INNOVATIVE CLINICAL TOOLS FOR OBJECTIVELY MEASURING LONGITUDINAL CHANGES IN KNEE ARTHROPLASTY PATIENT GAIT KINEMATICS AWAITING SURGERY

by

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Dedicated to the three people I love most in this world:

my mom,

my dad,

& my sister.

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ABSTRACT

Current clinical management of end-stage knee OA lacks objective functional assessments of patients. Markerless motion capture systems are a new technology that have the potential to facilitate efficient, well-integrated kinematic gait analyses within space-limited clinical environments, which previously limited the clinical uptake of standard technologies. Gait changes associated with end-stage knee OA have been identified, and there has been a growing recognition of functional and symptomatic variability within the patient population presenting for TKA. Extensive pre-operative waitlists for joint replacements contribute to greater patient pre-operative decline of PROMs, including pain, function, and quality of life. Understanding of the variability in patient pre-TKA function and the persistent functional deficits post-TKA will aid in targeting patient-specific improvements in gait and mobility throughout the TKA decision making process.

This thesis was a sub-study within a longitudinal research program focused on investigating the association of patient characteristics with declines in patient function awaiting TKA. The overarching goal is to optimize patient-specific objective joint function and mechanics post-TKA by tailoring robotic surgery to the patient's anatomy and function. The goals of this thesis were to facilitate the efficient collection of gait kinematics within a hospital clinic hallway, to analyze and define the repeatability of knee OA and TKA related kinematic gait metrics captured using this system, and to investigate the association of changes in gait kinematics over the TKA wait period in a cohort of end-stage knee OA patients with baseline patient factors.

A novel installation of a markerless motion capture system within a confined clinical hallway environment was successfully completed. A test-retest study of clinically relevant discrete knee angle gait outcomes collected with this system showed good-to-excellent repeatability. The clinical cohort study component of this thesis was the first to investigate changes in gait biomechanics of end-stage knee OA patients awaiting TKA. No significant changes in gait kinematics were observed on a group level, however, significant worsening of gait kinematics was found in one third of the patients. Patients with worsening gait presented with lower sagittal plane kinematics and higher knee adduction angle magnitudes at baseline, but no demographic or self-reported differences, highlighting the added sensitivity of an objective gait assessment during the wait period. Results of this initial investigation support the usage of longitudinal patient gait analysis over the TKA wait-period to potentially aid in surgical triage and prioritization.

The results from this thesis will allow for the increased clinical implementation of objective assessments of joint-level mechanics within end-stage knee OA populations. This serves as a valuable tool which can be used throughout the overarching research program and facilitate the high-volume collection of gait data on clinical cohorts, ultimately allowing for a better understanding of patient biomechanical deterioration or impact of treatment interventions. End-stage knee OA patients who demonstrated a worsening of their joint-level kinematics while awaiting surgery were not distinguishable at baseline by demographics or PROMs yet displayed biomechanical differences in their gait with stiffer sagittal plane angles and increased adduction magnitudes. These findings have implications regarding the clinical use of objective assessment tools to monitor patient function, especially in situations where long surgical wait periods are endured, as standard qualitative functional or patient-perceived outcomes may not capture this variability.

LIST OF ABBREVIATIONS USED

2D	Two-dimensional
3D	Three-dimensional
ACS	Anatomical coordinate system
AI	Artificial intelligence
BMI	Body mass index
DOF	Degrees of freedom
GRF	Ground reaction force
Hz	Hertz
ICC	Intra-class correlation coefficient
KA	Knee arthroplasty
KAA	Knee adduction angle
KAM	Knee adduction moment
KFA	Knee flexion angle
KFM	Knee flexion moment
MDC	Minimal detectable change
NRPS	Numerical Pain Rating Scale
OA	Osteoarthritis
OKS-PCS	Oxford Knee Score – Functional Component Subscale
PCA	Principal Component Analysis
PROM	Patient-reported outcome measure
ROM	Range of motion
SEM	Standard error of measurement
TKA	Total knee arthroplasty

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CHAPTER 1 INTRODUCTION

1.1 INTRODUCTION TO THESIS

This thesis was conducted as a sub-study of a longitudinal research program which aims to investigate the optimization of patient-specific objective joint function and biomechanics post-knee arthroplasty (KA) by enabling robotic surgery to be customized to the patient's anatomy and function. A comprehensive understanding of the pre-operative patient variability and its multifaceted relationships with joint anatomy, biomechanics, and surgical intervention will provide insight into how to approach surgical planning to target patient-specific biomechanics. This overarching study is investigating the association of patient characteristics and declines in patient function over the surgical wait period with post-operative surgical outcomes through the objective monitoring of patient biomechanics, activity, and clinically relevant outcomes. These efforts will contribute to the customization of clinical and surgical care, optimizing the surgical planning to meet individual patient needs. The study includes a cohort of patients receiving a primary robotic knee arthroplasty using the MAKO CT-Based Robotic System [Stryker Corporation, Kalamazoo, MI]. This research study is funded by the QEII Health Sciences Centre Foundation and Mitacs, and conducted in partnership with Nova Scotia Health, Division of Orthopaedic Surgery.

This thesis represents a sub-study of the above-described cohort study and has three major components. The first component was the integration of an optical motion capture system with markerless motion capture software to capture and model human movement kinematics within a clinic hallway at the Halifax Infirmary hospital in Halifax, Nova Scotia. As such a setup and application of motion capture is unique in the field, the setup, testing, and validation of a protocol for human gait analysis using this motion capture system were a key focus of this thesis, with the protocol developed to facilitate efficient and accessible gait analysis of knee arthroplasty patients in a clinical setting. The second component was the completion of an inter-session repeatability study using the markerless motion capture system and gait analysis protocol specific to our hospital hallway volume, and specific to outcomes that are highly relevant to clinical decision-making for knee arthroplasty. This component investigated the test-retest repeatability and measurement error of knee kinematics relevant to knee osteoarthritis (OA) and arthroplasty outcomes in a healthy cohort of participants collected with our markerless motion capture system at three time points longitudinally. The third component of this thesis involved the investigation of changes in gait kinematics of patients with knee OA on the surgical waitlist for total knee arthroplasty (TKA). A longitudinal assessment of patient gait kinematics over a 4-month period while on the wait list was performed, to quantify the changes in knee joint level kinematics and their relationship to baseline patient characteristics, self-reported outcomes, and kinematics.

The work completed in this thesis will allow for standardized gait analysis to be performed by our research group in a clinical setting, increasing patient throughput, and allowing for integration of gait analysis within the clinical assessment and surgical decision-making process. Further, the results from this thesis provide unique and initial information on changes in objective gait function while awaiting TKA and its association with baseline kinematics and patient characteristics.

1.2 THESIS OBJECTIVES

1.2.1 Repeatability of Knee Arthroplasty Gait Outcomes Using an AI Video-based In-clinic Hallway-installed Markerless Motion Capture System

Motivation: Current clinical management of end-stage knee OA lacks objective functional assessments of patients. Further understanding of the variability in patient pre-operative function [1], [2], [3], [4], [5] and persistent functional deficits post-TKA [2], [3], [6] is important to be able to better target patient-specific improvements in gait and mobility throughout the arthroplasty decision making process. Optoelectronic motion capture technologies are commonly used for gait analysis to non-invasively gather quantitative information of human gait and the impact of biomechanical pathologies [7]. Although gait analysis has been used extensively in research studies investigating the three-dimensional biomechanics of lower-body joints, the complexity, time inefficiency, and lack of operator procedure standardization have restricted the clinical uptake of motion capture [8]. Markerless motion capture technologies are an alternative to marker-based systems and provide fewer practical limitations regarding efficiency and operator expertise [8], [9]. Markerless AI-driven human pose estimation technologies use 2D video cameras paired with automatic human pose estimation, powered by deep-learning algorithms, to recognize a subject's key anatomical landmarks to estimate the pose of the body segments [10], [11], [12]. As a result, markerless motion capture can be smoothly integrated into different environments to provide a convenient and accurate method of performing motion capture on subjects. With the increasing use of this novel technology, studies have provided initial results on the comparability of joint kinematics from markerless motion capture versus traditional marker-based systems within laboratory-based environments [10], [13], [14], [15], [16], [17]. The influence of variable clothing worn by subjects during markerless motion capture collections [18], in addition to the inter-sessional repeatability of the joint kinematics captured with these systems have also been investigated [9], [19], [20]. Studies expanding the use of markerless motion capture to free-living environments have assessed the feasibility and reliability of joint kinematics collected in non-standardized locations (boxing ring, community rooms) [20], [21], [22], however no studies have investigated the potential for using these systems in a dimensionally limited space, such as a narrow hallway, which is most reflective of our clinical/hospital environment. It is therefore necessary to assess the quality and repeatability of the data collected within spaces that do not allow for optimal camera placement, visibility, or lighting effects, before the implementation of these systems within clinical spaces. Pairing clinical evaluations with objective kinematic joint assessments can assist in defining patient-specific indications for KA and support individualized treatment approaches which aim to slow OA progression through mechanical changes to the joint mechanics [1].

Objective: (a) To define the optimal camera setup and layout of a markerless motion capture system for an in-clinic hallway overground walking gait analysis protocol for knee arthroplasty patients, and (b) To install the markerless system and assess the repeatability of kinematic gait outcomes relevant to KA clinical decision-making using the defined protocol in (a).

Hypothesis: (a) A protocol will be defined which will successfully measure gait kinematics during overground walking using a markerless motion capture system in a clinic hallway. (b) The repeatability of sagittal plane knee kinematics will be comparable to previously reported values from marker-based motion capture systems. Frontal plane kinematics will have worse repeatability than those in the sagittal plane due to smaller ranges of motion during gait but will be better than previously reported values due to the elimination of anatomical marker placement effects.

1.2.2 Investigating Longitudinal Changes in Gait Kinematics Over the Waitlist Period in Patients Awaiting Total Knee Arthroplasty Surgery

Motivation: Extensive pre-operative waitlists for joint replacements contribute to greater pre-operative decline of self-reported measures [23], [24], [25], [26], [27], [28], including pain, functional ability, and quality of life, for patients awaiting TKA. The prioritization of TKA wait lists are largely influenced by professional clinical opinion [29], or through developed criteria [30], [31], [32] focusing on establishing radiographic presence of OA and patient-reported symptom severity through patient-reported outcome measures (PROMs). This approach may not prioritize patients whose radiographic results do not fully capture their functional severity, leaving them vulnerable to pre-operative decline. A stronger association of objective gait function has been shown with patient-perceived pain and function than with radiographic OA severity in the literature [33], which further supports the addition of a longitudinal objective functional assessment component of this clinical management, to effectively capture both the quantitative and qualitative variance experienced by these patients pre-operatively. Efforts to improve the communication of markers of surgical readiness from a kinematics perspective to the clinical team can further enhance the prioritization methods for TKA, with the goal of improving patient outcomes.

Objective: To examine if gait kinematics of patients awaiting knee joint arthroplasty change significantly during the surgical wait period and to examine the association of longitudinal gait changes with patient demographics, anthropometrics, PROMs and gait kinematics at baseline.

Hypothesis: Significant changes in sagittal plane gait kinematics will occur. The magnitude of change in knee joint kinematics over the surgical wait period will be highly variable between patients. Changes in the gait kinematics investigated will be related to the baseline patient-reported function and pain data, as previous work has found continued decline in these measures over the TKA wait period [23], [25].

1.3 ORGANIZATION OF THESIS

This thesis contains five chapters. Chapter 2 provides a literature review on biomechanical analyses of end-stage knee OA patients and relevant findings to TKA pre- and post-operative function, objective and patient-perceived functional assessment procedures, and motion capture technologies. Chapter 3 and Chapter 4 were written in manuscript format intended for separate submission to scientific journals. Objective 1 is addressed in Chapter 3, while objective 2 is addressed in Chapter 4. Chapter 5 contains concluding remarks on the collective findings of this thesis and recommendations for future work.

CHAPTER 2 BACKGROUND

2.1 END-STAGE KNEE OSTEOARTHRITIS

2.1.1 Osteoarthritis Disease Impact and Incidence

Osteoarthritis (OA) is a degenerative joint disease, most frequently affecting the knee joint [34], causing the largest rates of disability worldwide [35]. The most common symptom of OA is chronic pain; however, the presentation of OA varies greatly between patients, which can include decreased functional abilities and quality of life [34], [36]. OA progression and incidence increases with increasing age and bodyweight [34], [35], [37]. In Canada, the prevalence of diagnosed osteoarthritis is upwards of 14% of the adult population (4.4-million Canadians) [38]. As was once referred to as age related "wear and tear", it is now established that genetic factors [39], [40], joint injury [41], [42], and altered joint loading [43], [44], [45], [46] all affect the incidence and progression of OA, wherein 20% of the diagnosed cases of OA are in patients less than 65 years-old [38].

2.1.2 Knee Osteoarthritis and Risk Factors

OA can be present in any or all three knee compartments (tibiofemoral, patellofemoral), and affects all tissue surrounding that space. Great variance between structural joint OA incidence and OA physical symptoms are present [36], [47], particularly in lower-grade OA [36]. Many patients with pain and discomfort clinically present with minimal radiographic structural OA evidence, as well as structural presenting people with minimal pain or discomfort [47]. There is a higher prevalence of symptoms associated with radiographic knee OA in females [34], [35] and those of African descent [48]. The diagnosis of knee osteoarthritis is confirmed following positive diagnostic imaging findings and patient symptoms [49], [50], [51]. The Kellgren-Lawrence scale is a commonly used scoring system (rated 0-4) to determine the structural severity of knee OA from standing radiographs [52], where higher scores indicate increased structural OA severity due to the presence of osteophytes and narrowing of the joint space.

2.2 KNEE ARTHROPLASTY

2.2.1 Treatment

Surgical treatments of knee OA involve replacing affected components of the knee with implants in all compartments of the knee, in total knee arthroplasty (TKA), or only affected compartments, in unicompartmental KA (UKA). By surgically removing the damaged bone and cartilage from the tibiofemoral, and if needed, the patellofemoral joint surfaces, TKA is intended to reduce OA associated pain and symptoms, while increasing mobility and function of the knee. Implants are then fitted to the resected surfaces of the bones to provide new articulating surfaces for the knee joint. KA is an end-stage treatment option for patients who have not seen relief from more conservative OA management and treatment [53]. Clinical indicators for TKA surgery are frequently concentrated on establishing the presence of substantial radiographic evidence of OA and assessing patient-reported pain and function levels [29], [31].

2.2.2 Incidence and Demand for Surgery

In Canada, over 99% of primary knee replacements are performed to treat a knee OA diagnosis [54]. The population in Canada is aging, causing increased incidence in age-related diseases like OA [55]; and the demand for TKA surgery in Canada has been [54], [56], [57], and further influenced by a rising number of younger patients seeking treatment [58]. Extensive pre-operative waitlists for joint replacements resulting from the COVID-19 pandemic [54], [59], combined with the increased demand for TKA has put pressure on publicly-funded Canadian healthcare systems. Evidence-based benchmarks for TKA wait times in Canada have been established at 26 weeks (182 days) [60], [61]. Despite these targets, for example in the province of Nova Scotia only 38% of patients receive TKA surgery within the recommended target [60], which can have serious implications for their surgical outcomes. Patients who wait more than six months for TKA surgery have reported worsening pain, quality of life, and/or function both pre-operatively [23], [24], [25], [26], [27], [28] and post-operatively [62]. Efforts to improve the communication of objective markers of surgical readiness over to the clinical team can enhance the prioritization and triage methods for TKA with the ultimate goal of improving patient outcomes.

2.2.3 Conventional Knee Arthroplasty Procedures

The traditional standard of care TKA approach is to restore a neutral mechanical axis alignment (0 ± 3 degrees) of the femur and tibia [63], [64]. This is accomplished through cuts to the femoral frontal plane axis which augments its alignment with the tibia, however, this method has been critiqued with increased recognition of the variability of lower limb alignment in patients presenting for TKA [65], [66]. There has been varying levels of improvements in post-operative satisfaction and patient function [67], [68], [69] using more individualized alignment techniques that aim to be better targeted to the patient's anatomy [63], [64], as opposed to aiming for a standard mechanical alignment. Although limb and component malalignment have been shown to have an impact on implant survivorship [63], [70], [71], a further understanding of the interaction between optimal alignment and patient biomechanical and satisfaction outcomes is needed. Orthopaedic robotics technologies have the potential to help increase our understanding of optimal alignment and implant placement on a patient-level.

