Using biomechanics and MRi changes in Anterior Cruciate Ligament injured subjects to consider the implications for the development of knee osteoarthritis.

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Submitted to Cardiff University in partial fulfilment of the requirements for a PhD

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Acknowledgements.

First and foremost I would like to thank my supervisors, Robert van Deursen and Valerie Sparkes for their guidance and support, alongside Paulien Roos and Kate Button for contributing their time, energy and knowledge to developing the methods and assisting in data collection.

I would also like to thank the staff at Cardiff University Research Imaging Centre for allowing access to their resources and technical support alongside Kathleen Lyons whose time and clinical expertise was essential to the completion of the study. A big thank you also to Cardiff and Vale NHS Trust for granting access to information and the National Institute for Social Care and Health Research for providing essential research support.

To those who helped fund me throughout my research including Arthritis Research UK, Cardiff University and my employers, especially Marc Robinson and Adam Gethin/Neil Hill, I extend my eternal gratitude for helping keep a roof over my head and food on the table and allowing me to complete my thesis.

Finally to my friends and family, especially my Parents Maria and John, you have been there through the good times and the bad and supported me unwaveringly and believed in me even when I did not always believe in myself, for that I am indebted to you and eternally grateful.

Summary.

Background: The present study aimed to explore if risk factors associated with loading at knee were associated with degenerative changes in ACL injured groups.

Methods: **Part 1:** Biomechanics were investigated for gait, jogging and single legged squatting (SLS) in Anterior Crucitate Ligament Reconstructed (ACLR) (n=30), Anterior Cruciate Ligament Deficient (ACLD) (n=28) and controls (n=30). Analysis of biomechanics was also undertaken on a subgroup of ACLR (ACLR2) (n=10) 12.9±1.8 months after their first assessment. From the ACLR2 those with MRi (ACLM) were recruited (n=8).

Part 2: Comparison between the ACLM groups NHS diagnostic scans and a follow up scan was undertaken 27±11.7 months apart. Quantitative measurement of cartilage thickness and a semi-quantitative analysis developed from the Whole-Organ Magnetic Resonance Imaging Score (WORMS) was undertaken.

Part 3: Used a case series analysis incorporating individual participants' outcomes from the first two parts of the study.

Statistical analysis: Differences between ACLR, ACLD and control groups was performed using ANOVA. Longitudinal analysis was performed using a paired t-test and changes in MRi using a Wilcoxen signed-rank test.

Results: Biomechanics: No significant differences between groups existed for gait. For jogging ACLD and ACLR demonstrated reductions in peak knee extensor moment. The SLS showed a reduction in sagittal plane knee range of motion in the ACLD. The ACLD group had lower self-reported measures of function compared to the ACLR group.

Quantitative MRi: No significant differences in regional cartilage thickness between diagnostic and follow up scans was observed.

Semi-quantitative MRi: Significant improvement in total knee score was observed in ACLM.

Discussion: Despite increased loading being associated with the development of OA, the ACLD and ACLR groups maintained or decreased knee moments. Interestingly, the one ACLM participant with worsening of total semi-quantitative score had evidence of decreased extensor moment. However, reductions in net moment caused by a stiffening strategy may still lead to increased compressive forces that may have implications for knee health in the full ACLR and ACLD.

Conclusion: No evidence of degenerative changes was found in ACLM. However, individual's demonstrated degenerative changes in some features; this may suggest that OA is an end point but initiated and developed through different mechanisms.

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Glossary of Abbreviations.

3D	Three Dimensional
ACL	Anterior Cruciate Ligament
ACLD	Anterior Cruciate Ligament Deficient
ACLM	Anterior Cruciate Ligament MRi
ACLR	Anterior Cruciate Ligament Reconstructed
AMB	Anteromedial Band
AKSS	Acute Knee Screening Service
AL	Activity Level
ARUK BBC	Arthritis Research UK Biomechanics and Bioengineering Centre
BLOKS	Boston-Leeds Osteoarthritis Knee Score
BMA	Bone Marrow Abnormality
BOKS	Boston OA Knee Study
CGM	Clinical Gait Model
CLF	Central Lateral Femur
CLT	Central Lateral Tibia
CMF	Central Medial Femur
CMT	Central Medial Tibia
CUBRIC	Cardiff University Brain Research Imaging Centre
DMOADS	Disease Modifying Osteoarthritis Drugs
EMG	Electromyography
FOV	Field of View
FSE	Fast Spin Echo
GRF	Ground Reaction Force
ICC	Inter Class Correlation
IKDC	International Knee Documentation Committee
JSN	Joint Space Narrowing
JSW	Joint Space Width
Hz	Hertz
Kg	Kilogram
KOSS	Knee OA Scoring System
LAF	Lateral Anterior Femur
LAT	Lateral Anterior Tibia
LCF	Lateral Central Femur
LFTJ	Lateral Tibiofemoral Joint
LPF	Lateral Posterior Femur
m	Meter
mm	Millimeter
MAF	Medial Anterior Femur
MAT	Medial Anterior Tibia
MCF	Medial Central Femur

MDC	Minimum Detectable Change
MFTJ	Medial Tibofemoral Joint
MOAKS	MRi OA Knee Score
MOST	Multicentre OA Study
MPF	Medial Posterior Femur
MRi	Magnetic Resonance imaging
NISHCR CRC	National Institute of Social and Health Care Research Clinical Research Centre)
N.m	Newton meter
NHS	National Health Service
OA	Osteoarthritis
PC-IRT	Partial Credit Item Response Theory
PFJ	Patella Femoral Joint
PLB	Posterolateral Band
RCCK	Research Centre for Clinical Kinesiology
ROM	Range of Motion
s	Seconds
S.D	Standard Deviation
SE	Standard Error
SEM	Standardised Error of Measurement
SKA	Symptom and Knee Articulation
SLS	Single Leg Squat
SPGR	Spoiled Gradient Echo Sequence
SRM	Standard Response Mean
T	Tesla
TSK	Tampa Scale of Kinesiophobia
UK	United Kingdom
WORMS	Whole Organ Magnetic Resonance imaging Score

Chapter 1 Introduction.

Osteoarthritis (OA) is a physiological phenomenon diagnosed by both clinical and investigative criteria. Clinically, OA is defined as a narrowing of the joint line at greater than 50%, less than this is classified as pre-arthrosis (Louboutin et al., 2009). The classic view of OA being a degenerative disorder as a result of 'wear and tear' has been reviewed and is agreed that more complex dynamic mechanisms are involved involving biological, biochemical and biomechanical processes and these continue to be investigated (Ayral et al., 2005, Andriacchi et al., 2004). OA is associated with the progressive loss of articular cartilage, formation of osteophytes and joint remodelling with the corresponding symptoms of pain and functional movement loss (Dam et al., 2007, Louboutin et al. 2009, Hunter et al. 2006, Peterfy et al., 2004). Knee OA has been associated with several factors including age, body mass and previous trauma to the knee. Worldwide OA contributes greatly to disability, with OA of the knee being the most prevalent anatomical location (Louboutin et al., 2009). In the UK the prevalence of OA in the knee is cited as being more than 6 million people, accounting for approximately 10% of the UK's population at great expense to the NHS (Arthritis Research UK, 2014).

Limited knowledge exists about the initiation and progression of OA in the knee however previous knee injury, age, body mass and abnormal biomechanics have been cited as key risk factors for the development of OA (Hunter et al., 2006 and 2008). It is therefore important to understand and quantify the pathological changes made after trauma in the context of biomechanical adaptations. This information on 'pathological motion' could potentially supply a 'set of standards' to help in the diagnosis of musculoskeletal disorders and help determine the most effective treatment modalities (Andriacchi, 1990).

One of the most common forms of severe knee injury is that to the Anterior Cruciate Ligament (ACL), with incident rates being reported at approximately 30 per 100,000 of the population in the UK (Webb and Corry, 2000). In those with surgical repair, the re-rupture rate is cited as being between 2.3% to 13% in high level sporting populations depending on the demand of the sport (Myklebust and Bahr, 2005).

Injury to the ACL has been associated with degenerative knee changes and onset of early OA, although the underlying causal mechanisms for this remain theoretical in

principle. However this association has to be acknowledged, and several large scale studies have demonstrated that those with ACL injury go on to develop OA at an earlier time-point than would be expected in those having not suffered the injury. Lohmander et al., (2007) state that in a thorough evaluation of literature there is an obvious and profound association between ACL injury and development of early onset OA even after ACL reconstruction, despite the fact that subjective functional outcomes are improved when compared to those who remain deficient. Therefore a more in depth objective assessment of function, with more targeted outcome measures may give greater insight as to these underlying causal mechanisms.

Neuman et al. (2008) and Øiestad et al. (2010) in large scale epidemiological studies assessing which patients developed early OA after ACL injury and subsequent reconstruction, found that between 16 and 62% had developed radiographic OA within 15 years. Differences reported between studies have been correlated with associated risk factors, such as the removal of or severe repairs to the load bearing meniscus, with those having the meniscus removed having much increased rates of OA compared to those with no or only minor repairs.

Further knee trauma may also exacerbate the likelihood of OA occurring. This may take place in part due to incomplete rehabilitation, this can be caused by non-compliance to rehabilitation and/or the patient returning to demanding activities too soon. Returning to activity too soon may be self-imposed, or caused by clinical assessment errors as available outcome measures for identifying successful rehabilitation in the clinical setting may not be sensitive enough to detect insufficiencies in the ACL deficient (ACLD) or ACL reconstructed (ACLR) knee (Myklebust and Bahr, 2005). Thus meaning people are returning to sport too soon and underprepared for the demands of the sporting environment. Therefore the current study aimed to detect if differences in common activities performed during rehabilitation including gait and the more challenging activities of jogging and Single Leg Squatting (SLS) were evident post-rehabilitation. This may indicate that despite completion of rehabilitation biomechanical deficits exist in ACL injured participants that are potentially detrimental to long term knee health and a causal factor in the development of early onset OA.

Trying to generalise adaptation strategies in ACL injured patients is difficult due to differences in rehabilitation and/or surgical interventions and the time point from

injury/surgery at which the studies took place (Tashman et al., 2007; Rudolph et al., 2011; Risberg et al., 2009; Hurd and Snyder-Mackler., 2007). It appears that adaptations during jogging/running follow similar but exaggerated traits in ACL injured groups when compared with the findings from level gait (Karinikas et al., 2009; Rudolph et al., 2001; Berchuk et al., 1990), by avoiding full extension and decreasing knee moments. However literature on biomechanics in jogging on ACL injured groups is scarce and therefore this needs further evidence to help draw firm conclusions on adaptations or compensations in ACL injured groups in consideration of the above factors and in relations to the performance in other activities.

A vast majority of the studies on gait and jogging have focussed solely on sagittal plane kinematics and kinetics, therefore the present study has included frontal plane kinematic and kinetics to give a more thorough evaluation of adaptations within the knee. The SLS activity was included as despite its common use as an assessment tool in physiotherapy and rehabilitation settings to assess a patient's performance and map recovery after knee injury (Weeks et al., 2013), limited research has been conducted using the SLS. Despite its wide spread use, little is known about the validity and reliability of the SLS particularly with regard to comparing people with knee pathology to those with a healthy knee. The SLS is also challenging on the knee in a different way to gait and jogging requiring higher degrees of knee flexion.

Deficits for gait tend to have been reported in the short term after injury and indicative of a decrease in knee loading. More long term studies have shown indicators of knee loading can be returned to normal levels in ACLR and ACLD groups in lower demand activities like gait, however little is known about activities that place greater loading on the knee such as jogging and SLS in both these patient populations (Yamazaki et al. 2009). It may also be that a return to normal loading is detrimental to knee health if load distributing structures, such as the menisci, have been damaged transferring abnormal loads to the underlying cartilage or if a shift in loading has taken place on to areas of cartilage ill adapted to handle these loads (Andriacchi et al., 2006).

The most widely stated hypothesis as to why an ACL injury is associated with the development of early onset OA is an assumption that the stabilising role of the ACL, once disrupted may alter the normal movement pattern in the knee and that this change in loading, and/or shifting of the position of the femur on tibia, creates abnormal stresses through the knee cartilage and in turn leads to cartilage degeneration (Barrance

et al., 2006, Andriacchi et al., 2004; Andriachhi et al, 2009). However, to date no research study has attempted to link biomechanics, patient reported measures of function with longitudinal assessment of structures associated with degenerative knee change.

In the current study these potential deficits will be investigated using 3 Dimensional motion analysis. Both ACLD and ACLR groups will be assessed in terms of key performance, kinematic and kinetic outcome measures in comparison to controls. Evaluation of strength measurements and patient reported measures of knee function will also be analysed as these have been identified as risk factors for re-injury and also the development of OA (Louboutin et al., 2009). A sub-group of ACLR (ACLR2) was also assessed longitudinally at two time points' 12.9±1.8 months apart to investigate if biomechanics were altered or maintained, as this may have impacts for rehabilitation and long term knee health.

Changes in knee structures were measured in order to assess long term knee health and degenerative changes in structures that are associated with development of OA. This study has uniquely accessed MRi scans in a sub-group of ACLR (ACLM) that took part in the motion analysis aspect of the study in order to evaluate a battery of imaging diagnostic markers cited as potential indicators for the development of OA. Within the NHS setting at the time of suspected ACL rupture a patients' diagnosis is confirmed using MRi assessment. These diagnostic scans served as a starting point with which to compare to follow-up scanning undertaken at Cardiff University Brain Research Imaging Centre (CUBRIC), allowing an insight into long term changes in structures within the knee associated with degenerative change.

These scans were analysed using two methods; firstly a bespoke quantitative analysis routine which outlined cartilage in several MRi slices in the medial and lateral tibia and femur, from which measurements of regional cartilage thickness was undertaken. A second method adapted from the Whole Organ Magnetic Resonance Scoring tool (WORMS) which uses a semi-quantitative visual scoring of features, that are cited as being important in the development of OA (Peterfy et al., 2004). These features were also used by Bennell et al. (2011) and shown to have been associated with degenerative change in those with higher levels of dynamic knee loading in patients with OA. Features included cartilage morphology, meniscal integrity and bone marrow abnormality (BMA), these were again assessed in multiple regions in the tibiofemoral

joint. The methodology for the quantitative and semi-quantitative analysis is described in Chapter 4.16 and 4.17.

At present no disease modifying OA drugs (DMOADS) have been developed to combat OA. A combination of biochemical (cartilage matrix breakdown, volume and homogeneity) and MRI based markers (cartilage roughness, cartilage thickness, joint space width) have improved the diagnostic rate of OA and been used to map its progression. However different stages from initiation, progression and full scale OA, may show different prognostic and diagnostic markers that are affected by age, weight, genetics, trauma and biomechanics (Dam et al., 2009). The combination of this study's methodologies allows it to step into the gap between the pre-existing biomechanical literature, proposed theories for the development of OA after ACL injury and epidemiological findings assessing early OA in those having suffered an ACL injury alongside providing insight into the structural changes that take place in the knee in the early stages after ACL injury.

To extract the most information possible from the available data a case series style of analysis was undertaken in Chapter 7 and discussed in greater depth in Chapter 8. Although only a small number of participants could be assessed with MRi, this form of analysis allows for a deeper insight into an individual's changes in structures within the knee and how these were associated with the multiple risk factors associated with development of OA including demographics, motion analysis outcome measures, measurement of leg muscle strength and patient reported measures of function.

This was used to identify if common themes existed in those participants in the present study who had showed signs of degenerative change. This information can be used to generate more focussed outcome parameters with which to drive future research and to help create a deeper understanding of the risk factors and eventually mechanisms that influence the initiation, progression and the development of early onset OA in those suffering ACL injury.

This information could be used to help develop more targeted rehabilitation strategies that will allow patients to return to higher levels of function and in conjunction with long term monitoring of knee health identify those at risk of OA. If those at risk could be identified and the development of OA postponed, this could save the NHS millions of pounds and mean a reduction in clinical/surgical interventions in these patients, improving their quality of life in the long term.

Chapter 2 Literature Review (Part 1): ACL Injury and Biomechanics.

The search strategy for the following literature review can be found in Appendix 1.

2.1 ACL injury epidemiology.

Several studies have assessed the incidence of ACL injuries across a wide variety of sports. Lohmander et al. (2007) state that the highest incidence is seen in adolescents playing sports that require dynamic landing and pivoting such as basketball, football and skiing. It has also been noted that women have between a 3 to 5 time's higher risk of injuring their ACL than males when participating in these kind of sports.

In Denmark the annual incidence of ACL injury was reported to be approximately 30 people per 100,000 in 1991, based on in hospital clinical diagnosis of ACL rupture (Nielsen et al., 1991). A study in Sweden reported an annual incidence or 81 per 100,000 in the age range of 10-64 years (Frobell et al., 2007). This report by Frobell et al. (2007) used magnetic resonance imaging (MRi) to determine ACL injury, as opposed to solely clinical techniques as used by Nielsen et al. (1991). This could explain the disparity between the results as MRi is more accurate at detecting ACL ruptures in comparison to clinical assessment techniques (Frobell et al., 2007). In the UK an estimate of 30 ACL injuries per 100,000 people was reported by Webb and Corry (2000), this would lead to a figure of approximately 18,600 injuries in the UK per year.

Of those with complete ACL rupture incidence of OA from radiological findings (those showing degenerative changes in cartilage and bone from imaging without pain) is significantly higher than compared to symptomatic incidence (those patients presenting with pain). This demonstrates significant degenerative changes can take place in knee structures before the patient presents with symptoms of pain (Louboutin et al., 2009).

Lohmander et al. (2007) performed a systematic review of literature associating ACL injury with the development of radiographic OA. One hundred and twenty seven studies were identified (1970's to 2007), which included enough information from which to determine the level of development of OA. From the 127 studies reviewed the radiographic assessment methods were interpreted in terms of the Kellgren and

Lawrence (KL) criteria (Kellgen and Lawrence, 1957). The Kellgren and Lawrence system is a method of classifying the severity of knee osteoarthritis using five grades: Grade 0= No radiographic features of OA are present, Grade 1= Doubtful joint space narrowing (JSN) or possible osteophyte formation, Grade 2= Definite osteophytes and possible JSN, Grade 3= Multiple osteophytes, definite JSN, sclerosis, possible bony deformity, Grade 4=Large osteophytes, marked JSN, severe sclerosis and definite bony deformity (Kellgren and Lawrence, 1957). Lohmander et al. (2007) stated that OA was deemed to be present if the KL criteria JSN score was greater than grade 2, sum of osteophyte grades greater than 2, or a combination of a grade 1 JSN and a grade 1 osteophyte.

Lohmander et al. (2007) stated that there is an association between ACL injury and development of early onset OA and that reconstructive surgery does not appear to provide a protective mechanism against OA even if it is does improve functional knee outcomes in ACL injured groups. However one must be cautious in interpreting these results as data was collected from a number of studies with differing participant numbers and differing methodologies for determining OA, which in turn had to be standardised to the KL score for comparison (Lohmander et al., 2007).

Neuman et al. (2008) assessed 100 consecutive participants who had suffered an acute and complete ACL tear. These participants were observed over a period of 15 years with 23% having had an ACL reconstruction at a time point of an average of 4 years post injury. Neuman et al. (2008) discovered that 16% had developed radiographic OA in the tibiofemoral joint and all of these subjects had undergone a full meniscectomy. Interestingly participants who had not undergone meniscectomies had not developed tibiofemoral OA. This study concluded that activity modification combined with the non-removal of the meniscus created a favourable outcome in terms of OA development in ACL injured individuals.

Øiestad et al. (2010), as with Neuman et al. (2008), assessed participants for radiographic evidence of OA at a period of 10-15 years post ACL injury, however this group had all undergone reconstructive surgery. 181 participants were evaluated in the 10-15 year period following injury. It was discovered that in those with an isolated ACL injury, 62% had evidence of radiographic knee OA. Of those with associated meniscal and/or bone injuries in combination with the ACL rupture, 80% had radiographic signs of OA.

As with Neuman et al. (2008) the combination of injuries led to an increased prevalence of OA, but Øiestad et al. (2010) demonstrated a much higher prevalence of radiographic OA. This could be due to differences in methodology for assessing OA and as alluded to by Neuman et al. (2008) the time point at which the study took place. Øiestad et al. (2010) study took place much further from injury; consequently there was more time of exposure to the potential influences that cause the development of radiographic OA. Those with ACLR would also be more likely to return to higher levels of activity as well as more demanding activities; this could potentially cause degenerative damage if the knee is not fully stable, especially if other load bearing structures are damaged. This idea will be discussed in greater depth in forthcoming chapters.

2.2 ACL Anatomy and Dysfunctional Characteristics.

The ACL is one of the four major ligaments of the knee, along with the posterior cruciate ligament, lateral collateral ligament and the medial collateral ligament. The ACL is covered by a synovial membrane and its nerve supply is from the tibial nerve that penetrates the joint capsule and passes along the synovial sheath. Nerve fibres are present within the ACL ligament and are potential mediators in proprioceptive functioning (Karmani and Ember, 2003).

The ACL passes from the posterior aspect of the medial portion of the lateral femoral condyle and attaches in front of, and lateral to the anterior tibial spine. The ligament passes anteriorly, medially and distally from the femur to the tibia and is divided into two main groups. The anteromedial band (AMB) and the posterolateral band (PLB), when the knee is in extension the AMB is slack and the PLB is in tension, as the knee is flexed the PLB becomes slack and tension is present in the AMB (Karmani and Ember, 2003).

The knee ligaments, along with the nervous system and muscles, create a proprioceptive network creating stabilisation of the knee joint against external forces, damage to any one of these ligaments may potentially create severe instability in the knee (Karmani and Ember, 2003, Andriacchi et al., 2004). The ACL's main role is to provide stability against the anterior translation of tibia and is stressed by contraction of the quadriceps muscles; it is also active in determining the tibiofemoral axial rotation

with flexion of the knee (Beard et al., 1996, Barrance et al., 2006, Karmani and Ember, 2003).

2.3 A Developmental Framework for OA.

The primary hypothesis as to why the ACL injured knee is associated with the development of early onset OA is an assumption that once disrupted, the stabilising role of the ACL is reduced which ultimately increases loading, and/or shifting of the position of the femur on tibia, creating abnormal stresses through the knee cartilage leading to cartilage destruction (Barrance et al., 2006; Andriacchi et al., 2004; Andriachhi et al, 2009).

Andriacchi et al. (2004) proposed a framework for the 'in vivo pathomechanics of OA in the knee' including cellular 'biomarkers', which are a possible indicators of cartilage degeneration intrinsically linked to kinematic and kinetic parameters. In this framework, development of knee OA was broken down into two distinct phases, initiation and progression (Andriacchi et al., 2004). The initiation phase is started when healthy cartilage is exposed to injury or conditions which change the load bearing zones in the cartilage; this will in turn cause fibrillation of the cartilage and will occur more rapidly in acute cases where adaptation processes are unable to keep up with biomechanical alterations. There would then be a proposed increase in friction, which in turn would increase the sheer stress suffered by the cartilage, which is stated to affect regulation of metabolic factors.

The progression phase starts when the degenerative changes in the cartilage become more susceptible to damage caused by higher shear loads. Once knee OA is present, progression of OA will be enhanced by compressive loading, this is summarised in Figure 2.3.

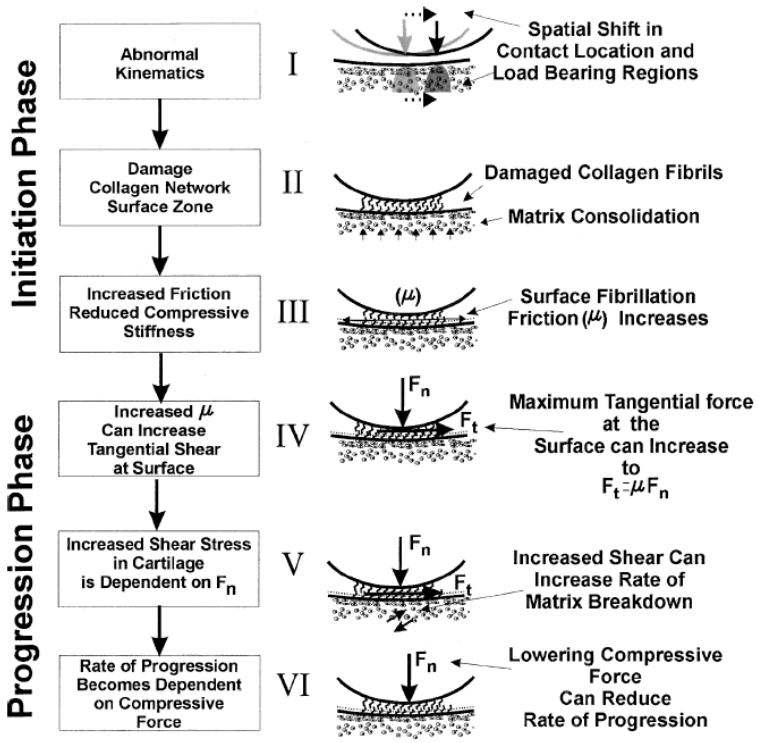


Figure 2.3 A Framework for the in Vivo Pathomechanics of Osteoarthritis at the Knee. This figure demonstrates a potential progressive path for OA in the knee. Reproduced with permission from Andriacchi et al. (2004).

This framework represents a mechanism by which changes will occur at a cellular level, however does not indicate the interrelationships between other factors that influence OA. If this pathway was supported by further research clinical practitioners could use the idea of lowering forces within the ACL injured knee to maintain better long term knee health by designing appropriate rehabilitation methods and advancing surgical techniques.

2.4 Mechanical Loading and OA.

In vivo measurement of knee loading and muscle activity, using knee kinematics, force measurement and Electromyography (EMG) can, when used in conjunction with each other, provide a detailed analysis of motion and muscle activity. Biomechanical assessment of participants may provide the opportunity to create a knowledge base of pathologies, across a number of disorders, as a result of musculoskeletal abnormalities. (Dennis et al., 2005).

Cartilage is at its thickest in the contact regions of the tibiofemoral joint. It has been demonstrated in several studies that cartilage thickness is influenced by loading and that abnormal loading causes cartilage changes (Kurz et al. 2005; Li et al. 2013; Andriacchi et al., 2009). The cartilage in the tibiofemoral plateau is thicker in the posterior portion of the lateral condyle and the anterior portion of the medial condyle. This is correlated strongly with tibiofemoral contact patterns during walking measured using computer modelling techniques (Andriacchi et al., 2004; Koo and Andriacchi, 2007). Kinematically, a proposed reason for the medial and lateral differences in peak cartilage thickness has been linked to the internal-external rotation that takes place during walking (Andriacchi et al., 2005; Scanlan and Andriacchi, 2011).

The internal peak knee abductor moment is typically larger than both the internal flexor and extensor moments and therefore is important when considering knee loading (Noyes et al., 1992). The internal peak knee abductor moment produced during walking has been shown to influence the loading of the medial and lateral parts of the knee (Andriacchi et al., 2004; Koo and Andriacchi, 2007) with OA most commonly occurring in the medial compartment, this has been related to an increase in internal peak knee abductor moments (Sharma et al., 1998; Mundermann et al., 2008).

Not only has a general link between abductor moment cartilage thickness and OA been discovered, it has been demonstrated that the internal knee abductor moment is predictive of clinical outcomes of treatment, severity of disease and disease progression (Sharma et al., 1998; Mundermann et al., 2008). The difference in response to load from healthy and medial compartment OA knees suggests that cartilage tissue responds differently once the degradation process has started to take place, signifying that cellular response is reduced and cannot adapt to the repetitive loads during walking.

Andriacchi et al. (2006) used a modelling approach to assess the potential impact on cartilage thickness of abnormal knee kinematics when comparing ACL injured to ACL intact knees. This combined participant specific gait data and finite element modelling of cartilage which was then exposed to simulated loads and measurements. Using this methodology Andriacchi et al. (2006) discovered that a rotational offset, which was evident in the ACLD group's kinematic data, created a significantly higher rate of cartilage loss when compared to those with an intact ACL without any differences in loading.

Although the cartilage loss was more rapid in those with ACLD , both the ACLD and ACL intact groups showed similar thinning patterns in the articular cartilage. The regions predicted for cartilage thinning initiated in the central region of the medial compartment and then moved to the medial boundary, which is where the first full cartilage thickness defects were discovered (Andriacchi et al., 2006). As with previous literature assessing cartilage degeneration patterns in clinical OA (Sharma et al., 1998; Mundermann et al., 2008) the primary area of degeneration was on the medial side of tibiofemoral joint, however an area of secondary wear was found on the central portion of the lateral aspect of the femur. The increased loss of cartilage on the medial side of the knee also caused a shift towards a more varus knee alignment throughout the progression of the simulation (Andriacchi et al., 2006).

Andriacchi et al. (2006) state that the data presented in the above study is supportive of the idea that rotational changes in knee kinematics in ACLD accelerated the process of cartilage degradation. This was specified to be caused by the shifting of contact locations from the thicker parts of the medial cartilage to areas of cartilage that are thinner and these areas not appropriately adapted to the increased stresses, thus accelerating cartilage loss compared to the intact ACL knee.

In addition to this Andriacchi et al. (2006) suggest that their results show a mechanical basis for the increased incidence of medial compartment OA in both ACLD and those with an intact ACL, caused by the morphologic variations in cartilage thickness and the difference in congruity between the medial and lateral compartments. This increased congruity in the medial compartment is cited as being a potential reason the medial compartment is more vulnerable to increased cartilage loss. Slight changes in tibiofemoral alignment create a much greater shift in contact location, compared to the less congruent lateral compartment, potentially to areas not well adapted to loading leading to cartilage breakdown.

The author suggests this paper should be evaluated in the context of the modelling assumptions that were made to both create and evaluate the cartilage model. The ‘thinning principles’ were based entirely on mechanical assumptions made at the early phase of gait when the knee is at its smallest degree of flexion and the ‘simple stresses’ that were applied may not take into consideration physiological loading in an in vivo situation. It is important to acknowledge that the modelling of the knee also did not

incorporate the menisci or other structures that will influence load distribution such as ligaments and musculature.

Andriacchi et al. (2006) acknowledged these limitations but stated that it was unlikely that adding more detail to the model, in terms of anatomy and more accurate representation of the load within the knee, would not likely influence the overall results of this study as it was comparing kinematic changes between the two groups under the same conditions. However the loads applied and resultant wear rates would be different in the physiological environment. Further to this Andriacchi et al. (2006) attempt to validate their assumptions by suggesting that the patterns of cartilage degeneration are the same as those discovered by participants with OA and in those who have early onset OA following ACL rupture. Andriacchi et al. (2009) suggest that evidence of early stage thinning may be a potential biomarker of the initiation phase of early OA in those with ACL rupture.

Assessment of cartilage has shown that areas that are loaded less during physical development are reported to have thinner and weaker cartilage structure (Bullough et al., 1992). Kinematic changes present in the ACL injured knee, may lead to changes in load distribution to areas of thinner cartilage not as effectively adapted to loading, this may play a role in the initiation and progression of early OA in ACL injured populations (Andriacchi et al, 2004; Chaudhari et al., 2008).

Hosseini et al. (2012) investigated the above hypotheses using dual fluoroscopy and MRi to create a 3D model of the tibiofemoral joint during a single leg lunge task in eight participants six months post-reconstruction. The uninjured limb was also assessed and used as the control condition. Hosseini et al. (2012) discovered that the ACLR knee demonstrated a combined lateral and posterior shift in peak contact deformation on the tibial plateau when compared to the uninjured knee. There was also a significant reduction in cartilage contact area and cartilage thickness in this contact area was thinner than in the uninjured knee. These results may support the idea that even though normal function is restored in some planes of motion, that deficits exist and that a shift in the contact location onto areas of cartilage that are unable to adapt to increases in loading may occur.

However, several limitations exist in this study; the small sample size makes meaningful conclusions difficult particularly applied to larger ACLR populations due to the strict inclusion and exclusion criteria imposed by this study. Also, although

contact locations were different no measures of loading were included in the analysis, therefore interpreting the loading conditions in the cartilage remains difficult. Finally, Hosseini et al. (2012) acknowledge that the task performed may not be representative of other more commonly performed tasks such as gait, jogging and hopping so interpretation of these results in other activities must be applied with caution.

In conclusion changes in loading using 3D computer models of ACL injured groups have demonstrated potential causal mechanisms by which this injury may initiate the progression of OA. However, these studies are limited by small sample size and lack of accurate representation of internal knee loading.

2.5 Spatiotemporal, Kinematic and Kinetic Patterns in Healthy Populations.

In order to understand pathological gait it is important to understand gait in healthy people. This chapter will describe spatiotemporal parameters used in gait analysis, as well as normal knee kinematics and kinetics, in order to set a background to which literature assessing gait and jogging in ACL injured groups, can be interpreted.

2.5.1 Spatiotemporal Parameters.

The gait cycle can broadly be defined at different stages that occur during a normal stride. A stride is defined as one foot being placed on the floor, then weight shifted onto the opposite limb (a step) and then returning weight to the first limb (Perry and Burnfield., 2010). This in turn is broken down into the stance phase (the point at which a foot touches the floor to the point at which the toe leaves the floor) which consists of around 60% of the gait cycle, and a swing phase when the foot is not in contact with the ground. In normal gait there is a period of time accounting for around 30% of the gait cycle when only one foot is in contact with the floor (from around 15-45% of the gait cycle), this is known as single support/stance (Perry and Burnfield, 2010).

Primarily, research into those suspected of having abnormal knee function is focused upon how the knee functions under loading conditions during the stance phase of gait and therefore the further subdivisions of gait from this point will focus upon this phase. The stance phase is often divided into initial contact or heel strike, loading response, mid stance, terminal stance and pre-swing (Perry and Burnfield, 2010).

2.5.2 Initial contact/Heel Strike.

During initial contact the primary task being performed by the limb is acceptance of weight being transferred from one limb to the other, to decelerate the limb and absorb impact. The hip is flexed and the knee is at minimum flexion, the ankle is dorsiflexed towards a neutral position. At this stage the other limb is in the pre-swing phase (Perry and Burnfield, 2010). The knee is at an angle close to 0 degrees, and internal knee moments at this point start to typically produce an internal knee flexor moment in response to the sagittal ground reaction force (GRF) acting anteriorly to the centre of the knee.

2.5.2 Loading Response.

During loading response the primary objectives of the limb are to absorb the impact of the weight transfer, to provide initial stability and to preserve enough momentum to ensure efficient progression of the gait cycle. The knee flexes from full extension to a position of flexion, whilst using the heel as a 'rocker' whilst the foot moves from a neutral to a position of plantar flexion in preparation for the next phase of gait (Perry and Burnfield, 2010). During this phase the net knee moment shifts rapidly from internal knee flexor moment toward a neutral knee moment, as the knee flexes an internal knee extensor moment is created in response to the GRF acting posteriorly in relation to the knee centre. This moment is typically largest at a point coinciding with peak knee flexion angle (Figure 2.5.4) (Craik and Otis, 1995).

2.5.3 Mid-stance and Terminal Stance.

Mid-stance and terminal stance combined represent the period of the gait cycle known as single limb support. Mid-stance begins when the opposite limb leaves the ground and continues until the centre of mass is aligned over the forefoot. The primary objectives during this phase are the progression of the limb and trunk, in a stable manner, over the static foot. The hip extends and the knee transfers from a position of flexion into near full extension as the foot dorsiflexes, providing forward momentum (Perry and Burnfield, 2010).

Terminal stance begins at the point the heel lifts off the ground and continues until the opposite heel strikes the ground, the bodyweight shifts towards the front of the foot, creating a forefoot rocker. The knee moves to a point of minimum flexion before again starting a new trajectory towards flexion. An increase in hip extension also puts the limb in a trailing position (Perry and Burnfield, 2010; Craik and Otis, 1995). During this phase the internal knee moment shifts from a peak internal extensor moment (at

peak knee flexion), to a neutral net knee moment and as the GRF forces the knee into minimum flexion. As the heel lifts off the ground, a peak internal knee flexor moment is produced (Figure 2.5.4) (Perry and Burnfield, 2010; Craik and Otis, 1995).

2.5.4 Pre-swing.

Pre-swing is the final phase of stance. The limb of interest responds to the shift in bodyweight to the opposite leg with an increase in plantar flexion, knee flexion and a reduction in hip extension. At this point the opposite limb is in a loading response. This phase is primarily to ensure progression of the gait cycle with a push off that not only propels the body forward but also prepares the limb for the swing phase (Craik and Otis, 1995; Perry and Burnfield, 2010).

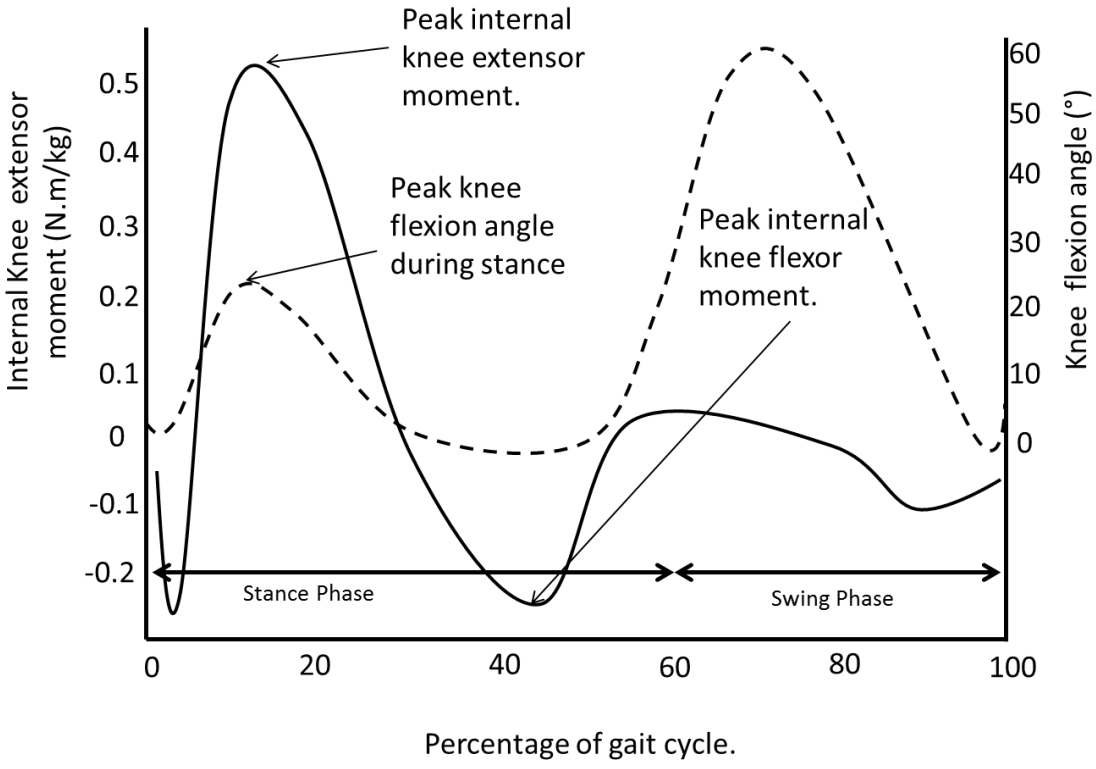


Figure 2.5.4 Sagittal plane knee moments and angles during gait.
Typical healthy internal knee extensor and flexor moment profile for gait (thick black line) alongside knee flexion angle profile (dashed black line). Peak internal knee extensor and flexor moments are shown corresponding with peak and minimum knee flexion angles during the stance phase. Adapted from Craik and Otis (1995) and Perry and Burnfield (2010).

2.5.5 Frontal Plane Mechanics.

Frontal plane internal knee moments (abductor moments) typically follow a double 'hump' pattern. These double humps correspond to key points in the sagittal plane motion of gait. The first and largest internal knee abductor moment (Figure 2.5.5) typically corresponds to the internal peak knee extensor moment shown above in Figure 2.5.4. The second internal knee abductor moment peak also coincides with the peak internal knee flexor moment demonstrated in the sagittal plane.

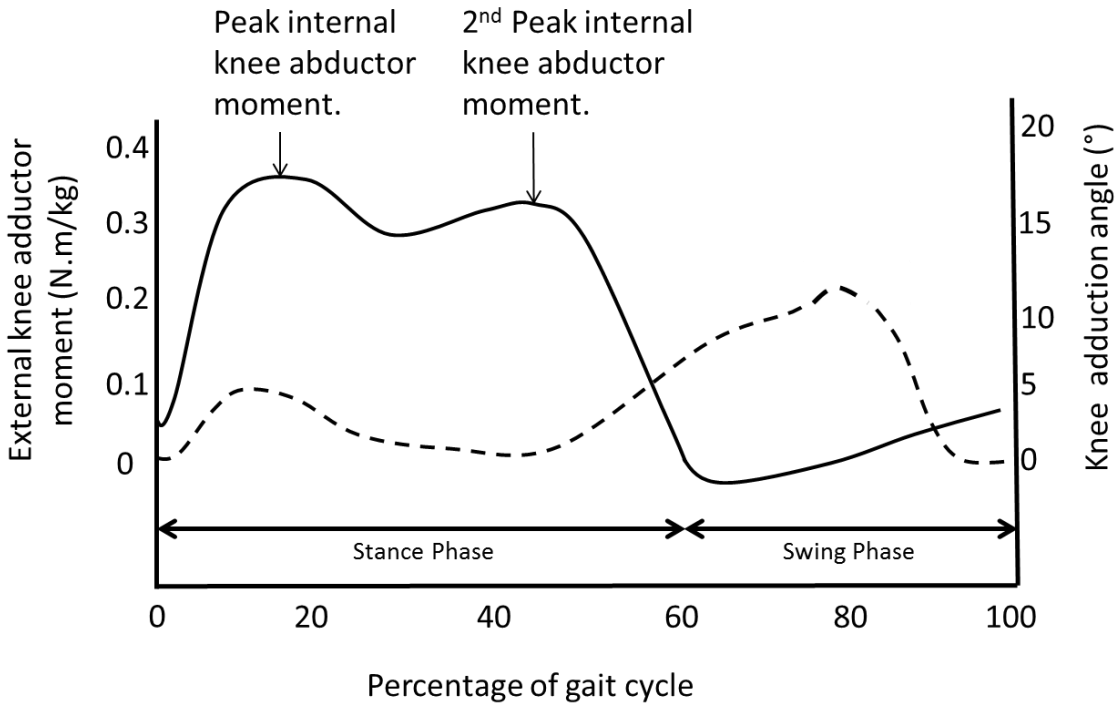


Figure 2.5.5 Frontal plane knee moment and angles during gait. Typical healthy internal knee abductor moment profile for gait (thick black line) alongside knee adduction angle profile (dashed black lines). First and second peak internal knee abductor moments are shown. Adapted from Perry and Burnfield, (2010).

It is worth noting that during jogging the knee follows the same pattern in the sagittal plane as during gait. However, the magnitudes of flexion angles and in turn internal

knee moments are markedly increased due to the increased knee angles and accelerations at the knee (Bush-Joseph et al., 2001). In the frontal plane the same for the first peak is also true however during jogging there is typically an absence of the second peak internal abductor moment (Bush-Joseph et al., 2001).

2.6 Gait and Jogging Adaptations in ACL Injured Groups.

2.6.1 Introduction.

This chapter aims to critically appraise research that evaluates the performance, kinematics and kinetic adaptations during level gait, jogging and SLS that take place in groups that have an ACL injury. This secton will focus upon literature evaluating groups that have had surgical intervention (ACLR), on groups who have had conservative treatment of their ACL injury (ACLD) and finally evaluating the few studies that have assessed the same participants in both the pre and post-surgical conditions.

From the literature reviewed the spatiotemporal outcomes measures used as indicators of gait performance, include gait velocity, stride length and stride time, single support time, double support time and cadence. Kinematic variables included knee flexion-extension, abduction-adduction and internal-external rotation angles. Kinetic variables covered a wide variety of outcomes including ground reaction forces in the vertical, anterior-posterior and medial-lateral planes, flexor and extensor, abductor-adductor and internal-external rotation moments.

Different studies have focused upon assessing kinematic and kinetic peaks and troughs across a selection of the varying points within the gait cycle described in Chapter 2.4. This does not only apply to analysis of maximum and minimum values of angles, moments and power, but also using variability measures such as range of motion (ROM) with which to compare injured participants with their healthy counterparts. Direct comparison of the same outcome measure values between studies can also be difficult. This is primarily due to the different normalisation techniques that are employed.

Some studies use absolute values, others use moments in relation to body mass, bodyweight or as a percentage of body mass or weight. These may also be further

normalised to either leg length or height. Alongside this there are different methods of data collection (2D and 3D) and mathematical methods for calculating performance, kinematic and kinetic values. Due to these factors results will generally be reported in this chapter in relation to increases and decreases in outcome measures of the ACL injured groups when compared to the controls (or in some studies the contralateral limb) within that specific study.

2.7 Gait and Jogging Spatiotemporal Adaptations in ACL Injured Groups.

2.7.1 Gait and Jogging Spatiotemporal Adaptations in ACLR.

Assessing spatiotemporal outcomes in ACLR Bush-Joseph et al. (2001), Georgoulis et al. (2003) and Butler et al. (2009) found that there were no significant differences in walking velocity between ACLR and controls, with Georgoulis et al., (2003) also demonstrating no differences in cadence between the ACLR group and controls. Webster and Feller (2011) also found in an analysis of both hamstring and patella graft ACLR groups there was no significant differences in walking velocity between the ACLR group and controls regardless of graft type.

Contrary to this Gao et al. (2010) demonstrated significant differences exist with regard to support times, with the ACLR group demonstrating a reduction in single leg support time on the injured limb and also an increase in duration of double leg support when compared to controls. There was however no difference between the injured and uninjured limb. Gao et al. (2010) hypothesised the shorter step length demonstrated in the ACLR group may be due to a reduction in extension during the stance phase and at the end of the swing phase. They also suggested that the non-injured limb had developed compensatory patterns alongside the injured limb.

Tashman et al. (2004) state that jogging is a more demanding activity mechanically on the knee joint and in turn the ACL graft than gait. Jogging also eliminates the double support phase of gait, which reduces the effect of adaptations or compensations that may be associated with the contralateral limb. Studies assessing performance of ACLR groups during jogging and running are limited in number. Bush-Joseph et al. (2001) assessed kinematics at a participant's self-selected jogging speed and they found that no significant differences existed between the ACLR group and controls (2.7m/s ACLR

vs 2.58m/s controls).

2.7.2 Gait and Jogging Spatiotemporal Adaptations in ACLD.

The studies mentioned below assessing ACLD have found a walking velocity of between 1.12-1.39m/s, which was found to be not significantly different to controls (Von Porat et al., 2006; Fuentes et al., 2011; Lindstrom et al., 2010; Roberts et al., 1999). In comparison to the gait velocity of the ACLR and controls in the studies reviewed above it can be seen that these values are within a similar range (ACLD 1.12-1.3 vs. ACLR 1.12-1.49m/s). Roberts et al. (1999), Von Porat et al. (2006) Alkjaer et al. (2003) and Georgoulis et al. (2003) also found no differences between ACLD and control groups with regard to other gait parameters such as cadence, step length, stance phase percentage and single and double support times.

Interestingly Lindstrom et al. (2010) did find a significant difference in gait velocity between men and women in their ACLD group, which was non-significant in the controls. Lindstrom et al. (2010) postulate that healthy females maintain a gait velocity similar to males by increasing their stride length and cadence, this may not have been possible in the ACLD female group due to restrictions in motion caused by the ACLD knee. Gao et al. (2010) also discovered a slower step speed and decreased step length when comparing the ACLD group to controls. As described for their ACLR group this may be due to a reduction in extension during the stance phase and at the end of the swing phase. The potential mechanisms that may protect the injured knee by avoiding full extension will be described in greater depth in Chapter 2.8.

Several other studies assessing gait in ACLD participants have not discussed the gait parameters other than to inform the reader as to whether the participants had walked at a self-selected gait velocity (Muneta et al., 1998; Berchuk et al., 1990; Beard et al., 1996), whilst other studies opted to use a standardised walking velocity. In the case of Wexler et al. (1998) this was chosen to be 1.1m/s and Alkjaer et al. (2003) selected a velocity of 1.25m/s. The potential influence of standardising walking velocity versus self-selected velocity on kinematics and kinetic parameters should be considered when interpreting the kinematic and/or kinetic results of these studies.

Assessing jogging performance in ACLD groups has been undertaken in a limited

amount of studies; Rudolph et al. (2001) assessed jogging performance in ACLD copers and non-copers versus controls at a self-selected jogging velocity. ACLD have been broadly categorised into three groups, copers, non-copers and adapters. Copers are those who return to normal sporting activities without episodes of giving way at the knee. Non-copers are those who have frequent episodes of giving way even during activities of daily living. Adapters are those who do not have episodes of giving way in activities of daily living but have modified their sporting activity as they experience knee instability in more demanding cutting and pivoting activities (Rudolph et al., 2001; Hurd and Snyder-Mackler, 2007; Button et al., 2008).

Rudolph et al. (2001) found no significant differences in velocity between copers and non-copers at 4 and 4.1m/s respectively (when velocity was normalised to leg length); this was however significantly slower than the controls who jogged with a velocity of approximately 4.8m/s. Stride length was also significantly shorter in the involved limb versus the contralateral limb in both copers and non-copers. Patel et al. (2003) and Berchuk et al. (1990) found that their ACLD group jogged at 2.6m/s and 2.8m/s respectively and in both studies this was not significantly different to their controls. These studies are contrary to the findings of Rudolph et al. (2001), although it is difficult to compare these studies as Rudolph et al., (2001) used a normalised jogging velocity per participants leg length whereas Patel et al. (2003) and Berchuk et al. (1990) used the participants absolute gait velocity and unlike Rudolph et al. (2001) these studies also did not describe any other temporal characteristics during jogging.

The results for jogging velocity in ACLD groups and their respective controls seem to be comparable with that of the ACLR studies described previously. The research described above also suggests that both ACL injured groups, regardless of surgical or conservative treatment modalities are capable of returning to normal jogging velocities. Therefore, kinematic and kinetic data is more easily comparable, as it is less likely to be influenced by adaptations in jogging velocity, in response to ACL injury and/or subsequent repair.

2.8 Gait and Jogging Kinematics in ACL Injured Groups.

2.8.1 Kinematics Adaptations in ACLR.

Variations in knee extension angles between ACLR and controls have been revealed in

some studies, with terminal stance knee flexion angle demonstrating significant increases in the ACLR group (Bush-Joseph et al., 2001). Alterations in knee flexion angle were noted by Karinikas et al. (2009) who found a significantly increased knee ROM when compared to controls. Karinikas et al. (2009) followed up these participants longitudinally at 6-12 and 12+ months post-surgery. At 6-12 months some kinematic differences still existed but at the 12+ month assessment all values for knee flexion angles had returned to non-significance compared to the uninjured leg.
However, Karinikas et al. (2009) used a standardised walking speed of 1m/s with all participants which can be considered a slower than normal walking speed, with self-selected mean walking speeds from other studies ranging between 1.12-1.49m/s. These walking speeds being outside the normal ranges may potentially influence gait mechanics, and any significant findings may not be truly representative of the kinematics and kinetic strategies employed by those with ACLR.

Devita et al. (1998) found that kinematics at the ankle, knee and hip had returned to normal patterns in the ACLR group six months after injury, which was supported by findings from Karinikas et al. (2009). Gao et al. (2010) also found that no differences in knee flexion pattern existed between the ACLR group and controls, although they did discover that the ACLR group demonstrated a significantly higher value of minimum knee flexion which was related to the shorter step length described previously for this cohort. There was also a significant timing offset in the ACLR group with the second flexion peak and toe off being delayed by approximately 2% of the gait cycle.

Several other studies have also demonstrated no differences in ACLR sagittal plane kinematics at the knee when compared to controls. This has been reported with regard to knee flexion angles during gait including; knee flexion angle at heel strike, knee flexion angle during loading response, peak knee flexion angle during mid-stance, knee flexion angle at toe off and peak knee flexion angle during swing phase (Bush-Joseph et al., 2001; Georgoulis et al., 2003 Webster et al., 2011).

A majority of studies assessing kinematics in ACL injured groups have focussed upon sagittal plane mechanics. More recently with the development of 3D motion analysis systems researchers are now able to analyse kinematics and kinetics in the frontal and axial planes of motion. At the time of writing few studies have assessed frontal and

axial kinematics in those with ACLR. Webster and Feller (2011) found that in the hamstring tendon reconstructed group a significantly reduced adduction angle compared to both a patella reconstructed group and controls throughout the stance phase of gait, although there was no difference between the patella tendon reconstructed group and controls.

Differences in the internal-external rotation of the knee have been demonstrated in ACLR groups, with a reduction in external tibial rotation, this was discovered throughout the stance phase and was found to be significantly reduced during the toe off phase of gait (Webster and Feller 2011; Gao et al, 2010) and mid-stance when compared to the contralateral knee (Webster and Feller, 2011). Webster and Feller (2011) found that 86% of their ACLR group had internal tibial rotations that were less than the mean for the uninjured knee and the controls. Georgoulis et al. (2003) also found a non-significant trend for increased internal tibial rotation.
It is worth noting that in the studies that have reported an increase in internal rotation there were separate controls and those that reported a decrease in internal rotation used the contra-lateral leg as control. This suggests that adaptations may take place in the uninjured leg and this may affect the interpretation of differences in the rotational kinematics as these values are given relatively to the uninjured limb when this is used as a control.

Gao et al. (2010) speculate that the offset in tibial rotation could be caused by an abnormally functioning ACL. The normal ACL has an oblique medial orientation from the tibia to the femur, if this orientation was not accurately recreated this could lead to offsets in rotation and a more internally rotated tibial position. Webster and Feller (2011) suggest that different placement of the graft and the type of graft used (single vs double bundle), may be capable of influencing knee kinematics and further research needs to be undertaken on surgical procedures in order to optimise knee motion after reconstruction. Alterations in tibial rotation patterns could potentially alter the tibiofemoral contact pattern. An example given by Gao et al. (2010) was that if the tibia had increased tibial rotation, this could shift the contact location to a more anterior position in the medial compartment of the tibial plateau. This would also lead to a more posterior contact location on the tibial plateau in the lateral compartment. It has been hypothesised that this shift in contact location could cause abnormal loading of cartilage that is ill adapted to this type of compressive loading, and repeated cycles of

abnormal loading could lead to the initiation of OA (Gao et al., 2010; Webster and Feller, 2011).

During jogging Karinikas et al. (2009) demonstrated a reduced range of motion in the injured versus contralateral limb in a period three to six months post ACL reconstruction, corresponding with significantly lower knee flexion and extension angles during the stance phase of jogging. At six to 12 months post injury these deficits in the injured versus contralateral limb still existed. However, at 12 months no differences in kinematics between limbs were evident. The aforementioned studies demonstrate that functional adaptations were more evident in more demanding activities. However, it is still an area of debate as to whether targeting a return to normal knee biomechanics is a positive or negative thing for the long term knee health of ACL injured groups, especially those who return to more demanding activities.

Karinikas et al. (2009) also demonstrates the importance that time since injury may have on the results of studies assessing function during jogging in ACL injured groups, as the participants assessed only recovered to normal knee biomechanics and strength at a time period over 12 months since their surgery. During running the subjects demonstrated a changed motor strategy which was time dependant, initially reducing knee angles and ROM. As there is normally an increase in knee joint angles and ROM during running when compared to gait, the initial restriction in knee ROM may be a protective strategy to reduce knee loading. Karinikas et al. (2009) demonstrated a correlation between muscle strength and knee angles, this may suggest that muscle strength is important in early stages of recovery in returning to a more normal knee function, but adaptations are reliant on more complex mechanisms than muscle strength alone.

Tashman et al. (2007) assessed downhill running at 2.5m/s, in 16 ACLR (6 females, 10 males) with a mixture of both patella (n=7) and hamstring reconstructions (n=9) at a period of five and 12 months post-surgery. Tashman et al., (2007) reported that ACLR group's knees at both time points demonstrated significantly increased knee adduction and external rotation angles when compared to the uninjured limb and there was no significant change between measurement times. However, no significant difference was found between limbs with regard to flexion and extension angles and this again did not vary with time. This was contrary to the results of Karinikas et al., (2009) at around 5-6

months post-surgery, however findings were similar at the one year time period for flexion and extension angles. Karinikas et al. (2009) did not investigate adduction or rotation angles at the knee. This emphasises the importance of assessing motion at the knee in more than just the sagittal plane, as differences may exist in other planes of motion in ACL injured groups.

2.8.2 Kinematics Adaptations in ACLD.

Several studies have assessed the sagittal plane kinematics in ACLD groups. Studies have evaluated changes in knee, hip and ankle kinematics, compared to either controls or the contralateral limb. Several studies have demonstrated kinematic changes at the knee in ACLD (Rudolph et al., 2001; Risberg et al., 2009; Hurd and Snyder-Mackler., 2007).

Rudolph et al. (2001) assessed ACLD divided into copers, non-copers and adapters. They found that non-copers produced less knee flexion excursion when compared to their contralateral limbs, and also to that of both the copers injured limb and the controls throughout the gait cycle. At heel strike, and during the loading response, no differences were found in the ACLD group's knee flexion angle when compared to the control condition (Georgoulis et al., 2003; Von Porat et al., 2006; Lindstrom et al., 2010; Muneta et al., 1998; Berchuk et al., 1990; Beard et al., 1996; Roberts et al., 1999; Hurd and Snyder-Mackler, 2007).

Hurd and Snyder-Mackler (2007) and Rudolph et al. (2001) described a stiffening strategy linked to a co-contraction of the quadriceps and hamstrings in non-copers. Hurd and Snyder-Mackler (2007) state that these co-contractions could result in higher knee forces, which may stabilise the knee, but also potentially overload knee cartilage, it remains to be seen if the adaptation strategies implemented in ACLD are protective or are detrimental to long term knee health.

Contrary to this Button et al. (2008) found that non-copers increased knee flexion at heel strike when compared to copers and adapters, although no controls were used for comparison. The increases in knee flexion angle described by Button et al. (2008) may be reflective of a decrease in quadriceps and hip extensor strength in their ACLD group.

An increase in knee flexion angle may also be a strategy to place the knee in a more

favourable position to increase hamstring activation and in turn increase knee stability. Beard et al. (1996) also demonstrated an increase in knee flexion angle and that hamstring activity in the ACLD limb was correlated with minimum knee flexion angle. Interestingly, EMG activity in the quadriceps was normal in the ACLD limb when compared to controls, this is contrary to the idea of quadriceps avoidance gait, and instead an increased activation of the hamstrings was cited as a potential aid to knee stabilisation.

During the mid-stance phase of gait Hurd and Snyder-Mackler (2007) and Beard et al. (1996) reported a significant increase in peak knee flexion angle in ACLD group's when compared to the controls. Alkjaer et al., (2003) also described a significant increase in peak mid-stance knee flexion angle in the ACLD copers when compared to controls; however the ACLD non-copers presented with no differences when compared to the controls.

Contrary to the studies above Berchuk et al. (1990) state that the ACLD group demonstrated a significant decrease in peak mid-stance knee flexion angle compared to controls but not when compared to the contralateral limb. Wexler et al. (1998) and Muneta et al. (1998) demonstrated that the ACLD group they investigated had no differences compared to controls in peak knee flexion angles throughout the stance phase of gait. During the terminal phase of stance Georgoulis et al. (2003) also found no differences in peak knee angles between the ACLD group and controls, which was supported by Lindstrom et al. (2010). This may indicate that when assessing ACLD for adaptations in groups that are not sub-divided by function, adaptations may not be discovered due to the influence of the overall group containing a mixture of copers, non-copers and adapters, washing out any strategies these sub-groups may exhibit.

Several studies have found that ACLD had a significantly higher knee flexion angle during terminal stance compared to the controls (Fuentes et al., 2011; Georgoulis et al., 2003; Lindstrom et al., 2010; Beard et al., 1996). The terminal stance phase of gait occurs at near full knee extension which submits the knee to an internal tibial torque that in the intact knee places strain through the ACL (Fuentes et al., 2011). In the absence of the ACL Fuentes et al., (2011) state that knee stability is dependent on the remaining structures in the knee, both the remaining passive structures such as the ligaments and menisci alongside active muscular control. These secondary knee

restraints have been reported to be less effective near full extension, an example of which would be the hamstring being a less effective synergist to mechanical stress in the ACL when nearing full extension (Fuentes et al., 2011). For this reason if ACLD subjects were to maintain normal knee kinematics and kinetics this may increase their vulnerability to further injury, thus adaptation strategies such as the one described by Fuentes et al. (2011) may be employed to avoid excessive knee loading and prevent long term degenerative changes to other structures which may influence the development of OA.

With regards to minimum knee flexion angle Gao et al. (2010) demonstrated that their ACLD groups were significantly less extended (more flexed) at the knee during the majority of mid-stance. This finding was also described by Muneta et al. (1998) and Roberts et al. (1999). Fuentes et al. (2011) also discovered significantly less knee extension during the terminal phase of gait. Wexler et al., (1998) demonstrated a time dependant decrease in knee extension angle between early and chronic ACLD groups. This increase in minimum knee flexion angle could again be representative of a strategy to protect the knee joint in the absence of the ACL, allowing a decrease in loading at the knee as described by Fuentes et al. (2011).

A shortfall in literature exists with regard to kinematics in both the frontal and axial planes of motion. Georgoulis et al. (2003) found no significant differences in peak knee adduction angles during gait when compared to controls throughout the entire gait cycle and these results were supported by Roberts et al. (1999). However Gao et al. (2010) found a significant increase in knee adduction angle in the ACLD group compared to controls during the stance phase of gait. It is proposed in those with an increase in adduction angles, there is an association with increased loading in the medial compartment of the knee which has been linked to degenerative OA changes in the knee (Webster et al., 2011; Butler et al., 2009).

Differences in rotational angles have been discovered by several studies. Georgoulis et al. (2003) found significant increases in internal tibial rotation compared to both controls and the ACLR group, taking the pattern of motion from external to internal rotation. Contrary to this Roberts et al. (1990) reported that their ACLD group demonstrated a decrease in maximum internal rotation and an increase in external knee rotation angles compared to controls. As described by Andriacchi et al. (2006), it may

be that rotational abnormalities at the knee are a key initiator in the progression of OA in ACL injured populations, as areas of the cartilage not commonly loaded may be subjected to increase loads they are not adapted to withstand. The studies discussed above have demonstrated different findings with regard to potential adaptations and/or deficits with regards to knee kinematics throughout the gait cycle in ACLD groups. There are many potential reasons for the disparity of these finding, these will be discussed in greater depth at the end of this chapter.

Only two studies in the literature had assessed knee kinematics during jogging in ACLD groups. Rudolph et al. (2001) suggested that non-copers demonstrated a trend towards less knee flexion at heel strike and a reduction in early stance peak knee flexion angle, whilst copers had similar knee kinematics compared to controls. Berchuck et al. (1990) also found no significant differences at the hip and knee with regard to angles of both the injured, uninjured and controls during the stance phase of running. With little literature in this activity it is difficult to assess the differences in kinematics and the potential strategies that may be employed in response to ACL injury. The reduction in knee angle may be representative of the previously described stiffening strategy to stabilise the knee joint in more dynamic activities, however more studies are needed to increase the understanding of kinematic adaptations during jogging (Hurd and Snyder-Mackler 2007; Fuentes et al., 2011).

2.9 Gait and Jogging Kinetics in ACL Injured Groups.

2.9.1 Kinetic Adaptations in ACLR.

Studies that have assessed kinetics in ACLR are small in number and have, as with kinematics, primarily focussed upon the sagittal plane. Bush-Joseph et al. (2001) found that the peak mid-stance internal extensor moment was slightly reduced and only 2 of their ACLR group demonstrated a quadriceps avoidance style of gait. This is partly characterised by a reduction in internal knee extensor moment, and has been reported as an adaptation strategy in those who are characterised as ACLD (Berchuck et al., 1990).

Devita et al. (1998) demonstrated that immediately post ACL surgery (before proper rehabilitation) internal knee extensor moment decreased to 57% of the controls. After rehabilitation knee extensor moment improved generally to the level of controls

throughout the stance phase of gait, but significant differences between these groups occurred at mid-stance. In the pre-rehabilitation condition ankle and hip extensor moments were analysed and the hip extensor moment increased to 37% greater than controls with no differences detected at the ankle. This created an overall effect of a comparable lower limb support moment in the ACLR group in relation to the controls.

Several studies have shown that in the sagittal plane no differences existed between ACLR and controls and that normal movement patterns in this plane had been restored (Devita et al., 1998; Karinikas et al., 2009; Georgoulis et al., 2003; Webster and Feller, 2011). Devita et al. (1998) state that although sagittal plane kinematics may be restored in ACLR this may not be representative of the loading and work patterns at the knee, and that it is these adaptations in loading that may cause future pathology. Devita et al. (1998) suggest the stress within the ACL is proportionate to the knee extensor force. The reduction in extensor moment noted in this study may therefore be a strategy to reduce stress through the knee joint, thus providing a protective mechanism. Karinikas et al. (2009) state a similar hypothesis for adaptation in the early stages of recovery after ACL reconstruction.

Bush-Joseph et al. (2001) found that no differences in loading at the knee occurred in their ACLR group and state that adaptations may be related to time since injury and surgery. This theory is supported by the work of Karinikas et al. (2009) who demonstrated a time dependant return to normal gait patterns. Georgoulis et al. (2003) suggest that if kinematics and kinetics are restored to normative values in ACLR, reconstructive surgery may be able to prevent abnormal knee loading and protect against further pathology. They also state that caution must be demonstrated when investigating solely sagittal plane kinematics and kinetics, as these do not allow a full and thorough analysis of the potential adaptations that occur after ACL injury which may take place in both the frontal and/or axial plane.

Butler et al. (2009) found that the ACLR group had significantly increased peak internal knee abductor moment when compared to controls. No other differences were found in frontal or sagittal plane kinematics or kinetics at the knee relating to both gender and ACL injury. Butler et al. (2009) state that this abnormal internal knee abductor loading may increase forces in the medial compartment and be a potential initiator for the development of OA. Contrary to this Webster et al. (2011) showed no

differences in knee abductor loading. They did acknowledge as only the contralateral limb was used as a control, adaptations may have taken place in the opposite limb so values may not be comparable to controls. The increased abductor moment in females may also make them more susceptible to developing OA due to the increased loading that may occur in the medial compartment.

Of the studies on jogging in ACLR only Bush-Joseph et al. (2001) assessed knee kinetics and demonstrated that the ACLR group significantly decreased their internal extensor moment which was more pronounced in jogging than in gait. The magnitude of internal extensor moment was found to be correlated with isokinetic measures of quadriceps muscle strength pertaining to those who had the weakest quadriceps demonstrating the largest reduction in internal extensor moment. No differences were found with regard to peak internal flexor moments between groups.

This demonstrates that in ACLR individuals whom are likely to be more active and return to higher levels of activity, assessing solely gait may not give a sufficiently thorough analysis to determine if kinematics and kinetics are appropriately restored after surgery. If adaptations exist in more dynamic activities, the author suggests this reduction in internal extensor moment may be acting as a protective strategy to prevent excessive loading in the ACL graft. This may have knock on effects on both performance on return to activity and implications for long term knee health.

2.9.2 Kinetic Adaptations in ACLD.

During gait Risberg et al. (2009), Hurd and Snyder-Mackler (2007) and Andriacchi and Dyrby (2005) found that internal knee extensor moments in the injured limb were lower than the uninjured limb, although Risberg et al. (2009) found this returned to a similar value after rehabilitation. In accordance with this Alkjaer et al. (2003) found a significantly decreased peak internal knee extensor moment during the stance phase of gait in ACLD when compared to controls. Peak knee extensor moment was significantly related to the peak knee flexion angle and at a given knee flexion angle controls produced significantly larger extensor moments than non-copers, with no difference being found between controls and copers.

In agreement with the findings above, Wexler et al. (1998) demonstrated a significant decrease in early mid-stance internal extensor moment and in maximum internal

extensor moment in the ACLD group when compared to controls. This corresponded with a significant increase in peak internal knee flexor moment. Wexler et al. (1998) also subdivided their ACLD into early, intermediate and chronic groups. Following this sub division it was discovered that significant decreases existed in internal knee extensor moments across these three groups at initial contact and early mid stance when compared to controls, showing a trend of decreasing knee extensor moment as time progressed. Terminal stance knee extensor moment was significantly increased in the chronic group, but not the early or intermediate group when compared to controls. Maximum internal knee extensor moment was also significantly decreased in the early and chronic, but not in the intermediate phase when compared to controls. Wexler et al. (1998) also demonstrated that across all 3 groups internal peak knee flexor moment was increased compared to controls but peak knee flexor moment was reduced near to the control values as time since injury increased.

Berchuck et al. (1990) discovered that in ACLD the internal knee flexor moment at heel strike was greater than the controls between heel strike and mid-stance. The ACLD group showed an absence of internal extensor moment seen in the controls. Instead they produced a significantly different internal flexor moment throughout most of the stance phase. This corresponded with a significant increase in hip flexor moment in both the injured and uninjured legs when compared to controls. Seventy five percent of the ACLD group in this study demonstrated quadriceps avoidance gait, characterised as a sustained internal flexor moment throughout the gait cycle as opposed to the normal biphasic pattern shown in Figure 2.5.4.

Wexler et al. (1998) also found a trend towards a reduction in internal knee extensor moment in the ACLD group. It was also suggested that the prevalence of quadriceps avoidance gait, as defined above, was correlated with time from injury. This suggests that adaptations in gait are time dependant and therefore the time of assessment in studies assessing gait biomechanics may influence the adaptations and strategies these studies describe. These changes towards a quadriceps avoidance gait were also interpreted as a reduction in quadriceps activity and an accentuation of hamstring activity.

Contrary to the strategy described at terminal stance described by Fuentes et al. (2011), at heel strike (where the knee is also in a position close to maximum extension), where

shearing forces have been demonstrated to be at their greatest the ACLD did not adapt their gait patterns (Wexler et al., 1998). The author suggests that the structures responsible for compensating for the absence of the ACL, in particular the surrounding muscles may be more able to respond and adapt more efficiently after heel strike as they are activated at a higher level. It may also be possible that the adaptation to avoid full extension at heel strike may take longer to reprogram than at terminal stance, or perhaps at heel strike the secondary restraints may be able to cope with the loads at this phase of the gait cycle (Berchuk et al., 1990; Rudolph et al., 2001).

Contrary to these studies Rudolph et al. (2001) found that internal knee extensor moments at the peak knee flexion angle was significantly lower in the non-copers compared to the uninjured limb and both limbs in both the copers and controls. Roberts et al. (1999) demonstrated that their ACLD group demonstrated no difference in kinematics at the knee at heel strike and throughout the stance phase of gait. Von Porat et al. (2006) also demonstrated no significant differences, both overall and by sub-classification (with regard to strength at a level above or below 90% of the uninjured limb) in internal knee extensor moment. There was however a relationship between knee extensor weakness and a lower internal knee extensor moment. Von Porat et al. (2006) also found that a majority of those with symptomatic OA (five of six participants) demonstrated a reduction in internal knee extensor moment.

Muneta et al. (1998) concluded that no differences in knee extensor moments in the ACLD injured limbs existed when compared to the uninjured limbs. Muneta et al. (1998) did however find a significant decrease in peak internal knee flexor moment when comparing the injured to the uninjured limb. The discrepancies in literature with regard to kinematic differences in ACLD groups could potentially exist because of the method of analysis, or absence of sub-classification of the ACLD group.

It has been demonstrated in the above literature, that when sub-classified, differences exist between ACLD copers, non-copers and adapters, that may influence kinematic and kinetic results when treating an ACLD cohort as one homogenous cohort. Other factors that may influence kinetic differences such as time form injury to assessment and rehabilitation methodology are described below in Chapter 2.11.

In studies that have assessed the same participants longitudinally, Ferber et al. (2002)

who evaluated gait kinetics in a group of ACL injured participants pre and post ACL reconstructive surgery found that in the ACLD condition the knee moment paralleled that of the controls throughout stance, whereas the ACLR at three months post-surgery demonstrated a similar pattern but in conjunction with a significantly increased internal extensor moment during the first half of mid-stance. They also discovered that during the second half of mid-stance the ACLR group demonstrated a significantly decreased internal flexor moment compared to the ACLD group and controls. The ACLR group also demonstrated increased knee flexor moment during the first half of mid-stance compared to the pre-surgical values. This would suggest that ACL reconstruction alters knee joint kinetics when compared to controls and their pre-surgical values. At first value this may seem reconstruction has a negative effect on knee loading, however caution must be aired as recovery of more normal gait mechanics may take longer than the 3 month period at which these ACLR were assessed (Karinikas et al., 2009).

During jogging activities Rudolph et al. (2001) demonstrated internal knee extensor moment at peak knee flexion angle was lower in non-copers in their involved limb, which was also significantly lower than both the limbs of the ACLD copers and controls. This was in agreement with Bush-Joseph et al. (2001) and Patel et al. (2003) who found that the internal knee extensor moment was significantly lower in the ACLD group when compared to the controls (Patel et al., 2003). This is also supported by findings from Berchuk et al. (1990) who found a significant reduction in internal knee extensor moment in the injured ACLD injured limbs compared to both the ACLD contralateral limbs and both limbs of the controls. The reduced knee extensor moment was described by Rudolph et al. (2001) as the 'hallmark of non-copers'. Rudolph et al. (2001) state it is important to account for functional ability when trying to uncover adaptations that may take place in ACLD.

Although ACLD copers moved with similar biomechanics to the controls, the non-copers limited their knee flexion and shifted knee loads away from the knee to the hip. It was proposed that co-contraction of the hamstrings, as suggested for level gait, may be a mechanism by which control of jogging is transferred away from the knee to the hip. However, this reduced knee motion in non-copers may lead to a reduction in the shock absorption capabilities of the knee joint and in turn lead to greater compression and shear forces, this may increase the risk of long term knee problems. Rudolph et al. (2001) suggest that the lack of relationship between quadriceps strength and internal

knee extensor moment in ACLD copers (which was significantly related in non-copers) may be an indicator of other factors playing a key role in knee stabilisation, and that muscle activation in terms of both timing and magnitude might be an important factor for adaptations in ACLD.

Patel et al. (2003) suggest that the relationship in jogging between quadriceps strength and internal peak knee extensor moment, which was not evident in level gait, is suggestive that higher demand activities require greater quadriceps strength to control knee stability than in lower demand activities. Rudolph et al. (2001) state that in the copers normal biomechanics and muscle timing may bode well for long term knee joint integrity although this is not supported by any literature looking at long term knee health in ACL groups to date. The literature discussed above assessed solely either ACLD or ACLR groups. Some studies however have assessed spatiotemporal, kinematic and kinetic outcomes in the same participants longitudinally in both ACLD and ACLR conditions.

2.10 Longitudinal Gait Adaptations.

Knoll et al. (2004) found that ACLD (consisting of both acute: 7-25 days post injury and chronic: 24-52 months post injury) demonstrated a significant reduction in stride length and in base of support in comparison to the uninjured limb. After reconstructive surgery these participants demonstrated the above differences at six weeks post-reconstructive surgery but at a follow up at around 4 months post-surgery, participants' injured limb mechanics had recovered to similar levels as the uninjured limb.

Knoll et al. (2004) reported that in the acute phase the ACLD group demonstrated a significant reduction in knee flexion excursion when compared to controls and this concurred with other studies on ACLD (Risberg et al., 2009; Hurd and Snyder-Mackler., 2007). However, those who were classified as chronic ACLD demonstrated a non-significant difference in knee excursion when compared to the controls. Ferber et al. (2002) also found no difference in sagittal plane knee kinematics between the chronic ACLD and controls. This emphasises the importance of considering the time of the assessment when evaluating differences demonstrated in studies on those with ACL injury.

The strategy of quadriceps avoidance gait described by Berchuk et al. (1990) described

as a reduction in internal extensor moment corresponding with a significant increase in hip flexion moment would also result in a reduced loading at the knee again serving as a protective strategy. Berchuk et al. (1990) suggest that this could be facilitated by increased hamstring co-contraction or avoidance of a quadriceps contraction during mid-stance. Interestingly abnormalities in the ACLD had a tendency to be present bilaterally rather than in just the affected limb.

Knoll et al. (2004) also suggested that the reduction in knee excursion in acute ACLD and early stages after ACLR is a mechanism to reduce net quadriceps activity which in has the potential to reduce anterior displacement of the tibia. This study verified that quadriceps activity was reduced in the vastus lateralis and medialis prior to and six weeks after surgery, verifying the idea of quadriceps avoidance. Reduction in extensor muscle activation could protect the knee against excessive tibial translation and a reduction in adductor longus activity (which was also noted), protects against excessive internal rotations of the knee at full extension angles such as heel strike and toe off.

Knoll et al. (2004) demonstrated that in a chronic ACLD group no significant differences were present when compared with controls with regards to knee kinematics and muscle activation patterns, perhaps suggesting that quadriceps avoidance does not exist in chronic ACLD groups. The marker system employed by Knoll et al. (2004) allowed for calculation of tibial translation, defined as the relative displacement between the tibial tubercle and the lateral femoral epicondyle. Using this method the ACLD group demonstrated a significantly larger tibial translation compared to the uninjured limb and controls during gait. This suggests that muscle activity adaptations attempt to, but fail, in reducing tibial translation in the ACLD knee.

Ferber et al. (2002) stated that no evidence of quadriceps avoidance was observed in any of the chronic ACLD group. This study using EMG found a reduction in vastus lateralis activity in the ACLD and this could be interpreted as a type of quadriceps avoidance. However as no differences were found in knee joint moment, power or angles the differences in vastus lateralis activity between the groups was unlikely to indicate quadriceps avoidance strategy. Ferber et al. (2002) suggest the higher and more prolonged hip extensor moment found in the ACLD group when compared to controls may be caused due to the higher demands placed on the hip due to increases in hip flexion.

This increase in hip flexor position may alter the length tension relationship of the hip extensor muscles and hamstrings to decrease anterior tibial translation.

The ACL injured groups analysed by Ferber et al. (2002), three months after reconstruction, demonstrated a similar pattern of flexion and extension to the controls. However the ACLR group had significantly more flexion during the late stance phase. It is difficult to ascertain the reason for the difference in results between Ferber et al. (2002) and Knoll et al., (2004) with regard to the post-surgery differences. This could be due to a combination of factors; the technique of reconstruction, rehabilitation methods and although only one month difference in terms of assessment from injury, in the early stages of recovery, this could possibly influence the kinematic differences between the studies. These factors will be discussed in greater depth in the limitations Chapter 2.12.

2.11 Gait and Jogging Adaptations in ACLD and ACLR: Conclusions.

In conclusion, differences in performance between ACL injured groups and controls may be influenced by a wide variety of limiting factors which are inherent within clinical research. Trying to generalise adaptation strategies in ACL injured groups is difficult due to these factors and the small sample sizes used in these studies. It does however appear that adaptation strategies appear to be time dependant, with time since injury being related to return to more normal gait in the ACLR, particularly in sagittal plane mechanics. However, more studies are needed to evaluate loading within the knee, particularly in the transverse and axial planes of movement, with larger sample sizes to fully understand the nature of gait adaptations in ACL injured groups. It appears that adaptations during jogging/running follow similar but exaggerated traits in the ACL injured cohorts when compared with the findings from level gait. However, literature on biomechanics in jogging on ACL injured groups is scarce and subject to the limitations discussed below making firm conclusions on adaptations or compensations in ACL injured groups difficult.

2.12 Limitations of Above Studies.

The primary limitations in all studies that are centred on patient research are related to the study's differing group demographics, data collection methodologies and outcome measurement calculation. This makes comparison between studies and generalising

results to the entire ACL injured cohort difficult. Described below are the key critical areas in which studies on both ACLR and ACLD groups show differences that may influence the comparison of results within each study. The wide variety of inclusion and exclusion criteria employed in the above research may influence the results of these studies. Factors such as associated injury to the ligaments, cartilage and in particular the menisci may influence movement patterns in ACL injured groups.

2.12.1 Sample Size.

The primary limitation in the above studies is the relatively small sample sizes in the majority of studies, as no studies demonstrated thorough power and sample size calculations. Sample sizes in the ACL studies above ranged from eight (Devita et al., 1998) to 35 (Karinikas et al., 2009), although this was subdivided into 17 patella tendon and 18 hamstring tendon reconstructions. These small sample sizes mean that achieving statistical power would be difficult. Contemplating the inherent variation in performance that is found within individuals, unveiling the adaptation strategies used by ACL injured groups would potentially require higher sample sizes to discover meaningful differences during gait and jogging.

2.12.2 Time from Injury or Surgery.

With regard to time from surgery the studies described above had mean time from surgery to assessment in the range of 3-12 months. Karinikas et al. (2009) demonstrate that there is a time dependent recovery of gait variables up to and beyond 12 months post-surgery. It could be hypothesised that the adaptation strategies (differences in kinematics and kinetics) discovered within the studies are only applicable at the time point at which the participants were assessed. Even within individual studies, a range of times of assessment from surgery are found which will make discovering meaningful differences difficult.

Some studies had also recorded time from injury to surgery (Webster and Feller, 2011; Georgoulis et al., 2003; Bush-Joseph et al., 2001; Webster et al., 2011; Knoll et al, 2004; Ferber et al., 2002) while the other studies had not. The influence of the time from injury to surgery on kinematics and kinetics post-rehabilitation needs to be more thoroughly investigated within the present study.

Within the ACLD studies time of injury to assessment ranged from 11 weeks to over seven years. If adaptations in ACLD gait patterns are time dependent, the wide variety

of time from injuries between and in some cases within studies may make meaningful comparisons and conclusions difficult to draw from these studies (Wexler et al., 1998).

2.12.3 Participant Matching.

It is to be commended that all of the studies reviewed had matched the ACL injured groups to the controls with regard to demographics such as height, body mass, age and gender (Bush-Joseph et al., 2001; Devita et al., 1998; Gao et al., 2010; Georgoulis et al., 2003; Webster and Feller, 2011; Beard et al., 1996; Berchuck et al., 1990; Muneta et al., 1998; Wexler et al., 1998).

Studies by Webster and Feller (2011), Butler et al. (2009), Rudolph et al. (2001) and Von Porat et al., (2006) strengthened their work further by matching for activity level although a majority of the studies had not (Bush-Joseph et al., 2001; Devita et al., 1998; Georgoulis et al., 2003; Gao et al., 2010; Webster et al., 2011).

The ACL injured groups within these studies ranged from an average age of 20-44 years, a mass of 74-92kg with a height of 1.72-1.81m, with the ACLR group tending to be more consistent demographically than the ACLD studies. Due to the consistency in demographics between the ACLR participants being assessed, it could be concluded that ACLR are relatively homogenous with regard to the mean age at which these participants are injured and their mean body mass and height. However the variation seen in the ACLD groups may make comparisons of these studies challenging.

As the studies on ACLD were categorised into copers, non-copers and adapters (Button et al., 2008; Alkjaer et al., 2003; Rudolph et al., 2001) in some studies but not in others (Risberg et al., 2009; Andriacchi and Dyrby, 2005), the strategies uncovered may be dependent on the participant's level of function and therefore grouping these participants together into one ACLD group, may mask the movement deficits in these participants.

2.12.4 Control Condition.

Karinikas et al. (2009), Webster et al. (2011) and Hurd and Snyder-Mackler (2007) were the only studies on gait in ACL injured groups to use solely the contralateral limb as a control. This means that the findings from these studies may be difficult to interpret compared to other studies ACL injured groups, as the contralateral limb has been demonstrated to undertake adaptations during gait (Gao et al., 2010).

2.12.5 Rehabilitation Procedure.

In most cases the level of adherence to the rehabilitation programmes that the ACL injured participants is not recorded. Generally, the studies seemed to have similar rehabilitation protocol outlines involving early restoration of ROM, balance and proprioceptive interventions. This often progressed onto sub maximal strengthening, cycling and exercises using other training devices such as the use of therapy bands and gym based muscle strengthening equipment.

The final stages of rehabilitation included maximal level strengthening, jump landings and more functional activities, followed by a return to non-pivoting sports then finally return to sport (Bush-Joseph et al., 2001; Karinikas et al., 2009; Webster and Feller, 2011; Devita et., 1998). Overall comparison is difficult as the duration, intensity and specific activities performed were not accurately specified and rehabilitation focus differed between studies. The studies by Gao et al. (2010) and Butler et al. (2009) did not describe in any detail the rehabilitation programme that their groups had undertaken. Rehabilitation factors may influence the recovery status of those even several months after surgery and therefore may be a limiting factor when applying the findings to the more general population of those with ACL reconstruction.

2.12.6 Surgical Procedure.

As well as pre-injury and post-surgical factors, the surgical procedure may also influence the gait mechanics in ACLR. Studies have assessed groups with patella tendon graft, Achilles tendon graft and hamstring tendon graft. Gao et al. (2010) included these grafts to form one ACLR group, while others have used a specific type of graft (Bush-Joseph et al., 2001). Several studies have performed analysis by graft type (Karinikas et al., 2009; Webster and Feller, 2011; Webster et al., 2005). These studies have demonstrated some differences on the influence of kinematics in relation to the type of graft used.

It has also been suggested by Scanlan et al. (2009) through assessing participants with a variety of graft types, that the orientation in the coronal plane of the graft, determined by MRi analysis, influences internal knee extensor moments. It was found that an increase in coronal graft angle correlated with a decrease in knee extensor moment. These differences in surgical techniques may be a limiting factor when comparing studies and drawing meaningful conclusions in patients with ACL reconstruction.

2.12.7 Measurement Tools.

Although these studies were undertaken using motion analysis systems differences will have existed between these systems. Evolution of motion analysis from 2 Dimensional to 3 Dimensional systems and the accompanying changes to calculation required to compute kinematic and kinetic variables may influence the accuracy of these results (Schache et al., 2006; McGinley et al., 2009).

This would be particularly evident in the frontal and axial planes as accurately calculating angles and in turn moments with movements that are subtle in natures are more difficult than that in the sagittal plane. Also, although systems may use similar mathematical principles to calculate knee kinematics and kinetics it is possible that there are also differences in these methods (Schache et al., 2006; McGinley et al., 2009). This means that reasonable sample sizes and statistical power become important to ensure that group differences are less likely to be influenced by systematic errors and that trends in data are likely to be caused by group differences (Schwartz et al., 2004).

2.13 Biomechanics of ACL Injury Hopping, Single Leg Squat and Muscle Strength.

After gait the most commonly researched activity in ACL injured groups is single leg hopping. Single leg hopping is a task used during rehabilitation as it is more demanding on the knee and are more representative of the loading and dynamic function in a sporting environment (Grindem et al., 2011).

Strength deficits in ACL injured groups, measured using isokinetic dynamometry, have been associated with abnormal kinematics and kinetics in the literature discussed previously (Patel et al., 2003; Karinikas et al., 2009). With studies demonstrating that internal extensor moment was found to be correlated with isokinetic measures of quadriceps muscle strength pertaining to those who had the weakest quadriceps demonstrating the largest reduction in internal extensor moment.

The single leg squat (SLS) is a commonly used tool in physiotherapy for assessing strength, muscular endurance and range of motion in the injured limb (Weeks et al., 2012), has a lack of scientific research assessing the differences in SLS mechanics and performance in pathological groups versus controls. A search of the literature at the time of writing found 1 article specifically relating to SLS performance biomechanics in ACL injured groups (Yamazaki et al., 2009).

2.13.1 Summary of Hopping Literature.

Risberg et al. (2009) state that the significantly increased hip extensor and ankle moments demonstrated in ACLD during hopping in conjunction with the reduction of knee moment and knee excursion after rehabilitation, suggest that a hip and ankle strategy is employed by the ACLD group to maintain knee loading at a lower level due to the absence of the stabilising role provided by the ACL. The study by Risberg et al. (2009) also assessed gait and found that the rehabilitation programme had returned gait parameters to that of the uninjured limb, suggesting that more dynamic tasks such as hopping take longer to establish normal knee function and loading patterns. The increase in hop distance in the injured limb to a similar level as the uninjured limb suggests an increase in quadriceps strength, although this was not quantified directly. However the changes in knee loading suggest that joint loading in hopping is controlled by several potential key factors, including the ability of the other joints to compensate to absorb deceleration forces and reprogramming of the proprioceptive system. Risberg et al. (2009) poses these questions; Firstly, are there other rehabilitation modalities to produce more normal knee function in ACLD? Secondly, does a return to more normal knee function in more dynamic, higher force tasks present a risk for further knee injury and dysfunction and act as a potential mechanism for the development of OA?

Denewith et al. (2010) suggest that bilateral differences during hopping in ACLR may be important as a clinical indicator for the progression of OA, as those activities that are more dynamic may cause adaptations in knee rotation movement under large axial loading which may exacerbate cartilage degeneration. As the injured limb was more extended during the landing phase of a hop, this stiffening strategy, as discussed in gait and jogging in some ACL injured groups, may be a strategy to increase knee stability.

Orishimo et al. (2010) also demonstrated that ACLR continued to have impairments in the involved limb. As with Denewith et al. (2010), knee ROM was reduced in the injured limb. The deficits at the knee and compensations at the hip and ankle indicate that measuring only hop distance as a marker of recovery does not fully examine the strategies and performance and loading taking place at a specific joint.

This is contrary to the idea proposed by Risberg et al. (2009) who assessed ACLD and stated that ACL injured participants should be able to return to normal function after restoring the mechanical stability of the ACL after reconstruction as adaptive strategies were still evident in this group of ACLR after rehabilitation. It is however important to

note that the impact of time on recovery in these patients is not fully understood in relation to hopping. It could be hypothesised that the lower moments and decreased knee ROM may be an adaptive strategy, to reduce anterior shear force. Orishimo et al. (2010) and Webster et al. (2005) suggest that adapted biomechanics are required to ensure normal loading conditions are maintained or reduced in the involved limb.

In conclusion it appears that deficits exist in those with both ACLR and ACLD with regards to biomechanics during a single leg hop, despite some studies demonstrating a return to normal function in other activities. This may be due to the higher demands placed upon the knee during a single leg hop. It is still uncertain whether it takes a longer time for a return to more normal biomechanics in more dynamic activities or if deficits will exist due to either the absence of or shortfalls in the reconstructive procedure.

2.13.2 Summary of SLS Literature.

Limited research has been conducted using the SLS despite its use as a common assessment tool in physiotherapy and rehabilitation to assess a patient's performance and map recovery after knee injury (Weeks et al., 2013). Despite its widespread use little is known about the validity and reliability of the SLS particularly with regard to comparing people with knee pathology to those with a healthy knee.

Crossley et al. (2011) demonstrated that the SLS, when used by trained physiotherapists, was a reliable tool for assessing hip dysfunction; however this study was undertaken on an asymptomatic cohort. DiMattia et al. (2005) state that despite the wide use of the SLS, there is no standardised method for prescription of this exercise and the relationship of the kinematic outcome measures to pathology and recovery are not, as yet, supported with motion analysis evidence.

The only study specifically assessing the SLS in ACL injured groups using kinematics, known to the author at time of writing, was undertaken by Yamazaki et al. (2009). Yamazaki et al. (2009) state the SLS is a useful tool in assessing lower limb kinematics in those with ACL injuries as it has been reported that the majority of injuries due to single leg landing come from valgus positioning of the lower leg. Yamazaki et al. (2009) found that a large proportion of their ACLD group could not successfully complete a full depth SLS and maintain balance. Therefore they evaluated a SLS of half depth.

Comparing injured and uninjured limbs, the injured leg of male participants demonstrated significantly less external knee and hip rotation, less knee flexion and more knee adduction than that of the uninjured leg of male subjects. The injured leg of female subjects also demonstrated more knee adduction than that of the uninjured leg of female subjects (Yamazaki et al. 2009). The population investigated by Yamazaki et al. (2009) were all ACLD and low functioning due to their requirement for ACL reconstructive surgery at a future date, and a majority of participants were unable to successfully complete a stable SLS. The study also did not investigate the side to side mechanics in the controls, which would have been an opportunity to investigate normal variation between dominant and non-dominant limbs, thus help in the interpretation of side to side differences with those with knee pathology.

In conclusion, little is known about the SLS and its relationship to kinematics and kinetics in pathological motion at the knee. As a tool that is commonly used by rehabilitation professionals, the author suggests that a thorough investigation of the SLS in both healthy populations, to obtain a suitable reference of normal knee function, and then in pathological conditions, in order to map deficits in lower limb function, should be undertaken for a wide range of pathologies in order to provide evidence for the efficacy of the SLS as a tool used in physiotherapy to assess knee function.

2.13.3 Strength Deficits in ACL Injured Groups.

Strength deficits have been associated with abnormal kinetics in those with ACL injury (Karinikas et al., 2009; Patel et al., 2003). Muscle strength is seen as a key indicator of recovery after ACL injury and deficits in both quadriceps and hamstring strength has been shown to exist in the post rehabilitation period (de Jong et al., 2007).

Lower limb dynamic stability is influenced in part by muscle strength (Besier et al., 2003) and muscle weakness has been hypothesized to be linked with the development of OA (Suter and Herzog, 2003). In ACL injured group's strength deficits in both the quadriceps and hamstrings have been reported to range from 5-40% and 9-27% when compared to the uninjured limb respectively (Thomas et al., 2013). Given that the quadriceps and hamstrings directly contribute to lower extremity stability, it is important to assess if strength deficits exist in ACL injured groups and to consider these in the context of both biomechanical deficits and their potential role in the development of further knee pathology.

Chapter 3 Literature Review (Part 2): MRi Methods for Assessing Knee Structures Linked to OA Development.

3.1 Introduction.

Accurate and precise measurement of cartilage in vivo together with other structures that constitute the knee joint, are important to determine the answers to some important clinical questions in the understanding, prevention and treatment of OA (Koo et al., 2005; Hunter et al., 2009; Hellio Le Graverand et al., 2010).

Radiography using conventional clinical systems including plain radiography and MRi are the simplest, most common and inexpensive methods for assessing pathology in the knee including OA. The mechanism by which plain radiographs are gathered means that they are capable of directly visualising osseous features that exist in the knee. These include features associated with OA such as osteophytes, subchondral sclerosis and subchondral cysts, which are typically combined with clinical opinion to diagnose OA. However, radiographs are limited as they cannot easily visualise soft tissue features and provide an indirect measure to assess cartilage thickness. MRi however has the capability to assess all of these features in greater detail and many others including direct visualisation of the cartilage and meniscus (Guermazi, Hunter and Roemer, 2009).

Studies have developed systems that quantitatively measure degenerative change in bone and cartilage in the knee joint. These typically use specialist MRi sequences and modelling of articular cartilage and bone to calculate a variety of biomarkers such as cartilage thickness, cartilage volume and joint space width (JSW). Other studies, using primarily clinically available MRI scans, have attempted to document indicators of degenerative change in multiple structures within the knee joint, using a scoring system applied by appropriate clinicians. This chapter will document the methods used in these studies, the results they have discovered relating to degenerative OA changes in both those with pre-existing OA and in those with ACL injuries.

3.2 Quantitative Methods.

Quantitative assessment of structures in the knee joint, particularly cartilage, in investigations in populations with, or cited as, being predisposed to developing OA, is dependent on the accuracy and reliability of the scanning sequence. Accurate techniques in segmenting the structures in the knee either manually or automatically is also of utmost importance. Accurate reconstruction of these segments to create cartilage models to detect what are potentially small changes in cartilage morphology between scans is also vital for the validity of results (Koo et al., 2005).

Koo et al. (2005) used a scanning protocol that used 1.5 Tesla with a fat-saturated 3D spoiled echo sequence. The purpose of the study was to determine the reproducibility of 3D cartilage thickness measurement in 4 healthy males. Areas of interest on the articular surface were defined according to the typical weight bearing regions when considering the sagittal plane knee angles during level gait. This was undertaken by drawing a line from the centre of a circle fitted to the femoral condyles through the tibia. The angle between the tibia and femur was used as an offset to approximate where zero degrees, or full extension, would be as the knee in the scan would have been slightly flexed. The expected load bearing regions of cartilage were then estimated from this reference angle using the kinematics found in the analysis of gait. These regions were also sub-divided into the lateral and medial compartments for assessment.

The inter-rater reproducibility was found to be improved using a rule based approach to segmentation, meaning that a checklist style protocol for decisions to be made during the segmentation process was more effective than solely a user defined decision making process. The intra-rater reproducibility test showed good reproducibility with regard to both cartilage thickness and volume, using a check list approach to analysis, with a coefficient of variation (CV) of 6.6% for cartilage thickness and 5.5% for volume being reported. Without the rule based protocol the CV was 8.3% and 7.5% with respect to thickness and volume, meaning that systems for assessing cartilage morphology should have a thorough and easily to follow protocol for analysis particularly if multiple raters are performing an analysis.

Koo et al. (2005) state that accuracy of measurement in quantitative methods that rely upon user defined segmentation of articular cartilage is reduced and that accuracy can also be influenced by the region being assessed within the knee. Therefore appropriate training and experience of those segmenting cartilage are of equal importance to that of

the image resolution, MRi slice thickness and the MRi technique employed when trying to assess cartilage morphology.

Li et al. (2005) used a similar cylindrical fitting method as Koo et al. (2005) in order to quantify cartilage distribution in the load bearing surfaces in the tibiofemoral joint. Cartilage quantification was reported on 6 controls, with an average age of 27 years, with no previous knee pathology. The cartilage was manually segmented, although there was no mention of level of proficiency of the segmentation operator.

Li et al. (2005) discovered that in the regions within the knee that would be expected to be loaded during gait; the cartilage was thicker than those that were not. In the medial condyle this was up to 40% greater in the loaded than unloaded areas and 20% higher in the lateral condyle. On the tibial plateau, cartilage thickening was apparent on the load bearing surfaces with a difference in cartilage thickness between the load bearing and non-load bearing parts of the lateral part of the tibial plateau.

The lateral part of the femur and tibia demonstrated greater cartilage thickness than the medial compartment. This is contrary to the discussions from kinematic studies that have assessed knee loading using external marker systems that demonstrate humans load their knees with a typical pattern of internal abductor moment throughout the gait cycle (Georgoulis et al., 2003; Butler et al., 2009; Webster et al., 2011). This would hypothetically mean that medial compartment of the tibiofemoral joint is loaded at a greater level in the medial than the lateral side. This may demonstrate a limitation of external marker systems in predicting internal knee motion discovered using MRi and modelling techniques. However MRi modelling techniques for measuring joint motion are usually performed on small groups (n=6 in Li et al., 2005) and are relatively novel in nature so the depth of literature to support this claim is limited. It is worth noting that no details on the participants' ethnicity were given, this may have influenced the results of this study as different ethnic background have demonstrated different patterns of knee OA. This could be hypothesised to be related to different loading patterns influenced by differences in alignment of anatomical structures (Zhang and Jordan, 2010; Felson et al., 2002).

Li et al. (2005) suggest that in certain pathologies and after injury to the knee, changes in point of loading and/or abnormal knee kinematics may load areas of cartilage ill adapted to these stresses and initiate degenerative cartilage change. The author proposes that an ACL injury may cause either a shift in loading towards areas of the

medial compartment ill adapted to loading, or an increase in medial compartment loading. This may be a causal factor in the early initiation of medial compartment OA that epidemiological studies have demonstrated in this population.

Andreisek et al. (2009) applied the hypothesis described by Li et al. (2005) and proposed by several other authors (Andriacchi et al., 2006; Chaudhari et al., 2008; Englund, 2010; Butler et al., 2009) to attempt to quantify cartilage change in those with ACL reconstructions 7 years following surgery. This study included 52 participants (28m, 24f) with a mean age of 33 and with no evidence of any other systemic disorder.

1.5T Scans were used with a fat saturated spoiled gradient echo sequence (SPGR), which created a slice thickness of 1.5mm and consisted of approximately 60 slices in the coronal plane. At follow up seven years following injury MRi scans were performed on both knees, with the uninjured limb used as the control condition. It is to be kept in mind that using the uninjured knee as a control has inherent limitations as some authors have suggested that adaptations in injured populations may take place in both the injured and uninjured limb, which may subject the injured limb to different loading conditions than a truly 'healthy' person without knee pathology (Gao et al., 2010).

The regions of the knee joint were manually segmented by one researcher who had more than 3 years' relevant experience. The sub-chondral bone area and the cartilage surface was outlined, the latter being divided into medial tibia, lateral tibia, central medial femur and central lateral femur. A bespoke algorithm assessed the size of the sub-chondral bone area and cartilage thickness across the sub-chondral bone area. Femur shape was also calculated by the method below in Figure 3.2.

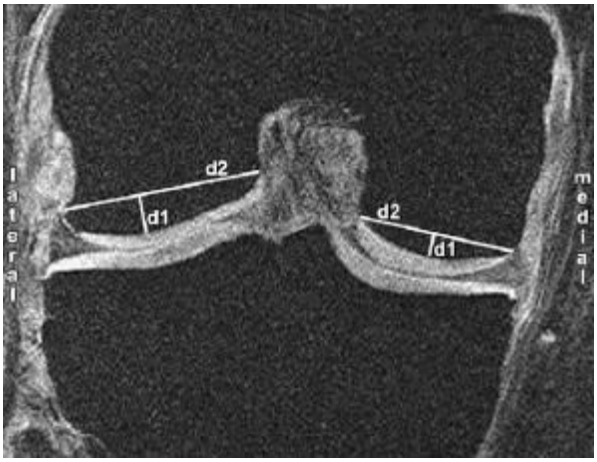


Figure 3.2 A method for assessing changes in femoral bone shape. The shape of the femur condyles was quantitatively assessed by the calculation: the ratio (r) between the maximal distance (d1) from the most inferior point of the femoral condyle to the horizontal reference line (d2) along the edges of the internal and external cortex of the medial/lateral femoral condyle. Reproduced with permission from Andreisek et al., (2009).

Andreisek et al. (2009) discovered that the sub-chondral bone area in the lateral femur was significantly smaller and in the medial femur was significantly larger in the control knee when compared to the operated side. However, there were no differences in cartilage thickness in any of the regions of the knee, except in the external lateral femoral sub-region, which was significantly reduced in thickness when comparing the injured versus non-injured limbs.

There was also no significant association between cartilage and meniscus lesions at the time of injury with cartilage thickness change. The ratio described above in Figure 3.2 was used as a measure of femoral shape change; this was significantly reduced in both the lateral and femoral aspects of the knee.

The study by Andreisek et al. (2009) was limited as data from MRi was unavailable from the time of injury for comparison to the more recent scans. Therefore, identifying longitudinal changes within each knee was not possible. There was also an absence of side to side comparisons within controls to examine if changes in bone shape were potentially due to natural variations and not due to long term changes caused by ACL injury.

Andreisek et al. (2009) concluded that there is evidence of changes in both sub-chondral bone area and femur shape after ACL injury; however no degeneration of

cartilage was evident. This could in part be explained by the fact that this group of ACL had a high rate of meniscal repair with very few meniscectomies, which have been associated with OA in other ACL studies (Neuman et al., 2008; Øiestad et al., 2010). Interestingly the 4 participants that had complete meniscectomies and severe cartilage lesions demonstrated a thinning of the cartilage within the central medial femur of 1.8, 8.3, 28.4 and 47.8%.

The study undertaken by Andreisek et al. (2009) found no changes in cartilage volume after a period of 7 years, despite the proposed theory that those with ACL injury would be predisposed to develop OA. This could potentially be that the methodology employed was not sensitive enough to detect cartilage change or that cartilage change takes longer to manifest. It does however offer alternative methodologies that did determine changes in knee structures in the ACL injured participants that can be employed using MRi. Li et al. (2013) also investigated cartilage morphology at a time point of at least two years after ACL reconstruction, consisting of a group of 30 males. These were compared to age and body mass matched controls.

As with Andreisek et al. (2009), Li et al. (2013) found no significant differences existed in cartilage thickness between groups across both the femur and tibia in either the lateral or medial compartment, this would be in conflict with the epidemiological studies carried out to assess OA prevalence in ACL injured populations. However, little is known about how cartilage changes in the early stages after ACL injury and in the early stages of OA (Frobell et al., 2010; Hellio Le Graverand et al., 2009). Research by Frobell et al. (2010) has demonstrated that there is thickening of the cartilage in the medial compartment in short term period of up to a year after ACL injury and this was stated to be related to swelling of the cartilage. This supports the idea that more research needs to be undertaken in those suffering with ACL injury at different time-points to attempt to define more accurately how cartilage morphology changes within the regions of the knee in the short, medium and long term.

Okafor et al. (2014) investigated the possibility that after ACLR that the anatomical orientation of the graft may be an important factor for preserving long term cartilage integrity. Using the non-injured limb as a control cartilage thickness was assessed for two groups of ACLR, one of which had been defined as ‘anatomically placed’ (n=10) creating normal knee motion and the other ‘non-anatomical’ (n=12) in which those participants demonstrated abnormal knee motion. These groups were assessed at a time

period at an average of 20 months post-reconstruction using high resolution MRi and segmented to create 3D models of both knees of each participant. The operative and contralateral knee models were registered to each other and a grid sampling system made site-specific comparisons of cartilage thickness.

Participants in the non-anatomic graft placement group demonstrated a significant decrease in cartilage thickness along the medial inter-condylar notch in the operative knee relative to the intact knee (8%). In the anatomic graft placement group no significant changes were observed. Okafor et al. (2014) state that these findings suggest that restoring normal knee motion after ACL injury may help to slow the progression of degeneration. Therefore graft placement may have important implications on the development of osteoarthritis after ACL reconstruction. This may in some part explain why both Li et al. (2013) and Andreisek et al. (2009) demonstrated no differences in cartilage thickness if their cohorts were consisting of those with normal knee motion. Nonetheless both Andreisek et al. (2009) and Li et al. (2013) state that assessing cartilage thickness using quantitative methods alone may miss key indicators for degenerative change that may precede cartilage loss, such as changes in bone and other articular structures and/or composition of cartilage assessed using signal intensity maps.

Several studies have also quantified cartilage morphology in patients with pre-existing radiographic or symptomatic OA. These OA cohorts are difficult to compare with the ACL population for several reasons. Firstly, these patients have already had an OA diagnosis therefore any changes in cartilage that are noted are not representative of an ACL population who may have no pre-injury OA. Secondly, the rate of cartilage loss may also be affected by age as the human bodies' ability to turn over new cartilage decreases with age. The age group in the studies detecting changes in OA are over 40, which would be higher than that in ACL injured cohorts described in Chapter 2.6-2.11 (Eckstein et al., 2010; Dam et al., 2009; Hellio le Graverand et al., 2010, Hunter et al., 2009; Bruyere et al., 2006).

At this age an OA cohort are less likely to be as physically active and have a higher body mass than younger populations (Eckstein et al., 2010; Hellio le Graverand et al., 2010; Hunter et al., 2009). These factors of age, activity level and body mass have been identified as risk factors for the development and progression of OA (Eckstein et al.,

2010). These factors may make direct comparison with the cohorts from ACL studies, which are a younger, generally more active and with a lower body mass difficult.

Studies that have assessed cartilage loss quantitatively using MRi scans in patients with pre-existing OA have found that degeneration appears to take place primarily in the medial compartment. Hunter et al. (2009) found that in a one year time period between baseline assessment and one year follow up, participants demonstrated a standard response mean (SRM) (calculated from the mean change in volume divided by the standard deviation change) for the central and medial tibia to be -0.096, the central medial femur -0.394 and the patella-0.198. It was noted that a majority of the participants (62%) already had notable degeneration in the medial compartment. The SRM for normalised cartilage volume for the central and medial tibia was -0.44, the central medial femur -0.338 and the patella-0.193. Hunter et al. (2009) concluded that there is evidence of cartilage loss, especially in the medial compartment of the knee, within a one year period; however this is less than reported in other studies. This could potentially be due to the differing methods employed between these studies to model cartilage and bone, including segmentation methods (manual verses automatic) and differing scanning sequences employed giving different quality images for analysis.

Eckstein et al. (2010) in assessing an elderly population with pre-existing OA discovered a significant loss of cartilage volume in the medial compartment compared to the lateral compartment over a one year period, which was greater in the medial tibia compared to the medial femur (-1.9% vs -0.5%). In a previous study Eckstein et al. (2009) demonstrated that participants with unilateral OA of the medial compartment that there was a 5.2, 18 and 44% reduction in cartilage thickness in the knees with evidence of Joint Space Narrowing (JSN) for sub-regions of the medial knee compartment when compared to knees with no JSN. The greatest difference was seen in the outer and central regions of the medial femoral compartment, which corresponds to the areas of the knee which are typically the load bearing regions of the knee across most activities of daily living (Eckstein et al., 2009).

Bruyere et al. (2006) discovered that in one year changes in medial tibiofemoral JSW (assessed using radiographs) were evident in a cohort of 62 participants with pre-existing OA; this was reported as a decrease of 6.7±20.5%. Changes in total cartilage volume were reported as a reduction of -0.4±16.7, and cartilage thickness (at a normalised location on the medial femur, defined after the cartilage volume model had

been produced) was reduced by 2.1±11.3%, but both of these were not significantly different from baseline. Lateral JSN was not associated with cartilage loss in terms of volume and thickness at any site; however medial compartment JSN was associated significantly with a reduction in cartilage volume and thickness in the medial compartment.

The above studies confirm what has previously been reported in epidemiological studies (Øiestad et al., 2010; Neuman et al., 2008) assessing OA changes in patients with OA occurs primarily in the medial compartment. The use of MRi and appropriate segmentation and modelling techniques can be taken as robust evidence that confirm these previous findings.

3.3 Semi-Quantitative MRi methods.

The previous chapter focusing on quantitative methods of determining degenerative changes in those with knee OA, has focused primarily on cartilage volume and thickness. However, other pathologies such as bone marrow lesions, bone oedema and osteophytes that are associated with OA are difficult to quantify using computer modelling techniques combined with MRi (Conaghan et al., 2006; Guermazi, Hunter and Roemer, 2009). It is also important to note that the specialised imaging sequences that are required to perform accurate quantification of structures within the knee are not viable in a clinical setting due to time constraints and the need to assess other features such a ligaments and muscles as these scans are diagnostic in nature. This demonstrates a requirement for semi-quantitative, visual analysis methods that are applicable for use with clinical diagnostic MRi sequences. This may provide more insight to structural abnormalities and changes within the knee that would be applicable to a wider patient group and can be assessed retrospectively (Conaghan et al., 2006; Guermazi, Hunter and Roemer, 2009). Structural abnormalities associated with OA that have shown good prognostic relationships with OA progression include both bone marrow abnormalities (Felson et al., 2003; Hunter et al., 2008; Neogi et al., 2012) and integrity of the meniscus (Slauterbeck et al., 2009; Hunter et al., 2006).

Amin et al. (2005) state that although radiographic evidence of JSN is associated with cartilage loss, this is not a sensitive measure and if used alone will miss a significant proportion of knees with longitudinal cartilage loss in periods of between 15 and 30 months. MRi has the ability to assess the knee as a whole organ, which has great

potential to provide greater insight incorporating a large number of articular features that have been associated with the progression of OA (Guermazi, Hunter and Roemer, 2009; Amin et al., 2005).

3.3 Semi-Quantitative Methods: Overview.

Guermazi, Hunter and Roemer (2009) identified 3 primary methods that have been developed for whole organ assessment of the knee in OA. These were the Whole Organ Magnetic Resonance Imaging Score (WORMS), the Boston-Leeds OA Knee Score (BLOKS) and the Knee OA Scoring System (KOSS). WORMS and BLOKS were stated to be the most commonly used scoring systems associated with mapping changes in OA from the available literature (Guermazi, Hunter and Roemer, 2009). These scoring systems have typically been developed by experts in radiology and OA and have assigned the scoring of these articular features according to their perceived importance in the pathology and progression of OA.

A systematic review by Hunter et al. (2011), whose research group has been heavily involved in the development of semi-quantitative scoring systems in knee OA discuss some of the evidence which led to the development and weighting of these scoring systems. Hunter et al. (2011) state that19 studies investigated the predictive power of articular abnormalities that can be identified on MRi as indicative of progression of knee OA. Meniscal integrity was discovered to be a key feature in the progression of OA. Participants who had meniscal tears showed a higher than average rate of cartilage loss (22% with damage versus 14% without). Global cartilage loss was significantly higher in those suffering with a severe meniscal tears compared to those without, and the relationship between meniscal injury and cartilage volume loss was greater in the medial meniscus than in the lateral side.

Complete ACL tears were found to have border-line significance on the progression of cartilage pathology and cartilage lesions located in the central region of the medial tibiofemoral compartment of the knee were more likely to progress than those in regions of the anterior, posterior and lateral compartment (Hunter et al., 2011). This is potentially due to this area being subjected to increased loading to areas ill-adapted to loading after injury as discussed previously. However, the risk of cartilage loss in the medial tibiofemoral compartment associated with ACL rupture after adjusting for meniscal injuries demonstrated there was no increased risk of progression of OA associated with ACL tear.

It appears other structures injured at the time of ACL rupture may be significant in the development of OA particularly that of the meniscus which is commonly injured and has a key role in load distribution on the knee (Slauterbeck et al., 2009).

Hunter et al. (2011) also evaluated several other articular features, some that were demonstrated to be linked with rapid progression of OA including the presence of severe meniscal extrusion and medial and lateral bone marrow abnormalities. Worsening in cartilage defect score (cartilage defect score is a pictorial scoring system to measure various types of cartilage abnormalities that is applied to different anatomical regions of the knee) was also associated with tibiofemoral osteophytes and areas within the knee with higher Bone Marrow Abnormality (BMA) scores had greater loss of cartilage and worsening of cartilage defect score.

Hunter et al., (2011) state that the responsiveness of the semi-quantitative assessment of cartilage morphology (SRM 0.55) is broadly consistent with quantitative assessment for the medial tibiofemoral joint. In addition the semi-quantitative assessment of BMA a structural target with good clinical and predictive validity of OA was also adequately responsive (SRM 0.43).

3.3.1 Assessment of the BLOKS Tool.

Hunter et al. (2008) investigated the reliability of BLOKS. This tool was developed from the relevant literature regarding the important articular features and their relationship to the development of OA. This was compiled by a collaborative group of UK and USA radiologists and rheumatologists.

Hunter et al. (2008) also tested the construct validity compared to WORMS with regard to BMA and also the predictive capability of mapping cartilage change longitudinally for each method. One hundred and twelve participants were recruited from the Boston OA Knee Study (BOKS). This entire cohort had been graded as having primary OA. At follow up at a period of between 15 and 30 months 86% of the participants were also re-evaluated.

Hunter et al. (2008) found a strong correlation (Spearman Correlation Coefficient= 0.63 in the medial compartment and 0.79 in the lateral compartment) between the BMA scales in this cohort between WORMS and BLOKS. In the medial tibiofemoral compartment a higher BMA score was related to greater cartilage loss in both WORMS and BLOKS. The association was higher in BLOKS than in WORMS. However, longitudinal changes in BMA were not associated with cartilage degeneration.

Hunter et al. (2008) concluded that BLOKS demonstrated moderate to good inter-reader reliability, ranging from 0.51 for meniscal extrusion up to 0.79 for meniscal tear. The reliability for other key features using weighted kappa was 0.72 for BMA grade, 0.72 for cartilage morphology and 0.62 for synovitis.

3.3.2 Assessment of the WORMS Tool.

Peterfy et al. (2004) developed the preliminary version of the semi-quantitative WORMS tool. Using 1.5T scanner with a clinical scanning protocol, reliability of this tool was assessed on 19 participants with symptomatic knee OA. Readings were scored independently by 2 senior radiologists following a 2 hour training session. Images were scored with regard to 14 articular features; cartilage signal and morphology, bone marrow abnormality, sub-articular cysts, bone attrition, marginal osteophytes, meniscal integrity, collateral ligament integrity, synovitis, loose bodies and peri-articular cysts and bursae.

All values for inter class correlation (ICC) were good to excellent with the lowest ICC being 0.61 and a majority were greater than 0.8. For cartilage and osteophytes these were greater than 0.9, with the worst agreement being for bone attrition, although the prevalence of this feature was rare. Many of the individual features were strongly associated with cartilage morphology in the medial compartment, particular marrow abnormality, bone cysts, bone attrition, osteophytes and meniscal damage (Spearman rho=0.73, 0.61, 0.56, 0.81, 0.75 respectively) (Peterfy et al., 2004).

Peterfy et al. (2004) concluded that MRi combined with WORMS, provides a more comprehensive picture of structural changes in OA and has excellent inter-rater agreement. The version presented in this paper (Peterfy et al., 2004) was not intended to be a final version but an initial step in a long term development of an accurate Knee OA scoring system.

Javaid et al. (2010) used WORMS as their primary outcome measure for the Multicentre OA Study (MOST). The primary aim of this study was to identify using clinical MRi if any of the articular features scored using WORMS in the early stages of OA were clinically important in the progression of the disease. Javaid et al. (2010) assessed the articular features in those with early but infrequent symptoms of OA but with no evidence of OA from plain radiographs.

This was a relatively large scale trial conducted on 155 participants (age range 50-79 years) assessing at baseline and approximately 15 months later. Those participants who developed frequent knee symptoms over the 15 month period were defined as cases while those who remained infrequently symptomatic were defined as the control group. Baseline MRi's were scored with regard to cartilage lesions, osteophytes, bone marrow lesions and cysts and all scores were adjusted for age, gender, race, body mass index (BMI), previous injury and site of the assessment clinic.

Of the 155 participants in the study 36 were defined as cases and 128 as controls. There was MRi evidence of cartilage damage in both the cases and controls. The prevalence of a severe cartilage lesion, BMA and osteophytes were significantly more prevalent in cases than in controls. However case status at 15 months was predicted by baseline status in only 2 locations, a BMA in the lateral patella and at the tibial subspinous sub-region.

This might be considered unusual considering that the progression of OA would usually be associated with changes in the medial compartment. However it may be that structural changes are not necessarily associated with symptoms and that certain locations of the knee such as the tibial subspinous and patella may produce more patient reported symptoms, due to increased sensitivity to pain in this location and increased strain on the ACL, which inserts in this region, and may be effected by tibiofemoral bone deformities caused in OA (Javaid et al., 2010).

In conclusion the study by Javaid et al. (2010) demonstrates that the WORMS tool is capable of detecting degenerative changes in the knee longitudinally but the predictive power of the progression of OA towards a symptomatic state using WORMS in a period of 15 months is difficult to assess. It does however appear that BMA is an important feature to assess when considering progression of OA.

Conaghan et al. (2006) performed Rasch Analysis on the WORMS tool. Rasch analysis is used to validate such scoring systems as it allows the determination of the sums of the subscale scores and the degree to which these scores can be used as a uni-dimensional interval level measurement tool. Conaghan et al. (2006) applied Rasch analysis to 2 studies both of which included participants with symptomatic knee OA.

When summating the scores at each site for the articular features identified in WORMS using the Rasch method the WORMS total score summary were found to be not

representative of the scoring of the individual components scores of WORMS suggesting that each articular feature score was not a uni-dimensional scale (Conaghan et al., 2006). However, Conaghan et al. (2006) state that this does not suggest the features identified and scored in WORMS are not important features in the pathology and progression of OA.

Conaghan et al. (2006) concluded that evaluation of these types of scoring tools typically relies on measures of reliability, validity, construct validity and responsiveness. It is important to note that uni-dimensionality of a scale is an important feature of internal construct validity, meaning that a feature assessed is an outcome measure relevant to measuring the progression of OA in its own right and not a by-product or result of another outcome measure. However, in the case of OA pathology this will be difficult, as changes in articular features are likely to directly interact with each other by the nature of physiological processes.

3.3.3 Comparisons of WORMS and BLOKS.

Lynch et al. (2010) compared the WORMS and BLOKS scoring system for the assessment of both prevalence and severity of cartilage lesion morphology, meniscal damage and BMA. Participants selected from the OA Initiative (OAI), were a sample of 115 knees with radiographic OA and at high risk of cartilage loss. These were based on risk factors associated with OA progression such as age and BMI. The knee MRi's were evaluated separately using both WORMS and BLOKS with a sub-set being revaluated for reliability testing. Baseline readings were used for comparison of the 2 methods for inter-rater reliability as well as presence and severity of damage to articular features at both the compartment and anatomical sub-region levels.

Lynch et al. (2010) demonstrated that both methods had high inter-rater agreement for all features (kappa for WORMS 0.69-1.0 and for BLOKS 0.65-1), with both methods having good agreement on the presence and severity of cartilage lesion morphology (kappa= 0.93). Both methodologies also reported good agreement for the score representing the extent and severity of BMA (kappa 0.74-0.80). This also applied for meniscal damage and extrusion; however the inclusion of meniscal signal and uncommon types of tear in the BLOKS tool may be advantageous if these were to prove clinically relevant in those with knee OA.

In conclusion both methods were similar in scoring both prevalence and severity of cartilage loss, BMA and meniscal integrity. Selecting between these methods should be

based on factors such as reader effort/time for training required, appropriateness of the goals of the study and performance of these scoring systems to map change longitudinally. The authors suggest that the WORMS methodology is described more thoroughly in the literature and the image representations given in the paper by Peterfy et al., (2004) are more easily available to researchers for interpretation of MRi scans, which gives it a distinct methodological advantage over BLOKS.

Felson et al. (2010) also assessed the BLOKS and WORMS tools with respect to longitudinal changes in those with pre-existing knee OA. MRi's were taken at baseline and at approximately a 24 month follow up in 113 knees from the OAI. They evaluated which cartilage loss score correlated best with radiographic joint space loss. They also assessed the validity of BMA and meniscal scores for the prediction of cartilage change.

Felson et al. (2010) noted that 33 of the knees demonstrated cartilage loss using BLOKS and 30 using WORMS, thus demonstrating a high agreement between the scales. In the medial tibiofemoral compartment both WORMS and BLOKS specified that 42% of the knees had joint space loss. Therefore, both tools had similar specificity but were not strongly associated with joint space loss findings from plain radiographs.

WORMS BMA score predicted cartilage score change more strongly than the BLOKS BMA variable, with some BLOKS BMA variables not associated with an increased risk of cartilage score change at all. Across the range of scores meniscal tear scores in BLOKS predicted cartilage loss with greater sensitivity than WORMS and the meniscal signal abnormality scored in BLOCKS, but not in WORMS, was also a predictor of cartilage loss (Felson et al., 2010).

Felson et al. (2010) concluded the BLOKS meniscal score was preferable to WORMS with regard to predicting degenerative cartilage change potentially due to the inclusion of pathologies not included in WORMS. However, BMA scoring in WORMS was preferable to BLOKS with regard to its greater sensitivity to predict cartilage changes, which is contrary to the findings of Hunter et al. (2008). WORMS is also an easier tool to score and was stated to not include any unnecessary measurement categories. However, neither method was conclusively better for scoring cartilage change longitudinally.

3.3.4 Assessment of the MOAKS Tool.

Hunter et al. (2011) stated that due to limitations existing in other semi-quantitative methods with issues relating to construct validity highlighted by Conaghan et al. (2011) and Guermazi et al. (2009) for scoring knee health. Hunter et al. (2011) attempted to resolve these issues by developing previous semi-quantitative into a new scoring tool called the MRi OA Knee Score (MOAKS). MOAKS was developed by a panel of experts in MRi and related to important features identified from the literature relating to the severity of knee OA and the potential for progression of the disease.

Two expert readers reported 20 MRi's, in addition one reader performing the analysis again 4 weeks later presented in a random order, to assess both the inter and intra rater reliability of the tool. Kappa scores for the inter-rater reliability were 0.36 for tibial cartilage and 0.49 for tibial osteophytes. Intra-rater reliability for tibial BMA number of lesions were 0.54 and synovitis 0.42 which would be regarded as low. In all other measures of reliability MOAKS rated as very good (0.61-1).

This tool, despite being claimed to be an development on pre-existing OA knee scoring methods, appears to provide no extra benefit in terms of both inter and intra-rater reliability when compared to both BLOKS and WORMS. This recently developed tool has also not been subjected to construct validation and its sensitivity to longitudinal structural changes.

3.4 Comparison of Quantitative and Semi-quantitative Methods.

Hunter et al. (2011) performed a meta-analysis to investigate the responsiveness and reliability of MRi based measures with regard to longitudinal structural change in knee OA in both quantitative and semi-quantitative methods.

Hunter et al., (2011) identified 84 published research studies for both quantitative and semi-quantitative methods. For the quantitative methods the inter and intra-rater ICC were rated as excellent (0.8-0.94) in respect to measurement of structural change, which as discussed in the previous chapter on quantitative methods focused primarily on measures of cartilage thickness and volume changes. The semi-quantitative measures all had moderate to excellent ICC scores (0.52-0.88) with the lowest score, corresponding to synovial intra-rater reliability, and the highest being for assessment of cartilage morphology.

The responsiveness analysis was undertaken using 42 research papers. This combined the SRM for quantitative cartilage change within the medial tibiofemoral joint and was reported as -0.86. For the semi-quantitative methods the SRM for the medial tibiofemoral joint was 0.55 corresponding to an increase in anatomical score linked to negative change, whereas the negative value for the quantitative methods was relating directly to loss of cartilage (Hunter et al., 2011).

Hunter et al. (2011) stated that MRi has evolved considerably over the past few years and that both quantitative and semi-quantitative methods have both good reliability and responsiveness and have the potential to map degenerative change in OA longitudinally. Both quantitative and semi-quantitative methods have their strengths and weaknesses, therefore it is important to assess the setting of research, the research aims and the applicability of the proposed tool to determine the best method to employ.

In conclusion, both quantitative and semi-quantitative techniques have been used to assess changes in participants with OA. Quantitative measurements use computerised image processing to assess typical cartilage morphology, including thickness and volume and it has also been applied to other articular features such as bone volume, BMA volume and meniscal position and volume. Semi-quantitative measurement of OA is typically much more dependent on the skills of the observer and generates data represented as a scale as opposed to a continuous measurement of change. Multiple methods for both techniques exist, semi-quantitative methods have an advantage of not requiring specialised imaging techniques and are easily applicable in a clinical setting to clinically grade scans with minimal training, providing the operator with a familiar tool with which to complete analysis.

However, these tools are derived from groups of experts who perceive what are meant to be important features in OA this may bias future studies as importance has been placed on certain articular features and their score value adjusted accordingly without conclusive evidence to support these claims. These systems are also time intensive and generally their reliability has not been as high as quantitative methods. It is important to note that although these methods have been developed to document articular changes longitudinally, this has primarily been in participants with pre-existing symptoms of OA. The applicability of this scoring tool to those suffering with an ACL injury has yet to be investigated, the key question would be to determine if a suitable knee scoring tool has been developed that is sensitive and reliable enough to detect changes in ACL

injured cohorts in the short to medium term, or whether a new tool designed specifically for this cohort needs to be developed.

3.5 Literature Summary.

ACL injuries are a common injury across many sports, with incident rates being reported at approximately 30 per 100,000 of the population in the UK (Webb and Corry, 2000). ACL injury is particularly evident in sports that require dynamic loading, rapid changes of direction and pivoting. Women have a 3 to 5 time greater risk of ACL injury when compared to men competing in similar sports (Lohmander et al. 2007).

ACL injury has been associated with the development of early onset OA, with studies showing a figure of 16%-62% of those suffering ACL injury having radiographic signs of OA at a time period of 10-15 years. Those patients suffering associated injuries and having meniscectomies were shown to be more likely to develop early onset OA than those with just an isolated ACL injury (Neuman et al., 2008; Øiestad et al., 2010).

The knee ligaments create, along with the nervous system and muscles, a protective proprioceptive network creating stabilisation of the knee joint against external forces. The ACL's primary role is to provide stability against the anterior translation of tibia and is stressed by contraction of the quadriceps muscles; it is also active in determining the tibiofemoral axial rotation with flexion of the knee (Beard et al., 1996, Barrance et al., 2006, Karmani and Ember, 2003).

The most widely discussed hypothesis as to why an ACL injury is associated with the development of early onset OA is an assumption that the stabilising role of the ACL, once disrupted may alter the normal movement pattern in the knee and that this change in loading, and/or shifting of the position of the femur on tibia, creates abnormal stresses through the knee cartilage and in turn leads to cartilage degeneration (Barrance et al., 2006, Andriacchi et al., 2004; Andriachhi et al, 2009; Scanlan and Andriacchi, 2011).

Several studies have demonstrated differences in performance between both ACLD and ACLR groups when compared to controls. However, differences between studies may be influenced by a wide variety of limiting factors which are inherent within clinical research. Trying to generalise adaptation strategies in ACL injured groups is difficult due to these factors and the small sample sizes used in these studies. It does however appear that adaptation strategies appear to be time dependant, with time since injury

being related to return to more normal gait in ACLR (Tashman et al., 2007; Rudolph et al., 2001; Risberg et al., 2009; Hurd and Snyder-Mackler., 2007). However, more studies need to evaluate loading within the knee, particularly in the frontal and axial planes of movement.

It appears that adaptations during jogging/running follow similar but exaggerated traits in the ACL injured cohorts when compared with the findings from level gait (Karinikas et al., 2009; Rudolph et al., 2001; Berchuk et al., 1990). However, literature on biomechanics in jogging on ACL injured participants is scarce and subject to the same variability in patient cohorts in terms of demographics and the limitations discussed above, making firm conclusions on adaptations or compensations in ACL injured groups difficult. In single leg hopping deficits in ACL injured groups when compared to a control condition appear more consistently in literature (Risberg et al., 2009; Orishimo et al., 2010). This may be due to the higher demands placed upon the knee during a single leg hop, it is still uncertain whether it takes a longer time for a return to more normal biomechanics in more dynamic activities or if deficits will exist due to either the absence of or shortfalls in the reconstructive procedure.

Limited research has been conducted using the SLS as a common assessment tool in physiotherapy and rehabilitation setting to assess a patient's performance and map recovery after knee injury (Weeks et al., 2013). Despite its widespread use, little is known about the validity and reliability of the SLS particularly with regard to comparing people with knee pathology to those with a healthy knee.
As a tool that is commonly used by rehabilitation professionals, thorough investigation of the SLS is required, to obtain normative values with respect to the knee and then in pathological conditions in order to map deficits in lower limb function, should be undertaken for a wide range of pathologies in order to provide evidence for the efficacy of the SLS as a tool used in physiotherapy to assess knee kinematics and kinetics.

In order to assess changes in cartilage and knee structures associated with OA, which can be linked to motion analysis and clinical data; both quantitative and semi-quantitative techniques have been developed. Quantitative measurements use computerised image processing to assess typically cartilage morphology, including thickness and volume, it has also been applied to other articular features such as bone volume, BML volume and meniscal position and volume (Koo et al., 2005; Andreisek

et al., 2009; Eckstein et al., 2010; Dam et al., 2009; Hellio le Graverand et al., 2010, Hunter et al., 2009; Bruyere et al., 2006).

Semi-quantitative measurement of OA, scoring articular features associated with degenerative changes, is typically much more dependent on the skills of the observer. Multiple methods for both techniques exist, however semi-quantitative methods have an advantage of not requiring specialised imaging techniques and are easily applicable in a clinical setting to clinically grade scans with minimal training, providing the operator with a familiar tool with which to complete analysis (Peterfy et al., 2004; Guermazi, Hunter and Roemer, 2009; Hunter et al., 2011).

However, these tools are derived from groups of experts who perceive what are meant to be important features in OA, this may bias future studies as importance has been placed on certain articular features and their score value adjusted accordingly without conclusive evidence to support these claims. It is important to note that although these methods have been developed to document articular changes longitudinally, this has primarily been in participants with pre-existing symptoms of OA. The applicability of this scoring tool to those suffering with an ACL injury has yet to be investigated, a key question would be if a suitable knee scoring tool has been developed that is sensitive and reliable enough to detect changes in ACL injured cohorts in the short to medium term, or whether a new tool designed specifically for this cohort needs to be developed.

3.6 Biomechanics Literature Summary: A Framework Based Approach.

Having assessed the data from the previously described studies, the following chapter describes the aforementioned studies' results in terms of kinetic adaptations in the context of the time frames at which they took place. This was undertaken as time from injury appears to be one of the key limiting factors when comparing studies and identify adaptation after injury in ACL injured groups and the links between these adaptations and the development of OA. The generalised plotting of the study's results in relation to a timeline will be used to create a framework of adaptations after ACL injury from which to generate research questions.

The outcome measure chosen for developing this framework was peak internal knee extensor moment, which was chosen for two key reasons. Firstly this study aims to identify if kinematic and kinetic parameters are associated with degenerative changes in

the tibiofemoral joint after ACL injury and secondly it is the kinetic evaluation of moments that are most closely associated with loading at the knee that has been cited as a potential causal mechanism in the development of early OA.

Although the literature suggests increases in internal knee abductor moment is associated with OA initiation, progression and development, unfortunately this parameter is not thoroughly investigated in the literature in order to use a model based approach for hypotheses generation; however for completeness these will be plotted were possible. This is also true for extensor moments during jogging, and these are also plotted to put into context the findings of the limited number of studies that have assessed internal knee extensor moment during this activity.

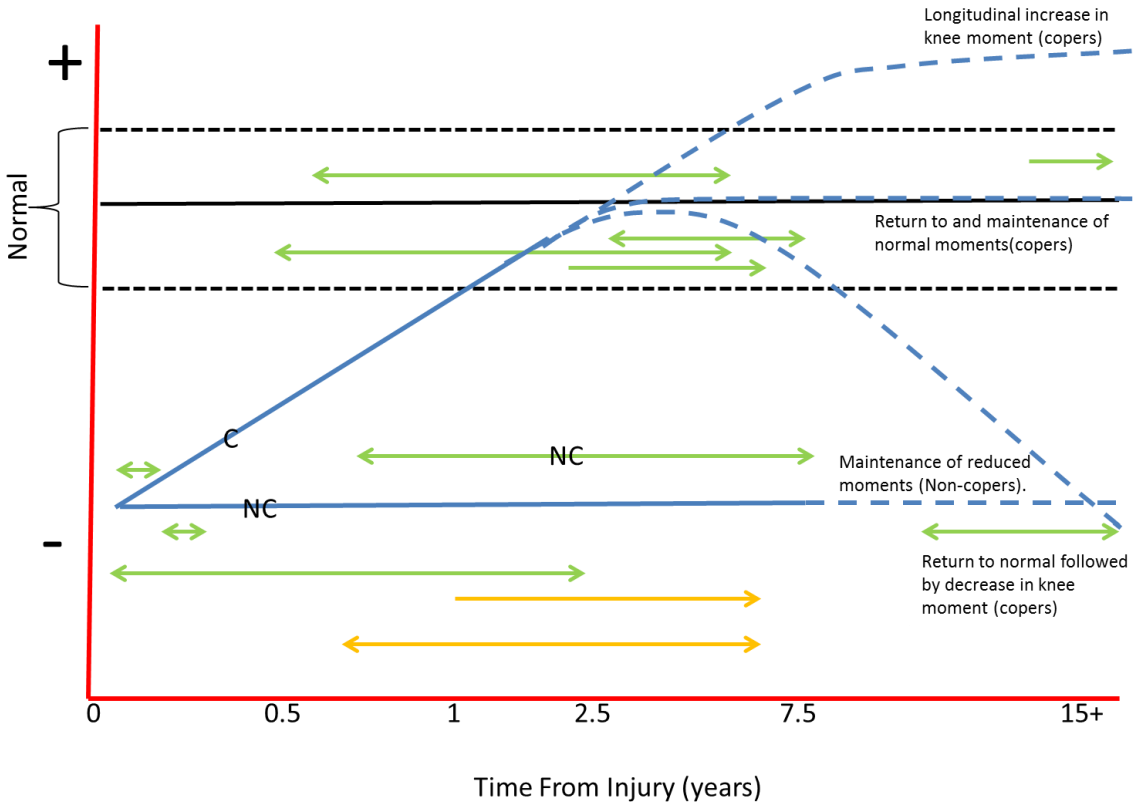


Figure 3.6.1 A framework for predicting future kinetic adaptations in ACLD.
Key: Light green lines=Individual gait studies on ACLD, horizontal length represents the time frame at which the study's participants were assessed since injury. Orange lines= Individual jogging studies on ACLD, horizontal length represents the time frame at which the study's participants were assessed since injury. +=Reported significant increase in internal knee extensor moment from control values. -=Reported decrease in internal knee extensor moment from control values. Continuous blue line= Model best fitting internal knee extensor moments ACLD post-injury adaptation trajectory data. Dashed blue line=potential direction for future adaptations. C=adaption line for copers. NC=adaptation line for Non-copers.

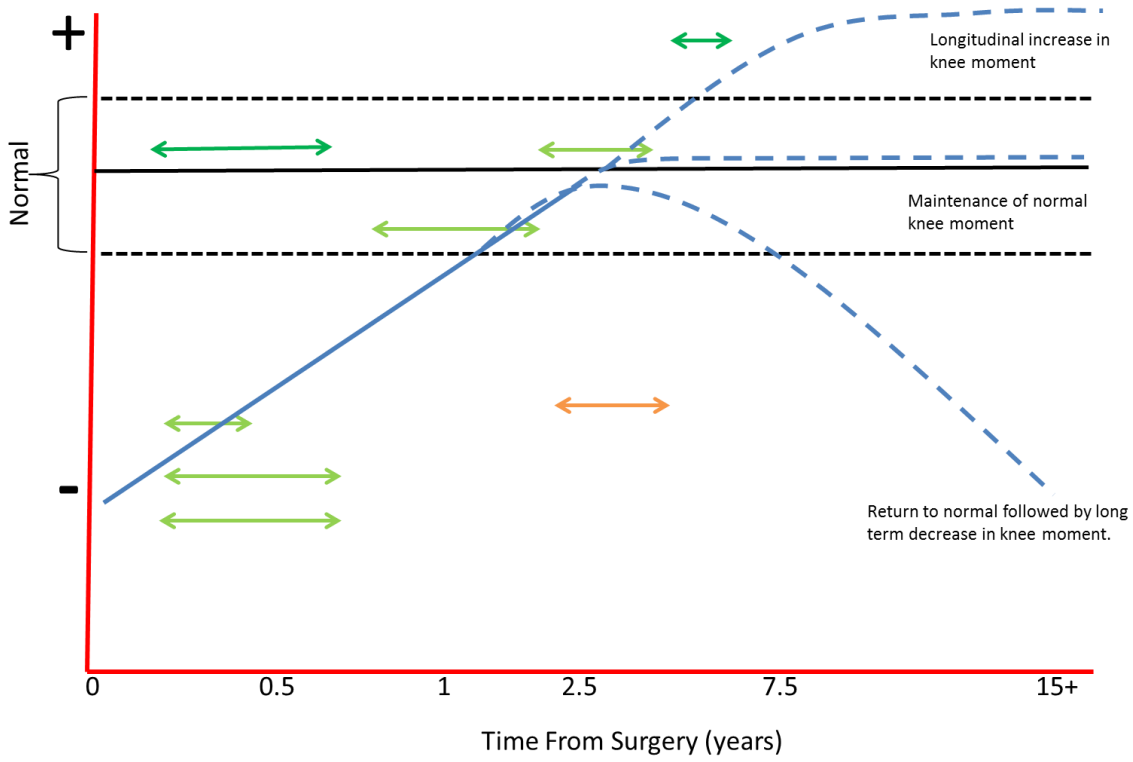


Figure 3.6.2 A framework for predicting future kinetic adaptations in ACLR.
Key: Light green lines=Individual gait studies on ACLR, horizontal length represents the time frame at which the study's participants were assessed since surgery. Dark green lines=Abductor moment during gait, horizontal length represents time frame from surgery at which assessment took place. Orange lines= Individual jogging studies on ACLR, horizontal length represents the time frame at which the study's participants were assessed since surgery. +=Reported significant increase in internal knee extensor/abductor moment from control values. -=Reported decrease in internal knee extensor/abductor moment from control values. Continuous blue line= Model best fitting internal knee extensor moments ACLR post-injury adaptation trajectory data. Dashed blue line=potential direction for future adaptations.

The thick continuous black line represents an imagined mean normal knee moment, with the dashed black lines representing the normal range of knee moments expected in a healthy population. It would be expected that this would be maintained longitudinally; therefore these lines run perpendicular to the horizontal red x axis, which shows the timeline after injury.

Along the red y axis an area that shows the direction of adaptation in these studies with the '+' representing an increase in moment compared to the normal range and the '-'

representing a decrease in moment compared to the normal range. This is NOT directly representative of knee moment values but an indicator solely of direction of adaption.

Several attempts were made using different methods to quantify these differences such as percentage difference from controls and converting measurements to a standardised unit of measurement. However the lack of data in some study's with which to convert to a standardised unit of measurement meant this was not possible. This combined with the different data collection tools and biomechanical modelling methods meant that values between studies were not directly comparable so the above approach seemed the only viable option with which to place studies on a timeline with some consistency.

Percentages were also not reflective of the sample size, so for example if the ACL groups' knee moment was 85% of the control value the significance is dependent on other factors that mean plotting these meaningfully was not achievable. Therefore a purely directional approach without the use of values was decided to be the most effective method to visualise these studies results in the context of their timeframes to create a model for recovery after ACL injury.

In the horizontal direction the green lines represent the approximate time frame at which the study took place post-injury. With regard to its position in relation to the normal range, if placed above this indicates an increase in moment, below a decrease in moment and if placed within the normal range demonstrates no differences were found when compared to controls. The orange lines represent data from studies assessing extensor moment during jogging in ACL injured patients and dark green lines represent the internal knee abductor moment.

The model for change over time for gait is shown as the continuous blue line. This line represents the adaption over time that agrees with the outcomes from the literature assessing knee moments. The dashed blue lines continuing on from the blue line represents the proposed future direction of adaptations where literature is scarce or non-existent at these time frames.

The increase of loading in time model would support the idea that early OA in these patients is associated with increases in long term knee loading after ACL injury, and supportive of the theory that adaptations in biomechanics precede physiological changes in structures and not vice versa. However data from the present literature does not support this and instead points towards one of the two following scenarios.

As both ACLD and ACLR appear to have a time dependant return to more normal knee moments during gait in the timeframes most comprehensively covered in the literature (solid blue line), it appears that the most likely future models for ACLD copers and ACLR would be maintenance of normal knee moments during gait.

The studies that have assessed copers and non-copers in the ACLD group separately show differences in long term outcomes. It would appear that the primary adaption is a decrease in knee loading in the early stages, then as time progresses a return to more normal knee moments in ACLR and ACLD copers whereas ACLD non-copers retain a decreased moment.

This is supported by jogging data, which although was not modelled due to lack of data, it is of note that in this more demanding activity the knee extensor moment appears to be reduced at all data points in ACLR as well as ACLD. This suggests that when activity demand is increased the knee cannot operate under conditions of normal loading so have to adapt to decrease loading at the knee.

The dark green lines in Figure 3.6.2 represent the studies that have assessed peak internal abductor moment, however again due to the lack of literature assessing this parameter no attempt at modelling this data was undertaken. Interestingly the abductor moment values demonstrated an increase in loading over time which is the opposite observed from knee extensor moments. Increased internal knee abductor moment has been associated with the progression of OA and is therefore identified as key parameter for investigation in the present study.

The structural changes in those with ACL injury and in those with pre-existing OA are discussed in the following chapter, which also evaluates methods for detecting degenerative change using MRi. This evaluation of structural changes, in combination with assessment of biomechanics, should give deeper insights into the relationship between biomechanics and structural changes after ACL injury.

3.7 MRi Literature Summary: Creating a Framework for Degenerative Change.

There is a lack of literature assessing changes in structures of the knee using both semi-quantitatively and quantitative methods longitudinally in those with an ACL injury or with pre-existing OA. The literature has shown that once cartilage starts to thin, it

degrades to severe OA. However, the cartilage response in the short and medium term remains largely unknown.

Within the literature on motion analysis different time points were assessed meaning a model of potential adaptations could be created for the early to mid-term periods after injury with which future hypotheses could be generated with an informed idea of the timelines and adaptations involved. For MRi analysis using quantitative and semi-quantitative methods information in these phases is not presently available.

This means that modelling degenerative changes after OA is difficult; however the model generated in Figure 3.7.1 for changes in cartilage thickness and Figure 3.7.3 for semi-quantitative scoring of structures has attempted to reconcile the literature, to create a series of potential models that describe the process of structural changes after ACL injury.

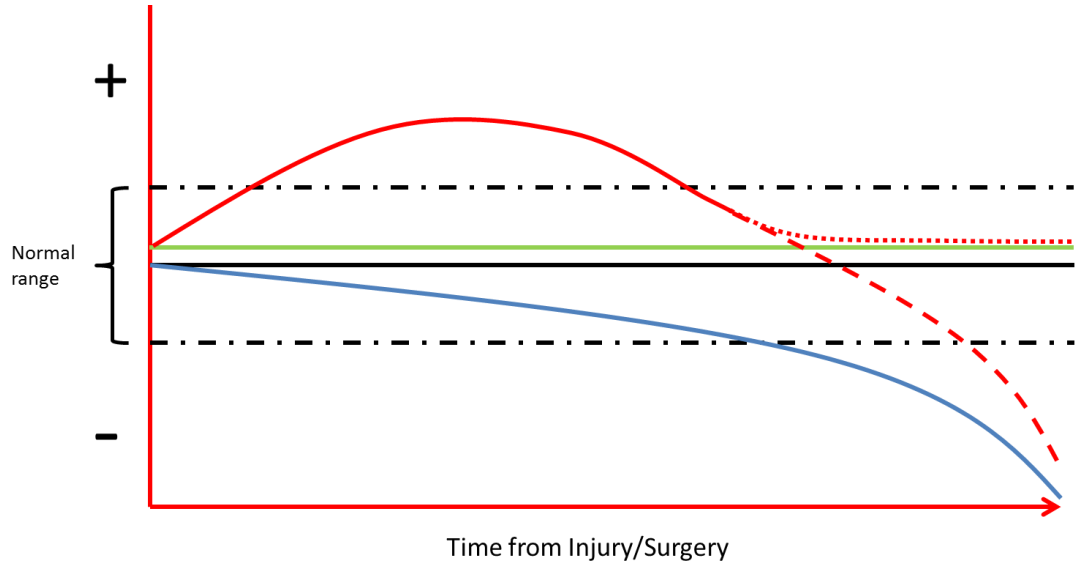


Figure 3.7.1 A framework for cartilage thickness changes after ACL injury. This framework is a generic plot of hypothesised cartilage changes that may happen after ACL injury/surgery with no specific identifiable timeframe applicable due to no appropriate literature available to model changes in cartilage thickness after ACL injury.
Key:+=Increase in cartilage thickness outside of normal variation. -=Decrease in cartilage thickness outside of normal variation. Solid black line = average cartilage thickness. Dashed Black lines= Normal physiological cartilage variation range. Solid green line=Model demonstrating cartilage maintains thickness. Solid red line=Model showing increase in cartilage thickness do to swelling post injury. Thick dashed redline=Period of cartilage thinning after initial swelling, leading to degenerative changes. Dotted red line=After initial swelling, cartilage returns to normal thickness range. Blue line=Model showing slow initial thinning of cartilage, that reaches a point where rapid thinning takes place.

Figure 3.7.1 plots the potential thickness changes in cartilage after ACL injury using the three defined models that can be ascertained from the literature. Firstly, there is no reduction in cartilage thickness within the timeframe that could be related to ACL injury (Solid green line). This model may be possible as advancements in surgical procedures and rehabilitation, including preservation of the meniscus (which has correlated strongly with reduced OA progression), might create a physiologically stable environment. This means the participant can continue to have a healthy knee within the timescales we might expect to see degenerative changes described previously in epidemiological studies.

The second model demonstrates an initial increase in measurement of cartilage thickness (Solid red line) that has been shown in some studies and cited as being an inflammatory 'swelling' response in the early stage after injury. This inflammatory response may contain cytokines that influence the rate of cartilage breakdown and growth; therefore there are two possible modelling pathways that can exist after the initial period of swelling.

Firstly the cartilage remains swollen until biological activity causes cartilage breakdown, this then degrades cartilage quality causing eventual thinning of the cartilage (Red thick dashed lines). Interestingly in this model if cartilage thickness was being measured in the intermediate phase (between points A and B), this would mean solely measuring cartilage thickness may not give an indication of the true condition of the cartilage health. Secondly, after initial swelling the cartilage responds by reducing thickness to its normal physiological state (dotted red lines) where it maintained.

Both of these modelling pathways may be viable and be influenced by a wide variety of inter-related risk factors that combine to determine the outcomes of knee health after ACL injury (Figure 3.7.2). Of these outcomes the present study has targeted key variables that have shown associations with OA (highlighted in red) including age, body mass, activity level, biomechanics, muscle weakness and structural damage caused by injury. Understanding the complex relationships between these variables and how they change over time is the key to unlocking both who and how people develop OA after ACL injury.

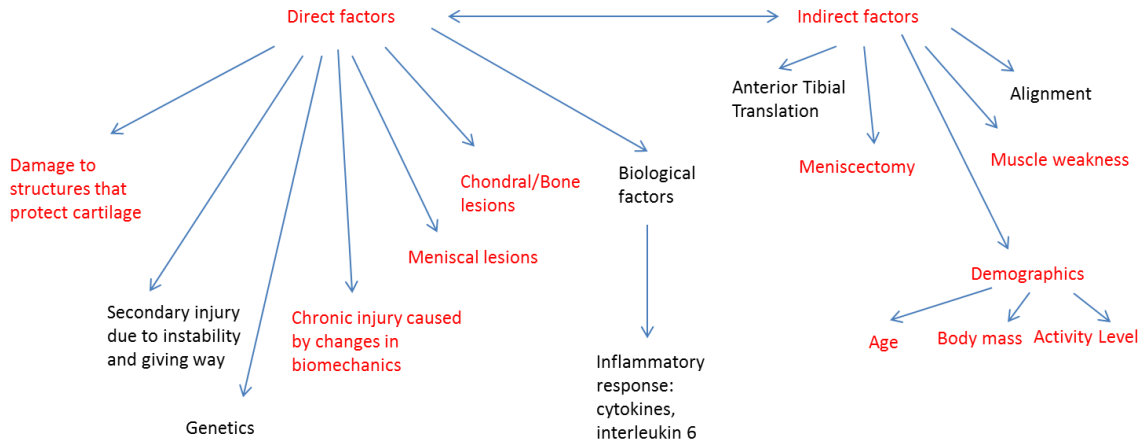


Figure 3.7.2 Risk factors for development of OA after ACL injury. Direct factors are those that have shown a direct and increased risk of the development of OA, whereas indirect factors have shown an association with development OA in certain populations or under specific conditions. Indirect factors will not necessarily carry the same risk as direct factors in the development of OA.

It is of note that semi-quantitative WORMS method only allows for measurement of swelling with the 'grade one' morphology score, having higher MRi signal intensity (appearing lighter) in the central portion of the cartilage and abnormal bulging on the cartilage surface (this is shown in Chapter 5.15.2). This does not however quantify increases or decreases in cartilage thickness in the same manner as quantitative methods. Therefore, the present study used both quantitative and semi-quantitative cartilage measures in conjunction with each other to get both a direct and morphological assessment of cartilage change.

The final model (solid blue lines) shows a more classical view of OA development, with cartilage degrading slowly in the initial period after injury, but then reaching a biological 'watershed' which, after reaching this point, then degrades rapidly into full OA, the rate at which this takes place would again be influenced by the aforementioned patient specific risk factors.

Structural abnormalities caused after injury have been shown to be potential mediators in the development of OA. Again due to lack of longitudinal data it is not yet understood how the key features identified from the literature (BMA, meniscal integrity and cartilage morphology) and targeted in the present study respond after ACL injury.

Figure 3.7.3 shows the framework for how scoring of structures using a semi-quantitative approach may change after injury, under the assumption they were damaged in the initial injury.

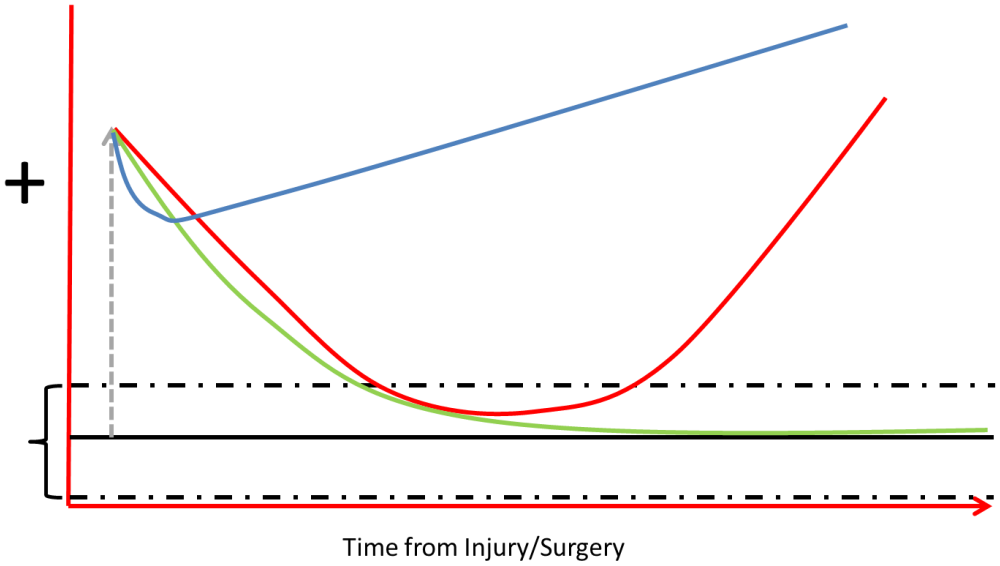


Figure 3.7.3 A framework for structural changes after ACL injury.
Key: +=increase (worsening) of structural integrity score. Blue dashed arrow=Worsening of score associated with injury. Thick black line=Average abnormality score in healthy knees. Dashed black line=Range of expected abnormalities in healthy populations. Solid red line=Model demonstrating initial decrease (improvement) in score, then further increase (worsening) of score. Solid green line=Model showing improvement of score back towards normal expected range. Solid Blue line=Model demonstrating initial short term improvement, then rapid increase of score toward severe degenerative structural changes.

In terms of modelling future changes in structures this is the most challenging as measurements may show marked improvements in the period after initial trauma. This may show initial and expected improvements in score of knee health. However, as time progresses damage caused by inflammation, in the case of BMA and deficiencies in structural integrity in the meniscus, may lead to more long term changes which create a worsening of knee health score. This idea is reflected in the first model (solid red lines).

Therefore trying to assess knee health using just one or even two data points has its limitations and must be put into a context of where that person sits on a time line from

injury. Ideally several assessment points are required with which to plot an accurate trajectory to fully model longitudinal structural changes after ACL injury.

The second model (solid green line) shows a return to normal levels of structural 'abnormality'. This may appear to be a contradictory notion, however at the time of writing no one has assessed a large scale population, across a broad number of age ranges, to explore if structural abnormalities would be expected even within a normal, healthy, functioning knee without any previous serious knee injury.

The final model (solid blue lines) shows that after damage to the structure, a very short term improvement in the feature may occur caused by surgery and unloading the knee after injury, but after a very short initial improvement the structures then degrade rapidly into a worsening of knee health.

In summary structural changes to cartilage thickness and scoring of structural changes to key anatomical features may use one or all of the previously described routes. The path with which knee health takes in an individual would be in large part influenced by the risk factors with which they possessed and regulation of biological activity after injury. By investigating these changes in individuals in combination with profiling for the above risk factors may be important to give insight as to who is most likely to develop early onset OA. This information may be used to target more focussed rehabilitation or advise lifestyle modification to delay the development of OA in these typically younger, healthy and more active populations. This in turn may potentially improve a patient's quality of life and reduce the long term burden on the health system.

3.8 Aims, Objectives and Hypotheses'.

3.8.1 Research Question.

Do those with an ACL injury demonstrate deficits in spatiotemporal, kinematic and kinetic outcomes across functional tasks, and are these associated with changes in articular features of the knee that may be indicative of degenerative change?

The above research question can be broken down into 2 primary aims:

3.8.1.1 Aims and Objectives 1.

Aim 1: To investigate if ACLD and ACLR participants demonstrate kinematic, kinetic, strength and clinical deficits when compared to each other and controls and if these deficits change longitudinally.

Objective 1: To determine knee kinematics and kinetics using a 3D motion analysis system and strength measurement using an isokinetic dynamometer. To assess subjective knee function using patient reported knee scores in ACLD, ACLR and controls.

These will be measured at two time points, post rehabilitation and at a follow up of approximately 1 year.

3.8.1.2 Aims and Objectives 2.

Aim 2: To determine if changes in articular features, associated with degenerative knee change, occur longitudinally in ACL injured participants and to explore if these are associated with kinematic, kinetic, strength and patient reported outcome measures.

Objective 2a: To develop tools capable of detecting changes in articular cartilage using clinical MRi sequences using a quantitative assessment technique.

In order to measure articular change quantitatively, by measuring cartilage thickness change for regions of the knee loaded during activities of daily living a bespoke method of segmentation, using the most appropriate scanning sequences available from clinical MR imaging will be developed. This will also be assessed for inter and intra rater reliability alongside validity.

Objective 2b: Semi-quantitative assessment of key articular features identified in the development of OA will be undertaken using an adapted version of an existing scoring system for measuring knee health.

3.8.2 Hypotheses.

3.8.2.1 Hypotheses': Kinematics and Kinetics.

1. ACLD participants will demonstrate significant differences in kinematics and kinetics in both the frontal and sagittal plane when compared to ACLR and controls.

2. ACLR participants will display significant differences to controls in frontal plane mechanics.

3. Significant differences in kinematics and kinetics will be more pronounced in higher demand activities. This will be more evident in the ACLD.

4. Participants kinematics and kinetics will change significantly between first and second assessment.

Null Hypotheses'

1. ACL injured participants will show no differences in kinematics or kinetics when compared controls across functional tasks.

2. At a 1 year follow up no significant changes will take place in the ACL injured groups' kinematics and kinetics during functional tasks.

3. No significant differences in kinematics and kinetics regardless of demand of activity.

4. The will be no changes in participants kinematics and kinetics between first and second assessment.

3.8.2.2 Hypotheses': Clinical Function and Strength Measurement.

1. Significant strength deficits will exist between both ACLR and ACLD with controls when assessing quadriceps and hamstring strength.

2. Significant reduction will exist between ACLD and ACLR with controls in subjective assessment of knee function.

3. Participants quadriceps and hamstring strength, alongside subjective assessment of knee function will significantly increase between first and second assessments.

Null Hypotheses'

1. ACL injured participants will show no differences in subjective measures of knee function when compared to controls.

2. ACL injured participants will also demonstrate no significant differences in hamstring or quadriceps strength when compared to controls.

3. No change will occur in knee function or strength measurement between first and second assessments.

3.8.3.3 Hypotheses': MRi Assessment of Articular Features.

1. Both semi-quantitative and quantitative assessment of articular features will show significant degenerative changes in articular structures associated with OA, between diagnostic scan and follow-up.

2. Changes in articular structures of the knee will be associated with demographic, kinematics and kinetics and subjective measures of knee function at the knee in ACL injured participants.

Null Hypotheses'

1. There will be no changes in both semi-quantitative and quantitative measurements of articular structures between diagnostic scan and follow up.

2. There will be no associations between demographics, kinematics, kinetics and subjective measures of knee function and changes in measurement of articular structures in the knee.

Chapter 4 Methods (Part 1): