PHYSICAL ACTIVITY TRACKING FOR END-STAGE KNEE OSTEOARTHRITIS PATIENTS SEEKING JOINT REPLACEMENT SURGERY

by

Kaitlin Genge

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Dedicated to Lila,

I love you and think of you every day.

Table of Contents

List of Tables

List of Figures

Abstract

Despite the known physical, mental, and disease management-related benefits of physical activity, many individuals with knee osteoarthritis are significantly less active than healthy age-matched individuals and often fail to achieve physical activity targets for the population. It is currently unknown how physical activity levels in the preoperative knee arthroplasty period relate to patient-specific characteristics, and how these relationships impact surgical outcomes. Objective monitoring of physical activity levels in the preoperative period is a valuable tool that clinicians and researchers can implement to gain a better understanding of patient quality of life and clinical disease severity.

This thesis was a subcomponent of a larger orthopedic robotics research program aimed at the customization of arthroplasty surgery based on patient-specific characteristics. The purpose of this thesis was to explore the relationships between physical activity levels (in terms of step counts and sedentary behaviors) and patient-specific characteristics in a population of end-stage knee osteoarthritis patients awaiting knee arthroplasty through the development of custom data processing tools implemented in a clinical population study. This included the development and testing of a bespoke step detection algorithm appropriate for a shank mounted IMU placement protocol and end-stage knee osteoarthritic population awaiting knee arthroplasty for implementation in a clinical population study. The algorithm developed in this thesis will be used for continued physical activity monitoring for the overarching robotics research program and may be used to guide the development of further custom step detection algorithms for applications in other populations.

The clinical study conducted in this thesis included end-stage knee osteoarthritis patients awaiting knee arthroplasty in Halifax, Nova Scotia, Canada. Step counts were found to be significantly lower in individuals with a higher body mass index and those with lower self-reported physical activity levels. Time spent sedentary was found to be significantly higher in females, individuals with a higher body mass index, and those with lower self-reported physical activity levels.

The final component of this thesis included the development of a visual tool for the representation of temporal physical activity intensity measured using IMUs in the clinical study population. The utility of the developed visual tool was explored through a series of three case studies on individuals from the clinical study population with similar summary physical activity metrics. The case studies revealed that temporal evaluation of physical activity provides insight on the methods by which individuals accumulate steps and limit sedentary activity throughout the day in a way that would not be easily identifiable in the absence of such a tool.

The data processing algorithms developed in this thesis allow for the exploration of physical activity in end-stage knee osteoarthritis patients awaiting knee arthroplasty with more depth and detail than has been previously reported in the literature. The findings of this thesis' clinical study identified associations between physical activity levels and patient-specific variables which can be used by clinicians to provide a more well-informed clinical assessment of disease state and can be used by researchers to guide further exploration of the relationships between patient characteristics and knee arthroplasty outcomes.

List of Abbreviations Used

BMI	Body mass index
CSV	Comma-separated values
CWA	Continuous wave accelerometer
HI	Halifax Infirmary
IMU	Inertial measurement unit
KA	Knee arthroplasty
MAD	Mean amplitude deviation
MEMS	Micro-electromechanical systems
OA	Osteoarthritis
OKS-PCS	Oxford knee score – pain component scale
OKS-FCS	Oxford knee score – functional component scale
PA	Physical activity
PHQ	Patient health questionnaire
PROMs	Patient-reported outcome measures
UCLA	University of California Los Angeles
WCWL	Western Canadian wait list

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Chapter 1. Introduction

1.1. Introduction

This thesis represents a sub-study of a larger research program which aims to optimize person-specific joint function after knee arthroplasty (KA) by customizing robotic knee surgery for patient anatomy and function. In order to target these patient-specific needs with surgical interventions, pre-surgical biomechanical, anatomical, and clinical characteristics need to be understood. The research program aims to develop and implement data driven approaches to monitoring these key features during the preoperative period to help inform future surgical customizations. The study uses the new MAKO surgical robotic system (Stryker Corporation, Kalamazoo, MI, USA, *https://www.stryker.com/*) which was recently installed in the Halifax Infirmary (HI). This is the second MAKO system in Canada; Halifax was chosen as the recipient of the device due to the quality of biomechanics and orthopedic research produced by Dalhousie University and NS Health. This research project is funded by the QEII Health Sciences Centre Foundation, and is being completed in partnership with Nova Scotia Health, specifically the Division of Orthopaedic Surgery.

This thesis has three major components. The first component involved the development of a data collection protocol and custom data processing algorithm to evaluate physical activity (PA) metrics from wearable inertial measurement units. The data collection protocol was developed to facilitate multi-day free-living activity assessment in such a way that participant recruitment, retention, and wear-compliance was optimized. The second component of the thesis involved a pilot clinical study examining objectively-measured PA levels of KA candidates with end-stage osteoarthritis (OA) of the knee. In addition to objective PA measures, patient-reported outcome measures (PROMs) and demographics were captured. Correlation analyses were completed to assess the association of PA outcomes with patient-specific characteristics and PROMs. The third component involved the development of a novel data visualization tool intended to present accelerometry data and PA intensity more specifically than general summary measures, such as daily step counts. This tool provides a more comprehensive capture of physical activity throughout the wear period, which can be used to further understand the methods by which individuals within the population achieve (or fail to achieve) PA targets.

Findings from this thesis contribute to the overarching research program by providing objective data on physical activity and its association with patient-specific characteristics, which can be combined with other factors - such as joint anatomy, biomechanics variables, and surgical data - to optimize personalized clinical planning of robotic surgeries.

1.2. Objectives

1.2.1. Step Count Assessment and Tracking for KA Candidates

Motivation: Step count is a relatively simple measure of physical activity that can be used by researchers and clinicians to evaluate how much a patient is moving on a daily basis. Step detection requires specific data processing and analysis which are dependent on the sensor used, the device placement, and the participant population [1], [2]. Existing objective step-detection devices often use proprietary data processing algorithms, which introduces a black box to the data analysis. For the purposes of this thesis, the ability to access raw data was essential to facilitate innovative algorithm development in alignment with the goals of the overarching research program. Furthermore, while hip and wrist placements are the most common for step detection devices [3], these placements do not allow for lower-limb specific analyses, such as free-living gait kinematic calculations. Shank placement is a better option than wrist or hip placements for this thesis because the body part of interest is the lower limb, specifically the knee. Since the IMU data obtained is specific to sensor placement, it is important that the data is processed accordingly, highlighting the need for a custom step detection algorithm for the specific purposes of this study's sensor protocol.

Step count guidelines are available for various populations, which suggest how many steps people should take each day for optimal health; for the present study population, a daily step count target of 7000 has been published [4]. Physical activity levels affect disease progression in a multitude of ways; not only by impacting radiographic disease progression, but also by influencing the overall presentation of the disease in terms of patient-reported pain, mental health, etc. Studies have identified complex relationships between step count and radiographic and clinical disease state, indicating that increased loading is beneficial for some, and detrimental for others [5], [6]. Lo et al. showed that radiographic and clinical severity of knee OA can be better predicted by combining measures of pain with physical activity levels, such as step count, rather than by pain assessment alone [7]. Other studies have also found correlations between psychological factors, such as stress level and self-efficacy, and physical activity levels, indicating that the assessment of PA levels can provide information related to both physical and mental health [8], [9]. Combining physical activity assessments with other clinically-relevant measures, such as pain and mental health, may allow for a more thorough assessment of a patient's disease state in the preoperative KA period. This may also be used to inform clinical decision making, including patient prioritization, surgical planning, and managing patient expectations around surgical outcomes.

Objective: (a) To develop and test a custom step detection algorithm for use in a population of end-stage knee OA patients awaiting KA, and; (b) To examine objectively-measured physical activity (step count) in the preoperative KA period and its association with patient characteristics (sex, body mass index (BMI), mental health scores, patient-reported pain levels, patient-reported PA levels).

Hypothesis: (b) Physical activity levels will be below the recommended daily step count for this population of 7000. Objectively-measured step counts will be lower in females than in males [10]–[12], in individuals with a higher BMI [13]–[15], in individuals with higher levels of depressive symptoms (lower mental health scores) [16], [17], in individuals with higher patient-reported levels of pain [18], [19], and in individuals with lower self-reported PA levels [20], [21].

1.2.2. Sedentary Activity of End-Stage Knee OA Patients Awaiting KA

Motivation: One way that physical activity levels can be objectively assessed is by classifying activity by intensity (sedentary, light, moderate, vigorous) [22]. In populations of senior adults, particularly those with end-stage knee OA, high levels of sedentary behaviours are commonly observed and are a significant risk factor for a wide range of illnesses and pathologies [23]. Semanik et al. found that sedentary time was significantly correlated with functional decline in those with or at high risk of developing OA, showing that more sedentary individuals showed a more rapid and significant decline in both gait speed and chair stand rate [24]. Evaluation of an individual's percentage of time spent sedentary, as well as monitoring for lengthy bouts of sedentary behavior [25], may be an effective way for clinicians to understand how OA patients spend their time throughout the perioperative period, and could influence their rehabilitation protocols. It is also appropriate to evaluate how patient-related variables such as PROMs and patient characteristics relate to sedentary behaviors during the preoperative period to help predict which characteristics of individuals may be associated with higher risk for rapid functional decline and worse surgical outcomes.

Objective: To examine the sedentary behaviors of KA candidates during the preoperative period, and its association with patient characteristics (sex, BMI, mental health scores, patient-reported pain levels, patient-reported PA levels).

Hypothesis: Objectively-measured time spent sedentary will be higher in females than in males [10], in individuals with a higher BMI [13]–[15], in individuals with higher levels of depressive symptoms (lower mental health scores) [16], [17], in individuals with higher patient-reported levels of pain [18], [19], and in individuals with lower self-reported PA levels [20], [21].

1.2.3. Weekly PA Intensity Mapping

Motivation: To further understand specific activity patterns, PA intensity levels can be presented in a temporal map in the preoperative period. This type of tool can provide a more specific representation of patient PA compared to summary PA metrics such as step counts and sedentary hours. A visual tool for the representation of PA in this population can provide detailed information to clinicians and researchers on the specific method by which patients achieve (or fail to achieve) activity targets. This information may be relevant for clinical assessments of patients in the preoperative period because studies have shown that the intensity of activity performed by individuals in this population may be associated with maintenance of performance-based function which is an indicator of patient disease state and quality of life [26], [27]. A clear visual representation of PA intensity temporally during the preoperative period may promote clinician uptake of pre-KA PA evaluation by facilitating ease of communication and identification of PA characteristics which are not clearly observable in the absence of such a tool. As of yet, similar analysis has not been done on a population of KA candidates throughout the preoperative period.

Objective: To develop a visual 'heat map' tool to represent activity intensity during the collection period and process preliminary data and present it in a case study to demonstrate the added value of evaluating PA temporally.

1.3. Organization of Thesis

Chapter 2 contains a review of background literature on physical activity in an end-stage knee OA population and its relationship to patient-specific characteristics. Chapter 3 outlines the thesis protocol, including the rationale for the chosen methodology and a detailed description of the data processing algorithms developed and applied to address the thesis objectives, while directly addressing objective 1(a). Objectives 1(b) and 2 are addressed in Chapter 4 through a pilot clinical study conducted to assess relationships between PA levels and patient characteristics. Finally, objective 3 is addressed in Chapter 5 through a case study presenting the developed visualization tool and discussing the value it adds beyond summary PA metrics. Chapter 6 contains concluding remarks on the outcomes of this thesis and recommendations for future work.

Chapter 2. Background

2.1. End-Stage Knee Osteoarthritis

2.1.1. Impact and Burden of the Disease

Osteoarthritis (OA) is a debilitating disease classified by the gradual degeneration of the articular cartilage and underlying bone of synovial joints [28]. In addition to tissue-level damage and degeneration, knee OA is characterized by functional disabilities, diminished mobility, and chronic pain. The progression and presentation of knee OA differs greatly among patients, partly due to the variability in joint degeneration within the three compartments of the knee [29], the unique loading of each individual's knee joint based on their gait biomechanics [30], and the frequency of loading applied to the joint based on the individual's physical activity (PA) levels [31]. Psychosocial factors also play a key role in the patient's interpretation of and ability to cope with their OA symptoms [32].

Over 4.3 million Canadians are burdened by this chronic disease, making it one of the most prevalent diseases in the country [33], [34]. In Nova Scotia, 1 in 4 people are diagnosed with OA at some point in their life, which is the highest incidence in Canada [35]. This high level of OA prevalence in Nova Scotia may be attributed to a number of factors including the relatively high levels of seniors over 65 years of age in the Atlantic provinces [36], the relatively high average barometric pressure and relative humidity in Nova Scotia [37], or lifestyle factors such as sedentary behaviors and diet. The high levels of burden associated with the disease, particularly in the elderly population [38], along with the predicted increase in disease prevalence in the coming years [39], emphasize the importance of clinical research focused on improving patient quality of life, including surgical outcomes.

2.1.2. Knee Arthroplasty for Treatment of End-Stage Knee OA

The standard treatment for individuals suffering from end-stage knee OA is surgical replacement of the joint in a total or partial knee arthroplasty (KA) procedure. KA involves surgical incision of the tissues around the knee joint so that damaged bone and cartilage of the distal femur, proximal tibia, and sometimes the patella, can be replaced. Once the damaged portions are resected, the joint is fit with prostheses. The surgical procedure is invasive and reserved for individuals who have progressed to the point that other, more conservative, approaches are no longer successful in managing their disease.

The main goals of surgical intervention for end-stage OA are the alleviation of pain, restoration of function, and improvement of quality of life [40]. This includes increasing the patient's ability to perform physical tasks and participate in physical and social activities to match that of healthy age-matched individuals, or at least to meet their own personal expectations of physical function. While knee arthroplasty is a well-established and generally successful treatment for end-stage OA patients, there are a number of individuals who remain unsatisfied after surgery; literature suggesting a dissatisfaction rate of approximately 20% [41], [42]. Some of the reasons commonly associated with post-surgical dissatisfaction are continued pain, a feeling of discomfort or instability in the joint, and unmet expectations in terms of function and physical ability [41]–[44].

2.2. Physical Activity in End-Stage Knee OA Patients

2.2.1. Importance of Pre-KA PA Tracking for Patient Assessment

Maintenance of physical function and the ability to perform daily PA are essential components of a healthy lifestyle. Regular PA contributes not only to physical health, but also mental wellbeing, disease prevention, and it is associated with reduced mortality rates [45]. Studies have been conducted which focus specifically on the impact of PA levels in older adults and lower-limb OA patients, which have identified the existence of strong correlations between PA levels and maintenance of optimal joint biomechanics [46], [47], health-related utility [48], and overall physical function [49]. Furthermore, PA levels have been found to be significantly lower in OA patients compared with healthy age-matched controls [50]. Studies have found that PA is an effective way to facilitate weight loss, preserve joint range of motion, improve strength, improve functional performance, and reduce overall symptoms of the disease [51]–[53]. In a systematic review of physical activity and lower limb OA, Kraus et al. also found that patients with consistent PA routines can sustain physical function better than those with lower PA levels [54]. These studies motivate the requirement for further analysis of the associations of objectively-measured PA levels with patient-specific characteristics and relevant clinical factors in the preoperative period.

Studies have identified a complicated relationship between step frequency and radiographic progression of knee OA [5] and limited research is available exploring the relationship between step counts and the clinical progression of knee OA [6]. Walking is the most common form of physical activity resulting in frequent loading of the knee joint, therefore it is appropriate to evaluate joint loading frequency in terms of step counts. Studies have found that in healthy knees, increasing the load on the cartilage (specifically the application of cyclic tensile strain) results in cartilage thickening, and thus helps to prevent OA onset and progression [55], [56]. Contrarily, in individuals with existing cartilage deficits, increased joint loading (related to higher knee adduction moment) may lead to more rapid disease progression [57], [58]. The literature seems to lack clear information on whether higher step counts are associated with improved disease state, however it is evident that this relationship is complex and requires further analysis. It is possible that certain patient characteristics may be linked to certain aspects of joint loading and its impact on disease state. Sedentary activity is another clinically relevant measure of physical activity levels. Studies have identified pathways by which excessive sedentary activity can lead to OA development and progression, including obesity, depression, joint level degeneration (such as loss of strength, stability, and range of motion), and changes at the cellular level [59], [60]. These findings indicate the importance of evaluating step counts and sedentary behavior in individuals with osteoarthritis to assess their roles in disease progression and to help identify characteristics of individuals who may be at higher risk of rapid disease progression, poorer quality of life, and worse KA outcomes.

2.2.2. Relationship Between PA and OA Patient Characteristics

Studies have continuously reported low levels of physical activity in the general population of end stage OA patients, some comparing PA levels in the population to healthy age matches [50], others assessing the population's ability to achieve published PA guidelines [61]. There is limited literature exploring how patient-specific characteristics are related to physical activity levels in end-stage knee OA patients. Certain studies have explored specific characteristics relating to radiographic and clinical OA progression, such as sex [13], [32], [62], body mass index (BMI) [15], [63], and mental health [64]–[66], but how these relationships relate to PA levels in the population remains unclear.

Sex:

Sex-based differences in various domains of knee OA have been reported numerous times in literature [67]–[70]. Previous studies have shown an association between sex and PA, suggesting that PA levels may differ significantly between males and females [11], [12]. This sex-based interaction may certainly translate to physical activity in a population of end-stage knee OA patients and is worth further exploring. It is difficult to accurately predict how males and females will differ in their reaction to disease state over time; however, women tend to respond more intensely than men to some of the key indicators of OA progression, such as increased pain and worsening mental health status [10], [71], indicating that women may also exhibit more severe symptoms of OA in relation to physical activity levels.

BMI:

Studies have found strong correlations between BMI and radiographic progression of knee OA [13], [63], [72]. Associations have also been identified between obesity and clinical progression of knee OA [15]. A systematic review by Lee and Kean explored the impact of BMI on OA incidence [14]; they reported that obesity is a significant risk factor for the development and progression of knee OA as both a biomechanical and metabolic disease. In terms of physical activity, a study exploring PA in Canadian adults identified that obese individuals participated in significantly less physical activity compared to those with a healthy BMI [73]. In a population of individuals with or at high risk of developing OA (a sub-cohort of the Osteoarthritis Initiative), higher BMI was found to be associated with decreased prevalence of meeting recommended physical activity guidelines [74]. Based on these findings, it can be hypothesized that individuals with higher BMIs may be more susceptible to low PA levels and excessive sedentary behaviors during the preoperative KA period.

Mental Health:

The prevalence of depression is significantly higher in physically ill populations compared with physically healthy populations [75]. Roshanaei-Moghaddam et al. reported baseline depression as a significant risk factor for the development of a highly sedentary lifestyle [16]. This relationship between mental illness and physical activity is bi-directional, as depressive symptoms can lead to lower PA, and low PA can lead to increased depressive symptoms. A study by Degerstedt et al. used patient-reported outcome measures (PROMs) to evaluate self-efficacy levels of individuals with OA and found that those with high self-efficacy scores also tended to report less pain and higher PA levels [17]. This leads to the consideration that mental wellbeing may play an important role in both the physical and psychological progression of knee OA. Studies have also identified depression as a risk for worse surgical outcomes after KA [65], [66].

Evaluating the associations between patient characteristics and pre-surgical PA may help identify patients who are more susceptible to leading highly sedentary lifestyles after surgical intervention (predisposing them to a number of comorbidities) and who are therefore at higher risk of experiencing post-surgical dissatisfaction. Once these associations are identified and understood, their potential utility in informing surgical triaging and planning will become more clear.

2.2.3. Relationship Between Physical Activity and OA Patient-Reported Pain

Self-reported pain levels vary greatly between individuals with OA. Patient-reported pain is a valuable metric for the assessment of the burden of the disease on a patient's life, as they can show a level of dissatisfaction that is not obviously present in other clinical measures [76]–[78]. The presentation of pain in an end-stage OA population is very complex, with some individuals reporting little to no pain, others reporting short periods of intense pain, and still others reporting incessant generalized pain [18], [79], [80]. An individual's pain experience can be impacted by psychological factors, such as depression and pain-related fear [81], as well as the use of medications for pain management [82]. Lower pre-KA pain levels have been found to be correlated with higher surgery satisfaction rates in OA patients [83], highlighting the important role that pain plays in disease progression and presentation.

Higher levels of patient-reported pain have been found to be correlated with lower levels of physical activity in individuals diagnosed with osteoarthritis [18], [84]. This decrease in PA is often caused by an individual's attempt to avoid the pain that often comes with movement [84]. This behavior, classified as fear-avoidance, is common in those with chronic pain-causing conditions, including osteoarthritis patients [19], [85]. These findings emphasize the potential impact that pain can have on individuals awaiting KA, both mentally and physically. Given that the pain associated with end-stage knee OA can be severe and debilitating, further research in this area may provide clarity on how individuals experience pain in the preoperative period and how the pain experience may relate to physical activity levels and patient-specific variables.

2.2.4. Relevance of PA Assessment in the Perioperative KA Period

The identification of patient variables associated with lower PA levels in the preoperative period can inform clinicians and researchers about the patient's quality of life and give insight on what patients are doing outside of the clinical environment. Understanding these relationships may help clinicians make decisions on OA patients' disease management and treatment, including assessing for surgical candidacy, patient triaging, and surgical planning, resulting in improved surgical outcomes for the patient population.

Triage:

Long surgical wait times and unclear prioritization strategies have been a common problem in Canada and internationally for many years. The Western Canada Wait List (WCWL) project was an initiative developed to examine wait times in the country and suggest better wait list management strategies; of particular interest in this project was exploring patient prioritization and triaging [86], [87]. They define prioritization tools as "a means to standardize the criteria for [surgical prioritization] decisions and make the ordering of patients in the waiting list as consistent as possible from region to region and physician to physician" [86], [87]. Reports from the WCWL outline the numerous factors that should be considered when prioritizing KA patient wait lists, highlighting the challenges associated with developing a simple, reproducible metric that effectively captures the quantitative and qualitative contributing factors. Physical activity monitoring in the preoperative period are generally limited to research protocols and are not standardly captured by clinicians for consideration in surgical triage. Current guidelines for the surgical triaging process, while vague, tend to place considerable emphasis on patient function and quality of life [86]–[90], suggesting that the assessment of PA levels in the preoperative period is a relevant metric to consider in the prioritization process. Furthermore, the assessment of physical activity levels in terms of step counts and sedentary behaviors is an objective tool which may help overcome some of the subjectivity associated with the current triaging process. Once relationships between patient characteristics and PA are explored and the multivariate associations between pre-operative PA, patients characteristics, and surgical outcomes are understood, physicians will be able to use this information to evaluate how patients should be prioritized based on their disease state, readiness for surgery, and predicted surgical outcomes.

Planning/Procedure:

One of the main goals of the overarching robotics research program is the patient-specific customization of KA procedures. Surgical robotic tools, such as the MAKO surgical robot gives surgeons the capability to plan surgical procedures with more specificity and execute the plan with increased accuracy compared to the current standard of care [91], [92]. As medicine shifts towards patient-specific surgical planning, a plethora of innovative tools can be used to help inform the surgical plan and implant selection including PROMs, objectively-measured physical activity outcomes, and biomechanical metrics.

Outcomes:

For those who are unable to manage their disease with more conservative treatment options and undergo KA, studies have found that physical activity levels do not significantly improve after surgical intervention for a number of patients [93], [94]. In fact, in many cases patients are less active after surgery than they were before [95]. While studies evaluating the associations between preoperative exercise programs (including strength training, endurance training, etc.) and KA outcomes (functional, pain, satisfaction, etc.) suggest that pre-KA exercise programs may impact length of hospital stay, knee flexion angles [96], and Tegner activity scores [97], a systematic review on the topic found insufficient evidence to draw conclusions [98].

Preoperative PA is a generally accepted pre-surgical OA management strategy, however there is limited literature exploring the impact of preoperative PA levels on surgical outcomes, highlighting the need for further research on this topic. One study by Twiggs et al. identified significant correlations between preoperative and postoperative step counts in a population of KA recipients [99]. In a study exploring sedentary behavior in the pre-KA period, higher levels of objectively-measured sedentary behaviours were found to be associated with significantly worse surgical outcomes (including OA symptoms, patient satisfaction, and functional activities, as assessed by the Knee Society Scoring System) [100]. These findings highlight the potential added value of pre-KA PA assessment for predicting surgical outcomes and managing patient expectations. Further exploration into the relationship between physical activity levels and patient-specific characteristics in the preoperative period may provide further insight on how these associations relate to surgical outcomes such as joint function, pain levels, and overall satisfaction.

2.3. Methods for Assessing Physical Activity

2.3.1. Subjective: Patient-Reported Outcome Measures

Clinicians and researchers commonly use subjective measures, such as those obtained through self-report questionnaires, to capture physical activity levels of patients; in fact, self-report surveys and questionnaires are the most common method of PA data collection [101]. This is a relatively easy and cost-effective way to evaluate an individual's daily levels of activity and ability to participate in social physical activities. PROMs are valuable when focusing on patient-centred care, as they allow clinicians and researchers to assess patient perspectives, quality of life, and other important aspects of the patient's clinical experience [102]. While various PA PROMs are available and validated; the selection of a PROM used in any study is dependent on numerous factors including the study population and the aspect of PA that the researcher is interested in (activity intensity, disease-specific PA outcomes, mobility, etc.) [103]. Some of the validated PROMs commonly used in research for PA assessment in individuals with knee OA are the Physical Activity Scale for the Elderly [104], the Lower-Extremity Activity Scale [105], and the University of California Los Angeles Activity Score [105].

2.3.2. Objective: Accelerometry and Inertial Measurement Units

2.3.2.1. A Brief History of Accelerometry

Accelerometers are tools that measure acceleration (rate of change of velocity) relative to a local reference frame by converting mechanical motion into electrical signal; they do this by detecting forces acting on a known mass [106]. Accelerometers date back to the 1920s, when they were designed for and implemented in a number of industrial engineering applications [107]. Large scale commercialization of accelerometers started in the early 1940s with the development of resistance strain gauges [106]. Around the same time, piezoelectric accelerometers were brought to market, which helped overcome issues associated with the transient responses of earlier accelerometers [108]. The first known accelerometer made specifically for human movement applications was developed in the early 1980s [109]. Despite certain barriers, including concerns about validity, reliability, and complexity [110], the use of accelerometers for physical activity monitors quickly became more common, with the annual publication rate on the topic increasing from less than 10 in 1981-1996 to nearly 90 in 2003-2004 [111].

2.3.2.2. Objective Monitoring of Physical Activity

The three common types of accelerometers in use today are piezoelectric, piezoresistive, and capacitive; the two latter are considered micro-electromechanical systems (MEMS), which simply refers to the presence of microscopic technology incorporating mechanical and electrical components. Each type of accelerometer is designed and optimized for its specific intended purpose and environment [112], [113]. Accelerometry for human movement detection generally uses MEMS devices, as they are small, relatively low-cost, and enhance sensor performance while reducing power consumption [112].

Physical activity trackers, which often incorporate inertial measurement units (IMUs) are becoming increasingly easy to access due to the miniaturization of technology and reducing costs associated with mass production. Many IMUs incorporate accelerometers and gyroscopes to detect tri-axial linear acceleration and tri-axial angular velocity, respectively [106]. IMUs are commercially available in a number of products including smart phones, smart watches, and fitness trackers. It is common for commercially available devices to perform data processing through proprietary algorithms, making it difficult or impossible to access raw data. There are also devices which are designed specifically for research purposes, such as ActiGraph, activPal, and Axivity sensors [112]. These research-intended devices sometimes provide raw, unaltered data, but there is limited literature available guiding the appropriate filtering and processing approaches necessary for the interpretation of this data in biomechanical applications, meaning that well-trained and skilled individuals need to be involved in this data processing. Studies have also shown that the accuracy of IMUs for physical activity monitoring is highly variable depending on the wearer population, the sensor used, the sensor placement, and the processing algorithms applied [1], [2]. A systematic review published in 2017 identified the hip as the most common sensor placement location in studies involving older adults [3]. This placement has been found to be better than some other common placements, such as the wrist, as it is closer to the centre of mass, and less prone to errors associated with upper body movements [1], [3]. Despite this finding, wear compliance is an issue for hip-worn sensors, as they generally need to be removed while sleeping and bathing. Additionally, this sensor placement is also not optimal for the calculation of lower limb kinematics, which is of increasing interest in clinical research.

Some of the potential uses of IMUs for human movement analysis include step detection, activity recognition, energy expenditure estimation, and activity intensity detection [111], [112] using either accelerometer, gyroscopic, or a combination of data from both sensor types. Societal and clinical shifts over the past 2 to 3 decades have placed a growing emphasis on the importance of physical activity for personal health, community health, and disease prevention. This, along with the rapid development of new technologies in engineering and medicine, highlights the importance of continued high-quality research in the field of human movement detection and physical activity monitoring, including objective measurements such as accelerometer-based approaches.

2.3.2.3. Added Value of Objective PA Monitoring

The rapid uptake of objective physical activity monitors has resulted in a number of studies evaluating the added value of objective activity tracking compared to PROMs for capturing PA. A systematic review by Skender et al. [20] evaluated the relationships between objectively- and subjectively-measured PA levels in adults, including those with various comorbidities such as OA, cancer, and fibromyalgia, and found that they were highly correlated; however it must be noted that IMU-based methods have been found to be slightly more specific and less prone to participant biases (such as recall bias) [21], [114]. In a population of individuals with OA, a common physical activity questionnaire (International Physical Activity Questionnaire-Short Form) was found to significantly overestimate patients' PA levels compared to accelerometry [115]. Urda et al.

demonstrated that the combination of objective and subjective PA measures is a more accurate way to assess physical activity levels and their interactions with other patient variables, when compared to either one method on its own [116], findings which were supported by those of Skender et al. [20]. Therefore, PA questionnaires are a valuable tool for assessing patient perception of their physical function, and in combination with objective PA measures, may be a valid indicator of patient quality of life and expectations around surgical outcomes.

Chapter 3. Thesis Protocol

This thesis is a sub-study of a larger research program aimed at the optimization of patient-specific joint function after knee arthroplasty (KA) by customizing robotic KA using the MAKO robotic surgical system (Stryker Corporation, Kalamazoo, MI, USA, *https://www.stryker.com/*). The study was approved by the Nova Scotia Health Research Ethics Board (REB File # 1028507).

3.1. Methodological Considerations

The protocol for this thesis required the collection of a combination of objectively-measured physical activity (PA) data, demographic information, and clinically-relevant patient-reported outcome measures (PROMs) in a population of end-stage knee osteoarthritis (OA) patients awaiting KA at the Halifax Infirmary. The assessment of objectively-measured PA involved continuous 7-day monitoring using an inertial measurement unit (IMU). To process the raw tri-axial accelerometer data and calculate step count in an end stage knee OA population, a custom Matlab (v.9.13) algorithm was developed. The patient-reported measures of interest included PA level, pain, and mental health. It is noted that additional objectives of the larger research program needed to be considered when developing this thesis' protocol.

3.1.1. Considerations Associated with the Larger Research Program

When developing the protocol for this thesis, objectives of the larger research program were considered to ensure that data collection protocols were consistent throughout the entire project. The research goals that needed to be considered are as follows:

a) Longitudinal tracking of PA outcomes: Objective and subjective monitoring of PA will be collected longitudinally throughout the preoperative period, and into the postoperative period. The protocol must be capable of capturing changes in PA between various time points.

b) Free-living assessment of knee kinematics using IMUs: Multiple IMUs can be used together to calculate joint angles in a free living environment. This type of analysis requires accelerometer and gyroscope capabilities, and the placement must be appropriate to determine the relative orientations of the thigh and shank.

c) Multi-centre collaboration between Dalhousie and McMaster University: There is the potential for multi-centre partnership between the orthopedic biomechanics research teams at Dalhousie (led by Dr. Janie Astephen Wilson) and McMaster (led by Dr. Dylan Kobsar).

3.1.2. Activity Tracking Protocol Rationale

When selecting an appropriate sensor for this research, a number of considerations were made. Since one of the goals of the project was to create a custom step detection algorithm, it was important to select a device which provided access to raw data. It was also essential that the IMU selected had a battery capable of collecting data for at least 7 days continuously at 100 Hz and ±8g [117], [118]. For future research projects within the overarching robotics study, there was also a requirement to obtain an IMU with both accelerometer and gyroscope sensors, as both are needed to calculate joint kinematics with body-worn sensors [119]. Based on these considerations, the team came to the decision to purchase the AX6 IMU Sensor (Axivity Ltd, Newcastle upon Tyne, UK, *www.axivity.com*), which met all the aforementioned requirements [118], and was suitable for the team at Dalhousie as well as for collaboration with McMaster.

The sensor placement and protocol for this study was chosen in an attempt to optimize validity of the data collection protocol without reducing participant wear compliance. This meant selecting a sensor location which was non-intrusive for participants while obtaining data that could be processed to accurately determine accurate step counts and activity intensities throughout the wear period. Based on similar published protocols [117], [120], the sensor placement that was chosen was approximately halfway between the lateral malleolus and lateral tibial condyle (approximately 2cm lateral to the anterior prominence of the tibia) on the surgical leg. This placement has been shown to be accurate for step detection and differentiating activity intensities using mean amplitude deviation (MAD) calculations. The sensor was oriented such that the positive x-axis (depicted by a small arrow on the face of the sensor) pointed approximately in the direction of gravity. This placement helped detect shank orientation to determine when the individual was in a prone or supine position. The sensor position and orientation are shown in Figure 1, below. The sensor was fixed to the shank using Hypafix transparent waterproof tape (BSN Medical

Canada (Essity), Laval QC, *www.medical.essity.ca*), which is a medical grade waterproof tape, approved for prolonged wear of 7+ days [121], [122]. This fixation method was chosen to improve wear-time compliance, as participants would not have to remove and reapply the sensor at any point during their data collection period.

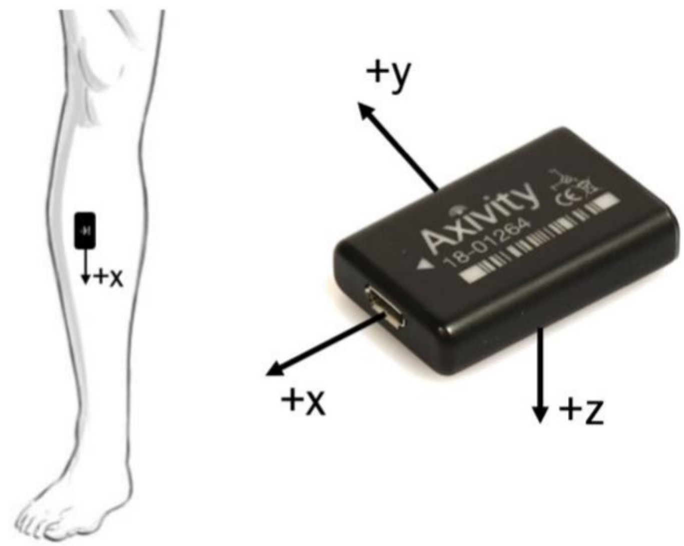

Figure 1: Position and orientation of the IMU for the study protocol. The sensor was placed on the shank of each participant's surgical leg, approximately halfway between the lateral malleolus and lateral tibial condyle, and approximately 2cm lateral to the anterior prominence of the tibia. The IMU was oriented such that the positive x axis pointed approximately in the direction of gravity (towards the ground).

3.1.3. PROMs Selection Rationale

A series of questionnaires were used to collect participant demographics and PROMs. The larger research program collects data from 6 questionnaires to capture clinically-relevant patient-reports, along with information on demographics, comorbidities, and medication use. The PROMs used for this thesis were selected to assess patient-reported physical activity levels, pain levels, and mental health scores. These questionnaires were selected in consideration of the long-term objectives of the overarching research project. All questionnaires used in this study are included in Appendix A.

To capture patient-reported physical activity levels, the University of California, Los Angeles (UCLA) Activity Score questionnaire was used. This questionnaire consists of a simple 10-point scale where patients indicate their average activity level from wholly inactive (1) to regular participation in contact sports (10). In a comparison of a number of other validated PA questionnaires, Naal et al. identified the UCLA Activity Score as the best subjective measurement tool for assessing PA in KA patients [123]. Multiple studies have validated this questionnaire for subjective PA collection in an elderly osteoarthritic population of arthroplasty patients, comparable to that of the present study [124]–[126]. These studies also identified that the UCLA Activity Score questionnaire is responsive to changes over time, which is an important consideration for future analyses within the robotics research program, as longitudinal changes begin to be assessed.

Patient-reported pain levels were evaluated using the pain subscale of the Oxford Knee Score (OKS-PCS). The Oxford-12 Knee Score was developed in 1998 to evaluate pain and function before and after total knee arthroplasty [127]. It was later established and verified that the scale could be split into a pain assessment portion (pain component scale, PCS) and a functional assessment portion (functional component scale, FCS) [128], [129]. The OKS-PCS consists of questions 1, 4, 5, 6, 8, 9 and 10 of the OKS [128]. The pain subscale has been validated numerous times, and has also been shown to capture significant changes within populations of KA patients throughout the perioperative period [130]–[133].

To evaluate mental health, the Patient Health Questionnaire (PHQ) for depressive symptoms was used. This questionnaire was developed to clinically assess the mental state of patients by evaluating their depressive symptoms, or lack thereof [134], [135]. The original questionnaire (PHQ-9) was modified to exclude the final question which asks about suicidal tendencies because it is unclear what this question intends to assess and because of the implications associated with the question. The updated PHQ-8 has shown comparable results to those of the original [136]. The PHQ-8 has been used and validated numerous times within populations of KA candidates, is capable of capturing changes in mental health status throughout the perioperative period, and is valid for the assessment of correlations between mental health scores and other variables, such as pain levels and patient satisfaction [65], [137].

3.2. Clinical Population Trial

3.2.1. Study Population

The study population consisted of individuals with end-stage knee OA, recruited from the participating surgeons' KA wait list. Patients awaiting surgery at the Halifax Infirmary were included in participant recruitment; including those receiving surgery with the MAKO robotic system, as well as those receiving conventional knee joint replacement surgery. Participants were recruited as early as possible once placed on the wait list to capture patients at the earliest stage of the wait period to support the longitudinal wait list component of the overarching study. 22 participants (13M/9F) were recruited between March 2023 and June 2023. Average participant age (years) and BMI (kg/m^2) were 69.1 ± 6.1 and 32.8 ± 7.3, respectively.

All participants included in the study were required to be over 18 years of age and capable of providing informed consent to participate. Exclusion criteria included neurological disorders impacting gait and mobility, non-OA-related lower limb pathology, other lower-limb surgery in the past year, and allergy to (or irritation caused by) adhesives.

3.2.2. Recruitment

Potential participants were contacted by the relevant physician's administrative staff to ask consent to release their contact information for research purposes. Those who consented to be contacted were recruited by the project's research coordinator within Nova Scotia Health's Division of Orthopedic Surgery. Over the phone, participants were informed of the purpose of the study, their role as a potential participant, and the consent form was explained in detail. Those who agreed to participate were then sent a link to the consent form and a series of questionnaires associated with demographic information and PROMs, as previously detailed in section 3.1.3 and shown in Appendix A. Once the participant had completed the consent, they were scheduled to meet with the research team at the Halifax Infirmary to begin their data collection period.

3.2.3. Materials

The materials that were procured for this thesis are listed below:

1. Axivity AX6 Inertial Measurement Unit *(Axivity Ltd, Newcastle upon Tyne, UK, www.axivity.com)*

The Axivity AX6 IMU is capable of collecting inertial data in 6-axes (linear and angular accelerations). Complete AX6 sensor specifications are available at: *https://axivity.com/files/resources/AX6_Data_Sheet.pdf.*

2. Hypafix transparent waterproof adhesive (*BSN Medical Canada (Essity), Laval QC, www.medical.essity.ca*)

Hypafix transparent waterproof adhesive is a medical-grade tape that is commonly used for the fixation of dressings, catheters, patches, etc. It is waterproof, bacteria proof, and latex-free. Hypafix tape can be used safely on the skin for seven days, making it an appropriate choice for this research project. This adhesive was selected based on similar published research protocols [121], [122].

3. Alcohol prep pads/sterile wipes - size medium, 2 ply cotton, 70% isopropyl alcohol (*The Stevens Company, Brampton, ON, www.stevens.ca/products*)

Alcohol prep pads were used to sterilize the AX6 devices before wrapping in Hypafix tape to reduce the risk of bacteria transfer between consecutive participants or between participants and the research team handling the devices. The pads were also used to sterilize participants' skin to remove excess oil, bacteria, etc. that may impact the integrity of the adhesive or the wear time compliance of the device [122].

4. Pre-paid Canada Post envelopes with tracking *(Canada Post Corporation, Ottawa, ON, www.canadapost-postescanada.ca)*

To ensure the AX6 sensors were returned to the research team in a timely manner, a pre-paid envelope was supplied to each participant to return their sensor at the end of the data collection period. Parcel tracking was required to ensure the privacy of participants was protected and due to the cost of the sensors.

3.2.4. Data Collection

To prepare for patient arrival, an AX6 IMU was configured for data collection using Open Movement's AX3/AX6 OMGUI Configuration and Analysis Tool *(Newcastle University, UK, https://github.com/digitalinteraction/openmovement)*. This is an open-source software which allows for the configuration of Axivity sensors for recording. The application also has data extraction and analysis capabilities, but these were not used for this study. IMUs were configured to collect data for 168 hours (continuous), starting 15 minutes after their scheduled clinic visit time. Sensors were set to collect tri-axial accelerometer data at 100 Hz with a sensitivity of ±8g; these settings were chosen based on manufacturer recommended settings [118] similar published protocols [117], and preliminary in-lab testing.

At the HI, participants met with the research team and all questions and concerns were addressed. Sensors were prepared by sanitizing with an alcohol prep pad and wrapping completely in Hypafix adhesive. The participants' skin was sanitized with an alcohol prep pad and the AX6 sensor was secured to the skin using Hypafix adhesive. The sensor was placed approximately halfway between each participant's lateral malleolus and lateral tibial condyle (approximately 2cm lateral to the tibia) on their surgical leg. The participants were informed that there may be some mild discomfort associated with wearing an adhesive product over 7 days, but in the case of any burning or itching they should remove the device and contact the research team. Participants were provided with a pre-paid envelope for the return of the AX6 sensor at the end of their data collection period. After the 7-day data collection period was complete, an automated message was sent to the participants' emails to remind them to remove and return their sensors. Axivity IMUs were retrieved at the Halifax Infirmary where they were sanitized and prepared for data extraction onto a hospital-based research desktop computer. To protect participant privacy, this computer was not connected to the internet.

3.2.5. Raw Sensor Data

Axivity sensor data were stored as a Continuous Wave Accelerometer (CWA) file, which is a proprietary binary file type that needs to be converted to a comma-separated values (CSV) file. One way to convert from CWA to CSV is by exporting the data in the proper format using Open Movement's OMGUI software. This method is appropriate for small data files but can be extremely time consuming for larger data files. Issues also arise when moving such large CSV files into Matlab, often causing the program to crash. CWA data can also be converted into CSV using a conversion code within Matlab itself. This is the method that was chosen for this project, as the computational power and time required to process large accelerometer files is much lower. An open-source Matlab code was used to complete this conversion (Copyright © 2012-2020, Newcastle University, UK. All rights reserved. *https://github.com/digitalinteraction/openmovement/blob/master/Software/Analysis/Matlab/CWA_readFile.m*).

Once converted into CSV format, the raw data obtained from the AX6 IMU may include date and time (from a built-in real time clock), sample number, time since recording start, battery level, up to three channels of accelerometer data, and up to three channels of gyroscope data (depending on the settings chosen when configuring prior to data collection). There are also temperature and ambient light sensors, which could be enabled upon configuration if needed. For this thesis, three axes of accelerometer data were obtained (x-, y-, and z-) at a frequency of 100 Hz and with a sensitivity of ±8g. This accelerometer data along with date and time were extracted for data analyses. Seven days' worth of raw data in CWA format at these settings takes approximately 370 megabytes of storage; once converted to CSV, the data grows to approximately 3 gigabytes.

3.2.6. Step Detection Algorithm

Filtering

A custom filtering and step detection algorithm was developed in Matlab to calculate step counts in the study population. A bandpass filter was used to remove noise caused by movements unassociated with ambulatory human motion. An upper limit of 15 Hz was chosen for the bandpass filter based on evidence that 99% of the power of frequencies of gait is contained below 15 Hz [138], [139], and because a spectral analysis from trial accelerometer data showed no significant signal components above 15 Hz. A lower bandpass limit of 1 Hz was selected based on similar published protocols [140], [141], and preliminary in-lab testing to optimize step count accuracy. A 12-second sample of accelerometer data from a 65-year-old end-stage knee OA patient awaiting KA at the

Halifax Infirmary during their 7-day data collection is shown in Figure 2 (2a: raw data and 2b: after application of bandpass filter).

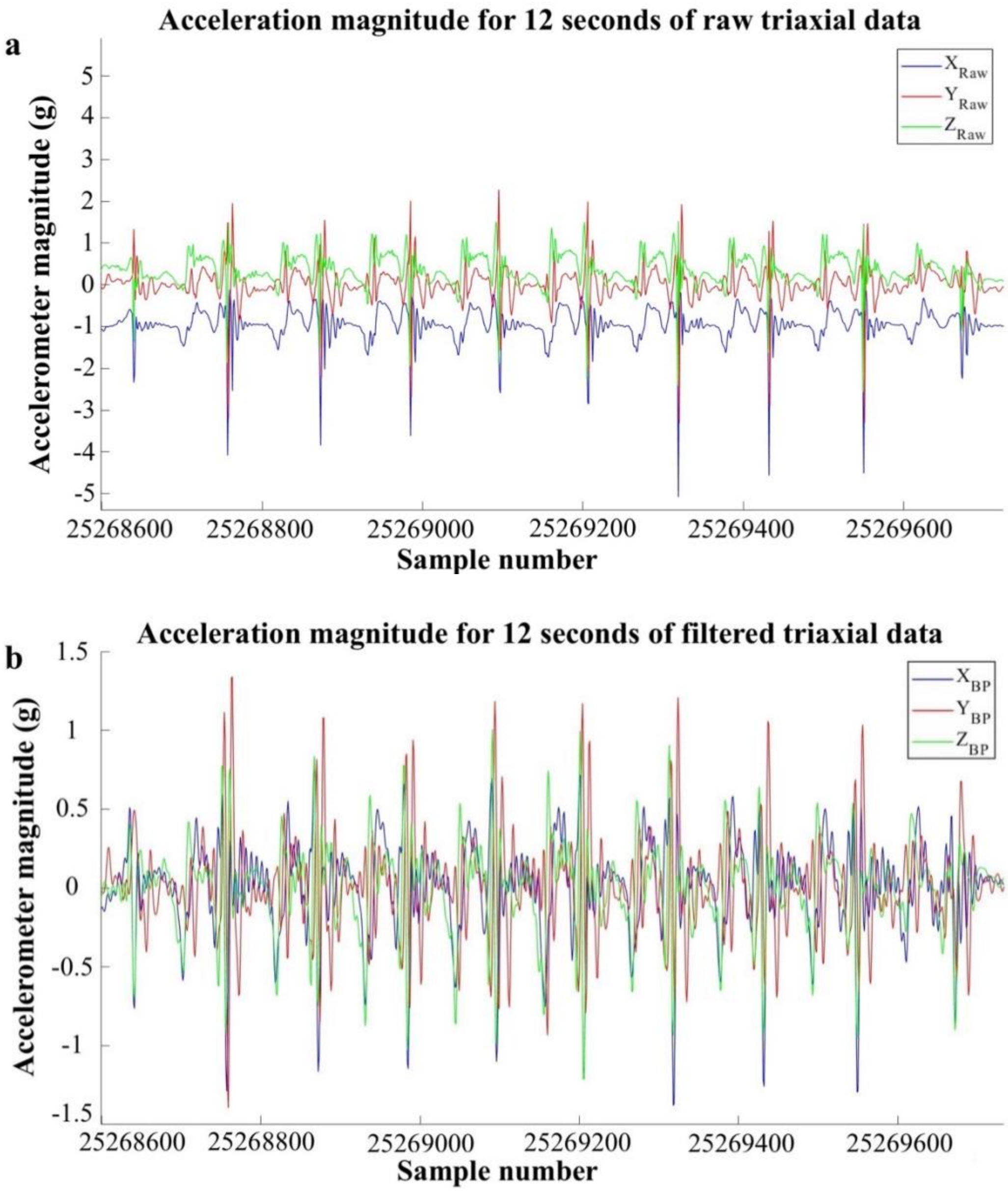

Figure 2: Twelve seconds of free-living accelerometer data collected from a 65-year-old end-stage knee OA patient awaiting KA at the Halifax Infirmary; (a) Raw accelerometer data in three axes. (b) Accelerometer data after applying a 1-15 Hz bandpass filter to each of the three axes.

The resultant acceleration norm was calculated (Equation 1) to combine the three axes of accelerometer data, because step detection tends to be sensitive to sensor placement and participant cohort [142]; this step is shown in Figure 3a (a continuation of the data filtering shown in Figure 2). A fourth-order Butterworth filter with a cut-off frequency of 10Hz, and a fourth order Savitzky-Golay filter were applied to the resultant acceleration vector to smooth the data, which helped to reveal distinct step-related peaks, as shown in Figure 3b.

Equation 1: $acc_N = \sqrt{acc_V^2 + acc_{ML}^2 + acc_{AP}^2}$

where acc_N is the 3D accelerometer norm, and acc_V, acc_{ML}, and acc_{AP} are the vertical, medio-lateral, and antero-posterior components of the acceleration, respectively.

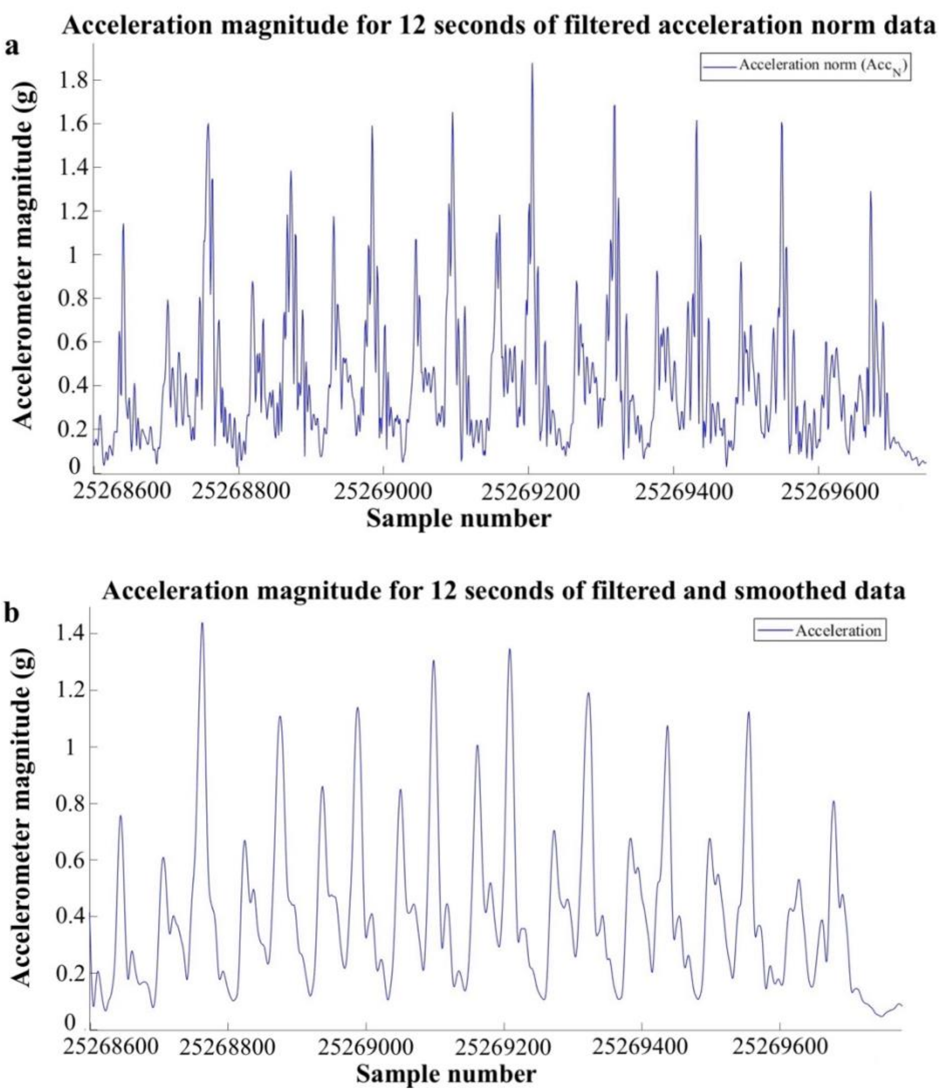

Figure 3: Twelve seconds of free-living accelerometer data collected from a 65-year-old end-stage knee OA patient awaiting KA at the Halifax Infirmary (continuation of data filtering shown in Figure 2); (a) Resultant acceleration norm calculated according to

Equation 1. (b) Acceleration norm after applying fourth-order Butterworth and Savitzky-Golay filters.

Step Detection

The filtered and smoothed accelerometer data was analysed to calculate step counts. The data processing algorithm went through a number of iterations to ensure it was appropriate for the specific sensor placement and protocol, each of which was tested for face and construct validity.

To arrive at a step detection algorithm that was appropriately counting steps, a number of criteria were laid out. These were tested by a combination of lab-based testing, free-living data collection with activity log, comparison with other validated step counting devices, and comparison of step counts in the population with those published in similar populations. Lab-based and free-living validation testing was performed on myself (a healthy 25 year old female with no lower limb pathologies or neurological disorders impacting gait and mobility). The following criteria were selected as bases of success for the algorithm, based on published values of AX6 IMU accuracy (relative to other accelerometers) [143]–[145] and face and construct validity requirements:

1. <u>Lab-based video comparison:</u> In a comparison with time-synchronized video data, the step detection algorithm should perform with at least 90% accuracy, independent of walking intensity or footwear.

   <u>Results:</u> Steps counted by the developed algorithm were compared to videos in ELAN (Version 6.5), which is a software that allows time synchronization of video and datasets. Timepoints in the video when a step was observed and times when a step was detected by the step-detection algorithm were compared against one another (Appendix B). Eight trials were completed (two of each of the following: barefoot and high intensity, barefoot and low intensity, shod and high intensity, shod and light intensity). The calculated accuracy of the algorithm was found to be 100% in barefoot trials and 98.9% in shod trials (slightly overcounting in some trials and undercounting in others). Intensity of walking did not affect step detection accuracy.

2. Free-living comparison with activity log: In a one-day free-living trial on a healthy participant, steps should be counted only when the participant logged bouts of walking. Steps should not be detected during sleeping hours or periods of self-identified sedentary activity.

   Results: The activity log for the 24-hour free-living trial helped identify two issues that needed to be addressed in the step-detection algorithm (Appendix B). Firstly, the reported wake-up time on the activity log was 7am, however 84 steps were detected between midnight and 7am due to movements during sleep, which prompted the addition of a sensor orientation requirement. Also, steps were detected from vibrations when riding the bus and car, therefore a minimum threshold was applied to remove errors from such vibrations. Once these processing steps were applied, the steps detected by the algorithm were consistent with the self-reported activities in the 24-hour log.

3. Comparison with Apple Watch: The Apple Watch (Apple, Cupertino, California, United States, *www.apple.com*) has not been largely validated in a free-living environment, as it is difficult to evaluate free living step counts, however this criterion was included because it is a trusted consumer tool for evaluating PA. In a one-day free-living trial on a healthy participant, the step detection algorithm should count steps within 15% below those reported by the Apple Watch (conservative, based on comparisons between Apple watch and other activity monitors, and findings that Apple Watch tends to overcount steps [146]).

   Results: Over a 24-hour free living trial, the steps counted were 6186 for Apple Watch and 5685 for the custom step-detection algorithm, meaning that the algorithm was well within the expected 15% range below Apple Watch.

4. Comparison with published step counts in similar populations: Mean step counts in the study population, calculated using the final step detection algorithm, should be comparable to other published mean step counts in individuals with lower limb OA (particularly those with end stage OA awaiting KA) within ±15% (based on observed variance in the population and reported Axivity IMU accuracy [145].)

Results: Relevant studies with reports of average daily step counts in this population were identified (Table 1). The step counts in these studies ranged from 5278 to 6476 steps per day. As will be noted in the results of Chapter 4, the average daily step count in the clinical study population is within this range.

5. Visual inspection of preliminary data in target population: Preliminary participant data from the clinical population study should show step detection at the appropriate times, as identified by visual inspection. Processed accelerometer data for the study protocol follows a distinct pattern of peaks, each of which should be detected as a step by the developed algorithm. This should be tested in the individuals with the highest and lowest walking intensities in the first ten participants included in the study, and periodically in other participants throughout the clinical population study.

   Results: Visual inspection of preliminary participant data was done for the least and most active participants from the first 10 participants recruited to the clinical study (Appendix B). Results showed that the step detection algorithm detected steps in the expected locations in the data, based on comparison between user-identified steps and algorithm-detected steps.

Table 1: Papers with similar data collection protocols reporting average daily step counts (SD) in knee OA patients.

Paper	Population	Average daily step count (SD)
Lützner et al., 2014	Pre-TKA pts	5278 (2999)
Twiggs et al., 2018	Pre-TKA pts	6409 (3228)
White et al., 2014	Radiographic knee OA	6476 (2613)
Chmelo et al., 2013	Knee OA pts KL Grade II-III	6209 (2554)

To achieve the above criteria, first a moving peak detection threshold was applied to the filtered data, which set the minimum peak detection cut-off to 130% of the moving average at that time point (calculated over 0.5-second windows). For steps to count, peaks needed to occur at least 40 samples apart (0.4 seconds). The unfiltered x-axis data had to average at less that -0.9g over the 2-second window surrounding step detection to ensure that steps were not counted when the participant was lying down (based on the sensor alignment outlined in Section 3.1.2). A walking bout condition requiring 10 steps to occur within 15 seconds was applied to remove step count errors from isolated non-ambulatory movements. The final processing step required at least one step with an acceleration norm magnitude greater than 0.7g per five counted steps to remove erroneous step detections arising during non-ambulatory movements such as driving and bussing. It is noted that the final step detection algorithm captures two steps per gait cycle (one from heel strike of the sensor-equipped leg, and one from toe-off of the sensor-equipped leg). Unilateral sensor placement complicates the detection of steps from the contralateral leg, but this data processing method allows for the detection of two steps per gait cycle. This method is appropriate because with each toe off of one leg, a step is performed by the other leg.

3.2.7. Sedentary Activity Algorithm

Data obtained in this thesis were processed to calculate activity intensity levels using MAD, a measure of distance of data points about the mean (Equation 2), which is a universal PA intensity classification algorithm, where higher intensity activity is associated with more deviation from the mean. MAD has been found to be comparable or superior to other classifiers, such as mean power deviation, skewness, and kurtosis [147], [148].

Equation 2: $$MAD = \frac{1}{n}|acc_{N,i} - \overline{acc}|$$

where $acc_{N,i}$ is the 3D acceleration norm on the i^{th} sample and $\overline{acc}$ is the average acceleration norm of the 500 samples surrounding $acc_{N,i}$.

MAD was calculated over 5-second epochs for the data collection period. Sedentary, light, and moderate activity intensity cut-offs (Table 2) were selected based on literature from a similar treadmill-validated study protocol on older adults [149], [150]. The total time spent sedentary was calculated by adding 0.01 seconds to a time counter for each sample with a MAD value below 0.0167g. Sedentary time is reported as the average percent of the day spent sedentary over the 6 central full days of data collection. It is important to note that these cut points were developed for sensor placement on the anterior thigh. Since the protocol of the present study uses shank placement for IMUs, it is likely that physical activity levels will be mildly overestimated, however similar threshold values for shank placement are not available in the literature. The thresholds used herein were developed from the most similar study protocol that could be identified in literature.

Table 2: MAD cut-offs used in this thesis, selected based on a similar published treadmill-validated protocol in older adults [149], [150].

Activity Intensity	**MAD Range**
Sedentary	$MAD_S < 0.0167g$
Light	$0.0167g \leq MAD_L < 0.0605g$
Moderate	$0.0605g \leq MAD_M < 0.5827g$
Vigorous	$0.5827 \leq MAD_V$

3.2.8. Longitudinal Data Collection

This thesis used data only from participants' first data collection in the preoperative period (as early as possible in their wait period). Participants were informed during the consent process that the goal of the study was to repeat the data collection process periodically throughout the preoperative and postoperative periods. Participant follow-up occurred, and will occur, at the following time points, with the intention of scheduling individuals for further data collections:

a) Every three months throughout the preoperative period;

b) At the pre-surgical appointment with the surgeon (approximately 2-3 weeks prior to the individual's scheduled surgery date), and;

c) Approximately three, six, twelve, and twenty-four months after surgery.

As the research program continues to progress and new components are added, such as the addition of a second IMU sensor on the thigh, participants will be asked to participate in these research components as well.

Chapter 4. Physical Activity Tracking of Knee Arthroplasty Candidates

4.1. Introduction

Physical activity (PA) is an important aspect of a healthy lifestyle, particularly for individuals with osteoarthritis (OA). It helps maintain physical health by contributing to improved organ function and disease prevention, and it is associated with reduced rates of premature mortality [49]. Regular PA is also associated with improved mental health, as it allows individuals to participate in physically demanding social activities and is associated with a better overall quality of life [48]. Regular PA aids in OA disease management by maintaining joint range of motion, joint biomechanics, and promoting muscle strength and stability of the joint [46]. Individuals with lower limb OA have been found to move significantly less than healthy age-matched individuals, predisposing them to a range of comorbidities and further disease progression [50], [151].

Complex relationships have been identified between PA levels and radiographic and clinical disease progression in an OA population with respect to step counts and sedentary activity [5], [6], [59], [60]. Studies suggest interactions between OA disease progression and patient characteristics, such as sex [32], body mass index (BMI) [15], mental health [65], and patient-reported pain levels [18]. Further exploration is required to determine if these relationships apply to disease progression in terms of PA levels as well. There is also an interest in identifying the added value of evaluating PA using objective measures compared to subjective measures alone (commonly used to capture PA levels for clinical and research purposes). Literature suggests that objective PA monitoring may be a more specific metric of actual PA levels [20] and that the combination of objective and subjective PA measures are likely more accurate in capturing clinically-relevant physical activity information than either one independently [116].

The end-stage treatment for severe knee OA patients is knee arthroplasty (KA), wherein the damaged portions of the joint are surgically removed and replaced with prostheses. Studies have shown varying degrees of association between post-KA PA levels and long-term surgical outcomes (including functional outcomes and overall patient satisfaction) [152]–[156]. The limited literature focused on the direct impact of objectively-measured preoperative PA levels on post-KA surgical outcomes suggest that higher preoperative step counts and lower levels of preoperative sedentary activity are positively correlated with postoperative outcomes (including decreased pain, and improved mobility and quality of life) [99], [157]. Brandes et al. stated that PA levels after KA seem to be more strongly influenced by pre-surgical PA levels than by the treatment itself [158]. These findings suggest the importance of objectively tracking PA during the preoperative period and assessing its relationship with clinically-relevant patient characteristics, to assist with pre-habilitation, patient triage, managing patient expectations, and the prediction of surgical outcomes. Existing studies in this area tend to be limited to PA monitoring during one session immediately prior to surgery [99], [157], [158].

The objectives of this study were to examine correlations between objectively-measured PA levels (in terms of step frequency and sedentary activity) and patient-specific variables in an end-stage knee OA population awaiting KA, and to evaluate correlations between objective- and subjective- PA measures to assess the potential added value of objective PA measures in the population.

4.2. Methodology

4.2.1. Participants

End stage knee OA patients were recruited from the participating surgeons' arthroplasty wait lists at the Halifax Infirmary. Inclusion criteria for this study were: over 18 years of age, end-stage knee OA patients awaiting arthroplasty, and capable of providing informed consent to participate. Exclusion criteria were: neurological disorders impacting gait and mobility, non-OA-related lower-limb pathology, and allergy to adhesives.

4.2.2. Data Collection and Processing

Individuals who agreed to participate completed consent forms and questionnaires (demographics and PROMs) on REDCap (Vanderbilt University, Nashville, TN, *https://www.project-redcap.org/*), a secure, web-based application designed for data capture in research studies. Participants completed 6 questionnaires at each data collection time point for the overarching robotics research program. Three of these were considered for this study (Appendix A): the University of California, Los Angeles (UCLA) Activity Score was used to capture patient-reported PA levels, the pain subscale of the Oxford Knee

Score (OKS-PCS) was used to capture patient-reported pain, and the Patient Health Questionnaire for depressive symptoms (PHQ-8) was used to capture mental health. At a regularly-scheduled clinic visit, each participant's surgical leg was instrumented with an AX6 (Axivity Ltd, Newcastle upon Tyne, UK, *www.axivity.com)* inertial measurement unit (IMU), configured to collect tri-axial accelerometer data for 168 hours continuously. The IMU was oriented such that the x-axis aligned approximately with the direction of gravity, and was fixed to the shank of the surgical leg with Hypafix transparent waterproof tape (BSN Medical Canada (Essity), Laval QC, *www.medical.essity.ca*). After 7-days of continuous wear, participants returned their IMU to the research team in a Canada Post pre-paid envelope (Canada Post Corporation, Ottawa, ON, *www.canadapost-postescanada.ca*), where it was sanitized and prepared for data extraction.

Three axes of accelerometer data were obtained (x-, y-, and z-) at a frequency of 100 Hz and with a sensitivity of ±8g. A custom step detection algorithm was applied to the raw triaxial accelerometer data (described in detail in section 3.2.6) to calculate participants' average daily step counts. Data were filtered with a 1-15 Hz bandpass filter, the acceleration norm, acc_N was calculated (Equation 1), and the data were smoothed using a fourth-order Butterworth filter with a cut-off frequency of 10Hz and a fourth-order Savitzky-Golay filter with a window size of 30 samples. The custom step detection algorithm was applied to the smoothed accelerometer data to calculate step count over the entire 7-day collection period. The average daily step count was calculated for the central 6 full collection days.

Activity intensity was characterized using mean amplitude deviation (MAD, Equation 2) [147], which was calculated over 5-second epochs for the entire data collection period. Sedentary activity was classified as a MAD value lower than 0.0167g [149], [150]. Average daily time spent sedentary was calculated for the central 6 full collection days.

4.2.3. Statistical Analysis

Pearson correlation analysis was used to assess relationships between objectively-measured PA (average daily step counts and average percent of day spent sedentary) and patient characteristics (BMI, mental health scores, patient-reported pain levels, and patient-reported PA levels). Correlation analyses were completed in Matlab (v.9.13), using the correlation coefficients function ([R,P] = corrcoef (A)). Sex differences were evaluated using two-tailed unpaired t-tests for average daily step count and average percent of day spent sedentary (reported as test statistic and p-value). These analyses were completed in Matlab using the two-sample t-test function ([h,p,ci,stats] = ttest2(A,B)). Statistical significance was set at $\alpha = 0.05$ for all tests. The selected effect size for statistical analyses (reported as Cohen's d values [159]) were based on findings from the literature. A medium effect size of 0.6 is appropriate for sex-based differences [160], self-reported pain [84], and self-reported mental health [161] and a high effect size of 0.9 is appropriate for correlations with BMI [162] and self-reported physical activity [163]. A high level of variability has been observed in all correlations between objective PA and PROMs due to the inherent subjectivity of self-reports [164]. For a significance of $\alpha = 0.05$, effect size of 0.6 (Cohen's d value indicating medium effect), and power of 80%, the required sample size was calculated in G*Power and found to be 17 for t-tests, and 19 for bivariate normal correlations. The detectable differences for an effect size of 0.6 are approximately 1500 steps per day and 4% daily sedentary time.

4.3. Results

4.3.1. Participants

Twenty-two participants (13M/9F) were recruited between March 2023 and June 2023. Participants were patients awaiting knee arthroplasty at the Halifax Infirmary. One outlier was identified by calculating leverage for each independent variable against step counts and sedentary time (determined by the hat matrices, Equation 3 and Equation 4). The excluded participant's BMI and mental health score both fell above the recommended exclusion thresholds for both step count and sedentary time (calculated as a leverage value that substantially exceeds the mean leverage values, Equation 5). Additionally, their average daily step count, average daily sedentary time, BMI, mental health score, and self-reported pain level fell outside 2 standard deviations of the means. All reported results from this point forward will exclude the aforementioned outlier (n = 21, 13M/8F).

$$\text{Equation 3:} \quad H = X(X^T X)^{-1} X^T$$

where H is the linear regression model's hat matrix and X is the design matrix.

$$\text{Equation 4:} \quad \sum_{i=1}^{n} h_{ii} = p \qquad 0 \leq h_{ii} \leq 1$$

where h_{ii} is leverage of the i^{th} observation in the sample (the i^{th} component of the diagonal of the hat matrix, H), n is the number of observations in the sample, and p is number of coefficients in the regression model.

$$\text{Equation 5:} \quad T = 2 \times \frac{p}{n}$$

where T is the recommended leverage value above which observations should be excluded (the recommended exclusion threshold), p is the number of coefficients in the regression model, and n is the number of observations in the sample.

The average age of the sample population was 69.1 ± 6.1 years, with ages ranging from 59 to 79 years. The average BMI was 32.8 ± 7.3 kg/m^2 with high prevalence of obesity (61.9%, BMI ≥ 30 kg/m^2) and overweight (85.7%, BMI ≥ 25 kg/m^2) as defined by Health Canada's guidelines for body weight classification in adults [165]. All participants self-reported their ethnicity as white. 90.5%, 47.6%, and 9.5% of participants reported intermittent or daily use of over the counter pain medications, non-steroidal anti-inflammatory drugs, and narcotic pain management medications, respectively (Appendix C).

Average self-reported PA level collected with the UCLA Activity Score was 4.5 ± 1.8 on a 1 (completely sedentary) to 10 (regular intense activities) scale with a median value of 4/10. Self-reported pain from the OKS-PCS averaged at 12.7 ± 5.3 on a 0 (incessant OA-related pain) to 28 (pain-free) scale. The average mental health score reported on the PHQ-8 was 4.8 ± 4.8 on a 0 (no signs of poor mental health) to 24 (severely depressed) scale.

4.3.2. Step Counts

Average daily step count varied significantly across the sample population, ranging from 2002 to 11050 steps per day, with an average of 6051 ± 2844. 12 participants (57%) did not achieve the recommended daily step count target of 7000 [4]. Significant correlations were identified between average daily step count and BMI ($p = 0.013$, $r = -0.53$, $r^2 = 0.28$), and self-reported physical activity score ($p = 0.011$, $r = 0.54$, $r^2 = 0.29$). Sex, self-reported pain level, and mental health score were not found to be significantly associated with objectively-measured daily step count (Table 3). Figures of step count versus sex, BMI, self-reported PA, self-reported pain, and mental health are shown in Appendix D.

Table 3: Summary of results showing mean (SD) of relevant metrics (age, average daily step count, average daily % sedentary, sex, BMI, self-reported PA, self-reported pain, and mental health scores), and their correlations with objectively-measured physical activity (average daily step count and average daily % sedentary); $^{+}$Assessed using UCLA (1-10 Activity Scale; 1 being little to no movement throughout the day, 10 being regular participation in high intensity activities); $^{++}$Assessed using OKS-PCS (0-28 scale; 0 being constant severe pain related to knee OA, 28 being no pain at all relating to knee OA); $^{+++}$Assessed using PHQ (0-24 scale; 0 being no signs of poor mental health, 24 being severe signs of depression); *$p < 0.05$ (significance).

n = 21	**Mean (SD)**	**Average Daily Step Count**			**Average Daily % Sedentary**		
		r	**r^2**	**p**	**r**	**r^2**	**p**
Age (years)	69.1 (6.1)						
Average Daily Step Count	6051 (2844)						
Average Daily % Sedentary	78.8 (6.6)						
Sex (M:F)	13:8			0.079			**0.021***
BMI (kg/m^2)	32.8 (7.3)	-0.53	0.28	**0.013***	0.51	0.26	**0.017***
Self-Reported PA (/10)$^{+}$	4.5 (1.8)	0.54	0.29	**0.011***	-0.54	0.29	**0.012***
Self-Reported Pain (/28)$^{++}$	12.7 (5.3)	0.017	<0.001	0.94	-0.13	0.016	0.58
Mental Health (/24)$^{+++}$	4.8 (4.8)	-0.11	0.012	0.64	0.25	0.061	0.28

4.3.3. Sedentary Activity

Sedentary activity showed slightly different associations with patient characteristics compared to step counts. Average percent of the day spent sedentary ranged from 68.8% to 91.0% across the sample population, with an average of 78.8 ± 6.6%. Statistically significant differences in sedentary activities were identified between males and females ($t(19) = -2.52$, $p = 0.021$), with females spending significantly more time sedentary than males. The average percent of the day spent sedentary was 76.3 ± 4.6% in males, and 82.9 ± 7.5% in females. Significant correlations were also identified between average percent of the day spent sedentary and BMI ($p = 0.017$, $r = 0.51$, $r^2 = 0.26$), and self-reported physical activity score ($p = 0.012$, $r = -0.54$, $r^2 = 0.29$). Self-reported pain levels and mental health scores were not found to be significantly associated with sedentary activity (Table 3). Graphs of sedentary time versus sex, BMI, self-reported PA, self-reported pain, and mental health are shown in Appendix D.

4.4. Discussion

The average daily step count of this study's sample population varied significantly, with the majority of participants not achieving the recommended target of 7000 steps per day [4]. This finding supports the hypothesis that preoperative physical activity levels are below the recommended level for most people awaiting KA. Research specifically targeting individuals with osteoarthritis has consistently shown low levels of physical activity and reduced step counts. As an example, a study assessing PA levels in individuals with or at risk of developing knee OA found that only 27% met the guideline of accumulating at least 150 minutes of moderate-to-vigorous physical activity per week, which corresponds to approximately 7,000 to 8,000 steps per day [74]. These findings highlight the challenges faced by this population in achieving adequate PA, which may translate to other health risks including declines in cardiovascular health, organ function [49], and mental health [48], emphasizing the importance of evaluating objective PA levels in individuals awaiting KA. Further research and tailored interventions are crucial to addressing the unique barriers and limitations associated with lower limb osteoarthritis and facilitating increased physical activity levels among affected individuals.

The average percent of day spent sedentary in the clinical study population was 78.8%, which is in agreement with a study on sedentary behaviors of individuals with OA from the Osteoarthritis Initiative [46]. The present study revealed a significant association between sedentary behaviors and patient characteristics, highlighting the relevance of considering individual factors when addressing sedentary behaviors in this context. The identification of sex differences, and correlations with BMI and self-reported PA provide valuable insights for the clinical assessment of OA in the KA preoperative period. While step count provides an indication of PA level, it does not capture prolonged periods of sitting or reclining, which can be captured by assessing sedentary behaviors. Excessive sedentary behaviors have specific health-related implications relevant to the OA population. Sedentary time has been found to be independently associated with worse physical function, pain, and stiffness in individuals with knee osteoarthritis, even after controlling for physical activity level [46], [94], [166], [167]. This suggests that sedentary behavior has unique effects on health outcomes beyond the influence of step count alone.

Significant differences in sedentary behaviors were found between males and females in this study, with females spending more time sedentary on average than males. This finding is consistent with literature that shows that females with symptomatic OA experience greater pain and functional limitations than males, leading to reduced mobility and decreased PA levels [168], [169]. These studies are not focused on any particular OA severity, but the present study specifically demonstrates these sex-based differences in an end-stage knee OA population. Literature focused on the specific challenges faced by females with knee OA in the preoperative KA period highlight differences in gait biomechanics [170], muscle strength and activation [171], and anatomical differences [172]. Studies evaluating sex-specific barriers to achieving PA targets have shown that females are significantly less physically active than men and that sociocultural challenges such as obligations associated with typical gender roles and lack of social support are commonly reported [173]–[175]; it is possible that these sociocultural barriers extend to female OA patients awaiting KA. Further research on the sex-specific burdens experienced by patients in this population can help inform patient prioritization and triaging by providing clinicians with more objective information relating to surgical need. By understanding the underlying factors contributing to sex differences in OA patients' PA levels, clinicians and researchers can develop more specific strategies to promote physical activity and manage disease progression in the preoperative period and potentially improve surgical outcomes. This information should also be considered and emphasized as the field transitions toward patient-specific surgical planning. Interestingly, significant differences were not identified between sex and step count. This finding may be related to differences in the specific means by which females and males accumulate steps throughout the day (i.e. the rapid accumulation of steps through bouts of high-intensity activities accompanied by lengthy sedentary bouts versus the gradual accumulation of steps during lower-intensity activities throughout the day accompanied by limited sedentary behaviors).

This study identified strong correlations between PA levels and BMI, with individuals with higher BMI exhibiting significantly lower step counts and more sedentary behaviors. It is important to note that the relationship between PA and BMI is bi-directional, as those with higher BMI tend to be less physically active, and those who are less physically active tend to have higher BMI [176]. The association identified herein agrees with existing research, which has consistently reported a negative relationship between BMI and PA levels in populations of varying demographics [166], [177]–[179]. The present study demonstrates these BMI-related PA outcomes in a population of individuals with end-stage knee OA, a topic which has not been extensively explored in the literature. The existing literature focused on the relationships between BMI and PA in OA patients mainly focuses on the potential benefits of weight loss for disease management and KA outcomes [166], [177]–[179], however these findings may also be relevant for the assessment of patient disease state (including function and PA levels) and quality of life (in terms of social participation).

A significant positive correlation was identified between objectively- and subjectively-measured physical activity levels in this study. Previous studies have reported varying levels of agreement between self-reported and accelerometer-based PA levels in adults, with some studies indicating that questionnaires overestimate PA relative to objectively-measured values, while others indicate that they underestimate [180]. Zahiri et al. found that UCLA questionnaire scores were significantly positively correlated with step counts ($p = 0.002$) in a sample of total joint arthroplasty patients but identified substantial variability in daily step counts for participants with the same self-reported score [163]. Similar outcomes were identified in the present study, with 9 individuals selecting 3/10 ("sometimes participates in mild activities, such as walking, limited housework and limited shopping") as their self-reported PA level, but their objectively-measured average daily step counts ranged from 2002 to 9091. Consistent with literature, these findings suggest that objectively-measured physical activity levels may be more specific and less prone to participant biases compared to subjective measures of PA [21], [114]. The findings from the present study support the notion that a combination of objectively- and subjectively-measured PA provides a more thorough patient evaluation in the preoperative KA period. The combined knowledge of an individual's perceived PA levels (as measured by questionnaires) and their objectively-measured PA levels (as measured by accelerometry) can be used by clinicians to manage patient expectations surrounding post-surgical function and ability to participate in physical and social activities. For instance, in individuals who consistently achieve daily PA targets for their population and self-report their physical activity level as relatively low, clinicians may predict that postoperative PA levels will not significantly increase; this information can be used to help manage patient expectations, to better assess readiness for surgery, and to help predict surgical outcomes relating to patient satisfaction [181].

Mental health scores and physical activity levels were not found to be significantly correlated in the study sample population. Literature exploring correlations between mental health scores and physical activity levels in individuals with moderate to severe knee OA have generally reported that worse mental health scores are associated with lower self-reported PA, lower step counts, and more time spent sedentary [182]–[184]. The findings of the present study may be attributed to the low levels of and low variability in depressive symptoms in the study's sample population. Hawker et al. found that in a population of knee OA patients, 25.8% of individuals experienced moderate to severe depressive symptoms (defined as a PHQ-8 score $\geq$ 10/24) [185], whereas the present study identified such symptoms in only 14.3% of participants. It is possible that these associations may be clearer in a larger sample population with more variability. While the PHQ-8 is a validated assessment tool in older adults [135], [186], it should be noted that older adults have repeatedly been found to underreport depressive symptoms [135], [187], [188]. Malkin et al. explored older adults' ability to identify mental illness and found that certain indicators of depression were often perceived as a normal part of the aging process, causing individuals in this population to self-report their mental health to be better than it actually is [187]. Based on this, it is important that the reported findings of the associations between self-reported mental health and PA levels are interpreted appropriately to ensure that mental wellbeing is not underestimated in the clinical evaluation of these patients.

Contrary to our hypothesis, there was no identified correlation between objectively-measured PA and patient-reported pain. Previous literature exploring the pain experience for knee OA patients has emphasized the complexity and inter-person variability in pain presentation and how it impacts an individual's life, including PA levels [18], [79], [80]. A wide range of pain values were reported throughout the study population, with the least pain reported being 20/28 and the highest being 3/28. Interestingly, the individual with the highest reported pain was found to meet or exceed the daily step count target of 7000 steps on 5 out of 6 collection days. These findings may speak to each individual patient's ability to maintain physical activity despite high levels of pain. The lack of correlation found herein may also be reflective of participants' lifestyle, where some individuals may have obligations such as work or family matters that require consistent PA, even while experiencing high levels of pain. It may be important for clinicians to consider how this impacts these patients' qualities of life and these behaviors may be useful in informing surgical prioritization and patient-specific pre-habilitation. Also, given that the selection of patients and scheduling of KA is a subjective process at the discretion of each surgeon in Nova Scotia, it is possible that some patients may over report pain and other subjective measures while on the wait list in the belief that this may expedite their access to surgery. A similar behavior was reported by Boring et al. studying the reasons why people over- or under-report pain; they found that the most common reason why patients over-reported pain levels in a clinical setting was to ensure treatment (including accelerated access to care) [189]. It is also important to consider the impact that changes in pain-management medication may cause throughout the perioperative period. The OKS-PCS asks patients to reflect on the past 2 weeks, and it is possible that recent treatments, such as corticosteroid injections, may result in differences between the retroactive pain reports and the actual physical activity levels during the data collection period [190], [191]. Information on medications was obtained from participants, but not controlled for in this study. These findings highlight the complexity of disease presentation in individuals with end-stage knee

OA. The assessment of objectively-measured PA levels and patient-reported pain may be useful for clinicians in assessing the patient's function and quality of life, and understanding the complex relationships between a patient's perceived disease state and objective metrics indicative of disease severity.

The primary limitations of this study were the relatively small sample size, and that the participants were recruited from a single centre (limiting the generalizability of the findings). Future research should include larger and more diverse sample sets, by recruiting from multiple institutions, representing various ethnicities, cultures, and socioeconomic backgrounds [192]–[195] to assess the validity of the present study's findings and explore relationships which could not be explored with this small sample size. Further research will be aimed at exploring how time on the wait list relates to differences in PA, how PA changes for individuals during the wait period, and how these measures relate to patient-specific characteristics in pre- and post-KA populations.

Furthermore, assessing PA through step count and sedentary activity metrics alone in this population has certain limitations that should be considered. Step count metrics may not capture the full spectrum of physical activities that individuals with knee osteoarthritis engage in, such as low-impact exercises or upper body movements that are important for maintaining overall fitness and functionality [74]. A study by Dunlop et al., assessing PA levels in older adults in the United States, emphasized that sedentary behavior should be assessed beyond just total sedentary time by considering the duration of uninterrupted sitting, breaks in sitting time, and types of sedentary activities performed [166]. Incorporating more comprehensive measures beyond step count and sedentary activity metrics, such as activity recognition or a more granular temporal assessment of PA intensity, would provide a more holistic understanding of PA levels in this population.

4.5. Conclusion

Incorporating objective PA tracking into the preoperative assessment for KA candidates presents the potential to improve clinical patient assessments throughout the perioperative period. It was demonstrated that individuals with knee OA tend to have PA levels below published targets, increasing their risk of comorbidities and further disease progression. Objective measurement of PA through accelerometers provides a more detailed assessment compared to subjective measures alone. Objectively- and subjectively-measured PA levels were found to be significantly correlated in the present study, however the combination of these two assessment tools provides a more detailed representation of a patient's lifestyle and PA levels in relation to their disease state. Both metrics can be considered by clinicians to compare patient perceptions of their daily function with objective measurements of their participation in physical activities, relating to patient expectations and post-surgical satisfaction.

Physical activity levels were found to be significantly lower in females, and individuals with higher BMI. These findings suggest that females and those with higher BMI may be more susceptive to reduced quality of life due to a potential decreased ability to participate in physical activities and may be at a higher risk of developing comorbidities associated with lack of PA. Females may face distinct challenges in the preoperative period (including biological, biomechanical, anatomical, and sociocultural barriers to achieving PA targets) which should be explored and considered by clinicians when assessing their disease state. Further research on the associations between sex and PA levels in this population, such as multivariate analysis of patient characteristics may provide more clarity on the specific considerations relevant in the assessment and treatment of males compared to females in the preoperative period. It is also likely that individuals with higher BMI face different challenges preoperatively, as the association between BMI and PA is bi-directional. The findings of the present study also suggest the potential utility of incorporating distinct considerations in the preoperative evaluation of patients based on these characteristics. The sex- and BMI-related differences observed in this study can be used by clinicians to help manage patient disease state in the preoperative period, better prioritize patients based on patient-specific characteristics, and predict post-surgical satisfaction relating to physical activity levels (based on pre-surgical expectations and predicted postoperative PA outcomes).

By incorporating PA tracking in the preoperative period, surgeons can better manage patient expectations, complete a more thorough assessment of pre-surgical prioritization, and better predict surgical outcomes based on patient-specific characteristics. Overall, the inclusion of PA measurement in surgical decision-making has the potential to enhance patient care and optimize surgical outcomes for KA candidates, by providing the clinical team with another useful and objective tool for patient assessment.

Chapter 5. A Novel Visualization Tool for Temporal Activity Tracking

5.1. Introduction

As discussed in Chapter 4, objectively tracking physical activity (PA) levels in the preoperative knee arthroplasty (KA) period can provide clinicians and researchers with valuable information relating to a patient's disease state and quality of life, which may relate to patient expectations for surgery and surgical outcomes. While the benefits of physical activity are well reported and PA is commonly recommended by clinicians for osteoarthritis disease management, people in this population consistently fail to meet public health PA guidelines [74], [196]. An average daily step count of 7000 steps has been reported in literature for patients in the present study population [4]. Individuals can achieve step count targets in a number of ways, depending on their lifestyle, pain levels and ability to tolerate pain from high intensity activities, and how much time they are able to dedicate to structured physical activities. Health Canada's *"24-Hour Movement Guidelines for Adults aged 65+"* offers several recommendations aimed at assisting older individuals in improving their physical activity levels to achieve the corresponding health benefits [197]. Thy encourage the reduction of sedentary time and suggest individuals trade light PA for more moderate to vigorous PA, suggesting that participating in higher intensity activities provides greater health benefits than simple reductions in sedentary time. Nova Scotia Health's guidelines for managing arthritis suggest "doing more physical activity as tolerated" and to try to obtain 30 minutes of moderate PA at least 5 days per week [198]. These guidelines suggest that the goal of simply increasing PA levels (by achieving certain step count targets and reducing time spent sedentary) should be more specific, and highlight the importance of participating in distinct types of activities to achieve the associated health benefits (at least 150 minutes of moderate-vigorous PA per week).

Limited literature exists exploring the impact of type of PA on knee osteoarthritis (OA) symptoms and KA outcomes, and the existing literature is inconclusive [27], [199], [200]. For instance, a systematic review on the topic suggests that an optimal knee OA exercise program should involve 3 supervised PA sessions per week, with one specific aim (improving aerobic capacity, improving quadricep muscle strength, or improving lower extremity performance) [201]; however, this recommendation does not align with PA guidelines from public health sources [197], [198], and the results of such a program have not been reported [23]. Some strategies that can be used to achieve step count targets are engagement in consistent low-intensity activity throughout the day, engagement in moderate activity throughout a portion of the day and low intensity or sedentary activity for the remainder, or participating in one or two shorter bouts of high intensity activity and spending the rest of the day doing low intensity or sedentary activities. This level of granularity in PA assessment has not been previously reported in a population of individuals with end-stage knee OA awaiting KA. The impact of activity intensity on OA-related outcomes in this population were explored in a cross-sectional study by White et al [26]. They found that replacing 60 minutes per day of sedentary activity with 60 minutes per day of light activity significantly reduced the risk of presenting with slow gait speed at the two year follow-up, and that the same benefits can be seen by achieving just 5 minutes of moderate to vigorous activity. These observations suggest that moderate to vigorous intensity activity may be associated with more significant functional benefits than light or sedentary activity, and that for individuals who are incapable of engaging in high-intensity exercise, light intensity activity may be a beneficial alternative to sedentary activity.

PA metrics are generally reported as summary values (such as average daily step counts, and average daily sedentary activity). These summary metrics are appropriate for providing a general overview of an individual's PA levels and assessing for factors associated with PA levels, however there are limitations to reporting PA in this way. Firstly, they do not provide information on the specific intensity of activities performed; for example, two individuals may have the same average step count, but one may achieve it through vigorous exercise while the other may achieve it through casual walking. Additionally, summary values may not capture the variability of PA levels throughout the day; for instance, an individual may accumulate most of their steps during a specific time period, while spending the rest of the day sedentary. This chapter will introduce a detailed visual tool used to assess PA intensity in 15-minute intervals throughout the week, helping overcome some of the limitations associated with objective PA measurements reported as summary values. The objective of this study was to develop a novel visualization tool to show temporal activity intensity of OA patients throughout the KA wait period and to demonstrate its use through a series of case studies to highlight the potential added value such a tool provides.

5.2. Methodology

5.2.1. Participants

End stage knee OA patients were recruited from the participating surgeons' arthroplasty wait lists at the Halifax Infirmary. Inclusion criteria for this study were as follows: over 18 years of age, end-stage knee OA patients awaiting arthroplasty at the Halifax Infirmary, and capable of providing informed consent to participate. Exclusion criteria were as follows: neurological disorders impacting gait and mobility, non-OA-related lower-limb pathology, and allergy to adhesives.

The case studies presented herein include 3 participants with similar average daily step count levels (within 10% of one another, based on the reported accuracy of Axivity IMUs and findings on the clinical significance of differences in step counts [202], [203]) such that the added value of a temporal PA assessment tool can be explored (beyond a simple step count or sedentary activity metric). Participants with an average daily step count above the daily target for the population of 7000 steps per day [4] were selected, such that their PA could be evaluated with more granularity to assess the means by which they attained the target step count. The case study participants' visual representations of PA were qualitatively compared to identify differing strategies used to accumulate steps and non-sedentary time. The visual representations of PA were also analyzed in conjunction with patient demographics and patient-reported outcome measures to highlight the potential clinical utility of the tool for PA assessment in the population.

5.2.2. Data Collection and Processing

Individuals who agreed to be involved in the study were sent a link to REDCap (Vanderbilt University, Nashville, TN, *https://www.project-redcap.org/*), a web-based application designed for data capture in research studies, where they completed their consent form, demographics form, and 6 questionnaires for the overarching robotics study. Three of these were considered for this study (Appendix A): the University of California, Los Angeles (UCLA) Activity Score questionnaire was used to capture patient-reported PA levels (1-10 scale; 1 being little to no movement throughout the day, 10 being regular participation in high intensity activities), the pain subscale of the Oxford Knee Score (OKS-PCS) was used to capture patient-reported pain (0-28 scale; 0 being constant severe pain related to knee OA, 28 being no pain at all relating to knee OA), and the Patient Health Questionnaire for depressive symptoms (PHQ-8) was used to assess patients' mental health (0-24 scale; 0 being no signs of poor mental health, 24 being severe signs of depression).

At a regularly scheduled clinic visit, an AX6 (Axivity Ltd, Newcastle upon Tyne, UK, *www.axivity.com)* inertial measurement unit (IMU) was fixed to the shank of the participants' surgical leg using Hypafix transparent waterproof tape (BSN Medical Canada (Essity), Laval QC, *www.medical.essity.ca*). The sensor was oriented such that its positive x-axis aligned approximately with the direction of gravity. Participants were instructed not to modify their regular activities during the data collection period (to "pretend the sensor was not there"). After 7 days of continuous wear, participants returned their IMU to the Halifax Infirmary in a pre-paid mailing envelope (Canada Post Corporation, Ottawa, ON, *www.canadapost-postescanada.ca*), where it was prepared for data extraction.

For this thesis, triaxial accelerometer data were obtained at a frequency of 100 Hz and with a sensitivity of ±8g. Activity intensity was characterized by calculating mean amplitude deviation (MAD) [147] on the unfiltered accelerometer norm over 5-second epochs. MAD cut-off thresholds for intensity classification were 0.0167g for sedentary activity, 0.0605g for light intensity activity, and 0.5827 for moderate activity intensity [149], [150]. Since vigorous-intensity activity is rarely observed in an end-stage OA population, moderate- and vigorous-intensity activities were combined (defined as $MAD_{mod\text{-}vig} \geq 0.0605g$).

A visual tool was developed to resemble a heat map, showing activity intensity in 15-minute increments throughout the central 6 full days of data collection. The "heat" of each 15-minute increment was determined by adding the intensity values (0 = sedentary, 1 = light, 2 = moderate, 3 = vigorous) of each sample (average of a 5-second window centred about the n^{th} point). The visual was created using Matlab's (v.9.13) image() function. The lowest intensity shown on the heat map is equal to 15 minutes of completely sedentary activity. The heat map is scaled such that the maximum value on the colour scale is equal to the maximum 15-minute intensity value observed in the sample cohort, as calculated by the sum of intensity values (0 to 3) of each sample in the window. This scaling was done so intensity maps of participants could be compared against one another. More details on the data processing involved in the development of the heat maps is shown in Appendix E.

5.3. Case Studies

The three participants chosen for the case study were all males with ages ranging from 65 to 74, and BMIs ranging from 25.3 to 30.1 kg/m^2. Their average daily step counts were all over 10,000 and within 10% of one another. There were some differences in sedentary behaviors with participant 2 spending significantly more time sedentary than participants 1 and 3. All 3 individuals reported physical activity levels higher than the average of the clinical study population. Participant 1 reported the most pain of the sample cohort, and mental health scores indicated low levels of depressive symptoms for all case study participants. Table 4 provides a summary of the three participants involved in the case study.

Table 4: Summary of case study participants' demographics, physical activity levels, and questionnaire results. $^+$Assessed using UCLA (1-10 Activity Scale; 1 being little to no movement throughout the day, 10 being regular participation in high intensity activities); $^{++}$Assessed using OKS-PCS (0-28 scale; 0 being constant severe pain related to knee OA, 28 being no pain at all relating to knee OA); $^{+++}$Assessed using PHQ (0-24 scale; 0 being no signs of poor mental health, 24 being severe signs of depression).

	Participant 1	Participant 2	Participant 3
Sex	M	M	M
Age (years)	65	68	74
BMI (kg/m^2)	30.1	26.1	25.3
Average Daily Step Count	10081	11051	10377
Average Daily % Sedentary	70.7	82.6	68.8
Self-Reported PA (/10)$^+$	6	6	8
Self-Reported Pain (/28)$^{++}$	3	10	16
Mental Health (/24)$^{+++}$	0	6	6

5.3.1. Participant 1: Consistent Low-Intensity Activity

Participant 1 (P1) was a 65 year old male with a body mass index (BMI) of 30.1 kg/m^2. This is the only case study participant with a BMI classified as obese [165]. His average daily step count was 10081 and he spent on average 70.7% of the day sedentary. P1 self-reported his PA level as 6/10 ("Regularly participates in moderate activities"), his pain level as 3/28 (the highest pain level reported in the patient cohort), and his depressive symptoms as 0/24 (no signs of poor mental health). He self-reported daily use of over the counter (OTC) medications. This individual has a diagnosis of end-stage knee OA with no reported comorbidities, and at the time of data collection was on the wait list for KA at the Halifax Infirmary. Despite achieving the daily step count target of 7000 steps [4] on 5 out of 6 collection days, and self-reporting a relatively high PA level, P1 reported that he was unable to engage in 20 minutes or more of exercise (described as 20 minutes or more of non-stop activity: swimming, jogging, rapid walking, cardio, weights/resistance) due to physical limitations and pain.

In the heat map developed for this participant's physical activity levels throughout the data collection period (Figure 4), it can be seen that this individual participated in consistent low to medium intensity physical activity. He did not engage in any intentionally higher-than-normal intensity exercise bouts, but rather achieved step count targets by spending the majority of waking hours engaged in passive movement. P1 shows that intense bouts of physical activity are not required to achieve daily step count targets. Based on the PA shown in this participant's heat map, it appears that P1 did not accumulate 150 minutes of moderate activity, as recommended by public health guidelines [197], [198]. The specific PA strategy adopted by P1 may be related to a number of factors including personal obligations requiring physical activity or the pain levels he experienced. The amount of physical activity obtained by this individual was higher than average for the population and may be sufficient to achieve the benefits associated with PA.

The evaluation of PA levels based solely on summary statistics reveals an unexpected relationship between pain and PA for this individual, as it would be predicted that someone experiencing such high pain levels would not be capable of achieving such high step counts and low levels of sedentary activity. It is possible that as OA progresses and pain prevents individuals from participating in higher intensity exercise, those who are willing and capable may adopt the strategy of engaging in prolonged low-intensity activity throughout the day to achieve step count targets. Visual analysis of PA provides clarity on how P1 managed to consistently reach step count targets, despite his reported pain. As reported by White et al., this is a beneficial way for individuals who are unable to engage in higher-intensity exercise to increase PA throughout the day in an attempt to meet PA targets [26].

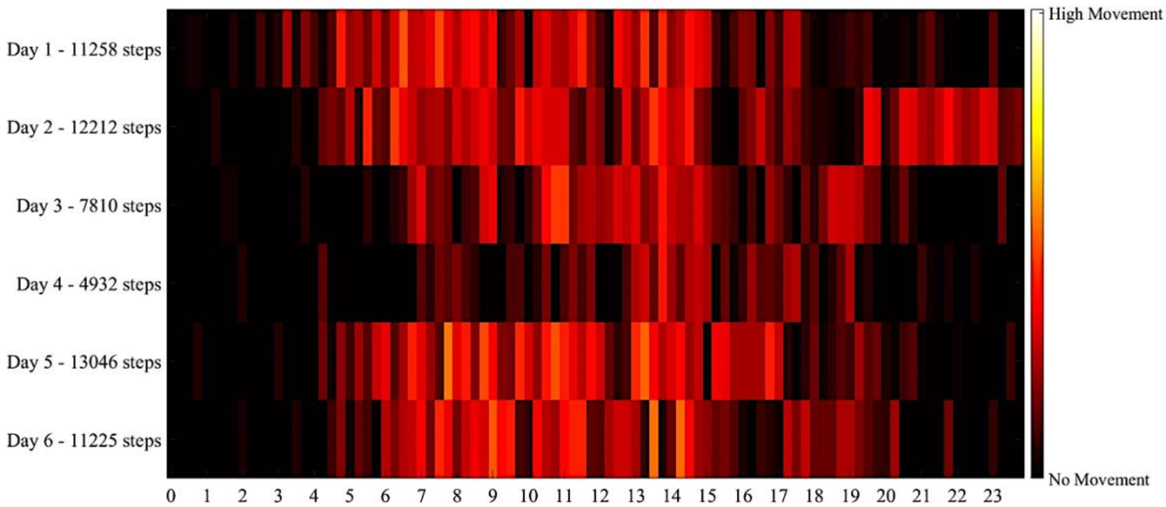

Figure 4: Heat map for case study participant 1 (65 year old male with a BMI of 30.1 kg/m^2, daily step count of 10081 and average 70.7% of day spent sedentary). This participant exhibited consistent low intensity activity throughout the week, achieving or exceeding the population's daily step count target of 7000 steps [4] on 5 out of 6 collection days.

5.3.2. Participant 2: Short Bouts of High-Intensity Activity

Participant 2 (P2) was a 68 year old male with a BMI of 26.1 kg/m^2 (classified as overweight [165]). His average daily step count was 11051and he spent on average 82.6% of the day sedentary. P2 self-reported his PA level as 6/10 ("Regularly participates in moderate activities"), his pain level as 10/28 (slightly more pain than the average of the sample population), and his mental health as 6/24 (low levels of depressive symptoms). He self-reported daily use of OTC medications. This individual has a diagnosis of end-stage knee OA, reported comorbid hypertension, and at the time of data collection was on the wait list for KA at the Halifax Infirmary.

This participant's heat map is significantly different than P1, exhibiting two short bouts of high intensity activity each day, combined with significantly more sedentary behaviors (Figure 5). This individual met or exceeded the recommended daily step target of 7000 steps [4] on all 6 of the data collection days, and appears to have participated in at least 150 minutes of moderate intensity activity per week, as recommended by public health guidelines [197], [198]. P2 engaged in high levels of sedentary activity outside of the structured high-intensity exercise bouts that he performed daily, as reflected in his average daily percent sedentary value of 82.6%.

In comparison to P1, summary statistics alone would suggest that P2 is doing a worse job of achieving PA guidelines, as step counts are not significantly different between the two, but sedentary time is significantly higher in P2. The visual evaluation of PA shows that in reality, P2 has simply adopted a different strategy to achieve PA targets. Based on the reported finding that 5 minutes of moderate to vigorous activity may offer the same benefits as 60 minutes of light intensity activity [26], it is possible that despite his higher sedentary levels, P2's PA is more beneficial for maintenance of performance-based function than P1.

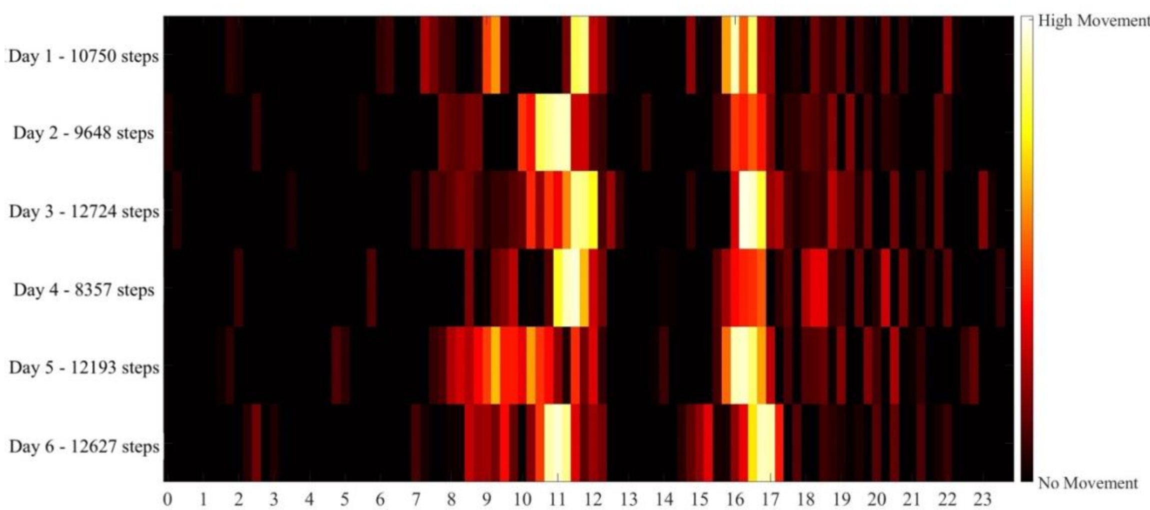

Figure 5: Heat map for case study participant 2 (68 year old male with a BMI of 26.1 kg/m^2, daily step count of 11050 and average 82.6% of day spent sedentary). This participant exhibited two bouts of high intensity activity each day (around 11:00am and 4:00pm), and spent the majority of the rest of the day sedentary. This patient achieved or exceeded the population's target of 7000 steps per day [4] on all 6 collection days.

5.3.3. Participant 3: Day-to-Day Activity Variability

Participant 3 (P3) was a 74 year old male with a BMI of 25.3 kg/m^2 (classified as overweight [165]). His average daily step count was 10377 and he spent on average 68.8% of the day sedentary. P3 self-reported his PA level as 8/10 ("Regularly participates in very active events such as bowling or golf "), his pain level as 16/28 (slightly less pain than the average of the sample population), and his mental health as 6/24 (low levels of depressive symptoms). He self-reported intermittent use of OTC and narcotic pain medications. This individual has a diagnosis of end-stage knee OA with no reported comorbidities and at the time of data collection was on the wait list for KA at the Halifax Infirmary.

In this individual's heat map for his data collection period (Figure 6), significant day-to-day variability is observed. P3 met or exceeded the recommended daily step target of 7000 steps [4] on 4 out of 6 of the data collection days, and appears to have accumulated the majority of active hours between 8:30 am and 1:30 pm. On the days when he did not meet step count targets, this participant exhibited high levels of sedentary activity; a behavior which would not be evident in summary metrics alone. P3 appears to use a strategy distinct from both P1 and P2 to exceed average daily PA recommendations; by significantly exceeding PA targets on *active* days while engaging in high levels of sedentary behavior on *inactive* or *recovery* days.

Day-to-day variability can be reported as a standard deviation of average daily step counts, but the heat map tool provides clarity and context to what that variability looks like with more granularity. Summary statistics for P3 tell a very similar story to those of P1, but as can be seen by comparing their heat maps, the methods by which they accumulated PA throughout the week are very different.

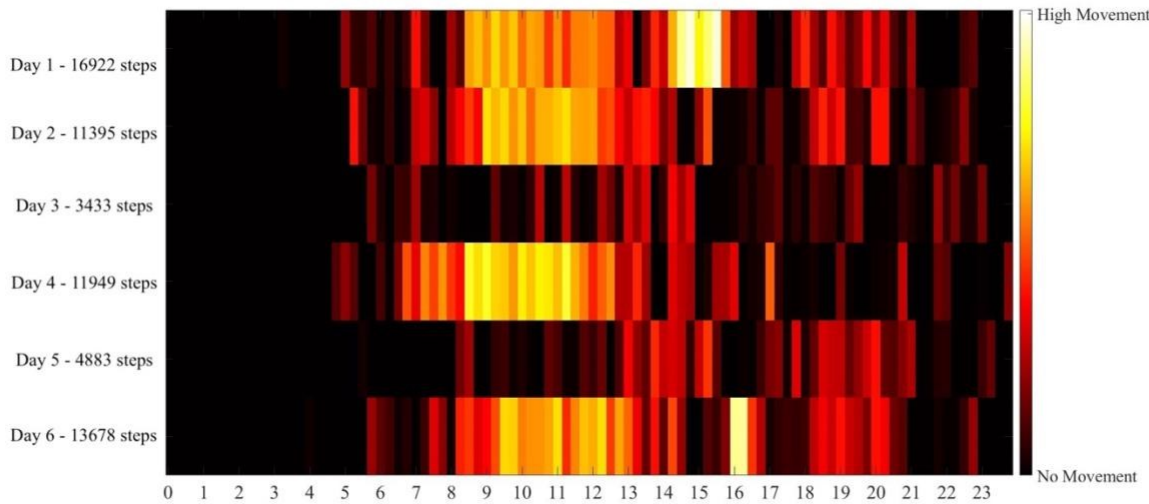

Figure 6: Heat map for case study participant 3 (74 year old male with a BMI of 25.3 kg/m^2, daily step count of 10377 and average 68.8% of day spent sedentary). This participant achieves or exceeds the population's daily step count target of 7000 steps [4] on 4 out of 6 collection days. Regular PA accumulation occurs on active days between 8:30 am and 1:30 pm. On active days he significantly exceeds the step count target, with significant drops in PA levels on inactive days.

5.4. Discussion and Concluding Remarks

The case studies presented herein demonstrate the utility of the developed visual tool for the presentation and interpretation of objectively-measured PA in a population of end-stage knee OA patients awaiting KA. As shown in the three participants studied, individuals accumulated physical activity in a variety of ways, by adopting distinct strategies potentially suitable for their pain tolerance, functionality, and way of life. Summary PA metrics, while useful for providing clinicians and patients with an overview of physical activity levels, are unable to capture the methods by which individual patients achieve (or fail to achieve) PA targets. This type of detailed PA assessment combined with findings in literature on the relevance of activity intensities may provide clinicians with useful information relating to patients' preoperative quality of life and help predict performance-based functional outcomes throughout the preoperative period and postoperatively.

Increasing PA levels is beneficial for individuals with knee OA for maintenance of physical health and function [49], improving mental health [48], and preventing clinical and radiographic disease progression [31]. PA guidelines for this population tend to suggest increases in PA and decreases in sedentary time including at least 150 minutes of moderate activity per week [197], [198]. The methods by which individuals in this population achieve these PA guidelines are not addressed in the literature, and are generally not assessed in objective PA analyses. While studies on objectively-measured PA oftentimes classify activity as sedentary, light, moderate, and vigorous intensity [84], [106], [114], [204], they do not evaluate these activity metrics with any further detail. The next step in detailed PA analysis in this population is the temporal tracking of PA intensity levels, such that the specific strategies patients use to accumulate physical activity can be understood. As demonstrated in the presented case studies, summary PA metrics are not detailed or specific enough to provide a thorough understanding of all relevant PA information in the population. These findings suggest that a more granular temporal approach to PA tracking may add value to the clinical assessment of patients in the preoperative period and may help researchers better understand the PA-related factors associated with OA patient function and quality of life.

In the future, this type of temporal PA intensity tracking tool may be used to evaluate differences between individuals, as well as differences between time points for the same patient. This tool may help clarify changes (or similarities) in summary PA metrics between time points that would otherwise remain unexplained without detailed temporal tracking, potentially providing clinicians with a clearer understanding of whether changes in PA are related to changes in disease state, seasonal changes, or other individual patient factors. For instance, in his clinic visit, P3 told the research team that he regularly golfs, which may be the source of accumulated PA on his active days. This, combined with the significant decrease in PA on his inactive days highlights the potential impact that seasonal changes may have on overall PA levels (i.e. when it is not golfing season, every day may look like an inactive day, resulting in significant decreases in summary PA metrics). Without the visual tool, it may be difficult to understand why PA levels change so significantly between time points, with no identifiable changes in disease state. This information could also be used by clinicians to encourage patients with similar PA routines to adopt other forms of exercise as seasons change or to inform targeted prehabilitation strategies for patients with consistently light PA routines, potentially resulting in decreased functional decline during periods when patients would normally be highly sedentary. The heat maps shown in the present study were interpreted qualitatively, however future efforts should incorporate quantitative temporal activity assessment using pattern recognition tools. This would allow for the incorporation of this information into modeling and quantitative analysis approaches to provide evidence for the specific role of various PA strategies on OA disease and KA outcomes.

The heat map tool presented herein provides a clear and comprehensive representation of PA intensity throughout the day, helping to address the limitations of traditional summary PA metric reporting. The case studies demonstrate the tool's ability to assist clinicians and researchers in identifying unique strategies employed by patients to achieve physical activity targets. The interpretation of these heat maps with patient demographics and outcome measures highlights the clinical utility of visual representations for assessing PA in the context of knee OA. In combination with findings related to the impact of PA intensity on OA symptoms and KA outcomes, this tool presents the potential to better inform treatment decisions and optimize patient care. This novel visualization tool paves the way for a more nuanced and personalized approach to PA tracking, ultimately enhancing clinicians' and researchers' understandings of the relationship between PA and OA in patients awaiting KA.

Chapter 6. Conclusion

6.1. Summary Of Thesis Outcomes

Physical activity (PA) is a relevant metric for the clinical assessment of individuals with end-stage osteoarthritis (OA) awaiting knee arthroplasty (KA), and further research in the field can provide valuable insights of PA in relation to the optimization of patient care. PA has been found to be associated with maintenance of physical function including joint biomechanics, improved quality of life, and improved surgical outcomes. PA is typically captured in research using patient-reported measures such as questionnaires; however, objective PA measurement tools have recently become more popular due to their increasing availability, decreasing size and cost, and literature highlighting the added value of such devices. Despite the recent surge in research centred on objective PA tracking, many areas remain insufficiently explored. The integration of objective PA monitoring tools in the clinical environment with a specific focus on end-stage knee OA patients is one such area. The overall goals of this thesis were to use objective activity tracking devices in this population to assess correlations between objectively-measured PA and patient-specific characteristics, to analyze their relevance for the clinical evaluation of patients in the preoperative period, and to develop a novel activity visualization tool aimed at presenting and analyzing patients' PA with more detail than summary PA metrics alone.

The first objective of this thesis was split into two components, both related to the assessment of PA levels in an end-stage knee OA population through step counts in the preoperative KA period. The first component was the development and testing of an accelerometer-based step detection algorithm appropriate for application in a clinical population of end-stage knee OA patients awaiting KA. Since limited literature was available guiding the development of a custom step detection program for raw accelerometer data, the algorithm underwent a number of iterations, each of which was appropriately tested for face and construct validity. The final step detection algorithm met all of the criteria laid out in the development phase (Section 3.2.6), including data comparison with lab-based video, comparison of detected free-living activity with an activity log, and comparison of detected steps with step counts from an Apple Watch in a free living trial. Step counts were calculated with the final algorithm in the clinical population study and the results were found to be comparable with those previously reported for end-stage knee OA populations. The second component of this objective was to use the developed step detection algorithm in a clinical population study of end-stage knee OA patients awaiting KA to analyze how step counts were associated with sex, body mass index (BMI), patient-reported PA, patient-reported pain, and mental health. As hypothesized, step counts were found to be significantly, negatively associated with BMI and positively associated with PA levels, with high BMI and low self-reported PA being associated with lower step counts. It was also identified that subjectively-measured PA was less specific than objective measures, with 9 individuals reporting their PA as 3/10 yet their objectively-measured average daily step counts ranged from 2325 to 9091. Unexpectedly, step counts of individuals in the population were not found to be impacted by the sex of the participant, nor by their self-reported pain or mental health.

The second objective of this thesis was to analyze how objectively-measured time spent sedentary was associated with sex, BMI, patient-reported PA, patient-reported pain, and mental health in a clinical population study of end-stage knee OA patients awaiting KA. In agreement with the findings from the analysis of associations with step counts, time spent sedentary was found to be significantly, positively associated with BMI and negatively associated with self-reported PA levels, with high BMI and low self-reported PA being associated with more time spent sedentary. Contrary to the findings from objective 1, a significant difference in time spent sedentary was observed between sexes, with females spending significantly more time sedentary than males within the studied sample. Again, sedentary behaviors of individuals in the population were not found to be impacted by participants' self-reported pain or mental health scores.

The third objective of this thesis was to develop a visual 'heat map' tool to represent activity intensity during the 6-day collection period, and to evaluate its added value for the clinical evaluation of PA through a series of case studies. The main finding of this work was the identified utility of the visual PA representation tool for evaluating the varying strategies that individuals in this population used to accumulate steps and non-sedentary time. The case studies presented in this thesis showed three individuals with similar summary PA metrics (step counts and time spent sedentary) but whose PA heat maps were very different upon visual inspection. The heat maps for the case study participants provided detailed information on PA behaviors which would not be clear or easily identifiable in the absence of such a tool.

6.2. Implications Of Thesis Research

The developed custom step detection algorithm (Section 3.2.6) is a valuable tool which can be used for further studies within the overarching research program to quantify PA in the end-stage knee OA population. The described methodology for the program development may also assist in guiding the development of future step detection algorithms for different study protocols and/or populations.

The findings of the clinical population study presented in this thesis will help fill the existing literature gap relating to the associations between objectively-measured physical activity levels and patient-specific characteristics in the end-stage knee OA population. Clinically relevant associations between PA metrics and OA patient characteristics have been identified (Chapter 4), which can help physicians and researchers understand patient quality of life and risk factors in the preoperative period. The added value of objective PA monitoring is also highlighted in the analysis of subjective compared to objective PA outcomes which show that subjective PA measures are less specific and may relate more to perceived PA levels, while objective measures are a more specific representation of actual activity.

The visual tool developed and presented in this thesis (Chapter 5) addresses the limitations associated with summary PA metrics by providing more detailed information on patients' temporal PA intensities. The case studies highlight the utility of evaluating physical activity intensities temporally during the preoperative period. In cases when individuals describe low quality of life associated with decreased ability to participate in physical activities, this type of tool may be useful for clinicians to gain a better understanding of what their PA routines look like, and the specific methods by which they are accumulating or failing to accumulate PA. This tool may also be useful in clarifying seemingly complex associations between an individual's summary PA metrics and other patient-reported outcomes, such as pain and quality of life. Temporal PA assessment may be less relevant for the assessment of individuals who fail to meet published PA guidelines due to clear physical limitations, as summary PA metrics may be enough to inform clinicians of these patients' physical activity levels.

6.3. Study Limitations

It is necessary to address the limitations of this thesis by acknowledging the constraints, weaknesses, and potential sources of bias that may have influenced the outcomes and interpretation of the research.

While the study was powered to report significant findings in the studied sample, a larger sample size would strengthen the applicability of the results reported herein. In particular, based on the sex-specific findings of the clinical study, it would be valuable to investigate the correlations between PA and patient-specific variables separately in males and females; however, a sample size of approximately 40 (20M/20F) would have been required to draw statistically relevant conclusions on this. Furthermore, it would be negligent to report findings from such a small sample size with the impression that they are representative of the entire clinical population, given that a number of clinically-relevant patient characteristics (such as ethnic and socioeconomic diversity and high levels of depression) were not demonstrated in this sample. The clinical population recruited for this thesis represents a small sample of individuals with end-stage knee OA awaiting KA in the Halifax, Nova Scotia, Canada area, and the study's findings may not be generalizable to the population as a whole.

As described in Chapter 4, significant correlations were not observed between PA levels and self-reported pain or mental health, contrary to what was hypothesized for the population [16], [17], [75]. A larger sample size with more variability in demographics and patient-reported outcome measures may clarify these findings to determine if they are reflective of the general population of individuals with end-stage knee OA awaiting KA or if they are specific to the sample population observed. For instance, as described in section 4.4, non-correlations between PA levels and mental health may have been caused by the study sample having generally low levels of depression compared to the population (14.3% of participants in the present study reporting moderate to severe depressive symptoms compared to reported values in similar populations near 25.8% [185]), it may have been attributed to population-wide underreporting of depressive symptoms, or it may be a valid reflection of the lack of associations between PA and mental health. It should also be noted that the reliability of patient-reported measures should always be considered, particularly in a population of older adults with chronic health conditions. The possibility always exists that participants' self-reports may be inaccurate or non-reflective of their true state due to the misconception that over-reporting symptoms will improve their likelihood of timely care [189] or because they lack the required knowledge to adequately self-assess through questionnaires [135], [187], [188]. In the present study, this limitation was mitigated as best as possible by selecting self-report questionnaire that have been tested and validated for the study population, however the inherent subjectivity of patient-reports in general highlights the need to ensure that participants are adequately educated on the purpose and meaning of each questionnaire they complete.

There were also limitations to this thesis associated with the analysis techniques used. While the step detection algorithm developed (Chapter 3) was tested for face and construct validity, a structured validation study in the clinical study population would verify the validity and reliability of the program for step detection. Furthermore, the sample size did not allow for multivariate analysis, which may have provided further insights on the associations between patient-specific characteristics and objectively-measured physical activity levels in the population. It is also noted that the intensity cut-off thresholds (Table 2) were developed for IMU placement on the thigh rather than the shank,. While these intensity threshold values were developed from the closest protocol that could be identified in literature to the present study, it is likely that activity intensity levels in the clinical study population were overestimated based on this limitation. For the temporal assessment of PA described in Chapter 5, further analyses using pattern recognition techniques are required to unveil the added value of such a tool in quantitative assessments of PA strategies and their clinical relevance in the population.

Furthermore, seasonable variability in physical activity levels (related to changes in weather and daily routines) was not controlled for in this study. Seasonable variability is a relevant factors in PA assessment [205], [206], including in those with osteoarthritis [207]. As identified in Section 5.4, seasonal activities (including participation in sports, and employment-related and personal obligations) may account for significant portions of daily PA accumulation which may vary between seasons. Interpretations of baseline PA levels and future analysis of changes in individual PA levels should consider this seasonal variability.

6.4. Recommendations and Future Work

The findings of this thesis suggest that clinicians and researchers should consider incorporating objective PA assessment into the preoperative KA assessment, as it has been shown to be associated with factors known to be related to OA disease state and to provide valuable information on patient quality of life. Furthermore, while objective PA assessment is significantly associated with subjective PA metrics, the present study suggests that objective measurements are more specific and may more accurately represent actual physical activity levels. Objective assessment of PA in this population should also be as detailed as possible because, as shown in this thesis, summary PA metrics may not be specific enough to capture all potentially clinically relevant characteristics of PA behaviors. Furthermore, the correlations identified between PA levels and sex and BMI highlight the clinical relevance of considering the distinct challenges faced by individuals with these characteristics. These findings suggest that clinicians should consider tailoring their pre-operative assessment and disease management strategies for such patient characteristics to optimize preoperative patient care and potentially improve KA outcomes in the population.

Future work in this field should attempt to address the limitations mentioned in Section 6.3. The sample size and single collection site limitations can be addressed by recruiting from multiple centres which all follow a common data collection and processing protocol. Active and strategic promotion of the research program in the study population is essential to optimize participant enrollment. The limitations associated with lack of diversity in demographics can also be addressed by recruiting from multiple sites, with a specific emphasis on targeting patients with varying ethnicities, cultures, and socioeconomic backgrounds for recruitment.

As the overarching robotics research program progresses, objective PA data will continue to be collected. Similar analysis on the associations between objectively-measured PA and patient-specific variables will be done as more participants are recruited. Participant PA data will also be collected longitudinally throughout the preoperative period and into the postoperative period, allowing for the identification of changes in PA and how these changes may relate to surgical outcomes. This analysis will provide insight on the associations between objectively-measured physical activity and clinical disease state, joint-related function, and overall patient quality of life. A thorough understanding of the role of PA in the presentation and progression of OA will allow clinicians to better assess patient disease state which will facilitate better management of patient KA expectations and may help inform patient-specific surgical planning. Moving forward, the research team also aims to assess free-living joint kinematics with a multi-sensor IMU protocol. Multi-centre recruitment has recently begun, as the research team connects with patients from both the Halifax Infirmary and Dartmouth General Hospital, which should increase the rate of participant enrollment and diversify the sample population. As study participants receive KA, the research team will combine preoperative patient data (including PA assessments from this thesis) with interoperative data from the MAKO surgical robotic tool and information collected postoperatively with the goal of identifying how preoperative and interoperative factors are associated with patient-specific surgical outcomes. By the conclusion of the overarching robotics research program the OA condition will be more thoroughly understood on a patient-specific level, providing the opportunity to customize KA surgeries to each patient in an effort to improve surgical outcomes of the population as a whole.

6.5. General Thesis Conclusion

The findings of this thesis provide valuable information on data processing techniques for step detection from raw accelerometry data, and associations between objectively-measured PA measures and clinically relevant patient-specific characteristics in a population of end-stage knee OA patients awaiting KA. The presentation of a novel PA visualization tool is another valuable outcome of this thesis. The work presented herein will contribute to the field of research on objective PA assessment for clinical populations by describing data processing and presentation methodologies and providing insight on statistically significant correlations between PA measures and patient characteristics. It will also contribute to the field of orthopedics, specifically in relation to OA and KA, by providing further insights on the relevance of the identified associations between PA and patient-specific variables in a clinical context.

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Appendix A. Patient-Reported Outcome Measures

UCLA Activity Score

- ☐ 1. Wholly inactive: dependent on others; cannot leave residence
- ☐ 2. Mostly inactive: very restricted to minimum activities of daily living
- ☐ 3. Sometimes participates in mild activities such as walking, limited housework, and limited shopping
- ☐ 4. Regularly participates in mild activities
- ☐ 5. Sometime participates in moderate activities such as swimming and can do unlimited housework or shopping
- ☐ 6. Regularly participates in moderate activities
- ☐ 7. Regularly participates in active events such as bicycling
- ☐ 8. Regularly participates in very active events such as bowling or golf
- ☐ 9. Sometimes participates in impact sports such as jogging, tennis, skiing, acrobatics, ballet, heavy labor, or backpacking
- ☐ 10. Regularly participates in impact sports

OKS-PCS

Question	Score				
	4	3	2	1	0
How would you describe the pain you usually have from your knee?	None	Very mild	Mild	Moderate	Severe
For how long have you been able to walk before the pain from your knee becomes severe (with or without a stick)	No pain >30 min	16 - 30 min	5 - 15 min	Around the house only	Not at all- severe on walking
After a meal (sat at a table), how painful has it been for you to stand up from a chair because of your knee?	Not at all painful	Slightly painful	Moderately painful	Very painful	Unbearable
Have you been limping when walking, because of your knee?	Rarely/ never	Sometimes/ just at first	Often/ not just at first	Most of the time	All of the time
Have you been troubled by pain from your knee in bed at night?	Not at all	Only one or two nights	Some nights	Most nights	Every night
How much has pain from your knee interfered with your usual work (including housework)?	Not at all	A little bit	Moderately	Greatly	Totally
Have you felt that your knee might suddenly "give way" or let you down?	Rarely/ never	Sometimes or just at first	Often or not at first	Most of the time	All the time

PHQ-8

Over the last 2 weeks, how often have you been bothered by any of the following problems?				
How often during the past 2 weeks were you bothered by...	Not at all	Several days	More than half the days	Nearly every day
Little interest or pleasure in doing things	0	1	2	3
Feeling down, depressed, or hopeless	0	1	2	3
Trouble falling or staying asleep, or sleeping too much	0	1	2	3
Feeling tired or having little energy	0	1	2	3
Poor appetite or overeating	0	1	2	3
Feeling bad about yourself, or that you are a failure, or have let yourself or your family down	0	1	2	3
Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
Moving or speaking so slowly that other people could have noticed. Or the opposite being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3

Appendix B. Step Detection Algorithm Validation Data

1. Comparison with video: The following dataset shows the first 20 steps compared between video and the step detection algorithm for 2 of the 8 completed trials; (a) Barefoot, and; (b) Shod. The step location numbers shown in the tables indicate the sample number where steps were observed. For context, the sampling frequency was 100 Hz.

(a) Barefoot

Time syncing:	**5th stomp (video):**	3.603
	5 stomp (data):	52534
	Offset:	52174

Step #	**Video time (s)**	**Expected step location (video)**	**Detected step location (algorithm)**	**Difference (1/100th second)**
1	5.705	52744	52746	2
2	6.289	52803	52804	1
3	6.94	52868	52872	4
4	7.59	52933	52928	-5
5	8.191	52993	52997	4
6	8.792	53053	53047	-6
7	9.409	53115	53118	3
8	10.076	53181	53173	-8
9	10.677	53241	53244	3
10	11.327	53306	53286	-20
11	12.045	53378	53378	0
12	12.696	53443	53441	-2
13	13.396	53513	53516	3
14	14.03	53577	53575	-2
15	14.731	53647	53651	4
16	15.398	53714	53707	-7
17	16.116	53785	53790	5
18	16.816	53855	53850	-5
19	17.567	53930	53932	2
20	18.284	54002	53976	-26

Steps counted (algorithm)	130
Steps taken (video)	130
% error	0

(b) Shod

Time syncing:	**5th stomp (video):**	5.388
	5 stomp (data):	3258
	Offset:	2719.2

Step #	**Video time (s)**	**Expected step location (video)**	**Detected step location (algorithm)**	**Difference ($1/100^{th}$ second)**
1	7.707	3490	3488	-2
2	8.36	3555	3556	1
3	9.071	3626	3617	-9
4	9.634	3683	3681	-2
5	10.212	3740	3738	-2
6	10.896	3809	3803	-6
7	11.917	3911	3907	-4
8	12.603	3980	3977	-3
9	13.268	4046	4036	-10
10	13.837	4103	4103	0
11	14.568	4176	4165	-11
12	15.217	4241	4229	-12
13	15.797	4299	4287	-12
14	16.388	4358	4355	-3
15	17.213	4441	4423	-18
16	17.883	4508	4493	-15
17	18.637	4583	4569	-14
18	19.302	4649	4637	-12
19	19.936	4713	4703	-10
20	20.653	4785	4773	-12

Steps counted (algorithm)	119
Steps taken (video)	120
% error	0.833

2. Comparison with activity log: The activity log (Supplemental Figure 1) and processed accelerometer data is shown below. Supplemental Figure 2 shows where errors were identified before the data processing algorithm was finalized and Supplemental Figure 3 shows after program finalization.

Activity Log – April 27, 2023

7:00 - got up

10:22 - got ready and made breakfast

10:50 - arrived at school

11:45 - walked to seminar

12:45 - walked back from seminar

2:40 - walked around building

3:30 - walked to dentist

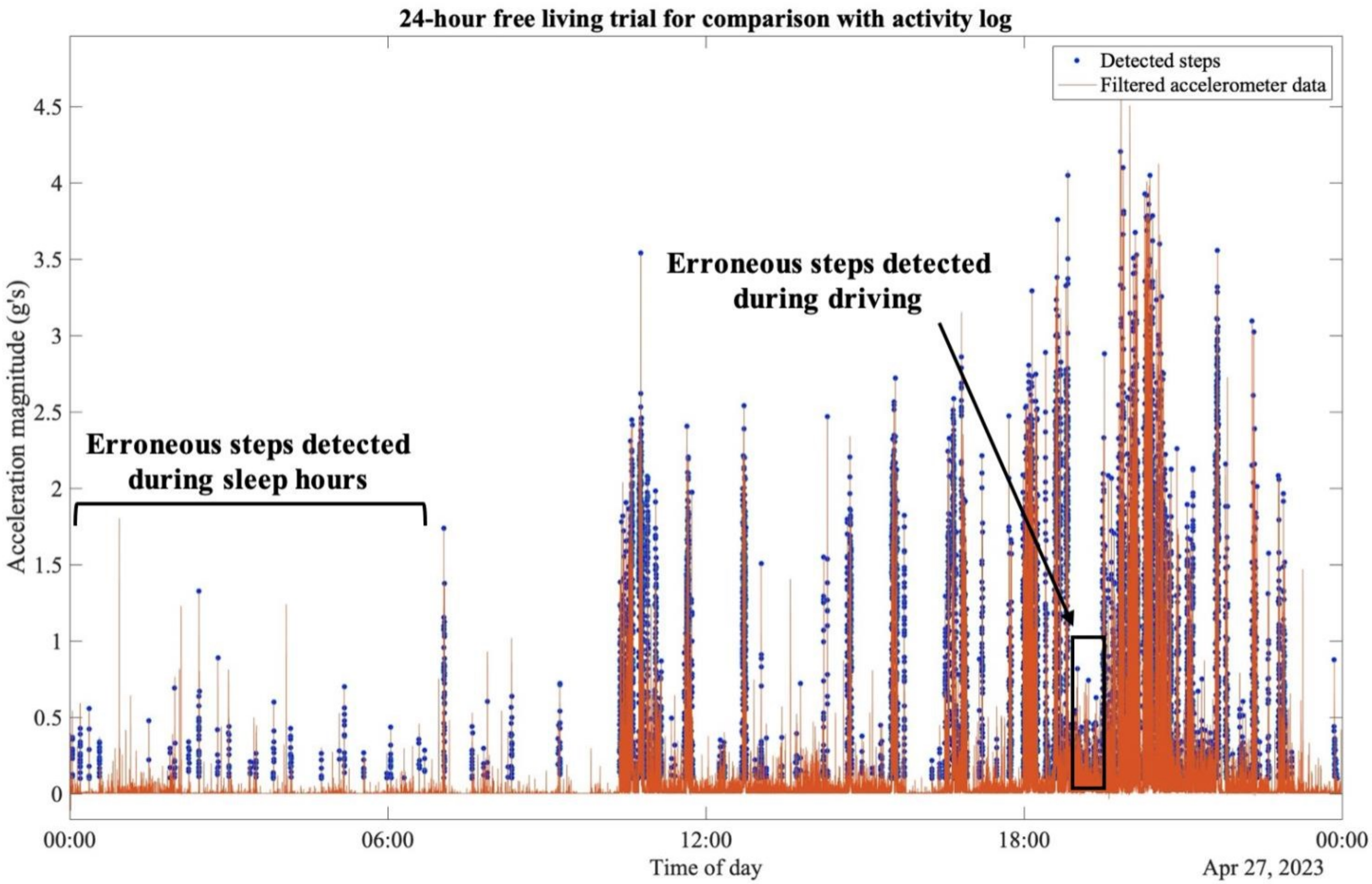
6:10 - walked dog

6:36 - walked to get car

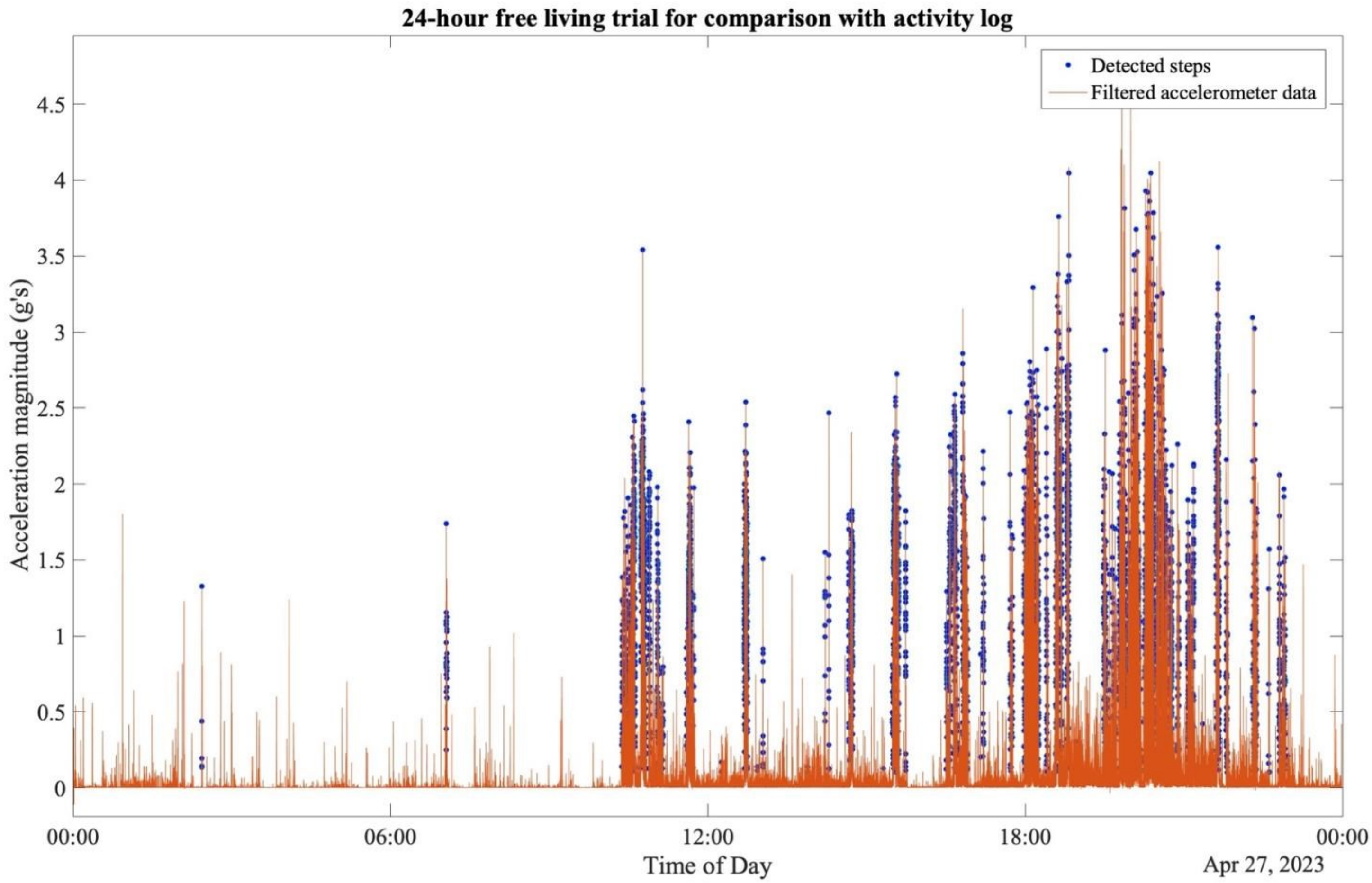
7:30 - arrived at laser tag

10:55 - bed

Supplemental Figure 1: Activity log for comparison with step detection algorithm.

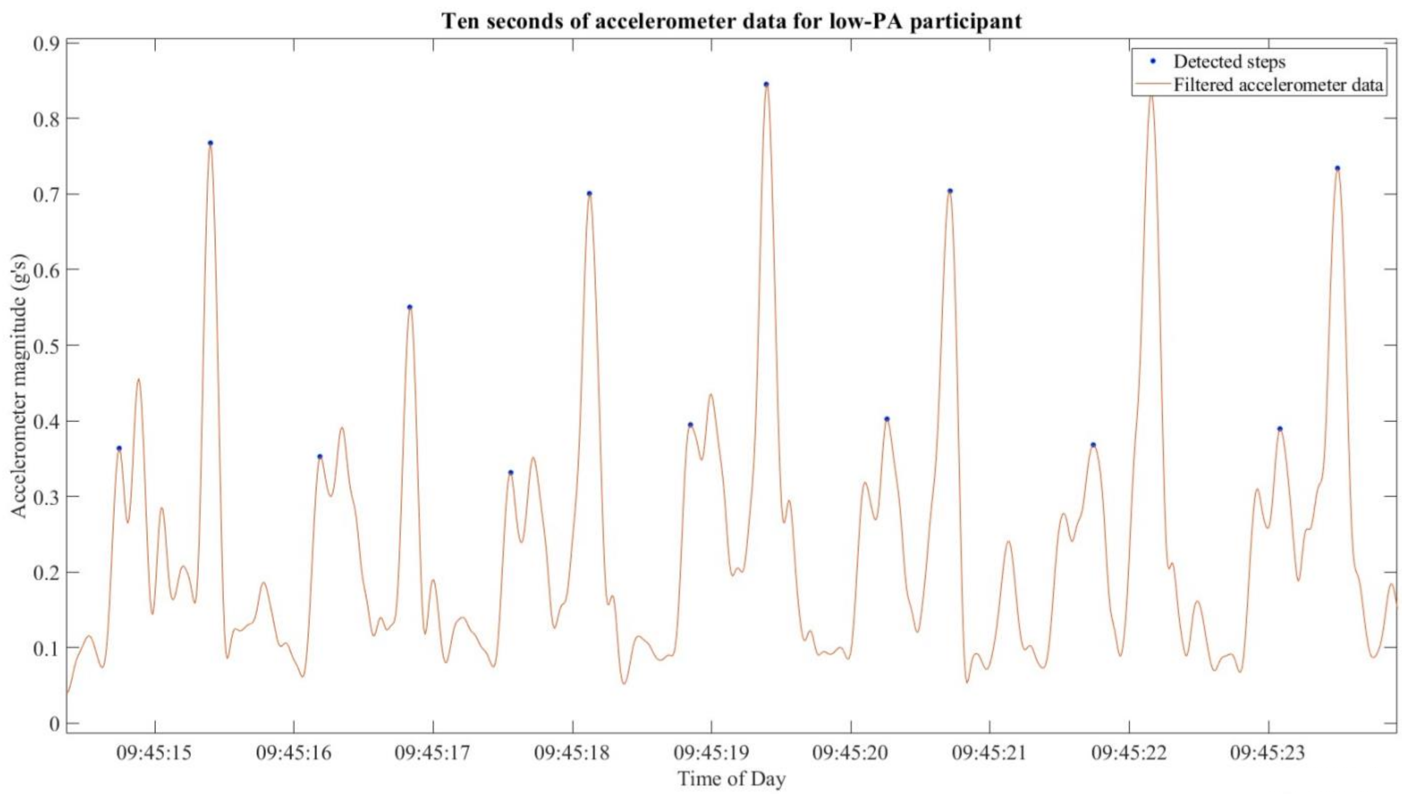


Supplemental Figure 2: 24-hour free living accelerometer data with identified times of disagreement with activity log.

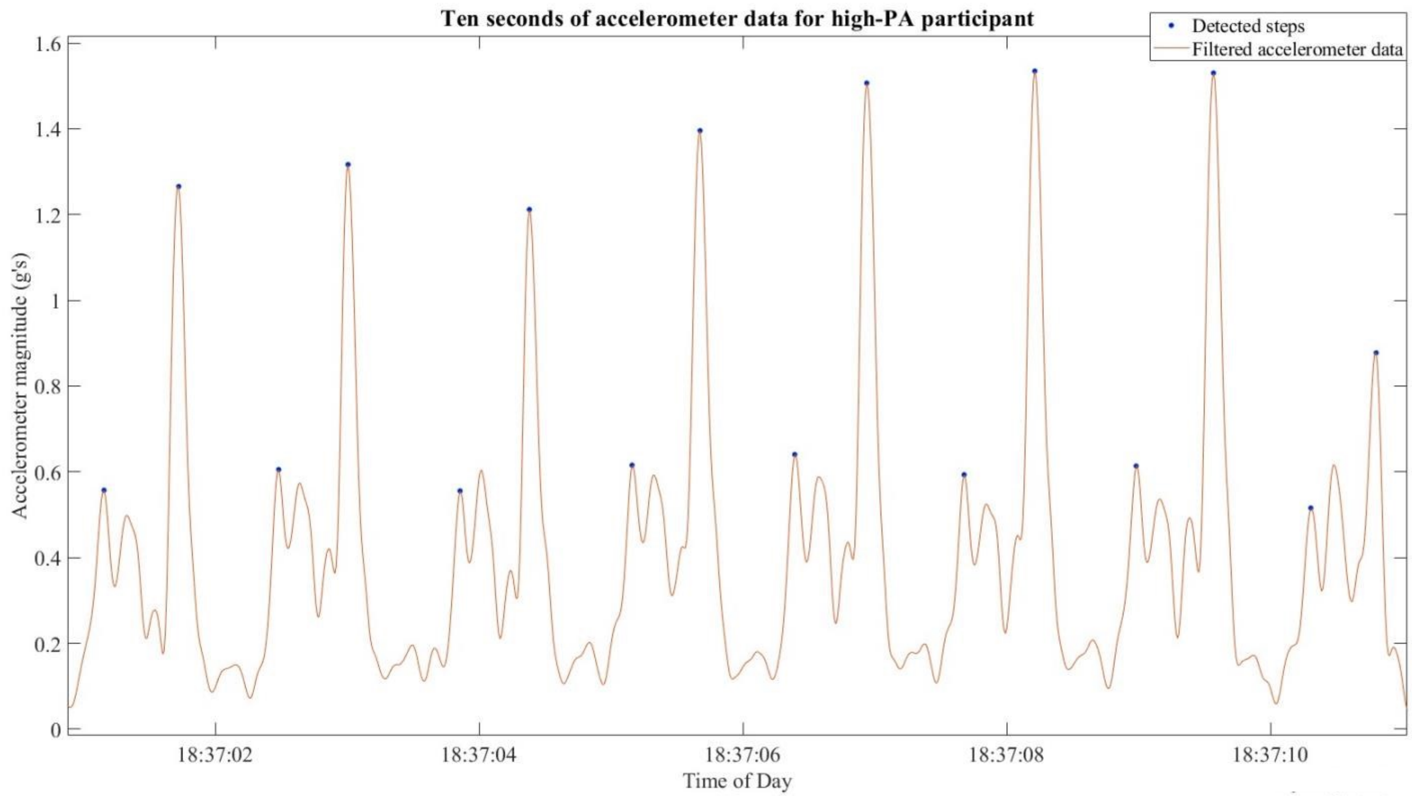


Supplemental Figure 3: 24-hour free living accelerometer data after correcting for identified errors.

3. Visual inspection of data from clinical population study: The images below show 10 second of filtered accelerometer data (showing locations of step detection) from the least active (Supplemental Figure 4) and most active (Supplemental Figure 5) participant of the first 10 recruited for the clinical population study.



Supplemental Figure 4: Ten seconds of filtered accelerometer data for the least active of the first 10 participants recruited for the clinical population study (68 year old female end-stage knee OA patient awaiting KA at the Halifax Infirmary, average 2002 steps/day and 90.4% of day sedentary). Blue dots indicate where steps were detected by the developed algorithm.



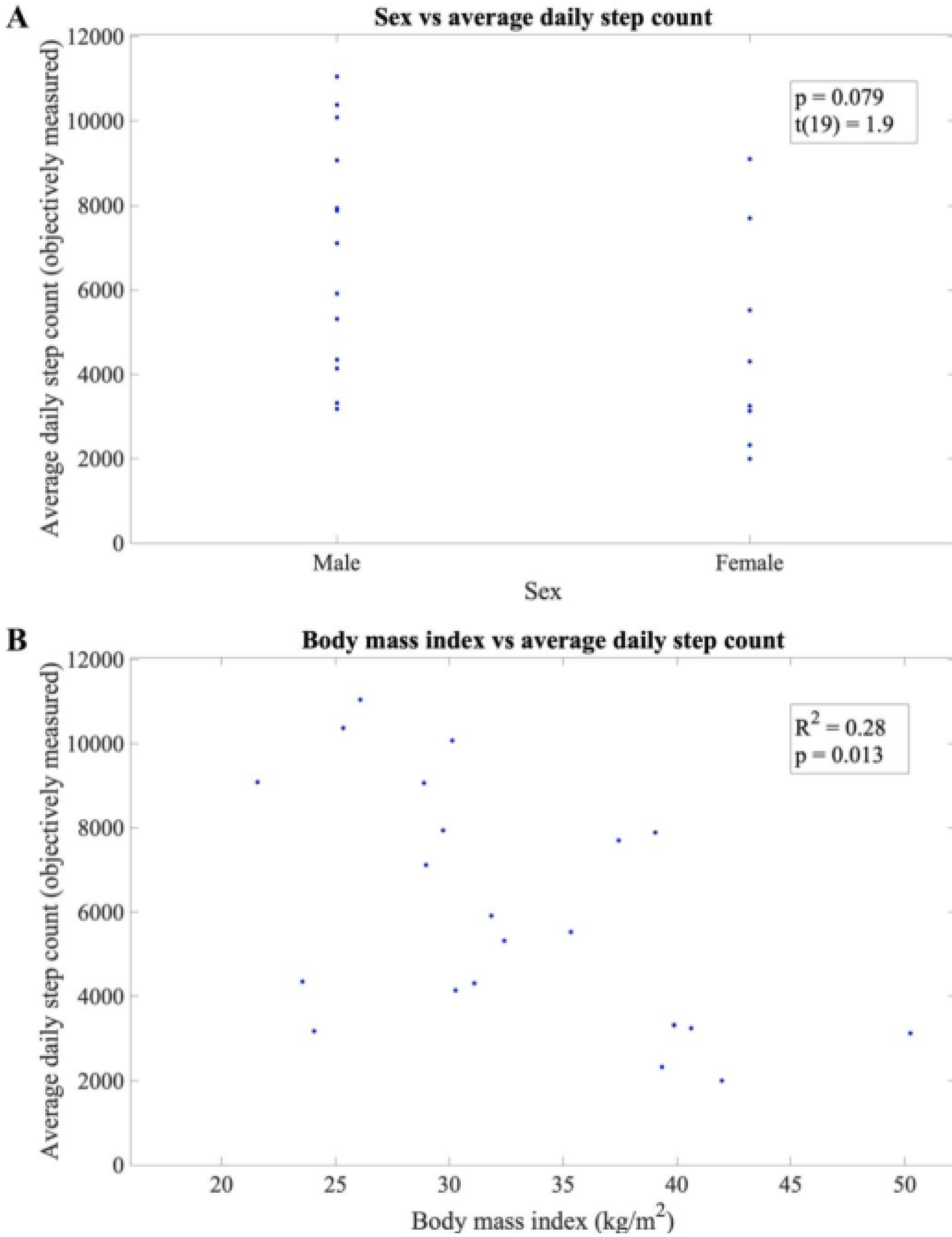
Supplemental Figure 5: Ten seconds of filtered accelerometer data for the most active of the first 10 participants recruited for the clinical population study (65 year old male end-stage knee OA patient awaiting KA at the Halifax Infirmary, average 10081 steps/day and 70.7 % of day sedentary). Blue dots indicate where steps were detected by the developed algorithm.

Appendix C. Self-Reported Medication Usage in Clinical Study

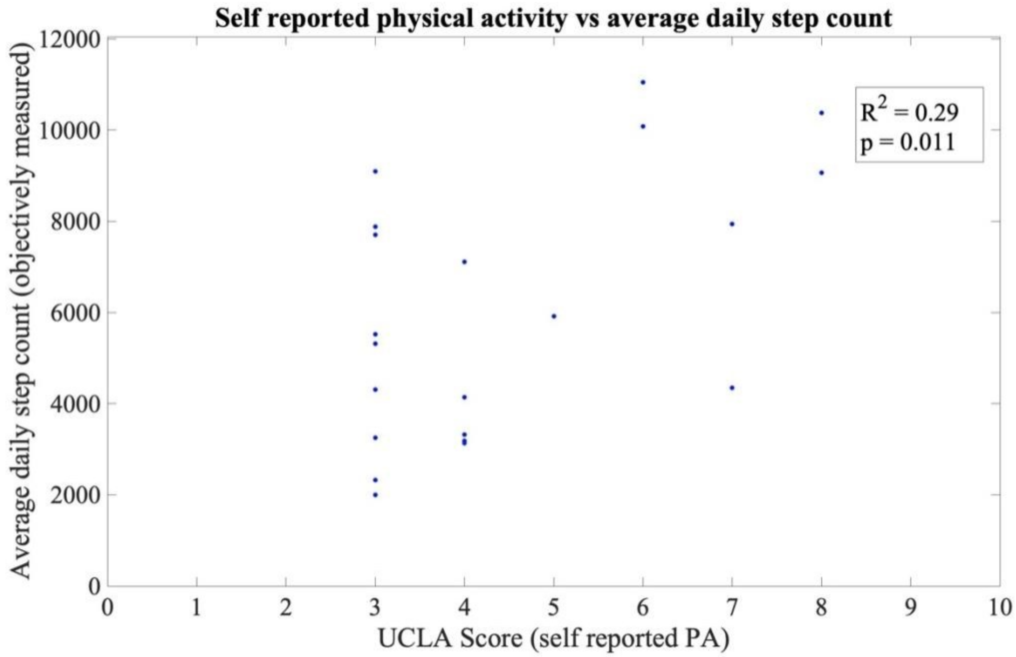
	Never Use (%)	Intermittent Use (%)	Daily Use (%)
Over the counter	9.5	28.6	61.9
NSAID	52.4	23.8	23.8
Narcotic	90.5	4.8	4.8

Supplemental Table 1: Self-reported use of medication for pain management in the clinical study population. Percentage of participants who selected each item is shown.

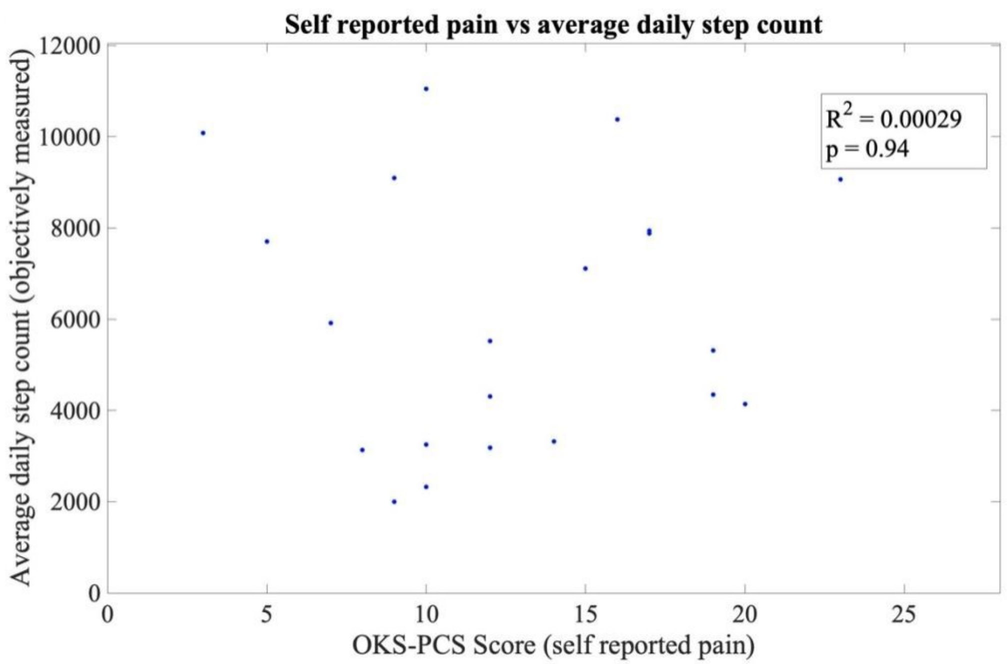
Appendix D. Physical Activity Correlation Graphs

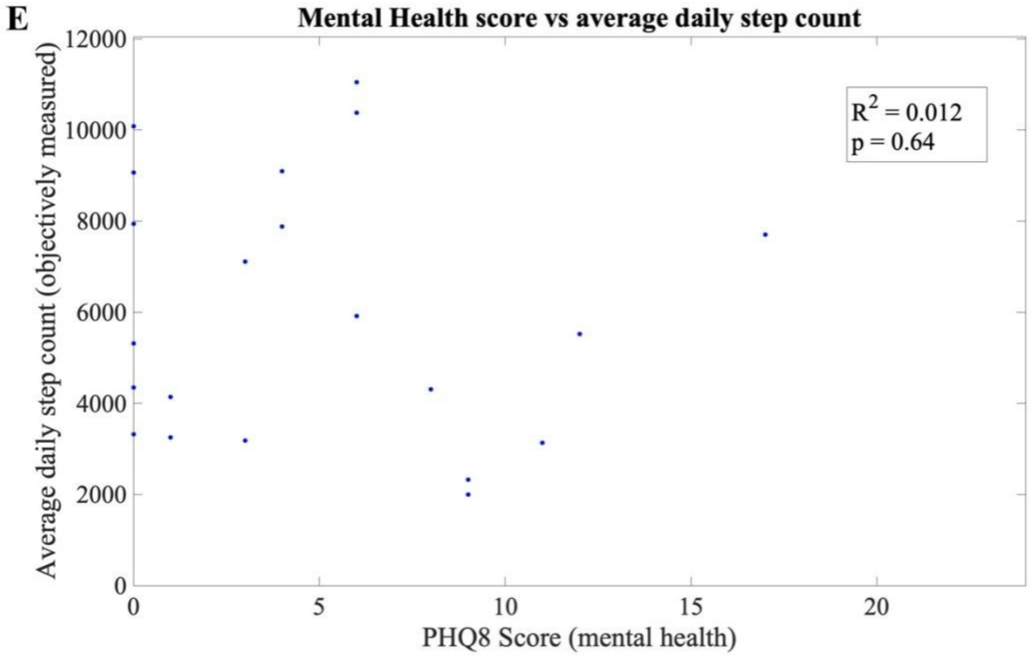


C


Self reported physical activity vs average daily step count
Average daily step count (objectively measured)
12000
10000
8000
6000
4000
2000
0
0
1
2
3
4
5
6
7
8
9
10
UCLA Score (self reported PA)
$R^2 = 0.29$
$p = 0.011$

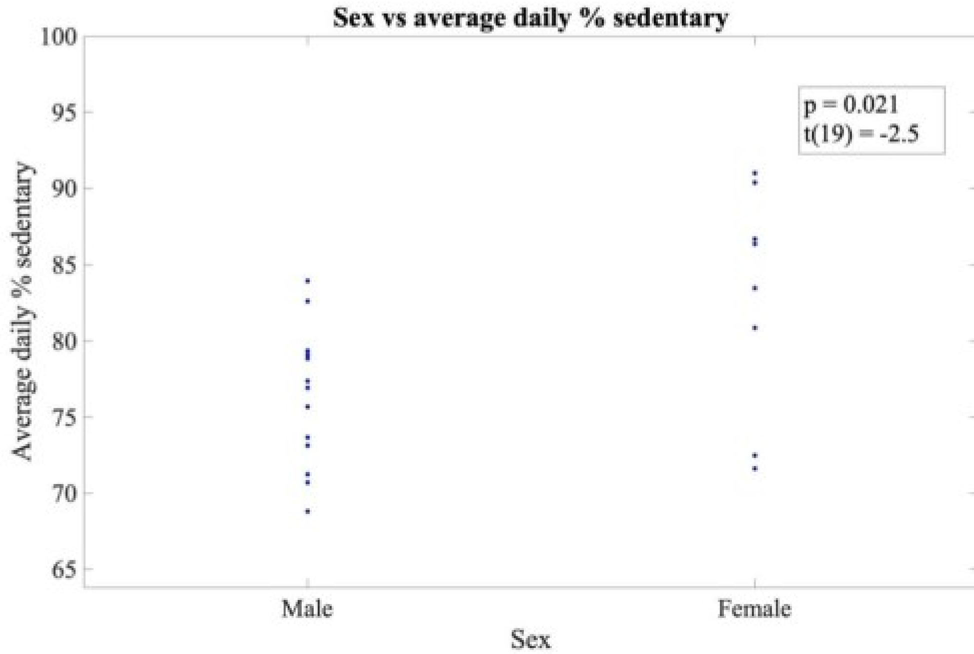
D


Self reported pain vs average daily step count
Average daily step count (objectively measured)
12000
10000
8000
6000
4000
2000
0
0
5
10
15
20
25
OKS-PCS Score (self reported pain)
$R^2 = 0.00029$
$p = 0.94$



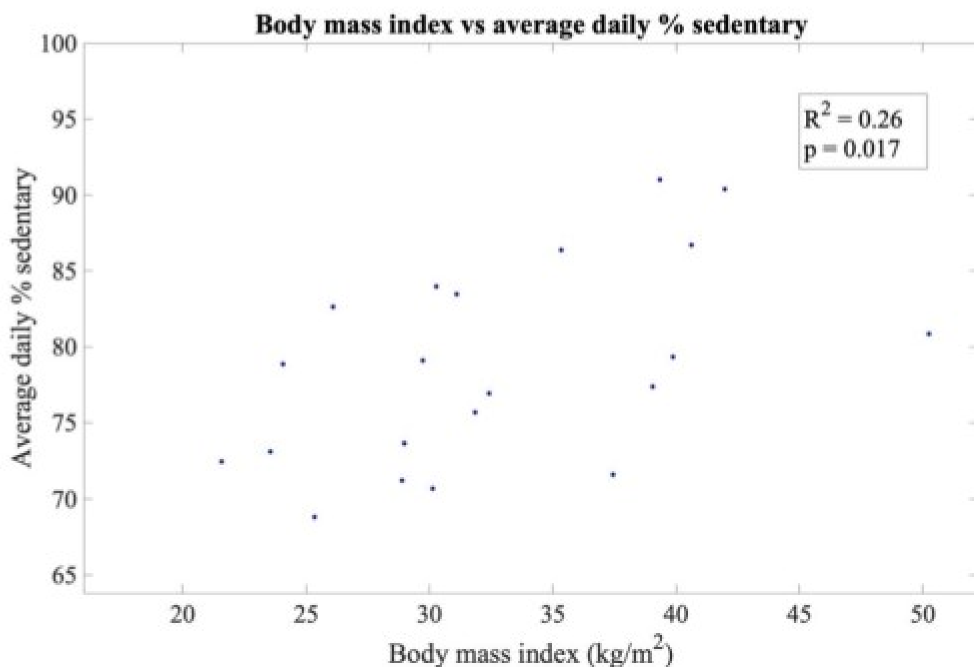
Supplemental Figure 6: Average daily step counts by patient-specific characteristics and their calculated correlation values. (A) Sex; (B) Body mass index (kg/m^2); (C) Self-reported physical activity level (1-10 scale UCLA Activity Score: 1 being little to no movement throughout the day, 10 being regular participation in high intensity activities); (D) Self-reported pain (0-28 scale OKS-PCS: 0 being constant severe pain related to knee OA, 28 being no pain at all relating to knee OA); (E) Mental Health Score (0-24 scale PHQ-8; 0 being no signs of poor mental health, 24 being severe signs of depression).

A



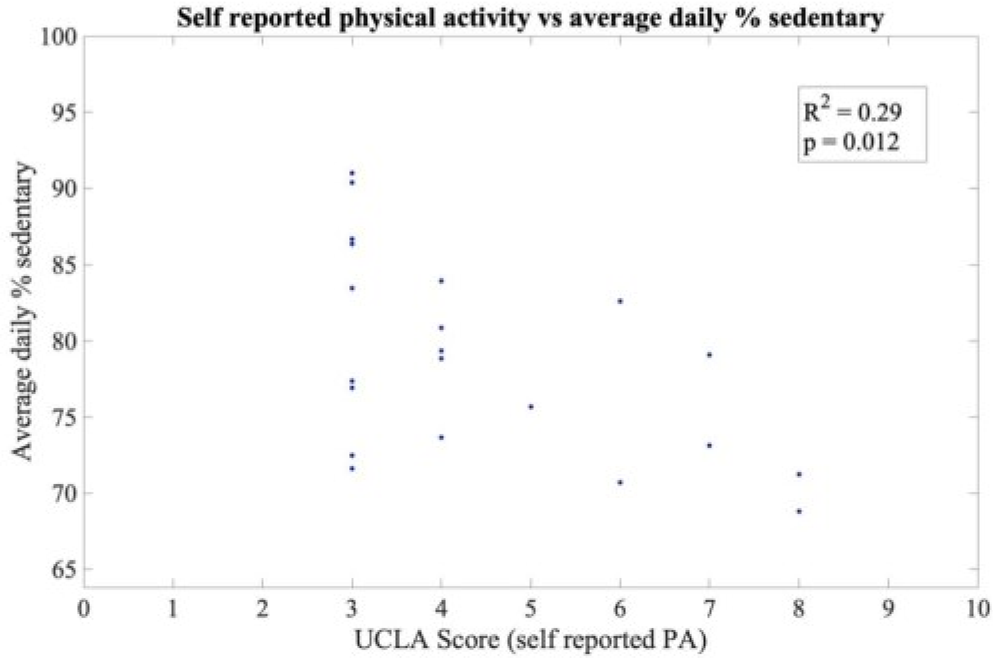
Sex vs average daily % sedentary
p = 0.021
t(19) = -2.5
Average daily % sedentary
100
95
90
85
80
75
70
65
Male
Female
Sex

B



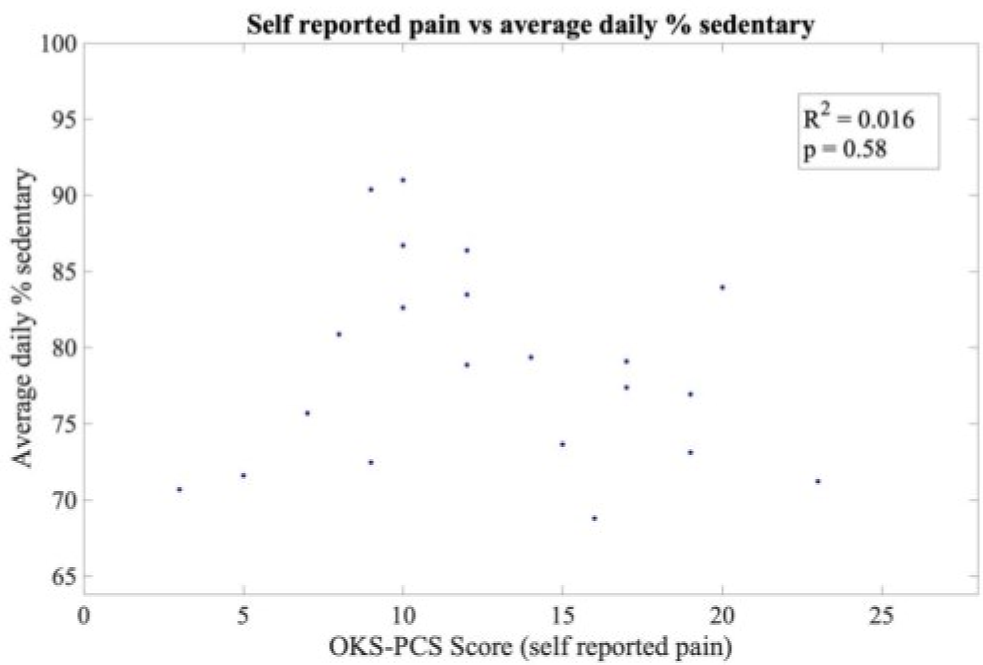
Body mass index vs average daily % sedentary
$R^2 = 0.26$
p = 0.017
Average daily % sedentary
100
95
90
85
80
75
70
65
20
25
30
35
40
45
50
Body mass index (kg/m^2)

C

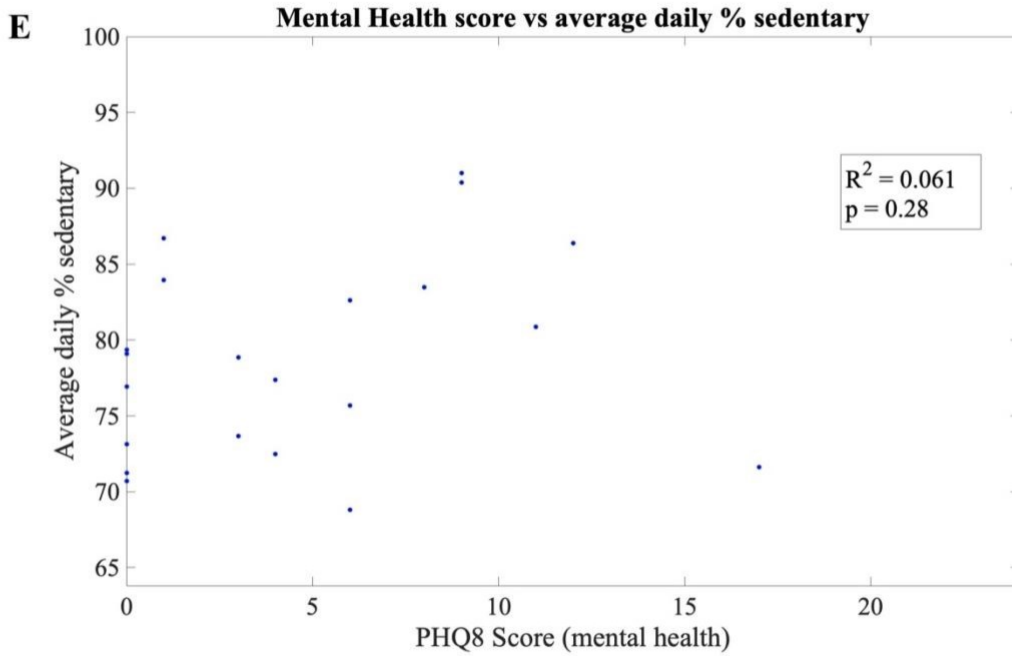


Self reported physical activity vs average daily % sedentary
R^2 = 0.29
p = 0.012
Average daily % sedentary
UCLA Score (self reported PA)
100
95
90
85
80
75
70
65
0
1
2
3
4
5
6
7
8
9
10

D

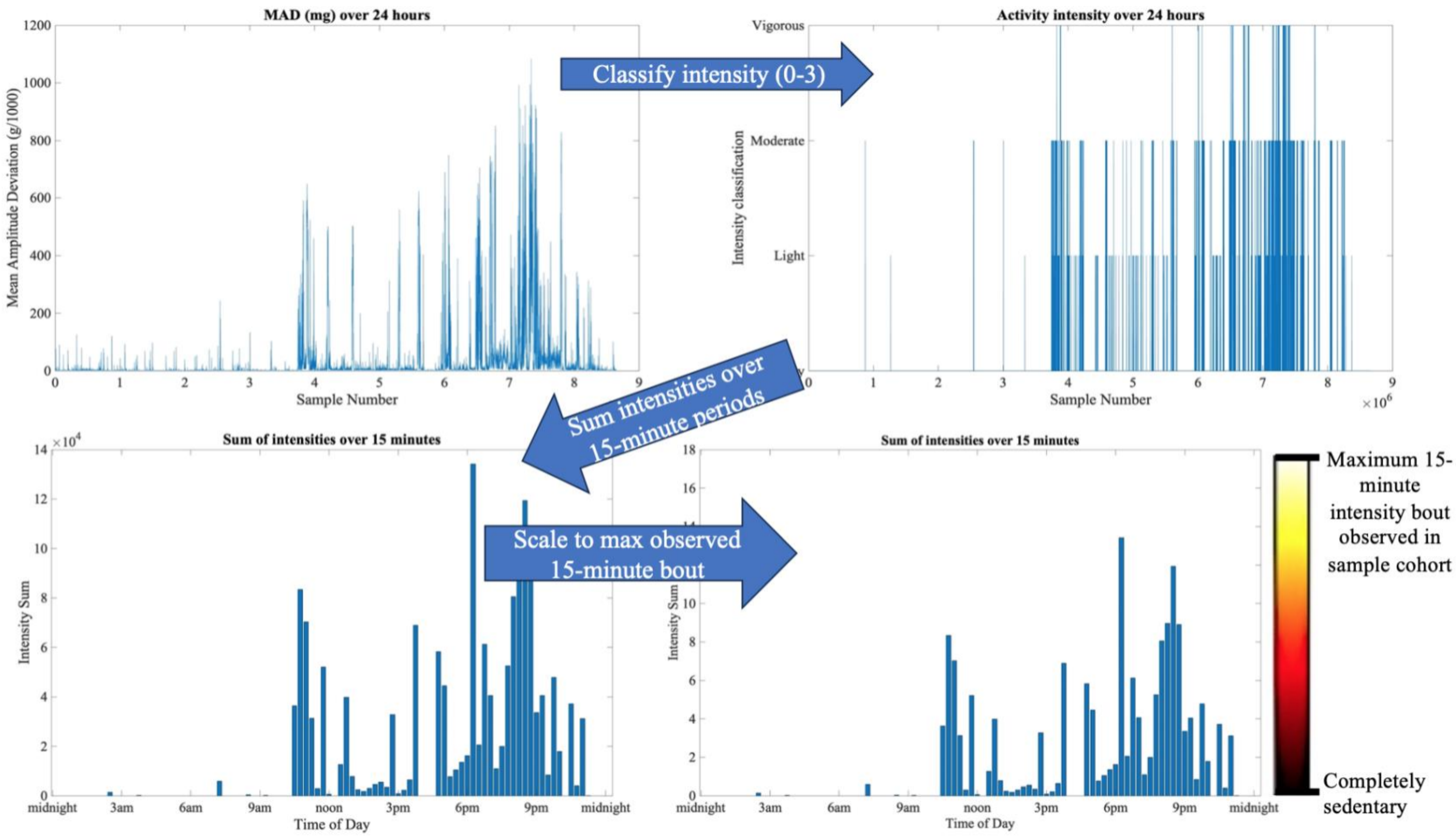


Self reported pain vs average daily % sedentary
R^2 = 0.016
p = 0.58
Average daily % sedentary
OKS-PCS Score (self reported pain)
100
95
90
85
80
75
70
65
0
5
10
15
20
25

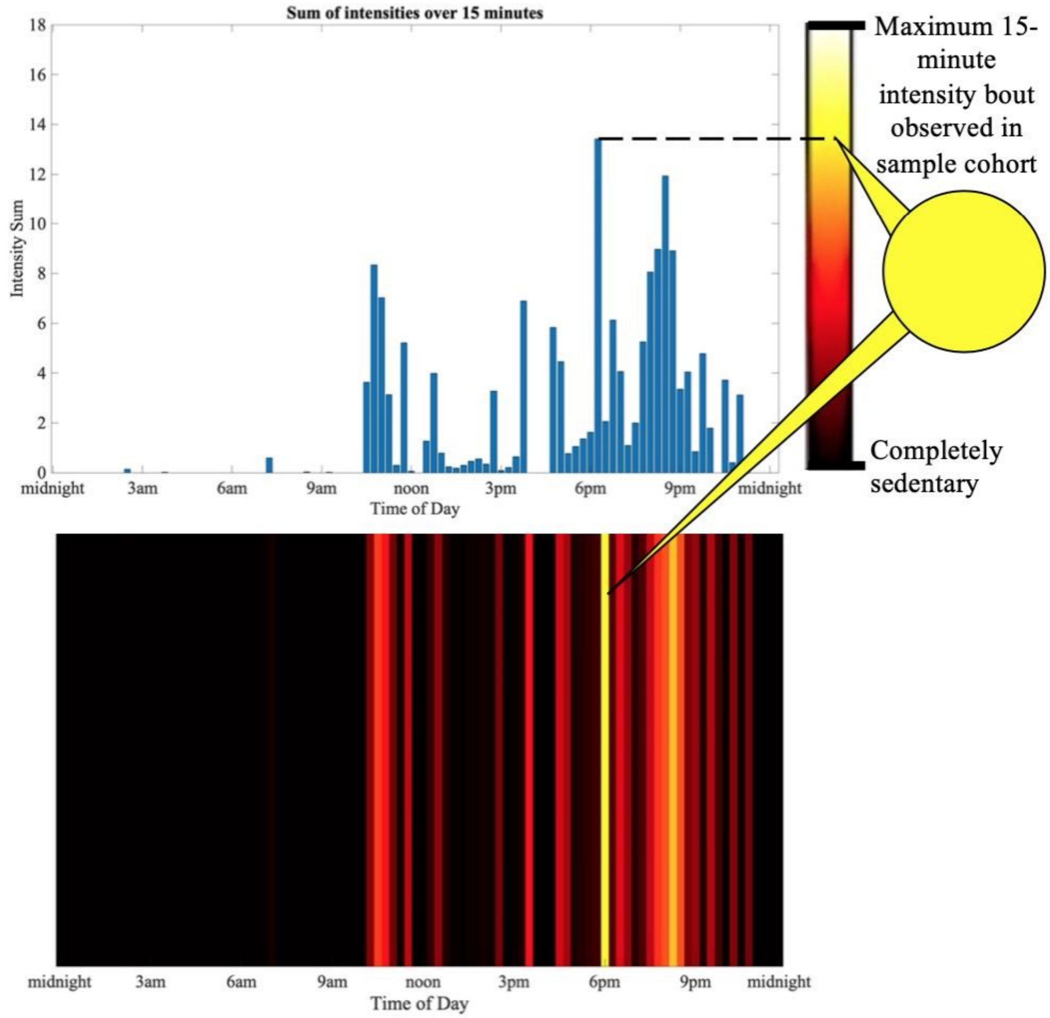


Supplemental Figure 7: Average percent of day spent sedentary by patient-specific characteristics and their calculated correlation values. (A) Sex; (B) Body mass index (kg/m^2); (C) Self-reported physical activity level (1-10 scale UCLA Activity Score: 1 being little to no movement throughout the day, 10 being regular participation in high intensity activities); (D) Self-reported pain (0-28 scale OKS-PCS: 0 being constant severe pain related to knee OA, 28 being no pain at all relating to knee OA); (E) Mental Health Score (0-24 scale PHQ-8; 0 being no signs of poor mental health, 24 being severe signs of depression).

Appendix E. Data Processing Steps for Heat Maps



Supplemental Figure 8: Data processing steps involved in the development of the heat maps for objective 3.



Supplemental Figure 9: Image of how processed data is translated to colours for the heat maps.