Knee joint kinematics associated with osteoarthritis in an older cohort

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Abstract

Osteoarthritis (OA) is a degenerative joint condition that affects roughly one third of adults over the age of 60. In the UK, this amounts to over 8 million people with the total cost of the disease to the economy estimated at £12 billion. Symptoms can include joint pain, stiffness, effusion (swelling of the affected joint) and reduced mobility.

Whilst the symptoms and diagnosis of the disease have been clearly defined in medical research, the underlying causes are not yet fully understood. It is thought that biomechanical factor's, and walking kinematics in particular, play a key role in OA aetiology. Furthering the understanding of these factors could lead to better treatments and help reduce prevalence through preventative measures.

A gait analysis protocol suitable for a clinical environment was developed to analyse the Newcastle Thousand Families Study birth cohort. This presented a unique opportunity to study an existing cohort of adults who are representative of the overall population. Gait analysis was performed on every able cohort member who attended for clinical assessment over a period of 16 months.

Females showed more significant differences in their gait than males. Of the differences found in males, most were found to be associated with altered cadence. Some variables among female participants were found to be associated with altered cadence, as well as body mass index (BMI), pain and stiffness. It was concluded that female gait is more susceptible to kinematic changes but that these changes are adaptations that slow disease progression. Males do not make these adaptations and show higher prevalence at later OA grades. Differences in cadence were thought to account for most differences in gait kinematics with BMI, pain and stiffness also contributing.

Overall, none of the variables measured seem likely to have caused the initiation of OA, however there is potential that the variables showing significant associations between grade 0 and 1 (particularly cadence) could be used for the prediction of OA incidence from gait and could be used as a supporting measure for other diagnostic tools.

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Chapter 1 Introduction

Gait analysis in a clinical environment can lend an objective and quantitative aspect to diagnoses, providing a clear and repeatable definition of variables defining a pathological condition. It can also offer insight into the underlying causes of conditions that are unclear from the symptoms presented, allowing the roots of a disease to be pinpointed and a more effective treatment or intervention designed.

1.1 Osteoarthritis

Osteoarthritis (OA) is a degenerative joint condition that affects roughly one third of adults over the age of 65. In the UK this amounts to over 8 million people [1], and in the US the figure is in excess of 28 million [2]. Symptoms can include joint pain, stiffness, effusion (swelling of the affect joint) and reduced mobility. In day-to-day terms, the effects can range from a joint that occasionally aches or is painful to walk on; to a severe pain that causes a significant detrimental effect on the lifestyle and quality of life of the sufferer. Severe cases of OA can be debilitating and often call for the affected joints to be replaced, but less severe OA can also have a significant impact on a person's life as a painful joint may dissuade the sufferer from physical activity.

Whilst the symptoms and diagnosis of the disease have been clearly defined in medical research, the underlying causes are not yet fully understood. Links have been established between OA and several factors, the first and foremost being ageing [3]. Joint injury from unexpected loading has also been connected to the initiation of OA, as bone remodelling occurs as the joint repairs itself. Body-mass index (BMI) has a well-established link with the incidence of OA with obese individuals more likely to develop OA [4]. Further, there is also evidence pointing to genetic factors playing a role in OA incidence [5]. It is also thought that biomechanical factors play a key role in OA incidence and are in fact linked to all of the factors mentioned so far. Additional mass will increase the loading within a joint and has the potential to cause damage. The sports that people play throughout their lives could also be causing joint damage and providing a site for OA to take hold [6].

OA starts with the degradation of cartilage within the joint. The cartilage forms part of an articulating structure. When surfaces move against one another there is the potential for damage to occur to either surface through friction. Therefore any movement of the joint has the potential to cause damage to the cartilage, and abnormal movement of the joint beyond what it is optimised for is likely to cause even more severe damage. Walking is one of the most common movements we all perform, and there is the potential that a person’s walking style may damage their cartilage and thus cause the initiation of OA.

Osteoarthritis is a progressive disease. Once OA initiates it will continue to develop within the affected joint and in almost all cases the symptoms will become increasingly acute [7]. We also live in an ageing population [8], with life expectancy increasing, so people are living longer and want to maintain the same quality of life. The progressive nature of the disease, in combination with this accelerating longevity in the UK, means that osteoarthritis treatment already places a substantial demand on healthcare services, and this will only increase in the future. Furthering understanding of how gait may be contributing to the initiation of OA is a first step to preventing it altogether, and it has been suggested that biomechanical factors form the core of the problem [9]. Establishing biomechanical factors as being involved in the initiation of OA could lead to better treatments for patients, maintaining quality of life as people age and reducing prevalence of the disease through pre-emptive measures.

1.2 Initiation

The first consideration when looking at the initiation of OA is that there are two types of OA, with different mechanisms of initiation; primary OA, where the initiation mechanism is not yet understood, and secondary OA, where damage to the joint from an event in life (e.g. breaking a bone) causes the disease to initiate [7]. As the initiation mechanism for secondary OA has already been identified, this study focused on identifying biomechanical factors which could have caused primary OA initiation.

Initiation of a disease is something that is hard to measure biomechanically as even if data were recorded before and after initiation of the disease, it would still be difficult to discern whether they were a cause or an effect of the disease. This problem is further compounded by the common lack of “before” gait data. OA sufferers do not tend to report problems to their doctor until they begin to suffer pain in their joints, and pain rarely occurs in the early stages of OA, as the changes occurring within the joint are insubstantial. This also means that it is unusual for a doctor to see initiation of OA within a joint, and thus little is known about the process.

A solution exists in the form of longitudinal cohort studies. These studies tend to track large groups of people throughout their lives or through large periods, with regular clinical assessments. The regularity of assessment combined with the long life cycle of cohort studies could be used to provide information on their gait both before and after OA initiation. The number of individuals present in a large cohort also brings with it increased statistical power, allowing statistical significance and directionality to be better established with regards to gait changes and OA initiation.

Finally, medical research studies typically use larger numbers of patients (n > 200) than are typically found in biomechanics studies (n = 10-100) in order to increase the power of a study and establish statistical significance in the results. For the results of a musculoskeletal biomechanics study to be readily accepted by the medical community, a study of similar size was needed.

1.3 The Newcastle Thousand Families Study

Osteoarthritis primarily occurs during later life, typically from age 50 onwards, with over a third of the UK population expected to exhibit the symptoms by age 65 [1]. However, there have been cases reported in individuals as young as 15 [10], although these are almost always cases of secondary OA. Thus, it would be most useful to study OA in subjects of an age in which it is most likely to occur as this provides the best chance of measuring gait both before and after initiation.

The Newcastle Thousand Families Study (NTFS) [11] presented a unique opportunity to study an existing cohort of adults, now all at age 62/63 years. It was opportunistic to use this cohort as the timing of the latest follow-up wave coincided with the timing of this study. However, use of the NTFS was also beneficial because it allowed access to an existing large group of subjects (over 300 in total) at a point in their life where OA could be entirely absent, developing or fully developed. Using existing information on OA prevalence within the UK population (roughly one third of the population [1]) it could be expected that at least 100 of these cohort members would already have developed OA within their joints, with yet more showing signs of undiagnosed OA. The rest of the cohort could provide baseline data on unaffected gait. Using these three groups, features that could have initiated the disease could be assessed, as well as comparing the gait of participants with developed OA to the results of other studies.

In addition, the study has tracked each member of the cohort since birth in 1947 and provides a wealth of medical and social information on each member at different stages of their lives, thereby allowing other factors with a suspected links to OA to be included in the analysis. The recruitment technique used was also free of bias, so this cohort could be seen as a representative sample of the population and so any findings have the potential to be applied to the wider population.

1.4 Challenge – Data collection in a clinical environment

Involvement with the NTFS brought with it several constraints which focused on practicality of running multiple clinical assessments side-by-side, and also limiting cohort attrition. As gait analysis was to take place alongside a range of other clinical assessments, time with the participant was limited to 25 minutes. The gait analysis would also have to be done in the clinical research facility where the rest of the tests were taking place, in order to further save time and avoid disruption for the participants. Gait analysis would have to take place with the participants wearing their own clothing, in order to preserve dignity, save time, and thus limit cohort attrition. Finally, every able member of the cohort was to undergo gait analysis and sub-setting was not allowed. This was aimed at promoting the integrity and completeness of the dataset.

Working in a clinical environment with limited time and space necessitated the design of a data collection protocol that was feasible within the constraints and yet also provided meaningful data with which to assess the initiation of OA in relation to gait. In addition, the protocol designed had to be able to record this data over the top of clothing, and be suitable for all members of the study to undertake.

1.5 Aims and Objectives

The aim of this study was to identify kinematic variables associated with OA initiation using the NTFS cohort and to provide baseline kinematic data for the cohort that could be used in future follow-ups.

The first objective was to develop and validate a gait analysis protocol that was quick and effective in a clinical environment, did not require a dedicated gait laboratory, and fitted within the limits of the overall NTFS clinical assessment. Once the protocol was finalised then gait analysis of the NTFS cohort commenced.

The second objective was to analyse the kinematic variables collected from the NTFS cohort gait analysis in relation to OA severity. The gait variables analysed focus on those with a previously reported link to OA [3, 12], and comparison with these studies helped establish validity of the data collected and also highlight areas where further work is needed or improvements can be made.

The final objective was to analyse the kinematic variables with a focus on OA initiation and to establish associations that would inform future follow-ups and other biomechanical studies. Whilst this study would be cross-sectional, and could therefore establish association but not direction between gait variables and OA, it is the first step on the road to a longitudinal cohort gait study of exceptional value.

1.6 Thesis Outline

Chapter 2 begins with an overview of the NTFS cohort and includes details of previous assessments that the cohort has undergone, and what assessments took place in the age 62/63 follow-up. It also includes the protocol for collection of data from other clinical assessments which were used in this study. The chapter then goes on to detail the conditions of involvement with the study stipulated by the NTFS steering committee. Finally, the chapter concludes with the formation of an engineering specification based upon the criteria for involvement in the NTFS.

Chapter 3 presents an in-depth look at OA from a biomechanical perspective, including symptoms and effects, current methods of diagnosis, why looking at OA and gait is relevant, the structure of the knee joint and methods of describing its motion, previous biomechanical analyses that have focused on the condition and the gait variables found to be associated with OA, and relevant variables for studying gait and OA. The chapter concludes with the criteria for excluding members of the NTFS cohort from the gait analysis in relation to OA (although their gait data was still collected).

An overview of the gait analysis methods available for use in a clinical environment is presented in Chapter 4 with reference to the conditions of involvement with the NTFS, and the challenges associated with gait analysis outside of a laboratory environment. Inertial sensors are selected as the most appropriate technology and a review is then presenting of their validation against established gait analysis methods. The chapter concludes with the selection of the inertial sensors from Xsens to be used in this study and an update of the engineering specification to reflect the use of inertial sensors.

Chapter 5 details pilot work conducted on the inertial sensors and includes a feasibility study comparing this system to an optoelectronic system, using a 4-bar linkage to provide repeatable mechanical motion simulating a knee joint.

Chapter 6 presents the design and development of a gait analysis protocol using inertial sensors that is suitable and viable in a clinical environment, and fits within the constraints of the NFTS.

Chapter 7 present the validation of the NTFS gait analysis protocol against a reference standard optoelectronic system. The affect of alterations to the protocol are also assessed. The final protocol is then included, and the gait variables that were analysed from the NTFS gait analysis are defined. The chapter concludes by detailing the statistical testing methods that were used on gait data from the NTFS cohort.

Chapter 8 presents the results of the NTFS gait analysis, together with other data collected by the study. It starts with a univariate analysis, looking at each variable individually in relationship to OA severity, and then moves on to adjust for potential confounding factors using a backwards stepwise regression.

Chapter 9 discusses the results of the NTFS gait analysis, including reference to previous studies found in the literature. The wider implications of the study are also discussed. The limitations of the work are then examined and the impact and future directions for this work are suggested. The chapter concludes with a summary of the findings of this study.

Chapter 2 The Newcastle Thousand Families Study

This chapter focuses on the Newcastle Thousand Families Study (NTFS) and starts by giving an introduction to the study and its cohort. It then moves on to detail what other measurements from this and previous studies on the cohort were used in this thesis, and how these were collected. Finally, the conditions of involvement with the study stipulated by the NTFS steering committee are described in detail, along with further additional considerations linked to working with patients in a clinical environment.

2.1 Introduction to the NTFS cohort

The Newcastle Thousand Families Study (NTFS) is a longitudinal epidemiological birth cohort study that began in 1947. Details of the NTFS cohort have appeared many times in the literature. The first 15 years of the study are covered in detail in 3 books [13-15], and the subsequent follow-up at age 32 has also been published as a book [16]. An International Journal of Epidemiology cohort profile [11] gave a complete outline of the cohort up to 2009.

The purpose of the study at inception was to investigate the high infant mortality rate in Newcastle compared to the rest of the UK, hypothesised at the time to be due to acute infections [11]. The study has evolved to include assessment of health outcomes, education, mental health, criminality and musculoskeletal measures. The cohort has been assessed using clinical assessment, questionnaires and interviews, and the volume of information available about this group, and the life each member has lived makes them one of the most studied groups of people in the world. The NTFS presented a unique opportunity to perform gait analysis on an existing large cohort that, due to its selection method, can be taken as representative of the larger population [11]. The data available from previous assessments of the cohort coupled with the statistical power that comes with having a study with a large numbers of participants, means that investigating the gait kinematic factors associated with osteoarthritis initiation and progression within this group could lead to conclusive results with real-world applicability and value.

The original cohort consisted of all but 4 of the 1146 children born in May and June of 1947 to mothers resident in Newcastle upon Tyne, forming a cohort of 1142 children. This method of selection ensured coverage of the entire social spectrum of the city and thus can be considered representative of the population at the time. In its current form, the sample consists of any traceable survivor of the original cohort and Table 2.1 gives details of the cohort size at each study interval up to and including the current study. A relatively low attrition rate has been seen especially when the high mobility of the population is considered.

Table 2.1 Cohort size at each study interval.

Years	**Cohort Age (years)**	**Participants**
1947	Birth	1142
1947-62	Birth to age of 15	1142 falling to 750 by 1962
1966	18	750
1969	22	442
1997-99	49-51	574 (questionnaire) 412 (physical assessment)
2009	62-63	433 (questionnaire) 350 (physical assessment)

In terms of the cohort continuing to be a representative sample of original cohort after attrition, those followed up at age 50 have been shown to be representative of the original cohort for all early life factors considered, with the exception of sex [17-19]. Finally, due to the design of the cohort recruitment process with the entire cohort being born within a two month period, this reduces the likelihood of age being an influential or confounding factor on many outcomes.

2.2 Additional data available

As mentioned in section 2.1, the cohort have been assessed at many points in their lives, and the data recorded about them has expanded and evolved over the years. Only some of this data was relevant to this thesis, and the protocols used for each measurement are described below.

2.2.1 Body-mass index at age 62-63 years

Body-mass index (BMI) is a measure of human body fat based on an individual's height and weight, although it does not actually measure body fat percentage. Height was measured using a standard clinical height scale, and weight was measured using clinical scales. Patients were fasted before arriving for clinical assessment so weight of food consumed could be neglected. BMI is calculated using Equation 2.1.

$$BMI = mass\ (kg)\ \div (height(m))^2. \tag{2.1}$$

2.2.2 WOMAC score at age 62-63 years

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) is a validated instrument [20] designed for the assessment of lower extremity pain and function in OA of the knee or hip. The score is assessed over three areas; pain, stiffness and function. Pain has 5 assessment questions, stiffness has 2 assessment questions, and function has 17 assessment questions. Each question asked the individual to rate the pain induced by an activity, stiffness at a time of day, or difficulty of a particular activity on a scale of one to eight. Sub-scores were calculated for each area, and an overall WOMAC score out of 192 was returned. A review carried out in 2001 by McConnell et al. [21] into the reliability and validity of the WOMAC score concluded that the index remained a valid tool for assessment.

2.2.3 Radiographs of the knee and Kellgren-Lawrence scoring

Radiographic images were acquired by the radiology department of the Royal Victoria Infirmary (RVI) in Newcastle upon Tyne and stored on their Picture Archiving and Communications System (PACS) using INFINNIT software (INFINNNIT North America, New Jersey). INFINNIT PACS allowed viewing of the digital images using high definition screens specially designed for analysis of radiographs. It also allowed optimisation of contrast, image size and picture sharpness, along with access to calibrated measuring tools.

Knee radiographs were analysed by a single clinician for evidence of OA. Measurements of joint space were taken (to the nearest 0.1mm) in medial and lateral compartments. The presence of osteophytes was graded in the medial and lateral compartments according to the Altman & Gold Atlas of Radiographic Images [76] with scores ranging from 0 (no osteophyte present) to 4 (large +/- multiple osteophytes). The presence of tibial spiking, sclerosis and deformity were noted as either present or absent.

Each joint was subsequently given an overall scoring for severity of OA according to the Kellgren & Lawrence [22] (KL) grading scale, which incorporates all of the parameters mentioned above. Images from the original description by Kellgren & Lawrence were used to guide scoring, which ranged from 0 (no evidence of OA) to 4 (severe OA). According to this grading scale a score of 1 is deemed to represent "possible OA", in contrast to the grading of osteophytes where a score of 1 represents "definite presence of osteophyte". In this study, a series of images were graded by a second musculoskeletal physician with extensive experience of scoring radiographs. Results show excellent inter-rater agreement (Cohen kappa coefficient of 0.82); intra-rater agreement was also excellent (Cohen kappa coefficient of 0.86).

2.3 Conditions of involvement

A birth cohort study with such a low attrition rate and participants who continually return for assessment and report that they enjoy it is a valuable commodity, and as such the steering committee for the NTFS are very protective of them. In order for gait analysis to become part of the age 62/63 follow-up assessments, the protocol developed had to fit within the conditions stipulated by the steering committee. These stipulations were made not only to protect the participants, but also to ensure that the gait analysis stayed within the ethical and practical boundaries of the study. In addition to these conditions of involvement, the study protocol was developed with the input of the study director and steering committee. Input was provided on the ethical, practical and social implications of any protocol decisions in order to facilitate a smooth ethical approval process and enjoyment of the study by participants.

2.3.1 Condition 1 – Location

During the age 49-51 follow-up, the majority of clinical assessments took place in the Clinical Research Facility (CRF) at the RVI in Newcastle upon Tyne. However, at this time the facility did not have access to a dual energy X-ray absorptiometry (DEXA) scanner for measuring bone mineral density and content. Therefore participants were required to travel to the Freeman hospital, located in the suburbs of Newcastle upon Tyne, for their DEXA scans. It was thought that while the data collected were very valuable, this journey added unnecessary time and complication to the participants visit. For the age 62/63 follow-up, the DEXA scanner located within the CRF was used (this had been purchased in the intervening period between the follow-ups, as well as the CRF facility having been built). As the X-ray department in the RVI hospital was used for taking the joint radiographs, the participants would be able to complete the entire clinical assessment within the same facility, shortening the total time needed for the assessment. It was therefore not permitted for the participants to travel to the gait laboratory at the School of Mechanical & Systems Engineering in Newcastle University and the gait analysis had to take place at the CRF.

2.3.2 Condition 2 - Time

There were a large number of measurements and activities to undertake when a participants attended for clinical assessment. It was the wish of the steering committee to make their visit as short as possible so that the participants did not have a bad experience of the assessment and did not feel their time was being wasted. This would hopefully ensure their participation in coming years. The time allotted for the gait analysis to take place was 25 minutes. This had to include greeting the participants and explaining what they were going to do, attaching the markers/sensors, calibrating the markers/sensors, and performing the gait assessment. Table 2.2 provides details of how much time was allotted for each of the clinical assessments for comparative purposes.

Table 2.2 Allotted time for each clinical assessment.

Assessment	Time Allotted (mins)
Anthropometric	15
Ultrasound	40
DEXA	45
Radiographs	60
MRI	45
Spirometry + Grip Strength	15
Cognitive	25

Hearing	15
Gait Analysis	25
Photographs	5

2.3.3 Condition 3 – Clothing

As mentioned, the intent of the steering committee was that participants would have a good experience of the clinical assessments and would be willing to attend future follow-ups. For this reason, dignity and comfort was a primary consideration and all markers/sensors to be used for the gait analysis would have to attach over the top of the clothing worn by the participant. This condition had a secondary benefit as asking a participant to disrobe and don specific clothing would add further time to the gait analysis protocol. It was permitted for the participants to be requested not to wear specific clothing types (this was detailed in the letter sent to them before they attended for clinical assessment) and for the participants to be barefoot during the gait analysis.

2.3.4 Condition 4 – Everyone

Throughout the NTFS it has been the intention that as many of the entire cohort be assessed at each interval, in order that there are as few gaps in the dataset as possible. There have been exceptions in studies at the ages of 32, 54 and 58 years where not all participants were contacted, or subsets of the cohort specifically used. For the age 62/63 years follow-up it was required that every able participant who attended for clinical assessment had the opportunity to take part in the gait analysis in order to have as a complete dataset as possible for the cohort at this age. The movements required for the gait analysis had to be suitable for every able member of the NTFS cohort to perform, from the most mobile and flexible to the least, with the exception of those who are unable to walk. Participants using walking aids also took part in the gait analysis and use of the walking aid was at their discretion and participants were only excluded from the gait analysis when it was either unethical or impractical for them to take part.

2.4 Additional advisement

In addition to the conditions of involvement set down by the steering committee, the study director for the NTFS was also involved in an advisory role during the development of the gait analysis protocol. Whilst the committee were aware in broader terms of what gait analysis entailed, they were not knowledgeable about the methods used and the various components of a gait analysis. There was, therefore, the potential that something unforeseen could be included in the protocol that would not be in keeping with their wishes of protecting of the cohort. Therefore, in any areas where a question was raised over whether it was permissible to do something, advice and clarity were sought from the study director.

2.5 Ethical Approval

Ethical approval for the study “The Newcastle Thousand Families Study – Their health and wellbeing at age 62 years” was granted by the Sunderland Research Ethics Committee acting as part of the NHS National Research Ethics Service, REC reference number 09/H0904/40. The gait analysis protocol was included in the overall ethics application.

2.6 Additional Considerations

Alongside the ethical approval granted for the study, there were some practical considerations to be made in order to ensure the comfort and enjoyment of the participants. The first of these was that they were given an explanation of the gait analysis protocol before commencing. This not only allowed the participant to feel more involved in the process and less like a subject for a test, but also gave them an idea of what to expect from the gait analysis and offer a chance to allay any concerns they may have.

Secondly, the attachment and removal of the markers/sensors used had to be as pain-free a process as possible. Double-sided tape is often used to attach markers/sensors and this can be painful to remove from skin, all efforts were taken to minimise this pain with gentle removal of the markers. Straps are also used for sensor/marker attachment and having a secure mounting is important for result quality, and this requires substantial tension in the strap. An over-tightened strap could be painful, so feedback from the participant when attaching straps was essential and a balance was struck between comfort and security of the attachment (although it always erred on the side of comfort when the attachment was deemed painful by the participant).

During the explanation of the calibration movements and trials it was made clear to the participant that the performance of both of these tasks was to be done only within their own comfort boundaries. A participant was not required to perform any movement that caused them pain or discomfort, although their judgement of this was at their discretion.

Finally, whilst the focus of this thesis was on knee joint movement, there may be future follow-ups of the NTFS that may require data on the ankle and hip joint movement. With this in mind, the protocol development included sensor attachment methods, positions and calibration movements the feet and pelvis. However, the validation study only dealt with measurement of knee joint motion as this was the focus of the thesis.

2.7 Engineering specification

In designing a protocol for the NTFS gait analysis, there were many requirements to consider. Therefore, it was proposed that engineering specification be created in order to keep track of these requirements. An engineering specification forms a list of requirements that a product must satisfy in ordered to be deemed fit for purpose. This list of requirements was based on the conditions of involvement in the NTFS, the additional considerations listed, and making this a relevant biomechanics study on the links between gait and initiation and progression of OA. The set of requirements that form the specification are set out in Table 2.3.

Table 2.3 Engineering specification detailing the requirements for the NTFS gait analysis protocol.

	List of requirements
A	Protocol must be feasible for use in the Clinical Research Facility at Royal Victoria Infirmary Newcastle.
B	Protocol must take no more than 25 minutes from start to finish.
C	Data collection must take place over the top of clothing.
D	Protocol must be suitable for every able member of cohort to perform.
E	Gait analysis procedure explained to all participants.
F	Minimise pain/discomfort during assessment.
G	Record data for hip, knee and ankle joints.
H	Accuracy and repeatability of data must be comparable to a reference standard system.
I	Variables relevant to the study of gait in relation to OA initiation and progression must be recorded.
J	Appropriate indicator of OA severity so that initiation as well as progression can be assessed.
K	Method must be portable and not require permanent installation.

2.8 Summary

This chapter has provided an introduction to the Newcastle Thousand Families Study cohort. It began by outlining the studies inception and then moved on to detail the other assessments that took place when participants attended for clinical assessment. The conditions of involvement with the study were then discussed in detailed, which included the reasoning behind each condition. The chapter then moved on to look at additional advisement during development of the gait analysis protocol, the ethical approval procedure, and addition considerations that had to be taken into account during protocol design and the subsequent clinical assessments. Finally, an engineering specification was created that included all the requirements for the gait analysis protocol and this will be referred back to in later chapters.

Chapter 3 Osteoarthritis

This chapter focuses on osteoarthritis (OA), and starts by reviewing the history of the disease. It then defines the disease and its symptoms and links these in to the methods used to diagnose the condition. The Kellgren-Lawrence (KL) grading scale used for radiographic identification of OA is looked at, and the methods used for OA diagnosis in the Newcastle Thousand Families Study (NTFS) are described. The causes for initiation of the disease and the theory of biomechanical initiation are then discussed. Previous studies on the links between OA and gait biomechanics are reviewed, and the chapter concludes with identification of the variables of interest with the intention of both diagnosing and predicting the initiation of OA from gait kinematics.

3.1 What is osteoarthritis?

Osteoarthritis is a joint condition in which there is a progressive softening and disintegration of articular cartilage, allowing the bones underneath the cartilage to contact and rub against each other. This contact and friction causes pain, swelling and loss of mobility in the joint. Over time this friction may also change the overall shape of the joint and thereby exacerbate the symptoms and rate of disintegration of cartilage. This disintegration is often accompanied by the growth of cartilage and bone at the edges of the joint, forming osteophytes (bony spurs) that can interfere with normal joint function and cause pain. The progressive nature of osteoarthritis and its deformation of the cartilage and bone means that once the disease has initiated in a joint it is unlikely that it will fully recover [7]. However, treatments for the disease can often slow or halt its progression and this can lead to some recovery of function of the joint and reduction of pain and swelling. Treatments include; exercise, weight control, rest and joint care, surgery, and medicines designed to reduce pain or stimulation of cartilage regeneration (e.g. glucosamine tablets) [7, 23].

3.2 The discovery of osteoarthritis

From the times of the first medical diagnoses up until around 1750, all forms of chronic arthritis were thought to be signs of gout. Gout is characterised by acute inflammatory arthritis and commonly presents itself as a red, tender, swollen joint. However, in 1782 (not published until 1802) Heberden was the first to report that some of the symptoms being seen in patients that are now accepted as being indicative of OA, had no connection to gout [24]. He also made specific reference to the bony spurs found on the affected joints. OA was differentiated from gout in several more instances, by Sandifort in 1793, Bell in 1824, and by Haygarth in 1805 [24]. Throughout the rest of the 19th century, recognition increased of these and other accompanying symptoms being a condition in its own right and not an expression of gout. By the beginning of 20th century the disease had been granted its own title of "osteoarthritis" [24], derived from the Greek words "osteo" meaning "of the bone", "arthro" meaning "joint" and "itis" meaning "inflammation".

The 20th century saw a dramatic expansion of medical techniques and rapid development of the technology available for diagnosis. One of the most important inventions of the period was the X-ray machine, and this was to prove an important tool in developing the understanding of OA. This led to a distinction being made between OA and rheumatoid arthritis [25], and also to the development of a radiographic scoring system by Kellgren and Lawrence [26] which is still in use today and used in this study.

3.3 Prevalence of osteoarthritis

The United States Centre of Disease Control (CDC) [27] estimates that OA affects 13.9% of adults aged 25 and older, and 33.6% of those aged 65 and older. This means that, for the United States, 26.9 million people are estimated to suffer from OA. A similar picture is seen in the United Kingdom with the National Health Service (NHS) reporting an estimated 8.5 million people suffering from OA [1]. It is also important to note that the figures from the CDC from 2005 show a rise from 21 million OA sufferers in 1990. This increase of 5.9 million OA sufferers is likely due to the ageing population phenomenon occurring in developed countries [8], but could also be due to increase in prevalence of risk factors for OA.

These overall figures from the NHS and CDC only tell part of the story of OA prevalence as several different joints can be affected, and prevalence figures also change depending on the diagnosis method used. Table 3.1 shows a breakdown of the prevalence by joint for symptomatic OA, taken from the CDC [27]. The figure for knee

OA is for adults aged 45 and over. When broken down by sex, the figures are 18.7% for females and 13.5% for males. It should be noted here that the prevalence of OA reported by different studies often disagree on the exact number. A recent review paper [28] looked at the overall prevalence of knee OA across 72 papers, and calculated an overall knee OA prevalence of 23.9% (27.3% for women, 21.0% for men).

Table 3.1 Prevalence of OA by joint in the US [2, 29, 30]

Joint	Prevalence (%)
Hand	8.0
Feet	2.0
Knee	16.0
Hip	4.4

The diagnosis method used can also affect the prevalence of OA reported for a population. Typically, radiographic methods yield a higher prevalence of OA than clinical examination [28], which may explain the discrepancy in the figures from the CDC [27] and those from Pereira et al [28]. The figures from the CDC were based on symptomatic OA, whereas those from Pereira et al were taken from a range of studies using both radiographic and clinical diagnoses.

3.4 Diagnosis of osteoarthritis

Due to the range and combination of symptoms that can be presented by a patient suffering from OA, no single test is able to conclusively diagnose the condition. Doctors use a number of methods to diagnose osteoarthritis currently; patient history, physical examination, and radiographic imaging. Typically two or more of these methods are used to diagnose osteoarthritis, with all three sometimes used. It should also be noted that gait is used as part of a physical examination and not as a separate method in its own right. Recent work has sought to quantify the changes in gait due to osteoarthritis and to couple this with new methods of classification using these variables, and this work will be detailed later in this chapter.

3.4.1 History

When a patient presents with a joint problem and OA is suspected, it is important to first differentiate OA from other conditions, such as rheumatoid arthritis. After the presenting symptoms have been classified, an assessment of the patient's occupation and social history is carried out. This is used to assess the lifetime loading of the patient's joints, since different occupations and activities can predispose someone to osteoarthritis and in some cases play a role in the initiation. Working in jobs which subject a joint to higher loads for longer periods than expected (e.g. carpet fitting, manual labour) lead to a higher risk of developing OA [31]. History of OA incidence within a family is also examined as research has been published that suggests some hereditary links for OA [32]. The patient's medical records are also reviewed to look at previous injuries to both the affected and unaffected joints. Damage to a joint through injury can provide an initiation site for OA, or can alter the geometry and kinematics of a patient's skeleton and lead to unexpected loading of another joint to compensate for a weaker one.

3.4.2 Primary or secondary osteoarthritis?

An examination of the patient's medical history allows a judgement to be made on whether their condition constitutes primary or secondary OA. Secondary OA is diagnosed when an associated reason with developing the disease can be clearly identified, such as a bone break or congential disorders. Primary OA is diagnosed when no initiating mechanism for the disease can be found [7].

Whilst the symptoms presented by patients suffering from primary or secondary OA are the same, when looking at disease initiation it is essential to discriminate between the two. The focus of this study was on identifying the mechanisms for primary OA initiation, as the initiation mechanisms for secondary OA are known. Therefore, the criteria formed for excluding NTFS cohort members from analyses in relation to OA initiation had to include factors that could have caused secondary OA. These will be detailed later in the thesis along with other exclusion criteria.

3.4.3 Physical examination

Historical assessment is then followed by a physical examination, designed to assess the severity of symptoms being presented and also to confirm any previous injuries or surgeries to the joint, and to check for any that have not appeared on the patient's records. A patient's gait is the starting point for physical examination as decreased mobility in a joint can often be seen clearly as a limp in one leg.

Following on from gait observation, the suspected joint is then examined for tenderness, crepitus (the crackling/popping sound heard during rough surface contact within a joint), swelling, and reduced range of movement. There are also specific examinations and movement tests for the knee joints that are recommended by medical textbooks on osteoarthritis [23]; Varus or valgus misalignment and deformity should first be assessed visually. Varus misalignment occurs when the knee joint centre is displaced laterally from the load bearing axis that runs down the middle of the leg, and valgus misalignment defines displacement in the medial direction from the loading bearing axis. The joint should also be palpated to check for effusion, tenderness, swelling and cysts on the back of the knee. Passive flexion-extension of the joint is used to assess the extent of a reduced range of motion. Medial-lateral and anterior-posterior laxity is also tested by applying stress in these directions to a partially flexed knee.

3.4.4 Radiographic Imaging

Radiographs are not generally used in diagnosis and are more commonly used to assess the structural severity of OA once it has been diagnosed in a physical examination. The typical OA features identified on radiographs are as follows;

- Joint-space narrowing (the knees image must be taken when weight bearing).
- Osteophytes.
- Subchondral bone thickening.
- Calcification of the cartilage.
- Small calcified foreign bodies.

These features are then applied to a grading scale which defines disease severity. One of the most commonly used scales is that developed by Kellgren and Lawrence [22], referred to as the Kellgren-Lawrence (KL) scale. It is this scale which was used in the radiographic image assessment for the NTFS cohort, and will be described in greater detail later in this later.

In addition to its use in diagnosis, radiographic imaging does serve a very important use when looking at the initiation of OA. Typically, OA does not cause pain in a joint until the disease severity reaches higher KL grade 2 or higher [33], and a patient would have no reason to report a problem with a joint until it started causing them pain or discomfort. The ability of radiographic images to show the initiation of the disease before severity increases and the joint begins causing the sufferer pain is vital in looking at factors which could be causing the disease to initiate.

3.4.5 Other methods

Along with radiographs there are other imaging methods used for assessment of OA. Ultrasound and magnetic resonance imaging (MRI) are better at detecting synovitis and effusion than clinical examination of a patient [7].

3.5 Defining OA severity

The previous sections have shown that there are various methods available for defining OA severity. Of these, clinical examination and radiographic scoring were both being performed as part of the NTFS age 63 follow-up, with osteoarthritis epidemiology a primary focus of the assessment wave. In addition, WOMAC score was also recorded, and this presents a measurement of OA severity that is very focused on patient welfare. It had to be decided which of these measures was the most appropriate for defining OA severity, when the focus of the study was on initiation of the disease.

Small radiographic changes that signal the initiation of OA do not usually cause pain to the sufferer [33] as no substantial changes have occurred in the joint in order to cause pain when articulating. Sufferers only report problems to their doctor when pain occurs, and this is usually in the latter stages of OA when the disease has developed (typically KL grade 2 onwards). Therefore, whilst pain is an important factor to consider from a patient welfare perspective, when looking at the initiation of OA it is not a good metric for defining disease initiation. However, pain in a joint can modify gait [34], therefore it is important to consider WOMAC scoring when analysing the results of the NTFS gait analysis. Gait alterations may have been caused by structural changes in the joint, but pain from these alterations will also be a contributing factor which may serve to exacerbate the alteration. It is highly likely that gait alterations due to structural changes or pain will interact strongly. For the purposes of this study, pain was included as a potential confounding factor in an attempt to adjust for alterations to gait due to joint pain.

Clinical examination suffers from some of the same problems as WOMAC scoring when looking at disease initiation. OA sufferers rarely go see a doctor for examination until the disease has developed and has started affecting their lives. In addition to this, a clinical examination can be used to diagnose the presence of OA, but a grading on severity is often then obtained from radiographic images.

The aim of this study was to assess gait changes in relation to OA severity, with a focus on the initiation stages of the disease. WOMAC score and clinical examination are effective at diagnosis and patient-focused measurement of the disease and its affect on the patient’s life, once the disease has already established itself within the joint. However, neither is appropriate for defining the initiation of the disease, or providing a repeatable quantitative measure of disease severity for comparing subject groups. Scoring of radiographic images provides for both these needs, and the Kellgren-Lawrence (KL) grading scale used by the NTFS is commonly used as a measure of OA severity biomechanics studies. Therefore, in the NTFS gait analysis, KL grade was used as a measure of OA severity.

The KL grading scale was developed by Kellgren and Lawrence in 1957 [22] and used the features listed in Section 3.4.4 to assess radiographic images of a joint suffering from OA, and assign a ranked severity. This provides a comparative measure for the severity of OA between subjects. The KL grading scale is shown in Table 3.2.

Table 3.2 The Kellgren-Lawrence grading scale [22].

Grade	Severity	Criteria
0	None	No features of OA.
1	Doubtful	Minute osteophyte, doubtful significance.
2	Minimal	Definite osteophyte, unimpaired join space.
3	Moderate	Moderate diminuation of joint space.
4	Severe	Joint space greatly impaired with sclerosis of subchondral bone.

3.6 Risk factors for OA

There are both mechanical and non-mechanical risk factors for OA and these were considered in conjunction with gait analysis data collected on the NTFS and could form the basis of future studies using the cohort data. This study's focus was on biomechanics and, as such, the biomechanical risk factors for OA have been considered separately.

3.6.1 Non-mechanical risk factors

OA is often referred to as "wear and tear" of the joint and all sites for OA show a tendency for increased prevalence of the disease with age [35]. Ethnicity is also a risk factor with Negroid and Oriental ethnic groups showing a lower prevalence than Caucasian groups [36]. Supporting these findings are geographic studies which show greater prevalence in European countries compared to those in Africa and Asia [37]. Finally, gender is a risk factor for OA with females showing a higher prevalence for OA [37].

Hereditary and genetic factors are also thought to increase the risk of developing osteoarthritis, although it is difficult to separate the influence of shared environment from genetic factors. Research looking at immigrant populations in 1995 found that Chinese individuals in the US have a lower prevalence of hip OA than US citizens [5]. This could point to genetic differences, but could also be linked to environmental factors. However, individuals living in the US with Chinese surnames (and therefore the implication of Chinese genes) also had a lower prevalence of hip OA compared to the rest of the population. Whilst not conclusive, this does provide an interesting example and support for hereditary factors playing a part in OA incidence.

A twin study in 1996 looked at genetic influences on OA incidence in women [38]. They found that 39% of the variance of osteoarthritis of the knee would be attributed to genetic factors. This genetic effect was consistent whether a radiographic or clinical method of diagnosis was used, and was also independent of environmental factors. A further study looking at radiographic knee OA progression in monozygotic (MZ) and dizygotic (DZ) twins [39] found a significant genetic component in the progression of medial knee OA. MZ twins (formed from the splitting of a single egg and containing identical genetic material) were found to have a significantly higher correlation of joint space narrowing and osteophyte formation in the medial compartment than DZ twins (formed from fertilisation of separate eggs by two separate sperm). This led to a heritability estimate of between 48% and 71%. No clear genetic influence could be found for lateral OA, although this conclusion is uncertain as there a low prevalence of cases of lateral OA compared to medial OA (2.3% compared to 17.6% for MZ twins, and 2.9% compared to 15.3% for DZ twins for joint space narrowing).

Low bone mineral density (BMD) is another risk factor that has been strongly linked to OA. Zhang et al. in 2000 reported that those with low BMD have been shown to have a lower risk of OA incidence compared to those with higher BMD [40]. The same relationship has been reported by another study [41] and there is no evidence to the contrary to the knowledge of this author. Whilst BMD is listed under the non-mechanical factors, it will be seen later in this chapter that associations with BMD may actually be a result of mechanical factors.

Injuries to joints sustained earlier in life can also increase the future risk of OA as they can result in initiation sites. A knee injury even as a child or young adult has been shown to significantly increase knee OA incidence in later life by around 8% ($p = 0.0045$) [42].

3.6.2 Mechanical risk factors

Obesity, measured using body-mass index (BMI), has previously been linked to OA prevalence [37]. There is also evidence to suggest that obesity is a cause of OA, and not a result of reduced mobility inducing a more sedentary lifestyle. Increased weight will influence the loading experienced by joints and any stresses induced by misalignment in the joint will be exacerbated by this.

Occupation is also thought to play a role in OA incidence because of the potential for some jobs to cause extreme loading on joints and therefore damage the cartilage. The Framingham study [43] found that men whose jobs had medium or higher physical activity demands (e.g. labourers) has a higher risk of knee OA. Similarly, knee OA was more common in men and women whose job involved much knee-bending (e.g. cleaners, carpet fitters).

Sports and other recreational activities have also been linked to OA incidence for the same reasons. Some sports may involve repetitive excessive loading of the joints and this can allow OA to initiate. Studies have found high prevalence of OA in former footballers [44] and former elite runners [45]. However, studies looking at recreational runners [46] show that a moderate level of sporting activity has no effect on OA incidence. This would imply that it is only the extremes of loading which cause OA incidence in the lower limbs and that exercise of a low or moderate intensity does not cause sufficient damage to the joints for OA to initiate.

Alignment and muscle strength are also important mechanical risk factors to consider. Weakness of the quadriceps muscles is associated with knee OA [47]. However some research actually views this muscle weakness as a cause of osteoarthritis [48]. A weak quadriceps muscle could be a result of pain and sedentary behaviour induced by OA. Alignment has been shown to have strong links with OA progression [49], but no results have been published that supports the links between alignment and incidence. From a mechanical perspective, alignment can be viewed as either a cause or effect of OA. Initial misalignment could cause the disease to initiate and the disease effects on gait kinematics then compounds the misalignment, or initiation of the disease could induce a misalignment which is then also compounded. Either of these would fit with the evidence linking OA progression to misalignment.

3.7 Why investigate OA and gait?

As detailed in Section 3.1, OA is the degradation of cartilage within a joint. However, the exact mechanism by which the cartilage degradation starts is currently unknown. A joint consists of two or more articulating surfaces, and the cartilage serves to lubricate these surfaces and reduce wear. Within any set of articulating surface, wear is likely to occur due to friction, and it is this friction which breaks down the cartilage. Cartilage is able to repair and replace itself under normal wear conditions, in the same way that the bearings on a mechanical machine are replaced periodically. However, when a joint performs a movement for which it is not designed or optimised for, damage can be done to the articulating surfaces. So, for instance, if a person was walking in a way that their joint was not designed for, then the damage to their joint from this movement would be greater than if their walking was within the design range of the joint.

It should be noted that it is not just walking that has the potential to cause unusual movement within a joint. Other movements, such as the sit-to-stand motion and stair walking [50] can be used to assess joint function. Both represent a movement with greater loading on the joint than found in walking and may help to highlight small changes in the joint due to OA which have a greater effect as load increase. However, neither was permitted for use in the NTFS gait analysis by the steering committee. Sit-to-stand motion was deemed to have a risk of causing orthostatic hypotension, a condition in which a person’s blood pressure falls suddenly when standing up or stretching [51]. This is more prevalent among older individuals [51] and the risk of this would mean a nurse would have to be present during the trials and there was not the staff availability to accommodate this. Stair walking was also deemed inappropriate on ethical grounds as there was a risk of individuals falling and injuring themselves. Normal walking is one of the most common activities performed in life, and represents a repeated movement and loading cycle that has the potential to cause damage to the cartilage and joint.

It has been noted in Section 3.4 that there are several methods for diagnosing OA. Currently, during diagnosis, one of the first things a doctor will ask a patient to do is to walk. This allows the doctor to assess the patient’s range of motion and symmetry of gait. This assessment is then followed up with specific exercises that passively move the joint and assess the movement levels and pain associated with them. Both of these procedures produce results that are subjectively interpreted by the doctor and, whilst experience will allow an individual practitioner to develop a consistent approach, there may be disagreement between doctors if assessing the same patient. Gait analysis is not only able to quantify the variables that doctors measure qualitatively when assessing gait, but can also provide a consistent repeatable method for assessing gait that allows for comparison between subjects. Of course, this is not to say that visual gait analysis would cease to serve a purpose. The fusion of visual and quantitative gait analysis by an experienced doctor, or a team of doctors and clinical scientists, would increase the value of gait analysis and provide more data to make a clearer diagnosis.

Many of the risk factors detailed in Section 0 come under the title of "mechanical risk factors" and could be detected using gait analysis. Alignment and muscle strength could affect, and be expressed by, the kinematics of movement and increased BMI could cause higher impacts and contact forces within a joint. Occupation and recreational activities are not things that can be directly measured from a gait analysis when attending for clinical assessment. However, they are important factors that should be taken into account during the analysis of gait and radiographic data.

In order to investigate OA and gait, it is important to know about the structure of the knee joint and the methods of describing knee joint motion. Sections 3.8 and 3.9 will deal with this. Section 3.10 provides a review of previous investigations into osteoarthritis looking at gait variables and the findings. Finally, Section 3.11 will draw together the results of the literature and define relevant variables for this study.

3.8 The knee joint

The knee joint is made up of four bones; the femur, tibia, fibula and patella. In addition to this, the quadriceps and hamstring muscles cross the knee joint as well as multiple ligaments. In essence, the bones provide structure, the muscles provide power and the ligaments provide stability, which all work together in the function of the knee joint. The articulating surfaces of each bone are protected by cartilage, which protects the bone and allows the surfaces to slide easily upon each other [52]. Figure 3.1 provides a guide to the structure of the knee joint.

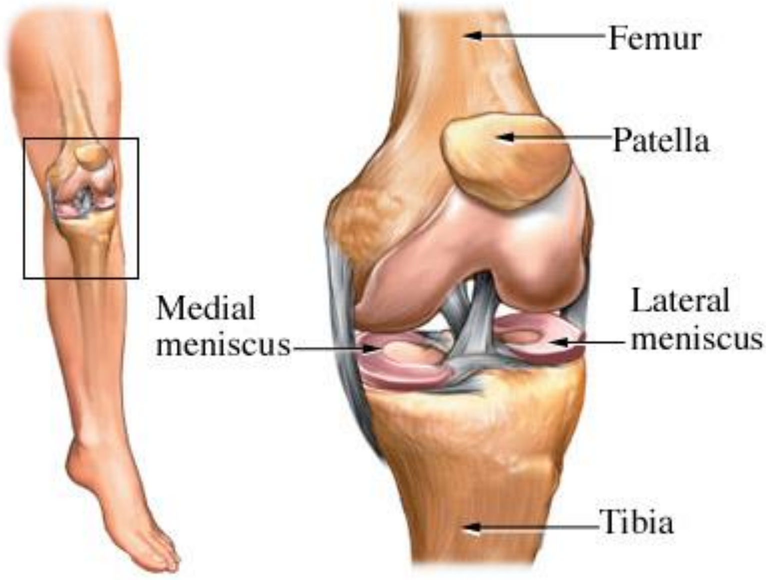

Figure 3.1 Diagram showing the internal structure of the knee joint [53].

The knee joint has a typical overall range of motion (RoM) of 140° in the sagittal plane. During walking the expected knee flexion/extension RoM in the sagittal plane is 60-70°. Movement of the knee joint does occur in the other anatomical planes during walking, with around 15-20° internal/external rotation and varus/valgus movement expected in the transverse and coronal planes respectively. Figure 3.2 provides a clear definition of the body anatomical planes. There are also two types of motion found between the articulating surfaces of the knee; rolling and gliding motion. Rolling motion initiates and occurs during flexion and consists of one bone surface rotating about the other. Sliding motion occurs at the end of flexion and consists of one surface translating across the other. During walking it is primarily rolling motion that occurs in the joint. Nevertheless, the combination of 3 potential axes of rotation, combined with translation of one bone relative to the other, makes the knee a 6 degree of freedom (DoF) joint. However, as shown later in this chapter, there are a multitude of methods that can be used to describe the motion of the joint, some of which do not take into account all 6 DoF.