2.2.4 Surgical Robotics Technologies

Surgical robotics systems allow for a surgeon to develop tailored surgical plans using patient-specific models of the knee, obtained from pre-operative imaging, like CT-scans [72]. Intra-operatively, the surgeon has access to real-time data of the patient's joint, such as the limb alignment and component positioning, simultaneously in all three dimensions [73]. This robotic system ensures correct implant placement through the restriction of cutting planes and boundaries on the bones. Benefits of this system are the increased accuracy and precision of the implant placement, as compared to standard arthroplasty [73], [74], [75].

Surgical robotic systems have gained widespread prevalence within the joint arthroplasty space. The implementation of robotic technology within surgery allows for distinctive pre-operative plans of implant positioning to be executed to a high accuracy [73], [74], [75]. As the technology is in its early uptake stages, much of the research investigating robotic-assisted TKA procedures reflect those of conventional knee arthroplasty techniques, and thus have been shown to produce long-term patient-perceived outcomes (function, pain, mental health) similar to standard knee arthroplasty surgery [74], [76], [77]. With the potential to implement customized surgical plans with high accuracy, the future of robotic-assisted TKA can implement future research on optimized implant positioning to patient anatomy [66], [78], [79] and function [2], [5], [80], resulting in improved patient-perceived and objective functional outcomes.

2.2.5 Patient-Perceived Outcomes after Knee Arthroplasty

Although the overarching goals of TKA are pain reduction and functional improvements [81], upwards of 33% of knee arthroplasty patients report remaining post-operative functional limitations [68], [82] and up to 11% report no clinical improvement in pain or function post-operatively [83]. Patient-reported outcome measures (PROMs) are a qualitative measurement tool commonly used within the TKA clinical assessment and research to measure and quantify the patients' perceived outcomes pre- and post-operatively [1], [84]. The subjectivity of measuring perceived function through PROMs has been well documented in the literature [85], [86], [87], [88], [88], [89], [90], wherein underlying levels of self-reported pain, psychosocial factors, and pain catastrophizing can influence the levels of self-reported physical function. Additionally, as trends increase for younger patients seeking TKA [57], higher expectations of post-operative physical function may become more prevalent [91], [92], [93].

A 2021 review from Wang et al. identifies PROMs capturing functional ability, pain levels, and quality of life that have been validated in the literature for cohorts of end-stage knee OA patients [94]. An example of one of these PROMs for pain and function is the Oxford Knee Score (OKS); a 12-question questionnaire developed to assess a TKA patient's perceived levels of pain and functional impairment from their knee during activities of daily living [95]. The OKS has been regarded as one of the most appropriate questionnaires for a knee arthroplasty-specific population [96]. Pain- and function-specific subscales (pain component scale, PCS; function component scale, FCS) of the OKS have demonstrated high internal consistency [85]. Evidence of the OKS score correlating with objective functional ROM of the knee is varied across the literature. A study from Maempel et al. demonstrated a worse OKS score was a significant predictor of decreased post-operative knee ROM in over 1000 unicompartmental KA patients [97]. In contrast, Soon et al. demonstrated no significant correlation between the OKS score and post-operative knee ROM in an Asian TKA cohort [98]. There has been a focus in the literature on post-KA measures of patient perceived function, however, understanding the relationship between pre-TKA PROMs and changes in objective measures of patient gait while awaiting TKA have not been explored.

2.3 BIOMECHANICS AND GAIT ANALYSIS

2.3.1 Objective Measurement of Patient Function

The complementary use of both performance-based functional testing and PROMs is recommended within the literature, as they capture different constructs of physical functioning [88], [90], [99], [100]. Standard performance-based tests may include range of motion (ROM) of joints, sit-to-stand testing, and timed walking tests, which are inherently easy to administer and can provide a more objective assessment of function when used with PROMs [78], [79]. Self-reported and performance-based measures can capture more broad levels of functional ability, however, lack comprehensive joint-level biomechanical evaluations. Post-TKA improvements in PROMs [84], [101], [102] and performance-based measures [84] have been shown despite continued deficits in patient biomechanics [84], [101], [102].

2.3.2 Gait Analysis

Gait analysis is a commonly used non-invasive method for quantifying kinematic and kinetic biomechanical abnormalities in patient function [103]. The pathomechanics of individuals with knee OA has been studied extensively using gait analysis protocols, which have provided valuable knowledge towards understanding the joint-level biomechanical characteristics of disease progression and the effect of surgical interventions [2], [5], [103], [104], [105], [106]. Traditional protocols to obtain objective data on the three-dimensional biomechanics of lower body joints have primarily relied on laboratory-based, marker-based optoelectronic motion capture systems.

2.3.3 Industry-Standard Laboratory-Based Gait Analysis

Optoelectronic motion capture systems use arrays of cameras to track the positions of body-fixed markers during movement; these markers can be the passive reflective type, which reflect under infrared light that is emitted from dedicated camera systems, or active, which self-emit infrared light to be tracked by the cameras sensors [107]. Markers are placed on specific anatomical landmarks to define the morphology of the segment, while clusters of markers attached to the limb segment track its motion [108]. Limb segments, assumed to be rigid bodies, are defined using a Cartesian coordinate system, where the joint connecting two segments specifies the relative motion, characterized within a joint coordinate system [109]. Corresponding joint angles are calculated using a sequence of Cardan-Euler rotations within an anatomical reference frame [109].

The addition of force platforms within the motion capture environment allows for kinetic analyses of gait to be performed, which defines the net external moments and forces on the joints. Using an inverse dynamics approach [110] (i.e. limb segments modelled as a chain from the ground up), three elements are needed to calculate joint moments: the ground reaction force (GRF) from the force platforms, the kinematics of the limbs, as well as anthropometric data of the limb segments. Joint moments can provide valuable information on joint loading [111], [112], which is of particular interest in knee OA populations, as alterations in knee joint moments are associated with knee OA gait patterns [104], [113] and progression of disease [46], [114].

While marker-based systems are prevalent in research, their clinical adoption has been limited due to several constraints, including time inefficiencies from extensive patient preparation procedures [8], [9], data processing expertise, and the requirement for an operator with in-depth anatomical knowledge to accurately position the optoelectronic markers on the patient's structural landmarks [115], [116]. Soft tissue artifact during movement occurs when there is relative displacement of the skin's surface with the underlying skeleton and tissues, and can be worse in patients with high amounts of subcutaneous fat and soft tissue [117]. Soft tissue artifact is a prevalent source of error in marker-based measurements [118], [119], as it opposes the rigid body assumption when calculating segment kinematics. Efforts to quantify and lessen its effect have been recognized in the literature [120], [121], [122], [123].

2.3.4 The Biomechanics of End-Stage Knee Osteoarthritis

Patients with severe knee OA present with significantly slower walking speeds than controls [64]–[66], reduced stride length [66]–[68], and longer time in the stance phase of gait [66], [69]. These measures can provide an overall estimate of patient function [90], however, are not specific to joint-level alterations during gait. Gait speed is a spatiotemporal parameter that is intrinsically linked to knee-joint biomechanics during gait [124], [125], [126], [127], however, it is also linked with OA disease severity [104], [128].

The most prevalent joint kinematic changes associated with severe knee OA are within the frontal and sagittal planes of motion. Previous gait studies have shown that individuals with advanced knee OA walk with lower peak flexion angles during the stance [104], [129], [130], [131], [132] and swing phases of gait compared to healthy controls [104], [129], [132]. Studies that have implemented statistical pattern techniques, such as Principal Component Analysis (PCA) to extract temporal gait waveform features, have found similar reductions in these sagittal plane gait patterns [133], [134]. Some patients with OA exhibit varus thrust in the frontal plane, which is a dynamic lateral motion of the knee when in the initial weight-bearing phase of stance [43], [135]. This frontal plane feature has been associated with higher loading in the medial knee compartment [58], a key component affecting the progression of knee OA [58]–[60], with significant associations of varus thrust patterns with increased radiographic knee OA progression [58], [59]. Other frontal plane changes in severe knee OA gait are higher overall magnitudes [132] and changes in the range of motion of the knee adduction angle during stance compared to controls [94], [99], [100], [101].

Changes to the joint kinetics during gait are present in patients with severe knee OA. In the sagittal plane, reductions of the knee flexion moment (KFM) in early stance and decreases in knee extension moments in late stance (i.e. minimization of KFM range) have been associated with severe knee OA gait [104], [134]. A stiffening of the sagittal plane knee kinematics described above, combined with a minimization in KFM range, could be attributed to the increased muscle responses to possible pain and instability in severe OA gait, attempting to increase joint stability and decrease knee joint loading [139]. In the frontal plane, changes in the knee adduction moment (KAM) have been associated with OA severity [104], [140], [141] and the presence of varus thrust [43], [135], [142].

2.3.5 Emerging Motion Capture Technologies - Markerless Systems

Automatic human pose estimation algorithms, using AI-driven feature recognition techniques, have been developed for use in synchronized multi-planar video camera configurations, which estimate the human pose during movement. In contrast to marker-based optoelectronic systems which use reflective markers within the 3D space to track segment movement, markerless algorithms rely on images from video recordings to determine the learned anatomical points of a subject at each data frame. An example of a biomechanics-focused markerless motion capture software is Theia3D (Theia Markerless Inc., Kingston, ON, Canada), which developed their training dataset to identify over 100 anatomical landmarks, on a collection of over 500,000 images that have been manually annotated each by at least two expert staff members [10]. A deep convolutional neural network-powered algorithm is used to apply the position of these discrete anatomical landmarks from the labelled training dataset onto each human, which then estimates the 2D joint positions within each frame of the collected data [9], [143]. The camera system calibration is then used to approximate the 3D joint positions within the space, which in combination with the anatomical landmarks, allow for the kinematic chain model to be scaled to the body at each data frame [9], [143]. An inverse kinematics approach is used to estimate the 3D pose (position and orientation) of each body segment throughout the trial [9], [143].

Markerless motion capture systems can be smoothly integrated into different environments to provide a convenient and accurate method of performing motion capture on subjects. These markerless systems offer significantly reduced set up time and eliminate the need for marker placement [115], making them more promising for uptake in busy clinical environments [9]. As the use of this novel technology has increased, initial comparability studies of joint kinematics calculated from markerless motion capture versus traditional marker-based systems within laboratory-based environments have been published [10], [13], [14], [15], [16], [17]. Although good agreement in most kinematic measures have been shown in these studies, it is crucial to understand the sources of error from both motion-capture modalities, before coming to conclusions on the comparability of measurements. The direct concurrent comparison of marker-based and markerless motion capture technologies must be tempered by the absence of direct measurement of bone motion, captured with fluoroscopy imaging, which is commonly referred to as ground truth data [117], [144], [145], [146], [147], [148]. Marker-based kinematic data includes errors from variability in operator marker application [118], [149], [150] and soft tissue artifacts [117], [119], [121], which both impact the estimations of joint centers and resulting joint kinematics, and can result in errors upwards of 5-degrees in lower limb angles. Markerless motion capture is subject to human error within the manual dataset labelling methods, which can impact the accuracy of these algorithms [11], [12], as such it is of importance for developers to include broad datasets that have been labelled by many experts to reduce excess bias. Transverse plane kinematics published from markerless systems as compared to marker-based motion capture, have shown poorer agreement than the sagittal and frontal planes, particularly for the thigh and shank segments and the knee joint angle [9], [10]. High amounts of within-session and between-between session variability [9] and large standard errors of measurement (SEM) (> 5°) [20] are displayed within these knee angles, which warrants caution when interpreting transverse plane kinematics and further exploration into the conditions to best produce transverse plane kinematics for analysis with markerless systems. Further limitations of markerless motion capture systems are inherent to the algorithms used; markerless motion capture algorithms that use set proprietary landmarking and model definition techniques allow for no control from the user during the pose estimation process. Although Theia3D allows for specification of a 2 or 3 degrees of freedom (DOF) model at the knee joint, this could pose a potential problem when desiring different degrees of freedom (DOF) at other joints or when dealing with augmented motion from patients with limb loss.

Ensuring the video data does not include any motion blur of the subject is of utmost importance, which requires the camera specifications and conditions to be optimized for the collection environment, including frame rate, shutter speed, and the lighting effects. Studies have investigated potential sources of error within kinematics measured from markerless motion capture systems, specifically; the influence of clothing worn by subjects during markerless motion capture collections [18], and the inter-sessional repeatability of the kinematic measures have also been investigated [9], [19], [20]. Few studies have begun to expand the use of markerless motion capture systems to non-laboratory free-living environments, where each assessed the feasibility and reliability of joint kinematics collected in non-standardized locations such as a boxing ring or community rooms [20], [21], [22]. No studies have investigated the potential for using these systems in narrow spaces, such as a clinical hallway, which is most reflective of our hospital environment. The quality and repeatability of the data collected within these hallway spaces, that do not allow for optimal camera placement or visibility, must be assessed before the implementation of these systems within clinical spaces.

CHAPTER 3 REPEATABILITY OF KNEE ARTHROPLASTY GAIT OUTCOMES USING AN AI VIDEO-BASED IN-CLINIC HALLWAY-INSTALLED MARKERLESS MOTION CAPTURE SYSTEM

3.1 ABSTRACT

Total knee arthroplasty (TKA) aims to provide patients with end-stage knee osteoarthritis pain relief, increased function, and a reduction of symptoms. Past research has highlighted persistent functional deficits in patients post-TKA and therefore understanding how to tailor surgical decisions more effectively to account for the pre-operative patient variability is important to reduce the post-operative burden of disability. Efforts to capture objective information on patient biomechanics have traditionally been isolated to laboratory-based marker-based optoelectronic motion capture systems, which have resulted in minimal clinical uptake due to lack of location flexibility, large collection time requirements, and therefore reduced patient throughput. The installation of motion capture systems within clinical environments is necessary to create patient-specific surgical plans and treatments that account for patient variability in objective measures of dynamic joint function. Markerless motion capture systems driven by AI models are a new technology that mitigate some of the time and location constraints of traditional systems and therefore offer more promise for uptake in clinical environments. Before adoption of the technology, it is important to ensure the validity of outcome measures that are relevant to arthroplasty surgery with this technology deployed in a clinic environment where ideal spatial layouts for capture volume are not possible. Therefore, the aim of this study was to analyze the day-to-day repeatability of knee kinematic gait outcomes relevant to knee arthroplasty surgery of a markerless motion capture system installed in a clinical hallway.

Healthy adults (13F/7M) participated in three gait analysis sessions using a markerless motion capture system installed in a hospital clinic hallway. Intraclass correlation coefficients ($ICC_{2,k}$) and standard errors of measurement (SEM) examined the day-to-day repeatability of discrete knee joint angle gait metrics. Seven of the eight kinematic outcomes had $ICC_{2,k}$ values over 0.88, indicating good-to-excellent repeatability for these measurements. SEM values observed were all less than 2°. Findings from this study indicate the repeatability of kinematic outcomes relevant to knee arthroplasty surgery collected with our markerless setup are comparable to previously published values from marker-based systems. We therefore have confidence in the adoption of markerless motion capture technology for in-clinic gait analysis for relevant outcomes for arthroplasty patients.

3.2 INTRODUCTION

Total knee arthroplasty (TKA) aims to provide patients with end-stage knee osteoarthritis pain relief, increased function, and a reduction of symptoms. Previous studies have highlighted continued functional deficits in patients post-TKA [1], [151]. Consequently, it is crucial to understand how to tailor surgical and clinical decisions more effectively to better account for pre-operative patient variability, aiming to diminish the post-operative disability burden. TKA surgery indicators are frequently concentrated on establishing the presence of substantial radiographic evidence of disease and assessing patient-reported pain levels [29], [31]. However, this approach may not prioritize patients whose functional limitations would benefit significantly from arthroplasty, leading to delays in accessing surgery [31]. The prioritization of surgical candidates also includes managing the expectations for KA surgery outcomes. Patients with higher pre-operative function often experience smaller functional gains post-surgery [3], [5], [152], which can result in lower satisfaction. Recognizing that some patients have a limited potential for functional improvement compared to others suggests a need for clear communication regarding expectations and/or continued innovation in the field to improve functional outcomes for all.

The motivation to incorporate motion capture systems into clinical settings is driven by the need for objective patient screening tools to monitor joint biomechanics at a patient-specific level [1]. Pairing clinical evaluations with objective kinematic joint assessments can assist in defining and clinically testing patient-specific surgical plans and treatments that account for patient variability dynamic joint function. Additionally, it can further assist the development of individualized treatment approaches which aim to slow OA progression through mechanical changes to the joint mechanics [1]. Traditional protocols to obtain objective data on the three-dimensional biomechanics of lower body joints have primarily relied on laboratory-based, marker-based optoelectronic motion capture systems. While these systems are prevalent in research, their clinical adoption has been limited due to several constraints, including a lack of location flexibility [9], extensive preparation time needed for patient motion trials, data processing expertise, and the requirement for an operator with in-depth anatomical knowledge to accurately position the optoelectronic markers on the patient's structural landmarks [115], [116]. Skin motion artifact during movement is a prevalent source of error in marker-based measurements [118], occurring when there is relative displacement of the skins' surface with the underlying skeleton, and can be worse in patients with high amounts of subcutaneous fat and soft tissue [117].

Video-based motion capture systems integrated with AI-driven markerless software for human post estimation are a new technology that mitigate limitations of traditional systems. These systems offer significantly reduced set up time and eliminate the need for marker placement [115], making them promising for uptake in busy clinical environments [9]. An established markerless motion capture technology, Theia3D (Theia Markerless Inc., Kingston ON) has developed a validated automatic human pose detection algorithm, powered by deep-learning networks, made intentionally for biomechanics research [10]. Previous studies investigating the Theia3D markerless algorithm repeatability and comparisons to marker-based motion capture technologies have been published [9], [10], [15], [20], [21], [153], [154], but it has not yet been validated in a space-constrained clinic hallway space for clinical outcomes specifically relevant to knee osteoarthritis treatment with arthroplasty. Therefore, the aim of this study was to examine the day-to-day repeatability of knee kinematic gait outcomes relevant to knee arthroplasty surgery collected with a markerless motion capture system installed in a clinical hallway, and, as a secondary objective, to use this information to define the standard error of these measurements and minimal detectable changes for clinical studies using the system.

3.3 METHODS

3.3.1 Subjects

Healthy adults (13F/7M) with no self-reported lower limb or gait pathologies were recruited from surrounding clinical offices and from word-of-mouth through the research team. Subjects were screened to exclude those under the age of consent, those unable to provide informed consent, those unable to walk continuously for 3 minutes without walking aids, and those with either neurological/motor disabilities affecting gait, lower limb protheses, or history of knee OA diagnoses. Each subject participated in three gait analysis collections at the Halifax Infirmary hospital, each taking place on different days or using different camera setup sessions, with a maximum of 45 days apart. Specific clothing/footwear type, fit, or colour [16], [155] was not instructed to the subjects, however, limitations of wearing thick-soled/work-style boots, high-heels, and long skirts were enforced. All subjects provided informed written consent, approved by the Nova Scotia Heath Research Ethics Board.

3.3.2 Data Collection Protocol and Analysis

A series of ten 2D video cameras (Sony, RX0ll) (60 Hz) on magnetic mounts were used to collect synchronized video data along the 2.4m x 9.1m stretch of clinic hallway (Figure 3.1). Before data collections, a calibration was performed for a minimum of one minute to compute the camera positions and orientation relative to one another using a calibration grid. Each new camera setup session involved camera placement and calibration within the hallway. No artificial lighting or modifications of the hallway environment were implemented. At each gait collection, subjects were instructed to walk at a comfortable, self-selected pace through the hallway volume, walking in alternating directions for a total of 8 passes through the volume or one minute, whichever occurred first.

After each gait collection, synchronized video data was downloaded from the cameras and Theia3D software (Theia Markerless Inc., Kingston ON) was used to estimate the three-dimensional pose (position and orientation) of each body segment during each frame of walking using the default inverse kinematic model [143] with 3 degrees of freedom (DOF) at the knee. Pose data was then further analyzed in Visual 3D software (C-motion Inc., Boyds MD) using an integrated model designed for Theia3D pose data and filtered with a low-pass fourth-order Butterworth filter at 8Hz. Three-dimensional knee joint angles were defined using a Cardan sequence based on the joint coordinate system definitions [109] and were time-normalized to foot contact events (heel and toe landmarks defined from Theia3D model). Gait cycles were defined from foot contact to next foot contact of the same leg, and defined along with foot off events according to methods by Zeni et al. [156]. A 4-metre-long section of hallway, central to the walking volume, was chosen as the analysis area (Figure 3.1). The first twelve gait strides occurring within the analysis section of the hallway were chosen for analysis for each collection.

Discrete gait metrics were extracted from each knee angle waveform for each subject. Metric selection was based on previous studies which investigated discrete gait kinematics within moderate to end-stage knee OA populations [104], [129], [157], [158]. Repeatability of the selected discrete kinematic gait metrics collected with the markerless system were calculated using previously described methods [9], [150], [159], [160], which have been implemented by others for similar repeatability protocols. Repeatability of the kinematic outcomes was assessed using the intra-class correlation coefficient (ICC) and the standard error of measurement (SEM). ICC values were calculated at the 2,k level, ($ICC_{2,k}$) for each kinematic outcome and 95% confidence intervals (CI) were calculated from each IC value. The SEM values were calculated ($SEM = \sqrt{RMSE}, where\ RMSE\ is\ the\ root\ mean\ squared\ error$) [161] using the mean values from each three sessions for all 20 subjects (60 values) with 95% CI. Minimal detectable changes (MDCs) in these kinematic outcomes based on the SEMs ($MDC_{90} = \sqrt{2} * Z * SEM, where\ Z = 1.645\ at\ the\ 90\%\ confidence\ level$) [162] were also reported to provide insight into meaningful changes in these outcomes above system error for clinical applications. All analyses were completed using custom MATLAB and Python scripts.

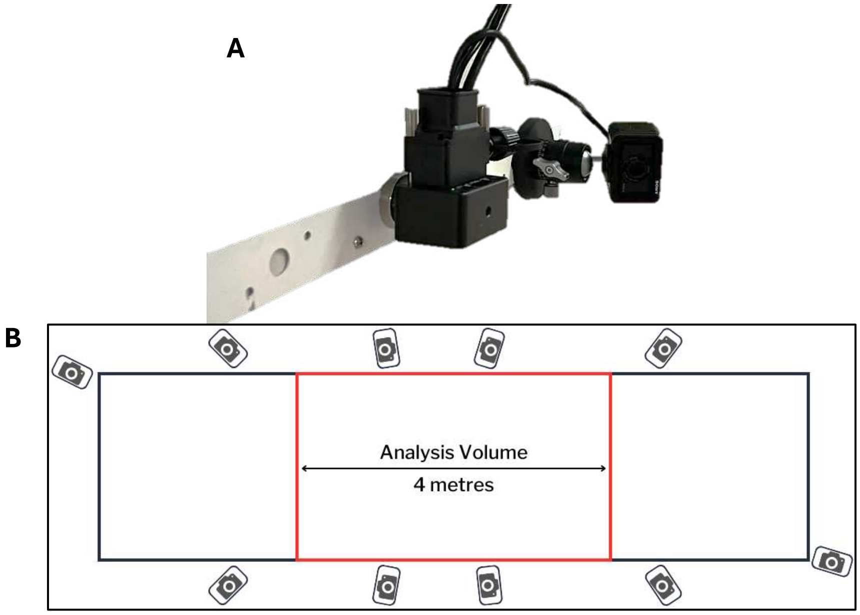
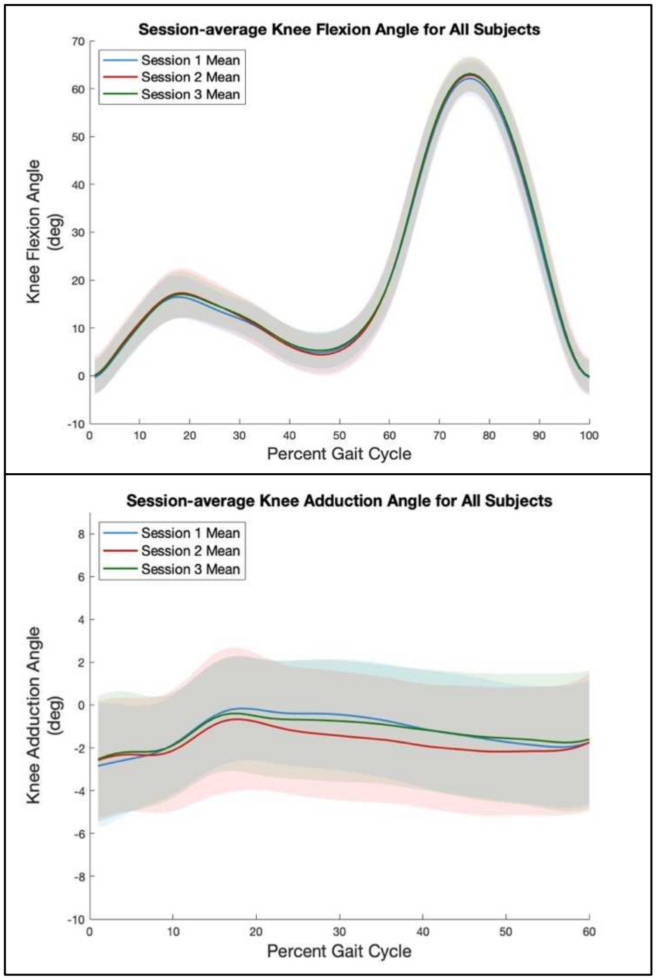


Figure 3.1 A) Sony RX0ll camera magnetically mounted to the hallway wall. B) Illustration of the data capture volume and experimental camera setup.

3.4 RESULTS

Twenty subjects (13F/7M) were recruited with a mean age of 36.8 ± 10.2 years, a BMI of 26.2 ± 3.4 kg/m^2, and participated in sessions 10.9 ± 11.6 days apart. Session-average knee flexion and adduction angles normalized to 100% gait cycle are plotted for all subjects in Figure 3.2. The key kinematic outcomes with repeatability and variability metrics are summarized in Table 3.1. Similar results were found across all reported metrics with most ICC$_{2,k}$ values indicating excellent repeatability (0.88 or greater for 7 of the 8 reported kinematic metrics). The lowest $ICC_{2,k}$ value was found for the knee adduction angle range of motion in stance ($ICC_{2,k} = 0.72$), while the highest value was found for the maximum knee flexion angle in stance phase ($ICC_{2,k} = 0.94$).

SEM values ranged from 1.28° (mean adduction angle in stance phase) to 1.85° (flexion ROM in stance phase) and were similar within the sagittal and frontal planes. MCD values calculated at the 90% confidence level using the SEM values ranged from 2.98°-4.30°.


Session-average Knee Flexion Angle for All Subjects

Session-average Knee Adduction Angle for All Subjects

Figure 3.2 Ensemble average waveforms for knee flexion (+ve) and adduction (+ve) angles for n=20 healthy adults. The shaded bands represent one standard deviation of each session group from their respective mean.

Table 3.1 Reported discrete kinematic (angle) knee metrics relevant to patient total knee arthroplasty.

Knee Metric	Session	Mean (SD) (°)	$ICC_{2,k}$ (95% CI)	SEM (95% CI) (°)	MDC_{90} (°)
1. Peak Flexion in Stance	1	17.3 (3.8)	0.94 (0.87, 0.97)	1.75 (1.48, 2.16)	4.1
	2	18.0 (4.8)			
	3	17.6 (4.4)			
2. Flexion ROM in Stance	1	18.1 (3.2)	0.91 (0.82, 0.96)	1.85 (1.56, 2.29)	4.3
	2	18.5 (4.8)			
	3	17.9 (3.6)			
3. Peak Flexion	1	62.6 (2.9)	0.88 (0.76, 0.95)	1.55 (1.31, 1.91)	3.6
	2	63.4 (2.9)			
	3	63.6 (3.0)			
4. Flexion ROM	1	63.4 (3.8)	0.93 (0.86, 0.97)	1.71 (1.44, 2.12)	4.0
	2	63.8 (4.4)			
	3	63.8 (3.9)			
5. Minimum Flexion in Late Stance	1	4.2 (3.7)	0.90 (0.79, 0.96)	1.79 (1.51, 2.21)	4.2
	2	3.8 (3.8)			
	3	4.6 (3.1)			
6. Peak Adduction in Stance	1	1.0 (2.3)	0.88 (0.74, 0.95)	1.46 (1.23, 1.81)	3.4
	2	0.6 (2.9)			
	3	0.9 (2.7)			
7. Mean Adduction in Stance	1	-1.3 (2.2)	0.90 (0.79, 0.96)	1.28 (1.08, 1.59)	3.0
	2	-1.7 (2.8)			
	3	-1.3 (2.6)			
8. Adduction ROM in Stance	1	4.5 (2.0)	0.72 (0.41, 0.88)	1.30 (1.09, 1.60)	3.0
	2	4.0 (1.5)			
	3	4.1 (1.7)			

Metrics defined during following ranges: 1. Between heel strike (0%) to 45% gait, 2. Maximum-minimum (between 0% to 45% gait), 3. Between 0 to 100% gait, 4. Between 0 to 100% gait, 5. Minimum between stance peak and swing peak, 6. Between 0% to toe-off, 7. Mean from 0% to toe-off, 8. Maximum-minimum (between 0 to 20% stance for minimum). SD = standard deviation, $ICC_{2,k}$ *= intraclass correlation coefficient type 2, k, SEM = standard error of measurement,* MDC_{90} *= minimal detectable change at the 90% confidence level.*

3.5 DISCUSSION

This study was the first to show that repeatable, clinically relevant knee kinematic gait outcomes can be readily captured with a markerless motion capture system in a space-limited clinic hallway environment. The ICC provides a unitless value of the total variance as a proportion of the variance due to between-subjects variance and within-subjects variance and can be influenced by the diversity of the patients in the dataset. Adding in the SEM provides a metric of the absolute reliability of the measure within individual subjects, giving insight into the systematic expected error session to session, not influenced by the variability between patients. The resulting 7 out of 8 reported $ICC_{2,k}$ values being over 0.88 indicated good-to-excellent repeatability of most measurements [163]. The two highest reported ICCs were for peak flexion in stance phase (0.94) and range of flexion over the gait cycle (0.93). Previous values published in the literature in marker-based motion capture repeatability studies range from 0.60-0.90 for comparable sagittal plane metrics [158], [164], [165], [166]. The ICCs for peak and mean knee adduction angle in stance were similar to those of the knee flexion angle metrics, except for the adduction angle ROM in stance metric (ICC = 0.72), which is supported by previous literature presenting frontal plane ROM ICC values (range: 0.38-0.60) [158], [164], [165].

SEM values observed were all less than 1.85° for the eight metrics. On a percentage level in comparison to the magnitude of the metric value, the SEMs for the sagittal plane metrics were smaller than the frontal plane. This shows that the measurements in the sagittal plane are more repeatable per degree measured, likely attributed to the larger movement in the flexion/extension axis [167] combined with the Carden sequence defining this axis first. Anatomical deviations in landmarking, with markers or with markerless algorithms, can lead to kinematic cross talk within adduction angle calculations [118], [168]. SEMs for the frontal plane metrics were numerically the smallest (1.28-1.46°), however on a percentage level were larger than the sagittal plane SEMs. This is consistent with previous studies using similar protocols and knee angle definitions [20], [158], [164], [166]. As compared to previous marker-based studies [158], [164], [165], [166], [169], [170], we reported higher ICC and smaller SEM values, indicating that our in-clinic markerless system resulted in less variance within-subjects over time and a more precise measurement capacity for the comparable metrics. As compared to previous markerless motion capture studies in laboratory-based or free living spaces [20], [171], we report comparable ICC and SEM values, indicating our narrow hospital hallway setup provides a suitable environment for markerless clinical gait analysis.

MDC values were calculated for each reported metric to provide an initial estimate of the range of standard error day-to-day within each metric. A review paper from McGinley et al. [167] suggested joint angle errors >5° are large enough to mislead clinical interpretation of the data, concluding that error values within 2-5° can be considered reasonable within the clinical context. The large difference in knee range of motion between the sagittal and frontal planes is important when interpreting measurement errors. Measurement errors >5° for the sagittal plane metrics result in a small percentage error, whereas in the frontal-plane, errors >5° can be upwards of 50% percentage error, and detrimental to the clinical validity of the measurements for our applications. In our study, SEM and MDC values were all below the 4.3°, with 5/8 metrics having MDC values <4°. From a measurement error perspective, our SEM values are within general clinically accepted bounds, and from a longitudinal data collection perspective, our MDC values also being within these bounds gives further confidence of the ability to detect change in these metrics over time. Careful interpretation of these MDC values will need to be taken when applying this system to different populations and studies, as changes from disease progression or gait interventions will need to be documented, thus determining if these MDC values are clinically relevant.

Within marker-based motion capture systems, discussions over reporting relative ROM measurements versus absolute peak metrics due to larger between-session errors in the latter, are documented [170], [172], [173], and have been attributed to the misalignment of the anatomical coordinate systems (ACS) between days. It has been shown that reporting ROM values (relative to the movement performed) experienced less between-day variation leading to a better reliability [170], [172], [173]. A past comparable study from Ferber et al. [173] reported maximal day-to-day change for peak reported values to be larger than the corresponding ROM excursion values for each joint/plane; peak angle difference values reached upwards of nine-times larger than the peak excursion difference values. The ACS alignment in this markerless system is achieved by AI-driven algorithms, which, although does contain error effects derived from the algorithm, removes the large effect of varying ACS alignment experienced in marker-based systems. This resulted in comparable day-to-day variability in ROM and peak metrics in our study.

The knee metrics we report in this paper are all relevant to knee OA severity and response to arthroplasty treatment, as shown in past literature [104], [131], [132], [138], [158]. Past studies have showed the effects of TKA on post-operative patient kinematics and have also shown the impact individual pre-TKA gait kinematics has on post-operative kinematics [3], [4], [5]. The progression of knee OA varies significantly from one patient to another, with respect to radiographic severity and symptomatic severity [47], [174], [175], [176], [177], and does not follow a homogeneous pattern across the patient population. The ability to monitor the change in kinematic variables that are directly related to post-TKA kinematics and outcomes, can help aid clinical decision making during pre-operative triage for certain patients.

3.6 LIMITATIONS

This study used a healthy subject cohort, motivated by the main objective of determining the repeatability of the system within the hallway location, and therefore may not fully represent the variability in knee osteoarthritis gait kinematics. However, these results provide good evidence for a repeatable, feasible protocol for multi-session markerless clinical gait studies in a busy clinic hallway space. Each of the 20 subjects had varying time between visits for subsequent sessions, spanning a maximum of 45 days. Although these subjects were self-identified to have no gait pathologies, where negligible changes in their gait function were expected over the study collection period, the variation between follow-up visits was not kept consistent subject-to-subject and may have influenced the results. Purposefully, clothing was not controlled for in this study, except the exclusion of long skirts/coats and thick-soled work-style boots/shoes, to ensure a non-homogeneous clothing-style of the participants. Research on the effects of varying clothing styles and colours have been published [16], [155], however allowing for a mix of clothing attire in this repeatability study ensures no bias in the accurate identification of anatomical features.

3.7 CONCLUSIONS

This is the first study to use a novel installation of a markerless motion capture system within a confined clinical hallway environment to collect human gait data. In this study, we investigated the test-retest repeatability of clinically relevant discrete knee angle gait outcomes using a markerless motion capture system. Gait data collected over three sessions showed good-to-excellent repeatability. The implementation of a markerless motion capture system within the orthopaedic clinic will allow for an on-site, efficient collection of gait data from knee arthroplasty patients, greatly relieving the burden of collection time and travel associated with traditional off-site laboratory gait collections. Clinical partnerships are nurtured with consistent on-site collaboration, and the translational relevance of the gait data collected can be ensured. It now poses as a feasible option for majority of patients, and moving forward allows for clinical integration of gait analysis, which has historically been a consistent hurdle with existing marker-based technologies, from a personnel bandwidth perspective as well as an insufficient population perspective.

CHAPTER 4 INVESTIGATING LONGITUDINAL CHANGES IN GAIT KINEMATICS DURING THE WAITLIST PERIOD IN PATIENTS AWAITING TOTAL KNEE ARTHROPLASTY SURGERY

4.1 ABSTRACT

Constraints of publicly funded healthcare systems, particularly in Canada have put high stress on the healthcare system. This has led to extended wait times for patients to access surgery, wherein effective management including patient triage on the waitlist for arthroplasty is critical. Joint kinematics during walking change with the progression of knee osteoarthritis (OA), and patients in the end-stages of OA awaiting total knee arthroplasty (TKA) have significantly altered walking kinematics. However, there has been little investigation into if and how gait kinematics change over the wait period for knee arthroplasty. The purpose of this study was to examine longitudinal changes in walking knee joint kinematics in the pre-operative period, to examine patient factors that relate to gait kinematics decline during the pre-operative wait period, and to examine differences in baseline patient factors between those whose gait kinematics worsen during the wait period compared to those who did not.

Thirty-eight patients (15 follow-up) with end-stage knee OA awaiting robotic-assisted TKA underwent two gait analyses, approximately four months apart, using a markerless motion capture system in the clinic hallway, and sagittal and frontal plane joint angles were calculated. On a group level, knee kinematic metrics did not significantly change over the wait period. Significant associations of baseline gait kinematics with patient demographics, and self-reported function were identified. Kinematic gait changes over the wait period were significantly associated with baseline gait kinematics. Five patients experienced significant worsening of gait kinematics who

presented at baseline with lower sagittal plane kinematics and higher knee adduction angle magnitudes. Objectively measured gait measures may be a more sensitive indicator of mobility worsening during the arthroplasty wait period that other patient factors or subjective outcomes.

4.2 INTRODUCTION

Knee osteoarthritis (OA) is a progressive, degenerative disease which presents with symptoms including increased pain and stiffness, decreased functional ability, and poor quality of life [35]. In countries with universal public healthcare systems such as Canada, patients awaiting total knee arthroplasty (TKA) often experience extended wait times [56], [60]. Evidence-based benchmarks for TKA wait times in Canada have been established as 26 weeks (182 days) [60], [61]. Despite these targets, for example in the province of Nova Scotia only 38% of patients receive TKA surgery within the recommended target [60], which can have serious implications for their surgical outcomes. Patients who wait more than six months for TKA surgery have reported worsening pain, quality of life, and/or function both pre-operatively [23], [24], [25], [26], [27], [28] and post-operatively [62]. While it appears the surgical demand outweighs the healthcare system capacity, there are no comprehensive or universally accepted guidelines for informing surgical candidate triaging.

While TKA generally provides patients with relief of symptoms and increased joint function, it has been shown that nearly 20% of patients are unsatisfied post-KA with lingering pain or functional deficits [178], [179], [180]. Post-surgical dissatisfaction has been related to pre-operative patient biomechanics and observed lack of perceived and objective improvements in joint function after arthroplasty [3], [5], [152]. Knee OA affects gait biomechanics through the spectrum of clinical disease progression [104], [134]. Gait biomechanics have been shown to improve after TKA, but are rarely restored to asymptomatic levels and patterns [6], [151], [157], [181]. Both pre-operative patient-specific gait mechanics and the extent of improvements in these mechanics following TKA may play a role in determining both the objective gait and patient-perceived outcomes after surgery [5], [6], [152]. Pre-operatively, patients with higher functioning gait patterns may have a diminished potential for knee mechanic improvements post-TKA [5], [152], and in some instances, a potential for worsening of gait patterns [2], [3]. There is a need to understand and identify patients who are at risk of declining while waiting for surgery and to understand how declines can affect post-surgery outcomes.

The primary objective of this study was to examine the changes in gait kinematics among TKA patients awaiting knee arthroplasty surgery, and how these changes relate to demographics, baseline patient-reported pain and function, and gait kinematics. The secondary objective was to compare baseline variables between patients who exhibited significant worsening of gait during the wait period and those who did not.

4.3 METHODS

4.3.1 Patients

Patients diagnosed with end-stage knee OA using clinical and radiographic criteria were recruited from participating surgeons' knee arthroplasty surgical waitlists (MD, GR, JL) to participate in the study. Exclusion criteria included any neurological disorders affecting gait and mobility, any other lower limb surgery in the past year, systemic inflammatory arthritis, and/or an inability to provide informed consent. All patients provided informed written consent, approved by the Nova Scotia Heath Research Ethics Board.

4.3.2 Data Collection

This was a study on a subset of patients recruited for an overarching longitudinal study examining changes in gait biomechanics, physical activity, and clinical outcomes during the wait period for robotic-assisted knee arthroplasty surgery and in response to surgery at multiple post-operative timepoints perioperatively. At each visit, all patients completed a series of questionnaires that included demographics and anthropometrics, and a series of patient reported outcome measures (PROMs). PROMs included the Oxford Knee Score Functional Subscale (OKS-FCS) [95], the Numerical Pain Rating Scale (NPRS) [182], the UCLA Activity Scale (UCLA) [183], and the EQ-5D [184]. Patients were further asked to take part in a markerless gait analysis in the clinic hallway (described below) and were fitted with shank-fixed inertial measurement unit (IMU) sensors to record step-based activity levels for a one-week period after their clinic visit (data not included in this study). The current study includes only the OKS-FCS (APPENDIX A), NRPS (APPENDIX A), and gait analysis data collected at two timepoints in the pre-operative period: baseline and at a second pre-operative visit (T2) approximately four months after the baseline visit.

4.4 GAIT ANALYSIS

Three-dimensional (3D) kinematics of the lower extremity joints were recorded using a markerless, video-based motion capture system that included ten synchronized video cameras (Sony RXOll) arranged strategically along a 2.4m x 9.1m stretch of a hospital clinic hallway to maximize viewing volume for overground walking, and using a protocol with good to excellent day-to-day repeatability for knee kinematic outcomes in this setup (Chapter 3). Video data of patient walking trials was recorded at 60Hz. Each patient walked overground along the hallway at a continuous self-selected comfortable pace, alternating directions for 8 passes or 1 minute of walking. Each patient wore their own clothing and footwear and were only asked to refrain from wearing long skirts, thick-soled boots, and/or heeled shoes.

4.5 GAIT DATA PROCESSING

The synchronized video data was first processed using Theia3D (Theia Markerless Inc., Kingston ON) software to estimate the three-dimensional position and orientations (pose) of the body segments using an inverse kinematic model with three degrees of freedom at the ankle, knee, and hip joints (knee outcomes presented in this study). Visual3D software (C-motion Inc., Boyds Maryland USA) was used to process and calculate the lower extremity joint angles and stride characteristics within the central 4m-long section of the hallway (Chapter 3, Figure 3.1). Pose data was lowpass filtered with a 4th order Butterworth filter at 8Hz and data from the first 10 gait cycles of the surgical leg were analyzed, where a gait cycle was defined as foot contact to foot contact of the same leg (foot contact = maximal anterior distance of the proximal foot from the pelvis [156]). Three-dimensional knee joint angles were defined using a Cardan sequence based on the joint coordinate system [109] and were time-normalized to foot contact events. Ensemble average sagittal- and frontal-plane knee angle waveforms (101 data points) were created from the first ten viable gait cycles from each visit, for each patient. Gait speed was calculated for each patient as the average speed across all 10 gait cycles (stride length ÷ stride time).

Gait outcomes: Eight discrete knee angle metrics, relevant to knee arthroplasty outcomes [2], [129], [151] and shown in this thesis (Chapter 3) to be day-to-day repeatable in the current setup in healthy participants, were averaged over the 10 gait cycles. These parameters included (Table 4.1): knee flexion angle peak and range over the gait cycle (KFA Peak, KFA Range), knee flexion angle peak and range in stance phase of the gait cycle (KFA Peak^S, KFA Range^S), minimum flexion angle in late stance (KFA Min^{LS}), and adduction angle peak, mean, and range in stance (KAA Peak^S, KAA Mean^S, KAA Range^S).

Table 4.1 Reported kinematic (angle) knee metrics relevant to patient total knee arthroplasty.

Metric	**Definition**	**SEM (95% CI) (°)**	**MDC$_{90}$ (°)**
1. KFA Peak (°)	Maximum flexion angle (0-100%) of gait cycle	1.55 (1.31, 1.91)	3.6
2. KFA Stance Peak (°)	Maximum flexion angle between 0- 45% of gait cycle	1.75 (1.48, 2.16)	4.1
3. KFA Range (°)	KFA Peak – min. angle between 0-100% of gait cycle	1.71 (1.44, 2.12)	4.0
4. KFA Stance Range (°)	KFA Stance Peak – min. angle between 0-45% of gait cycle	1.85 (1.56, 2.29)	4.3
5. KFA Minimum Late Stance (°)	Minimum flexion angle between KFA Stance Peak and KFA Peak	1.79 (1.51, 2.21)	4.2
6. KAA Peak Stance (°)	Maximum adduction angle between 0% gait cycle to toe-off	1.46 (1.23, 1.81)	3.4
7. KAA Stance Range (°)	KAA Peak Stance – min. angle between 0-20% of gait cycle	1.30 (1.09, 1.60)	3.0
8. KAA Stance Mean (°)	Mean angle between 0% of gait cycle to toe-off	1.28 (1.08, 1.59)	3.0

Metrics defined during following ranges: 1. Between heel strike (0%) to 45% gait, 2. Maximum-minimum (between 0% to 45% gait), 3. Between 0 to 100% gait, 4. Between 0 to 100% gait, 5. Minimum between stance peak and swing peak, 6. Between 0% to toe-off, 7. Mean from 0% to toe-off, 8. Maximum-minimum (between 0 to 20% stance for minimum). SD = standard deviation, SEM = standard error of measurement, MDC$_{90}$ = minimal detectable change at the 90% confidence level.

To define further features of knee kinematics during walking that have been shown to be relevant to knee arthroplasty [2], [5] and that describe the temporal pattern variability in knee joint angles, principal component analysis (PCA) was applied to the knee angle waveforms [133], [134]. PCA was applied to the flexion/extension angle data over the gait cycle and to the adduction/abduction angle data over the stance phase of the gait cycle separately. Observations from baseline (n=38) and T2 (n=15) gait trials for all patients were included in the principal component (PC) models (n=53 observations). Principal components (PCs) were defined that describe the directions of pattern variability within the gait metrics, and PC scores were calculated for each patient by projecting their data onto each PC as an indication of how much their gait waveform aligns with each PC pattern. The interpretation of the PCs was done using the PC eigenvector plots and interpreting representative patient waveforms of the 95th (high) and 5th (low) percentile for each PC score [185] (APPENDIX B). PC features were retained which showed importance to knee arthroplasty and end stage OA, as previously reported in the literature [2], [5], [151].

4.5.1 Statistical Analysis

Change in Kinematic Outcomes (Primary Aim): Paired t-tests were used to examine if gait kinematic outcomes changed significantly between baseline and T2 visits during the wait period. Pearson's correlation analysis was used to examine correlations between baseline patient data (demographics, PROMs, and gait kinematics) and changes in the gait kinematic outcomes during the wait period (change = T2 - baseline). Sex differences in the reported kinematics were evaluated using two-tailed unpaired t-tests. A significance of 0.05 was set for all statistical tests.

Worsening Subgroup Analysis (Secondary Aim): Patients were categorized as part of the worsening group if they experienced a significant reduction in at least one sagittal plane metric from the baseline to T2 visit. Previously reported standard error of measurement (SEM) and minimal detectable change (MDC) values of each sagittal-plane knee metric were used to define a minimum threshold of worsening (Chapter 3, Table 3.1). Differences in the baseline data, T2 data, and magnitude of change in outcomes were compared between the worsening and non-worsening groups using t-tests ($\alpha = 0.05$). All analyses were completed using custom MATLAB, Excel, and Python scripts.

4.6 RESULTS

Thirty-eight patients (19F/19M) were recruited at baseline with a mean age of 68.2 ± 7.9 years and a BMI of 32.7 ± 7.3 kg/m^2. A subset of 15 patients (6F/9M) completed a second gait analysis session 130 ± 17.9 days after the baseline visit (subset age: 69.8 ± 6.5 years, BMI: 35.1 ± 7.6 kg/m^2). Patient demographics, gait speed, and PROMs at baseline and T2 are presented in Table 4.2 for the full group and follow-up subgroup. There were no significant differences between the baseline-only patients (N=23) and the second-visit subgroup (N=15) at baseline for age, speed, OKS-F, and NPRS. The second-visit subgroup had a significantly higher BMI (affected by a higher mean weight; baseline (N=23) mean: 86.9 kg, sub-group mean: 100.6 kg).

Table 4.2 Demographic, speed, and PROM data for whole group (N=38) and follow-up groups (N=15) at Baseline and Time 2 (T2).

	Baseline			**Time 2**
	All (N=38)	Baseline-Only (N=23)	Follow-Up Group (N=15)	Follow-Up Group (N=15)
Sex (F/M)	19/19	13/10	6/9	
BMI (kg/m^2)	32.7 (7.3)	30.7 (6.3)	35.9 (7.8)[a]	
Age (years)	68.2 (7.9)	67.7 (8.8)	68.9 (6.4)	
OKS Functional	11.3 (3.1)	11.1 (3.0)	11.6 (3.2)	
NPRS	6.2 (2.3)[ϕ]	5.9 (2.5)[γ]	6.5 (1.9)	
Speed (m/s)	1.02 (0.19)	1.00 (0.19)	1.05 (0.19)	1.01 (0.23)

Values presented as mean(SD); SD = standard deviation; OKS-FS scored from 0-20 (0 most severe). NPRS scored 0-11 (11 worst pain). [ϕ]NRPS for n=37 patients at baseline. [γ]NRPS for n=22 patients at baseline.

Baseline (N=38) ensemble average sagittal and frontal plane knee angle gait waveforms for all subjects' surgical knees are presented in Figure 4.1. For the follow-up group, ensemble average sagittal and frontal plane knee angle gait waveforms at baseline and T2 for the surgical knees are presented in Figure 4.2.

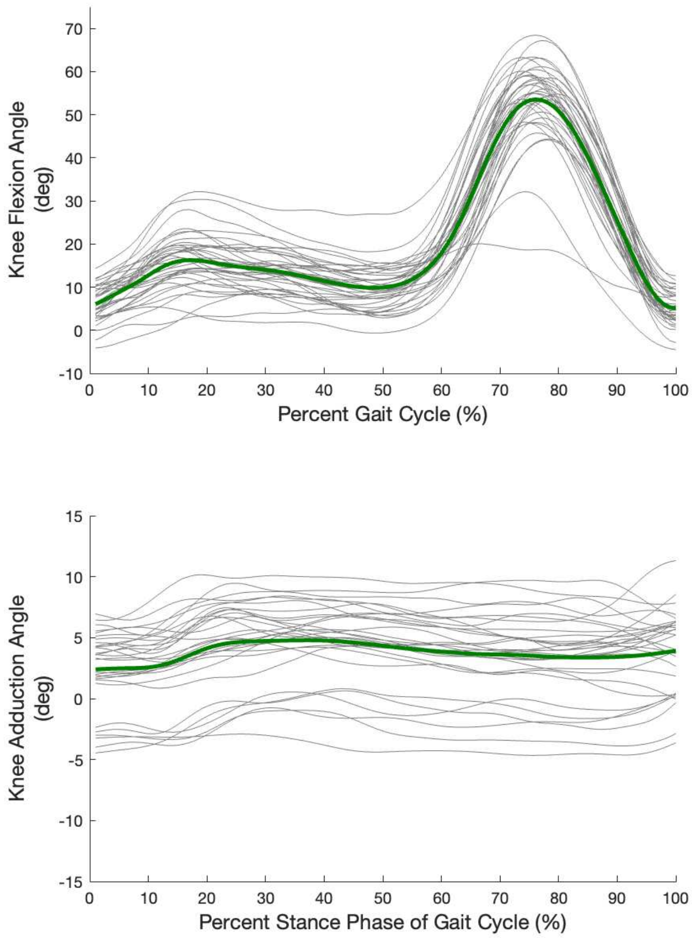


Figure 4.1 Sagittal and frontal plane knee angle waveforms plotted for each participant (N=38) at baseline (T1). Green bolded lines represent the average for all participants.

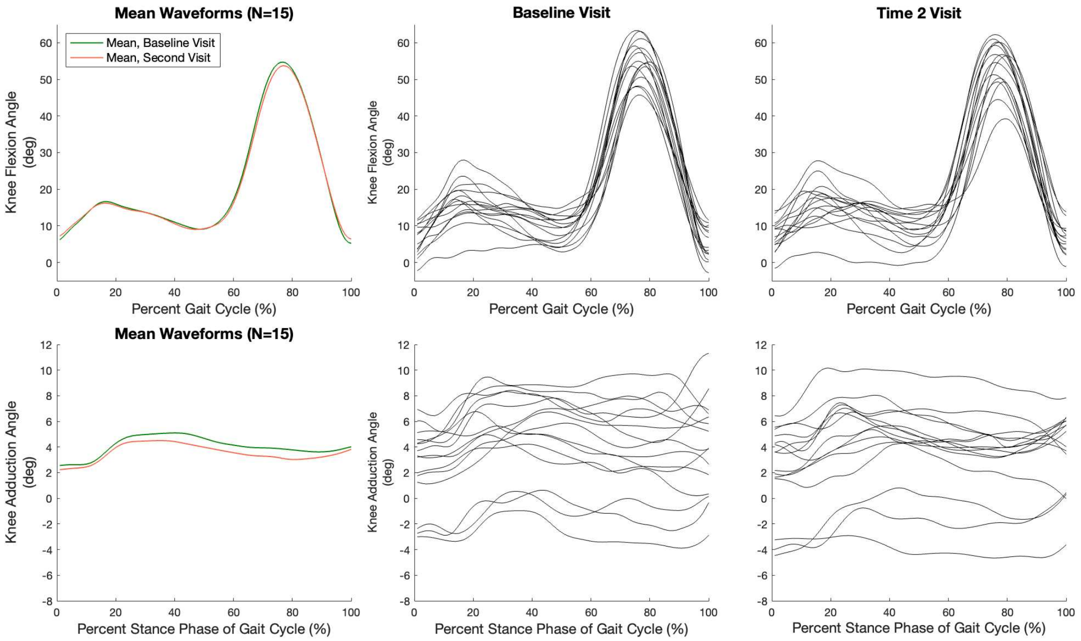


Figure 4.2 Sagittal and frontal plane knee angle waveforms plotted for each follow-up group patient (N=15) at baseline (T1) and second visit (T2).

4.6.1 Longitudinal Change in Gait Outcomes

Patient kinematic data at baseline and T2 are presented in Table 4.3 for the full group and follow-up subgroup. Three sagittal and frontal plane PCs were retained for further analysis. These PCs captured 85.1% (sagittal plane) and 98.0% (frontal plane) of the variability within the patient waveform data, and further interpretations for each are included in APPENDIX B. There were no significant differences in discrete kinematic or PC score gait outcomes from baseline to T2 on a group level (Table 4.3).

Table 4.3 Kinematic data for whole group (N=38) and follow-up groups (N=15) at Baseline and Time 2.

		Baseline		Time 2
Kinematic Parameter		All (N=38)	Follow-Up Group (N=15)	Follow-Up Group (N=15)
Discrete Metric				
KFA Peak (°)		54.5 (9.0)	55.4 (5.4)	54.8 (6.3)
KFA Peak^{S} (°)		17.6 (5.9)	17.9 (5.1)	18.1 (5.6)
KFA Range (°)		49.0 (8.8)	49.7 (7.2)	48.8 (7.6)
KFA Range^{S} (°)		12.2 (4.2)	12.2 (4.3)	12.2 (4.4)
KFA Minimum^{LS} (°)		9.0 (5.0)	8.3 (3.7)	7.9 (4.5)
KAA Range^{S} (°)		4.8 (1.7)	4.5 (1.8)	4.5 (1.5)
KAA Mean^{S} (°)		3.1 (4.5)	4.0 (3.4)	3.6 (3.4)
KAA Peak^{S} (°)		5.5 (4.7)	6.6 (3.6)	6.2 (3.3)
PC Gait Feature	Variance Explained (%)			
KFA PC1: gait cycle flexion angle magnitude	56.8	0.4 (50.1)	3.9 (33.0)	-0.9 (38.7)
KFA PC2: stance-to-swing angle range	25.3	-1.9 (32.3)	6.2 (25.1)	4.8 (28.8)
KFA PC4: mid-to-late stance-phase range	3.0	-0.2 (10.5)	-0.2 (9.8)	0.5 (11.9)
KAA PC1: stance-phase adduction angle magnitude	95.1	-1.3 (45.7)	8.3 (34.2)	3.2 (34.1)
KAA PC2: early stance-to-midstance range	2.2	0.9 (6.5)	-1.0 (7.4)	-2.2 (6.3)
KAA PC4: heel strike-to-early stance range	0.7	0.3 (4.0)	-0.1 (2.9)	-0.7 (3.4)

PCs were defined in the direction of the provided interpretation, larger values = higher magnitudes, negative values = opposing direction from interpretation.

Pearson's correlations of baseline variables with change in knee kinematic outcomes are presented in Table 4.4. Plots of significant associations are provided in APPENDIX C.

Sagittal Plane: A baseline to T2 decrease in KFA range in stance was significantly associated with lower baseline BMI and a higher baseline knee adduction range from heel strike to early-stance (KAA PC4). A baseline to T2 decrease in the range of stance phase flexion to extension angle (KFA PC4) was significantly associated with female sex and lower baseline knee adduction range in stance and trended towards greater baseline heel strike to midstance differences in knee adduction angles (KAA PC2; $p \leq 0.06$). A baseline to T2 decrease in the overall magnitude of the flexion angle during gait (KFA PC1) trended towards significant associations with a lower knee adduction angle range in stance ($p \leq 0.06$).

Frontal Plane: Baseline to T2 increases in the peak knee adduction angle in stance were significantly associated with smaller baseline knee adduction angle ranges during stance, and greater early-to-midstance adduction angle differences (KAA PC2) at baseline. Increases in knee adduction range in stance from baseline to T2 were significantly associated with male sex and lower baseline adduction angle range during stance.

Table 4.4 Correlation results (r value) of baseline values and Δ-kinematics.

		Change Values					
		Δ Speed	Δ KFA Range^{S}	Δ KAA Peak^{S}	Δ KAA Range^{S}	Δ KFA PC1	Δ KFA PC4
Baseline Values	Age	-0.11	-0.14	-0.20	-0.34	0.32	0.08
	BMI	0.25	**0.51***	-0.11	0.42	-0.17	-0.03
	Speed	-0.14	-0.45	0.33	-0.07	-0.02	0.13
	OKS-F	0.15	-0.30	-0.07	-0.26	0.32	0.36
	NPRS	-0.32	-0.03	0.26	0.13	-0.14	-0.06
	KFA Peak	0.19	-0.24	0.08	0.07	0.35	0.04
	KFA Peak^{S}	-0.32	-0.26	0.18	0.26	-0.12	-0.37
	KFA Range	0.39	-0.18	-0.02	-0.19	0.46	0.38
	KFA Range^{S}	0.03	-0.32	0.08	-0.09	0.18	0.14
	KFA Minimum^{LS}	-0.37	-0.17	0.16	0.01	-0.28	-0.25
	KAA Peak^{S}	0.40	0.41	-0.42	-0.40	0.17	0.47
	KAA Mean^{S}	0.29	0.34	-0.32	-0.30	0.01	0.39
	KAA Range^{S}	0.33	0.39	**-0.63***	**-0.63***	0.50$^{\uparrow}$	**0.68***
	KFA PC1	-0.16	-0.34	0.21	0.16	0.01	-0.27
	KFA PC2	0.38	-0.02	-0.05	0.01	0.28	0.24
	KFA PC4	-0.24	-0.22	0.19	0.18	0.08	-0.36
	KAA PC1	0.29	0.33	-0.31	-0.30	0.00	0.38
	KAA PC2	0.03	0.30	**-0.52***	-0.43	0.12	0.50$^{\uparrow}$
	KAA PC4	-0.31	**-0.62***	0.46	0.08	0.15	-0.32

^{S} *= metric over the stance phase of gait cycle.* ^{LS} *= metric at the late-stance phase of gait cycle.* ***Bolded**** *values show significance at* $p < 0.05$. $^{\uparrow}$ *= significance of* $p \leq 0.06$.

4.6.2 Worsening Subgroup Analysis

Of the 15 patients with T2 data, five patients were identified who exhibited significant worsening (i.e. away from healthy, asymptomatic direction [104], [151]) of at least one sagittal-plane metric between baseline and T2 (Table 4.1). At baseline, there were no statistically significant differences between groups for demographic, patient-reported outcomes, discrete or PC gait kinematic metrics (Table 4.5). The worsening group at baseline showed trends towards lower flexion angle magnitudes (KFA PC1), higher adduction angle magnitudes (KAA PC1), smaller KFA stance range (and KFA PC4), smaller KFA peaks, smaller KFA stance ROM, and larger mean KAA compared to the non-worsening group ($0.08 < p < 0.108$).

From baseline to T2, the gait worsening group had a significantly greater decrease in KFA peak ($p < 0.05$) and knee flexion angle magnitude (PC1; $p < 0.005$) than the non-worsening group (Table 4.5, Figure 4.3). At T2, the worsening group had significantly worse sagittal plane gait kinematics including lower KFA overall magnitudes (PC1, $p = 0.01$), lower KFA stance phase range ($p = 0.05$), and lower peak KFA ($p = 0.04$). The worsening group also had higher stance peak knee adduction angles, ($p=0.03$), and higher stance mean adduction angles ($p = 0.03$) than the non-worsening group.

Table 4.5 Baseline, mean change, and T2 demographic, speed, PROMS, and gait kinematics data for the worsening (N=5) and non-worsening groups (N=10).

	Worsening Group (N = 5)			**Non-Worsening Group (N = 10)**		
	Baseline	Change	T2	Baseline	Change	T2
Sex (F/M)	2/3			4/6		
BMI (kg/m^{2})	36.5 (8.9)			35.4 (7.6)		
Age (years)	69.4 (7.4)			68.7 (6.3)		
OKS Functional	10.0 (3.0)			12.4 (3.2)		
NPRS	6.9 (2.7)			6.3 (1.5)		
Speed (m/s)	1.00 (0.17)			1.08 (0.20)		
Discrete Metric						
KFA Peak	52.4 (6.1)	-2.7 (2.0)*	49.7 (7.3)*	56.9 (4.6)	0.4 (2.4)*	57.3 (4.1)*
KFA Peak^{S}	15.5 (5.6)	-1.1 (2.4)	14.4 (6.4)	19.0 (4.8)	0.9 (3.3)	20.0 (4.4)
KFA Range	47.2 (9.6)	-1.9 (2.2)	45.3 (10.8)	51.0 (5.9)	-0.4 (3.2)	50.6 (5.3)
KFA Range^{S}	10.3 (3.6)	-0.4 (4.2)	10.0 (2.4)*	13.1 (4.5)	0.1 (2.7)	13.2 (4.9)*
KFA Min.^{LS}	8.1 (4.6)	-1.2 (2.8)	6.9 (5.9)	8.4 (3.4)	0.0 (2.3)	8.4 (3.9)
KAA Range$^{S\ \&}$	4.1 (1.4)	0.5 (1.7)	4.6 (1.1)	4.7 (2.0)	-0.3 (1.6)	4.4 (1.7)
KAA Mean^{S}	5.5 (2.1)	0.04 (2.2)	5.5 (2.1)*	3.3 (3.8)	-0.7 (1.4)	2.6 (3.5)*
KAA Peak^{S}	7.6 (1.8)	0.4 (1.7)	8.0 (1.9)*	6.1 (4.2)	-0.8 (1.9)	5.3 (3.5)*
PC Gait Feature						
KFA PC1	-12.9 (34.1)	-22.8 (7.0)*	-35.7 (33.7)	12.2 (30.6)	4.2 (17.9)*	16.4 (28.6)
KFA PC2	6.1 (38.5)	-5.9 (19.6)	0.2 (47.0)	6.2 (18.0)	1.0 (9.9)	7.2 (17.0)
KFA PC4$^{\&}$	-4.7 (9.1)	0.4 (12.1)	-4.3 (10.6)	2.1 (9.8)	0.8 (11.4)	2.9 (12.3)
KAA PC1	23.1 (20.9)	-0.3 (23.6)	22.8 (21.4)	0.9 (38.0)	-7.5 (14.3)	-6.6 (35.9)
KAA PC2	-0.4 (7.5)	-0.3 (6.1)	-0.7 (7.1)	-1.3 (7.7)	-1.7 (5.7)	3.0 (6.2)
KAA PC4	-0.7 (2.9)	-1.5 (1.4)	-2.2 (4.1)	0.2 (3.0)	-0.2 (2.9)	0.1 (2.9)

*Values presented as mean(SD); SD = standard deviation. * = significant ($p < 0.05$) differences between worsening and non-worsening groups at time point. $^{\&}$ = Significant sex-related differences in magnitude of change from baseline to T2 for all N=15 in follow-up group.*

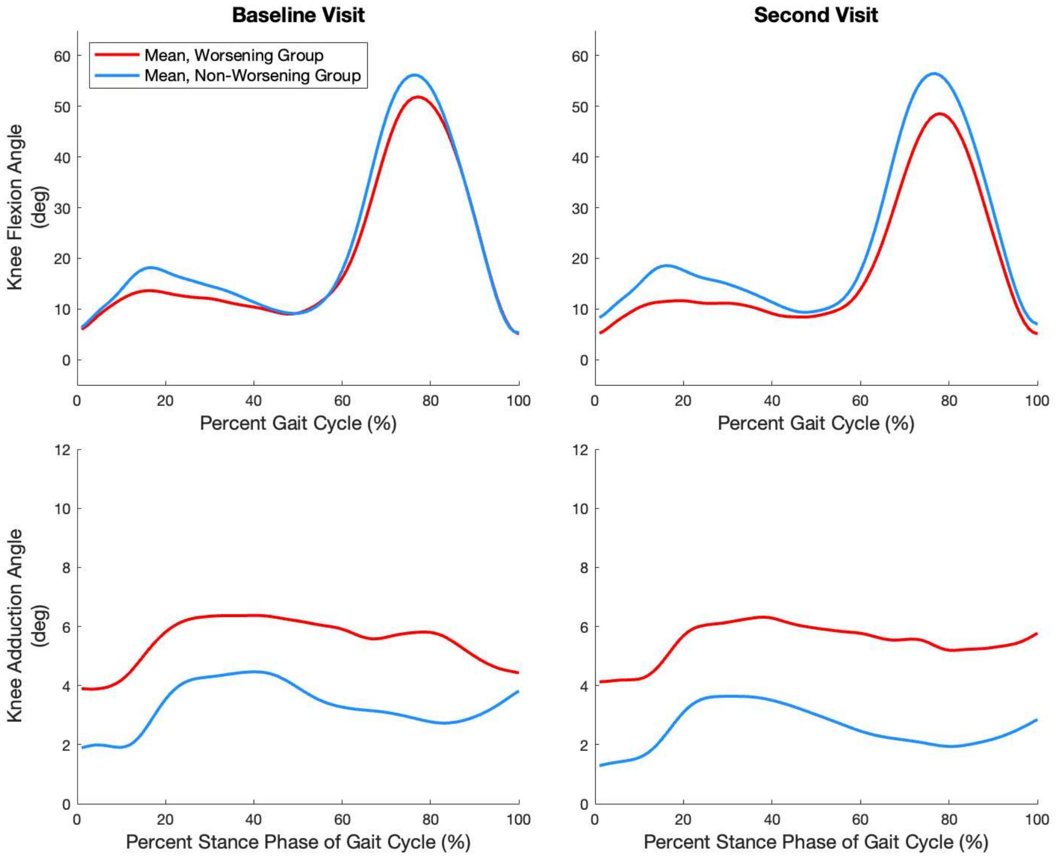


Figure 4.3 Sagittal and frontal plane knee angle waveforms for the second visit sub-group participants at baseline and T2.

4.7 DISCUSSION

Previous studies have provided evidence on the impact of TKA on patient gait biomechanics from before to after surgery [2], [5], [129], [151], [157], as well as the association of waiting for TKA with continued deterioration in pain, anxiety, quality of life and self-report function [23], [24], [25], [26], [27], [28] and lower levels of post-operative satisfaction [62] and function [186]. This study was the first to investigate the potential impact on objectively measured gait biomechanics while awaiting TKA. On a group level, knee kinematics during gait did not significantly change while waiting for knee arthroplasty surgery, however patient to patient variability was high, and some patients showed significant gait kinematics decline while waiting.

Female sex was significantly associated with a greater increase in knee adduction angle range and a greater decrease in stance-phase flexion-extension angle range (KFA PC4) from baseline to T2. Differences in gait biomechanics present in OA females that do not occur in males. Altered knee adduction moment (KAM) loading and sagittal plane motion and loading have been previously observed in female OA gait [4], [187]. These sex-specific manifestations of OA within patient joint mechanics could pose an influential factor of end-stage worsening of kinematics.

A lower baseline BMI was associated with a greater decrease in KFA range in stance from baseline to T2. As the incidence of knee OA increases with higher BMI [188], and with BMI associated with OA progression [189], [190] and alterations in knee OA gait mechanics [191], this was an unexpected finding of our study. This finding may involve multivariate factors, such as sex [192] and knee alignment effects [189], [193], although this was not analyzed in a multivariable analysis in our current study due to small sample sizes.

The magnitude of change of the kinematic variables from baseline to T2 were not significantly associated with baseline self-reported pain. Within the literature, Maly et al. found a significant inverse association of knee flexion-extension angle excursion during gait and self-reported pain within a population with varied OA severity [194], and Stauffer et al., although they did not report OA severity of the cohort, also found a significant inverse association of knee flexion range in stance with severity of knee pain [195]. This could suggest gait alterations are associated with perceived pain in less-severe grades of knee OA, however, the relationship may be less clear at more severe stages of the disease. Evidence on the influence of self-reported pain with worsening knee OA gait kinematics is yet to be established within the literature [196]. Changes in the reported discrete sagittal plane metrics showed no significant associations with baseline self-reported function. This suggests that patient-perceived function is a tool to globally indicate the degree of functional ability, however, may not be sensitive enough to prognostically reflect risk of function worsening over time.

A key finding was that changes in knee kinematics during gait over the wait period were most associated with the reported baseline gait kinematics than the PROMs or demographics/anthropometric variables. In our study, a higher knee adduction range at baseline was associated with having greater reductions in frontal plane metrics (KAA Peak, KAA Range; $p < 0.05$) and less reduction of sagittal plane knee angle stance phase range of motion (PC4 $p < 0.05$). There is literature evidence of significant variability in the direction and amount of frontal plane angle changes during gait in OA patients over time [131], [136], [137], [138], and our study would support this finding, with no group level significant change in these measurements over time, but with significant person-to-person variability.

Higher baseline knee adduction range from heel strike to early-stance (PC4), representing a varus thrust characteristic [197] in higher PC scores, was associated with greater reductions of the knee flexion angle range in stance ($p = 0.01$). Varus thrust, a measure of dynamic frontal-plane instability, has been associated with altered joint loading [43], [135], [142], lower sagittal range of motion [198], [199], and altered muscle activation [198], [200], [201] during gait in patients with knee OA. Greater varus thrust magnitudes have been shown to correlate with greater medial and lateral quadriceps and hamstring co-contraction [200] and lower knee extensor and flexor strength [201]. The added compensatory muscle co-contraction from attempting to stabilize the joint during gait may not be good in terms of long-term function, but necessary for these patients in the moment to reduce pain and instability. Implications of varus thrust on the sagittal plane mechanics have not been thoroughly investigated in the literature, but our current results suggest that higher varus thrust in patients with severe knee OA was associated with further sagittal plane stiffening potentially in response to the associated instability.

We chose to represent worsening of gait kinematics with changes in the sagittal plane knee kinematics only, wherein a majority of compensatory mechanisms and gait stiffening develop throughout OA progression [104], [131], [202], [203]. There are also significant changes in sagittal plane kinematics present in severe OA gait compared to earlier disease phases [104]. This decision is also relevant to post-TKA functional outcomes; Outerleys et al. found frontal plane knee mechanics, which are primarily targeted with standard TKA procedures, to be the most significant contributors in discriminating between pre- and post-TKA gait, and pre-TKA deficits in sagittal plane biomechanics were less improved [2]. As this study did not control for only medial compartment OA, defining the worsening of frontal plane kinematics to be associated with the directionality of changing knee adduction angles is not relevant to our population [45], [204], [205], whereas a decrease in the magnitude and range of sagittal plane kinematics is universally worse regardless of OA location and severity.

Patients who displayed a significant gait worsening walked with more severe sagittal plane gait kinematics and greater knee adduction kinematics at baseline, when compared to the non-worsening group (Figure 4.3) ($p < 0.05$). Although this worsening group was small (n=5), which limited the statistical power to detect more kinematic differences at baseline or to perform multivariable analyses, two sagittal plane PC scores trended towards significance between the worsening and non-worsening groups at baseline: flexion angle magnitude (PC1, $p \leq 0.1$) and flexion stance phase range of motion (PC4, $p \leq 0.1$). Higher baseline knee adduction angle magnitudes within this group are potentially associated with a more structurally severe presence of OA [131], [203]. The stiffer sagittal plane kinematics exhibited by the worsening group at baseline, paired with larger knee adduction angles, help support a "lower functioning" OA gait phenotype of these patients (cluster of low-functioning, dynamically varus patients with stiff sagittal plane knee gait) [206]. The worsening group experienced significantly greater reductions of the knee flexion angle magnitude than the non-worsening group from baseline to T2, which suggests a potential for further worsening of kinematics during gait for these patients, which could have more severe consequences on their surgical outcomes.

The kinematic differences observed between the worsening and non-worsening groups at baseline, the lack of differences in other factors, and the significant correlations between changes in kinematics and baseline kinematic measures, support the added value and sensitivity of objectively capturing patient gait dynamics during the pre-surgical waiting period as a potentially clinically relevant monitoring tool. Given the small sample size of the current investigation, further research should and will examine these associations in larger patient cohorts with more multivariate statistical approaches.

4.8 LIMITATIONS AND CONSIDERATIONS

Our investigation focused solely on the sagittal and frontal planes, choosing to not include the transverse plane knee kinematics. Transverse plane kinematics, particularly at the knee joint, are observed to have the largest measurement errors [9], [20], [167] (Standard error of measurement: > 5°, Root-mean squared difference: > 3.5°) and lowest reliability [167] (Intra-class coefficient: 0.34 < 0.87) when performing motion capture of human gait. The small range of knee motion in the transverse plane during gait, coupled with the long-axis alignment of the thigh and shank segments during this motion, results in larger errors within transverse plane data [167]. Higher tibial external rotation in stance [138], [207], as well as lower transverse plane ROM [131], [138], has been shown in severe knee OA cohorts compared to less severe OA cohorts, and it is plausible that with the stiffening of gait in other planes, changes in transverse plane mechanics may worsen over time. However, our ability to measure change in these small measurements over time is limited and therefore we decided to not focus on it in the current study.

Additionally, our study contained a relatively small sample size, using initial clinical data on this population collected using a validated protocol with markerless motion capture technology. Despite the limited sample, significant differences and associations were identified that support the need for continued investigation into gait biomechanics changes during the wait period for arthroplasty surgery. The sample size, and particularly the small sample size of the worsening subgroup, may limit the generalizability of our findings to larger groups, and so caution should be taken when drawing conclusions based on the current results. We did not have static frontal plane alignment available for this cohort at the time of this study, however future work will incorporate static alignment information to understand how anatomical differences among joints may contribute to understanding kinematic deterioration during the wait period. The 4-month follow-up time frame may also have limited the results of our study; as studies have shown continued declines in patient-reported metrics on the wait period upwards of 6-months [23], [24], [25], [26], [27], [28], longer wait times would likely show more severe changes in gait kinematics. Lastly, the demographics of patient group analyzed in this study displayed a homogeneous age range which can limit interpretation generalizability of the analysis results.

This study did not investigate the gait kinetics and muscle activation changes over the surgical wait period. As this study analyzed initial data collected from a research program integrating efficient, streamlined, and high-volume motion capture into clinical environments, only changes in knee kinematics were investigated at this time. Changes in joint-level patient mechanics during knee OA progression are multifactorial, including changes in muscle activation patterns [134], [139], [208] and joint loading and moments [104], [134], which all impact the patient kinematics during gait. In the future, linking these kinematic changes with the kinetic environment is important for understanding the full spectrum of change in gait mechanics.

4.9 CONCLUSIONS

This study was the first to investigate changes in gait biomechanics of end-stage knee OA patients on the waitlist for TKA. Although there were no significant changes in gait kinematics on a group level, there was significant patient to patient variability and significant worsening of gait kinematics was found in one third of the patients. Patients with worsening gait presented with lower sagittal plane kinematics and higher knee adduction angle magnitudes at baseline, but no demographic or self-reported differences, highlighting the added sensitivity of an objective gait assessment during the wait period. Results of this initial investigation support the usage of longitudinal patient gait analysis over the TKA wait-period to potentially aid in surgical triage and prioritization. Future work should include larger longitudinal patient datasets to further characterize the multivariate relationships between baseline patient anatomical differences, kinematic worsening, and symptomatic worsening while awaiting TKA.

CHAPTER 5 CONCLUSIONS

5.1 SUMMARY OF THESIS OUTCOMES

Objective, instrumented gait analysis can provide valuable insights into patient joint-level function that are not captured by the standard patient-reported outcome measures (PROMs) or qualitative functional testing [84], [101], [102]. Gait changes associated with end-stage knee OA have been identified [104], [113], [127], [203], and there has been a growing recognition within current research of great functional and symptomatic variability within patient groups presenting for TKA [2], [3], [4], [5], [206]. The clinical uptake of gait analysis during the evaluation and triaging of patients with end-stage knee OA can provide further insight into patient functional variability and functional deterioration over the surgical wait period, which remains insufficiently investigated. Markerless motion capture systems are a new technology that have the potential to facilitate efficient, well-integrated kinematic gait analyses within clinical environments. The goals of this thesis were to facilitate the efficient collection of gait kinematics within a hospital clinic hallway, to analyze and define the repeatability of knee OA and TKA related kinematic gait metrics captured using this system, and to investigate the changes in knee gait kinematics over the surgical wait period in a cohort of end-stage knee OA patients awaiting TKA and the association of these changes with baseline patient factors.

The first component of this thesis aimed to integrate an optical motion capture system with markerless software within a hospital clinic hallway to facilitate overground kinematic gait analysis. Video cameras were arranged in the 2.4-metre-wide hallway in a configuration which optimized camera visibility for overground gait collection. The initial setup and protocol testing used an iterative approach with cameras arranged on tripods in the Dynamics of Human Motion lab at Dalhousie University to ensure data capture within the proposed volume prior to moving to the clinical location.

The second component of the thesis was a test-retest study within this hospital hallway volume on 20 healthy participants at three timepoints to quantify the inter-session repeatability of discrete sagittal and frontal plane kinematic metrics relevant to end-stage knee OA and TKA [2], [104], [129], [151] using the markerless motion capture system. Intraclass correlation (ICC) and standard error of measurement (SEM) values were found to be very good-to-excellent, and comparable to those previously reported in the literature [158], [164], [165], [166]. As hypothesized, sagittal plane metrics displayed better repeatability than frontal plane metrics.

The third component of this thesis was to investigate the changes in gait kinematics over the surgical wait period in a clinical group of patients with end-stage knee OA. Patient gait kinematics were longitudinally assessed over a 4-month period on the waiting list, which aimed to quantify changes in knee joint-level kinematics and their association with baseline patient characteristics, self-reported pain and function, and kinematics. There were no significant group-level changes in gait kinematics, however, there was variability of gait changes among patients and one third of patients displayed significant worsening of gait kinematics. The patients who displayed gait worsening presented with lower sagittal plane kinematics and higher knee adduction angle magnitudes at baseline, however, showed no significant baseline differences in demographics or self-reported pain or function.

5.2 IMPLICATIONS OF THESIS RESEARCH

This thesis integrated a markerless motion capture system into a clinical environment, which will allow for the increased clinical implementation of objective assessments of joint-level mechanics within end-stage knee OA populations. This serves as a valuable tool which can be used throughout the overarching research program and can contribute to the high-volume collection of gait data on clinical cohorts, ultimately allowing for a better understanding of patient biomechanical deterioration or impact of treatment interventions.

The inter-session study results (Chapter 3) will add to the existing literature that has investigated the repeatability of markerless motion capture technologies. This study was the first to define the absolute repeatability of discrete kinematic metrics relevant to OA and TKA cohorts using a markerless motion capture system within a unique clinical environment, which is critical information needed to help inform the next steps for clinical translation of motion capture systems. This information can have implications for the triage and management of patients presenting for TKA, to allow for patient-specific objective functional characteristics to be measured and considered during this process. This research has implications for the efficacy of markerless motion capture within non-laboratory or space-limited environments, demonstrating that with increased developments of motion capture technology, systems can be adapted to collect repeatable measures of human movement with efficiency, not burdened by clothing, space, or operator error to the extent of previous technologies.

The longitudinal investigations performed in Chapter 4 address the gap within the literature on the potential functional changes in end-stage knee OA patients awaiting TKA. Assessing patient gait over the wait period provided information on the variability in objective function among patients during this time. On a group-level, significant changes in knee joint-level kinematics were not present during this period, however, on a patient-level, one third of patients experienced significant worsening of knee joint gait kinematics. These patients were not distinguishable at baseline in demographic or self-reported pain or functional measures, however displayed differences in their baseline gait mechanics with stiffer, reduced sagittal plane angles and increased varus angle magnitudes during walking. These findings have implications regarding the clinical use of objective assessment tools to monitor patient function, especially in situations where long surgical wait periods are endured, as standard qualitative functional or patient-perceived outcomes may not capture this variability.

5.3 LIMITATIONS AND CONSIDERATIONS

There are several limitations of this work. Participants in Chapter 4 were primarily from the Halifax, Nova Scotia area, and as such, may represent a relatively homogeneous dataset from an ethnicity/socioeconomic perspective that should be accounted for when interpreting these results. The patient cohort also had a relatively small age band; therefore, it is difficult to overly interpret any significant age-effects. Therefore, the current results should be interpreted in this context and may not be generalizable to the entire or worldwide adult population with end-stage knee OA.

Although significant associations were identified, the statistical power for finding other potential differences between subgroups was limited in a population of 15 patients, with 5 worsening, which also limited our ability to perform multivariable analyses. Larger sample sizes should be used to further strengthen the results from the clinical longitudinal study in Chapter 4. This study provided an investigation into longitudinal changes observed over the wait period for TKA in a cohort with end-stage knee OA using initial data from a novel setup of a markerless motion capture system. The addition of more participants will increase the potential of capturing more representative levels of clinical diversity (e.g. age, ethnicity, socioeconomic status, mental health status), as well as statistically relevant conclusions to be drawn on multivariable analyses related to this. This longitudinal study captured the change in kinematics over a four-month period, which should be considered when interpreting results. A four-month period was investigated to align with the timeline of this thesis and may not have been a sufficient time-period to observe the extent of pre-operative kinematic changes within this cohort.

This research did not investigate the kinetics and muscle activation changes over the surgical wait period. As this thesis presented initial efforts to integrate efficient, high-volume kinematic motion capture system into a clinical environment, only kinematic gait outcomes were validated and investigated at this time. Changes in joint-level patient function during knee OA progression are multifactorial; changes in muscle activation patterns [46], [47], [130], [139], [208], joint loading and moments [46], [47], [104], [113], and pain [194], [196], [209] all impact the patient biomechanics during gait. Limitations of the generalizability of the gait changes identified over the TKA waitlist period are inherent to our representation of these changes in only within a kinematic domain of the sagittal and frontal planes of the knee joint.

Considerations of the markerless deep learning vision algorithm, wherein the training dataset from internet images could contain age, ethnic, positional, or clothing biases, need to be taken into account. This could affect the accurate measurement of individuals who present differently from the training dataset attributes.

5.4 RECOMMENDATIONS AND FUTURE WORK

Future work from the overarching research program this thesis contributed to will be incorporating additional pre-operative variables (physical activity outcomes, free living gait, morphology, anatomy) and linking them to surgical and post-operative outcomes. This is future work that is already being explored by our team. In addition, efforts to leverage the standardized data collection procedures of markerless motion capture systems can look towards multi-center partnerships; higher data sharing and gait analysis collection volumes that are required for more advanced analytics, can be possible. The development of more advanced processing and computing infrastructures will allow for progress in real-time processing and data feedback that is more appropriate for clinician users, whereas currently, this system is operating in a manual, research context.

The repeatability study in Chapter 3 was designed to establish the repeatability of discrete knee kinematics relevant to our clinical application collected with a markerless motion capture system. This is valuable as these metrics have not been previously investigated in the literature using markerless technology, but also provides a future framework for assessing additional metrics of interest and assessing the impact of different system setups and locations as we expand our research program. Recommendations for future work include defining the whole-waveform kinematic segment/angle variability and repeatability of transverse plane kinematics, as to not limit the data able to be confidently presented from the system.

Future work investigating the impact of the surgical wait period on patient function could include the anatomical alignment of the patients and characterization of the affected OA compartments in the knee. This would allow for further classification of the baseline patient cohort, to support the identification of patient factors related to kinematic decline while awaiting surgery. The collection of objective neuromuscular control data can provide further information which may help to identify multivariate differences between deteriorating groups on the waitlist. The addition of functional testing to the gait analysis protocol, observed with the markerless motion capture system, is a great opportunity for future research. Alterations in patient gait with knee OA have been extensively studied in the literature, however, objective functional assessment of activities such as stair ascent/descent [210], [211], sitting-to-standing [212], and incline/decline walking [213] may identify additional changes in patient joint-level function that are related to kinematic deterioration, further helping to identify them during clinical triaging and management processes.

Lastly, a nod to the work I find most exciting in the future. As efforts to further classify and phenotype patients with knee OA are taken, in hopes of identifying those most susceptible to poor post-operative TKA outcomes, I believe high laxity and hypermobile patient groups should be investigated in addition to those groups that naturally separate based on factors of demographics, PROMs and biomechanical variables [3], [206], [214], [215]. Patients with increased joint hypermobility (i.e. increased angular range of motion in a joint), whether due to genetic factors or trauma, can display increased knee mobility [216]. Greater varus-valgus joint mobility has been associated with deteriorations in ligament integrity with age, and a reduction in the knee joint space from OA progression [217]. Severe joint mobility is linked to a higher incidence and structural progression of knee OA [218] and may compromise joint stability.

To effectively tailor surgical TKA procedures to the patient, the association between the joint movement and the active and passive stability of the joint needs to be established with the abovementioned patient-factors, as surgical procedures do not just affect the bone mechanics, but those of all surrounding soft tissues as well. This is an area of research that has not been investigated contributed to by: 1. The reduced clinical uptake of motion capture systems, and 2. The inability to accurately capture objective passive mobility data on patients in standard clinical assessments or surgical procedures, both of which are aided with the use of in-clinic markerless motion capture systems and surgical robotics systems. There is an exciting opportunity to longitudinally monitor characteristics and changes in patient gait over the TKA wait period, which can be further supported by collecting objective data on the passive mobility of the knees during surgery using surgical robotic systems.

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APPENDIX A Patient-Reported Outcome Measures

Numerical Pain Rating Scale (NPRS)

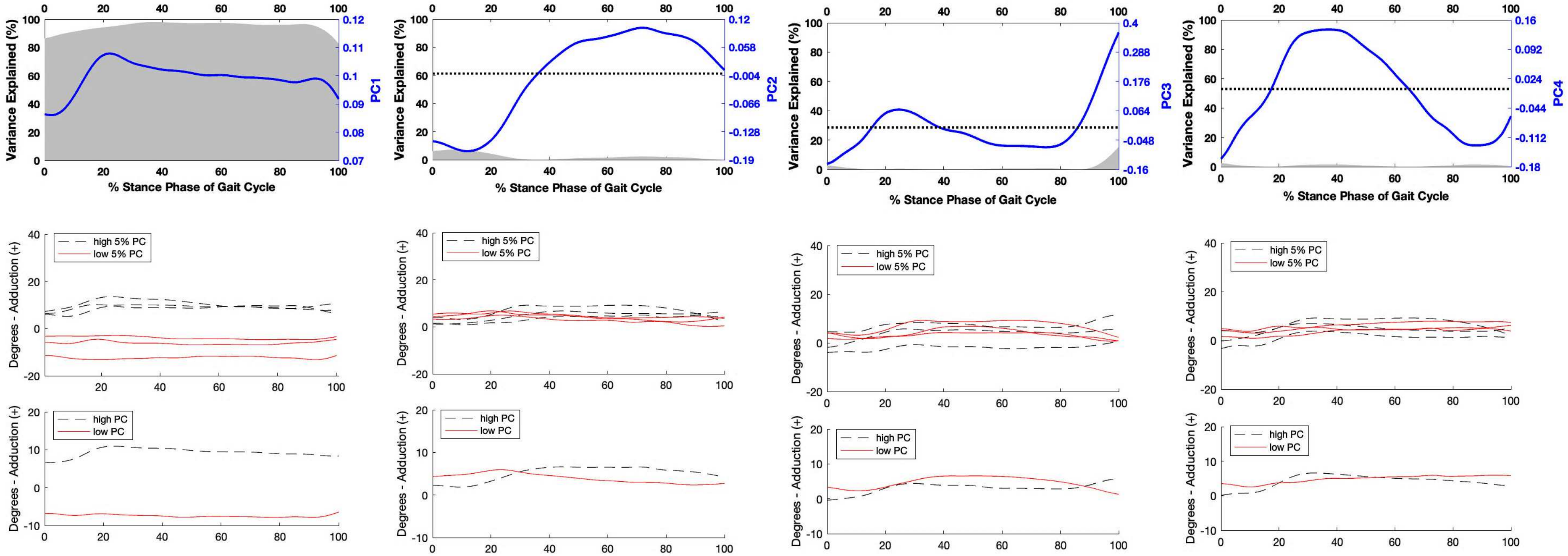
OSTEOARTHRITIS PAIN AND SYMPTOMS (11-item NPRS)										
Describe your **average pain levels over the last week**. Please give a number from 0 to 10, with 0 meaning no pain and 10 meaning the worse pain, to describe your average pain over the past week:										
0	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
No Pain										Worst Pain
Describe your **average pain over the last 24 hours**. Please give a number from 0 to 10, with 0 meaning no pain and 10 meaning the worse pain, to describe your average pain over the past 24 hours										
0	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
No Pain										Worst Pain
Describe your **worst pain over the past 24 hours**. Please give a number from 0 to 10, with 0 meaning no pain and 10 meaning the worse pain, to describe your worst pain over the past 24 hours										
0	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
No Pain										Worst Pain

Oxford-12 Knee Score Functional Component Subscale

OKS-FCS					
Question	**Score**				
	4	3	2	1	0
Have you had any trouble with washing and drying yourself (all over) because of your knee?	No trouble	Very little trouble	Moderate trouble	Extreme difficulty	Impossible to do
Have you had any trouble getting in and out of a car or using public transport because of your knee? (whichever you tend to use)	No trouble	Very little trouble	Moderate trouble	Extreme difficulty	Impossible to do
Could you kneel down and get up again afterwards?	Yes, easily	With little difficulty	With moderate difficulty	With extreme difficulty	No, impossible
Could you do the household shopping on your own?	Yes, easily	With little difficulty	With moderately difficulty	With extreme difficulty	No, impossible
Could you walk down a flight of stairs?	Yes, easily	With little difficulty	With moderately difficulty	With extreme difficulty	No, impossible

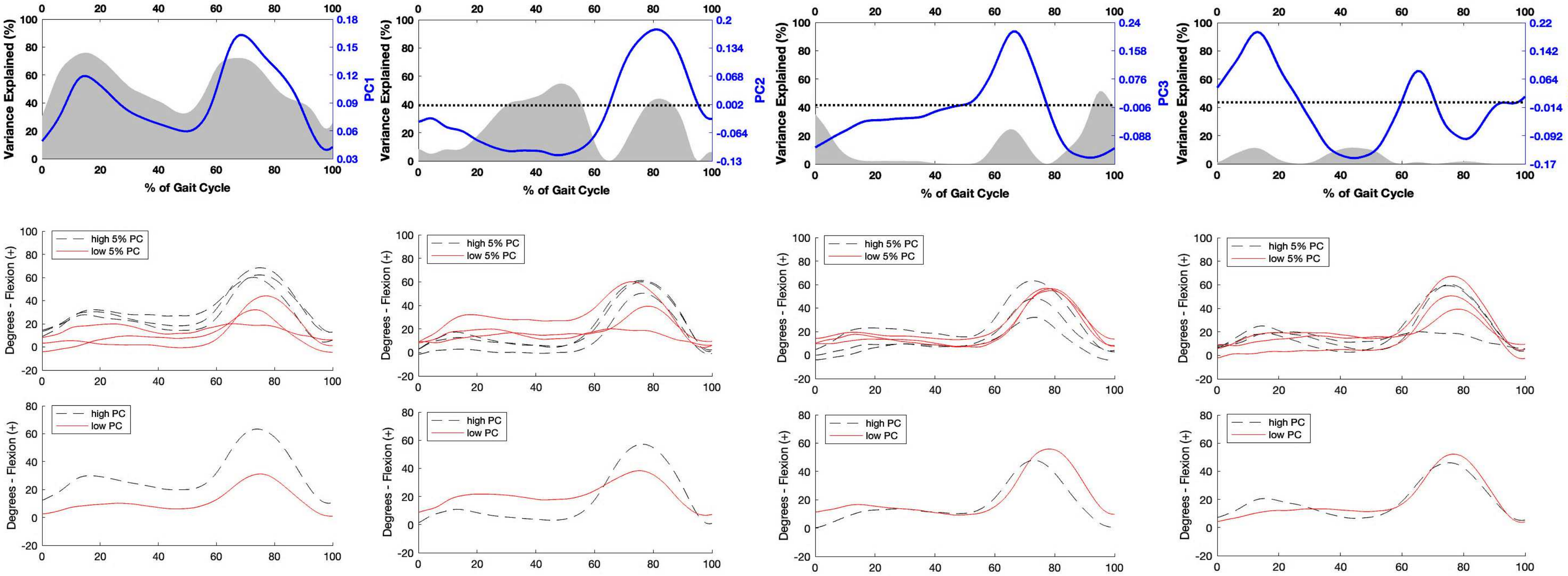
APPENDIX B Principal Component Analysis Results

Knee adduction angle principal component eigenvector plots. Top row: Eigenvector and percent variance explained. Middle row: waveforms associated with 95th and 5th percentile PC scores. Bottom row: mean waveform associated with 95th and 5th percentile PC scores. These plots were used to interpret the knee adduction angle PC features in Chapter 4 (n = 38 participants, 53 waveforms). Definitions of PC interpretations are found in Supplementary Table B.1.



Supplementary Figure B.1 Knee adduction angle principal component eigenvector plots (L-R: PC1, PC2, PC3, PC4).

Knee flexion angle principal component eigenvector plots. Top row: Eigenvector and percent variance explained. Middle row: waveforms associated with 95th and 5th percentile PC scores. Bottom row: mean waveform associated with 95th and 5th percentile PC scores. These plots were used to interpret the knee flexion angle PC features in Chapter 4 (n = 38 participants, 53 waveforms). Definitions of PC interpretations are found in Supplementary Table B.1.



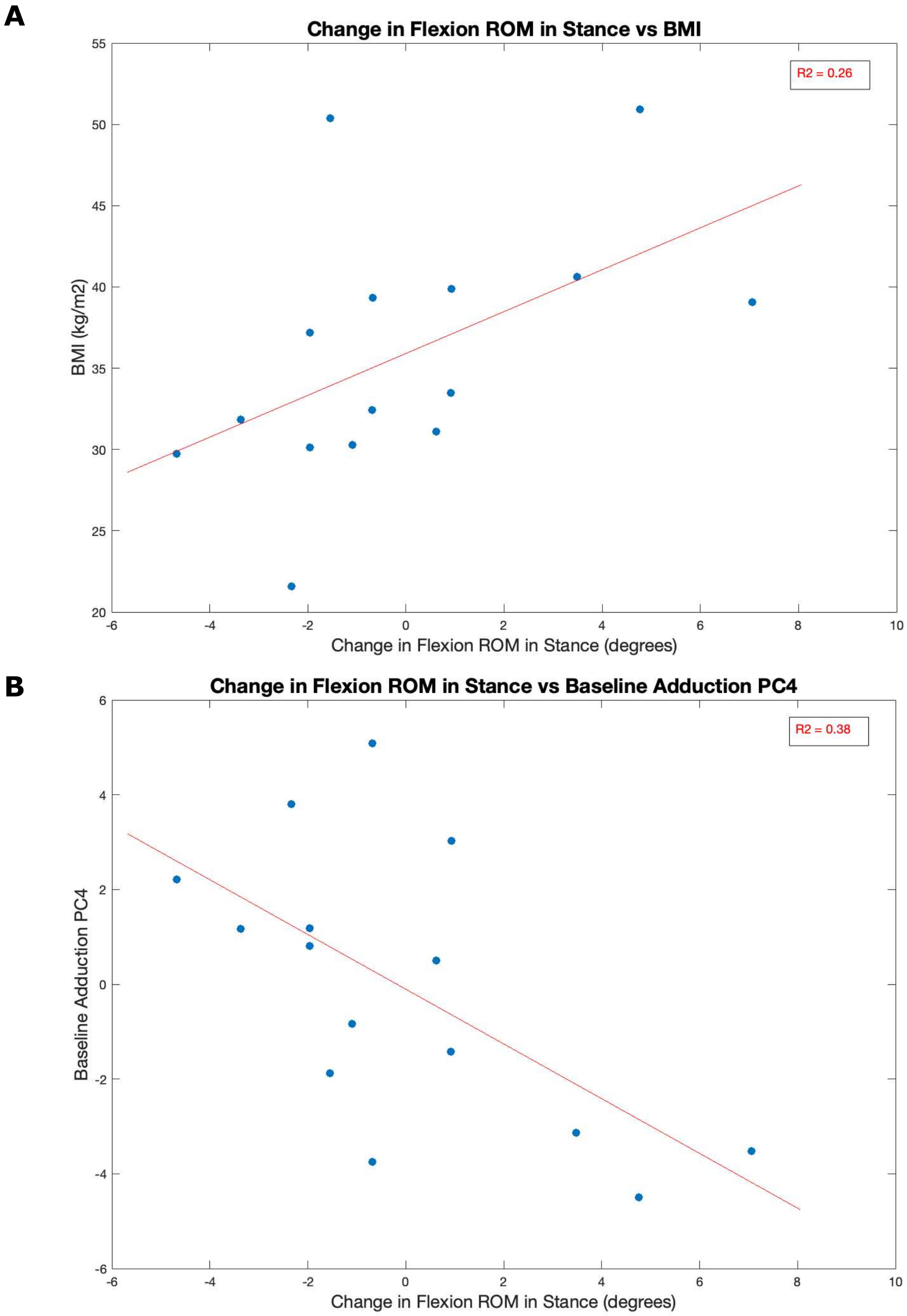
Supplementary Figure B.2 Knee flexion angle principal component eigenvector plots (L-R: PC1, PC2, PC3, PC4).

Supplementary Table B.1 Principal Component Analysis Results.

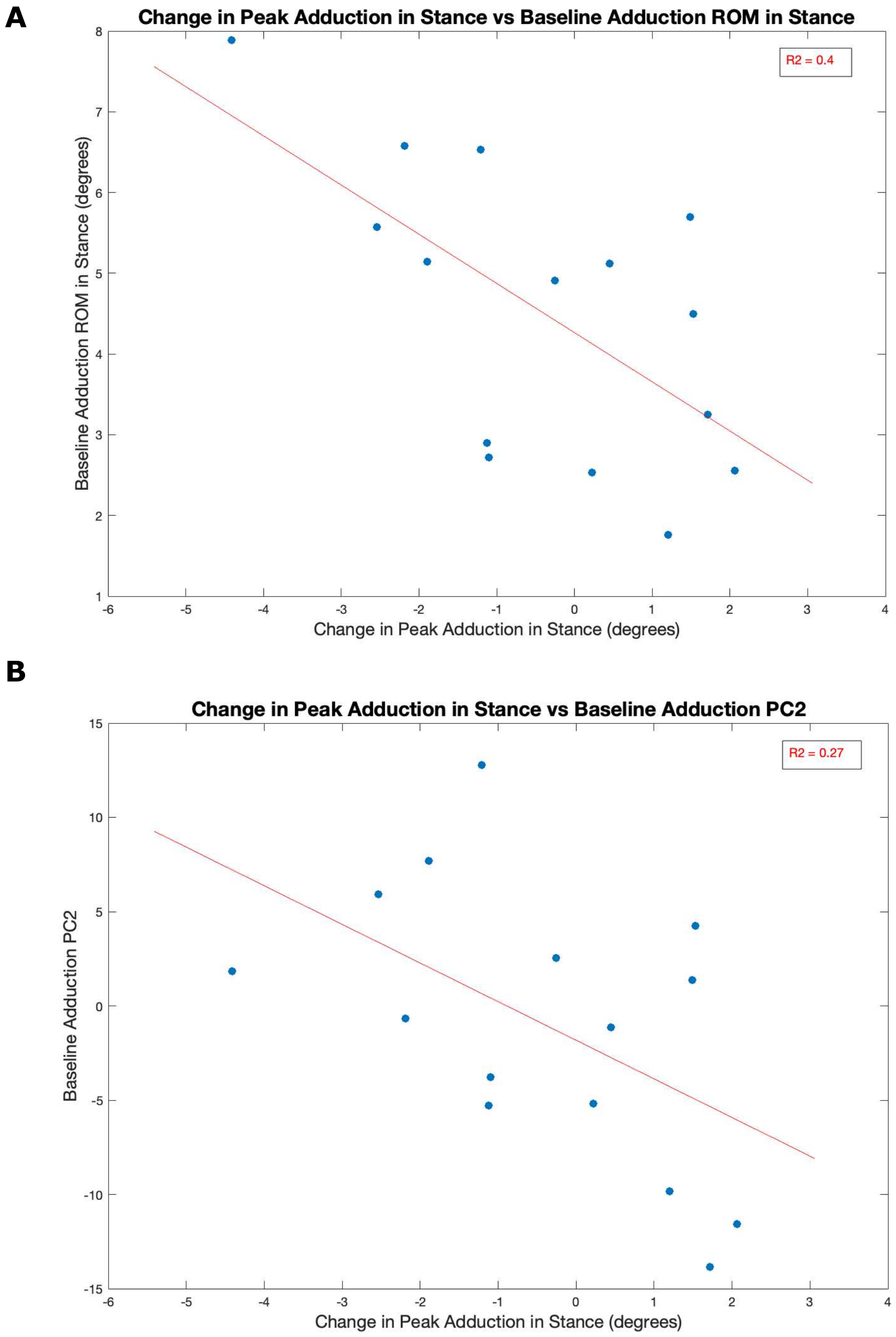
Gait Feature	**High PC Score Description**	**Variance Explained (%)**
Sagittal Plane		
PC1: overall magnitude of knee flexion angle over gait cycle	High overall magnitude of knee flexion angle over gait cycle	56.8
PC2: difference between peak stance phase and swing phase knee flexion angle	Greater difference between peak stance (smaller) and peak swing (larger) phase knee flexion angle	25.3
PC4: stance phase knee flexion angle range	Greater difference between peak stance (larger) and terminal stance (smaller) phase knee flexion angle	3.0
Frontal Plane		
PC1: overall magnitude of the knee adduction angle in stance phase	Higher overall magnitude of knee adduction angle during stance	95.1
PC2: difference between early (10-20% stance) and midstance (50-70% stance) knee adduction angle	Difference between early stance (less adduction) and midstance (more adduction) knee adduction angle	2.2
PC4: heel strike-to-early stance (30% stance) knee adduction angle range	Difference between heel strike (more abduction) and early stance (more adduction) knee adduction angle	0.7

APPENDIX C Significant Correlation and T-test Results

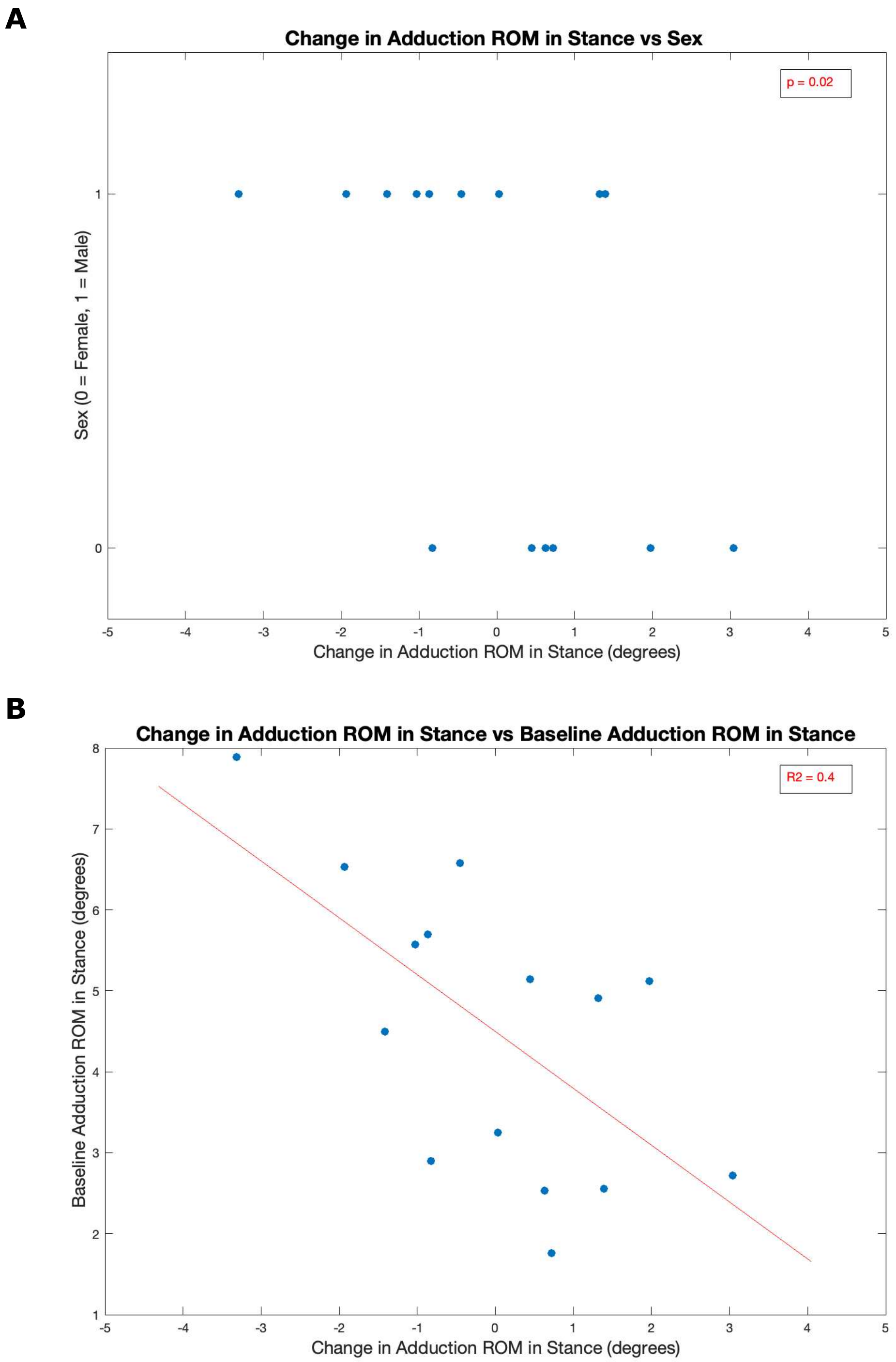
Significant ($p < 0.05$) correlation and t-test results of baseline values with change in gait kinematics from baseline-T2 for follow-up group patients (N = 15).



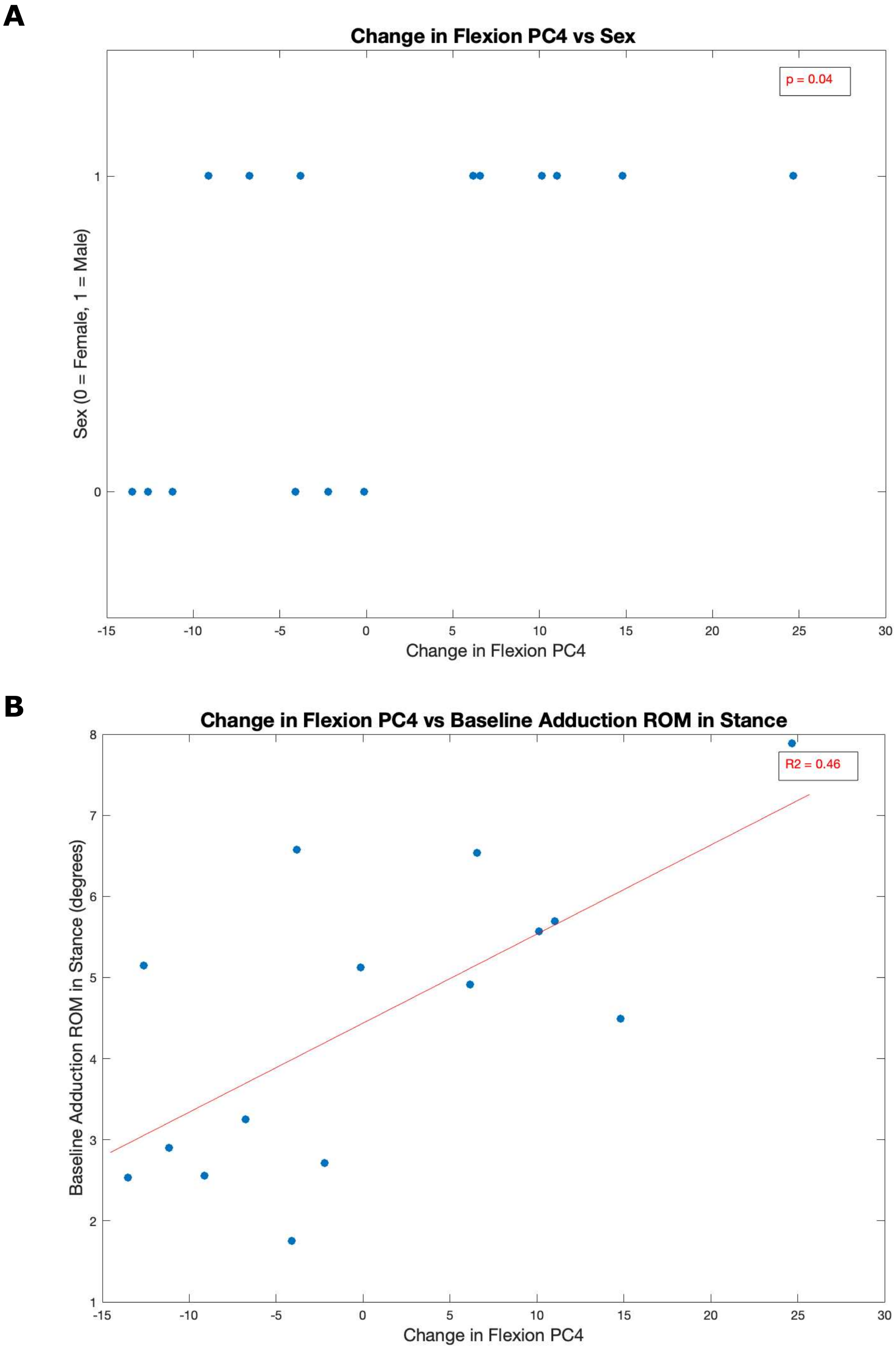
Supplementary Figure C.1 Change in flexion angle ROM in stance by (A) BMI; (B) baseline adduction angle PC4.



Supplementary Figure C.2 Change in peak adduction angle in stance by (A) baseline adduction angle ROM in stance; (B) baseline adduction angle PC2.



Supplementary Figure C.3 Change in adduction angle ROM in stance by (A) sex-differences from two-tailed unpaired t-test; (B) correlation results with baseline adduction angle ROM in stance.



Supplementary Figure C.4 Change in flexion angle PC4 by (A) sex-differences from two-tailed unpaired t-test; (B) correlation results with baseline adduction angle ROM in stance.