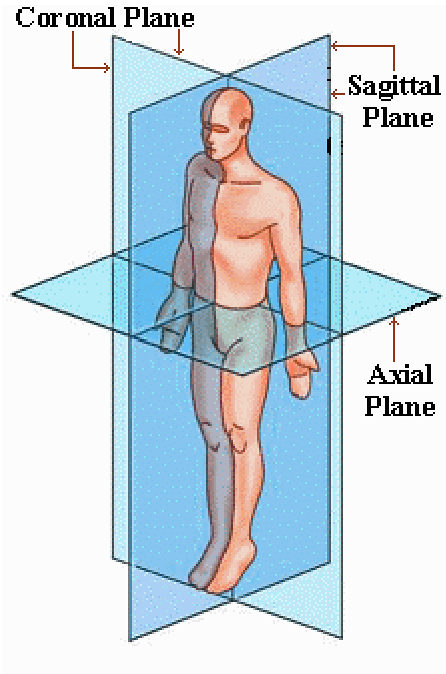

Figure 3.2 Definition of the body anatomical planes commonly referred to in gait analysis [54].

Aside from the rolling and gliding motions above, there is an unusual property of the knee referred to as the “screw-home” mechanism, which is crucial when considering knee stability for standing upright [55]. This mechanism effectively accomplishes locking of the knee joint and reduces the work performed by the muscles during standing. This mechanism occurs in the last 20 degrees of knee extension. External rotation of the femur relative to the tibial plateau occurs due to a difference in radius of curvature of the medial and lateral condyles (the medial femoral condyle being longer than the lateral condyle). This results in a tightening of both cruciate ligaments. This rotation continues until the ligaments become taut and the tibia lies in a position of maximum stability relative to the femur. This position achieved is actually one of slight hyper-extension of the joint. We shall see later that this locking mechanism can affect kinematic descriptions of the knee joint [56]. It is also important to note that this locking mechanism for the knee joint occurs in the last 20 degrees of knee extension. This is a feature present in a normal gait cycle, with the knee joint entering this angle range as heel-strike approaches, and has the potential to stay in this range during most of the stance phase.

3.9 Description of knee joint kinematics

Along with a variety of technologies that have been employed to record gait, there are many methods in which this information can then be processed to give a description of the knee joint kinematics. It was concluded in Section 3.8 that the knee is a 6 DoF joint. However, assumptions can be made about the joint that decrease the number of DoF and make kinematic calculations simpler and also make interpretation of data easier.

One option is to ignore translations, with 3 axial DoF used to describe joint rotations. A further DoF can be lost from this model by assuming either no internal/external rotation or no varus/valgus movement of the joint. A planar description of the knee joint can also be used which allows only for flexion/extension of the joint and translation of the bones in the sagittal plane. Finally, a 1 DoF description can be made by assuming the joint to be a hinge with a fixed centre of rotation. The description chosen to model the knee joint must be appropriate for the data collected, e.g. it would not be possible to properly model a 6 DoF knee joint if only orientation data were collected. During the data analysis process it is also important to consider the limitations that the model used could have imposed on the data and any potential sources of error introduced.

The choice (or constraint) of the model of the knee joint chosen, and the number of DoF it has, will then influence the description of the joint kinematics. If a 6 DoF model is chosen, then rotation and translation in all 3 body planes can be described. Flexion/extension, internal/external rotation and adduction/abduction can be reported as rotations, and medial-lateral shift, anterior-posterior draw and compression-distraction can be reported as translations. It should be noted that these sets of rotations and translations are not always mutually perpendicular, and as such there can be crosstalk between them. For instance, medial-lateral movement of the bones will likely be accompanied by abduction/adduction due to the uneven surface of the bone. Another example is the screw-home locking mechanism described in Section 3.8, which can cause internal/external rotation as flexion/extension occurs.

Euler angles are another method that can be used to describe joint kinematics and involve decomposing a rotation matrix describing the 3D rotation between two segments in a defined three order. The order of rotations is usually specific to the joint and motion you are interested in, with the choice of order aimed at avoiding the potential for gimbal lock to occur. Typically, the first rotation in the order is the one about which most of the motion occurs. In the case of the knee joint, the first rotation is about the z-axis, as this represents flexion/extension and exhibits the greatest range of motion out of the knee joint axes. Euler angles are quite similar to the methods used by clinicians to describe joint motion and, as such, facilitate easier communication of results. However, Euler angles describe rotation about a point and are unable to present data on the translation of bones within a joint, only relative rotation.

Another method for the description of knee kinematics is to use the helical axis description of motion [57]. This description links the rotation and translation of the joint, so that as the joint rotates it also translates along its axis. In reality, the axis of rotation of the knee joint is not constant and changes with flexion/extension angle [55]. The advantage of using the helical axis for joint description is that it provides information about the actual axes of rotation, compared to Euler angles which can lead to crosstalk between axes. However, joint motion using the helical axis requires both angle and position to be reported and interpreted together [57]. This is substantially different from the clinical descriptive methods used and can lead to difficulty in communicating results to clinicians.

One of the most commonly used methods for describing joint kinematics is the joint coordinate system (JCS) proposed by Grood and Suntay [58]. This is also the system recommended for the reporting of knee kinematic data by the International Society for Biomechanics [59]. In this method, one axis is taken from each of the bodies. In the case of the knee joint, the flexion/extension axis is taken from the femur and the internal/external rotation axis is taken from the tibia. The third axis is formed from the cross-product of these two and is termed the “floating axis”. One of the advantages of this method is that the order of rotations does not have to be specified as is the case with Euler angles. The body fixed axes are formed using joint anatomy and so either a precise anatomical calibration is required or invasive identification of anatomical points. It is also possible to apply the JCS to orientation data and take anatomical axes from each segment without fixing the position of the axes of rotation within the joint.

The methods of knee kinematic description described above are the main ones used in biomechanics. A descriptive method will be chosen during the protocol development chapter that fits within the constraints of the study, with the technology chosen, and still returns meaningful data.

3.10 Knee osteoarthritis and gait

Over the past 20 years there have been numerous investigations into the effects of OA on gait and also into what biomechanical factors may be causing the initiation of the disease. Whilst the following review is not exhaustive of the literature, it provides a balanced representation of the progression in knowledge and understanding of the condition in relation to gait.

In 1992, Messier et al. published a paper [60] focusing on the effects of OA on gait, strength and flexibility. They compared a group of 15 knee OA suffers and a group of 15 healthy controls using a force plate and single video camera perpendicular to the direction of movement. OA assessment was performed using radiographs and graded on the KL scale. Most of the patients were shown to have KL grade 2 OA (KL 2.2±0.15). The results showed that these OA sufferers had decreased mean knee angular velocity and knee range of motion. No difference was found in any of the spatiotemporal variables apart from normalised stride length.

In 2001, Kaufman et al. [61] performed a larger study on 139 adults (mean age 57) diagnosed with early stage knee OA and compared their gait characteristics against those of 20 healthy control subjects (mean age 30). An optoelectronic system and force plate was used to capture data on level walking and stair ascent and descent. They found that for level walking the OA sufferers had 6° less peak knee flexion than healthy controls. Figure 3.3 shows a typical knee flexion movement from an OA sufferer compared with the normal range (shaded region). Whilst the graph stays almost entirely within the normal range a distinct flattening of the curve can be seen during the stance phase (roughly 0-60% of gait cycle) implying increased stiffness in the knee joint. OA subjects also showed significantly lower knee extensor moments which were conjectured to be a method of minimising pain in the joint. Cadence was also significantly reduced during walking for the OA subjects. The stair ascent and descent exercises did not show any differences in the range of joint motion, however speed and knee extensor moment was found to be significantly smaller for OA sufferers for both activities. This again implies a pain management technique. The study also had sufficient numbers to perform a comparison between sexes. Female OA subjects were found to have significantly greater peak knee flexion and no significant difference in velocity. The female subjects also generated greater knee extensor moments than their male counterparts. This is in agreement with females being at greater risk of OA than males [36].

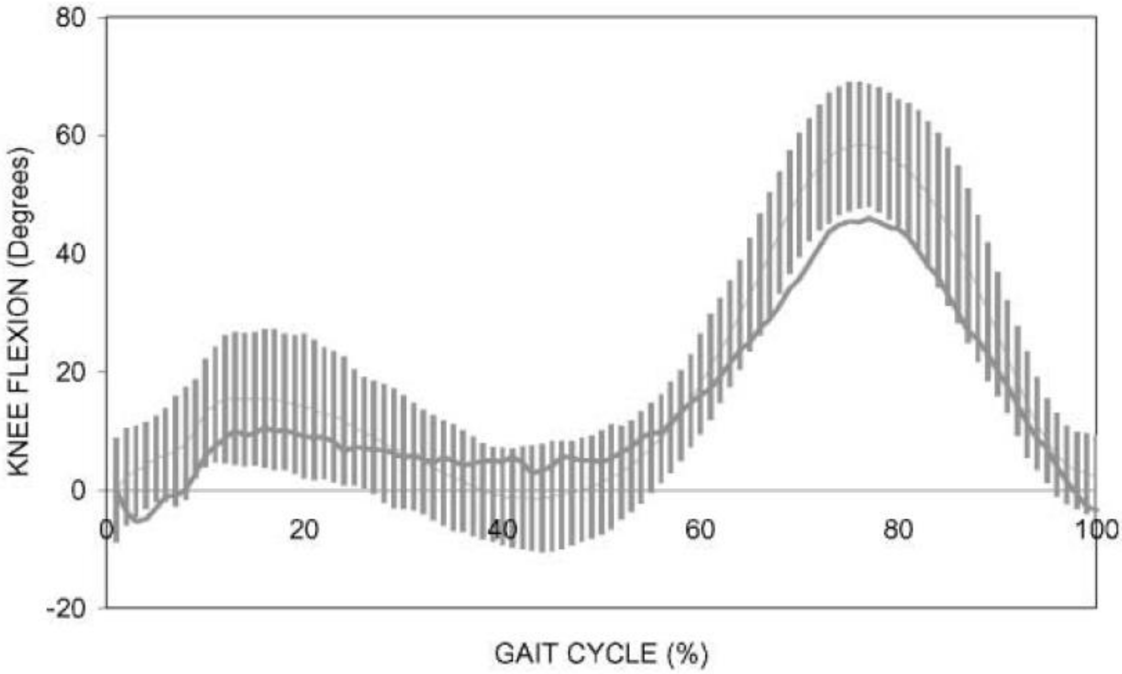

Figure 3.3 Knee flexion during level walking. The shaded region represented the normal range, defined as ±2 standard deviations from the mean. The line represents typical knee flexion movement from an OA sufferer [9].

The issue of sex differences in osteoarthritic gait was further investigated by McKean et al. in 2007 [62]. They studied a group of 39 OA sufferers diagnosed with moderate knee OA (within the range KL grade 1-3), and who were awaiting knee arthroscopy, against 42 healthy subjects. An optoelectronic system and force plate was used to collect walking data on all subjects at self-selected walking speed. Female OA patients exhibited significant differences in knee flexion angle and knee moments in all planes. However, it is unknown whether these biomechanical differences are a contributing factor to females having a higher risk factor for OA, or are a measure of the difference in biomechanical effect OA has on each sex. It could also be noted that no link was found between gait and disease severity. This, in itself, seems unlikely as OA is a progressive disease and symptoms such as stiffness become progressively worse over time. There is also no information given on how many subjects at each KL grade were included so it is difficult to assess the validity of the conclusion.

Al-Zahrani and Bakheit [12] investigated the gait characteristics of patients with severe knee osteoarthritis using an optoelectonic system, force plate and EMG system.

They performed gait analysis on 58 patients (44 female, 14 male – again demonstrating the sex distribution of the disease), with 25 healthy subjects used as controls. Table 3.3 shows the results obtained. Gait characteristics of OA patients were found to be significantly different from healthy controls for all but one of the variables measured (ankle plantarflexion in stance). The reductions in knee flexion and moments are greater than those found in the studies of McKean [62] and Kaufman [61], giving further strength to the progressive nature of OA producing a progressive decline in gait function. It is also interesting to note that the presentation of the data by Al-Zahrani and Bakheit is unusual. It is typical to present either mean and standard deviation, or median and inter-quartile range (IQR). Present the mean and IQR is unusual because, by definition, the mean would be exactly between the upper and lower quartiles.

Table 3.3 The mean and IQR of the spatiotemporal, kinematic and kinetic parameters of gait of the control subjects and the patients with OA [12].

	Control (n = 25)		OA (n = 58)		
Variable	Mean	IQR	Mean	IQR	P-value
Walking speed (m/s)	1.17	1.04-1.29	0.55	0.37-0.72	<0.001
Stride length (m)	1.27	1.18-1.40	0.75	0.63-0.92	<0.001
Mid-stance (% cycle)	30.05	29.72-30.25	34.16	31.58-35.70	<0.001
Mid-swing (% cycle)	80.06	79.70-80.47	84.03	81.54-85.21	<0.001
Hip extension in stance (°)	38.59	33.90-43.00	26.63	21.00-33.45	<0.001
Knee flexion (loading phase) (°)	14.30	9.60-18.40	4.41	2.25-6.25	<0.001
Knee flexion (swing) (°)	60.10	55.60-65.20	34.78	27.65-45.20	<0.001
Ankle plantarflexion (stance) (°)	30.88	23.50-35.60	19.01	15.90-22.70	<0.12
Ankle dorsiflexion (swing) (°)	22.74	17.70-26.40	27.76	21.20-33.10	<0.02
Knee moment (mid-stance) (°)	0.10	0.02-0.24	0.33	0.17-0.49	<0.001
Knee power (mid-stance) (°)	0.11	0.00-0.27	0.01	0.04-0.06	<0.004
Ankle moment (pre-swing) (°)	0.79	0.61-0.91	0.57	0.36-0.78	<0.002
Ankle power (pre-swing) (°)	3.86	2.91-4.53	1.46	0.53-2.31	<0.001

In 2004, Astephen and Deluzio [63] applied a multivariate gait data analysis technique to data collected using an optoelectronic and force plate system on 50 end-stage knee OA patients and 50 asymptomatic controls. The multivariate analysis technique used principle component analysis (PCA) to produce a ranking showing which combination of variables could explain the most variation between groups, and giving a breakdown of what each combination consisted of and how the variables within each were weighted. This method is effective in including the synchronisation of different changes in gait that are otherwise difficult to analyse due to the volume of data produced. Figure 3.4 shows what feature 1, which described 18.46% of the variation between subjects, consisted of. It is primarily kinetic variables that make up this feature, with some kinematic and spatiotemporal ones. Unfortunately, no further information is given on the breakdown of other sets of variables that describe differences between the groups. The authors also state that this technique may only be effective on groups of patients from opposite ends of the OA spectrum as this presents a scenario where substantial changes in gait may be observed, although the technique is generalised and should work for comparison with more subtle differences.

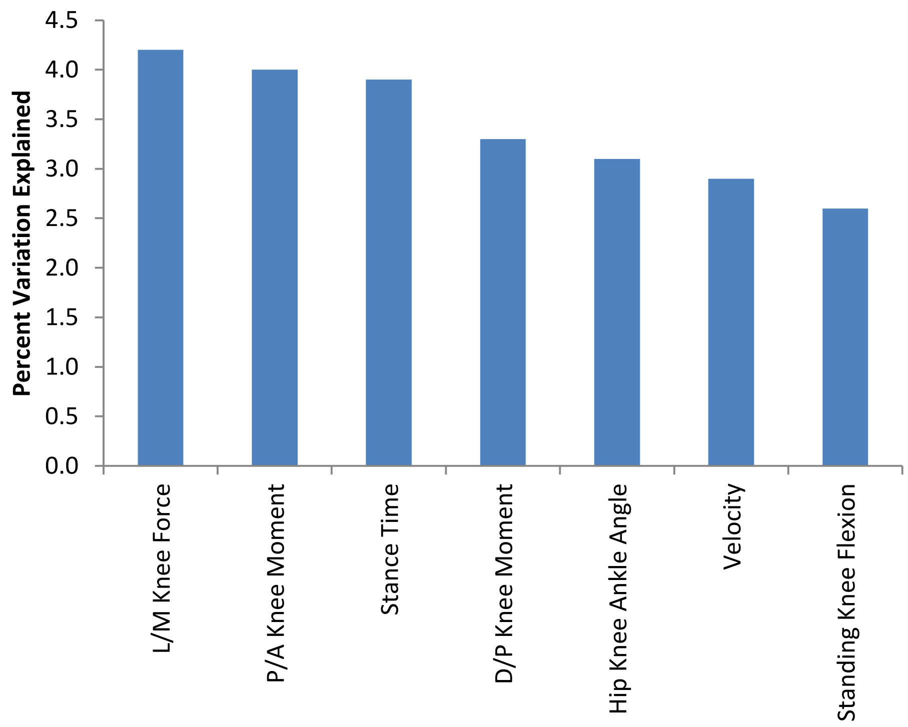

Figure 3.4 Major contributing factors to feature 1 (important in the stance phase of the gait cycle). The values of the percentage variation explained for the seven major contributors of feature 1 are shown. Each major contributor had a percentage variation explained of at least 50 per cent of the maximum percentage variation explained [63].

Childs et al. [64] compared a group of 24 knee OA sufferers against a group of 24 healthy controls. Knee OA presence was defined as clinical and radiographic evidence and grade 2 or higher on the KL scale. Gait recording was performed using an electromagnetic system, a force plate and a surface EMG system with subjects performing both walking and step ascent tasks. During the walking task it was found that OA sufferers had a higher knee angle at heelstrike (4.5° versus 1.4° for healthy subjects) and also had a lower knee flexion range of motion in the loading response phase of stance (15.7° versus 19.5°). This agrees with the conclusions of Messier et al. in that knee OA causes a decrease in function of the affected joint. OA subjects also demonstrated lower peak vertical ground reaction forces than controls and this could be connected with the subjects attempting to minimise pain in the affected joint. Finally, OA subjects were also found to have longer periods of muscle activation which could represent and contribute to the stiffening of the joint.

Throughout these gait analysis studies, either self-selected or pre-defined walking speeds were used. In 2006 Bejek et al. [65] sought to quantify the effect of walking speed on gait parameters of OA sufferers. The OA group consisted of 20 control subjects and 20 knee OA sufferers, all classified as having severe radiographic symptoms (KL grade 3-4). An ultrasound-based gait analysis system (incorporating electromyography sensors) was combined with an instrumented treadmill to record 3D kinematic and kinetic data. Subjects walked at four different speeds, from 1-4 km/h in increments of 1 km/h unless incapable (in which case gait at higher speeds was not recorded). It should be noted that patients with both hip and knee OA were assessed in this study, however only the data for knee patients is included here as this was the focus of the present work. Of the 22 parameters assessed, only 5 were found not to be affected by gait speed, although interestingly the motion of the knee joint was included in this unaffected group. Previous research has shown knee joint motion to be affected by gait speed so this presents a conflict [66]. However, this could be an effect of treadmill walking, which has been shown to produce increased cadence, smaller stride length and stride time, and reductions in the majority of joint angles [67]. When comparing the gait of osteoarthritis and control groups in the study by Bejek et al., statistically significant differences were found in 13 of the 22 parameters measured, including; cadence, double support phase length, and motion of knee joint. The decrease in motion of the knee joint resulted from a combination of increased minimal knee flexion and decreased maximal knee joint flexion. Gait asymmetry was also assessed, and this was shown to be increased in the OA group. The conclusion of the study was that most of the biomechanical parameters measured were affected by gait speed, although it would have been useful if the study had included a measurement of the preferred walking speed of the subjects.

Also in 2006, Henriksen et al. [68] looked at the impulse-forces generated during walking and the alterations to these with the incidence of knee OA. Ten patients diagnosed with radiographic knee OA, and who suffered pain during walking, were compared to ten healthy control subjects using an optoelectronic system and a force plate sampling at 1000 Hz. The transmission of the shock wave generated by heel-strike was measured at their shank and sacrum, and their joint kinematics at heel-strike was also assessed. This research showed no significant differences between the two groups for ground reaction forces, shock wave propagation and heel-strike joint kinematics.

Following on from the work of Astephen in 2004 [50], Deluzio and Astephen in 2007 [69] used a group of 50 end-stage knee OA patients to look at the gait waveform data of three variables; knee flexion angle, flexion moment and knee adduction moment. As with the previous investigation, a force plate and optoelectronic system was used to collect gait data and a control group of 63 healthy subjects was also used. The authors then used principle component analysis (PCA) to compare the two groups. Before reviewing the results of the PCA, it is useful to look at the graph comparing knee flexion of the OA and control groups in Figure 3.5. A distinct flattening of the knee flexion angle during the stance phase can be seen, in line with the results of Kaufman in 2001 [61]. Statistical analysis of the PCA scores showed that OA patients knees were less flexed throughout the gait cycle than the controls, and also that they had less range of motion in the joint. OA subjects were also shown to have a smaller range of flexion moment during gait and a lower flexion moment during the first half of the stance phase. A lower adduction moment in early stance was also shown in the OA subjects. A discriminatory analysis was also performed in order to rank the importance of each component in discriminating between the OA and healthy groups, which in effect is moving towards using gait to diagnose OA. The results of this discriminatory analysis, in ranked order, were; amplitude of flexion moment, range of motion during flexion, magnitude of flexion moment during stance and magnitude of adduction moment during stance.

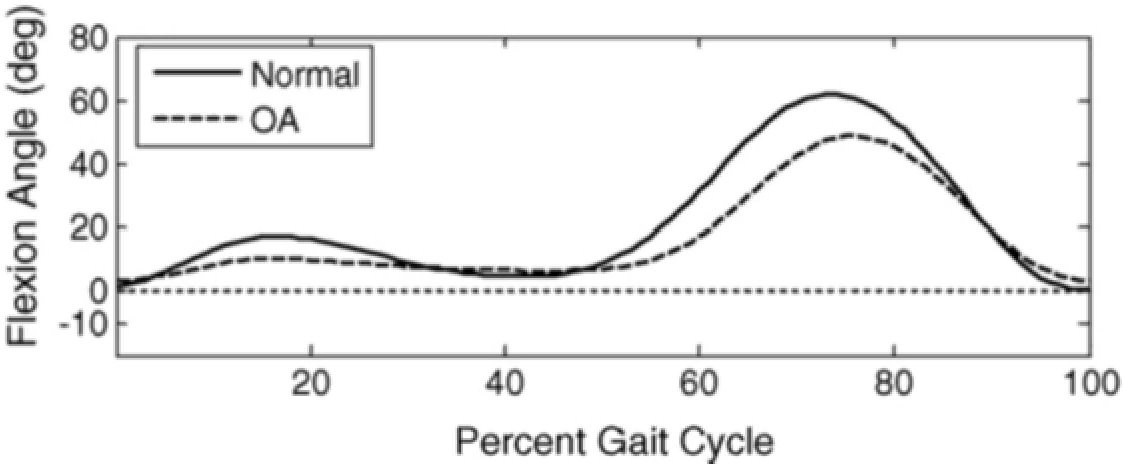

Figure 3.5 Mean knee flexion/extension angle waveform data for the OA patients (dashed) and the control group (solid) [69].

Knee adduction moment is influenced by small kinematic changes in other joints, and Guo et al. [50] investigated the effect of foot progression angle on this variable. Ten subjects presenting KL grade 1-3 OA were analysed using an optoelectronic system and force platform. Subjects walked at a self-selected speed with their natural foot progression angle (FPA) and again with FPA increased by 15°. Knee adduction moment typically has two peaks at the start and end of the stance phase, and increasing the FPA caused the peak towards the ends of stance to decrease during walking. This agrees with data reported studying similar FPA alterations in healthy subjects [70]. It is thought that the increased FPA decreased the ground reaction force lever arm for the second peak by moving it closer to the joint centre. Whilst the study used a small group of patients with varying severities of OA, the work of Guo et al. is useful in providing potential strategies to reduce damaging forces in the knee joint.

In 2007, Landry et al. [71] used the PCA technique previously developed [55] to look at the effect of walking speed on OA. An optoelectronic system and force plate was used to collect data, and 41 patients with radiographic grade 1-3 on the KL scale were compared against 43 asymptomatic patients. Two gait speeds were analysed: self-selected and 150% of self-selected speed. They found that the OA patients had similar stride characteristics and joint kinematics to the control group. This does not agree with the majority of the literature. The kinetic measurements were found to differ between the two groups, and the conclusion drawn was that the kinematic changes are a result of the OA process, with the kinetic changes being linked to incidence of the disease. Increased walking speed was found not to alter this relationship between the two groups, although it did accentuate differences where they previously existed. Therefore, having patients perform a fast walk when attempting to diagnose OA using gait could lead to a greater differences in kinematics between groups. However, there is still the risk that asking patients to walk at a faster speed could cause additional changes to their gait which may erroneously be taken to be indicative of OA. Furthermore, some patients may be unable to walk at the required speed, which could be linked to the severity of their OA.

The studies discussed so far have been cross-sectional in nature and have measured gait at one point in time. Lynn et al. in 2007 [72] published an investigation in which longitudinal changes in gait kinetics were assessed in relation to changes in OA symptoms. Kinetic gait data were collected on 28 healthy older adults who returned 5-11 years later for the same assessment, at which stage they were approximately 72 years old. Of the 28 subjects, 15 had knees that developed osteoarthritis during the intervening period using radiographic measures, and 2 of the subjects had both radiographic OA changes and accompanying symptoms. No difference was found between those whose OA had progressed radiographically, but had no accompanying symptoms, and those who remained healthy. However, in the cases of the 2 subjects with both radiographic and symptomatic diagnosed OA, changes in knee adduction moment were seen that correlated with the affected knee joint compartment. The conclusion can be drawn that an abnormal gait pattern can lead to the development of OA, but that without the development of clinical symptoms, gait function abilities are retained. Whilst the results of this study are useful, the small number of people who then developed OA that affected their gait means that further longitudinal studies are required to establish the true effect of a bi-directional process.

With the increasing use of inertial sensors, Turcot et al. [73] investigated the possibility of using acceleration signals obtained during gait to discriminate between 9 OA patients showing radiographic evidence of OA (KL grade 1-4) and 9 healthy subjects. An optoelectronic system was used to collect kinematic data and accelerometers were attached to the femur and tibia. Whilst the difference between the knee flexion patterns was not statistically significant, the peak knee flexion during both stance and swing phases, shown in Figure 3.6, does show a distinct difference. The acceleration data was presented in two areas; external accelerations measured directly by the sensors, and internal accelerations estimated in the functional coordinate system using a mathematical transformation. External accelerations in the anterior-posterior

(AP) direction were found to be significantly different between the groups. Internal accelerations were found to be significantly different in the medio-lateral (ML) and AP directions. Features in the ML acceleration data could be related to excess varus-valgus movement of the joint during loading, and the AP data implies that the OA subjects were absorbing the load of heel-strike in a less efficient way.

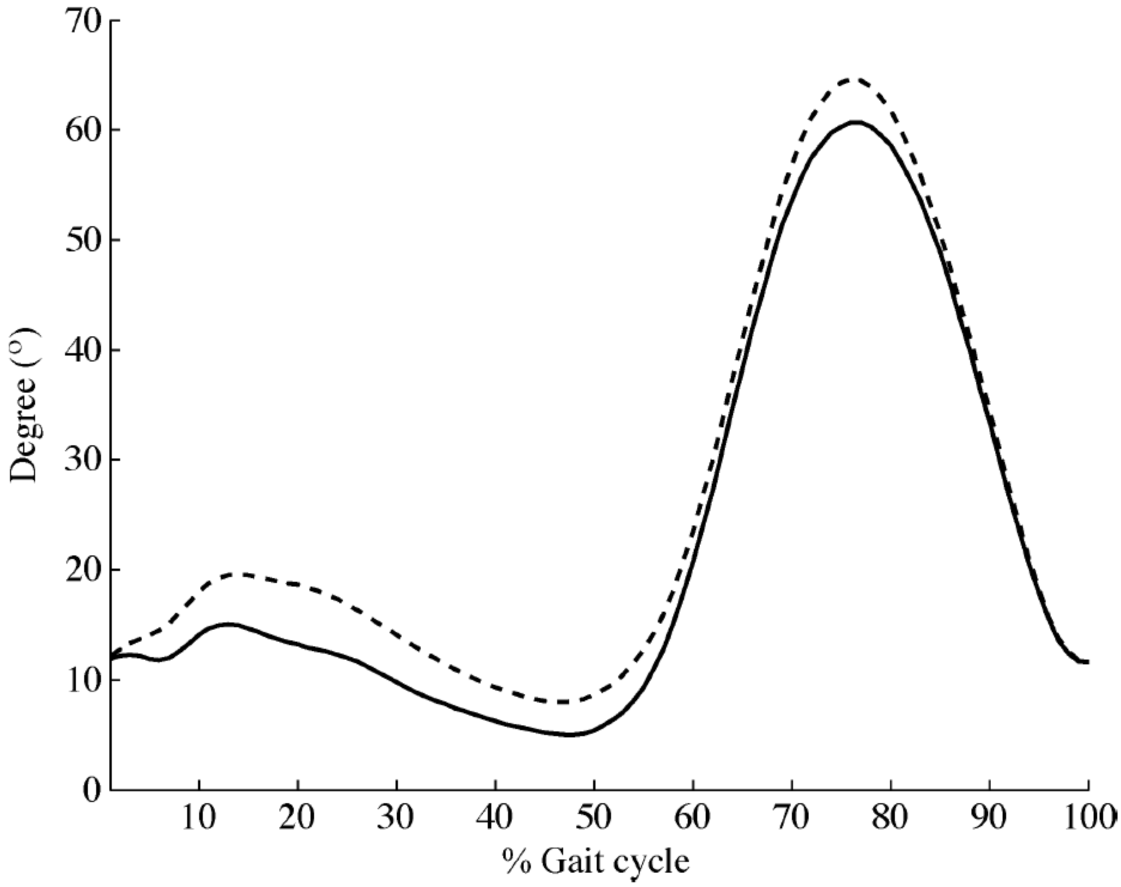

Figure 3.6 Mean knee flexion/extension patterns in degree (°) of OA (solid line, n = 9) and asymptomatic (dashed line, n = 9) groups during gait [73].

Previous investigations have typically involved an OA and a control group, and compared kinematics between the two. Briem and Snyder-Mackler in 2009 [74] looked at the inter-limb differences in 32 patients with moderate knee OA (KL grade 2-3). An optoelectronic system and force plate was used to collect gait data. Asymmetry was seen between affected and unaffected knees for flexion and adduction. However adduction moment of the knee showed no significant difference between affected and unaffected joints. This is thought to be a result of compensatory hip movement in the frontal plane.

In 2009, Zeni and Higginson [75] investigated the relationship between dynamic knee joint stiffness and OA severity using a group of 12 severe OA patients (KL grade 4), 22 moderate patients (KL grade 2-3) and 22 healthy control subjects. Dynamic joint stiffness is defined as the gradient of a line when joint moment is plotted against joint angle and represents the resistance that soft tissues offer in response to an applied moment across a joint. A higher dynamic joint stiffness might indicate an effort to mediate unwanted moments across a joint. An optoelectronic system and instrumented treadmill were used to collect kinematic and kinetic data. Stiffness was found to increase with increasing OA severity, with the severe group found to have significantly higher dynamic joint stiffness than the moderate and control groups. No significant differences were found between the moderate and the control groups.

The same authors then used the same data to assess kinematic differences between asymptomatic controls and moderate and severe OA sufferers over a range of walking speeds (1.0 m/s, self-selected and “fast”) [76]. Walking at a self-selected speed produced the greatest number of significantly different variables. Knee sagittal plane motion was found to be significantly different between all three groups, decreasing with OA severity, which is likely to be a result of increasing stiffness in the joint found in the previous study, coupled with mechanical alterations in the joint causing pain and therefore gait adaptations to minimise this. Peak vertical ground reaction force (GRF), knee flexion moment and loading rate were also found to be significantly different, and these are all likely to be pain-reduction strategies. At 1.0 m/s only loading rate was found to be significantly different between groups ($p = 0.009$), although this is not unexpected. By reducing walking speed, the movement becomes less subconscious and more conscious as the subject is aware that they are not walking at their normal speed at which they are accustomed. A slower walking speed will also mean that body segments are moving slower and that the accelerations experienced at impact are lower.

Pain is generally accepted in the literature as a gait modifier, and patients will employ pain management strategies in their gait to reduce this. It is difficult to separate the effect of joint pain on gait, and in 2010 Henriksen et al. [34] employed a method of inducing joint pain using hypertonic saline injections directly into the infrapatellar fat pad of the knee joint of a healthy group of 36 subjects (18 male, 18 female). This healthy group was also compared to a group of moderate and severe OA sufferers who did not have the injections into their joints. An optoelectronic system and force plate was used to record data. When pain was induced in healthy knees, a significant reduction was seen in the first and second peak adduction moment, the peak extensor moment and the peak flexor moment. Maximum and minimum knee flexion angles were also affected by pain, however no significant change was seen in the knee joint angle at heel strike. In the comparison part of the study, moderate OA patients walked with lower first and second peak adduction moments than the severe patients, with the healthy controls having greater values than both OA groups. The implication is that lowering the peak adduction moment is a pain management strategy, but one that cannot be implemented when OA symptoms become severe, possibly due to mechanical changes in the joint becoming extensive. The knee joints angles showed no significant difference between OA severities or the healthy controls, despite the controls having 2.5° less flexion at heelstrike and 4.2° more flexion in late stance.

Changes in the moments about the knee joint will cause changes in the joint contact forces and this change could be what actually causes damage to the articulating surfaces of the joint. Richards and Higginson [77] estimated the knee contact force (KCF) in patients with varying degrees of OA severity (KL grade 2-3 for moderate OA and grade 4 for severe OA) and a healthy control group. An optoelectronic system and instrumented treadmill were used to collect gait kinematic and kinetic data and an EMG kit used to collect muscle force data. Two peaks occur in KCF during stance phase and the second peak KCF was found to decrease significantly with increasing OA severity, whereas the first peak KCF only decreased for the severe OA subjects. The decrease in the second KCF can be taken as an indication of less muscle force being produced and this would go some way to explaining why gait speed decreases with increasing OA severity. Double support time was also found to increase significantly with increasing OA severity.

Astephen et al. [33] in 2011 investigated the associations between joint biomechanics and neuromuscular control and moderate OA, looking at the differences between radiographic changes and pain severity. Data was collected on a group of 40 OA patients (with a range of severities) using an optoelectronic system, force plate and EMG system. Radiographic OA severity was found to be correlated with knee adduction moment during stance ($R^2 = 0.21$, $p = 0.003$) and maximum knee flexion angle over the whole cycle ($R^2 = 0.11$, $p = 0.03$) with higher knee adduction moments and lower maximum flexion angles associated with more severe OA. Pain was found to only be significantly associated with gait speed and neuromuscular activation patterns, specifically lower lateral gastrocnemius and higher medial hamstring activation.

Cartilage adaptation is one of the key physical features of OA. Koo et al. [78] examined the relationship between cartilage thickness and knee joint kinematics. In order to avoid the cartilage changes associated with OA which may be the cause or result of altered knee joint kinematics, 17 healthy volunteers were used and their gaits recorded with an optoelectronic system and force plate. Cartilage thickness was analysed using MRI. The results showed a significant correlation between medial femoral cartilage thickness and knee flexion angle at heel-strike, with a higher flexion being associated with thicker cartilage.

Debi et al. [79] explored the relationship between single limb support phase length and the WOMAC self-evaluation questionnaire. A GAITRite system (CIR Systems, US) was used to record the single limb support phase length, cadence, velocity and step length of 125 OA patients. Single limb support phase length was found to have a stronger correlation with WOMAC score than with OA grading, and also had a stronger correlation than any of the other spatiotemporal variables measured. The implication of this work is that pain is a greater modifier of gait than radiographic OA, and pain levels strongest correlation being with single limb support phase length supports the theory that the loading of the joint causes the pain.

Also in 2011 (as part of the Baltimore Longitudinal Study of Ageing) Ko et al. [80] looked at the difference in gait patterns between older adults with and without knee osteoarthritis. A group of 41 OA sufferers (17 symptomatic, 24 asymptomatic) were compared to 112 non-OA sufferers. An optoelectronic and force plate system was used to collect gait data and both “usual” and “fast” walking speeds were analysed, as well as another “usual” walking speed trial after the procedure had been completed (roughly 30 minutes after the first walking trial). At usual walking speed, gait speed and stance phase length were found to differ significantly between OA and non-OA groups, but not within the OA group (symptomatic vs asymptomatic). At fast walking, stance phase length and knee range of motion were found to differ significantly between OA and non-OA groups. Interestingly, in the usual walking speed trial conducted 30 minutes after the assessments had started, gait speed, stance phase length and knee range of motion were all found to be significantly different between the OA and non-OA groups. This could imply an effect of habituation or relaxation, which was not present at the start of the assessment exercise and after 30 minutes participants assumed a more natural gait. Alternatively this could be viewed as an effect of fatigue after 30 minutes of activity that affected OA sufferers more.

Most recently in 2012, Kubinski and Higginson [81] investigated the effect of a weighted walking task on gait kinematics. The purpose of this was to look at the different loading strategies induced by weighting and how adaptation to extra weight varied between healthy and osteoarthritis individuals. A group of 20 individuals with knee osteoarthritis were compared to 20 age- and sex-matched healthy individuals, using an optoelectronic system and instrumented treadmill. Whilst the measurements were recorded at a constant walking speed of 1.0 m/s, subjects were also asked to provide a self-selected walking speed. Overall, OA subjects walked significantly slower than healthy subjects, with approximately a 12% decrease in walking speed between groups. In total there were 4 groups for the statistical analysis; weighted and un-weighted walking tasks for both healthy and knee OA groups. Comparing the groups for the un-weighted tasks, the only significant differences were found in initial double support phase length and load rate. For the OA group, only the initial double support phase length was found to be significantly different during the weight bearing task, whereas in the healthy individuals the hip flexion angle at foot-strike was found to be significantly different, as was the initial double support phase length. The conclusions from this work were that OA individuals have less capacity to adapt their kinematics during weight bearing tasks, and that even in un-weighted tasks the OA individuals showed differences during the loading phase of gait.

This review of the existing literature on the links between osteoarthritis and gait kinematics has highlighted several areas of interest. There are common gait features which are consistently shown to be significantly linked to osteoarthritis severity. These being; knee adduction moment, knee flexion angle, stiffness and walking speed. In the more recent publications there has also been a shift towards analysing the part of stance phase immediately following heel-strike. There has also been a distinct flattening of the knee flexion graphs during stance phase for OA sufferers and this is indicative of a decline in knee function. Finally, OA sufferers have been shown to differ during the loading phase of gait, when weight is being transferred onto an affected joint.

Previous work in the field of biomechanics has focused on gait kinematics, gait kinetics and neuromuscular control [12, 33, 61]. There have also been studies on the effects of pain caused by OA on gait [34]. OA severity is usually established using radiographs which are graded using the Kellgren-Lawrence (KL) scale [22]. However, many of these studies group OA severities together into “moderate” OA (typically KL grade 1-3) [62, 64, 74] and “severe” OA (KL grade 4) [76]. In his review paper, published in 2010 [82], Englund concluded that research needs to focus on the early stages of OA in order to understand the role of biomechanics in initiation of the disease.

These previous studies have typically grouped OA grading into groups for “moderate” (typically KL grade 1-3) and “severe” (typically KL grade 4). In order to assess the affect of OA initiation and progression on gait kinematics it is important to look at each grading individually, otherwise a degree of resolution is lost. In order to do this, sufficient subject numbers are required for each OA grading, and this may be why previous studies decided to group their KL grades in order to increase the size of each group and allow reliable statistical analysis. The NTFS cohort provided a cohort of sufficient size that each grade had sufficient numbers to allow statistical analysis between grades, as well as with ‘controls’.

3.11 Relevant gait variables for this study

Before a method for the gait analysis of the NTFS cohort was developed, it was important to identify what variables were of interest when looking at gait in relation to OA. This final section provides a summary of the variables from the literature that were found to be linked with OA.

Spatiotemporal parameters have been shown to provide a good distinction between OA and asymptomatic patients. Cadence, walking speed, stance phase length, double support phase length, and stride length have all been found to be significantly different between groups.

Sagittal and transverse plane knee joint angles have also been used to distinguish between groups in previous studies. Overall range of motion and stance phase range of motion of the knee joint in the sagittal plane are useful, and the knee joint angle at heel-strike has also been shown to be an important factor. The shape of the stance phase curve is of interest as well. Transverse plane range of motion of the knee joint is a good indicator of stability of the joint and the tranverse plane joint angle at initial contact would be linked to the instantaneous joint moment at heel-strike.

Kinetic variables such as flexion and adduction moments about the knee joint also differ between subject groups, as well as the forces experienced by the joint during walking and particularly at heelstrike and in the loading phase.

Medical history and current evaluation of the cohort will allow identification of previous injuries or current ailments that may have affected gait and therefore mask, replicate or aggravate the kinematic changes as a result of OA. This was used to determine whether a participant was excluded from the final analysis based upon the criteria for exclusion. There were also several variables that were important to consider as confounding factors when looking at the links between OA and gait kinematics. BMI was one of the most obvious, with BMI showing a clear link with OA [37] and BMI also altering the loading within a knee joint. Pain whilst walking was also included as potential confounding factor as pain in a joint naturally promotes gait alteration to minimise pain.

Before development of gait analysis protocol began, it was important to note that whilst all these variables may be useful, it may not be possible to measure all of them. The gait analysis method chosen, and the protocol developed for the NTFS cohort gait analysis, had to strike a balance between fitting within the constraints of the study and recording relevant variables.

3.12 Summary

This chapter has shown that there are multiple methods of diagnosing OA, and that there are several different tests that can be performed when assessing movement in relation to the disease. The methods of describing knee joint motion have been detailed. It has also gone through extensive literature on previous studies looking at OA and gait, and identified variables previously linked with OA. Table 3.4 summarises the information from this chapter relevant to gait analysis protocol development. This information will be assessed in conjunction with the engineering specification created in Section 2.7 during the technology selection and protocol development.

Table 3.4 Summary of the information found in this chapter relevant to NTFS gait analysis protocol development, including; indicators of OA, tests for assessing joint movement, methods of describing knee joint motion, and relevant variables for assessing OA in relation to gait found in the literature. Both sit-to-stand motion and stair climbing have been excluded from the tests for assessing joint movement as they have risks associated with orthostatic hypotension, but have been included here for completeness.

Indicators of OA
Clinical examination
Radiographic imaging
Pain Scoring
Tests for Assessing Joint Movement
Gait
Sit-to-stand motion (excluded)
Stair climbing (excluded)
Methods of Describing Knee Joint Motion
Full 6 DoF description
Helical axis
Euler angles
Joint coordinate system
Relevant Variables
Spatiotemporal parameters
Sagittal and transverse plane knee kinematics
Flexion and adduction moments
Joint contact forces
Accelerations and forces at heel-strike
Confounding variables to include in analysis

Chapter 4 Selecting an Appropriate Technology for Gait Analysis

Motion analysis has expanded vastly since its inception in the 1880's by Eadward Muybridge [83]. The methods available have swelled to include video cameras, optoelectronic systems, electromyography, inertial systems, force plates, goniometers, and a plethora of other technologies employed in novel and creative scenarios. As with many other aspects of science, technology continually develops and methods come in and out of fashion depending on the current state of the art. With this expansion and development, it has become increasingly difficult to select the most appropriate technology for gait analysis.

This chapter deals with the selection of an appropriate method for gait analysis of the Newcastle Thousand Families Study (NTFS) that allowed the examination of kinematic features of gait. It begins by discussing the challenges associated with performing gait analysis in a clinical environment and the essential criteria that the method needed to meet. This is followed by a brief overview of the motion analysis methods commonly available. The chapter then moves on to how an appropriate method, taking into account both the constraints of the NTFS, was selected, and the variables of interest, with inertial sensors being identified as the most appropriate method. An explanation of inertial sensors and a review of their use for gait analysis are presented. The chapter then looks at the use of inertial sensors in clinical settings and also how inertial sensors have been used so far in the investigation of osteoarthritis (OA). Finally, this chapter concludes with the selection of a system supplier and the preliminary testing of the system to establish its feasibility for joint angle measurement using a 4-bar linkage.

4.1 Gait analysis in a hospital environment – the challenges

Gait analysis in a hospital environment has several major advantages associated with it; patients attending for gait analysis can attend for other tests in the same visit, and thus cut down on inconvenience and increase the ability for assessment of association with other clinical data. Hospital environments are also a more familiar setting for a patient than a gait laboratory and they may feel more comfortable. Finally, recruitment for studies is a major task for any gait study and working in a hospital environment allows news of relevant studies to be communicated to patients by their physicians.

A dedicated gait laboratory allows environmental and logistic variables to be tightly controlled. The space available would have been chosen and designed to be suitable for the actions to be performed and provide sufficient space for equipment and personnel. The space would also have been chosen in order to accommodate the technology being used for analysis and the time frame allowed for each subject would be more than sufficient for the activity taking place.

In a clinical environment the circumstances are somewhat different. Finding a large unused room within a hospital is a rare occurrence and gait analysis technology will not often be accorded a private space within a facility. Therefore, it must fit in existing space within the hospital and co-habit with other equipment, studies and functions associated with the space. For example, corridors are sometimes used for gait assessment as they provide a large enough space for gait to be established, but they are also used for transit by others using the hospital. Similarly, hospital bays provide a suitable venue for attachment of markers/sensors and have privacy screens to preserve modesty, but they may also be used for assessment and treatment of patients of the hospital.

Whatever the space allocated for gait analysis to take place, it is unlikely that researchers would be allowed to permanently fix optoelectronic cameras or other systems to the walls as these would require repair after use, detract from the multi-purpose aspects of the space provided, and cause potential hazards for patients around the hospital. From the researcher's perspective, a hospital is a public space and there are issues of security with leaving expensive equipment here. So any system chosen for gait analysis in a hospital environment has to be able to adapt to whatever space is provided and must also be portable so that it can be moved around as required and not require permanent fixture.

The essential requirements for a gait analysis system to be used in a clinical environment are that:

- The system will measure the variables of interest to the study.

- The system will fit within the space provided by the hospital for gait analysis to take place.
- The system is portable and does not require permanent installation.

The following section presents an overview of the common methods of gait analysis and in each case the technology will be assessed based on the criteria listed above.

4.2 Overview of common methods of gait analysis

As mentioned, gait analysis has expanded to encompass a variety of methods that can measure a variety of kinematic and kinetic variables. Before moving onto selecting an appropriate system it was important to understand how each method works, what each method offers and what its drawbacks are. It is important to note that while many other techniques exist, only the most commonly used gait analysis methods have been considered, and that the evaluation of the systems has focused on practicality and portability.

4.2.1 Optoelectronic systems

Optoelectonic systems are the most commonly used technology for motion analysis [84] and are widely accepted as being the gold standard for data capture, due to extensive iterative development of the technique. They provide accurate kinematic data and, with the current software, interface easily with other technologies such as force plates.

Optoelectronic systems function by converting light signals into electrical signals and track the light emitted or reflected by markers attached to a subject. The system consists of several cameras (usually 6 or more) arranged to capture the area of interest on a subject. For gait analysis of both legs, the arrangement would typically form a circle. The cameras are calibrated so that their positions relative to each other is known and the capture volume formed is well defined. The cameras then track markers attached to a subject, of which there are two types; Active markers emit a signal that is tracked by the cameras and typically come in the form of small LEDs, whereas passive markers reflect near infra-red light emitted by the cameras. The position of each marker within the capture volume is then calculated based on the signal from each camera and their known positions with respect to each other. In order to generate a three-dimensional position for a marker it must be seen by at least 2 cameras and the more cameras that see the marker the less error there will be in its computed position.

Once the position of each marker has been found at each time-frame, these data can be fed into a pre-defined or custom-made model to compute joint angles. The joint angle calculation uses the markers on one segment to define a set of anatomical axes and similarly for the following segment. The angle between the two anatomical axes is then calculated at each time point, producing the joint angle in 3-dimensions over the period. This angle can then be expressed using whatever convention is appropriate.

As stated, these systems provide accurate kinematic data about the movement of a subject. However there are a few drawbacks. The quality of the kinematic data produced is dependent on accurate placement of markers on a subject relative to bony anatomical landmarks or other features. The models used to calculate joint angles use several kinematic constraints and contain no capacity for checking if a marker has been placed in the proper position. Therefore, improperly placed markers will affect the formation of the anatomical axes and thus the calculation of joint angles. Linking into the accuracy of the marker placement, the effect of intra- and inter-operator repeatability of marker placement should be considered [85]. Two operators may place markers in different locations on the same subject, leading to differences in the model produced and thus differing joint kinematics. A single operator may place the markers in slightly different places each time, again leading to variation.

Another problem associated with optoelectronic system is “skin movement artefact” [86-88]. Markers can be placed over bony anatomical landmark in order to form a coordinate system. However the skin is not rigidly attached to these structures and will move and stretch over them during movement. An example of this is would be the movement of the skin over the anterior superior iliac spine. However skin movement artefact does not just happen at bony landmarks; contraction and relaxation of muscle mass can cause skin movement and distort the position of markers relative to the underlying skeleton. Methods have been proposed to deal with skin movement artefact, but there is as yet no standardised technique [89].

There are also other practicalities associated with using an optoelectronic system. As six cameras or more are typically required, this requires a substantial space (typically greater than $10m^2$) in order to accommodate the equipment and also form a suitably sized capture volume and Figure 4.1 shows an example of the typical layout of optoelectronic and the capture volume formed. Camera positioning is another factor that can affect as the more cameras that see each marker, the more accurate the data produced will be. Ideally, cameras would be mounted on the walls or ceiling to give a stable mounting position and this requires a space devoted purely to motion capture. By mounting cameras on tripods, optoelectronic systems are also portable, but they still require some effort to transport and time to set up.

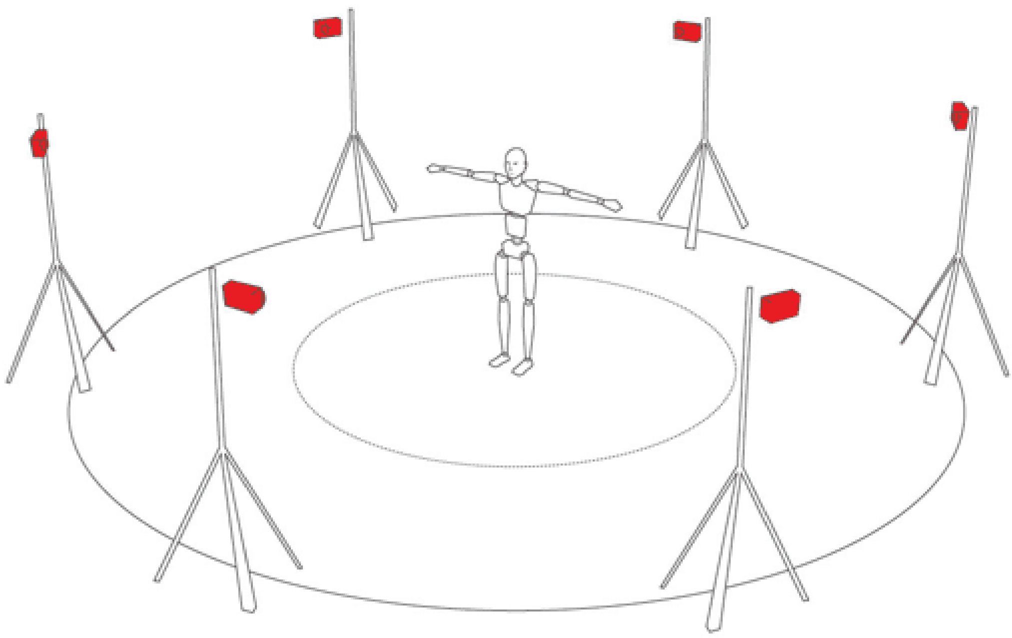

Figure 4.1 Typical optoelectronic camera setup to form a capture volume, image used from Optitrak website (NaturalPoint, USA).

So, whilst optoelectronic systems are a well established and accurate technology for kinematic measurement of movement, they do have some drawbacks with respect to inter- and intra-rater repeatability and also their space requirements in order to form a capture volume.

4.2.2 Force plates

Like optoelectronic systems, force plates have also been the subject of continuous iterative development over many years. They measure the ground reaction forces generated by objects in contact with them and, from this, kinetic data can be calculated.

Force plates typically consist of a steel plate with an embedded sensor. They are available in a variety of configurations; the simplest ones use a single sensor that will return only the vertical component of the force applied to the platform. More complex set-ups use multiple sensors and can return the three-dimensional components of an applied force, as well as the moment of the force and centre of pressure. Force plates containing more sensors are also capable of detecting and differentiating multiple force applications (Kistler Group, Switzerland). The sensors come in the form of either load cells or force transducers. When a load is applied to the plate it is detected by the cells/transducers and this is then converted into an electrical signal. The magnitude and direction of the force is calculated from this electrical signal using the position of the cells/transducers and the signal recorded by each of them. This is done for each time interval, and force plates can achieve sampling rates of 1000 Hz or more [90]. Force plates come in a variety of sizes, and the size of the force plate used, the number of sensors within it, and the range of readings it can measure are chosen to suit the application.

Force plates are commonly used in gait analysis studies where the ground contact forces are a variable of interest [91, 92] or where joint contact forces are thought to be important [77, 93]. They provide accurate force data at high sampling rates that can then be used to calculate kinetic data using inverse dynamics. They are calibrated using either an object of known mass or using the pole-test method [94] and are a quick process.

However, there are some drawbacks to using force plates, and once again these are related to portability and practicality. Most force plates are set into a frame in the floor and form a permanent installation as part of a gait laboratory. In order to increase portability the plate could be set in a portable frame, with ramps leading up onto it, but these can suffer problems with damping of unwanted vibrations and stability of the mountings. There is also the risk that the ramps may alter the subject’s gait and thus the ramps should ideally be followed by a level section of walkway to allow gait to stabilise again, which add further bulk to the set up. In addition to this, force plates are quite heavy which further decreases portability.

With the force plate representing a finite area on which foot contact has to take place, this creates problems similar to those of the capture volume with the optoelectronic system. If the subject does not land their foot fully on the force plate during gait then complete information of the forces and moments present during the ground contact phase of their gait are not recorded, and there is also the risk of the subject missing landing on the force plate entirely. Whilst practice and training can lead to a subject reliably landing on the force plate, this training takes time and it could be argued that such training and focusing on the force plate could induce a subconscious change in their gait.

Force plates, like optoelectronic systems, are a well established and commonly used method and capture accurate force data that can be used to calculate kinetic variables. However they have some drawbacks relating to mounting requirements and also training of participants to reliably land their foot on the force plate in each trial.

4.2.3 Inertial measurement units

Inertial measurement units (IMU) consist of a combination of accelerometers and/or gyroscopes, both of which work on the principle of the measurement of inertia (the tendency of an object to resist a change in motion). They are capable of measuring kinematic data in the form of orientations of limb segments, and also kinetic data in the form of accelerations and angular velocities.

Accelerometers operate on a spring-mass principal. Two charged plates are separated and the capacitance between them is a function of their separation distance. One plate is suspended over the other on a flexible mounting and acceleration causes this mounting to flex causing a change in plate separation and thus a change in capacitance. This change in capacitance is measured and then the change in separation is calculated. Gyroscopes are based on the principle of conservation of angular momentum. A spinning wheel or disc is mounted within a series of gimbals, allowing three-dimensional rotation of the disc. The large angular momentum of the disk means that an external torque applied to it causes a much smaller change in orientation then it would otherwise. The external torque is minimised by mounting the disc within gimbals and its orientation remains nearly fixed regardless of the motion of any body segment it is fixed to. The gyroscope therefore forms a fixed reference frame which can be used to obtain the orientation of body segments. The combination of accelerometers and gyroscopes form’s an inertial measurement unit, capable of measuring both the orientation of a limb segment and the accelerations experienced by it.

In comparison to optoelectronic system and force plates, IMU's are a relatively young technology, but one that has become increasingly popular for gait analysis since the late 1990's with more studies reporting their use due to rapid progression of the technology [84]. They are also portable as the sensors themselves are typically very small and data can be collected by a data logger attached to the subject, thereby freeing the subject from any capture volume constraints [90].

However, IMU's do have some disadvantages, the most prominent of these being integration drift. Small errors in measurement of acceleration and angular velocity propagate into large errors in position via double integration and, since each new reading is calculated from the previous one, the errors are cumulative. Therefore, a correction must be periodically applied from another sensor, which in the case of IMU's for gait analysis is usually a magnetometer used to correct the heading reading. Unfortunately, magnetometers also suffer their own problems caused by variations in the local magnetic field [95, 96]. Large distortions in the magnetic field can cause them to produce a false reading and therefore the correction applied to the IMU is also false. As a solution, fusion algorithms are often employed that simultaneously use the magnetometer to correct the IMU, and the IMU to correct the magnetometer.

A further shortcoming of IMU's is that they record orientation, but not position, so whilst joint angles can be calculated directly, the position of the segments in three-dimensional space cannot. Indirect calculation can be performed used a double integration of the acceleration signal. However, this has the same caveats as previously described for double integration [97]. Recently, some work has been done on a process that assumes zero-velocity when an inertial sensor attached to the foot is in contact with the floor, and using this to compensate for integration drift and calculate stride length [98]. This method has been validated for accelerations measured using an optoelectronic system but has yet to be applied to an inertial sensor. As a result of not returning positional data IMU's cannot return spatiotemporal variables such as walking speed. However, it is still possible to measure cadence [99].

IMU's, whilst being a young technology in comparison to optoelectronic systems and force plates, offer a solution for gait analysis that is both portable and adaptable to the environment within which it is placed, but with the drawbacks of not being able to measure positional data and being affected by disturbances in the local magnetic field.

4.2.4 Electromyography

Electromyography (EMG) systems are used to detect and measure the electric current produced by muscles during contraction and thereby detect which muscles are being used during an activity, and how and in what combinations they activate.

Sensors can be placed on the skin (surface EMG) or fine wires can be inserted into the muscle of interest (intra-muscular EMG). These sensors then detect the electrical signal generated during muscle contraction and this is passed through a signal amplifier before it is recorded for later analysis. Unlike the other techniques mentioned previously, EMG does not produce kinematic or kinetic data. Instead, it can identify which muscles are used to perform an action, how the work needed to perform the action is distributed between the muscles, and can also give an indication of abnormal muscle performance [100]. Typically, EMG systems are combined with other technologies for gait analysis in order to provide both the muscle activation data and the kinematic or kinetic data [90]. Looking at these in conjunction can provide a multi-layered view of how the person walks and how they are controlling their gait.

Modern EMG sensors can be very small and light and can record data either via a data logger or via wireless transmission back to a computer [101]. This frees them from the constraints associated with optoelectronic systems and force plates in a similar way to IMU's.

EMG systems do have some disadvantages associated with them. As mentioned, there are two methods of attaching the sensors, surface and intra-muscular. Intra-muscular sensor attachment is an inherently invasive procedure and can be painful during both insertion and movement, and the wires can be difficult to remove and sometimes cause damage to the surrounding muscle tissues. Surface mounted sensors do not encounter these problems. However, they can return erroneous readings for a specific muscle, as other muscles lying around or on top can cause cross-talk in the signal [102]. Each muscle signal muscle then is distinguished using its motor unit action potential (MUAP) and the expected activation pattern for that muscle. Differences in muscle layout, mass and density between participants can also make distinguishing different muscles more difficult [90].

EMG systems provide data on muscle activation. The systems are portable and free from capture volume constraints. However there are some difficulties associated with sensor attachment methods and distinguishing between signals from muscles in the same locality.

4.2.5 Marker-free systems

Marker-free systems are perhaps the most recent gait analysis technology and, as such, are one of the least developed and accurate. However, they are capable of returning kinematic data and offer a level of freedom that is unparalleled in comparison to the other systems mentioned.

Marker-free systems, as the name suggests, use no markers attached to the subject. Instead they use a video camera (or set of video cameras) to record an activity performed by the subject. The cameras are normally set up to record data in one (or several) of the three anatomical planes. This video data is then digitised, either manually or using an automated system. This involves identifying and marking joint centres on the video data. Manual digitisation requires these points to be marked on each frame of the video, whereas automated digitisation requires manual digitisation of the first frame and then uses a set of constraints to automatically digitise the rest. Examples of these constraints are segment length, velocity and pixel intensity. Once all frames have been digitised, the joint angles are then calculated for each plane of movement.

Marker-free systems have several advantages, the foremost of which is their portability. A single camera system to capture motion in the sagittal plane could easily be carried by a person, and set up time is minimal with the important parameters being the focus of the camera and ensuring it is perpendicular to the plane of movement. There is also no marker attachment to deal with which reduces inter-rater error. This method also avoids participants having to disrobe or change clothing.

There are some disadvantages associated with marker-free systems. If a subject is wearing clothing this could make it more difficult (or even impossible with loose clothing) to track the motion of their body underneath. This is fundamentally the same problem as that created by skin motion artefact. There are also inaccuracies associated with the digitisation process; an incorrect manual digitisation of the first frame would then impact upon the automation of the process, and the quality of any manual digitisation process is based upon the operator’s judgement [103]. Once again, judgement of the initial manual digitisation would be affected heavily by the clothing worn by the subject.

Marker-free systems provide a portable solution for gait analysis with a minimum of inconvenience to the subject. However, they are susceptible to problems associated with tracking of the underlying anatomy which then leads to errors in the calculated joint angles.

4.2.6 Electromagnetic systems

Electromagnetic systems work on the principle of disturbance of a homogeneous magnetic field by a ferrous metal or electronic device. A base station produces a homogenous magnetic field in the surround area and each object produces a unique disturbance that allows tracking of the position and orientation of the body segment they it is attached to.

Electromagnetic systems have several advantages. They provide both position and orientation of body segments, but do not require a line of sight as would be the case with an optoelectronic system. They are also portable and the disturbance objects can be secured attached over the top of clothing, or underneath clothing if appropriate and practical. Also, unlike inertial sensors, they do not suffer from integration drift.

However, there are a few disadvantages of using an electromagnetic system. Typically the capture volume created takes the shape of a sphere centered on the base station which generates the magnetic field and the radius of this sphere is dependent on the strength of magnetic field produced. Capture volumes can be as large as 2-4m in diameter but this requires a powerful field emitter. Electromagnetic systems are also not appropriate for use around patients fitted with pacemakers as they can interfere with the normal operation of the device.

4.3 Selection of an appropriate technology

The overview in the previous section has highlighted that there are several technologies available for gait analysis in a hospital environment, each with its own advantages and disadvantages. In order to select an appropriate technology for gait analysis of the NTFS cohort these must all be assessed in relation the engineering specification set out in Table 2.3 (Section 2.7, page 14) and the information found on previous work on OA and gait in Chapter 3. The selection process first considered the conditions of involvement as, without compliance with these, the gait analysis would not have taken place at all. In addition, it was also considered whether the system would be able to measure some (or all) of the variables of interest listed in Table 3.4.

Optoelectronic systems were the first method to be excluded from selection, as markers normally attach directly to the skin which wound contravene requirement C. There existed the option of using a lycra suit with markers already attached. However the intention of attaching the markers over a participants clothing, while primarily to preserve dignity, was also to avoid them having to disrobe at all and adding time to an already tight schedule given the wide range of other clinical assessments. An optoelectronic system would also have required a substantial space in order to position cameras and form a capture volume, and the 2m wide corridor allocated to perform the walking trials did not provide space for this.

Force plates are the next technology to be excluded by the criteria because they require fitting into the floor, or for a raised walkway to be build around them with a ramp leading up to this. Fitting a force plate into the floor of the corridor is not an option available as it would require substantial building work and would breach requirement K (Table 2.3). Building a removable walkway which the force plate could fit into was the other option, but this was discounted as the method has to be portable, quick to set-up and take down, and easy to store. A portable walkway would require significant storage space and would take time to assemble each morning as it could not be left in place overnight.

Electromagnetic systems were appropriate for data capture within almost all conditions of the NTFS steering committee. However, it was possible that one or more of the study members who attended for clinical assessment would have a pace maker and this would make them unable to perform the gait analysis. Requirement D states that all able NTFS cohort members had to be recorded. Exclusion based upon having a pacemaker was not permissible, so therefore electromagnetic systems were excluded.

This left inertial systems, electromyography and marker-free systems as remaining options. Marker-free systems were rejected because while they are portable and do not require any marker attachment, the technology does have some problems with clothing worn over limb segments. In addition to this, whilst the technology shows great potential, it is currently not far enough advanced to produce data with repeatability that is comparable to other systems that measure kinematics.

Electromyography and inertial systems provide very different types of data, but both are available as a wireless system with a data logger attached to the subject and the sensors used by both systems are small and lightweight. However, electromyography systems by their very nature require direct contact with skin and this would therefore require the subject to disrobe during the gait analysis in order for the sensors to be attached, which would be in breach of requirement C. Clothes could then be placed on top of the sensors in order to preserve modesty, but this disrobing and then dressing would add more time onto the proceedings which is to be avoided and may conflict with requirement B.

This led to the decision that inertial sensors were the best choice for this study. They can attach over the top of clothing, can provide temporal on cadence and gait cycle phase lengths, kinematic data about joint angles, and also kinetic data on accelerations experienced by limb segments [104-106]. Inertial systems are also portable and can be carried by a single person, and is easy to store and can be operated from a laptop by a single person. The following section will now assess in more depth previous studies focusing on validation of inertial sensors for gait analysis.

4.4 Previous validation of inertial sensors for gait kinematic measurement

As inertial systems have grown in popularity over the past ten years much work has focused on benchmarking them against the “reference standard” optoelectronic systems, and it is important to review the literature to see how they compared, what protocols proved the most effective for obtaining comparable results with an inertial system, and what the potential problems are when using an inertial system. For the purposes of this review inertial measurement units (IMUs) will be taken to mean sensors combining readings from accelerometer and gyroscopes, and in addition to these incorporate magnetometers. It should be noted that this is an overview of how inertial sensors have been used for gait analysis, their performance and success in this role, and how well they compare to other methods of gait analysis. Specific features of protocols, such as sensor attachment and calibration methods, are reviewed in detail in Chapter 5.

Williamson and Andrews in 2001 [107] reported the comparison of an accelerometer and gyroscope system against an electrogoniometer for measurement of knee joint angle and angular velocity on both real and simulated knee joints. The error for the simulated knee joint angle was found to be 2.1° and 4° for the real knee joint angle. However, there may be errors associated with the electrogoniometer reading due to the separation of its attachment points being variable and therefore inducing strain and possibly movement of the attachment points. This paper demonstrated a clear application and testing of inertial sensors against an established method, albeit not an optoelectronic system, and the system proved to have great potential. A calibration method for defining body anatomical axes is not specified by the authors.

In 2002, Mayagoitia et al. [108] presented a comparison of a bespoke inertial system against a Vicon optoelectronic system for measurement of shank angle, shank angular velocity, knee linear acceleration and shank angular acceleration. Two accelerometers and a gyroscope were attached to an aluminium strip, and then secured on the frontal medial aspect of each shank with Velcro strapping. Subjects walked at 5 different walking speeds. The results presented showed that the inertial system produced results very close to those of the optoelectronic system, but with errors increasing at the highest walking speeds. It was postulated by the authors that these errors were likely due to the increase in vibration of the sensor at higher walking speeds, which seems reasonable, considering the attachment method used was Velcro strapping, the secureness of which can vary.

Whilst not focusing on gait kinematics, Luinge and Veltink [109] published a paper featuring a comparison of an IMU system, consisting of three-dimensional accelerometers and gyroscopes, against a Vicon (Oxford Metrics, UK) optoelectronic system for measurement of upper body kinematics. Their focus was not on joint angle calculation, but on methods to improve orientation estimation of the sensors and reduce the drift experienced. Their conclusion was that orientation drift was caused almost entirely by heading error. Heading error can be corrected by either using biomechanical constraints on the body segments, or by employing a magnetic field sensor as seen in other studies.

Bergmann et al. in 2009 [110] reported a comparison of inertial and optoelectronic systems for measurement of hip, knee and ankle joint angles during stair ascent. Six Xsens IMU’s (Xsens Technologies, Netherlands) were compared against a

Codamotion optoelectronic system (Leicestershire, UK) and only joint motion around the transverse axis was considered. They found strong correlations (e.g. Pearson correlation coefficient = 0.999 for knee angles) between the joint angles measured by the two systems, along with mean RMSE angles of 4-5 degrees, indicating good general agreement between the optoelectronic and inertial systems. The authors had previously performed an unpublished pilot study comparing both systems and found a much lower RMSE value and a Pearson correlation coefficient of 0.999. The disparity between the pilot study and the gait study reported was thought to be due to a misalignment between the two coordinate systems. IMUs were placed at the midpoint of a segment, whereas optoelectronic markers are located on bony landmarks, creating two different coordinate systems. Compounding this will be the skin movement experienced by the optoelectronic markers, and the rotational displacement of the IMUs caused by changes in muscle contour during contraction/relaxation. Looking more closely at the comparison of the systems, the knee joint range of motion reported shows the highest level of agreement between the two systems. The ankle range of motion is overestimated by the inertial system, as is the thigh angle. Whilst it has been stated that the difference in coordinate system could cause this discrepancy, it is also possible that the definitions of each segment are causing this. The foot segment in the inertial system is formed using measurement of one sensor and therefore assuming the foot to be a rigid segment, which is not the widely accepted standard [111]. The thigh angle for the optoelectronic system is likely to have been heavily influence by skin movement as the markers were placed on the greater trochanter and lateral femoral epicondyle. Overall, the IMUs proved to be as repeatable as the optoelectronic system, and the discrepancies between the two systems can be explained by the difference in coordinate systems and segment definitions, although there is no easy solution to either of these problems.

In 2008, Picerno et al. [112] used 4 Xsens MTx sensors to measure three-dimensional hip, knee and ankle joint angles while walking and compared against a Vicon optoelectronic system. In this study, retro-reflective markers were attached directly to the IMUs as well as the common anatomical landmarks. Their protocol is unique in the literature for its use of a calibration procedure using a fifth sensor (discussed fully in Chapter 5). Their results showed that, for all joints, there was a clear hierarchy in the accuracy of angular measurements when compared to the optoelectronic system; flexion/extension was the most accurate, followed by the adduction/abduction angle, with the internal/external rotation angles being the least accurate. Repeatability of the measurement showed a similar hierarchical relationship. The use of markers on the IMUs themselves to form the technical frames for the optoelectronic system means that both systems were affected by the same soft tissue artefact, although this study does not mention the artefact that would be experienced by placing the markers at anatomical landmarks. Whilst the authors state that the tests were conducted in a “controlled magnetic field environment”, no explanation of how this was achieved is offered and the greatest error appearing in the internal/external rotation measurement would support the magnetic field not being homogeneous and affecting the measurements.

O’Donovan et al. [113] in 2007 assessed a bespoke IMU system consisting of two tri-axial accelerometers, rate gyroscopes and magnetometers. They described a postural and functional calibration method designed around knee flexion that defines the body anatomical frames. The sensors were compared against an Evart 3D (Motion Analysis Corporation, USA) optoelectronic system for 12 exercises involving rotation of the ankle joint about all 3 axes. A similar hierarchy was shown in the joint angle measurement as was seen in the work of Picerno et al. [112], with flexion/extension angles being the most accurate with root mean squared error (RMSE) of $<1°$, and internal/external rotations the least accurate, with RMSE of $>3°$. The authors suggest the explanation that the flexion/extension movements were performed about an axis approximately orthogonal to both the reference vectors used to define the sensor to segment orientation, thus resulting in the most accurate measurement. Internal/external rotation measurements were performed around the acceleration reference vector, formed when the subject performed a standing full-body rotation of 180-360 degrees. The accuracy of this reference vector relies on there being no out of plane movement of the sensors during the movement, something that is unlikely to occur. Proximity of the sensors to the floor may also mean that the magnetometer reading is affected by local magnetic field disturbances, and this would also fit in with the internal/external rotation reading being the least accurate, as when a subject is standing this would be analagous to a heading reading. However, the angles measured were still comparable to an optoelectronic system and actually showed greater agreement than those measured by Picerno et al., despite these having a more precise calibration procedure for defining anatomical frames. It should be noted that this system was static, and that further complications may arise when the sensors are mobile and are moving in a non-homogeneous local magnetic field.

In 2010, Cutti et al. [114] reported the development of the “Outwalk” protocol for clinical gait analysis using inertial sensors, designed to be suitable for knee amputees and children with cerebral palsy, and to be fast and practical in a clinical environment. This involved a static supine calibration procedure and their focus at this stage was to look at repeatability of goniometer measurement of static hip and knee flexion before putting the protocol into practice, as this is used in the static calibration procedure. Having found the repeatability of the goniometer measurement to be comparable to an optoelectronic system using the CAST protocol [115], they then went on to perform an in-vivo assessment of the protocol using 4 healthy volunteers [116] and comparing the system to an optoelectronic system using the same CAST protocol as before. They concluded that the Outwalk protocol with inertial sensors was comparable to the optoelectronic system using the CAST protocol, with similar levels of accuracy for hip, knee and ankle joint angles in the sagittal plane, and hip joint angles in the transverse plane. All other joint angles measurements suffered from decreased accuracy, but it was concluded that this disparity was due to differences between the protocols and the coordinate systems used.

In 2008, Cloete and Scheffer [117] sought to benchmark an inertial system using the Xsens sensors against a Vicon optoelectronic system for full-body motion capture. The sensors were mounted on the Moven lycra bodysuit provided by Xsens, and the “Gollum” marker model was used for the optoelectronic capture [118]. They found the sagittal plane measurements of the hip and knee angles to be comparable to that of the optoelectronic system, whilst the transverse and coronal plane angles are marginally comparable. For the ankle joint, none of the angles are comparable, and this is likely due to a difference in the way each system calculates the ankle joint angles. Other discrepancies between the two systems were accounted for by movement of the lycra bodysuit over the skin, similar to the skin movement artefacts typically experienced by optoelectronic systems.

This literature review has shown that over the past 10 years, the use of inertial sensors for gait analysis has increased and a multitude of new protocols have been proposed and validated. Validation is typically done using a Vicon optoelectronic system as the “gold standard” against which the inertial systems are compared. The results typically show comparable measurement of sagittal plane joint angles for the hip and knee joint. The ankle joint sagittal plane angle is a little less predictable and is heavily influenced by the marker set used for the optoelectronic system and the joint angle calculation method employed by the inertial system. Measurements of the transverse plane are usually the next most accurate measurement with coronal plane angles reported as the worst, although some studies report these as being on a par with each other. Measurement of the sagittal plane joint angles of the knee joint are what is of most interest to this work, and as such inertial sensors are a suitable technology. Not only does the literature prove them to be comparable to optoelectronic system in terms of accuracy.

4.5 Problems associated with inertial sensors

Whilst in the previous section inertial sensors were shown by the literature to provide accurate and repeatable measurement of sagittal plane joint angles, it is important to be aware of their limitations and the factors that can affect them. This section will briefly deal with four of the main problems that can affect inertial sensors, and the precautions that can be taken to limit these effects.

4.5.1 Integration drift

All inertial systems suffer from integration drift to varying degrees. With integration drift, small errors in the measurement of the acceleration and angular velocity are integrated into larger errors in velocity, and this effect is then further compounded when the signal is integrated to obtain position. The new position is calculated from the previous position and the resulting accelerations and angular velocities experienced, and so errors due to integration drift are carried forward and can very quickly build up in an inertial system.

One method to combat integration drift is to employ a third sensor which provides an additional reading to provide a correction and compensate for the drift. In the case of IMUs for gait analysis, this is typically a magnetometer which corrects for the heading drift using the earth’s magnetic field, although GPS systems can also be used depending on the degree of precision required. However, magnetometers have their own problems, and these will be discussed in the next section.

4.5.2 Ferromagnetic disturbances

Whilst including a magnetometer in an IMU can offset the effects of integration drift, these sensors themselves are sensitive to disturbances in the local magnetic field. A magnetometer measures the strength or direction of a magnetic field, and uses this to measure magnetic north and provide a reference reading for resetting of heading drift in IMUs. However, distortions in the local magnetic field can affect the validity of the magnetometer readings. Ferromagnetic materials, such as iron, can cause these distortions and the magnitude of the distortion will vary depending on the amount of material present and the sensors proximity to it.

Most gait analysis takes place inside buildings and iron is a common building material, thereby making the entire volume enclosed by the building susceptible to ferromagnetic disturbance. De Vries et al. in 2009 [96] undertook a study to examine the ferromagnetic disturbances in 3 different gait labs. Figure 4.2, taken from their paper, shows clearly how the magnetic field can vary at floor level, even over such a small area.

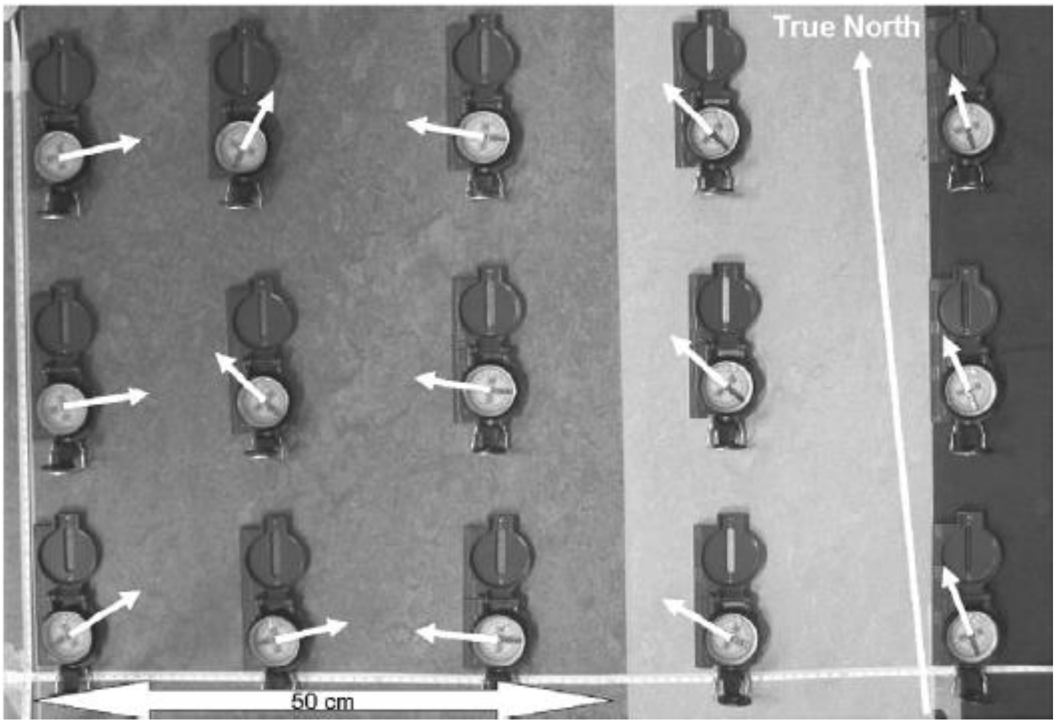

Figure 4.2 Compass reading taken over an area of laboratory floor by De Vries et al. [90].

They tested the magnetic field direction at 5cm and 180cm above the floor level, and found that at 5cm the standard deviation of the magnetic field direction was 30 degrees, whereas at 180cm it was only 3 degrees. This stark contrast clearly shows the effects of proximity to a high metal content surface. They then went on to assess how this disturbance affected the stability of orientation estimates from the IMUs, under two scenarios; one starting from a "safe area" where the magnetic field was known to have the correct direction, and another starting from an "unsafe area" where the magnetic field was known to be distorted. Two different filters, a quaternion filter and Kalman filter, were also looked at, giving a total of 4 conditions for each height reading. The Kalman filter had been developed in 2005 by Roetenberg et al. [95] with the specific focus of compensating for magnetic disturbances. In both starting conditions the Kalman filter performed better than the quaternion filter. The starting condition only had an effect on the orientation estimates of the Kalman filter when it was within 5cm of the floor, with the error from starting in an "unsafe area" being double that of starting in a "safe area". The authors recommend that measurements be performed above a height of 40cm, but that this is less important when using a Kalman filter. Starting in a "safe area" where the magnetic field has the correct direction is important, and restricting recording time to 30 seconds per data recording will also help to reduce errors.

4.5.3 Resonance

Resonance is a phenomenon that occurs when a system vibrates at its natural frequency. This can cause the amplitude of vibration of the system to increase and in the case of inertial sensors the readings from the accelerometers would become unreliable. The natural frequency of a system is calculated using the Equation 4.1, where "m" is the mass of the system and "k" is the stiffness.

$$Natural\ frequency = \frac{1}{2\pi}\sqrt{\frac{k}{m}} \tag{4.1}$$

Typical accelerometers have a natural frequency of around 10 kHz. However, when they are combined with a gyroscope and magnetometer to form an inertial measurement unit, there is an increase in the effective mass and therefore a decrease in the natural frequency. If the sensor is also attached to a frame and casing, this will further increase the mass. Previous research has shown that combining multiple sensors and mounting them in this way can decrease the natural frequency to around 20 Hz [119], which is close to the frequency components of gait. The recommendation of this study was that an inertial sensor should ideally have a natural frequency above 20 Hz for biomechanical applications. It was shown in the same study that it is possible to increase the natural frequency by increasing the stiffness of the system or by altering the attachment method. In the study by Forner-Cordero et al. [119] pre-loading of the system using bandages increased the natural frequency significantly with the mass of the bandages not affecting the measurements significantly. This will be taken into consideration when looking at methods of attachment of inertial sensors.

4.5.4 Secure attachment

In addition to a method of attachment that increases the natural frequency of a system, a secure attachment is also required. During the calibration of an inertial system, the orientation of each sensor to its underlying segment is defined and this is essential for calculation of joint angles. If sensor-to-segment orientation changes after the calibration of the system this will then affect the joint angles calculated and will invalidate the data. Therefore it is essential that the sensors are attached securely, using a method and positioning that will ensure minimal movement of the sensors relative to their underlying segments, and in a way that can be done for all participants. This will be a key consideration discussed in Chapter 5.

4.6 Selection of a supplier

Having reviewed the literature on modern uses of inertial sensors, and also looked at the problems associated with them, it was next necessary to select/design a system for use in the NTFS gait analysis. Designing a bespoke system would have some advantages; the sensor component sensitivity could be precisely specified, bespoke systems are typically smaller and more compact, data can be recorded and processed as the user wishes. However, the design and manufacture of a bespoke system is a complex and lengthy task and one which would not be feasible within the course of this research. Therefore it was decided that an “off-the-shelf” commercial system would be used.

There are a variety of companies producing inertial sensors for use in gait analysis. Xsens, InterSense (InterSense Incorporated, USA) and Shimmer (Shimmer Research, Ireland) all provide off-the-shelf kits designed for biomechanical analysis of movement. Several of the more recent validation studies reviewed in Section 4.4 [110, 112, 114, 117] use a system provided by Xsens Technologies. The MTx sensors recommended for use in motion analysis comprise a three-dimensional accelerometer, gyroscopes and magnetometer, and are available with a full acceleration scale of either 5G or 18G, depending on the user's requirements. The technical specifications of the Xsens MTx sensors are shown in Table 4.1. A sensor fusion algorithm is employed to produce an orientation estimate for the sensor. The fusion algorithm uses the measurement of gravity and Earth magnetic north to compensate for the integration drift, often called an Attitude and Heading Reference System. In order to compensate for magnetic disturbances, the sensors also employ a Kalman filter which has been shown to reduce the effect of magnetic field disturbances [95], although attention should still be paid to this. There are also a range of scenarios built into each sensor which use assumptions about the acceleration and magnetic field to obtain orientation. For the purposes of this study the "Human" scenario would be the most appropriate, as the "Human_large_accel" scenario is intended for fast movements where large accelerations may occur during impact.

Table 4.1 Xsens MTx sensor specifications.

Dimensions (L x W x H)	38 x 53 x 21 mm
Weight	30g
Gyroscope full scale	± 1200 deg/s²
Accelerometer full scale	± 50 m/s²
Magnetometer full scale	± 750 mGauss

The MTx sensors are connected to a data logger, the Xbus Master unit, in a daisy-chain configuration. The Xbus Master records the readings from all attached accelerometers, stores a packet of data in its buffer, and then burst transmits this back to a laptop via Bluetooth. The bandwidth provided by the Bluetooth connection is one of the limiting factors in the choice of sampling rate and the type of data recorded. The Xbus Master itself is attached to an adjustable strap which fits around a subject's waist, chest, or other convenient attachment area, and it should be placed so as not to interfere with the subject's movement, or the sensors. The data recorded by the sensors and transmitted back to the laptop can be either processed or raw data and, for the purposes of this study, raw data was recorded to ensure no level of detail was lost.

Finally, the system is operated by the MT Manager software supplied with the Xbus kit and developed by Xsens. They also offer a data processing package, MVN Studio. However there were some reservations about working with this; the software is supplied as a "black box" system, so any calculations, filtering, and smoothing of data, are not visible or available to the user. Precision is important in measuring joint kinematics and the researcher must be able to account for all the calculations and manipulations of their data in order to support results. Therefore using the manufacturers processing software in this case would be inappropriate.

Xsens were chosen as a supplier as they offered a complete inertial system including; sensors, data logger and software, with the option to record data in its raw format and to process it using different software. The system was also affordable, portable, and had already been validated by several studies against a reference system (see Section 4.4). A seven-sensor kit was selected as this would allow recording of lower limb kinematics with one sensor on each segment.

4.7 Summary

This chapter has focused on the selection of an appropriate technology for gait analysis of the NTFS cohort. It began with establishing the practical challenges of performing gait analysis in a hospital environment and then moved on to an overview of the common methods of gait analysis available, and the advantages and disadvantages of each with reference to the intended application. It then established the selection of inertial systems as the appropriate technology for the NTFS gait analysis. Following on from this a literature review on the modern uses of inertial systems for gait analysis was presented, with a focus on the benchmarking and validation of these systems against established methods. A key point to take from this literature review is that there is no standard protocol for gait analysis with inertial sensors, with most researchers designing a bespoke protocol, although there were commonalities between these. However, sagittal plane joint angles were consistently well recorded, with varying degrees of success for the joint angles in the other planes. The problems associated with inertial sensors were also discussed, and attention had to be paid during the protocol design to magnetic field disturbances and secure sensor attachment. Finally, a supplier of an inertial system was selected and the technology detailed. The next chapter goes on to detail pilot studies that were conducted to test the suitability of the Xsens sensors for joint angle measurement in a clinical environment, before development of a complete gait analysis protocol commenced.

Chapter 5 Pilot Tests

Before purchasing a full inertial system and commencing on the development of a complete gait analysis protocol, some preliminary pilot tests were required to assess the feasibility of using inertial sensors for gait analysis in the Clinical Research Facility (CRF), and also to assess their feasibility for measuring joint angles. Xsens provided an Xbus demo kit containing two sensors in order to perform these studies. This chapter starts off with testing of the magnetic field variation in the Wilson Horne corridor of the CRF where gait analysis took place. It then goes on to feasibility testing of the sensors using a mechanical linkage to simulate joint motion.

5.1 Magnetic field testing of the Wilson Horne corridor

5.1.1 Introduction

As mentioned in Chapter 4, inertial sensors can be affected by variations in the local magnetic field. The magnetometer is used to correct integration drift, but in itself can be affected by disturbances in the local magnetic field due to ferromagnetic materials or large items of machinery. It was therefore necessary to test the magnetic field variation in the Wilson Horne corridor to ensure that use of the magnetometers to correct heading drift in the inertial sensors was going to provide useful integration drift correction and not make matters worse.

5.1.2 Methods

To measure the magnetic field in the corridor, two systems were used. The first was a standard navigational compass with an adjustable bezel, purchased from an outdoor pursuits shop. This gave a measurement of the magnetic field direction within the corridor. The second system was an MTx sensor. The sensor contained a magnetometer and the raw data recorded by this can be viewed and analysed before it is used in creating an orientation measurement. The magnetic field is measured in arbitrary units (AU’s) that are normalized to the earth magnetic field strength. The magnetic field normal reading is found by calculating the root-mean-squared (RMS) value of the magnetic components in each sensor direction (x, y and z). It was also recommended by Xsens that the variation of the magnetic field normal reading recorded by the sensors be measured, and that for reliable readings this should not go beyond a range of 0-2 AU's.

It should be noted that homogeneity of the local magnetic field is what is important when testing an area for suitability. The magnetometer reading of true north is used to correct the integration drift in the sensor, and it is important that this measurement remains constant otherwise the corrections applied will change. However, the direction of the heading used to correct the integration drift is not dependant on it being true north, but rather on the direction not changing during the course of data being recorded. For instance, the magnetometer might read true north to be 40° different to its actual reading, due to local magnetic field disturbance. However, as long as this offset remains constant then the integration drift correction will still function as intended. Therefore, the relative change of magnetic field direction along the corridor compared to the starting point was assessed.

A wooden trolley was used in order to perform the tests. It was a requirement that the trolley's surface and structure be made of wood, as if it were made of metal then this could compromise the magnetic field reading by further interfering with the measurement devices. The only metal in the trolley was in the casters and screws, which were a sufficient distance from the surface on which the measurement devices were placed so as not to have interfered with the measurements. The height of the trolley's surface from the floor was 40cm. Three tests were then performed. Figure 5.1 shows the layout and dimensions of the Wilson Horne corridor where the magnetic field measurements took place.

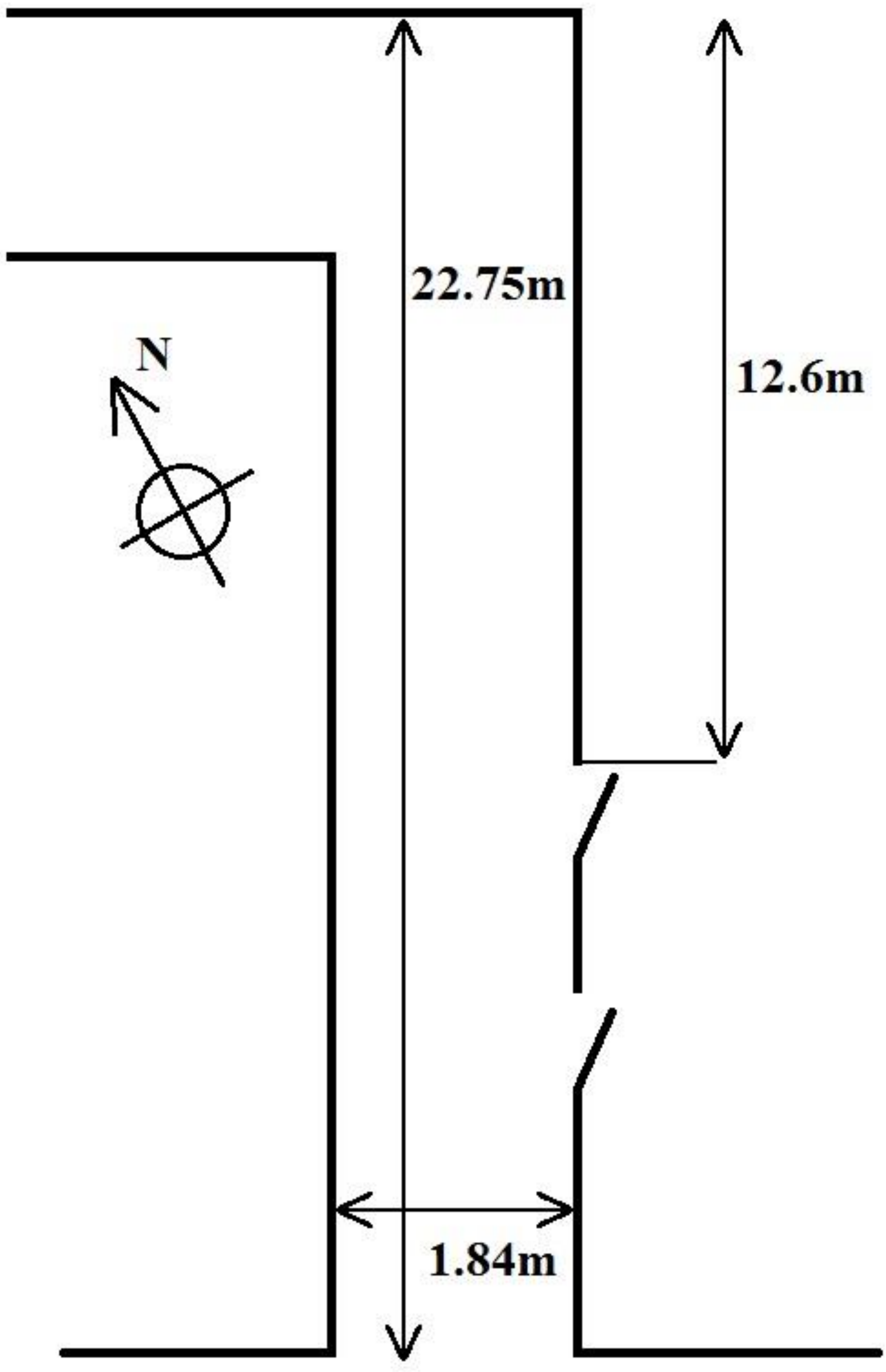

Figure 5.1 Layout and dimensions of the Wilson Horne corridor where magnetic field testing took place.

Test 1; the compass was fixed on the trolley with tape and the bezel adjusted so that the 0° reading was parallel with the left edge of the trolley. Figure 5.2 shows the compass fixed to the trolley surface with the appropriately adjusted. The trolley was pushed against the north wall so it lay parallel to the surface. The direction of magnetic north was then measured. This was repeated 5 times with the trolley moved away from the wall after each trial and replaced in the same position. The compass remained fixed in the same place on the trolley, thereby keeping the reference frame constant for each measurement. The purpose of this test was to assess the repeatability of the magnetic field direction at the north end of the corridor where trials were likely to start. Figure 5.3A shows the positioning of the trolley relative to the wall of the corridor.

Test 2; the trolley and compass set-up from Test 1 was used for Test 2. This test began at the north end of the corridor, and the trolley was pushed down the corridor in a southerly direction for 10m. The trolley was stopped at intervals of 1m so that compass readings could be recorded. Care was taken not to rotate the trolley as it was pushed down the corridor. This was repeated 5 times. The purpose of this test was to assess the variation in magnetic field direction. Figure 5.3B shows the position of the trolley relative to the corridor and direction of progression during the trial.

Test 3; the MTx sensor was fixed on the trolley with tape. The position of the MTx sensor is the same as that shown for the compass in Figure 5.2 and Figure 5.3. This test also began at the north end of the corridor, and the trolley was pushed down the corridor in a southerly direction for 10m. Care was taken not to rotate the trolley as it was pushed down the corridor. MTx sensor readings were recorded wirelessly using the MT Manager software provided by Xsens. This was repeated 5 times. The purpose of this test was to assess the variation in magnetic field normal reading by the MTx sensor.

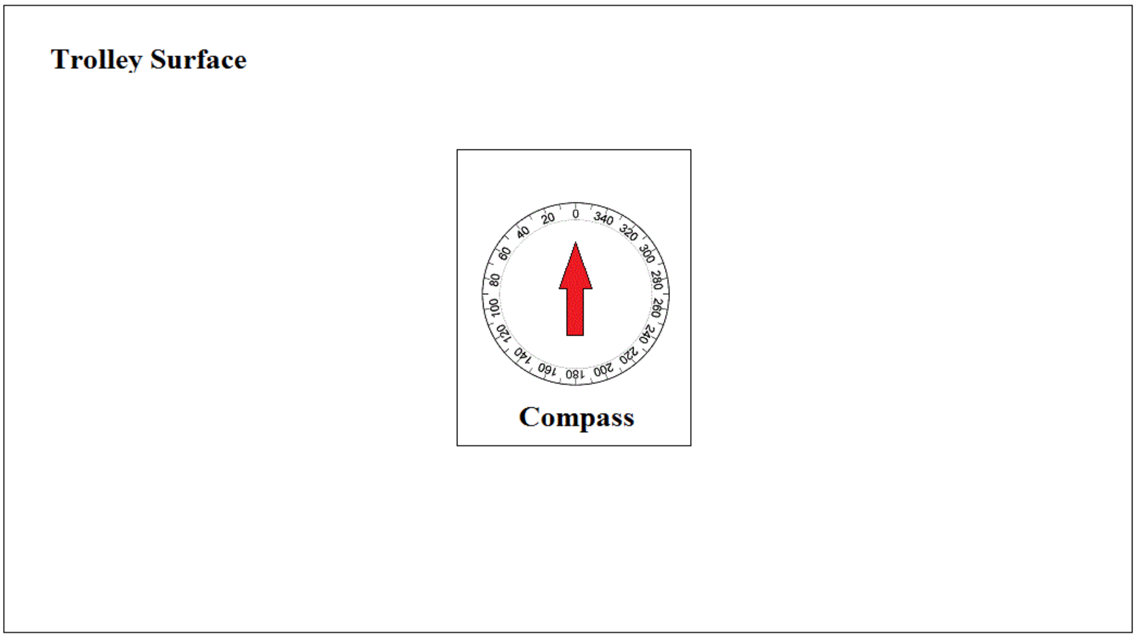

Figure 5.2 Compass fixed to trolley surface for use in Test's 1 and 2.

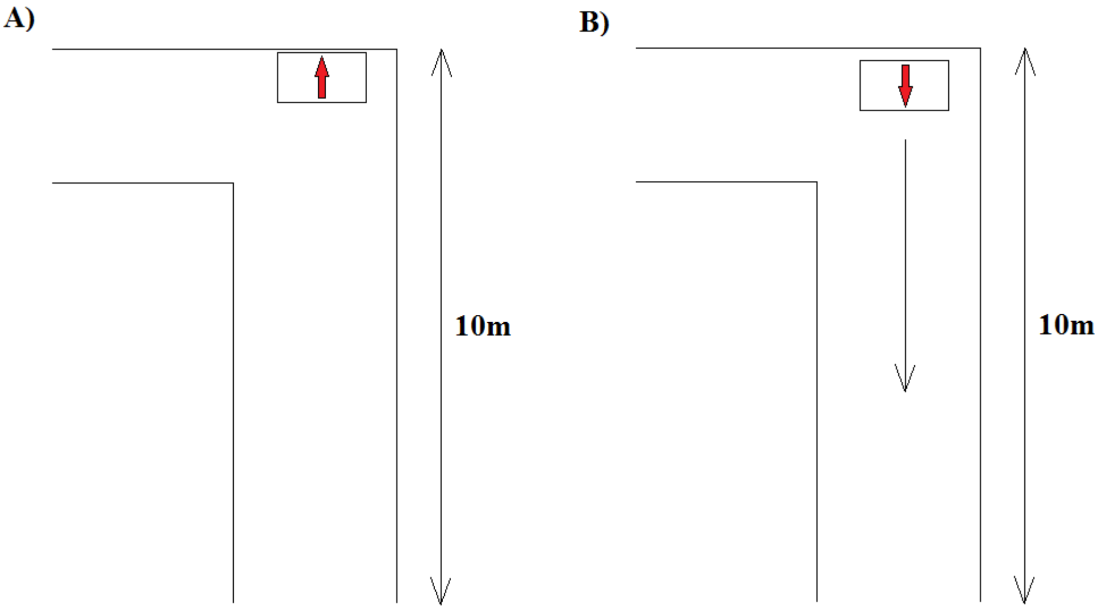

Figure 5.3 A) Position and direction of trolley and bezel in Wilson Horne corridor for Test 1, B) Position, direction of trolley and bezel, and direction of progression in Wilson Horne corridor for Test 2. The red arrow indicates the direction of 0° on the compass bezel.

5.1.3 Results

For Test 1, the compass reading for each trial was reported The mean reading across all 5 trials was 329.6° with a standard deviation of 0.55°. For Test's 2 and 3 the ranges of the values recorded for the both the compass and MTx sensor were calculated for each trial and this gave a measure of how much the magnetic field was varying along the corridor. In both cases, reporting the range of readings was a better measure of magnetic field homogeneity than reporting the mean and standard deviation; e.g. There could have been one point in the corridor where the magnetic field was substantial different from the surround area. However, this was only one reading out of many and may not have been shown clearly by the mean and standard deviation. Reporting of the range ensured no masking of individual readings which were substantially different from the surrounding area. Results from Test 1 are shown in Table 5.1. Results from Test 2 are shown in Table 5.2. Results from Test 3 are shown in Table 5.3.

Table 5.1 Results from Test 1 – compass in static position at north end of Wilson Horne corridor.

Trial No.	Compass Reading (°)
1	329
2	330
3	329
4	330
5	330

Table 5.2 Results from Test 2 – compass moved in southerly direction down Wilson Horne corridor.

Trial No.	Compass Readings (°)		
	Maximum	Minimum	Range
1	159	141	18
2	158	142	16
3	159	139	20
4	161	141	20
5	163	146	14

Table 5.3 Results from Test 3 – MTx sensor moved in southerly direction down Wilson Horne corridor.

Trial No.	**Magnetic Field Normal (AU)**		
	Maximum	**Minimum**	**Range**
1	1.51	0.63	0.87
2	1.62	0.42	1.20
3	1.65	0.63	1.02
4	1.60	0.64	0.96
5	1.73	0.59	1.11

5.1.4 Discussion

The magnetic field direction in the Wilson Horne corridor was analysed and was found to be close to true north in the northern end of the corridor. The variation of this value along the corridor was also reasonably stable, with an average range of variation of 17.6°. It should be noted the extreme values of this variation occurred within the last metre of the trial, implying that the magnetic field was become increasingly disturbed from a distance after 9m along the corridor. If this trend of increasing disturbance were to continue then measurements using the magnetic field direction to correct integration drift may not be reliable after 10m along the corridor. This data was supported by the magnetic field normal readings from the MTx sensors which remained within the range recommended by Xsens (0-2).

The north end of the Wilson Horne corridor's magnetic field was reasonably homogeneous until a distance of 10m was reached. This seems logical as the Wilson Horne corridor ends at a corner of the building, and the CRF facility is located on the top floor, therefore giving a minimum of metal structure surrounding this volume. It should be noted that these tests were conducted at a distance of 40cm from floor level. This is representative of height of the human knee joint from the floor during standing for a human of height 177cm. A previous investigation [96] found that disturbance became greatest at floor level. This is a reasonable conclusion as this represents proximity to ferromagnetic materials used in the building construction. Therefore, orientations reported by sensors in close proximity to the floor may not be as reliable as those reported at 40cm.

5.1.5 Conclusion

These data supported the conclusion that use of the magnetometer to correct heading drift in the MTx sensor is permissible. The work of de Vries et al. [96] recommended that trials should start in an area of little or no magnetic field disturbance and that trials should be shorter than 30 seconds. As the north end of the Wilson Horne corridor represented an area of little magnetic field disturbance, and walking 10m takes considerably less than 30 seconds for a healthy individual, the north end of the Wilson Horne corridor was deemed suitable for gait analysis using inertial sensors that included a magnetometer.

5.2 Mechanical simulation of joint motion

5.2.1 Introduction

Before development of a full data collection protocol, including calibration procedure and method of calculating joint angles, it was useful to test the measurement of joint angle using a repeatable mechanical motion. This would give an indication of how repeatable the system was in measurement of joint motion. This mechanical joint motion could also be measured using a reference standard system, and the comparison of the two systems measuring the same motion would be a useful starting point for validating the inertial system against the reference standard. This comparison will be in line with those typically found in the literature validating inertial systems against optoelectronic systems [114, 117].

5.2.2 Methods

It was decided that a four-bar linkage would be used as this was readily available and also simulated sagittal plane knee joint motion, one of the gait variables found to be linked to OA in Section 3.10. By attaching the inertial sensors to 2 linked arms this would provide joint motion in one plane that could be measured. Whilst it is accepted that the four-bar linkage is not a complete representation of the knee joint, it does provide repeatable one degree of freedom motion and can be used to assess both the accuracy and repeatability of the sensors for joint angle measurement.

A four-bar linkage is the simplest moveable closed-link chain. It consists of four bodies, called bars or links, connected in a loop by four joints [120]. In the case of the four-bar linkage available for this testing, three of the bars were mobile and the fourth bar was immobile and was formed by the board to which the other linkages were attached. Figure 5.4 shows a picture of the four-bar linkage used. Two bars are shown in red, one bar is shown in yellow, and the fourth immobile bar is the blue frame to which the others are attached. Four single DoF joints can be seen in silver, linking all four bars.

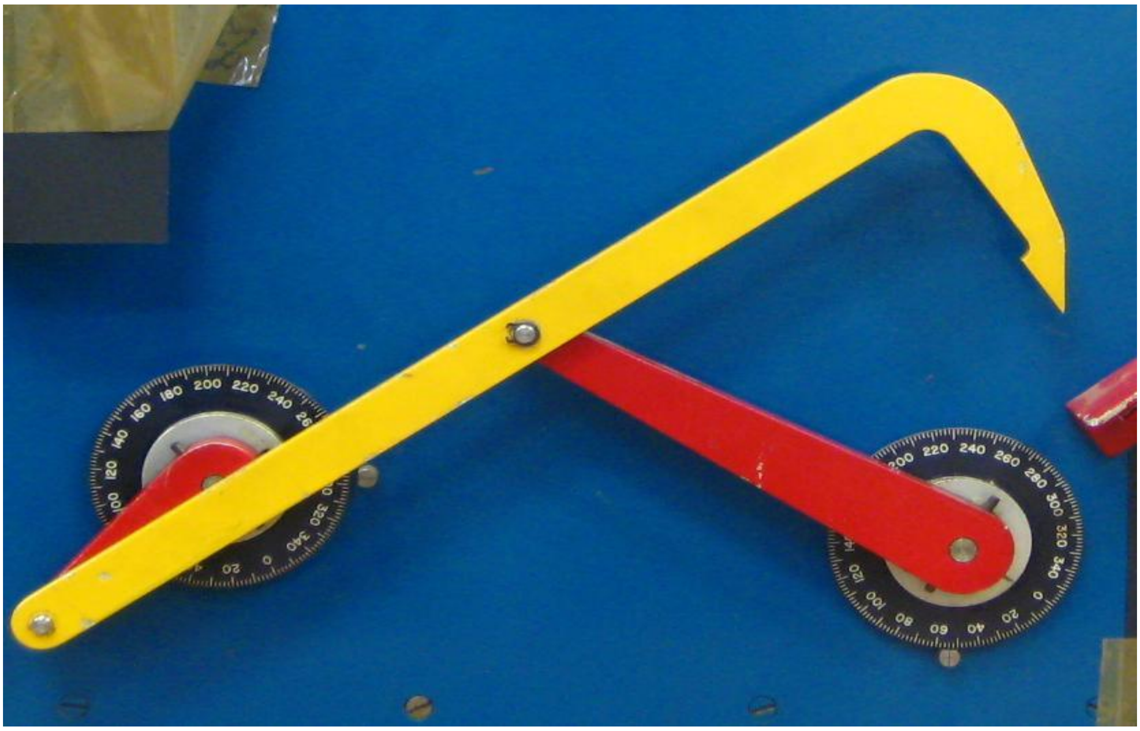

Figure 5.4 Four-bar linkage used for repeatable mechanical simulation of sagittal plane knee joint motion.

Two MTx sensors were attached to two of the linkages using double sided tape with their x-axes aligned with the long axis of each linkage. This coordinate frame alignment meant that calibration to obtain sensor to linkage orientation was not necessary as the motion of the sensor-fixed coordinate system could be assumed to represent the movement of the linkage arm to which it was attached. Figure 5.5 shows the attachment scenario for the sensors and four-bar linkage, and the angle measured by the sensors. Five trials consisting of five complete rotations of the system were recorded, which would allow assessment of both intra- and inter-trial repeatability. A sampling rate of 50 Hz was used.

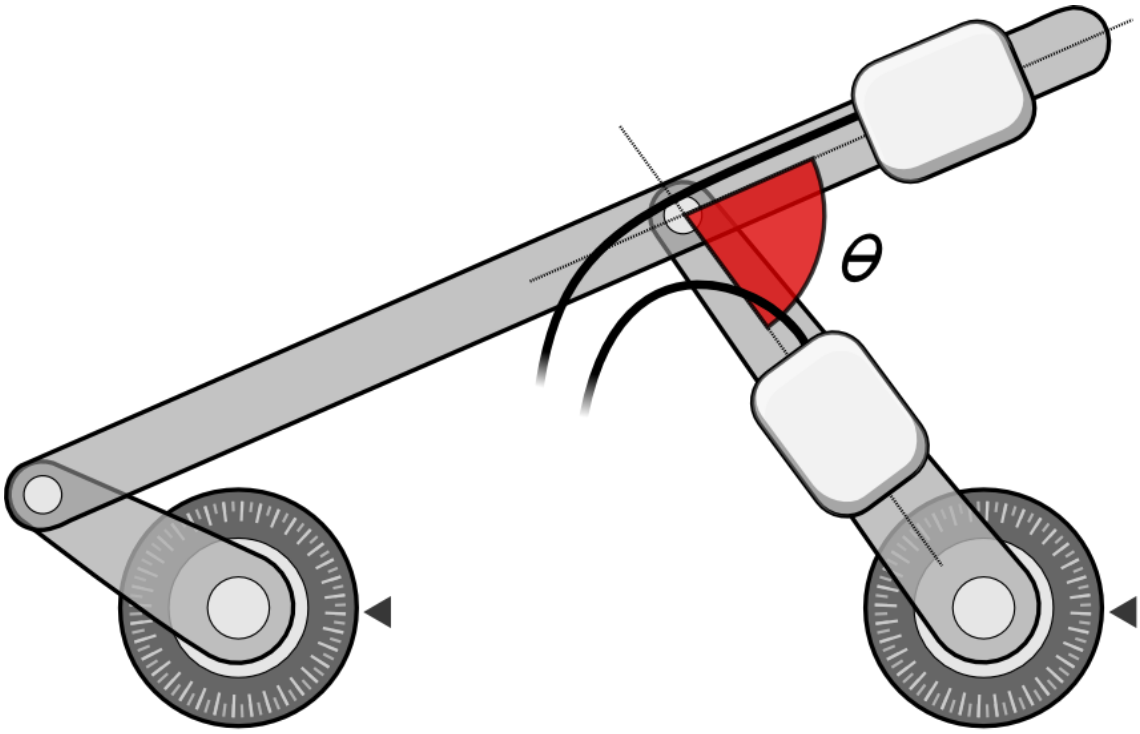

Figure 5.5 Four-bar linkage with inertial sensors attached measuring the angle between the two linkages (θ).

The same four-bar linkage had been used in an unpublished pilot study which compared a marker-free motion capture technique to a Vicon optoelectronic system. As the four-bar linkage had sustained no damage or wear during the intervening period its motion was assumed to be the same and the optoelectronic data previously recorded for its motion can be used to compare with that measured by the inertial system. The data from the Vicon optoelectronic system was collected using a Vicon 512 OES (Vicon Ltd, Oxford, UK), sampling at 50 Hz. Two 14mm reflective markers were attached to the centre line of each segment on the 4-bar linkage. The vector defining the centre lines of each segment were calculated to obtain the angle θ. Five trials consisting of five complete rotations of the system were recorded.

When assessing repeatability of the MTx sensors for recording joint motion, both intra- and inter-trial repeatability were assessed. Intra-trial repeatability was reported using the mean and standard deviation of the angle measured during 5 consecutive rotations of the system in each individual trial. Inter-trial repeatability was reported using the mean and standard deviation of all rotations from all trials, a total of 25 rotations in total. The same method was applied to the angles recorded by the Vicon system. Difference between the measurement of the angle θ by both systems was assessed using a 2-tail paired t-test.

5.2.3 Results

The mean and standard deviation of the angles found across the five rotations for each inertial system trial are shown in Table 5.4. Looking at each trial individually gives a measure of intra-trial repeatability for inertial sensor measurement of the mechanical joint angle. Looking at all trials together gives a measure of inter-trial repeatability. The mean and standard deviation of the angles measured by both the Xsens and Vicon systems are shown in Table 5.4. A 2-tail paired t-test showed ranges of motion that were not significantly different between the two systems (p=0.07).

Table 5.4 Intra-trial repeatability of inertial sensors for measurement of four-bar linkage motion.

Trial No.	θ min ± SD (°)	θ max ± SD (°)
1	52.9 ± 0.1	123.6 ± 0.1
2	53.0 ± 0.1	123.7 ± 0.1
3	53.0 ± 0.1	123.7 ± 0.1
4	53.0 ± 0.1	123.7 ± 0.1
5	53.0 ± 0.1	123.7 ± 0.1
All trials	53.0 ± 0.1	123.7 ± 0.1

Table 5.5 Comparison of joint angles and range of motion measured by inertial sensors and optoelectronic system.

System	Mean θ min ± SD (°)	Mean θ max ± SD (°)
Inertial sensor	53.0 ± 0.1	123.7 ± 0.1
Optoelectronic	58.0 ± 0.4	128.0 ± 0.4

5.2.4 Discussion

The inertial sensors showed good intra- and inter-trial repeatability for measurement of planar mechanical joint motion. In all cases the variation of values measured for the maximum and minimum joint angles represented less than 0.5% of overall range of motion, indicating good intra-trial repeatability. Good inter-trial repeatability was also shown as the maximum difference between any two trials was less than 0.5% of the range of motion measured.

The maximum and minimum joint angles measured by inertial sensors showed greater repeatability (SD = 0.04°) than the optoelectronic system (SD = 0.4°). A 2-tailed paired t-test show no significant difference between the two systems, although there was a difference between the values measured for maximum and minimum joint angle. However, the difference was consistent across all the trials, and the range of motion of the joint measured by the two systems did not differ. It is therefore thought that this systematic difference of 5° between the two systems could be related to a difference between the axes and frames constructed in these studies, and what was defined to be 0° of rotation.

5.2.5 Conclusion

The repeatability of inertial sensors for simple angle measurement has been tested on a four-bar linkage providing a repeatable planar mechanical joint motion, and the sensors were found to be comparable in accuracy to an optoelectronic system and also showed greater repeatable of joint angle measurement.

5.3 Summary

Two pilot studies have been conducted; the first assessed the feasibility of using inertial sensors containing a magnetometer in the CRF at Newcastle RVI hospital. The study confirmed that the first 10m of the north end of the Wilson Horne corridor presents a sufficiently homogeneous magnetic field to not adversely affect inertial sensors orientation readings and to allow correction of integration drift using the measured value of magnetic north. The second study used a repeatable planar mechanical motion to perform a preliminary assessment of the MTx inertial sensors repeatability and accuracy in measurement of joint angle. The MTx sensors were found to have accuracy comparable to the Vicon optoelectronic system used as a reference standard, and to have greater repeatability of planar joint angle measurement than this system.

From the results of these pilot studies it was concluded, in conjunction with the results from the literature review in Section 4.4, that the inertial system from Xsens would be suitable for development of a protocol for gait analysis of the NTFS cohort. These results supported commencement of the design of a protocol for gait analysis of the NTFS cohort using Xsens MTx sensors.

Chapter 6 Data Collection Protocol Design

In order to develop a protocol that adhered to the engineering specification developed in Chapter 2, this chapter starts by including the specification so it can be easily referenced during the protocol design. It then moves on to detail the space available in the Clinical Research Facility, and then selects an appropriate walking trial based upon this. The sensors selected in Section 4.6 are then summarised, and the chapter then goes on to review, select and develop appropriate methods for sensor calibration, joint angle measurement and gait event detection.

6.1 Design of a protocol to an engineering specification

Previously, in Chapter 2, an engineering specification was created that detailed the list of requirements for the NTFS gait analysis protocol (Table 2.3). Table 6.1 shows the engineering specification in its current form that will be referred to during protocol development.

Table 6.1 Engineering specification referred to during protocol development.

	List of requirements
A	Protocol must be feasible for use in the Clinical Research Facility at Royal Victoria Infirmary Newcastle.
B	Protocol must take 25 minutes from start to finish.
C	Data collection must take place over the top of clothing.
D	Protocol must be suitable for every able member of cohort to perform.
E	Gait analysis procedure explained to all participants.
F	Minimise pain/discomfort during assessment.
G	Record data for hip, knee and ankle joints.
H	Accuracy and repeatability of data must be comparable to a reference standard system.
I	Variables relevant to the study of gait in relation to OA initiation and progression must be recorded.
J	Appropriate indicator of OA severity so that initiation as well as progression can be assessed.
K	Method must be portable and not require permanent installation.

6.2 The Clinical Research Facility

The Clinical Research Facility (CRF) is situated in the Leazes Wing of the Royal Victoria Infirmary (RVI), Newcastle upon Tyne. Its purpose is to provide dedicated care facilities for patients and practical support to researchers carrying out clinical research, and provided the ideal setting in which to carry out the wide-ranging clinical and physical assessments for the NTFS age 62-63 years follow-up.

The Wilson Horne corridor within the facility was selected as a venue for gait analysis trials, as no other area provided sufficient space. Figure 5.1 shows the layout and dimensions of the Wilson Horne corridor. The dimensions of the corridor are 22.75m long by 1.84m wide, providing adequate length for the gait analysis to take place. At the southern end the corridor had offices on one side that were in regular use. A nearby consulting bay provided sufficient privacy for sensor attachment, and also allowed the entire gait analysis procedure to be explained to participants before starting, so that any concerns they had could be allayed and to make sure they were comfortable with the whole experience. It also provided sufficient space and freedom of movement for the subject to get accustomed to moving around with the sensors attached.

6.3 Walking trial design

6.3.1 Starting the walking trials

The first decision to be made with regard to the walking trial design was where to start the walking trials. As mentioned in Section 4.5.2, magnetic field disturbance can adversely affect inertial sensor orientation readings. The pilot study in Section 5.1 assessed the magnetic field variation in the Wilson Horne corridor and found it to be close to true north at the northern end of the corridor, and sufficiently homogenous up until around 10m down the corridor. The south end of the Wilson Horne corridor contains several offices in regular use. There was a risk that traffic from these offices could interrupt a walking trial and cause an alteration in the person’s gait, or halt them altogether. Avoiding interruptions to walking trials is a key consideration.

Considering the practicalities of having a sufficient space for walking trials, the desire to avoid interruption in the trials, and the magnetic field variation in the Wilson Horne corridor, it was decided that all walking trials would start at the north end and proceed in a southerly direction. This gave sufficient space for the trials to take place, minimised the potential for interruption, and stayed within an area where the magnetic field exhibited little variation.

6.3.2 Walking speed

Walking speed was another factor that had to be considered in the trial design. Previous studies have asked subjects to walk at “slow”, “preferred” and “fast” speeds [76] and this has proven effective. However, it was a subject’s preferred walking speed that was of interest in this study, as this would produce the most natural gait and represents the kinematics which occur the most frequently [12, 61]. Therefore participants were asked to walk at a self-selected speed indicative of what they considered to be their ‘normal’ walking speed.

6.3.3 Trial length

As mentioned in Section 6.3.1, trials began at the north end of the corridor and proceeded in a southerly direction. Selecting a trial length that would minimse the potential for traffic to interfere with the walking trials was important.

The first consideration was the range of the bluetooth wireless transmission system used by the Xsens Xbus system. The wireless range was tested and the bluetooth signal was lost at a distance of around 25 metres with no obstructions present. This was sufficient for use in the corridor as there were no obstructions between the bluetooth transmitter and receiver, and thus wireless transmission range was not a limiting factor.

In deciding on the length of a walking trial, there were two options; either a participants could be asked to walk a fixed distance to a marker, or else asked to walk a fixed number of steps. There are drawbacks to each of these methods. If a participant was asked to walk to a marker, they may see it as a challenge to be completed in the least possible time, and therefore would increase their walking speed as a result of this. Section 6.3.2 specified that the participant’s natural, self-selected walking speed was of interest.

Conversely, if a participant was asked to walk a fixed number of steps there is the potential that the additional cognitive load induced by counting their steps would affect their gait. A study on stroke patients and healthy control subjects has shown that cognitive load did not have a significant effect on the stride duration and cadence of the healthy individuals [121] but had more of an effect on the stroke patients. Individuals having suffered stroke or presenting with other pathologies likely to affect their cognitive ability were excluded under the exclusion criteria detailed in Section 7.8 (page 124). In addition, the impact of this dual task scenario was lessened due to several practice walking trials taking place before any data was recorded. Therefore it was decided that participants would be asked to walk a fixed number of steps.

A distance of ten strides was chosen for the trial length. This made sure participants finished the walking trial before they reached the frequently used rooms, whilst also allowing them to establish their gait. This trial length also minimised the chance of a subject walking far enough down the corridor as to move into the area where the local magnetic field became distorted (see Section 5.1.4), and also meant that the length of each trial recording was less than 30 seconds which is in keeping with the recommendations by de Vries et al. [96]. Of the 10 steps recorded, the first and last pairs of strides were not analysed as these represented the subject establishing their gait, and preparing to halt.

6.3.4 How many walking trials?

The choice of how many walking trials to perform was influenced by two factors; the number needed to order to collect sufficient data on a patient's gait, and the time available given that sensor attachment, calibration, trials and sensor removal all had to occur within a 25 minute window (requirement B in Table 6.1). It was anticipated that sensor attachment would take around 5 minutes, leaving 20 minutes for the sensor calibration, walking trials and sensor removal. Demonstrating the sensor calibration routine, and giving the subject time to practice, was estimated to take 4-5 minutes. Sensor removal after the trials was anticipated to take 3-4 minutes. This left approximately 10-11 minutes for the calibration procedure and walking trials. This allowed for 3 repeats of the walking trials with a few minutes spare in case there were any unforeseen problems. Each walking trial provided 6 strides of data for each subject, so that over 3 trials a total of 18 strides per subject were obtained.

6.4 Sensors selected

A seven-sensor Xbus kit produced by Xsens Technologies (Xsens, Netherlands) was selected for gait analysis of the NTFS cohort. This consisted of seven MTx sensors which include a three-dimensional accelerometer, gyroscope and magnetometer, and an Xbus Master unit. The sensors are connected to the Xbus Master unit, which stores and transmits the data back to a laptop via bluetooth. The system is operated by the MT Manager software supplied and raw data was recorded. A complete description of the system selected can be found in Section 4.6.

6.5 Sensor attachment method

Three principal methods of attaching inertial sensors for gait analysis were available. These are: bone pins, double sided tape or glue, and elastic strapping. Inertial sensors on bone pins provide very accurate data on motion within and by a limb segment as they are not subject to the skin movement artefacts. However, they require a surgical procedure to attach, can be painful when moving about, and may leave a scar, and is in breach of requirement F. The use and justification of a surgical procedure also makes the ethical approval process much more difficult. The NTFS gait analysis was to be strictly non-invasive, so for these reasons bone pins were immediately discarded as a viable method of attachment.

A lycra bodysuit could be used for sensor attachment, with the sensors mounted in secure pockets on this. However, this has some inherent disadvantages, the first of which being that in order to wear the suit a subject would first have to disrobe and change into it. Requirement C does not allow this. In addition to this, bodysuits work best when they are tailor-made to fit the individual, which would not be practical or financially viable when working with large subject numbers. Finally, in a study in 2008 by Cloete and Scheffer [117], it was thought that the motion of the lycra bodysuit over the skin accounted for much of the disparity in joint angle measurement between the inertial and optoelectronic systems.

Double sided tape or glue has been used to attach inertial sensors directly to the skin [110, 119] and provides a secure attachment that can be easily removed without damage to the skin, provided the right adhesive is use. Suitable adhesives would be water-soluble bonding agent used by professional make-up artists or the adhesives found on toupee tape, as they are both suitable for use on the skin, are removed easily, and are sweat-resistant. However, it was stipulated that sensor attachment must take place over the top of clothing (requirement C). Attaching a sensor directly to clothing use glue or tape would not allow the sensor to accurately track the joint segment underneath.

Elastic strapping is the method most commonly found in the literature [110, 119, 122, 123]. The sensor is mounted on an elastic strap that passes round a subject’s limb segment. Fastening of straps is usually done with Velcro and this provides a secure fastening method and also makes the sensors quick to remove. The straps either incorporate a pocket/slot for the sensor to sit in, or have an exoskeleton attached on which the sensor sits [108, 113, 124]. Straps can be placed over the top of clothing and have an adjustable circumference, thus making them suitable for all participants and satisfying requirements C and D. In combination with the elastic nature of the material this provides an attachment method that will accommodate a wide range of body sizes.

Elastic straps were the only attachment method that fit within the conditions of involvement of the NTFS, and would also provide a secure attachment method. Xsens supply straps that are custom-made for the MTx sensors, therefore these were used for sensor attachment. Each strap consisted of a plastic holder for the MTx sensor and strong Velcro attachment points on the straps.

However, using a strap for the attachment of a sensor on the foot had some problems. A strap passing around the sole of the participant's foot might cause an alteration in their gait due to discomfort. Therefore it was decided to use double-sided tape to attach the foot sensor directly to the skin, and to then secure the sensor with surgical tape. Whilst removal of clothing is not allowed by the NTFS conditions, removal of footwear was permissible and did not violate requirement C. It is possible that removal of the sensors attached with double-sided tape could be painful, however if it is done carefully this can be avoided. It should be noted that it is possible that the sensation of having the sensor on their foot may also cause an alteration in gait, although it is not expected to be to the same extent. Table 6.2 shows the sensor attachment method chosen for each segment.

Table 6.2 Summary of sensor attachment methods by location.

Segment	Attachment Method
Pelvis	Velcro strap
Thigh	Velcro strap
Shank	Velcro strap
Foot	Double-sided tape

Strap tension needed to be considered during attachment. It was mentioned in section 4.5.3 that resonance can affect the measurements from inertial sensors when the sensors vibrate at, or close to, their natural frequency. The addition of frames and casing around inertial sensors typically lowers their natural frequency to around 20 Hz due to the increase in mass [125]. The only way to then raise this natural frequency is to increase the stiffness of the system during attachment by pre-loading the system using the tension in attachment bandages/straps [119]. Pre-loading of the system using attachment bandages was shown to increase the natural frequency of the system [119] in the work of Forner-Cordero et al., although attachment tightness was not measureable in this study and was dependant on the pain capacity of the subjects. It was recommended that the natural frequency of above 20 Hz would be sufficient for biomechanical measurements in most circumstances. Bergman et al. [110] also reported the attachment of sensors using both double-sided tape and Velcro straps (1 sensor on each limb segment). In both that paper, and that from Mayagoitia [108], it is clearly stated that the straps were attached tightly with a preloading force in order to decrease measurement errors. Whilst this seems a sensible decision, it was noted that care must be taken that the strap tightness does not alter the participants gait or cause them any pain (requirement F). In this thesis, the attachment tightness once again depended on the pain capacity of the NTFS participants, however a level of tightness was achieved to sufficiently raise the natural frequency of the system to above 20 Hz, given that the sensors themselves without any attachment pre-loading have a frequency of 20 Hz. In addition to this, the MTx sensors themselves have a low pass filter which ensures that no high frequencies are passed to the output filter.

6.6 Sensor attachment positions

Choice of marker/sensor attachment position was a crucial part of protocol design as much of the inter-trial repeatability of a technique hinges upon repeatable placement of the sensors/marker, giving a clear and stable definition of the anatomical axes of each limb segment. This was necessary in order to provide data that was as accurate and repeatable as other systems more commonly used in gait analysis, which would satisfy requirement H. It was also necessary to attach sensors to all lower body segments to record data for movement of ankle, knee and hip joint, in order to satisfy requirement G.

Marker attachment positions for optoelectronic systems are traditionally chosen for their proximity to anatomical landmarks. A wire-frame model of each body segment is then constructed from these markers and the anatomical axes subsequently defined. Locating a marker relative to a bony landmark improves inter-trial repeatability of these anatomical axes definitions as it gives a reference point for the required marker position.

When using inertial systems a relationship is defined between the technical frame of the sensor and the anatomical frame of the limb segment to which it is attached using a calibration procedure. The relationship defined between the two sets of axes will change depending on where the sensor is placed on the segment. Once defined, this relationship will only be altered if the sensor is displaced relative to the underlying limb segment. Therefore, a key requirement for this inertial system was sensor attachment positions that ensured minimal movement of the sensor relative to the segment during gait.

The dorsal surface of the foot, in line with the fifth metacarpal was chosen for the attachment of the foot sensor. This provided an even surface for the double-sided hypoallergenic tape to adhere to, and also adequate area either side of the attachment location for securing the sensor with surgical tape. It also represented a mid-foot position that will maximise its stability [114]. This attachment method means that the subject must be barefoot during the walking trials and has the added benefit of removing the effect of footwear on gait. It was noted that participants may not be used to walking on hard surfaces without footwear and this scenario may alter their gait.

The proximal end of the medial tibia was chosen for attachment of the shank sensor as it provides a flat surface for the sensor to rest upon. Other studies have used an attachment position just above the lateral malleolus [114]. However, this has the potential for the straps to slip down due to the curvature of the segment. The elastic Velcro strap passed around the shank with the sensor positioned 5cm distal of the tibial tuberosity on the medial surface of the tibia. In this position the strap sat above the maximum curvature of the shank, therefore preventing the strap from slipping down due to gravity. The medial surface of the tibia has been used in other studies to provide a stable attachment position [110].

Due to the larger muscle mass and skin movement present on the thigh segment it was difficult to select an appropriate attachment position. The larger muscle mass would mean that the effects of muscle contraction and relaxation on the straps would be greater. Optoelectronic systems typically position markers close to the knee joint flexion axis. However, this position would be beneath the curvature of the muscles and may lead to the straps slipping down and so a more proximal position was required. The front of the thigh was also unsuitable as the quadriceps muscle would be contracting and relaxing beneath the sensor and may cause excess roll of the sensor and accentuate the joint angle measurement. Placing the sensor on the lateral surface of the thigh, 10cm proximal to the lateral femoral epicondyle, provided a flat surface where the quadriceps and hamstring muscles meet. This is supported by Bergmann et al. [110].

Optoelectronic systems use markers placed on the anterior and posterior superior iliac spine points on each side to form a definition of the pelvic frame. Placing an inertial sensor on any of these points would create a similar definition of the pelvic frame (after calibration). However, placing the sensor on a bony outcrop would not be a stable position. The sacrum is attached to the pelvis and experiences little movement relative to the pelvis. Placing the sensor over the sacrum would allow for an acceptable definition of the pelvic frame whilst simultaneously providing a flat area for the sensor to rest.

Figure 6.1 shows the Xsens MTx sensors attached to a subject in the chosen positions using the Velcro straps provided by Xsens. Figure 6.2 shows the attachment of the foot sensor using double-sided tape, with surgical tape over the top to further secure it.

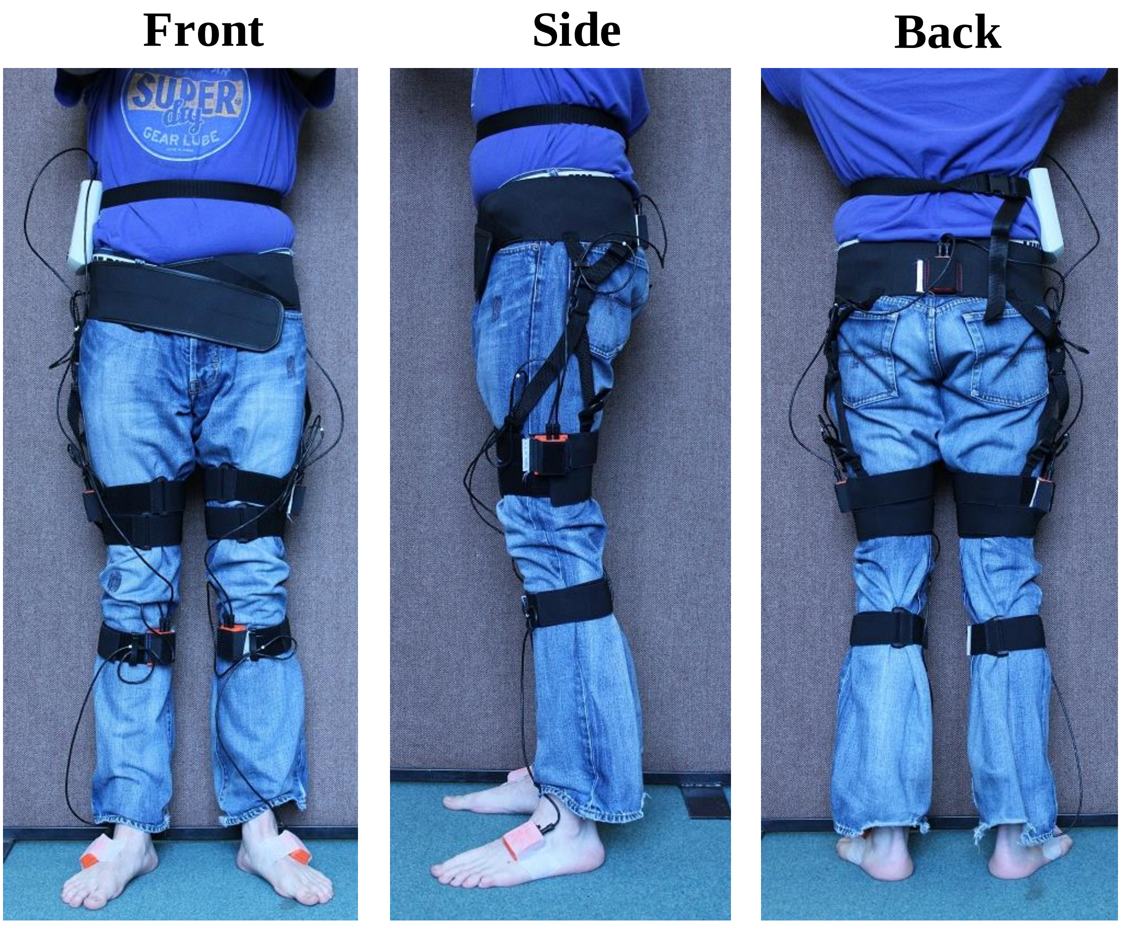

Figure 6.1 Sensor attachment positions for Xsens MTx sensor using custom-made Velcro straps.

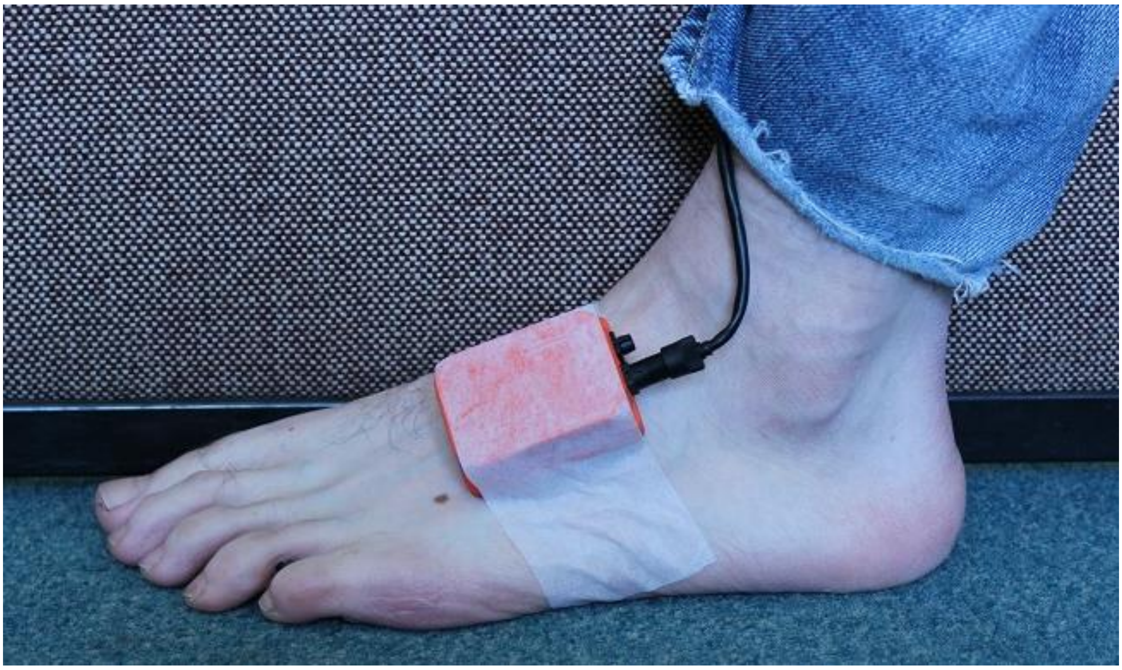

Figure 6.2 Attachment of MTx sensor to dorsal surface of foot using double-sided tape and surgical tape.

In all cases, the attachment straps would have to be sufficiently tight as to limit the movement of the sensor relative to the segment. This also has the added effect of raising the natural frequency of the strap and sensor system as the natural frequency increases with the pre-loading force from the bandage [119], as discussed in Section 6.5.

6.7 Calibration of inertial sensors

The definition of the sensor to segment orientation for each sensor is a crucial step for the use of IMU's in gait analysis to understand where the sensor is positioned relative to the underlying skeleton. Without this it is impossible to calculate joint angles and other variables. A more precise calibration of the sensors will produce more accurate and repeatable data, which satisfied requirement H. It was also important that the calibration was reasonably quick to perform in order to satisfy requirement B. This section will first review the different calibration methods proposed in the literature, and then move on to the design of a calibration routine based upon the ideas and recommendations found in the literature.

6.7.1 Calibration methods in literature

Several calibration methods with varying degrees or success have been proposed in the literature. All of them define the rotational displacement between the sensor frames and the segment anatomical frames.

The work of Bergman et al. in 2009 [110] used the MTx inertial sensors from Xsens for measuring joint angles during stair ascent. Their calibration routine involved aligning the X- and Z- axes of the sensors with the sagittal plane and gravity respectively. This was done in static stance phase. The system was compared to an optical motion analysis system (Codamotion, UK) and joint angles were calculated for the sagittal plane only. The systems showed no statistically significant difference for measurement of the knee joint angle. However, the inertial system consistently over-estimated both the ankle and hip joint ranges of motion. The standard deviations for the two systems were similar for each joint, implying that the definition of the anatomical frames is the source for the difference. The calibration routine for this method has produced accurate results for the knee joint, but not the others. This anatomical frame definition is sensitive to the placement of the sensors and has potential for inter-rater repeatability issues. Aligning the sensors axes with the anatomical planes would also take more time than was available in this study.

Another calibration method proposed by Picerno et al. [112] used an inertial sensor mounted on a frame with pointers, as shown in Figure 6.3. The pointers are aligned with anatomical landmarks on each segment and this aligns the sensor axes with the anatomical ones. The relationship between the orientation of the sensor attached to the body segment and the sensor in the frame, gives the technical to anatomical rotation matrix needed to transform sensor data into anatomical frame data. This method was compared against an optoelectronic system for measurement of the hip, knee and ankle angles during level walking. Flexion/extension angles for all joints were found to show the highest agreement, with internal/external rotation showing the biggest difference between systems. The method was found to be a valid alternative for the measurement of 3D joint kinematics, although rotations about the long axis of a segment should be treated with caution. The calibration technique is thorough and provides a definition of the anatomical frames equivalent to that used by an optoelectronic system. However, the technique requires time and precision, and at the moment does not take into account the repeatability of identifying anatomical landmarks. There is also some slight concern over the frame itself; inertial sensors incorporating a magnetometer are sensitive to disturbances in the local magnetic field. The material for the sensor frame used in the calibration is not stated, and if this were metal, and the disturbance not suitably taken into account, it could cause problems with obtaining a reliable reading.

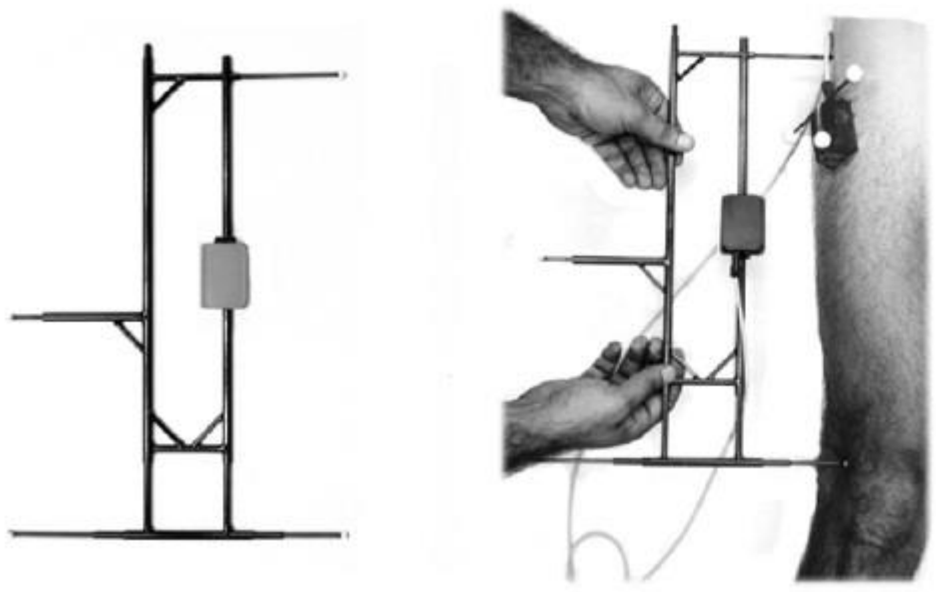

Figure 6.3 Inertial sensors mounted in calibration frame used by Picerno [106].

O'Donovan et al. in 2007 [113] used another approach for calibration. After secure sensor attachment, the subject performed a full rotation about the long axis of the body in standing position. This defined the long axis (y-axis) of each body segment. The subject then performs a knee flexion/extension and ankle dorsi/plantar flexion in a seated position. Assuming alignment of the medio-lateral axes of both segments, this movement defines the z-axis of segment. The cross product of the two calculated axes gives the x-axis, and hence a complete definition of the anatomical axes for each segment. The sensors were compared to an optoelectronic system (Motion Analysis Corporation, US) for measurement of ambulation. Flexion/extension angles were again found to be the most accurate, with internal/external rotations being the least accurate once again. This technique does not rely on accurate positioning of the sensors or pointers, and is quick to perform. The movements required are also simple to perform so there is less chance for subject error in the calibration routine.

The Outwalk program, developed by Cutti et al. [114], used a combination of functional movements and static postural measurements to calibrate their sensors (Xsens, NL). A flexion/extension movement was used for the knee, and then static captures of the subject either standing up straight or in the supine position were used to complete the definition. It should be noted that in the static standing position the feet are pointing straight forward and are parallel, providing a definition of 0 degrees internal/external rotation. The protocol was found to be accurate for all but the ankle internal/external rotation. The validation of this technique also compares results to those from Picerno [112] and found similarities in the results, implying that the simplification of the calibration process had not affected results. Once again, the calibration movements present little chance for subject error as the movements are all passive.

Favre et al. [126] proposed a similar calibration routine to the study by Cutti et al. A flexion/extension of the knee joint defined the medio-lateral axis, and an ad/abduction of the leg about the hip defined the antero-posterior axes. The final anatomical axis is defined as the cross-product of these. A static capture in neutral standing posture was used to define zero values for all three axes. The method demonstrated repeatability that was comparable to that reported for an optoelectronic system. The report also compared this functional calibration procedure against one using alignment of the sensor and body anatomical frames with the functional calibration procedure found to be more accurate.

The methods reviewed present a range of calibration procedures, including static poses, functional movements, and the identification of anatomical landmarks or the alignment of sensors with the body anatomical frames. The development of a calibration method for the NTFS gait analysis will now be described, combining elements of each of these and focusing on minimising the time taken to perform the calibration whilst preserving accuracy and repeatability of joint angles measured.

6.7.2 Calibration method development

The calibration method for the NTFS gait analysis had to be rapid and reliable (requirements B and H), and able to be performed on any of the cohort who could walk, regardless of mobility and flexibility (requirement D). It was also preferable that the method did not involve passive movements as this has the potential for causing pain if the subject’s comfortable range of motion for the joint is exceeded (requirement F). As previously mentioned, the experience of this gait analysis procedure is an important consideration, as it is hoped that all the participants will return for future follow ups and take the gait analysis part of this study from cross-sectional to longitudinal, further increasing its value and conclusions. The calibration would also have to take place either in the sensor attachment bay, or in the corridor where the trials are to be performed. Finally, as this was to be a portable method, a minimum of extra equipment had to be used since this would detract from the portability of the method (requirement A).

The method of aligning the sensor frames with the body anatomical frames [110] was immediately rejected on the grounds that the procedure would take too long and make it difficult to meet requirement B, and it could lead to intra- and inter-rater repeatability issues due to the subjective placement of the sensors relative to the anatomical frames. In addition to this, the sensor attachment points had already been defined and only the thigh sensor position would allow for frame alignment. The use of an extra inertial sensor mounted on a pointer frame [112] was also rejected, as whilst this would produce the most accurate calibration, the extra time and equipment needed for this are unavailable.

The calibration method developed for this protocol was a combination of the static and functional calibration methods detailed in the literature. The theory behind this calibration procedure was to rotate the sensor in the sagittal plane, and to use the gravity vector measured at the start and end of the movement to construct the anatomical axes. Figure 6.4 shows an example of a movement that changes the orientation of the sensor within the sagittal plane (in this case, the thigh sensor).

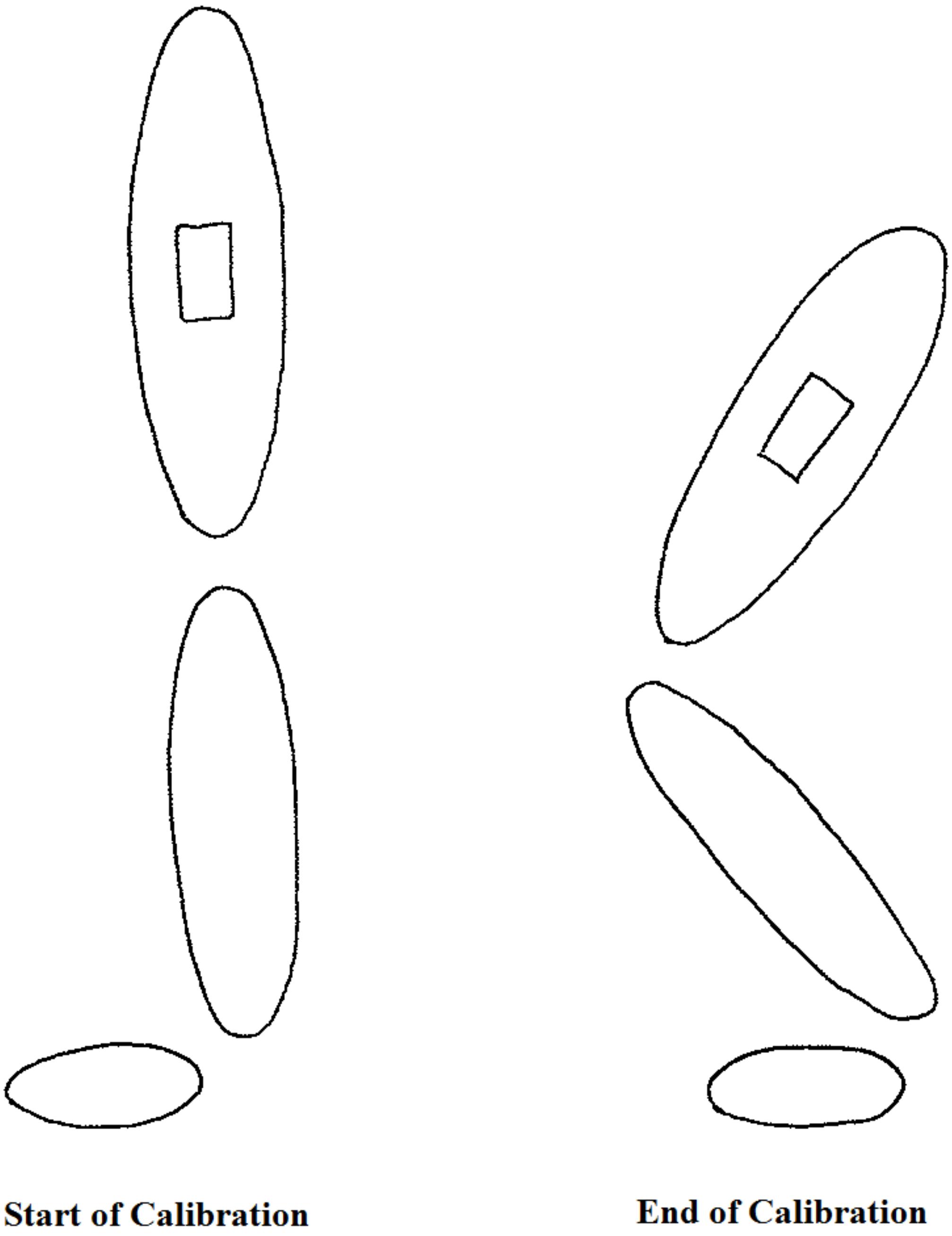

Figure 6.4 Example of left thigh calibration movement illustrating reorientation of MTx sensor within the sagittal plane.

Figure 6.5 shows an MTx sensor measuring the gravity vector at the start (G1) and end (G2) of a movement. The gravity vector in the starting position (G1) was used to define the anatomical y-axis of each segment, perpendicular to the transverse plane. The segment was then moved to a different orientation within the sagittal plane and the relative orientation of the sensor with respect to the gravity vector was measured again (G2). The cross-product of the measured gravity vectors gave the anatomical z-axis perpendicular to the sagittal plane. Finally the cross-product of the anatomical y- and z-axes gave the anatomical x-axis, perpendicular to the coronal plane.

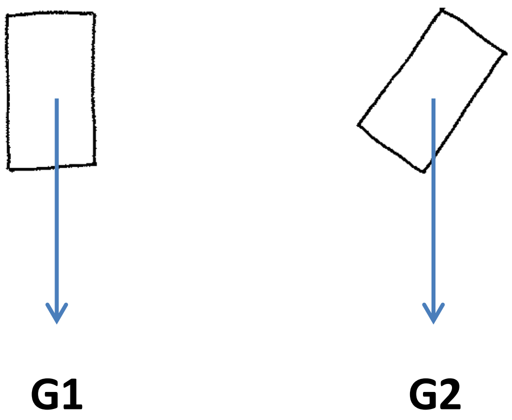

Figure 6.5 Change of orientation of sensor during calibration movement measuring the gravity vector at the start (G1) and end (G2) of the movement.

Whilst this study only required sensor data describing the knee joint, all sensors were calibrated so that future studies could look at motion of the hip and ankle joint. A total of four movements were performed for the calibration routine, with each movement calibrating a different sensor or group of sensors. Each movement started with the participant standing with their legs straight and feet at a comfortable width apart so that the ankle-hip axis was perpendicular to the floor. The thigh and shank sensors were calibrated using a squatting movement with the subject keeping their knees pointing forward so the rotation of the sensor occurred only in the sagittal plane. Figure 6.6 shows this movement. Each foot sensor was calibrated by lifting the foot at the heel, with only the toe remaining in contact with the floor, and moving the foot backwards until it came to rest at an angle against the wall. The waist sensor was calibrated by bending at the waist from the hips. In all cases, the range of motion for these calibration movements was that which the subject could perform comfortably without pain or discomfort.

Figure 6.6 Squat calibration movement used to calibrate the thigh and shank sensors.

It should be noted that this calibration routine assumed movement took place only in the sagittal plane. Out-of-plane movement would have affected the accuracy of the body anatomical frame definition. To combat this, during the squat movement the subject was asked to keep their knees in line with their toes as they performed the squat.

Finally, the attachment straps may move during each walking trial due to muscle contraction and relaxation. This could change the relationship between the sensor frame and the body anatomical frame, thus invalidating it for the next trial. Calibration of the sensors was, therefore, done before each walking trial to redefine the sensor-to-segment relationship.

6.8 Gait event detection using inertial sensors

In order to separate the data recorded for each participant into gait cycles, it is necessary to identify gait events. Traditional methods of identifying gait events have used footswitches. In the case of an optoelectronic system a height threshold can be set and, if a foot marker moves and stays below this for a period of time, this forms the definition of stance phase. Velocity and acceleration values from an optoelectronic system can also be used to define gait events.

With the increased use of inertial sensors, there have been several publications on gait event detection using inertial sensors. In 2005, Sabatini et al. reported on a study that assessed foot walking features using inertial sensors attached to the shank and foot [127]. As part of this they compared detection of walking features using the inertial sensors to a foot-switch. The angular velocity recorded by the gyroscope in both the foot and shank sensors was used to define gait events. Compared to the footswitch, the foot inertial sensor detected toe-off around 35ms earlier and with no systematic difference for the heel-strike. The shank inertial sensor showed the reverse, with heel-strike detected around 10ms later and no systematic differences for toe-off.

Another study tested the use of a single inertial sensor placed on the sacrum to identify gait events during running [99]. Acute acceleration spikes in the antero-posterior direction were used to identify heel-strike and toe-off. The results were compared against those obtained by an optoelectronic system and force plate, with the sampling rate for all three systems being 100 Hz. Agreement for heel-strike timing was very high, whilst toe-off was detected earlier with the inertial system than with the reference system. The authors postulated that this could be due to changes in the support of body mass which would not be detected by the camera system. It should also be noted that whilst a single sensor at the sacrum was shown to record gait events, this was for a running gait only. The accelerations experienced during running are higher than those for walking and this increase in acceleration magnitude may have aided the sensors in detecting the gait events.

In 2006, Jasiewicz et al. [128] used an inertial sensor attached to the dorsal surface of the foot to detect gait events. They compared the detection of both heel-strike and toe-off events using foot linear accelerations, foot angular velocities and shank angular velocities against footswitches. They conducted their study using 26 healthy volunteers with a large age range (5-79 years), and 14 with spinal-cord injuries, giving a comparison of each method for measurement of gait detection for both normal and pathological gait. Linear acceleration and angular velocity were found to be as accurate as footswitches for detecting gait events. For normal gait, all three methods utilising inertial sensors were equally accurate when compared to footswitches, however for pathological gait the angular velocity of the shank sensor proved not to be accurate.

An adaptation of the linear acceleration method developed by Jaseiwicz et al. [128] has been selected for use as the study design bore similarities to this thesis. The efficacy of the method for detecting gait events in both normal and pathological gait was assessed for a range of ages, and it was found that the foot sensor gave accurate results for both. The healthy subject group in the study by Jaceiwicz et al. had a large age range and the method of gait event detection proved effective for all ages. The sensors were attached to the dorsal surface of the foot. Finally, the sampling rate used by Jaceiwicz et al. was set at 25 Hz. One of the key factors in event detection will be sampling rate, and if a sampling rate of 25 Hz was found to be suitable then a higher sampling rate should only improve accuracy. An adaptation of the method by Jaciewicz was necessary due to the method use to define the interrogation windows and thus identify the acceleration signal defining a gait event.

The foot linear acceleration method developed by Jaciewicz et al. [128] uses the vertically directed acceleration to identify heel-strike, which will be in the z-direction primarily for the foot sensors in the work presented by this thesis. In the method by Jaciewicz et al., an interrogation window of ±100ms for the acceleration data was used around the peak of ankle dorsiflexion. The peak acceleration in the z-direction was then found and this is defined as the heel-strike event. For the work in this thesis it was decided to create an interrogation window using the minimum knee flexion angle as measurement of knee flexion was more reliable than ankle dorsiflexion using the protocol developed.

For identification of toe-off events Jaciewicz et al. used the acceleration in the forward direction, which is the y-direction for foot-sensors in this work. This method used the peak plantarflexion to define the interrogation window for finding the peak acceleration in the y-direction. This was again not possible in this study, however it was also not possible to use the knee-flexion angle as knee-flexion at toe-off is not a maximum or minimum value (as was the case with creating the interrogation window for heel-strike accelerations). Maxima and minima are mathematically distinctive features of a waveform, where gradient changes from positive to negative (or vice versa), and thus are relatively easy to find computationally. Finding a subtle change in gradient, with no change in sign and the value of which could be different for each subject, would not be a robust method of identifying an interrogation window. Instead, the heel-strike timings previously calculated were used to separate the trial into individual gait cycles. The estimated position of the toe-off event was then manually defined by the operator by viewing the forward acceleration signal and identifying the peak following heelstrike. This estimated position was then used to define an interrogation window of ±100ms and the peak acceleration then identified mathematically.

6.9 Description of knee joint motion

Previously, Section 3.9 went through a range of methods that can be used to describe knee joint motion. Inertial sensors were selected as the most appropriate measurement method for this study (based on the list of requirements found in Table 2.3), and a decision was required on which description of knee joint motion was to be used for the NTFS cohort.

Inertial sensors provided data on the orientation of the limb segment to which they are attached, but not its position. It is possible to obtain segment position from inertial sensors data via double integration of the acceleration measurements, but this carries with it substantial inaccuracies due to integration drift. The lack of reliable positional data for body segments meant that the helical axis description of the knee joint motion was not available for use, as this reports orientation and positional changes together as rotations around a screw axis. This left the joint coordinate system (JCS) and Euler angle descriptions of joint motion as available options.

Both the JCS and Euler angle descriptions of data are similar to those used by clinicians when describing knee joint motion during clinical examination.

Therefore, the ease of communication of gait analysis results does not suggest a preference for either method. The JCS devised by Grood and Suntay [58] was originally based on mechanical axes defined relative to anatomical landmarks. The JCS is formed by selecting an axis from each segment forming the joint, with the third axis a "floating" axis, defined by the cross-product of the two body-fixed axes. This methodology can still be applied to orientation data and so this provided no discriminator between the two.

In the literature detailing previous studies that have validated inertial sensors for measurement of gait kinematics (Section 4.4), both methods were found to have been used to successfully describe knee joint motion by other researchers. However, there is a preference in the literature for using the Euler angle convention for analysing inertial sensor data in relation to joint motion, with multiple studies reporting use of this method [110, 112, 129, 130]. Euler angles are also less susceptible to errors in the definition of the anatomical frames than helical axes [131]. Therefore, Euler angles were used for the description of knee joint motion in the NTFS gait analysis. The order of rotations used was ZYX, which was the same as those used in previous studies using Euler angles to interpret knee joint motion and appropriate as most of the joint motion occurred about the Z-axis (flexion/extension).

Before moving on to describing the method of calculating Euler angles for the knee joint, it is important to note the limitations of this method of describing joint motion. This description of knee joint motion does not describe any of the translations of bones during joint movement, and only returns rotations about a fixed point [90]. This is therefore not a complete descript of the joint motion. In addition, the rotation of the joint is assumed to take place about a fixed point when in fact the knee joint flexion axis changes with flexion of the joint. Therefore, an Euler angle representing knee flexion may not give a complete descript of the actual flexion angle of the joint.

6.10 Calculation of Euler angles for knee joint motion

In order to extract Euler angles for a joint, the segment-to-segment rotation matrix had to first be calculated. This required combining the sensor-to-segment rotation matrices defined by the sensor calibration with the sensor-to-global rotation matrices recorded by the sensor for each sample during the walking trials. In the calculation steps below, the following notation system was used. A single capital R in bold represented a 3×3 matrix that defines the rotation matrix from one coordinate system into another. The superscript following the capital R represents the starting coordinate system, and the subscript following the capital R represents the final coordinate system after the transformation. For example $\boldsymbol{R}_{B}^{A}$ represents the rotation matrix from coordinate system A to coordinate system B. Table 6.3 presents a list of the subscript and superscript notations used, and their definitions. Table 6.4 presents a complete list of the rotation matrices used in calculation of the segment-to-segment rotation matrix.

Table 6.3 Superscript and subscript notation used for identification of rotation matrices.

Symbol Used	Definition
G	Global frame
TA	Thigh anatomical frame
SA	Shank anatomical frame
TS	Thigh sensor-fixed frame
SS	Shank sensor-fixed frame

Table 6.4 Known rotation matrices used in the calculation of segment-segment rotation matrix for the knee joint.

Matrix	Definition
$\boldsymbol{R}_{TA}^{TS}$	Thigh sensor frame to thigh anatomical frame.
$\boldsymbol{R}_{SA}^{SS}$	Shank sensor frame to shank anatomical frame.
$\boldsymbol{R}_{G}^{TS}$	Thigh sensor frame to global frame.
$\boldsymbol{R}_{G}^{SS}$	Shank sensor frame to global frame.

Equation 6.1 was used to calculate the rotation matrix from the thigh anatomical frame into the shank anatomical frame. This produced a 3×3 matrix describing knee joint motion. A ZYX rotation sequence had been specified. Decomposition of the matrix in Equation 6.2 yielded angles ψ, θ and Φ. These represented rotations about the Z-, Y- and X-axes respectively. Table 6.5 clarifies the movement represented by each angle produced in the matrix decomposition. No filtering of joint angle data was performed.

$$\boldsymbol{R}_{SA}^{TA} = \left[\boldsymbol{R}_{TA}^{TS}\right]^{-1} \boldsymbol{R}_{SA}^{SS} \, \boldsymbol{R}_{G}^{TS} \left[\boldsymbol{R}_{G}^{SS}\right]^{-1} \tag{6.1}$$

$$R_{\psi}R_{\theta}R_{\phi} = \begin{bmatrix} cos\theta cos\psi & sin\phi sin\theta cos\psi - cos\phi sin\psi & cos\phi sin\theta cos\psi + sin\phi sin\psi \\ cos\theta sin\psi & sin\phi sin\theta sin\psi + cos\phi cos\psi & cos\phi sin\theta sin\psi - sin\phi cos\psi \\ -sin\theta & sin\phi cos\theta & cos\phi cos\theta \end{bmatrix} \tag{6.2}$$

Table 6.5 Definition of movement for each angle produced from matrix decomposition.

Angle	Movement definition
ψ	Flexion/extension
θ	Internal/external rotation
Φ	Adduction/abduction

6.11 Sampling rate

The Xsens Xbus system was capable of achieving sampling rate up to 512 Hz. However, when using the wireless transmission protocol, the sampling rate was affected by the number of sensors being used and the type of data being transmitted. A throughput of 20 kilobytes per second was available for the bluetooth wireless transmission method, which allowed a maximum of 20,000 bytes to be sent every second. Data was transmitted in the raw data format with orientations reported as a rotation matrix. Equation 6.3 shows the calculated data rate for a sampling rate of 50 Hz.

$$[(7 \times 20) + 2 + 7] \times 50 = 7450\ kbytes/sec \tag{6.3}$$

This data rate is well below the limit, and allows for the sampling rate to be raised to 120 Hz (17,880 kB/s). However, this higher sampling rate is close to the limit of the wireless transmission protocol and it was cautioned by Xsens that this may cause problems. Therefore, a sampling rate of 50 Hz was chosen.

6.12 Gait variables

Section 3.11 summarised the gait variables from the literature that have been found to have a link with OA. This list must now be reviewed, bearing in mind the sensors selected and the gait analysis protocol designed, in order to select variables which have the potential to be measured reliably by the methods chosen and are also relevant when looked at the link between OA initiation and gait.

Of the variables found to be relevant to this study from Section 3.10, inertial sensors had the potential to measure all of them, except anything required knowledge of spatial parameters or force components. This, therefore, excluded walking speed, stride length and flexion and adduction moments. There was the option to measure walking speed and stride length by integrating the acceleration signal from the inertial sensors to obtain position. However, this was deemed not reliable enough to be worthwhile (although could be looked at in the future if techniques for reliable integration of acceleration improve). There was also the option that flexion and adduction moments could be obtained by combining the accelerations experienced by each body segment and the mass of the body segment. However, as measurement of individual body segment masses was not performed, this would require estimation of the segment mass from anthropometric scaling. In addition to this estimation of segment mass, the acceleration recorded by the sensor may not provide an accurate reading of the acceleration experienced by the segment. Soft tissue movement, strap tightness and sampling rate might affect the recording of acceleration. It was therefore decided that this was not a variable that would be analysed, although, as with spatial parameters, there is the potential for this to be done in future should techniques evolve that prove sufficiently robust.

Whilst ground reaction force at heel-strike could not be measured with inertial sensors, the acceleration experienced by the foot sensor could be seen as a proxy of this. If a person were striking the ground with more force, then a higher acceleration would be recorded. Heel-strike force has been linked with OA in previous studies [104], although the measurement of the acceleration induced by heel-strike has some of the caveats mentioned above when discussing the use of acceleration signal for calculating moments about a joint; soft tissue movement and sampling rate may both affect the accurate measurement of acceleration signal. Therefore, interpretation of the heel-strike acceleration results should be done with caution and bearing these limitations in mind.

From the review of validations of inertial sensors in Section 4.4, it became clear that sagittal plane kinematics were relatively easy to obtain using inertial sensors and also provided accurate data in comparison to reference standard systems used. Conversely, transverse and coronal plane data proved much more difficult to obtain reliably for other studies. Therefore it was decided that sagittal plane kinematics would be focused on as these have proved the most reliable to obtain with inertial sensors during the literature review in Section 4.4 and have also been linked with OA in Section 3.10.

Finally, whilst spatial variables such as walking speed and stride length could not be measured, it was possible to measure temporal variables such as cadence and gait phase lengths. These have been linked to OA in the literature (Chapter 3) and the method adapted to measure gait events for this study was previously proven to be as accurate as a reference standard foot-switch (Section 6.8). Initial double support phase length was also selected. This represents the phase of the gait cycle when weight is being transferred from one foot to the other in preparation for toe-off. A longer initial double support phase length would indicate a slower transfer of weight and could be interpreted as weight being gingerly applied to a painful joint. The sagittal plane range of motion of the knee joint during the first 0.1s of stance phase represents the period of time following heel-strike when the joint is flexing to absorb the impact of heel-strike and starting to accept load transferred from the contralateral joint. The range of motion in this phase indicates how much joint movement occurs in the initial stages of load acceptance. Movement in this period could be seen as either entirely subconscious or determined by musculoskeletal structure, or influenced by bracing of the individual before impact.

Sagittal plane kinematics and temporal variables have been chosen for analysis in relation to OA initiation. However, there are many features within these two areas that could be recorded and analysed. The literature review of previous investigations into OA and gait (Section 3.10) highlighted sagittal plane kinematic and temporal variables that have shown a link with OA. Therefore, these variables were selected for analysis in this study.

Table 6.6 lists the kinematic, kinetic and temporal variables selected for analysis in the NTFS gait analysis based on previous work that has found a link between each variable and OA (Chapter 3, Section 3.10). This satisfied requirement I of the engineering specification.

Table 6.6 Kinematic, kinetic and temporal variables selected for analysis in the NTFS gait analysis.

Variable
Cadence
Single support phase length
Initial double support phase length
Peak knee flexion timing
Knee sagittal plane range of motion
Knee sagittal plane range of motion during the stance phase
Knee sagittal plane range of motion during the loading phase
Knee sagittal plane range of motion during the first 0.1s of stance phase
Knee sagittal plane peak flexion angle
Knee sagittal plane mean flexion angle
Knee sagittal plane mean flexion rate
Knee sagittal plane landing angle
Normalised vertical acceleration at heel-strike

6.13 Summary

This chapter began by reviewing the list of requirements for the NTFS gait analysis protocol to satisfy and then moved on to review the space available for gait analysis. Walking trial design was then reviewed and decision made on where to start the trials, walking speed, trial length, and how many walking trials would take place. The protocol design then moved on to summarise the sensors selected and identify appropriate attachment methods and positions. A review of calibration methods used for inertial sensors was performed and an appropriate calibration method then designed based upon this review. Methods of gait event detection using inertial sensors were reviewed and a method was adapted to fit the data available to this study. Euler angles were chosen to describe knee joint motion was chosen and the method of calculating knee joint angles described. Finally, a sampling rate was chosen for the sensors, and gait variables were selected for analysis based upon the results of the literature review of OA and gait in Chapter 3. Validation of the protocol designed was the next stage of this study.

Chapter 7 Protocol Validation

Chapter 6 developed a protocol for gait analysis of the NTFS cohort. Before gait analysis could start, this protocol required validation against a reference standard system. This chapter begins with the selection of a reference standard system. It then goes on to detail the protocol validation tests that will be used for assessing accuracy and repeatability of the NTFS gait analysis protocol using inertial sensors. The chapter then goes on to the methods used for assessment and the results obtained. These results are discussed and conclusions drawn, with recommendations for the protocol made. The final protocol is included, with these recommendations taken into account. The gait variables to be analysed from the NTFS gait analysis are then detailed, and the level of accuracy reported for each variable specified and justified. Finally, the statistical methods to be used for the analysis of the NTFS gait analysis results are described.

7.1 Choosing a reference standard system

The first task during the protocol validation was choosing a reference standard to compare the NTFS gait analysis protocol against. The purpose of a reference standard is to provide a well recognised and established measurement method which the accuracy and repeatability of the data recorded by the protocol developed can be compared against. Choosing such a system will aid acceptance of the validation of the protocol (and thus the results of the NTFS gait analysis) by the research community.

A Vicon (Vicon, UK) optoelectronic system was selected as this represented a commonly-used, well established and accepted technology (see earlier review of opto-electronic system in Section 4.2.1). In addition to choosing the system to compare the NTFS protocol against, a model and marker set to be used for the Vicon system also had to be chosen. There is a wide variety of models and marker sets available, some with specialist applications and others designed to be more general and flexible. The Plug-In-Gait (PIG) model and marker set for the lower body was chosen. The lower body PIG model and marker set was designed following the recommendations of several papers [132, 133] on the recording and calculation of movement data.

It is noted that in the selection of a reference standard system, and the model and marker set to be used with it, there will be errors associated with each of these. This is unavoidable, but must be taken into account when drawing conclusions from the results of a comparison.

7.2 Methods

7.2.1 Subject

This purpose of this validation study was to compare the measurement of knee joint by two systems. There is a wide range of variability in human gait, therefore it was decided to use a single subject for this validation study. Both systems would be measuring the same subject and therefore a direct comparison could be made. It was suggested that the subject group be expanded to include multiple subjects of varying ages and body types. However, there was not sufficient time to accomplish this before the commencement of the NTFS age 63 follow-up.

7.2.2 Vicon system set-up

A six camera Vicon T20 motion capture system was used, with the cameras set out in a circular arrangement to form a typical capture volume for gait analysis (see Figure 4.1 in Section 4.2.1). Data was recorded using an MX giganet box and a PC running Vicon Nexus software. A sampling rate of 50 Hz was used as this has commonly been found in gait studies using optoelectronic systems, and was also the sampling rate of the Xsens system. Joint angles were processed by the Vicon Nexus software using the PIG model.

Fourteen spherical markers, each 25mm in diameter, were used. Table 7.1 describes the attachment positions for the PIG lower body marker set and were those specified by the Vicon PIG user manual. Figure 7.1, Figure 7.2 and Figure 7.3. from the Vicon PIG user manual, show the marker attachment positions from the front, back and side respectively. Markers were attached using double-sided tape and their bases further secured with surgical tape. Marker attachment was performed by a single experienced researcher.

Table 7.1 Description of marker positions for PIG lower body marker set.

Marker Name	Attachment Position
LASI	Left anterior superior iliac spine.
RASI	Right anterior superior iliac spine.
LPSI	Left posterior superior iliac spine.
RPSI	Right posterior superior iliac spine.
LTHI	Over the lower lateral 1/3 surface of the left thigh, in line with the hip and knee joint centres.
LKNE	On the flexion/extension axis of the left knee.
LTIB	On the lower lateral 1/3 surface of the left shank.
LHEE	On the left calcaneous at the same height above the plantar surface of the foot as the toe marker.
LTOE	Over the second metatarsal head of the left foot, on the mid-foot side of the equines break between the fore-foot and mid-foot.
RTHI	Over the upper lateral 1/3 surface of the right thigh, in line with the hip and knee joint centres.
RKNE	On the flexion/extension axis of the right knee.
RTIB	On the lower lateral 1/3 surface of the right shank.
RHEE	On the right calcaneous at the same height above the plantar surface of the foot as the toe marker.
RTOE	Over the second metatarsal head of the right foot, on the mid-foot side of the equines break between the fore-foot and mid-foot.

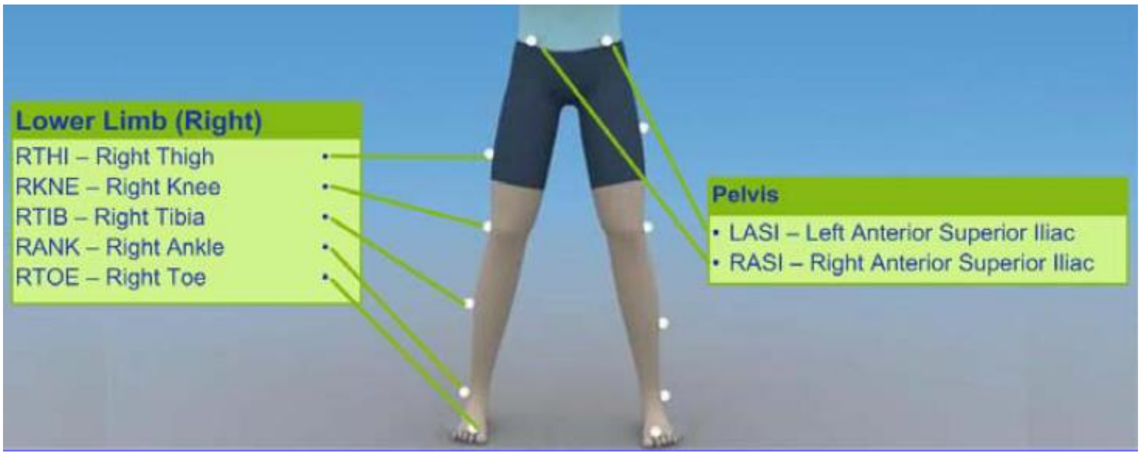

Figure 7.1 Front view of marker placement for PIG lower body model.

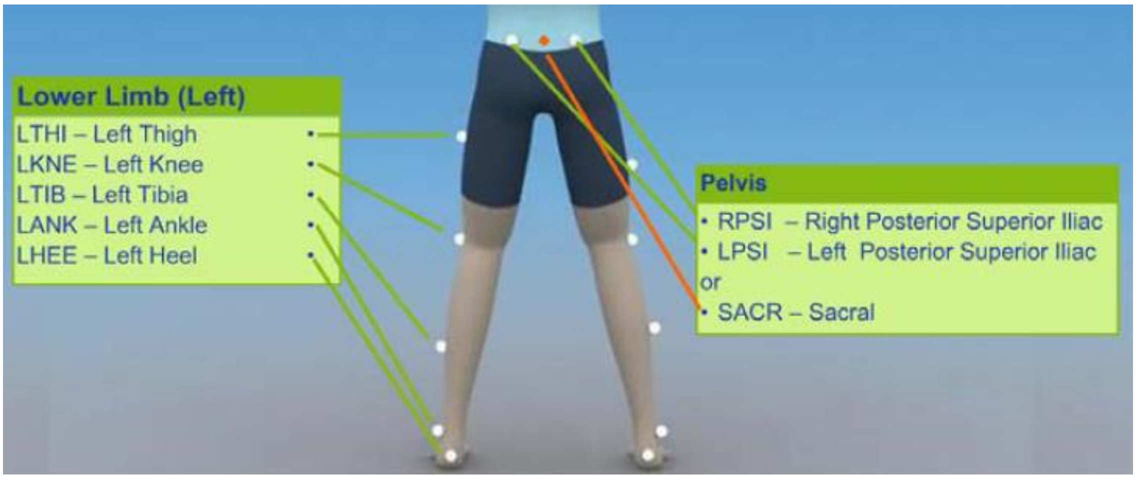

Figure 7.2 Back view of marker placement for PIG lower body model.

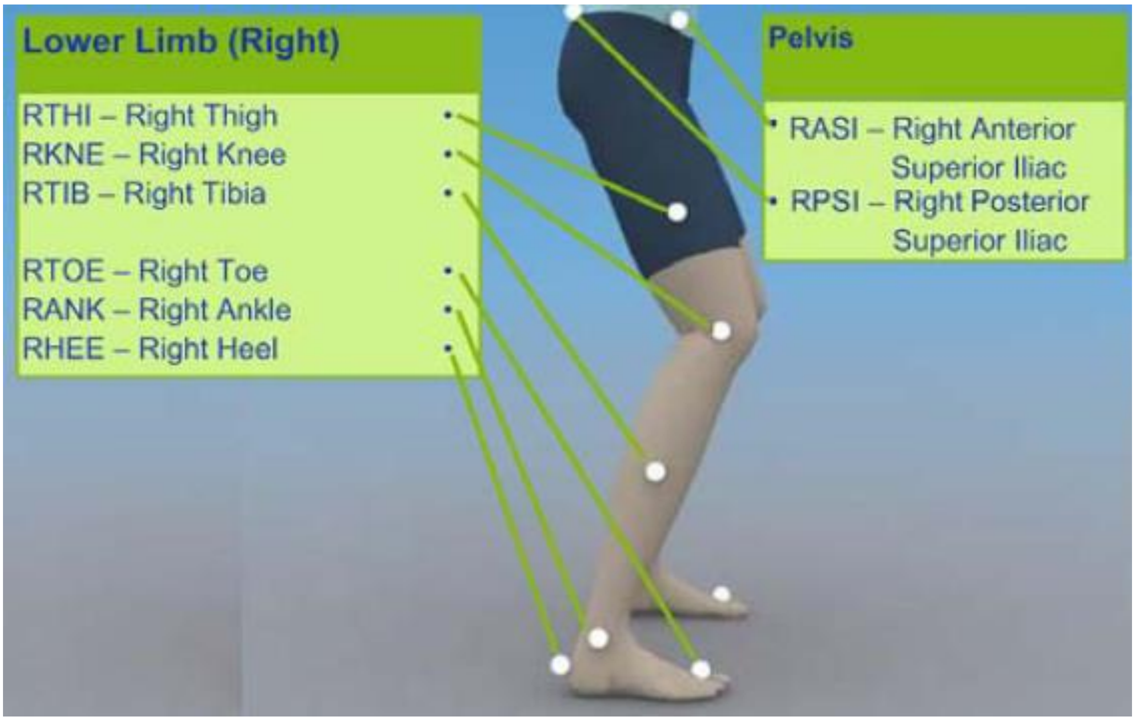

Figure 7.3 Side view of marker placement for PIG lower body model.

7.2.3 Xsens system set-up

The standard NTFS data collection protocol designed in Chapter 6 was used to collect data for the Xsens system. Tests to assess the effect of alterations to the protocol are detailed later in Section 7.3.

7.2.4 Trial design

Due to the attachment positions of the Vicon markers and MTx sensors, it was not possible to record with both systems simultaneously, as the sensor straps lay over the marker attachment positions in most cases. Fifteen complete gait cycles were recorded for each system using the protocols stated. When testing alterations to the NTFS gait analysis protocol, fifteen complete gait cycles were recorded for each alteration.

7.2.5 Results analysis

As the Vicon and Xsens systems did not record data on the same gait cycle simultaneously, it was not possible to compare individual trials. Therefore, the average gait cycle across all fifteen trials was calculated for each system and these were then compared by calculating the root-mean-squared error between the two systems. This is a method that has been used before in comparisons between optoelectronic and inertial systems [112].

A two sample T-test was also used to compare the range of motion (RoM) of the knee joint in the sagittal plane measured by each system. In this case, the sagittal plane RoM for each trial was calculated and these formed the datasets ($n = 15$ for each system). The RoM has also been used by other studies to compare measurement of knee joint angles by two systems [12, 134]. The standard deviation of the sagittal plane RoM measurement can also be used to compare the repeatability of the two systems.

Once the comparison with the Vicon system had been established it was the intention to assess how alterations to the standard protocol affected its repeatability. For each alteration to the protocol an F-test was used to compare the variance of the knee sagittal plane RoM for the altered and standard protocols. A non-significant result for the F-test would indicate equality of variance between the two protocols and thus no effect on repeatability.

Joint angles were quoted to an accuracy of 0.5°. A significance level of 0.05 was set for all statistical tests.

7.3 Protocol alterations

7.3.1 Removal of calibration movements before every trial

In Section 6.7.2 it was decided that calibration of the sensor would take place before every trial in case the straps had move during the previous walking trial and altered the sensor-to-segment orientation. However, removal of these additional calibration movements would save time, and so it was decided to test the affect of removing them and only calibrating the sensors once before the first walking trial.

7.3.2 Displacement of sensors from specified attachment position

Sensor attachment positions were chosen in order to provide a stable attachment position that aims to minimise the movement of the sensor relative to its underlying segment. However, inter-rater repeatability of marker attachment can be a problem when using optoelectronic systems and it was possible that this same issue could occur with attachment of the MTx sensors if multiple operators were used. Therefore, the effect of misplacement of the MTx sensors was tested. Sensors were displaced from their intended attachment locations along the long axis of each segment. The thigh sensors were moved distally by 6cm and the shank sensor was moved proximally by 4cm. The directions for displacement were chosen as they represented the direction in which movement may naturally occur during walking trials due to the combined effects of muscle contraction/relaxation and gravity. Each sensor displacement test was performed individually with the others sensors in their specified positions.

7.3.3 Material types

As the MTx sensors were to be attached over the top of clothing, it was important to test the effect of a range of material types that might be worn by participants when they attend for clinical assessment. Denim trousers, lycra tights, cotton suit trousers and cotton tracksuit bottoms were chosen for testing. These material types represented typical clothing that might be worn and also represented a range of elasticity and friction, with low elasticity and high friction (denim) through to high elasticity and low friction (lycra). The standard NTFS gait analysis protocol was used during assessment of material types.

7.3.4 Sensor sampling rate

A sampling rate of 50 Hz was specified in Section 6.11 as this has been commonly used in other gait analysis studies. There was sufficient bandwidth to accommodate a sampling rate of 120 Hz, however this was right on the limit of the bandwidth available and may cause problems with data buffering and transmission. Therefore it was decided to test the effect of increasing the sampling rate to 120 Hz, both on measurement of knee joint motion and on data integrity.

7.3.5 Simulation of excess adipose tissue

The cohort being studied had the potential to contain a wide range of body types and sizes, where excess adipose tissue could affect sensor readings. In order to simulate an overweight participant, hydration gel packs were used to simulate excess adipose tissue. These packs were placed underneath the thigh sensor straps as this was where the most adipose tissue tends to the found on the legs.

7.4 Validation Test Results

Figure 7.4 compares the measurement of knee flexion/extension movement during walking for the Vicon and Xsens systems over all 15 walking trials. The root-mean-square error between the two systems was 1 degree. The mean and standard deviation of the knee flexion/extension RoM measured by each system is included in Table 7.2. No significant difference was found in the measurement of knee flexion/extension RoM ($p = 0.47$).

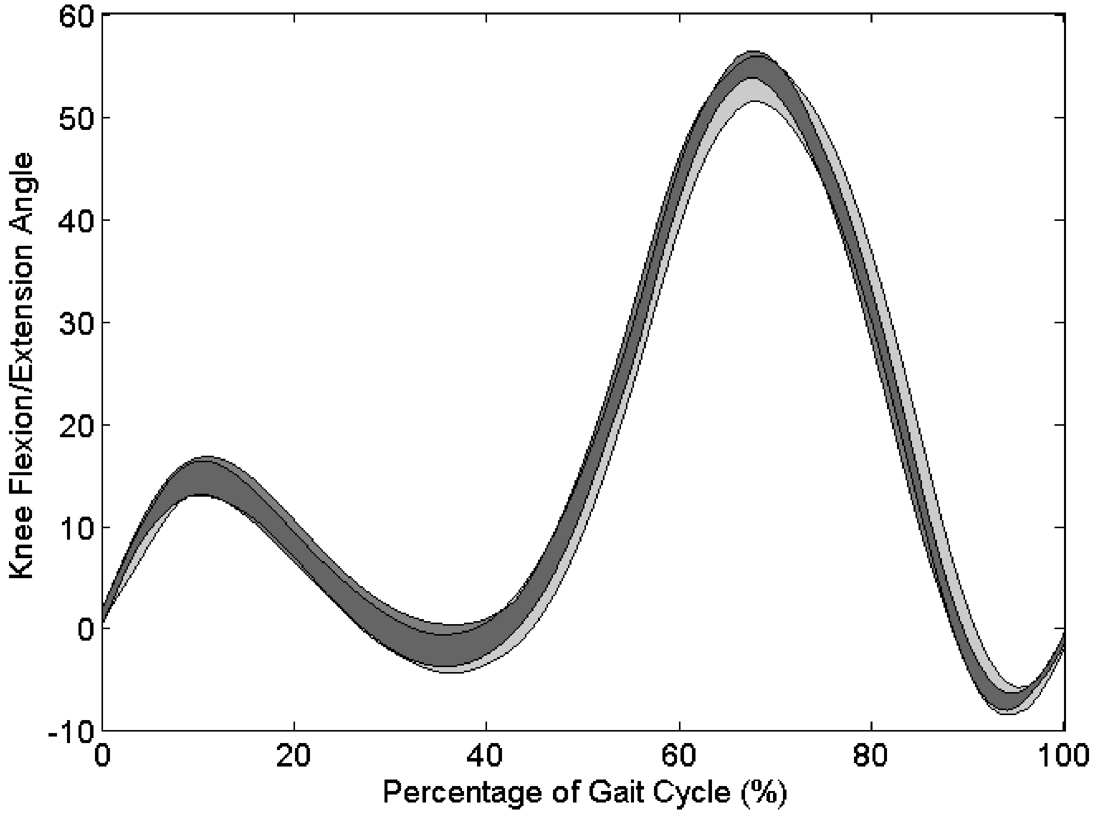

Figure 7.4 Comparison of knee flexion/extension measurement by the Vicon (light gray) and Xsens (dark grey) systems for the same subject over 15 trials.

Table 7.2 Mean knee flexion/extension RoM measured by Xsens and Vicon systems.

Scenario	**Knee flexion/extension RoM (°) Mean (SD)**
Xsens	61.5 (1.28)
Vicon measurement	59.5 (1.59)

The mean and standard deviation of the knee flexion/extension RoM for the standard protocol and each protocol alteration is shown in Table 7.3, as well as the results of each F-test.

Table 7.3 Mean and standard deviation for knee flexion/extension RoM for each protocol alteration and the standard protocol, including results of F-test for statistical significance between the each protocol alteration and the standard protocol.

Scenario	Knee RoM (°) Mean (SD)	F-test Result (p =)
Standard protocol	61.5 (1.28)	N/A
Reduced calibration	65.5 (5.19)	0.001
Shank sensor displacement	60.5 (1.60)	0.200
Thigh sensor displacement	62.5 (2.91)	0.002
Material type – denim	61.0 (1.75)	0.120
Material type – lycra tights	61.5 (1.33)	0.551
Material type – cotton suit trousers	61.0 (1.26)	0.350
Material type – cotton tracksuit bottoms	61.0 (1.35)	0.391
Sampling rate 120 Hz	61.5 (1.20)	0.400
Loose tissue simulation	62.0 (1.66)	0.170

7.5 Discussion

The repeatability of the ranges of motion measured by the inertial sensors for the knee joint was comparable to that measured by the optoelectronic system, and showed no statistically significant difference. The comparison of measurement of knee joint flexion/extension in Figure 7.4 supports this. The inertial systems measurement of knee flexion/extension remained within the measurements recorded by the optoelectronic system. The RMSE of 1° is similar to that reported by Picerno et al. [112] and for the unpublished pilot study reported by Bergman et al. [110], further supporting the inertial system having measured the knee joint flexion/extension as well as the optoelectronic system. It should be noted that whilst the optoelectronic system is being used as a reference standard system, it will also have its own errors associated with marker placement and assumptions during calculation of joint angles.

The reduction in the total number of calibration movements performed, with the calibration movements before the second and third trials removed, resulted in significantly decreased repeatability for the measurement of knee flexion/extension. The implication of this is that the sensors did experience movement relative to the underlying body segment during the walking trials. However, the repeatability of the protocol when all the calibration movements were included produced repeatability comparable with an optoelectronic system; therefore it was deemed an adequate solution.

Displacement of the shank sensor also produced no significant effect on the repeatability of knee flexion/extension RoM measurement. The shank sensor sits on a bony surface at the proximal end of the medial tibia, with little movement of the muscle tissue beneath the sensor strap to displace it, and this was thought to be the reason for no significant difference being found. Displacement of the thigh sensor caused the standard deviation of the knee flexion/extension RoM to more than double, indicating a significant decrease in repeatability. The thigh sensor had the greatest muscle mass beneath it and therefore muscle contraction and relaxation caused the sensor to move during gait.

None of the materials tested caused a significant decrease in repeatability of knee flexion/extension RoM measurement. The results for denim, whilst not significant, were noticeably lower than those for the other material types. The low elasticity of denim means that when the material was pulled tight during flexion, the tension will transfer directly to the sensor straps and displace them from their intended positions. It is possible that with varying fits of denim clothing, the effect of the material may be more or less pronounced (for tighter or looser fitting clothing respectively).

Sampling rate had no significant effect on the repeatability of the joint angle measurements. However, it was noted that when using a sampling rate of 120 Hz the system would experience “buffer overflow” error. The error was diagnosed as being related to the buffer used within the Xbus Master data logging unit. This buffer stores the data recorded in “packets” and then burst transmits them back to the receiver. The more data recorded per second and buffered for transmission, the more likely it is that a buffer overflow error may occur. This error results in some samples of data being lost, as the system gets rid of the data causing the error and begins recording and transmitting again. In order to avoid the error entirely it was recommended that a sampling rate be chosen that keeps the data rate below 60-65% of the maximum (20 kb/s). 50 Hz was selected as the most appropriate sampling rate. Antonsson and Mann [135] recommended a sampling rate of greater than 30 Hz in order to adequately record human gait kinematics, and 50 Hz is commonly used as a sampling rate for optoelectronic system measuring gait kinematics. Therefore 50 Hz is sufficient to capture sagittal plane knee kinematics and gait events.

The adipose tissue simulation showed a slight decrease in repeatability for the knee flexion/extension RoM, likely due to the instability in attachment surface, but these still remained within expected values and the change was not significant.

7.6 Conclusion

From the validation testing it was first concluded that the NTFS gait analysis protocol had accuracy and repeatability comparable with the reference standard of an optoelectronic system. An RMSE of 1° was found between the two systems for measurement of knee joint flexion/extension, which is comparable with other inertial sensor validation studies [110]. This satisfied requirement H of the engineering specification. Alterations to the protocol were tested, with removal of calibration movements before the second and third trials, and displacement of the thigh sensors distally from its intended attachment position were found to significantly affect repeatability of knee flexion/extension measurement. Care must be taken in placement of the thigh sensor, and calibration movements must take place before every walking trial. No material type had a significant effect on repeatability, however denim did show markedly different results from the other material types tested. Therefore it was decided to request participants not to wear denim trousers when they attended for gait analysis. Finally, whilst increasing the sensor sampling rate did not significantly affect knee joint flexion/extension measurement repeatability, it did cause problems with integrity of the data. Therefore it was decided to keep the sampling rate at 50 Hz, as originally specified.

7.7 Final protocol

This section draws together the decisions made with regards to protocol design and concisely summarises the gait analysis protocol developed, incorporating any adaptations made to the protocol as a result of the validation testing.

The sensors were attached using custom-made, elastic, Velcro straps (Xsens, NL), with the exception of the foot sensor which was attached using double-sided, hypoallergenic tape and secured with surgical tape. The foot sensors were positioned on the dorsal surface of the foot, in line with the fifth metacarpal head. The shank sensors were positioned on the proximal end of the medial tibias, 5cm distal to the tibial tuberosities. The thigh sensors were positioned 10cm proximal to the lateral femoral epicondyles. The final sensor was attached over the sacrum. All sensors were connected to a data logger attached around the subject's waist on a separate strap. The data were captured at a sampling rate of 50 Hz, and transmitted wirelessly.

A set of calibration movements were performed to describe the orientation of each sensor relative to its body segment. The subject stood in an adjustable foot frame with legs straight and feet aligned with the frame, and this provided a repeatable starting posture for each trial, ensuring joint angles in all planes are close to 0º. The thigh and shank sensors were calibrated using a squatting movement with the subject keeping their knees pointing forward so the movement occurred primarily in the sagittal plane. The foot sensors were calibrated by lifting the foot at the heel, with only the toe remaining in contact with the floor, and moving the foot backwards on the foot-frame until the foot comes to rest at an angle. The waist sensor was calibrated by bending at the waist from the hips. In all cases, the range of motion for these calibration movements was that which the subject could perform comfortably without pain or discomfort.

For the trials, the participants started off in the foot frame and then performed a walk of ten paces at a self-selected speed down the corridor. At the end of the trial they remained facing in the direction of travel until recording was stopped. They then returned to the foot frame, and the calibration movements and trials were repeated twice in sequence. Finally, the protocol ended with the removal of the sensors from the subject.

All participants were barefoot during the protocol and were specifically requested not to wear jeans when attending for clinical assessment. Female participants were asked to wear trousers.

7.8 Exclusion criteria

It was noted in Section 3.4.2 that it is important to distinguish between primary and secondary OA when looking at initiation of the disease by gait. Participants with secondary OA were excluded from the analysis because another external factor had influenced the initiation of the disease, and the results analysis focused on healthy participants and those with primary OA. The criteria for diagnosing secondary OA are very broad and encompass many measures that were not obtained during this study. Therefore, secondary OA exclusion was based upon; congenital disorders of the knee joint, diabetes, inflammatory diseases and injury to the joints [7]. It was noted that there is the potential that some causes of secondary OA were not identified, e.g. genetics, inactivity due to a sedentary lifestyle. Therefore it is possible that some of the final group used for analysis of OA initiation in relation to gait may include some cases of secondary OA. It was not possible at this stage to exclude these individuals, however in the future it may be possible to review participants exclusion to encompass all causes of secondary OA. This will be taken into account during results analysis.

Along with exclusion based upon the diagnosis of secondary OA, there were also diseases that are likely to affect a participants gait and it would be difficult to discern whether OA or another pathology was causing differences found in gait variables. The decision on whether to exclude a participant based upon diagnosis of pathology was based upon the potential for the given pathology to have affected the biomechanics of the musculoskeletal system, for the pathology to be causing pain whilst walking, or for the pathology to have adversely affected the participants balance and coordination. If the accepted symptoms of a pathology exhibited by a participant included any of these symptoms, then the participant was excluded from analysis.

Diagnosis of osteoarthritis in any other joint apart from the knee also necessitated exclusion from the results analysis as it would be difficult to discern which joint pathology had caused changes in gait. Any other form of arthritis in a joint also led to exclusion from the results analysis. Finally, joint replacement in any joint of the lower extremity led to exclusion from the gait analysis as the effect of this upon gait would be difficult to separate from affects due to an OA joint. Table 7.4 list the pathologies that resulted in exclusion of NTFS participants from the results analysis looking at OA initiation through gait.

Table 7.4 Criteria for excluding NTFS participants from results analysis relating to OA initiation through gait.

Criteria
Diagnosis of secondary OA.
Facioscapulohumeral muscular dystrophy.
Ataxia.
Parkinsons.
Guillana-Barré syndrome.
Stroke.
OA in other joints.
Hip replacement.
Knee replacement.

7.9 Calculation of gait variables selected for analysis

With the protocol finalised, and its repeatability validated, it was important to clearly define the variables collected that would be analysed with respect to the Kellgren-Lawrence (KL) grade, based on the review in Section 3.11 of relevant gait variables for this study. To avoid ambiguity the calculation of all variables used needed to be defined.

Cadence was calculated between the 3rd and 8th heel-strike events of a participants walking trial, representing 5 strides, according to Equation 7.1.

$$Cadence = no. strides \times \frac{60}{time\ taken\ (s)} \qquad 7.1$$

Single support phase length was calculated as the time between toe-off of one gait cycle and heel-strike of the following gait cycle and expressed as a percentage of the overall gait cycle length. Initial double support phase length was calculated as the time between heel-strike of one foot and toe-off of the opposite foot and expressed as a percentage of overall gait cycle length. Peak stance phase flexion time was calculated as the time at which the first peak flexion occurred during stance phase and expressed as a percentage of overall cycle length.

Knee sagittal plane range of motion (RoM) was calculated by subtracting the minimum value of knee flexion during a gait cycle from the maximum value of knee flexion during the same gait cycle. Knee sagittal plane RoM in the stance phase was calculated by subtracting the minimum value of knee flexion from the maximum value of knee flexion during the period between heel-strike and toe-off for each gait cycle. Knee sagittal plane RoM in the loading phase was calculated by subtracting the minimum value of knee flexion from the maximum value of knee flexion during the period between heel-strike of one foot and toe-off of the opposite foot. Knee sagittal plane RoM during impact phase was calculated by subtracting the minimum value of knee flexion from the maximum value of knee flexion during the first 0.1s of stance phase.

Peak flexion angle was defined as the maximum value of knee flexion achieved over the whole gait cycle. Mean knee flexion angle was calculated by taking the average knee flexion value over the whole gait cycle. Mean knee flexion rate was calculated by numerically differentiating the knee flexion data and taking the average of this over the whole gait cycle. Knee sagittal plane landing angle was defined as the angle of knee flexion at the time of heel-strike.

The ground reaction force exerted on the body depended on both how hard a participant struck the ground and also their body mass. As a force plate was not used, acceleration was used as a measure of heel-strike force. Vertical acceleration at heel-strike was found from the acceleration measured by the foot inertial sensor in the global z-direction (global vertical) as this was the closest sensor to the point of impact. In order to negate the effect of body mass and to determine if participants were striking the floor harder as a result of their gait, the vertical acceleration at heel-strike was normalised to body mass. A summary of the variables selected for analysis and the units they were recorded in is given in Table 7.5.

Table 7.5 NTFS gait variables selected for analysis in relation to KL grade.

Variable name
Cadence (strides/min)
Single support phase length (%)
Initial single support phase length (%)
Peak stance flexion timing (%)
Knee sagittal plane range of motion (°)
Knee sagittal plane range of motion in stance phase (°)
Knee sagittal plane range of motion in the loading phase (°)
Knee sagittal plane range of motion in the impact phase (°)
Knee peak flexion (°)
Knee mean flexion over gait cycle (°)
Knee mean flexion rate over gait cycle (°/s)
Knee sagittal plane landing angle (°)
Normalised vertical acceleration at heelstrike (m/(kg s^2))

7.10 Level of accuracy of reported group variables

Cadence was measured as the number of strides per minute and as such was reported to the nearest integer value. All variables reported as a percentage of overall gait cycle length were reported to the nearest integer percentage. As the sampling rate is 50 Hz, a gait cycle duration of over two seconds for all participants would be required to have considered reporting a higher accuracy. Joint angles were measured to the nearest half degree; therefore joint angles for each group were reported to one decimal place. Similarly, rate of change of joint angle was also reported to one decimal place. Finally, acceleration data from the sensors was recorded to three decimal places, and mass was recorded to two decimal places; therefore normalised vertical acceleration at heelstrike was reported to two decimal places.

7.11 Statistical methods for assessing gait analysis variables in relation to OA

As osteoarthritis is a disease that will progress at a different rate in each sufferer, it is reasonable to assume that the data will not be normally distributed. Therefore, non-parametric statistical methods are required as these make no assumptions about the normality of data. Non-parametric methods compare the distributions of two or more groups. The median is a robust description of the middle of a dataset as it is not as strongly affected by the presence of outliers as the mean. Therefore the median will be reported in the descriptive statistics for each variable.

A chi-squared test was used to examine the effect of sex and body side on OA incidence. When the association between a gait variable and KL grade was found, a Mann-Whitney test was first performed to assess differences in the gait variable between sexes. If no differences were found at all KL grades then sex was ignored in subsequent inter-grading analysis. The inter-grading analysis started with a Kruskal-Wallis test to examine differences between groups. If this returned a significant difference ($p < 0.05$), then a Mann-Whitney test was performed between successive groups to find where the difference lay. If sex was not able to be ignored then these tests were performed for each sex individually.

Other factors were included that could potentially have altered a participant's gait, and any changes in gait may in fact have been an expression of these confounding factors, rather than purely a change in gait kinematics. Pain and stiffness were treated as possible confounding factors as they have been shown to produce alterations in gait [34, 136] and osteoarthritis patients often suffer pain whilst walking. BMI was also treated as a confounding factor and has also been linked to the incidence of OA [137]. Finally, some studies have shown that changes in speed can cause alterations in gait kinematics[65, 71]. Whilst the protocol was incapable of calculating walking speed due to lack of spatial data, cadence could be used as a proxy of walking speed. In order to assess the effect of these confounding factors, a backwards stepwise regression was then performed on each kinematic variable against KL grade, with WOMAC pain score, WOMAC stiffness score, BMI and cadence included in the model. The exception to this will be when looking at cadence, in which case cadence cannot be included as a confounding variable. The R^2 values and regression coefficients will be reported for each analysis.

7.12 Summary

A suitable reference standard for comparing the NTFS gait analysis protocol against was chosen. A methodology for the validation testing was then developed and suitable tests chosen. The accuracy and repeatability of the NTFS gait analysis protocol was validated against the reference standard, and protocol alterations assessed. Calibrating the sensor before every trial improves the repeatability of the protocol. Thigh sensor movement artefact has been shown to have the greatest effect on repeatability, and attention should be paid to minimising the movement of this sensor during gait. Denim material under the straps had the largest effect on repeatability of joint angle and so should be avoided. The final protocol to be used for the NTFS gait analysis is then included for clarity. The chapter then moves on to select the gait variables that will be analysed in relation to OA severity, and the calculation method for each of these. Finally, the statistical tests used to assess the changes in each gait variables in relation to OA severity are detailed and justified.

Chapter 8 Results

This chapter details the results obtained from the analysis of gait variables in relation to other relevant clinical assessment data (detailed in Chapter 2) on the Newcastle Thousand Families Study (NTFS) cohort. The chapter begins with basic summary statistics of the cohort members who underwent gait analysis, and then moves on to detail the results for each variable recorded. The sample size for each variable is included in the title of each table for clarity. Data for each gait variable is presented in the form of a bar chart for ease of viewing, with the exact values for the data included in Appendix A.

8.1 Summary of basic cohort statistics

Figure 8.1 shows the attrition of the NTFS cohort since inception and the final number of participants included in the NTFS gait analysis. This group comprised of ninety-seven males and 114 females. The mean age for both sexes was 63±0.1 (mean±SD) and the range was 62-63. The mean ages did not differ significantly between males and females ($p = 0.797$). Table 8.1 and Table 8.2 show the height, weight and BMI for males and females respectively. Table 8.3 shows a summary of the number of participants presenting with each KL grade. The KL grade used for this table is the most severe KL grade present in either of the knees of each participant and this is used for analysis of variables that are not knee-dependant (eg. cadence). More females than males had grade 0 and grade 1 OA, and more males than females had grade 2, grade 3 and grade 4 OA. There was little difference between sexes at grade 2. A chi-squared test to examine the effect of sex on OA incidence returned a p-value 0.092, indicating no significant difference between male and female incidence of OA at all grades. It should be noted that there was only one female participant with grade 4 OA in either knee. It was not possible to perform an intra-sex comparison between females with grade 3 and grade 4 OA due to small numbers. Table 8.4 gives a summary of the participant numbers presenting with each KL grade broken down by both knee (right or left) and sex. These are the groupings used for knee-dependant variables (eg. Sagittal plane knee range of motion). For grades 1, 2 and 4, there were more instances of right knee OA than left knee OA. A chi-squared test for statistical significance was used to examine the effect of body side on OA incidence in males and females separately. A value of p = 0.876 was returned for males and a value of p = 0.500 for females. This indicates no significant difference in OA incidence in the left or right leg for both sexes, allowing body side to be ignored in subsequent analyses.

Table 8.1 Male anthropometric data (n = 95) at age 62-63 years.

Variable	**Mean**	**Range**	**Standard Deviation**
Height (cm)	174.6	160.6 – 186.0	5.3
Weight (kg)	84.6	60.4 – 131.8	12.9
BMI (kg/cm²)	27.8	20.3 – 42.6	4.0

Table 8.2 Female anthropometric data (n = 111) at age 62-63 years.

Variable	**Mean**	**Range**	**Standard Deviation**
Height (cm)	160.8	145.4 – 174.5	6.3
Weight (kg)	71.1	47.3 – 125.5	13.6
BMI (kg/cm²)	27.6	18.5 – 47.6	5.4

Table 8.3 Frequency of KL grades by sex at age 62-63 years.

KL Grade	**0**	**1**	**2**	**3**	**4**
Male	3	53	32	5	4
Female	12	68	29	4	1
Total	15	121	61	9	5

Table 8.4 Frequency of KL grades by knee and sex at age 62-63 years.

Grade	**0**		**1**		**2**		**3**		**4**	
Knee	**R**	**L**	**R**	**L**	**R**	**L**	**R**	**L**	**R**	**L**
Male	4	7	58	57	28	26	4	5	3	2
Female	12	18	72	70	26	23	3	3	1	0
Total	16	25	130	127	54	49	7	8	4	2

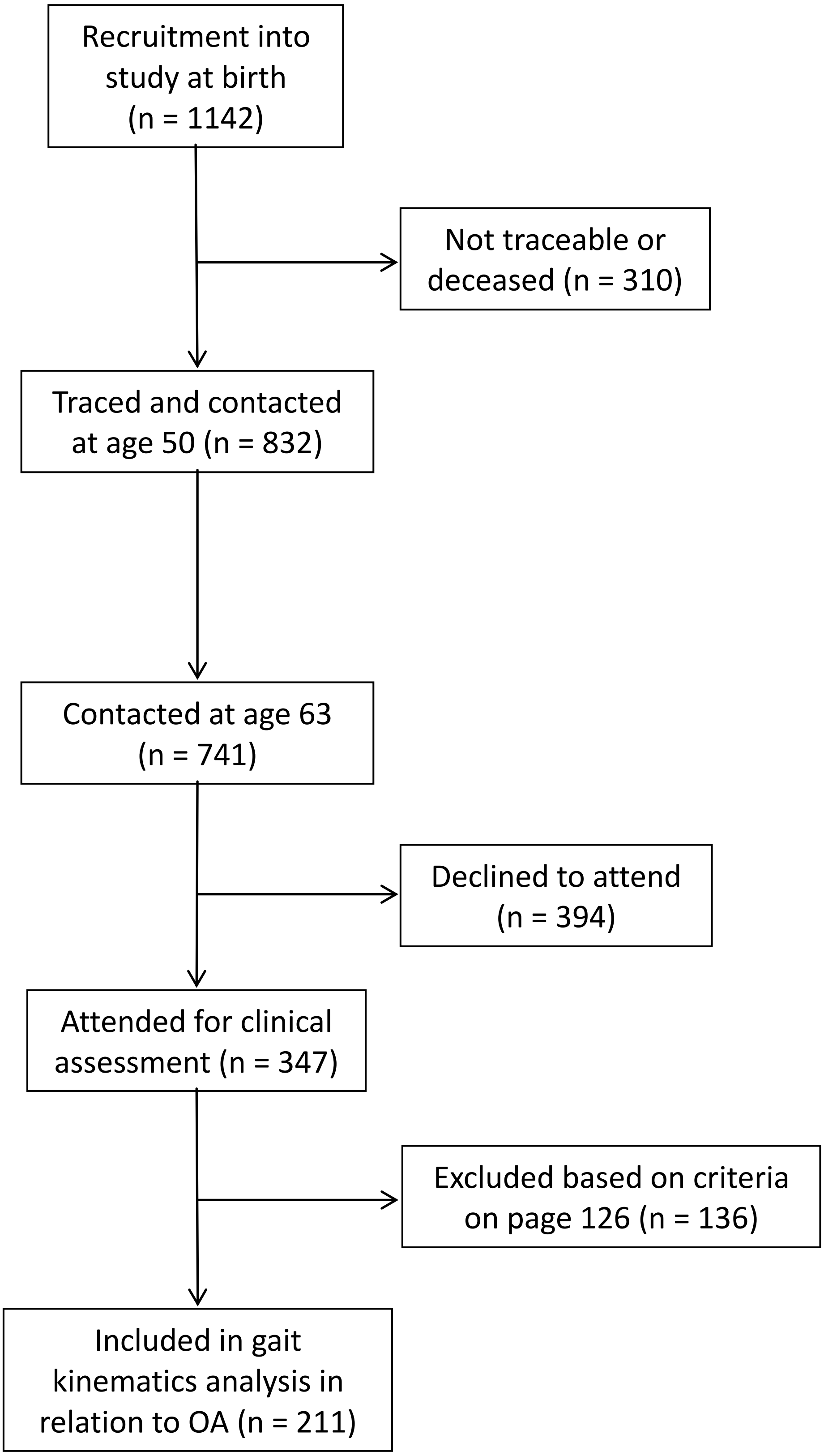

Figure 8.1 CONSORT diagram showing cohort attrition and final number of participants included in NTFS gait analysis.

8.2 Potential confounding factors

As detailed in Section 7.11, there were several potential confounding factors to consider when looking at the relationship between gait kinematics and KL grade. The method of assessing these was to include them as variables in a backwards stepwise regression analysis. The confounding variables chosen were WOMAC pain score, WOMAC stiffness score, BMI and cadence. WOMAC pain score, WOMAC stiffness score and BMI were subject to the same statistical analysis procedure as the gait variables (with regression analysis excluded). Cadence was included in the analysis of kinematic variables.

8.2.1 WOMAC pain score

Median WOMAC pain score for the entire cohort was 1 (interquartile range (IQR) 0 – 8). Figure 8.2 shows the median WOMAC pain score for each KL grade, by sex.

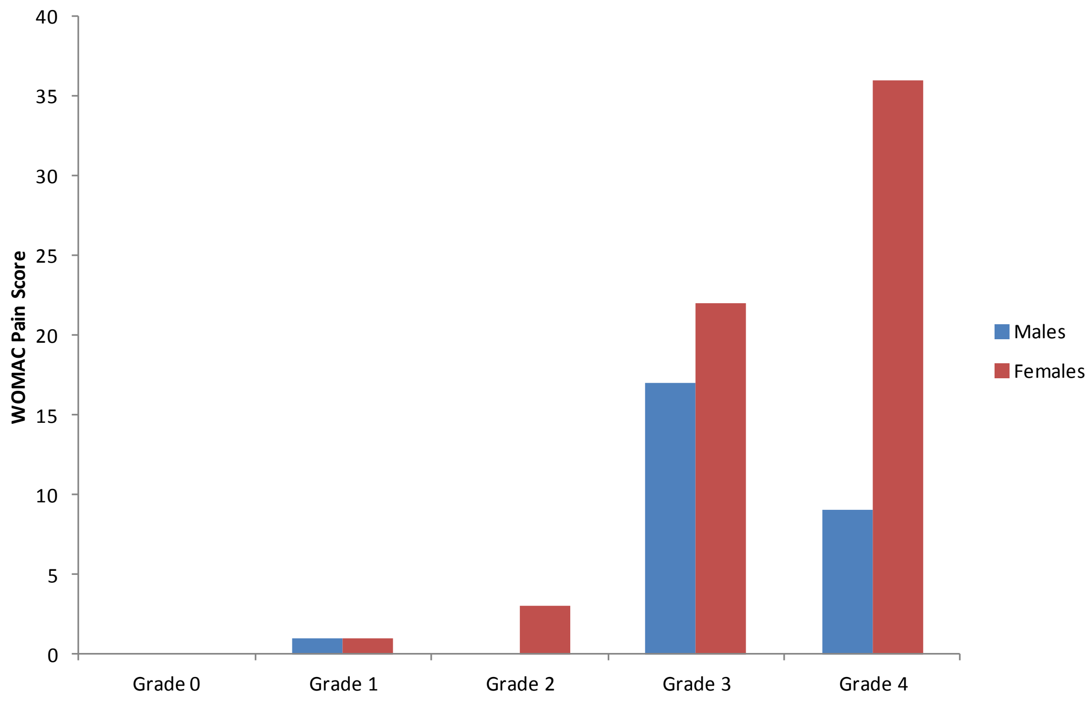

Figure 8.2 Median WOMAC pain score for each KL grade, by sex.

Table 8.5 shows the results of a Mann-Whitney test examining associations between sexes at each grading for WOMAC pain score. No significant associations were found between sexes for any grading allowing sex to be ignored in subsequent inter-grading statistical analysis.

Table 8.5 Results of Mann-Whitney test for statistical significance of sex within OA gradings for WOMAC pain score at age 62-63 years.

	P-value
Grade 0	0.500
Grade 1	0.362
Grade 2	0.173
Grade 3	0.209
Grade 4	N/A

A Kruskal-Wallis test for statistical significance returned a value of p = 0.001, indicating a significant association. Table 8.6 shows the results of a Mann-Whitney test performed between successive groups for WOMAC pain score. A significant association was found between grade 2 and grade 3.

Table 8.6 Results of Mann-Whitney test for statistical significance between OA gradings for WOMAC pain score at age 62-63 years.

Groups Tested	**P-Value**
Grade 0 vs Grade 1	0.287
Grade 1 vs Grade 2	0.567
Grade 2 vs Grade 3	0.001
Grade 3 vs Grade 4	0.584

8.2.2 WOMAC stiffness score

Median WOMAC stiffness score for the entire cohort was 0 (IQR 0 – 4). Figure 8.3 shows the median WOMAC stiffness score for each KL grade, by sex.

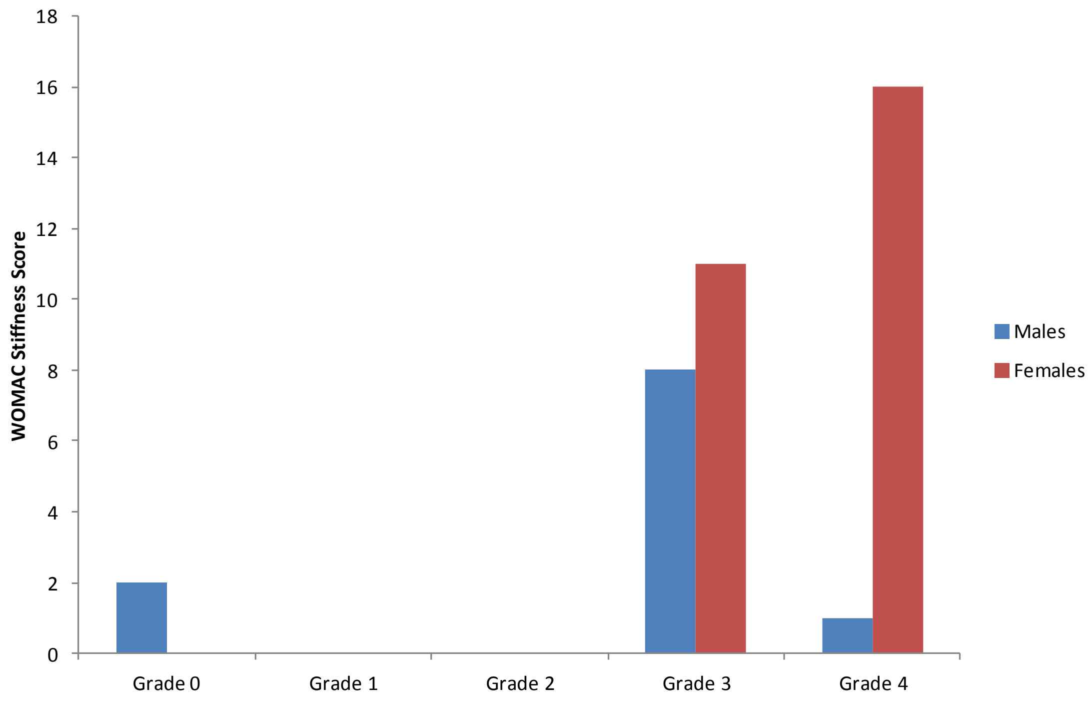

Figure 8.3 Median WOMAC stiffness score for each KL grade, by sex.

Table 8.7 shows the results of a Mann-Whitney test examining associations between sexes at each grading for WOMAC stiffness score. No significant associations were found between sexes for any grading allowing sex to be ignored in subsequent inter-grading statistical analysis.

Table 8.7 Results of Mann-Whitney test for statistical significance of sex within OA gradings for WOMAC stiffness score at age 62-63 years.

	P-value
Grade 0	0.119
Grade 1	0.851
Grade 2	0.217
Grade 3	0.175
Grade 4	N/A

A Kruskal-Wallis test for statistical significance returned a value of $p = 0.001$, indicating a significant association. Table 8.8 shows the results of a Mann-Whitney test performed between successive groups for WOMAC stiffness score. A significant association was found between grade 2 and grade 3.

Table 8.8 Results of Mann-Whitney test for statistical significance between OA gradings for WOMAC stiffness score at age 62-63 years.

Groups Tested	P-Value
Grade 0 vs Grade 1	0.531
Grade 1 vs Grade 2	0.457
Grade 2 vs Grade 3	0.004
Grade 3 vs Grade 4	0.300

8.2.3 BMI at age 63 years

Median BMI for the entire cohort was 26.90 kg/m² (IQR 24.46 – 30.01). Figure 8.4 shows the median age 63 BMI for each KL grade, by sex.

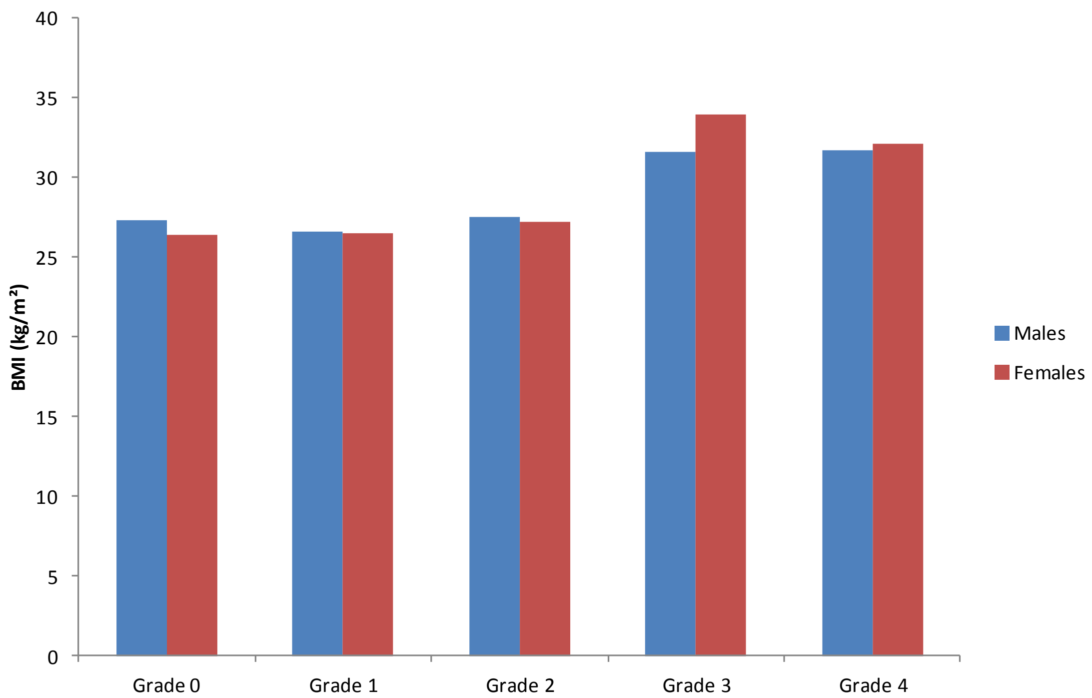

Figure 8.4 Median BMI at age 62-63 years for each KL grade, by sex.

Table 8.9 shows the results of a Mann-Whitney test examining associations between sexes at each grading for BMI. No significant associations were found between sexes for any grading allowing sex to be ignored in subsequent inter-grading statistical analysis.

Table 8.9 Results of Mann-Whitney test for statistical significance of sex within OA gradings for BMI at age 62-63 years.

	P-value
Grade 0	0.293
Grade 1	0.344
Grade 2	0.698
Grade 3	0.314
Grade 4	N/A

A Kruskal-Wallis test for statistical significance returned a value of p = 0.001, indicating a significant association. Table 8.10 shows the results of a Mann-Whitney test performed between successive groups for BMI. Significant associations were found between grade 1 and grade 2, and between grade 2 and grade 3.

Table 8.10 Results of Mann-Whitney test for statistical significance between OA gradings for BMI at age 62-63 years.

Groups Tested	**P-Value**
Grade 0 vs Grade 1	0.913
Grade 1 vs Grade 2	0.038
Grade 2 vs Grade 3	0.013
Grade 3 vs Grade 4	0.876

8.3 Spatiotemporal gait variables

For each of the gait analysis variables it was decided to treat knees individually, therefore the sample size increased to 422 knees. The only exception to this was for cadence where the data reported were for an individual and not for each knee individually.

8.3.1 Cadence

Median cadence for the entire cohort was 109 strides/min (IQR 100 – 114). Figure 8.5 shows the median cadence for each KL grade, by sex.

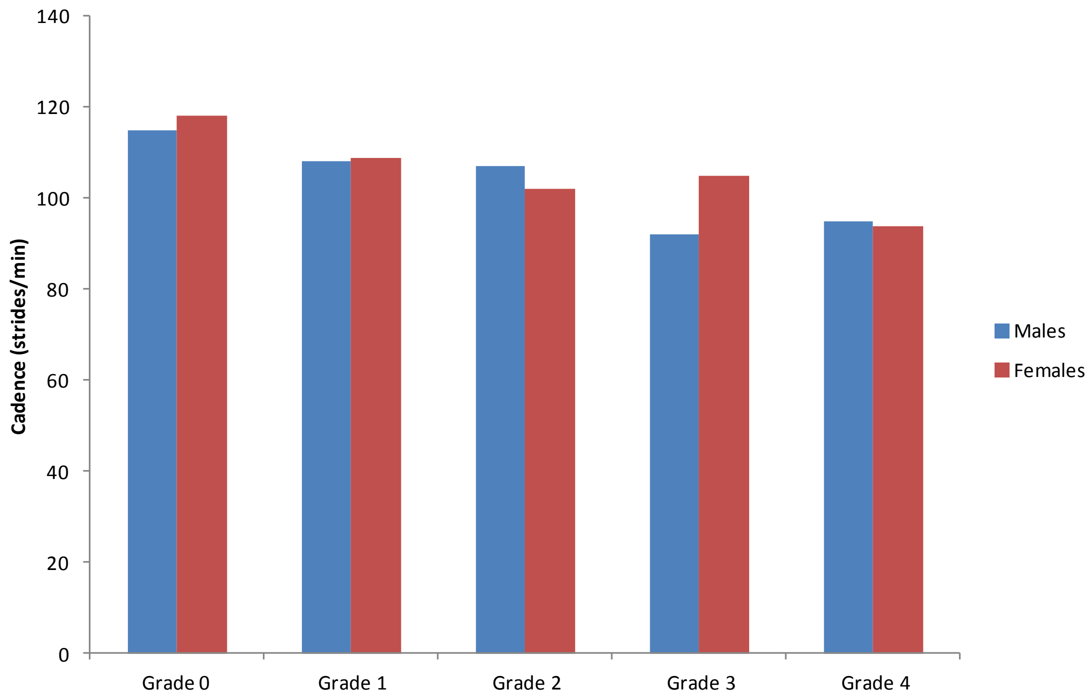

Figure 8.5 Median cadence for each KL grade, by sex.

Table 8.11 shows the results of a Mann-Whitney test examining associations between sexes at each grading for cadence. No significant associations were found between sexes for any grading allowing sex to be ignored in subsequent inter-grading statistical analysis.

Table 8.11 Results of Mann-Whitney test for statistical significance of sex within OA gradings for cadence at age 62-63 years.

	P-value
Grade 0	1.000
Grade 1	0.302
Grade 2	0.919
Grade 3	0.270
Grade 4	1.000

A Kruskal-Wallis test for statistical significance was used to examine associations between OA gradings and returned a value of p = 0.001, indicating a significant association. Table 8.12 shows the results of a Mann-Whitney test performed between successive OA gradings for cadence. A significant association was found between grade 0 and grade 1 only, although grade 2 and grade 3 were close to being significantly different.

Table 8.12 Results of Mann-Whitney test for statistical significance between OA gradings for cadence at age 62-63 years.

Groups Tested	P-Value
Grade 0 vs Grade 1	0.017
Grade 1 vs Grade 2	0.503
Grade 2 vs Grade 3	0.075
Grade 3 vs Grade 4	0.286

Performing a stepwise regression analysis and including WOMAC pain score, WOMAC stiffness score and BMI did not change the statistical significance, with a value of F < 0.001 and all variables were included in the model. The R^2 value for cadence against KL grade was 0.092, and when WOMAC pain score and BMI were included in the model, the overall R^2 rose to 0.194. Regression coefficients from the final model are shown in Table 8.13. KL grade, WOMAC pain score and BMI were significantly negatively associated with cadence, whilst WOMAC stiffness score was significantly positively associated with cadence.

Table 8.13 Final regression model for cadence against KL grade and confounding factors.

Variable	Regression Coefficient (95% CI)	P-value
KL grade 0	Reference	N/A
KL grade 1	-5.71 (-9.54, -1.88)	0.001
KL grade 2	-7.31 (-11.57, -3.07)	0.001
KL grade 3	-15.20 (-22.36, -8.03)	0.001
KL grade 4	-15.01 (-24.34, -5.69)	0.001
WOMAC pain score	-0.63 (-0.87, -0.39)	0.001
WOMAC stiffness score	1.13 (0.60, 1.66)	0.001
BMI (kg/m^2)	-0.26 (-0.52, -0.01)	0.001

8.3.2 Single support phase length

Median single support phase length for the entire cohort was 29% (IQR 28 – 31). Figure 8.6 shows the median single support phase length for each KL grade, by sex.

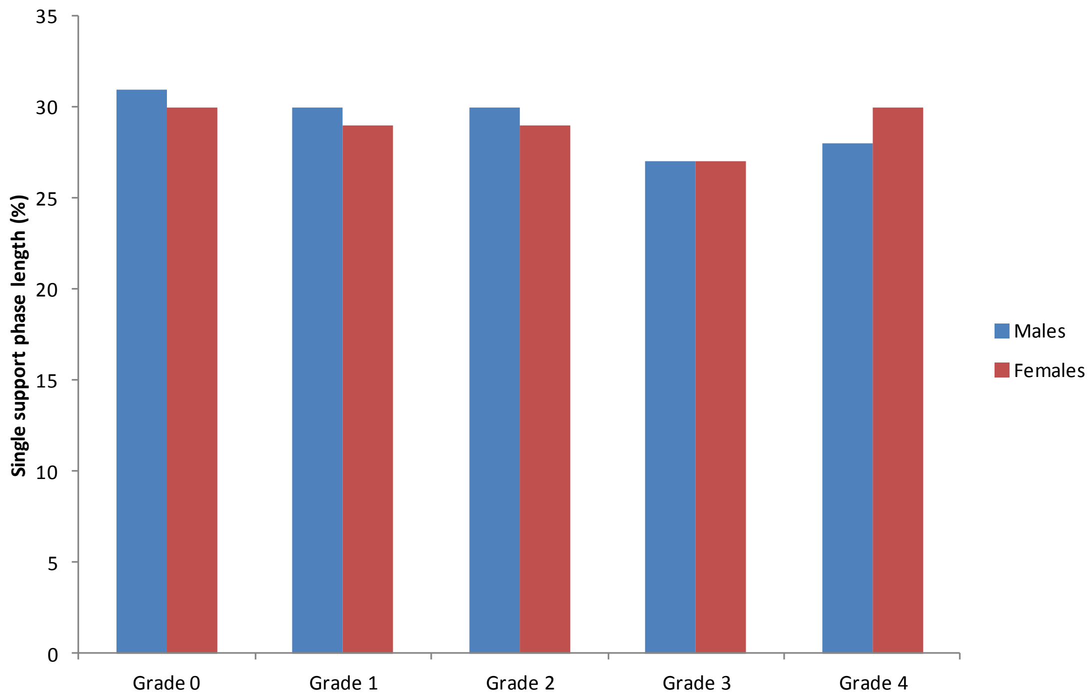

Figure 8.6 Median single support phase length for each KL grade, by sex.

Table 8.14 shows the results of a Mann-Whitney test examining associations between sexes at each grading for single support phase length. Significant associations were found between sexes for grade 1 and grade 2, therefore in subsequent inter-grading statistical testing sexes were treated individually.

Table 8.14 Results of Mann-Whitney test for statistical significance of sex within OA gradings for single support phase length at age 62-63 years.

	P-value
Grade 0	0.691
Grade 1	0.005
Grade 2	0.005
Grade 3	0.957
Grade 4	N/A

A Kruskal-Wallis test for statistical significance returned a value of $p = 0.015$ for men and a value of $p = 0.01$ for women, indicating a significant association for males and females. Table 8.15 shows the results of a Mann-Whitney test performed between successive male OA gradings for single support phase length. A significant association was found between grade 2 and grade 3. Table 8.16 shows the results of a Mann-Whitney test performed between successive female OA gradings for single support phase length. A significant association was found between grade 0 and grade 1.

Table 8.15 Results of Mann-Whitney test for statistical significance between male OA gradings for single support phase length at age 62-63 years.

Groups Tested	**P-Value**
Grade 0 vs Grade 1	0.167
Grade 1 vs Grade 2	0.508
Grade 2 vs Grade 3	0.054
Grade 3 vs Grade 4	1.000

Table 8.16 Results of Mann-Whitney test for statistical significance between female OA gradings for single support phase length at age 62-63 years.

Groups Tested	**P-Value**
Grade 0 vs Grade 1	0.026
Grade 1 vs Grade 2	0.205
Grade 2 vs Grade 3	0.134
Grade 3 vs Grade 4	N/A

Performing a stepwise regression analysis for males and including WOMAC pain score, WOMAC stiffness score, BMI and cadence led to the removal of KL grade, WOMAC pain score and WOMAC stiffness score from the model, with the a value of $F<0.001$. The R^2 value for single support phase length against KL grade was 0.112, and when BMI and cadence were included and OA grading excluded, the overall R^2 rose to 0.413. Regression coefficients from the final model are shown in Table 8.17. BMI was significantly negatively associated with single support phase length, whilst cadence was significantly positively associated with single support phase.

Table 8.17 Final regression model for male single support phase length against KL grade and confounding factors.

Variable	Regression Coefficient (95% CI)	P-value
KL grade 0	Reference	N/A
BMI (kg/m²)	-0.14 (-0.20, -0.70)	0.001
Cadence (strides/min)	0.12 (0.09, 0.15)	0.001

Performing a stepwise regression analysis for females and including WOMAC pain score, WOMAC stiffness score, BMI and cadence led to the removal of WOMAC pain score and WOMAC stiffness score from the model, with the a value of $F < 0.001$ for the final model. The R^2 value for single support phase length against KL grade was 0.057, and when BMI and cadence were included, the overall R^2 value rose to 0.545. Regression coefficients from the final model are shown in Table 8.18. KL grade and BMI were significantly negatively associated with single support phase length, with the exception of KL grade 4 which was significantly positively associated with single support phase length along with cadence.

Table 8.18 Final regression model for female single support phase length against KL grade and confounding factors.

Variable	Regression Coefficient (95% CI)	P-value
KL grade 0	Reference	N/A
KL grade 1	-0.18 (-0.87, 0.52)	0.045
KL grade 2	-0.77 (-1.62, -0.7)	0.045
KL grade 3	-1.15 (-2.84, 0.54)	0.045
KL grade 4	2.30 (-0.89, 5.49)	0.045
BMI (kg/m²)	-0.09 (-0.14, -0.04)	0.001
Cadence (strides/min)	0.13 (0.11, 0.15)	0.001

8.3.3 Initial double support phase length

Median initial double support phase length for the entire cohort was 21% (IQR 19 – 22). Figure 8.7 shows the median initial double support phase length for each KL grade, by sex.

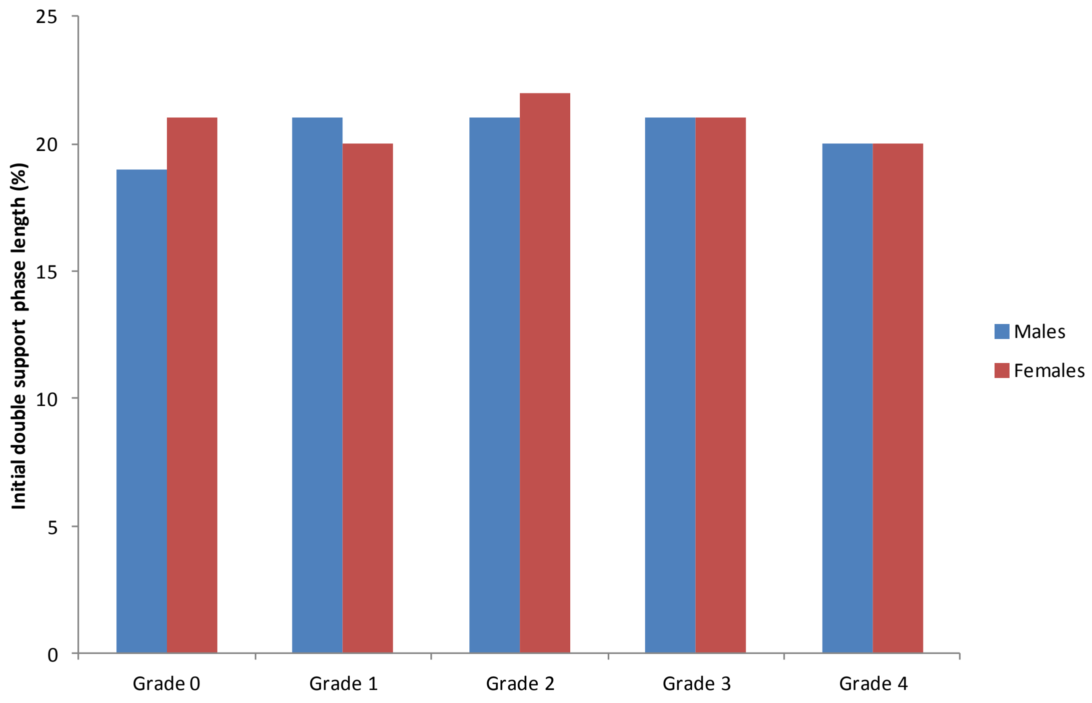

Figure 8.7 Median initial double support phase length for each KL grade, by sex.

Table 8.19 shows the results of a Mann-Whitney test examining associations between sexes at each grading for initial double support phase length. Significant associations were found between sexes for grade 0 and grade 2, therefore, in subsequent inter-grading statistical testing, sexes were treated individually.

Table 8.19 Results of Mann-Whitney test for statistical significance of sex within OA gradings for initial double support phase length at age 62-63 years.

	P-value
Grade 0	0.041
Grade 1	0.610
Grade 2	0.002
Grade 3	0.957
Grade 4	N/A

A Kruskal-Wallis test for statistical significance returned a value of $p = 0.096$ for men and a value of $p = 0.003$ for women, indicating a significant association for females but not for males. Table 8.20 shows the results of a Mann-Whitney test performed between successive female OA gradings for single support phase length. A significant association was found between grade 1 and grade 2.

Table 8.20 Results of a Mann-Whitney test for statistical significance between female OA gradings for initial double support phase length at age 62-63 years.

Groups Tested	P-Value
Grade 0 vs Grade 1	0.200
Grade 1 vs Grade 2	0.001
Grade 2 vs Grade 3	0.989
Grade 3 vs Grade 4	N/A

Performing a stepwise regression analysis for females and including WOMAC pain score, WOMAC stiffness score, BMI and cadence led to the removal of KL grade, WOMAC pain score and WOMAC stiffness score from the model, with the a value of F<0.001. The R^2 value for initial double support phase length against KL grade was 0.001, and when BMI and cadence were included and OA grading excluded, the overall R^2 value rose to 0.488. Regression coefficients from the final model are shown in Table 8.21. BMI was significantly positively associated with initial double support phase length and cadence was significantly negatively associated with initial double support phase length.

Table 8.21 Final regression model for female initial double support phase length against KL grade and confounding factors.

Variable	Regression Coefficient (95% CI)	P-value
KL grade 0	Reference	N/A
BMI (kg/m²)	0.08 (0.03, 0.14)	0.001
Cadence (strides/min)	-0.12 (-0.15, -0.10)	0.001

8.3.4 Knee sagittal plane peak flexion timing during stance phase

Median knee sagittal plane peak flexion timing during stance phase for the entire cohort was 18% (IQR 17 – 20). Figure 8.8 shows the median knee sagittal plane peak flexion timing during stance phase for each KL grade, by sex.

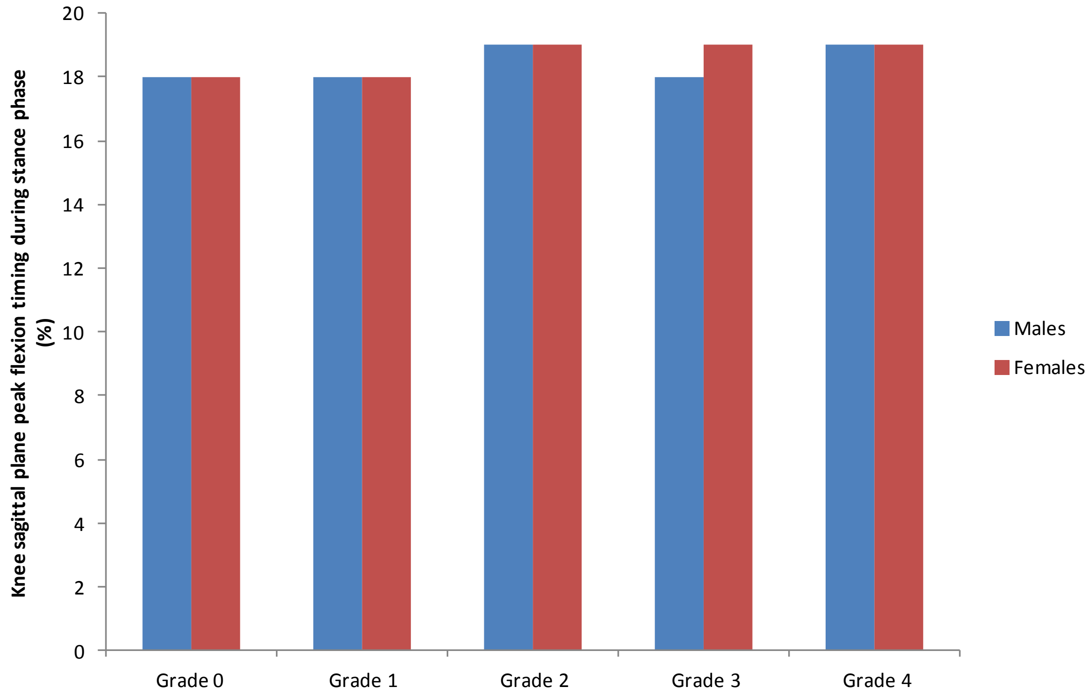

Figure 8.8 Median knee sagittal plane peak flexion timing during stance phase for each KL grade, by sex.

Table 8.22 shows the results of a Mann-Whitney test examining associations between sexes at each grading for knee sagittal plane peak flexion timing during stance phase. No significant associations were found between sexes for any grading allowing sex to be ignored in subsequent inter-grading statistical analysis.

Table 8.22 Results of Mann-Whitney test for statistical significance of sex within OA gradings for knee sagittal plane peak flexion timing during stance phase at age 62-63 years.

	P-value
Grade 0	0.871
Grade 1	0.300
Grade 2	0.908
Grade 3	0.704
Grade 4	N/A

A Kruskal-Wallis test for statistical significance returned a value of p = 0.124, indicating no significant association.

8.4 Kinematic variables

8.4.5 Knee sagittal plane range of motion

Median knee sagittal plane range of motion for the entire cohort was 61.2 degrees (IQR 56.1 – 65.9). Figure 8.9 shows the median knee sagittal plane range of motion for each KL grade, by sex.

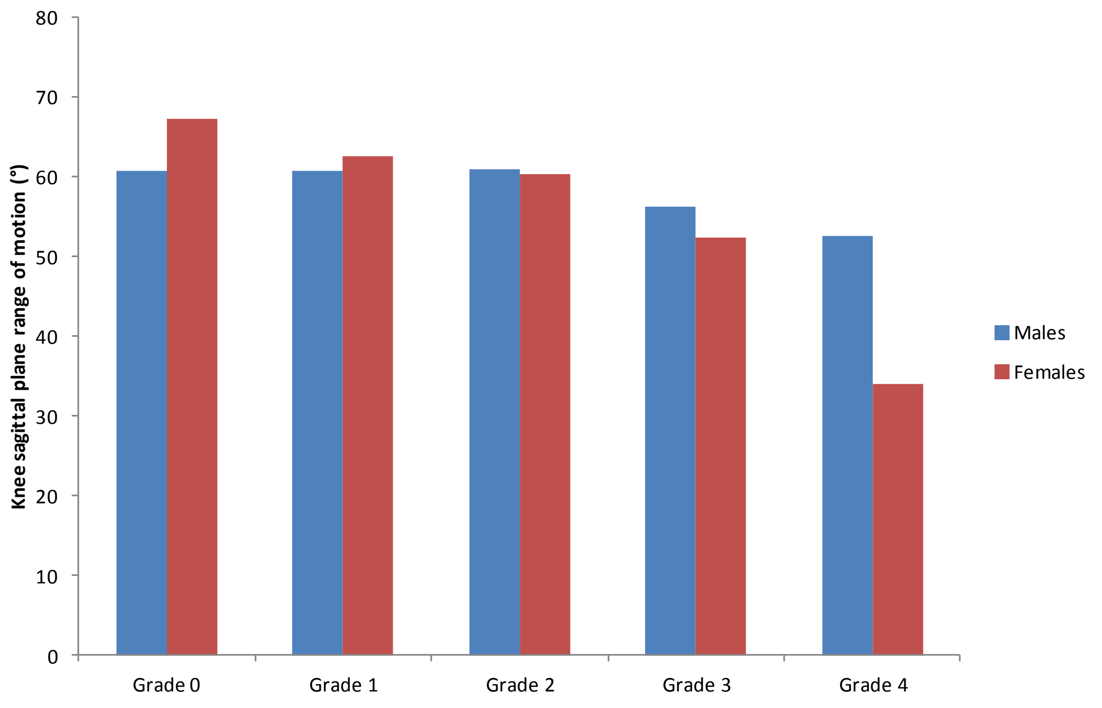

Figure 8.9 Median knee sagittal plane range of motion for each KL grade, by sex.

Table 8.23 shows the results of a Mann-Whitney test examining associations between sexes at each grading for knee sagittal plane range of motion. A significant association was found between sexes for grade 0 only, therefore in subsequent inter-grading analysis statistical testing sexes were treated individually.

Table 8.23 Results of Mann-Whitney test for statistical significance of sex within OA gradings for knee sagittal plane range of motion at age 62-63 years.

	P-value
Grade 0	0.006
Grade 1	0.180
Grade 2	0.899
Grade 3	0.551
Grade 4	N/A

A Kruskal-Wallis test for statistical significance returned a value of p = 0.009 for males and 0.001 for females, indicating a significant association for both sexes. Table 8.24 shows the results of a Mann-Whitney test performed between successive male OA groups for knee sagittal plane range of motion. A significant association was only found between grade 2 and grade 3. Table 8.25 shows the results of a Mann-Whitney test performed between successive female OA groups for knee sagittal plane range of motion. Significant associations were found between all gradings.

Table 8.24 Results of Mann-Whitney test for statistical significance between male OA gradings for knee sagittal plane range of motion at age 62-63 years.

Groups Tested	**P-Value**
Grade 0 vs Grade 1	0.685
Grade 1 vs Grade 2	0.145
Grade 2 vs Grade 3	0.039
Grade 3 vs Grade 4	0.854

Table 8.25 Results of a Mann-Whitney test for statistical significance between female OA gradings for knee sagittal plane range of motion at age 62-63 years.

Groups Tested	**P-Value**
Grade 0 vs Grade 1	0.002
Grade 1 vs Grade 2	0.005
Grade 2 vs Grade 3	0.042
Grade 3 vs Grade 4	N/A

Performing a stepwise regression analysis for males and including WOMAC pain score, WOMAC stiffness score, BMI and cadence led to the removal of KL grade, WOMAC pain score, WOMAC stiffness score and BMI with a value of F < 0.001. The R^2 value for knee sagittal plane range of motion against KL grade was 0.131, and when cadence was included and KL grade excluded, the overall R^2 value rose to 0.286. Regression coefficients from the final model are shown in Table 8.26. Cadence was significantly positively associated with knee sagittal plane range of motion.

Table 8.26 Final regression model for male knee sagittal plane range of motion against KL grade and confounding factors.

Variable	Regression Coefficient (95% CI)	P-value
Cadence (strides/min)	0.36 (0.23, 0.50)	0.001

Performing a stepwise regression analysis for females and including WOMAC pain score, WOMAC stiffness score, BMI and cadence led to the removal of WOMAC stiffness score and cadence, with a value of F < 0.001. The R^2 value for knee sagittal plane range of motion against KL grade was 0.226, and when WOMAC pain score and BMI were included, the overall R^2 value rose to 0.328. Regression coefficients from the final model are shown in Table 8.27. KL grade, WOMAC pain score and BMI were significantly negatively associated with knee sagittal plane range of motion.

Table 8.27 Final regression model for female knee sagittal plane range of motion against KL grade and confounding factors.

Variable	Regression Coefficient (95% CI)	P-value
KL grade 0	Reference	N/A
KL grade 1	-3.81 (-6.46, -1.15)	0.001
KL grade 2	-7.20 (-10.47, -3.93)	0.001
KL grade 3	-6.67 (-13.43, 0.08)	0.001
KL grade 4	-25.44 (-38.02, -12.85)	0.001
WOMAC pain score	-0.16 (-0.27, -0.06)	0.003
BMI (kg/m²)	-0.27 (-0.47, -0.07)	0.008

8.4.6 Knee sagittal plane range of motion during stance phase

Median knee sagittal plane range of motion during stance phase for the entire cohort was 51.4 degrees (IQR 47.1 – 55.4). Figure 8.10 shows the median knee sagittal plane range of motion during stance phase for each KL grade, by sex.

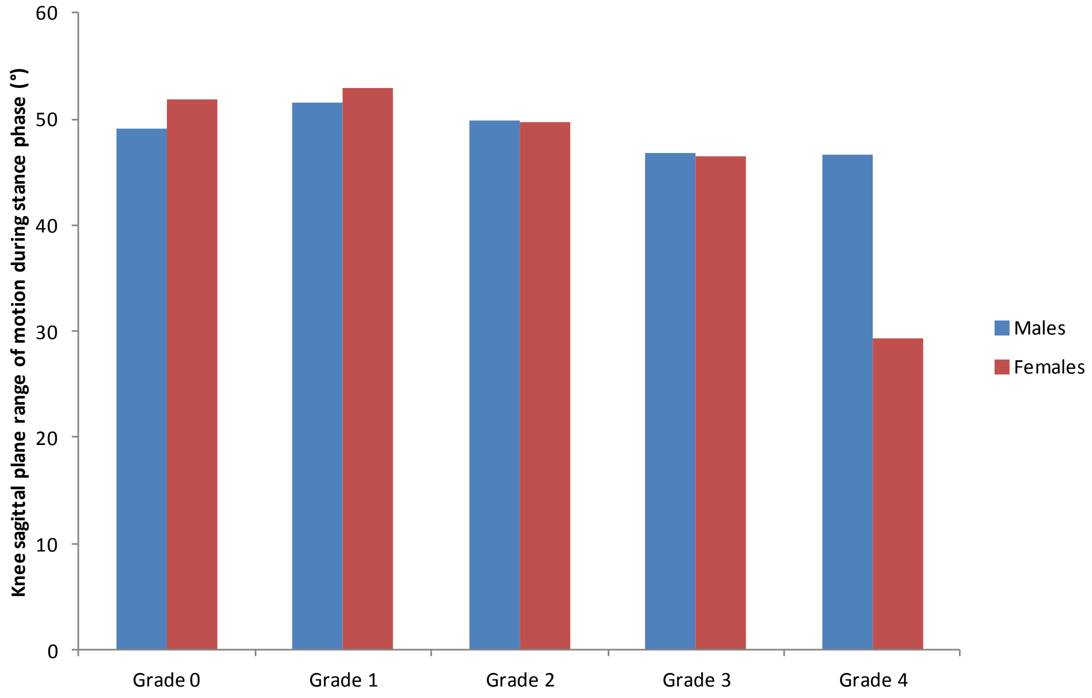

Figure 8.10 Median knee sagittal plane range of motion during stance phase for each KL grade, by sex.

Table 8.28 shows the results of a Mann-Whitney test examining associations between sexes at each grading for knee sagittal plane range of motion during stance phase. Significant associations were found between sexes for grade 1, therefore in subsequent inter-grading statistical testing sexes were treated individually.

Table 8.28 Results of Mann-Whitney test for statistical significance of sex within OA gradings for knee sagittal plane range of motion during stance phase at age 62-63 years.

	P-value
Grade 0	0.171
Grade 1	0.030
Grade 2	0.714
Grade 3	0.871
Grade 4	N/A

A Kruskal-Wallis test for statistical significance returned a value of $p = 0.129$ for males and $p = 0.006$ for females, indicating a significant association for females but not for males. Table 8.29 shows the results of a Mann-Whitney test performed between successive female OA groups for knee sagittal plane range of motion during stance phase. A significant association was found between grade 1 and grade 2.

Table 8.29 Results of Mann-Whitney test for statistical significance between female OA gradings for knee sagittal plane range of motion during stance phase at age 62-63 years.

Groups Tested	**P-Value**
Grade 0 vs Grade 1	0.552
Grade 1 vs Grade 2	0.013
Grade 2 vs Grade 3	0.068
Grade 3 vs Grade 4	N/A

Performing a stepwise regression analysis for females and including WOMAC pain score, WOMAC stiffness score, BMI and cadence led to the removal of WOMAC pain score, WOMAC stiffness score, BMI and cadence, with a value of $F < 0.001$. The R^2 value for knee sagittal plane range of motion during stance phase against KL grade was 0.149. Regression coefficients for the final model are shown in Table 8.30. KL grades 1 was significantly positively associated with knee sagittal plane range of motion during stance phase and KL grade 2, 3 and 4 were significantly negatively associated with knee sagittal plane range of motion during stance phase.

Table 8.30 Final regression model for female knee sagittal plane range of motion during stance phase against KL grade and confounding factors.

Variable	Regression Coefficient (95% CI)	P-value
KL grade 0	Reference	N/A
KL grade 1	0.72 (-1.70, 3.15)	0.004
KL grade 2	-2.88 (-5.82, 0.06)	0.004
KL grade 3	-4.14 (-10.03, 1.75)	0.004
KL grade 4	-22.71 (-33.87, -11.55)	0.004

8.4.7 Knee sagittal plane range of motion during loading phase

Median knee sagittal plane range of motion during loading phase for the entire cohort was 16.9 degrees (IQR 13.4 – 19.9). Figure 8.11 shows the median knee sagittal plane range of motion during loading phase for each KL grade, by sex.

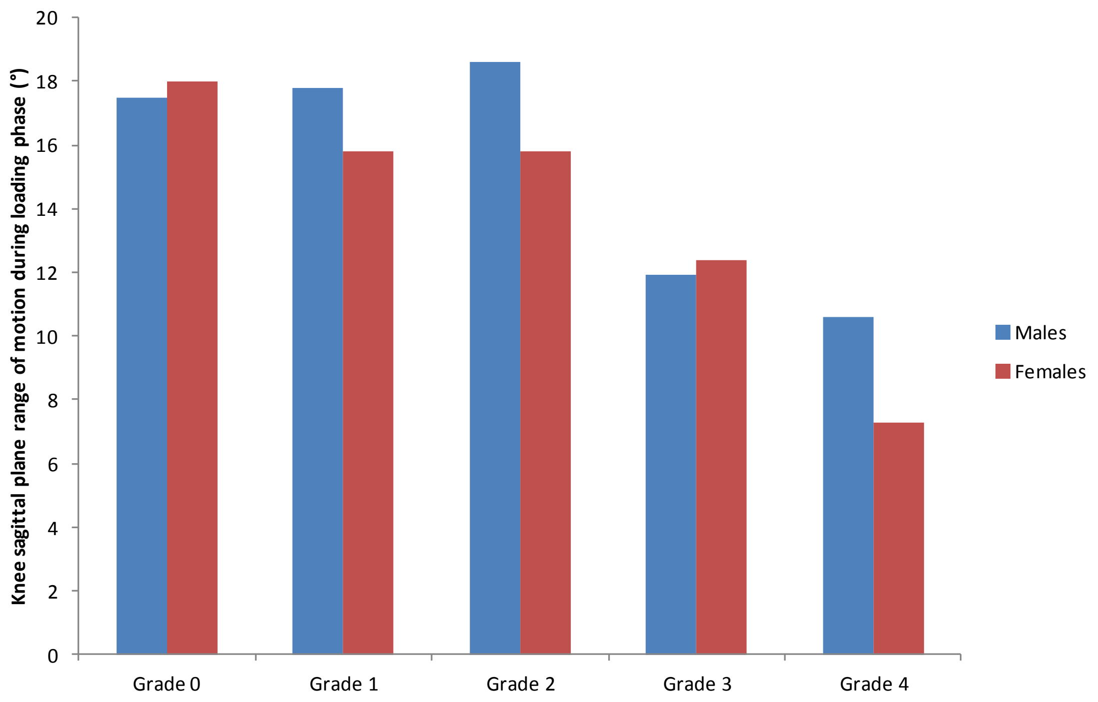

Figure 8.11 Median knee sagittal plane range of motion during loading phase for each KL grade, by sex.

Table 8.31 shows the results of a Mann-Whitney test examining associations between sexes at each grading for knee sagittal plane range of motion during loading phase. Significant associations were found between sexes for grade 1 and grade 3, therefore in subsequent inter-grading statistical testing sexes were treated individually.

Table 8.31 Results of Mann-Whitney test for statistical significance of sex within OA gradings for knee sagittal plane range of motion during loading phase at age 62-63 years.

	P-value
Grade 0	0.418
Grade 1	0.003
Grade 2	0.004
Grade 3	0.704
Grade 4	N/A

A Kruskal-Wallis test for statistical significance returned a value of $p = 0.006$ for males and $p = 0.137$ for females, indicating a significant association for males but not for females. Table 8.32 shows the results of a Mann-Whitney test performed between successive female OA groups for knee sagittal plane range of motion during loading phase. A significant association was found between grade 2 and grade 3.

Table 8.32 Results of Mann-Whitney test for statistical significance between male OA gradings for knee sagittal plane range of motion during loading phase at age 62-63 years.

Groups Tested	**P-Value**
Grade 0 vs Grade 1	0.457
Grade 1 vs Grade 2	0.461
Grade 2 vs Grade 3	0.020
Grade 3 vs Grade 4	0.760

Performing a stepwise regression analysis for males and including WOMAC pain score, WOMAC stiffness score, BMI and cadence led to the removal of KL grade, WOMAC pain score, WOMAC stiffness score and BMI, with a value of $F < 0.001$. The R^2 value for knee sagittal plane range of motion during loading phase against KL grade was 0.084, and when cadence was included and KL grade excluded, the overall R^2 value rose to 0.200. Regression coefficients from the final model are shown in Table 8.33.

Cadence was significantly positively associated with knee sagittal plane range of motion during the loading phase.

Table 8.33 Final regression model for male knee sagittal plane range of motion during loading phase against KL grade and confounding factors.

Variable	Regression Coefficient (95% CI)	P-value
Cadence (strides/min)	0.33 (0.20, 0.44)	0.001

8.4.8 Knee sagittal plane range of motion during impact phase

Median knee sagittal plane range of motion during loading phase for the entire cohort was 5.7 degrees (IQR 3.3 – 8.2). Figure 8.12 shows the median knee sagittal plane range of motion during impact phase for each KL grade, by sex.

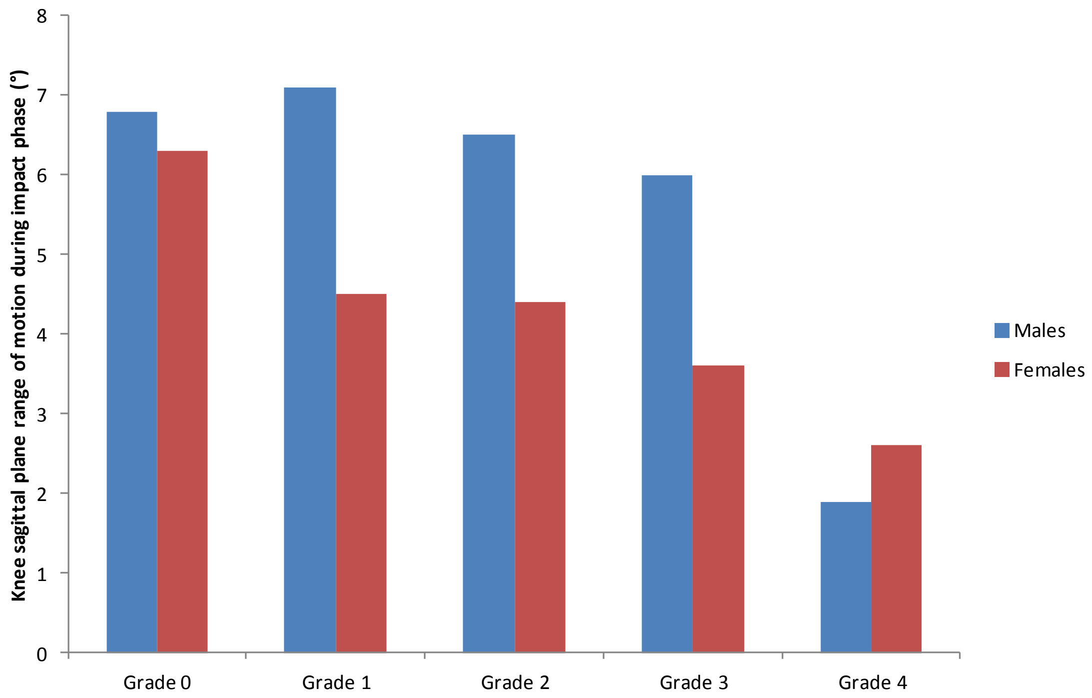

Figure 8.12 Median knee sagittal plane range of motion during impact phase for each KL grade, by sex.

Table 8.34 shows the results of a Mann-Whitney test examining associations between sexes at each grading for knee sagittal plane range of motion during impact phase. Significant associations were found between sexes for grade 1 and grade 3, therefore in subsequent inter-grading statistical testing sexes were treated individually.

Table 8.34 Results of Mann-Whitney test for statistical significance of sex within OA gradings for knee sagittal plane range of motion during impact phase at age 62-63 years.

	P-value
Grade 0	0.825
Grade 1	0.001
Grade 2	0.001
Grade 3	0.626
Grade 4	N/A

A Kruskal-Wallis test for statistical significance returned a value of $p = 0.019$ for males and $p = 0.012$ for females, indicating a significant association for both males and females. Table 8.35 shows the results of a Mann-Whitney test performed between successive male OA groups for knee sagittal plane range of motion during impact phase. A significant association was found between grade 2 and grade 3. Table 8.36 shows the results of a Mann-Whitney test performed between successive female OA groups for knee sagittal plane range of motion during impact phase. A significant association was found between grade 0 and grade 1.

Table 8.35 Results of Mann-Whitney test for statistical significance between male OA gradings for knee sagittal plane range of motion during impact phase at age 62-63 years.

Groups Tested	**P-Value**
Grade 0 vs Grade 1	0.952
Grade 1 vs Grade 2	0.530
Grade 2 vs Grade 3	0.063
Grade 3 vs Grade 4	0.198

Table 8.36 Results of Mann-Whitney test for statistical significance between female OA gradings for knee sagittal plane range of motion during impact phase at age 62-63 years.

Groups Tested	P-Value
Grade 0 vs Grade 1	0.002
Grade 1 vs Grade 2	0.431
Grade 2 vs Grade 3	0.861
Grade 3 vs Grade 4	N/A

Performing a stepwise regression analysis for males and including WOMAC pain score, WOMAC stiffness score, BMI and cadence led to the removal of KL grade, WOMAC pain score, WOMAC stiffness score and BMI, with a value of $F < 0.001$. The R^2 value for knee sagittal plane range of motion during impact phase against KL grade was 0.093, and when cadence was included and KL grade excluded, the overall R^2 value rose to 0.365. Regression coefficients from the final model are shown in Table 8.37. Cadence was significantly positively associated with knee sagittal plane range of motion during the impact phase.

Table 8.37 Final regression model for male knee sagittal plane range of motion during impact phase against KL grade and confounding factors.

Variable	Regression Coefficient (95% CI)	P-value
Cadence (strides/min)	0.24 (0.18, 0.30)	0.001

Performing a stepwise regression analysis for females and including WOMAC pain score, WOMAC stiffness score, BMI and cadence led to the removal of KL grade and BMI, with a value of $F < 0.001$. The R^2 value for knee sagittal plane range of motion during impact phase against KL grade was 0.001, and when WOMAC pain score, WOMAC stiffness score and cadence were included and KL grade excluded, the overall R^2 value rose to 0.331. Regression coefficients from the final model are shown in Table 8.38. WOMAC stiffness score and cadence were significantly positively associated with knee sagittal plane range of motion during impact phase and WOMAC pain score was significantly negatively associated with knee sagittal plane range of motion during impact phase.

Table 8.38 Final regression model for female knee sagittal plane range of motion during impact phase against KL grade and confounding factors.

Variable	Regression Coefficient (95% CI)	P-value
WOMAC pain score	-0.09 (-0.18, -0.01)	0.026
WOMAC stiffness score	0.21 (0.04, 0.39)	0.015
Cadence (strides/min)	0.14 (0.11, 0.18)	0.001

8.4.9 Knee sagittal plane peak flexion angle

Median knee sagittal plane peak flexion angle for the entire cohort was 61.5 degrees (IQR 56.8 – 66.3). Figure 8.13 shows the median knee sagittal plane peak flexion angle for each KL grade, by sex.

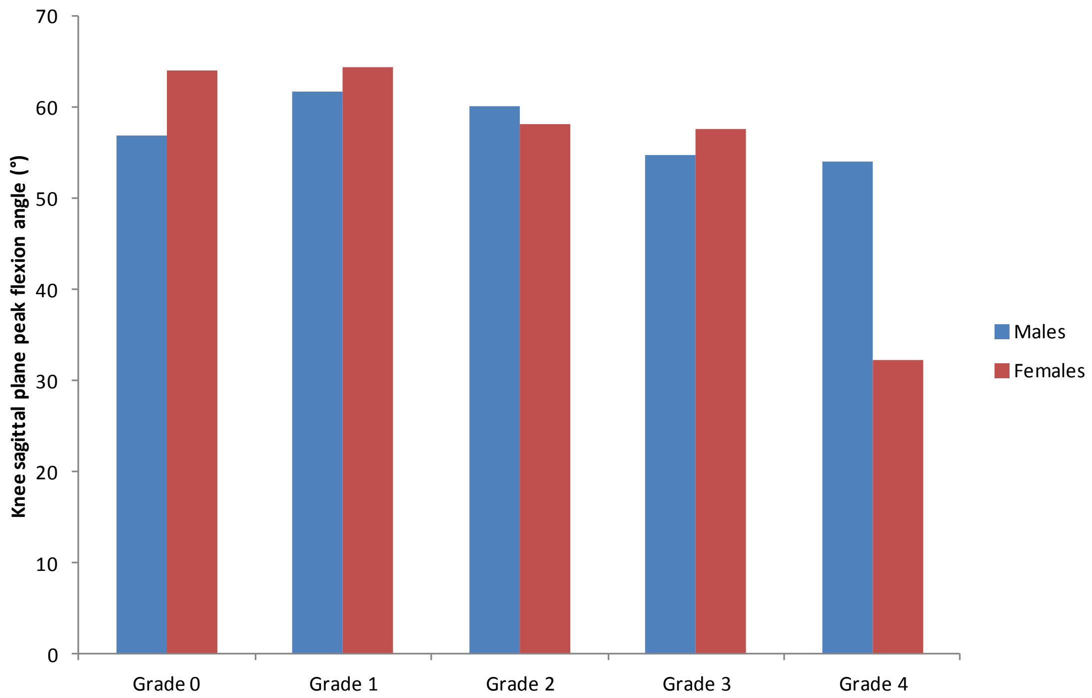

Figure 8.13 Median knee sagittal plane peak flexion angle for each KL grade, by sex.

Table 8.39 shows the results of a Mann-Whitney test examining associations between sexes at each grading for knee sagittal plane peak flexion angle. Significant associations were found between sexes for grade 0 and grade 1, therefore in subsequent inter-grading statistical testing sexes were treated individually.

Table 8.39 Results of Mann-Whitney test for statistical significance of sex within OA gradings for knee sagittal plane peak flexion angle at age 62-63 years.

	P-value
Grade 0	0.001
Grade 1	0.002
Grade 2	0.637
Grade 3	0.416
Grade 4	N/A

A Kruskal-Wallis test for statistical significance returned a value of p = 0.001 for males and p = 0.001 for females, indicating a significant association for both males and females. Table 8.40 shows the results of a Mann-Whitney test performed between successive male OA groups for knee sagittal plane peak flexion angle. Significant associations were found between grade 0 and grade 1, grade 1 and grade 2, and grade 2 and grade 3. Table 8.41 shows the results of a Mann-Whitney test performed between successive female OA groups for knee sagittal plane peak flexion angle. A significant association was found between grade 1 and grade 2.

Table 8.40 Results of Mann-Whitney test for statistical significance between male OA gradings for knee sagittal plane peak flexion angle at age 62-63 years.

Groups Tested	**P-Value**
Grade 0 vs Grade 1	0.014
Grade 1 vs Grade 2	0.060
Grade 2 vs Grade 3	0.030
Grade 3 vs Grade 4	0.760

Table 8.41 Results of Mann-Whitney test for statistical significance between female OA gradings for knee sagittal plane peak flexion angle at age 62-63 years.

Groups Tested	**P-Value**
Grade 0 vs Grade 1	0.499
Grade 1 vs Grade 2	0.001
Grade 2 vs Grade 3	0.637
Grade 3 vs Grade 4	N/A

Performing a stepwise regression analysis for males and including WOMAC pain score, WOMAC stiffness score, BMI and cadence led to the removal of KL grade, WOMAC pain score, WOMAC stiffness score and BMI, with a value of $F < 0.001$. The R^2 value for knee sagittal plane peak flexion angle against KL grade was 0.104, and when cadence was included and KL grade excluded, the overall R^2 value rose to 0.120. Regression coefficients from the final model are shown in Table 8.42. Cadence was significantly positively associated with knee sagittal plane peak flexion angle.

Table 8.42 Final regression model for male knee sagittal plane peak flexion angle against KL grade and confounding factors.

Variable	Regression Coefficient (95% CI)	P-value
Cadence (strides/min)	0.33 (0.17, 0.49)	0.001

Performing a stepwise regression analysis for females and including WOMAC pain score, WOMAC stiffness score, BMI and cadence led to the removal of WOMAC pain score and WOMAC stiffness score, with a value of $F < 0.001$. The R^2 value for knee sagittal plane peak flexion angle against KL grade was 0.247, and when cadence was included, the overall R^2 value rose to 0.317. Regression coefficients from the final model are shown in Table 8.43. KL grade and BMI were significantly negatively associated with knee sagittal plane peak flexion angle and cadence was significantly positively associated with knee sagittal plane peak flexion angle.

Table 8.43 Final regression model for female knee sagittal plane peak flexion angle against KL grade and confounding factors.

Variable	Regression Coefficient (95% CI)	P-value
KL grade 0	Reference	N/A
KL grade 1	-0.06 (-3.08, 2.96)	0.001
KL grade 2	-7.42 (-11.10, -3.75)	0.001
KL grade 3	-6.45 (-13.80, 0.88)	0.001
KL grade 4	-29.56 (-43.43, -15.69)	0.001
BMI (kg/m²)	-0.33 (-0.55, -0.11)	0.003
Cadence (strides/min)	0.10 (0.01, 0.20)	0.049

8.4.10 Knee sagittal plane mean flexion angle

Median knee sagittal plane mean flexion angle for the entire cohort was 20.9 degrees (IQR 18.2 – 24.0). Figure 8.14 shows the median knee sagittal plane mean flexion angle for each KL grade, by sex.

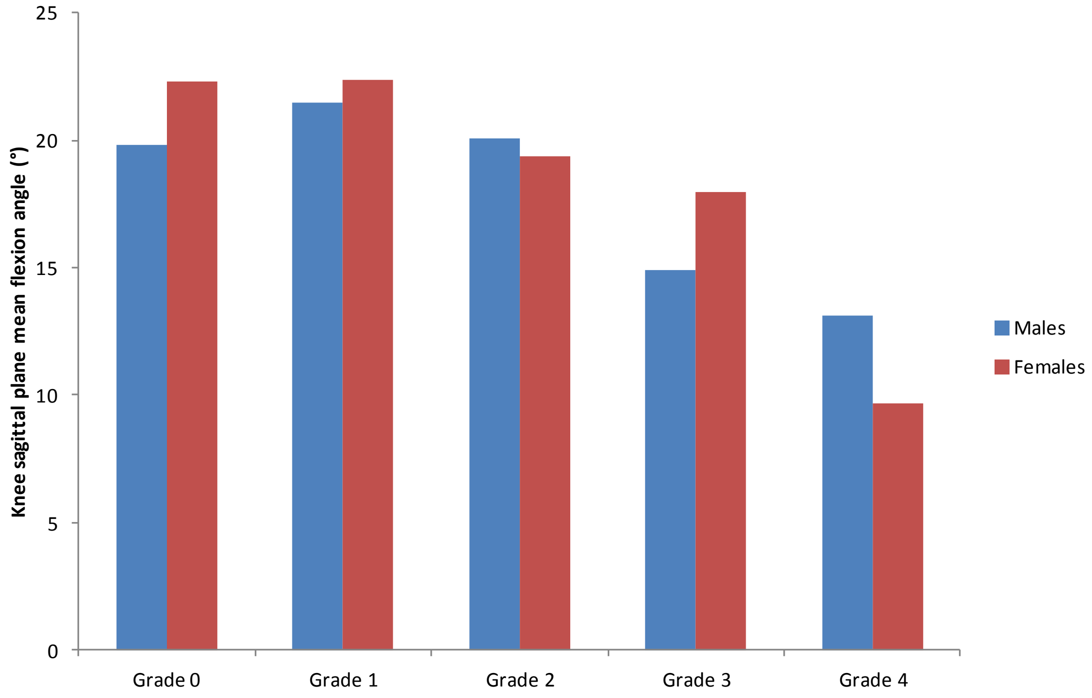

Figure 8.14 Median knee sagittal plane mean flexion angle for each KL grade, by sex.

Table 8.44 shows the results of a Mann-Whitney test examining associations between sexes at each grading for knee sagittal plane mean flexion angle. Significant associations were found between sexes for grade 0, therefore in subsequent inter-grading statistical testing sexes were treated individually.

Table 8.44 Results of Mann-Whitney test for statistical significance of sex within OA gradings for knee sagittal plane mean flexion angle at age 62-63 years.

	P-value
Grade 0	0.024
Grade 1	0.202
Grade 2	0.201
Grade 3	0.626
Grade 4	N/A

A Kruskal-Wallis test for statistical significance returned a value of $p = 0.001$ for males and $p = 0.001$ for females, indicating a significant association for both males and females. Table 8.45 shows the results of a Mann-Whitney test performed between successive male OA groups for knee sagittal plane mean flexion angle. Significant associations were found between grade 1 and grade 2, and grade 2 and grade 3. Table 8.46 shows the results of a Mann-Whitney test performed between successive female OA groups for knee sagittal plane mean flexion angle. Significant associations were found between grade 1 and grade 2.

Table 8.45 Results of Mann-Whitney test for statistical significance between male OA gradings for knee sagittal plane mean flexion angle at age 62-63 years.

Groups Tested	**P-Value**
Grade 0 vs Grade 1	0.054
Grade 1 vs Grade 2	0.028
Grade 2 vs Grade 3	0.013
Grade 3 vs Grade 4	0.581

Table 8.46 Results of Mann-Whitney test for statistical significance between female OA gradings for knee sagittal plane mean flexion angle at age 62-63 years.

Groups Tested	**P-Value**
Grade 0 vs Grade 1	0.758
Grade 1 vs Grade 2	0.001
Grade 2 vs Grade 3	0.219
Grade 3 vs Grade 4	N/A

Performing a stepwise regression analysis for males and including WOMAC pain score, WOMAC stiffness score, BMI and cadence led to the removal of WOMAC pain score, WOMAC stiffness score and BMI, with a value of $F < 0.001$. The R^2 value for knee sagittal plane mean flexion angle against KL grade was 0.159, and when cadence was included, the overall R^2 value rose to 0.233. Regression coefficients from the final model are shown in Table 8.47. KL grades 1, 2 and cadence were significantly positively associated with knee sagittal plane mean flexion angle and KL grades 2 and 3 were significantly negatively associated with knee sagittal plane mean flexion angle.

Table 8.47 Final regression model for male knee sagittal plane mean flexion angle against KL grade and confounding factors.

Variable	**Regression Coefficient (95% CI)**	**P-value**
KL grade 0	Reference	N/A
KL grade 1	2.91 (-1.28, 7.10)	0.033
KL grade 2	2.46 (-1.81, 6.72)	0.033
KL grade 3	-1.63 (-6.87, 3.59)	0.033
KL grade 4	-2.56 (-8.41, 3.29)	0.033
Cadence (strides/min)	0.16 (0.07, 0.26)	0.001

Performing a stepwise regression analysis for females and including WOMAC pain score, WOMAC stiffness score, BMI and cadence led to the removal of WOMAC pain score and WOMAC stiffness score, with a value of $F < 0.001$. The R^2 value for knee sagittal plane mean flexion angle against KL grade was 0.143, and when cadence and BMI were included, the overall R^2 value rose to 0.256. Regression coefficients from the final model are shown in Table 8.48. KL grade 1 and BMI were significantly positively associated with knee sagittal plane mean flexion angle and KL grades 2, 3, 4 and BMI were significantly negatively associated with knee sagittal plane mean flexion angle.

Table 8.48 Final regression model for female knee sagittal plane mean flexion angle against KL grade and confounding factors.

Variable	**Regression Coefficient (95% CI)**	**P-value**
KL grade 0	Reference	N/A
KL grade 1	0.78 (-1.29, 2.86)	0.007
KL grade 2	-3.28 (-5.80, -0.76)	0.007
KL grade 3	-2.15 (-7.18, 2.88)	0.007
KL grade 4	-9.59 (-19.09, -0.08)	0.007
BMI (kg/m²)	-0.26 (-0.41, -0.11)	0.001
Cadence (strides/min)	0.09 (0.03, 0.16)	0.008

8.4.11 Knee sagittal plane mean flexion rate

Median knee sagittal plane mean flexion angle for the entire cohort was 130.2 degrees/s (IQR 112.3 – 145.3). Figure 8.15 shows the median knee sagittal plane mean flexion rate for each KL grade, by sex.

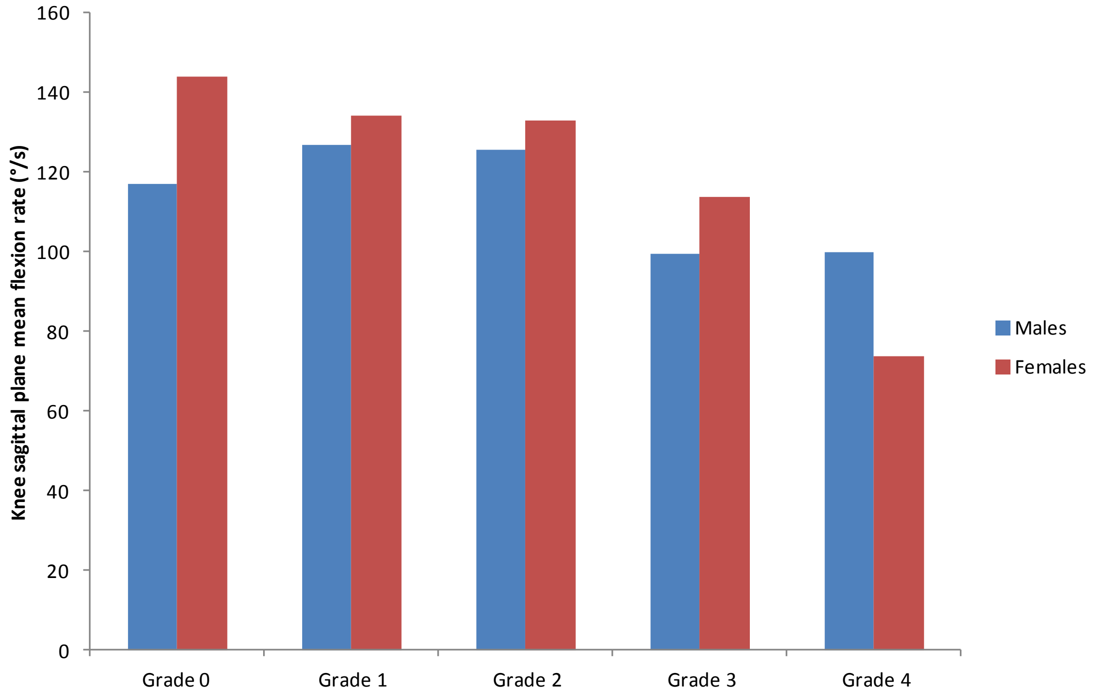

Figure 8.15 Median knee sagittal plane mean flexion rate for each KL grade, by sex.

Table 8.49 shows the results of a Mann-Whitney test examining associations between sexes at each grading for knee sagittal plane mean flexion rate. Significant associations were found between sexes for grade 0 and grade 1, therefore in subsequent inter-grading statistical testing sexes were treated individually.

Table 8.49 Results of Mann-Whitney test for statistical significance of sex within OA gradings for knee sagittal plane mean flexion rate at age 62-63 years.

	P-value
Grade 0	0.001
Grade 1	0.008
Grade 2	0.354
Grade 3	0.416
Grade 4	N/A

A Kruskal-Wallis test for statistical significance returned a value of $p = 0.006$ for males and $p = 0.011$ for females, indicating a significant association for both males and females. Table 8.50 shows the results of a Mann-Whitney test performed between successive male OA groups for knee sagittal plane mean flexion rate. A significant association was found between grade 2 and grade 3. Table 8.51 shows the results of a Mann-Whitney test performed between successive female OA groups for knee sagittal plane mean flexion rate. A significant association was found between grade 0 and grade 1.

Table 8.50 Results of Mann-Whitney test for statistical significance between male OA gradings for knee sagittal plane mean flexion rate at age 62-63 years.

Groups Tested	**P-Value**
Grade 0 vs Grade 1	0.178
Grade 1 vs Grade 2	0.854
Grade 2 vs Grade 3	0.022
Grade 3 vs Grade 4	0.760

Table 8.51 Results of Mann-Whitney test for statistical significance between female OA gradings for knee sagittal plane mean flexion rate at age 62-63 years.

Groups Tested	**P-Value**
Grade 0 vs Grade 1	0.012
Grade 1 vs Grade 2	0.325
Grade 2 vs Grade 3	0.352
Grade 3 vs Grade 4	N/A

Performing a stepwise regression analysis for males and including WOMAC pain score, WOMAC stiffness score, BMI and cadence led to the removal of KL grade, WOMAC pain score, WOMAC stiffness score and BMI, with a value of $F < 0.001$. The R^2 value for knee sagittal plane mean flexion rate against KL grade was 0.096, and when cadence was included and KL grade excluded, the overall R^2 value rose to 0.516. Regression coefficients from the final model are shown in Table 8.52. Cadence was significantly positively associated with knee sagittal plane mean flexion rate.

Table 8.52 Final regression model for male knee sagittal plane mean flexion rate against KL grade and confounding factors.

Variable	Regression Coefficient (95% CI)	P-value
Cadence (strides/min)	2.20 (1.81, 2.58)	0.001

Performing a stepwise regression analysis for females and including WOMAC pain score, WOMAC stiffness score, BMI and cadence led to the removal of WOMAC pain score, WOMAC stiffness score and BMI with a value of F < 0.001. The R^2 value for knee sagittal plane mean flexion rate against KL grade was 0.084, and when cadence was included, the overall R^2 value rose to 0.516. Regression coefficients from the final model are shown in Table 8.53. KL grade was significantly negatively associated with knee sagittal plane mean flexion rate and cadence was significantly positively associated with knee sagittal plane mean flexion rate.

Table 8.53 Final regression model for female knee sagittal plane mean flexion rate against KL grade and confounding factors.

Variable	Regression Coefficient (95% CI)	P-value
KL grade 0	Reference	N/A
KL grade 1	-2.52 (-11.06, 6.01)	0.016
KL grade 2	-11.11 (-21.44, -0.79)	0.016
KL grade 3	-16.57 (-37.25, 4.11)	0.016
KL grade 4	-44.65 (-83.77, -5.53)	0.016
Cadence (strides/min)	1.70 (1.42, 1.98)	0.001

8.4.12 Knee sagittal plane landing angle

Median knee sagittal plane landing angle for the entire cohort was 2.2 degrees (IQR -0.7 – 5.8). Figure 8.16 shows the median knee sagittal plane landing angle for each KL grade, by sex.

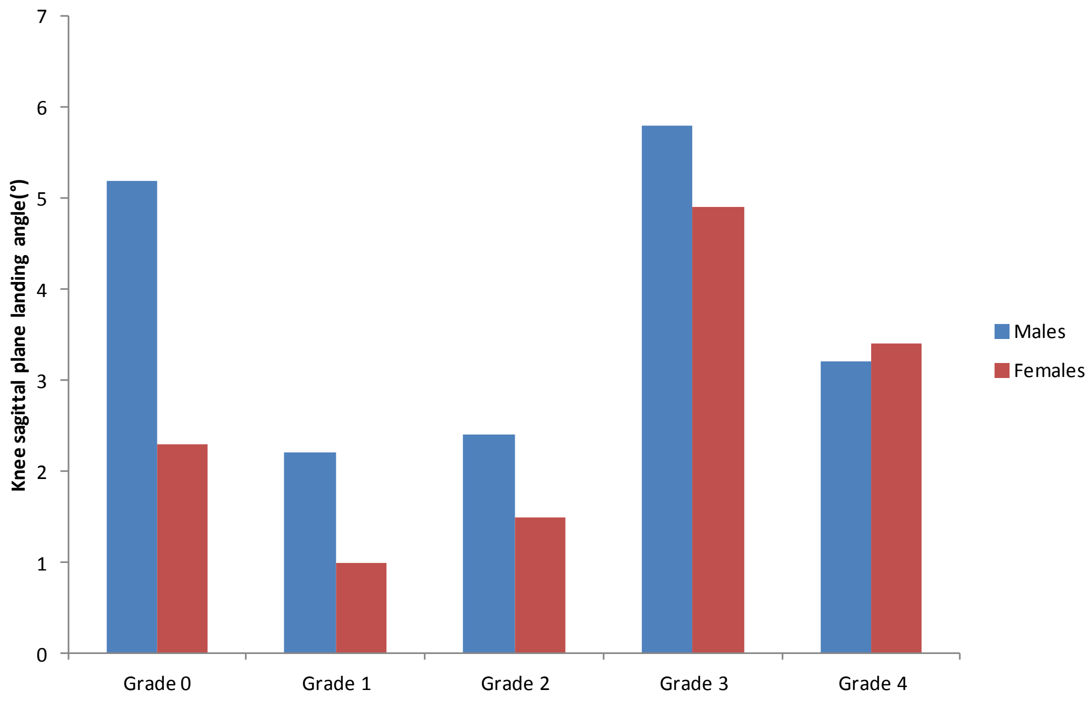

Figure 8.16 Median knee sagittal plane landing angle for each KL grade, by sex.

Table 8.54 shows the results of a Mann-Whitney test examining associations between sexes at each grading for knee sagittal plane landing angle. A significant association was found between sexes for grade 1, therefore in subsequent inter-grading statistical testing sexes were treated individually.

Table 8.54 Results of Mann-Whitney test for statistical significance of sex within OA gradings for knee sagittal plane landing angle at age 62-63 years.

	P-value
Grade 0	0.339
Grade 1	0.029
Grade 2	0.259
Grade 3	0.626
Grade 4	N/A

A Kruskal-Wallis test for statistical significance returned a value of $p = 0.350$ for males and $p = 0.137$ for females, indicating no significant association for both males and females. As no link was found between KL grades, no regression analysis was required.

8.4.13 Normalised vertical acceleration at heelstrike

Median normalised vertical acceleration at heelstrike for the entire cohort was 0.39 m/(kg s²) (IQR 0.34 – 0.49). Figure 8.17 shows the median normalised vertical acceleration at heelstrike for each KL grade, by sex.

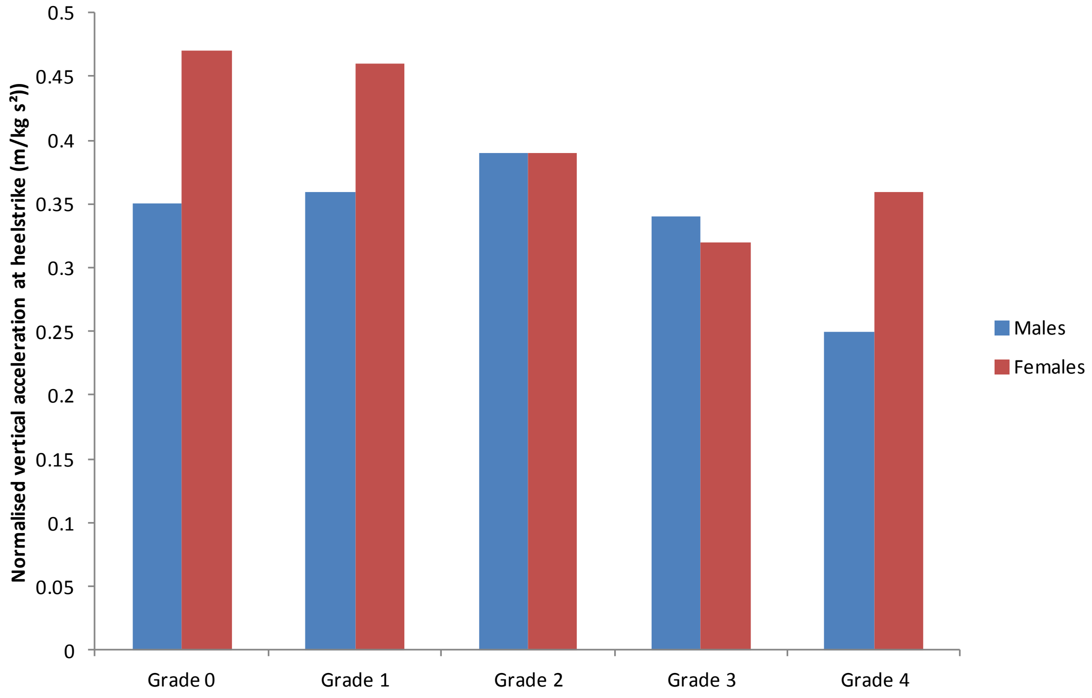

Figure 8.17 Median normalised vertical acceleration at heelstrike for each KL grade, by sex.

Table 8.55 shows the results of a Mann-Whitney test examining associations between sexes at each grading for normalised vertical acceleration at heelstrike. Significant associations were found between sexes for grade 0 and grade 1, therefore in subsequent inter-grading statistical testing sexes were treated individually.

Table 8.55 Results of Mann-Whitney test for statistical significance of sex within OA gradings for stance phase length at age 62-63 years.

	P-value
Grade 0	0.003
Grade 1	0.001
Grade 2	0.214
Grade 3	0.680
Grade 4	N/A

A Kruskal-Wallis test for statistical significance returned a value of $p = 0.006$ for males and 0.010 for females, indicating a significant association for both sexes. Table 8.56 shows the results of a Mann-Whitney test performed between successive male groups for normalised vertical acceleration at heelstrike. A significant association was found between grade 3 and grade 4. Table 8.57 shows the results of a Mann-Whitney test performed between successive female groups for normalised vertical acceleration at heelstrike. A significant association was found between grade 1 and grade 2, and grade 2 and grade 3.

Table 8.56 Results of Mann-Whitney test for statistical significance between male OA gradings for normalised vertical acceleration at heelstrike at age 62-63 years.

Groups Tested	**P-Value**
Grade 0 vs Grade 1	0.714
Grade 1 vs Grade 2	0.156
Grade 2 vs Grade 3	0.196
Grade 3 vs Grade 4	0.016

Table 8.57 Results of Mann-Whitney test for statistical significance between female OA gradings for normalised vertical acceleration at heelstrike at age 62-63 years.

Groups Tested	**P-Value**
Grade 0 vs Grade 1	0.520
Grade 1 vs Grade 2	0.036
Grade 2 vs Grade 3	0.033
Grade 3 vs Grade 4	N/A

Performing a stepwise regression analysis for males and including WOMAC pain score, WOMAC stiffness score, BMI and cadence led to the removal of WOMAC pain score, with a value of $F < 0.001$. The R^2 value for normalised vertical acceleration at heel-strike against KL grade was 0.086, and when WOMAC stiffness score, BMI and cadence were included, the overall R^2 value rose to 0.545. Regression coefficients from the final model are shown in Table 8.58. KL grades 1, 4 and BMI were significantly negatively associated with normalised vertical acceleration at heel-strike and KL grade 2, 3, WOMAC stiffness score and cadence were significantly positively associated with normalised vertical acceleration at heel-strike.

Table 8.58 Final regression model for male normalised vertical acceleration at heel-strike against KL grade and confounding factors.

Variable	**Regression Coefficient (95% CI)**	**P-value**
KL grade 0	Reference	N/A
KL grade 1	-0.03 (-0.10, 0.04)	0.009
KL grade 2	0.01 (-0.06, 0.07)	0.009
KL grade 3	0.03 (-0.05, 0.11)	0.009
KL grade 4	-0.07 (-0.16, 0.02)	0.009
WOMAC stiffness score	0.01 (0.00, 0.01)	0.004
BMI (kg/m²)	-0.01 (-0.02, -0.01)	0.001
Cadence (strides/min)	0.01 (0.00, 0.01)	0.001

Performing a stepwise regression analysis for females and including WOMAC pain score, WOMAC stiffness score, BMI and cadence led to the removal of KL grade and WOMAC pain score, with a value of $F < 0.001$. The R^2 value for normalised vertical acceleration at heelstrike against KL grade was 0.001, and when WOMAC stiffness score, BMI and cadence were included and KL grade excluded, the overall R^2 value rose to 0.456. Regression coefficients from the final model are shown in Table 9.4. WOMAC stiffness score and BMI were significantly negatively associated with normalised vertical acceleration at heel-strike and cadence was significantly positively associated with normalised vertical acceleration at heel-strike.

Table 8.59 Final regression model for female normalised vertical acceleration at heel-strike against KL grade and confounding factors.

Variable	**Regression Coefficient (95% CI)**	**P-value**
KL grade 0	Reference	N/A
WOMAC stiffness score	-0.01 (-0.01, 0.00)	0.049
BMI (kg/m²)	-0.01 (-0.02, 0.00)	0.001
Cadence (strides/min)	0.01 (0.00, 0.01)	0.001

Chapter 9 Discussion

This chapter starts by looking at the prevalence of OA seen in the NTFS cohort compared to what was expected. It then moves on to provide a summary of both the univariate and multivariable statistical analysis for each variable. These results are then compared with other studies and their implications in relation to gait as a mechanism for initiation and progression of osteoarthritis are discussed. A wider view of this study is then taken and main learning points that could be applied in other studies are discussed. The strengths and weaknesses of the methods used are then explored with potential areas for improvement highlighted. Directions for future work and how to extend the scope of the work already done are examined. Finally, the conclusions from this thesis are drawn together and summarised in a set of learning outcomes.

9.1 Prevalance of osteoarthritis in the Newcastle Thousand Families Study cohort

Out of the original 1142 participants recruited at the inception of the study [11], 347 attended for clinical assessment. Of these, 136 were excluded from the analysis of OA initiation in relation to gait kinematics using the exclusion criteria detailed in Section 7.8. Following application of the exclusion criteria, 211 participants remained for us in analysis of gait kinematics in relation to OA initiation.

Based upon data from previous studies [27], roughly 70 out of these 211 participants were expected to have OA. However, 196 out of the 211 were diagnosed radiographically as having KL grade 1 or above. This is much higher than the expected prevalence. The data from previous studies has been based upon self- or doctor-reported OA for a population. In Section 3.5 it was discussed that patients only seek medical advice if a joint is causing them pain or affecting their quality of life. Changes seen at KL grade 1 are minimal and structural changes to the joint resulting in pain, swelling or reduced mobility are rarely seen until KL grade 2 or higher is reached. For the NTFS cohort, 75 participants out of 211 reported KL grade 2 or higher which is in keeping with the prevalence expected from previous studies.

9.2 Main findings of Newcastle Thousand Families Study gait analysis

The full results of the Newcastle Thousand Families Study gait analysis are included in Chapter 8. This section provides a summary of the main findings.

Cadence was the only variable not found to differ between sexes. A significant association was found between Grade 0 and Grade 1, and the association between Grade 2 and Grade 3 was close to significance, even after adjusting for pain, stiffness and BMI.

For males, the significant associations found between KL grades are detailed in Table 9.1. Table 9.2 shows the final regression models for gait variables found to have significant associations between KL grades for males.

Table 9.1 Significant associations found between KL grades for males.

Groups Tested	**Significant associations found**
Grade 0 vs Grade 1	Peak flexion angle
Grade 1 vs Grade 2	Mean flexion angle
Grade 2 vs Grade 3	Single support phase length Knee RoM Knee loading phase RoM Knee impact phase RoM Peak flexion angle Mean flexion angle Mean flexion rate
Grade 3 vs Grade 4	Normalised vertical acceleration at heel-strike

Table 9.2 Final regression models for significantly associated gait variables for males.

Variable	**Final Regression Model**
Single support phase length	BMI, Cadence
Knee RoM	Cadence
Knee loading RoM	Cadence
Knee impact RoM	Cadence
Peak flexion angle	Cadence
Mean flexion angle	KL Grade, Cadence
Mean flexion rate	Cadence
Normalised vertical acceleration at heel-strike	KL Grade, Stiffness, BMI, Cadence

For females, the significantly associations found between KL grades are detailed in Table 9.3. Table 9.4 shows the final regression models for gait variables found to have significant associations between KL grades for females.

Table 9.3 Significant associations found between KL grades for females.

Groups Tested	**Significant associations found**
Grade 0 vs Grade 1	Single support phase length Knee RoM Knee impact phase RoM Mean flexion rate
Grade 1 vs Grade 2	Initial double support phase length Knee RoM Knee stance phase RoM Peak flexion angle Mean flexion angle Normalised vertical acceleration at heel-strike
Grade 2 vs Grade 3	Knee RoM Normalised vertical acceleration at heel-strike

Table 9.4 Final regression models for significantly associated gait variables for females.

Variable	**Final Regression Model**
Single support phase length	KL Grade, BMI, Cadence
Initial double support phase length	BMI, Cadence
Knee RoM	KL Grade, Pain, BMI
Knee stance phase RoM	KL Grade
Knee impact phase RoM	Pain, Stiffness, Cadence
Peak flexion angle	KL Grade, BMI, Cadence
Mean flexion angle	KL Grade, Cadence
Mean flexion rate	KL Grade, Cadence
Normalised vertical acceleration at heel-strike	Stiffness, BMI, Cadence

9.3 Interpretation of the findings from this study

Only cadence was not found to be significantly different between sexes. Debi et al. [79] conducted a study that looked at cadence in OA patients with KL grades 1-4. Individual cadence values for each grade are not reported but the average cadence across all KL grades was 105.3 steps/min. For participants of the NTFS gait analysis showing signs of radiographic OA, average cadence was 106.6 steps/min which is similar. Cadence was significantly different between grade 0 and grade 1, and close to significance between grade 2 and grade 3. This is supported by the work of Ko et al. [65]. Whilst they measured walking speed and not cadence, they found a significant association between patients with knee OA and healthy controls. This significant association between grade 0 and grade 1 implies that the presence of mild OA within the joint affects cadence, but does not further affect it until substantial structural changes have occurred within the joint as a result of disease progression. This is supported by the regression coefficients for OA gradings, which show -5.71 and -7.31 for grade 1 and grade 2 respectively, and then jump to -15.20 and -15.01 for grades 3 and 4. Had participant numbers in the grade 3 and 4 groups (n = 9 and n = 5 respectively) been higher, this change would likely have become significant with increased statistical power. WOMAC pain score, WOMAC stiffness score, and BMI were all included in the regression model for cadence, but with much lower regression coefficients. However, their addition did cause an increase in R-squared value from 0.092 to 0.194, implying that their addition more than doubled the amount of variability explained between the KL grades. It would appear that OA initiation affects cadence which, given the small radiographic changes and low pain level induced by these, might instead imply that OA sufferers walked with reduced cadence before incidence of OA. The decrease in cadence in the latter radiographic stages of OA is likely a reflection of the increased degradation of the joint to the point at which its function is substantially impaired.

Single support phase length showed significant associations between KL grades 2 and 3 for males and between grades 0 and 1 for females. Debi et al. [79] found the single support phase length for group of 125 OA patients with mixed sex and KL grading to be 36.7%. Astephen et al. [33] also found single support phase length to be around 36% for OA patients. This compares with 29% found for the OA sufferers within the NTFS cohort and implies that they spent less time in single support phase. Stance phase length has been shown to be related to walking speed [76] and the patients in the work of Astephen et al. showed no significant associations between the KL grades for walking speed. Whilst walking speed was not measured for the NTFS cohort, cadence did differ significantly between KL grades and it is suggested that this caused the association in single support phase length. The OA group in the NTFS cohort showed lower average WOMAC pain and stiffness scores than those of the OA patients in the work of Debi et al., which should lead to a longer single support phase length. It is possible that measurement of gait events using inertial sensors was not as reliable as the GAITRite system (GAITRite, CIR Systems Inc) used by Debi et al., as gait event detection using a pressure mat is analogous to using foot-switches which are considered to be the gold standard for gait event detection. Landry et al. [71] found a significant association between OA patients and healthy controls for stance phase length, with OA patients spending 36.3% of the gait cycle in single support phase compared to 37.4% for healthy controls. Whilst the relationship is mirrored by the NTFS cohort, the figures themselves are more in agreement with Debi et al. McKean et al. [62] also found a significant association between moderate OA sufferers (KL grade 1-3) and healthy controls for stance phase length ($p = 0.03$), and this is also supported by values found by Astephen et al. [33] (35.8% single support phase length).

Ko et al. [80] also looked at stance phase length and found a significant association between healthy controls and patients with knee OA, a result that was seen in this study for women, but not for men. Ko et al. also found a significant association between stance phase length for asymptomatic patients and healthy controls. In the female participants of the NTFS cohort, a significant association was found between grades 1, 2 and 3, but not between grade 0 participants and those with grade 1 OA. The stance phase lengths recorded for the grade 0 group in the NTFS cohort were also around 5% greater than those of the healthy controls in the study by Ko et al. Whilst pain and BMI associations between the OA groups for the two studies could explain an association in stance phase length, it seems unusual that an association of 5% is found between healthy participants of the studies, and lends further credence to the theory that the method of gait event detection with the inertial sensors was not as good as those used in other studies. BMI and cadence were included in the regression models for single support phase length for both sexes and KL grade was only included for females. The single support phase is when all the participants mass is supported by one leg, and thus BMI was expected to be included in the regression model as higher BMI would mean greater loading in the knee joint. BMI was not found to be significantly different between sexes and significant associations were found between grades 1 and 2, and grades 2 and 3. Association in cadence was found to be close to significance between grades 2 and 3 and BMI was included in the regression analysis. It is thought that it is the increased joint loads caused by an increase in BMI that contributed to the significant association seen in single support phase length. For males, the inclusion of BMI and cadence in the regression model increased the R^2 value from 0.112 to 0.413 with KL grade excluded. A similar jump in R^2 values was seen in females (0.057 to 0.545) when KL grade was also included. Both regression models showed a positive association between cadence and single support phase length and a negative association between BMI and single support phase length.

Initial double support phase length showed a significant association between grades 1 and 2 and females, but not between any grades for males. Initial double support phase length represents the period when body weight is being transferred from one leg to another before swing phase begins and is sometimes referred to as the loading phase. Cadence and BMI were included in the regression model for initial double support phase length. The significant association found between grades 1 and 2 for females can perhaps be explained by increase in pain and stiffness between these grades, although it was not found to be significant. There was also no significant association found between sexes for BMI, implying that males do not adapt their loading regime to mitigate the effects of increased BMI. Whilst increased BMI may have caused a reduction in single support phase length in males due to higher joint loading, the time over which this loading was applied to the joint before single support phase began did not differ significantly. This implies that whilst males may have adapted to decrease the time over which a joint remains loaded, they did not change how fast the load was applied. This is backed up by no significant associations being found between KL grades for peak flexion time during stance phase, as an increase in this would indicate a decrease in loading rate (the same load applied over a longer period of time). Finally, knee flexion angle at heel-strike was not significant between KL grades, further supporting the conclusion that no change was made in the loading of the joint despite degradation of the joint due to OA as the flexion angle at heel-strike is the starting point for the system to flex and transfer body weight onto the limb.

The time to first peak flexion angle during stance phase did not show any significant associations between KL grades for males or females. Childs et al. [64] also looked at the time to first peak flexion during stance phase and found there to be no significant association between OA patients and healthy controls, which is in agreement with this study. Their values were expressed as a percentage of stance phase and were 27-28% for both groups. Assuming stance phase to represent roughly 60% of the gait cycle, this converts to peak flexion during loading phase occurring at 16-17% of gait. The NTFS cohort showed first peak flexion during stance phase to occur at 18-19% of the gait cycle. There is substantial similarity between the results of Childs et al. and this study and this similarity is even more noticeable when it is taken into account that 60% stance phase length is a low estimate and that it is likely to be greater than this. For males, the NTFS cohort results were supported by the results for initial double support phase length and knee flexion angle at heel-strike. For females, knee flexion at heel-strike supported the results for time to peak first flexion during stance phase, but initial double support phase length did not. However, it has been suggested by Childs et al. that the method for measuring gait events using inertial sensors was not as accurate as if foot-switches had been used. Whilst this would not affect the measurement of first peak flexion angle timing, it could affect the measurement of heel-strike timing and gait cycle length. If either of these were not measured correctly then the timing of the first peak flexion angle as a percentage of gait cycle would be affected. However, any errors in gait event detection should be applied to all participants randomly and therefore any associations in time to first peak flexion angle between KL grades should not be due to bias.

Knee RoM over the entire gait cycle showed a significant association between grade 2 and grade 3 for males and between all KL grades for females. Kaufman et al. [61] reported knee RoM as around 60° for healthy individuals and 45-50° for severe OA patients. The trend between the two groups is the same as that found for the NTFS cohort, with knee RoM decreasing from 60-65° in healthy controls to 35-55° in severe OA sufferers. Al-Zahrani et al. [12] also looked at knee RoM in severe OA sufferers and found a similar relationship to Kaufman et al., with RoM decrease from 65° to 35-50° in OA sufferers. This is again similar to the NTFS cohort. Whilst the study of Turcot et al. [73] did not focus on knee RoM, a graph comparing knee flexion-extension patterns of the two groups showed little difference in RoM. However, the KL grades measured by their study were not reported, so it is difficult to compare with the results of this thesis. Had the OA sufferers presented with grade 1-2, then their results were similar to those found in the NTFS cohort. Ko et al. [80] reported that the knee RoM of healthy controls compared to grouped asymptomatic and symptomatic OA sufferers was close to significance. The knee RoM reported for asymptomatic and symptomatic OA sufferers was 55.46° and 53.82° respectively. These are similar to the values reported for grade 3 and grade 4 of the NTFS cohort, although no KL grades were specified in the work of Ko et al. In the case of males in the NTFS cohort, KL grade was not significant after adjustment for cadence, implying that differences in cadence were responsible for differences in knee RoM rather than OA. It is also noted that the only significant association for males was between grades 2 and 3. This is thought to be the stage at which disease severity starts to make substantial mechanical changes in the joint, and pain from the joint also increases, so a difference in knee RoM between these grades would be expected. For females, KL grade was included along with pain and BMI included in the regression model. This represented one of the few cases where cadence was not included in the regression model. KL grade on its own explained 22.6% of variation between grades, and the inclusion of pain and BMI increased this to 32.8%. The implication of this is that the presence of OA within the joint was causing a kinematic adaptation, perhaps through mechanical changes in the joint, as pain was only shown to be significant between grades 2 and 3. BMI was significant between grades 1 and 2, and grades 2 and grade 3. The lack of significance between grade 0 and grade 1 coupled with no significant effect of pain between grade 0 and grade 1, implies that the kinematic differences may have been present before onset of OA and that pain as a result of disease progression and increased BMI have caused an amplification of their effect.

Stance phase RoM showed no significant associations between KL grades for males but showed a significant association between grade 1 and grade 2 for females. Turcot et al. [73] showed a similar relationship for stance phase RoM between OA patients and healthy controls, although the overall magnitude of flexion was lower for the OA group. As with knee RoM, this is in contrast to the results of the NTFS study. However, sex-specific results were not reported for the study by Turcot et al., whereas for the NTFS study a significant association was shown between sexes for knee stance RoM. Given the small number of individuals present in the work of Turcot et al. (nine OA patients, nine healthy controls), the combination of sexes during kinematic data analysis may have masked these differences and led to their data showing no difference. The combination of sexes is understandable given the small subject numbers as drawing conclusions from statistical tests would have been more difficult had sexes been separated and group sizes further decreased. For females, only KL grade was included in the final regression model and this was the only case where KL grade appeared on its own in a regression model. Stance RoM represents the ease of flexion of the knee joint whilst loaded and the implication from the regression analysis is that cadence, BMI, pain and stiffness did not affect the ease of flexion. The difference between stance RoM for grades 2 and 3 was close to significance, and it is thought that higher numbers in each grading would have caused this difference to become significant. This implies that the progression of the disease may have caused functional changes in the joint that are expressed purely mechanically and not as pain.

Knee RoM during the loading phase showed a significant association for males between grades 3 and 4, but not between any grades for females. Al-Zahrani et al. [12] found a significant association between OA patients and healthy controls for loading phase knee RoM as well. In the regression analysis for the NTFS cohort, KL grade was excluded and cadence included in the model, implying differences in loading RoM were due to differences in cadence. The walking speeds of the two groups in the work of Al-Zahrani et al. were significantly different and it is thought that, if a regression analysis were performed on their knee loading phase RoM data, then this would account for the associations shown. Childs et al. [64] found healthy controls to walk with a mean of 19.5° of flexion in the loading phase whereas OA sufferers (KL grade 2 and above) walked with a mean of 15.7° of flexion in the loading phase. The decrease seen in NTFS cohort was smaller, with 17.5-18° for healthy controls and 16° for an average of grades 2, 3 and 4. However, the breakdown of the KL grades in the group used by

Childs et al. is not known and if their group included more patients with KL grades 3 and 4 then this could explain the difference in results. Zeni et al. [76] also looked at loading phase RoM and found healthy controls to have a loading RoM of around 18°, moderate OA sufferers (KL grade 2-3) around 14° and severe OA sufferers (KL grade 4) around 10°. The NTFS cohort showed similar knee flexion during the loading phase when they were grouped in the same way and sex ignored.

Males in the NTFS cohort showed a significant association between grade 3 and grade 4 for impact phase knee RoM and females showed significant associations between grade 0 and grade 1. As with several other variables for males, the regression analysis excluded KL grade and only included cadence, implying that differences in cadence were associated with the impact phase knee RoM associations. In the regression model for females, pain, stiffness and cadence were included and KL grade excluded. KL grade on its own explained 0.1% of variation between grades, whilst the inclusion of pain, stiffness and cadence and the removal of KL grade explained 33.1% of the variation. The implication of this is that the significant association between grade 0 and grade 1 was not due to presence of OA. This is supported by the results for males which excluded KL grade from the regression model entirely. However, it also seems unlikely that this association would be due to pain and stiffness as there is no significant association for these variables between grades 0 and 1. Cadence was significantly different between grades 0 and 1, and therefore it is concluded the relationship shown by impact RoM is an expression of changes in cadence.

In the case of peak flexion angle, significant associations were found between grades 0 and 1, and grades 2 and 3 for males, and between grade 1 and grade 2 for females. Kaufman et al. [61] reported that the peak flexion angle for knee OA sufferers to be 6° less than that recorded for healthy controls. Whilst the KL grade used to define OA severity is not specified by Kaufman et al., the inclusion criteria listed (e.g. “involved joint is primary factor limiting physical activity” and “joint pain with passive range of motion”) are indicative of severe OA. Given the assumption that the OA group used were severe OA sufferers, this agrees with the peak flexion angles from the NTFS gait analysis which show around 5-6° less flexion for grade 4 OA patients and some grade 3 patients. Kaufman et al. also reported that female OA sufferers had significantly greater peak knee flexion during walking, which is supported by the grade 2 and 3 participants of the NTFS cohort, but not by grade 4. However, grade 4 contained only 1 female participant, so use of this group in the comparison is not justified. Turcot et al.

[73] also found around 5° less peak knee flexion for OA sufferers compared to healthy controls, similar to that found for KL grades 3 and 4 in the NTFS cohort, although without any detail on OA disease severity from Turcot et al. it is difficult to compare. Briem et al. [74] found a significant association in peak knee flexion between healthy controls and OA sufferers with KL grade 2-3, with a value of 4.4°. This is similar to the association reported between healthy participants of the NTFS cohort and those with KL grade 3 OA. However, those with KL grade 2 OA did not show this response. A breakdown of the KL grade of the patients in the study by Briem et al. is not given, so if there were more patients with KL grade 3 then grade 2, this could explain the differences between the studies. For males in the NTFS cohort, cadence was the only significant variable. The pattern of associations between KL gradings for peak flexion angle were similar to those found in cadence, and imply that the decrease in cadence is expressed as a decrease in peak flexion angle. The association between grade 1 and grade 2 is close to significance, however as these two groups both had large numbers ($n = 115$ and $n = 53$), it is not expected that this would have become significant with increased sample size. For females, the regression analysis for peak flexion angle included KL grade, BMI and cadence. The R-squared value for KL grade alone was 0.247, and with additional variables included in the regression this rose to 0.317. This implies that KL grade is explaining more of the association between KL grades for peak flexion angle than the other regression variables. However, females showed a significant decrease in knee RoM at all grades. The decrease in peak flexion angle could be an expression of this, although it would seem logical that it would have caused a decrease in peak flexion angle between all grades, not just grades 2 and 3.

For males, mean flexion angle was significantly different between grades 1 and 2, and grades 2 and 3, with grades 0 and 1 being close to significance. For females, mean knee flexion angle showed a significant association between grades 1 and 2 only. Astephen et al. [33] found a significant correlation between mean knee flexion across the entire gait cycle and disease severity. The mean knee flexion angle for males in the NTFS cohort agreed with this, with significant associations found between healthy participants and those with KL grades 1, 2 and 3. This agrees with the findings of Astephen et al. Only females showed significant association between grades 1 and 2. The study by Astephen et al. contained over twice as many males than females. This could explain the difference between their results and this study, as the results were averaged across both sexes in the work of Astephen et al. A significant correlation was also found between gait speed and WOMAC pain severity in the work of Astephen et al., and in the NTFS cohort pain was significantly associated with cadence. For both sexes in the NTFS cohort, cadence was included in the regression analysis, but KL grading was also included, implying that it was not just differences in cadence that explained the significant associations between the groups. The regression coefficients for males for this variable are unexpected. For grade 1 and grade 2 they are 2.91 and 2.46 respectively, indicating that an increase in KL grade produces an increase in mean knee flexion. Then for grade 3 and grade 4 they are -1.63 and -2.56, indicating that this further increase in KL grade decreases the mean knee flexion. This latter relationship is likely due to pain and stiffness being increased in this group and therefore it being both more difficult and more painful to flex the knee. The relationship for the earlier KL grades indicates that for early stages of OA it is actually easier to flex the knee than when no OA is present in the joint. The author has no satisfactory explanation for this at present. For females, the addition of cadence in the regression model increased the R-squared value from 0.143 to 0.256. This is a larger increase than that shown for peak knee flexion (which showed a similar relationship between KL grades), both in overall magnitude and also relative to the original R^2 value. This would imply that BMI affects the limits of knee flexion, but not the overall ease of flexion of the joint.

Mean flexion rate showed significant associations between KL grades 3 and 4 for males, and between grades 0 and 1 for females. Messier et al. [60] also looked at knee flexion rate across the whole gait cycle with OA patients showing significantly lower knee angular velocity than controls. Messier et al. measured knee angular velocity to be around 130 °/s for healthy controls and around 120 °/s for OA sufferers. In their study, OA sufferers had a KL grade of 2.2 ± 1.5, indicating moderate OA. The healthy individuals in the NTFS cohort had an angular velocity of 136 °/s and the grade 2 and 3 OA sufferers had an angular velocity of 126 °/s. Whilst the NTFS cohort overall showed higher knee angular velocities, the magnitude of the decrease with OA severity between the two matching groups was the same (10 °/s in both cases). For males in this study the final regression model excluded KL grade and included only cadence. This is a result that has been seen in other variables for males in this study, and the implication is that changes in cadence alone were responsible for any changes in mean flexion rate. For females in this study the final regression model included KL grade and cadence. KL grade on its own explained 8.4% of the variation between grade 0 and grade 1, and when cadence was included this rose to 51.6%. This implies that the significant association found in mean flexion rate between grades 0 and 1 was an expression of cadence.

Knee flexion angle at heel-strike did not show significant associations between KL grades for either sex. Childs et al. [64] also looked at knee flexion at heel-strike and found OA patients had significantly higher knee flexion at heel-strike than healthy controls, with OA patients having a mean flexion angle at heel-strike of 4.5°. In the NTFS gait analysis, knee flexion angle at heel-strike did not show significant associations for males or females at any KL grade. The magnitude of knee flexion at heel-strike from the OA sufferers in the NTFS cohort is similar to those found in the study by Childs et al. It is suggested that higher subject numbers in the NTFS gait analysis may have contributed to the difference in findings and that had the study by Childs et al. had greater subject numbers, this may have resulted in the same trend being shown. Henriksen et al. [34] reported that OA patients walked with 2.5° more flexion at heel-strike, and this is similar to the flexion angle at heel-strike of the grade 3 and 4 OA patients in the NTFS cohort. In both studies the difference in knee flexion angle at heel-strike between subject groups was not significant.

Normalised vertical acceleration at heel-strike showed significant associations between grades 3 and 4 for males, and between grades 1, 2 and 3 for females. Zeni et al. [76] did not find the vertical ground reaction force at heel-strike to be significantly different between groups. Whilst the NTFS gait analysis did not measure ground reaction force, vertical acceleration at heel-strike was recorded and could be seen as a proxy for vertical ground reaction force. Given the low sampling rate (50 Hz) using in the NTFS cohort compared to the force plate used by Zeni et al. (1800 Hz), the results from the NTFS gait analysis for normalised vertical acceleration should be treated with caution as the sampling rate may not have been sufficient to fully capture the accelerations generated by heel-strike. For males in the NTFS cohort, pain, stiffness and BMI were all included in the regression model along with KL grade. This implies that changes in normalised vertical acceleration at heel-strike were likely part of a pain management strategy aimed at reducing the force through the joint. The R^2 values for the regression support this, with KL grade on its own explained 8.6% of variation between the groups. When pain, stiffness and BMI were added, 54.5% of variation was explained. However, these results should be treated with caution due to the low numbers for grade 3 and grade 4 OA ($n = 9$ and $n = 5$ respectively), and the sampling rate used (50 Hz). For females, stiffness, BMI and cadence were included in the regression model and KL grade excluded. Both BMI and stiffness were negatively associated with vertical acceleration, implying that a heavier patient with a stiffer limb would experience a smaller vertical acceleration. At first, this relationship seems counterintuitive, but when viewed as a pain management strategy it does seem logical. However, pain was not significantly associated with normalised vertical acceleration at heel-strike.

In drawing together these results, the first thing that should be considered is cadence, as it does not differ significantly between sexes. However, cadence has been included in more regression analyses for men than for women. Therefore, either differences in cadence must affect one sex more than another or, differences in cadence do not have any effect and can be ignored. This second possibility was discounted as it is included in many of the regression models. Therefore any differences in cadence may affect one sex more than another.

It is possible that cadence was defined before the development of radiographic OA and also that these changes in cadence were responsible in part for changes seen in kinematic variables. This is supported by the inclusion of cadence in the regression analysis for 15 out of the 17 variables that showed significant associations between one or more KL grades. The evidence for cadence being defined before disease initiation is not conclusive by any means. However, it cannot be explained why the disease would cause a decrease in cadence at initiation, but then not cause any further change in cadence as severity increase. At disease initiation, the physical changes that occur are small whereas as severity increases the physical changes become more substantial and affect the mechanical function of the joint. This supports the conclusion that cadence is defined before disease initiation and not significantly affected by its progression. It could be argued that as BMI, pain and stiffness were included in the regression model for cadence, these factors could be the reason why a change in cadence between groups was observed. However, none of BMI, pain or stiffness differed significantly between grades 0 and 1, so this cannot explain the significant association found between these groups. Other changes in gait kinematics could be an expression of this difference in cadence and these changes are then exacerbated by increasing disease severity causing mechanical changes and increased pain and stiffness in the joint. This theory is supported by the difference in cadence between grades 2 and 3 being close to significance, and for BMI, pain and stiffness the difference between grades 2 and 3 was found to be significant.

More significant associations in females than in males implies that females may be more susceptible to kinematic alterations as a result of the disease. This was supported by the conclusions of McKean et al. [62]. Cadence was included in fewer of the regression models for females, and never on its own, whereas for males it was included in every regression model and was the only variable included on five occasions. This means that less of the variation in kinematics between KL grades for females can be explained by differences in cadence. Of the other regression variables, BMI was included five times for females and only twice for males, implying that changes in BMI have more of an effect on female kinematics than on male kinematics. Stiffness was included twice for females and pain included once. For males, stiffness was included once and pain was not included at all. The implication of these regression models is that female kinematics are more susceptible to changes due to pain and stiffness, although these variables were only included in the regression models for three variables so this conclusion should be treated with caution. Such alterations made by females could be seen either as adaptations aimed at mitigating the effects of the disease on their gait and reducing any pain or stiffness they experience, or as differences in walking kinematics that exist before the development of OA.

When assessing the potential for kinematic variables to initiate OA, it was expected that significant associations would be found between grade 0 and grade 1, and not between grade 1 and grade 2. This would imply a variable was defined before disease initiation and that the initial stages of disease progression had little effect on it. Subsequent disease progression into stages 3 and 4 would be expected to cause a change in kinematics as the severity of the disease can impair joint function, and the pain and stiffness from the joint can increase. This increase in pain and stiffness could cause gait adaptations aimed at pain management. Of the variables analysed for males, only peak flexion angle showed this relationship. This might indicate disease initiation and the regression analysis excluded KL grade and included cadence. For females, single support phase length, impact RoM and mean flexion rate showed this relationship. Of these variables, only single support phase length was not concluded to have been an expression of cadence. Single support phase length represents the entire body’s weight being supported on one limb. BMI was negatively associated with single support phase length and it seems reasonable that an increase in BMI would cause a decrease in single support phase length as this would be decrease the time in which the joint is maximally loaded. Overall, none of the variables measured seem likely to have caused the initiation of OA, however there is potential that the variables showing significant associations between grade 0 and 1 (particularly cadence) could be used for the prediction of OA incidence from gait and could be used as a supporting measure for other diagnostic tools.

9.4 Does gait have the potential to diagnose and predict OA?

In Chapter 1 of this thesis, it was hoped that “establishing biomechanical factors as being involved in the initiation of OA could lead to better treatments for patients, maintaining quality of life as people age and reducing prevalence of the disease through pre-emptive measures”. This now brings us to the question of “does gait have the potential to diagnose and predict OA?” In this authors opinion, yes, although the answer will be split into two sections dealing with diagnosis and prediction separately.

9.4.1 Diagnosis

One of the benefits of this study was the size of the cohort available for gait analysis. This allowed advanced statistical methods to be used to draw conclusions about a large group of subjects. However, were any of these conclusions to be applied to an individual, there is a chance that they may not produce a correct diagnosis. The results of this study only prove that given a set of variables, a patient is statistically likely to present with the disease, with 95% confidence of the diagnosis being correct. Therefore, in order for gait analysis to gain acceptance as an alternative and valid method of OA diagnosis, more data is needed to increase the statistical likelihood of a correct diagnosis being made.

In working in a clinical environment, the author became aware of how stringent the approval procedures can be for new methods of testing for diseases. They require conclusive evidence, a near-unified opinion and approval, and high reliability. It is this author’s opinion that, currently, gait analysis cannot satisfy these criteria. There is fragmentation is the methods used in studies both in terms of hardware, and the software and analysis models used to extract data. There is also dispute over which variables are relevant, and no single study has looked at every gait variable. Indeed, this work with the NTFS cohort chose not to study several variables, for practical reasons, which have shown strong links to OA.

Unification is what is now required within the gait analysis community. Some of this has already happened, with the International Society of Biomechanics producing standard methods of defining joint movement which everyone can use. However, there is no requirement to use these, and justification can be made for departure from standard methods. But without a standard method it is difficult to compare studies, and also to combine their data to form a body of proof that gait analysis can diagnose OA.

Gait analysis studies have shown good evidence for substantial gait changes due to OA, but the field does not yet possess the level of proof needed to be incorporated into the spectrum of OA diagnosis methods available. However, with more data, larger studies involving numbers of subject equal to greater than the size of the NTFS cohort, and a standard methodology allowing data from different studies to be analysed in conjunction with one another, it is this authors belief that this goal is fully achievable.

9.4.2 Prediction

The question of whether gait analysis can be used to predict OA before it initiates is a much more difficult one to answer. In order to predict OA, information is required on the conditions prior to and just after initiation of the disease. However, there are obstacles in the way of acquiring data in each of these scenarios.

One of the issues in detecting early osteoarthritis is that symptoms can be hard to identify. Pain is not always experienced in the early stages of the disease and radiographic changes can be small. None of the methods of diagnosis currently available give a conclusive judgement on presence of the disease just after initiation, and the patient may not even visit the hospital until disease has progressed. If no pain is being experienced by a joint, a patient is unlikely to visit the hospital to have the joint examined and thus the disease is not detected until the later stages when it has already established itself within the joint and is causing pain.

One way to increase the likelihood that OA is identified early on in its progression would be to add clinical and radiographic examination into annual health check-ups. This may allow early signs of the disease to be identified and the patient could then be recruited into a gait analysis study.

This addition to annual health check-ups could also provide data on each patient before the disease initiated. Gait data on an individual before a disease initiates is rare, and typically a healthy control group is used for comparison. However, this is not a substitute for patient specific data before the disease initiated, and it is this author's opinion that this is essential for building a method of predicting OA. Adding gait analysis into annual health check-ups would allow both "before" and "after" data on each individual to be collected. Up until recently, the obstacles to this were practical ones, with gait analysis being time consuming and expensive to perform, and expertise being required for analysis of the data. This study, along with others, has developed a method that is portable, fast, relatively cheap, and easy to perform. There is still expertise required in the interpretation of the data, but the data collection can be done by anyone with only a short amount of training required. Gait data collection should not stop being viewed as a specialist technique, and instead seen as a useable tool.

This will in then provide a much larger database of gait data, with information about an OA sufferers gait before and after initiation of the disease. It is only with this longitudinal data that prediction of a disease can even begin to occur. With cross-sectional data theories surrounding OA initiation can be suggested, but without longitudinal data confirming the conditions prior to and post-initiation, these remain only as theories. Increasing the gait database through further studies and making gait analysis a common tool for health screenings is a key step in moving towards prediction of OA from gait.

9.5 Wider implications of this work

So far this discussion has focused on the results of analysis of individual gait variables, comparing them to the results from previous studies, and analysing them with a focus on how they may be initiating OA within the knee joint. It has also discussed how the technological approach developed should be incorporated into medical practices in order to enhance the diagnosis and possible prediction of OA. However, it is also important to view this study within the whole field of OA research and see what conclusions can be applied to other studies, not necessarily involving gait.

The decision was made to use KL grade as a measure of OA severity, instead of a more patient oriented measure such as pain scoring (Section 3.5). The decision was justified because pain due to osteoarthritis usually occurs after the disease has initiated and progressed to KL grade 2 or higher within the knee joint [33]. Therefore, in a study focusing on OA initiation, using pain scoring as a measure of severity would not have provided information on those participants with early stages of the disease and would only highlight those with developed OA. However, so as not to ignore the effect of pain on a participant’s gait, the WOMAC scores were included in the backwards stepwise regression model to assess any affect pain may have had on gait variables. Section 9.1 discussed the prevalence of OA seen in the NTFS cohort and highlighted the difference found in prevalence when KL grade 1 was included (with prevalence more than doubling with the inclusion of KL grade 1). When only KL grades 2 and above were used, prevalence of OA in the NTFS cohort mirrored the expected prevalence. This further emphasised that using a measure of OA severity based upon pain is not appropriate when looking at initiation of the disease and that a radiographic measurement such as a KL grade should be used as it is capable of discerning the early stages and initiation of the disease. However, this conclusion should be tempered with caution, as the radiographic diagnosis of early stage OA within a joint is likely to be determined by the experience of the clinician grading the radiographs.

As mentioned, WOMAC scores were included as confounding factors in regression modelling for each gait variable in order to assess whether differences between OA severities were due to pain caused by the affected joint. No studies could be found which combined the study of OA severity, pain and gait kinematics or that including the level of pain experienced by participants in their analysis. Whilst any measurement of pain is inherently subjective, it should still be included in data analysis as it is a potential confounding factor when looking at the links between OA severity and gait kinematics.

Leading on from the use of confounding factors in data analysis are the analysis methods themselves. This study followed a logical decision process to arrive at the statistical methods used. A key feature of the methods used was that normality of the data was not assumed and non-parametric tests were chosen. This is a sensible assumption as a sample of the population used to look at a disease which will initiate and progress at different times and rates in each participant would not lead to normally distributed data. However, the statistical methods employed in previous studies often assume normally distributed data. It is possible that differences in recruitment method (a representative birth cohort versus a targeted recruitment from an OA clinic for example) may lead to the data from these studies being normally distributed, although this still seems unlikely given the progressive nature of OA. Furthermore, proof of normality of the data (such as skewness) was not found to be reported in any of the studies that were reviewed in Chapter 3. This leads to the conclusion that normality of the data was assumed and not checked. Therefore, the statistical tests used on the data may not have been appropriate, with the knock-on effect that the analysis and interpretation of the results could then be called into question. Careful selection of an appropriate and justifiable statistical analysis method is an important consideration for any study.

Finally, the recruitment method used for this study was free from the bias that might be found when recruiting from an OA clinic. As discussed earlier in this thesis, recruitment from an OA clinic would be unlikely to include any participants with recently initiated OA as the disease would not have developed enough to be causing pain within the joint. Therefore, looking at initiation of the disease using targeted recruitment of participants is unlikely to yield any meaningful results as it effectively leads to looking at the wrong group of people. A birth cohort, or any cohort that provides an unbiased cross-sectional view of the population, would be an effective way of recruiting with the intention of looking at the initiation of a disease where the causes of initiation are not understood.

9.6 Strengths of this work

The large number of participants for the gait analysis is the first strength of this work. Gait analysis studies with over 200 participants have not been found in the literature. Coupled with this is the fact that the group of participants in this study is representative of the overall population. Recruitment for a study can compromise the representativeness of the sample used and mean that the results cannot be applied to the larger population. The recruitment method for the Newcastle Thousand Families Study did not suffer from these recruitment criteria problems, as everyone born within a 2 month span in 1947 was included. There is some risk that the factors behind the high infant mortality rate that spawned the study could affect the representativeness of the cohort, but at present this is unquantifiable.

The recording of individual KL grades by an experienced clinician and the use of these in the analysis is another strength. In the literature, only three studies were found that considered individual KL grades [33, 73, 79]. All other studies grouped several KL grades together and considered either “moderate” or “severe” levels of OA. In addition to this, no study in the literature had the analysis focused on the differences between healthy ‘controls’ and those with KL grade 1. Analysing the differences between these two groups is most likely to uncover biomechanical causes of the disease, as analysis during the later stages of OA makes it impossible to distinguish whether any changes found were causes or effects of the disease.

Accounting for the effects of joint pain and stiffness on gait, as well as the effect of BMI and cadence, has been done in other studies and was important to include here, particularly when looking at possible biomechanical causes of disease initiation.

The protocol provided a less expensive alternative to optoelectronic systems, whilst maintaining comparable repeatability and accuracy. The protocol was also required to fit within strict time, space, practical and ethical constraints, and this was accomplished. No complaints about the procedure were received and participants seemed to engage well with the gait analysis. The protocol was also performed on every able member of the NTFS cohort, and its adaptability to all the body types presented should be recognised. This protocol has the potential to be used in other settings, particularly in clinical research.

9.7 Weaknesses of this work

It is likely that having osteoarthritis in one knee joint will affect the kinematics of the other healthy knee joint. Lewek et al. [138] looked at the difference between the kinematics of uninvolved joints and healthy controls, and whilst differences were found in laxity of the joint, excursion of the joint was not significantly different to the controls. However, Liikavainio et al. [139] found no significant gait asymmetry in moderate OA sufferers. Briem et al. [74] found peak knee flexion angle showed significant side-to-side interactions between involved and uninvolved limbs. There is no conclusion within the literature on how an involved joint will affect an uninvolved joint, nor on the extent of the effect. It is also unknown how OA in both joints, but with varying severities, would affect the kinematics. However, none of these factors have been accounted for in the analysis of the NTFS cohort gait kinematics.

When analysing disease initiation and progression, it is best to work with longitudinal data, since changes can then be observed over time and related to initiation and progression of the disease in question. Conclusions drawn from a cross-sectional study are speculative and cannot firmly tie variables to the initiation of a disease; they provide associations between kinematic variables and osteoarthritis but cannot show anything related to the direction of the association. Therefore, any conclusions drawn from the NTFS gait analysis should be treated as associations until further supporting work is done or another gait analysis performed on the cohort in a few years to make the study longitudinal. However, this analysis has provided baseline data for the NTFS cohort as well as being a study in its own right.

Forces and moments that influence how the knee joint is loaded have previously been linked to OA [12, 63, 76] and have been implicated as being involved in the initiation of OA. However, within the constraints of the NTFS clinical assessment and the practicalities of developing a practical, portable gait analysis solution in a hospital environment, this was simply not possible. A force plate would have required installation in the floor of the corridor used (or another appropriate space found and a force plate installed there), and this was not permitted by the Clinical Research Facility. The use of a portable force plate was considered with a raised ramp and runway either side of it. However this did not fit within the portability condition, or the size of storage area available. The corridor in question also had to remain accessible for staff and patients of the hospital, and a force plate and raised runway would have prevented this.

Repeatable and accurate data were provided only in the sagittal plane. Calibration of inertial sensors was performed by a functional movement which defined an axis of rotation. Each axis of rotation for a joint should ideally be defined by its own functional movement. Due to the time constraints of working in conjunction with many other clinical assessments, it was not possible to calibrate every function axis. In hindsight, due to the focusing on knee joint angles for this thesis, it might have been better to use the time available to calibrate all three axes for the knee joint instead of one for each joint. However, another stipulation of the study was that motion of all three joints had to be recorded. If the motion of a joint had been recorded without its axes being defined, then the data would be of no use.

The sampling rate chosen for this analysis (50 Hz) was sufficient for recording of knee angles and gait events. However, the results for normalised vertical acceleration at heel-strike should be treated with caution as the sampling rate may not have been sufficient to fully record the event. Unfortunately, the sampling rate was determined by the bandwidth available for wireless transmission of data. A sampling frequency of 100 Hz was tried. However, this caused some recording errors relating to buffer overflow and meant that, on occasion, data was lost. It was deemed more important to ensure recording of complete gait cycle data than to have a higher sampling at the risk of missing data.

It is also possible that the straps used to attach the sensors may have had an effect on the gait kinematics. Any change made to a mechanical system has the potential to affect its function. Straps attached tightly around body segments are likely to have an effect, initially due to discomfort. Participants reported that they initially felt affected by the straps, but that by the time they had completed some practice calibration movements and trials they felt comfortable in them.

Finally, the inertial sensors returned orientation data, but not spatial data, therefore it was not possible to measure variables such as stride length, width and walking speed. These have been shown as relevant variables when looking at the osteoarthritis and gait [79]. However, it may be possible to calculate these from current data. A method referred to as “strap-down integration” has been reported [140] to calculate displacement data from inertial sensors and it would be interesting to look at this in the future.

9.8 Direction for future work

The analysis presented in this thesis considers knees individually for all variables except for cadence. It would be useful to look at the interaction between involved and uninvolved joints, similar to the study performed by Briem et al. [74]. This study focused on patients with one healthy and one osteoarthritic joint, and the NTFS cohort could be used to replicate and extend this analysis to look at the effect both knees being affected by OA, but with varying severities.

The NTFS has been running for almost 65 years, with assessments taking place throughout this period. It is intended that another follow-up be performed on the cohort at around age 70. Performing gait analysis again as part of this assessment would move the study from cross-sectional to longitudinal in nature and increase the value of its findings dramatically. Comparing the progression of OA severity to changes in kinematics with the participant numbers present in the study would allow suggested kinematic changes brought on by the disease to be confirmed. Furthermore, analysis of the gait at age 63 of those who have gone on to develop OA, and comparing this to the gait variables suggested as candidates for initiation in this thesis, would be of great value to biomechanical research on the topic.

Another area for future work would be to further analyse the gait data recorded at age 63 for the cohort in ways that were outside of the research included in this thesis. Looking at OA by individual knee compartment could be of interest, as could analysis of joint space narrowing, both of which were available as part of the radiographic assessment. The WOMAC scoring system could also be looked at with individual scores assessed, or scores analysed in quartile categories instead of as discrete values. Finally, the incidence and severity of OA in relation to fractures and other events that could have altered the musculoskeletal system could be analysed.

Further kinematic variables could also be extracted from the existing data. The method of Pfau et al. [140] for calculating displacement from inertial sensor data using strap-down integration could be investigated. The gait data collected could also be combined with a classification system, such as the one developed by Beynon et al. [134], could turn this large dataset into a potential tool for diagnosis of the condition and also help to identify study members who are at risk of developing OA. These predictions could then be checked in subsequent cohort follow-ups.

Finally, if a follow-up were to take place, the range of assessment methods should be expanded. At the time of protocol design, the focus was on practicality and portability whilst still providing relevant data with good integrity. With a longer development period, improved methods could be developed. The use of a GAITRite pressure mat would provide valuable data on foot pressure distribution and foot progression angle, whilst also measuring gait speed, stride length and timing of gait events. Other studies have also suggested assessing the kinematics of stair climbing as well as of walking, as the former represents a high-loading scenario. The design of a moveable (and perhaps instrumented) set of stairs could be undertaken in order to provide another assessment method.

9.9 Conclusions

Whilst there are some limitations of this, the largest single study to date to assess the initiation of OA and its effects on kinematics, several conclusions can be drawn. The first is that, for the variables measured, female gait kinematics are more susceptible to change due to OA than male gait kinematics. This is supported by the work of McKean et al. [62]. Cadence could explain the male kinematic differences for most variables, but less so for females. BMI, pain and stiffness scoring also featured in the regression analyses more often for females, so it would appear that a female gait is more inclined to adaptation to other factors than male gait. This could possibly explain why prevalence of OA in NTFS cohort for males is lower than that of females for grade 1 OA, but is greater than that of females at higher severities. Female joints may be more prone to develop the disease as a result of their gait kinematics, but females make adaptations early on to negate its effects. In contrast, male joints are less prone to disease initiation as a result of gait, but a lack of adaptation means a more rapid increase in severity. Females have more kinematic changes that could be linked to the initiation of the disease and this would therefore explain the higher prevalence.

A further conclusion of this study was that differences in cadence could explain many of the spatiotemporal and kinematic differences found between groups. It was included in all regression models for males and 7 regression models for females. Therefore, it would seem that differences in cadence may be responsible for many differences found in gait. This is supported by the work of Landry et al. [71] and Zeni et al [76]. Cadence itself only showed a significant association between grades 0 and 1, which suggests that differences in cadence were defined before OA initiation. It could be concluded that this difference in cadence is an expression of gait kinematics changes as a result of the disease. However very few of the variables for which cadence was included in the regression analysis showed significant kinematic associations between grades 0 and 1. Therefore, it was concluded that these kinematic differences are a result of differences in cadence, rather than the converse, and that the changes in cadence were exacerbated by BMI, increasing disease severity and the effects of pain and stiffness in the joints. These factors combined to cause a change in kinematics. Overall, none of the variables measured seem likely to have caused the initiation of OA. Rather, a difference in cadence defined before OA initiation then goes on to express itself in gait kinematics as the disease progresses in severity. The cause for differences in cadence before disease initiation is unknown, and could be a result of muscle development that then influences the walking style.

The wider implications of this thesis were that choosing a measuring of OA severity must be appropriate for the analysis taking place. Confounding factors should also be included in results analysis, and appropriate statistical methods should be chosen logically and justified with no assumptions made about normality of data. Finally, recruitment methods for studies should be sought that are free from bias and produce a representative sample of the overall population.

Learning outcomes for this thesis are as follows;

- Inertial sensors represent a promising technology for fast, efficient gait analysis in a clinical environment and could be employed as a further method of diagnosis that is faster and cheaper than radiographic imaging.
- Further development of inertial sensor protocols are needed in order to produce good quality coronal and transverse plane data whilst maintaining a fast and efficient protocol.
- Female kinematics are more susceptible to change due to OA than male kinematics.
- Differences in cadence could explain variation of kinematic and spatiotemporal variables, and thus should be included in analyses.
- Spatiotemporal and sagittal plane kinematic variables seem unlikely to cause OA initiation, but could be useful in improving early diagnosis of the disease.
- The metric chosen for defining OA severity must be appropriate for the focus of the study and the analysis taking place.
- Confounding factors should be included in statistical analyses so that their effects are not ignored, as rarely do things act in isolation.
- Appropriate statistical methods must be chosen and fully justified, with no assumptions made about the normality of data.
- Study recruitment can produce bias in the results and affect the validity of applying conclusions to overall population, and the effect the recruitment method chosen may have had must be considered in the results analysis.

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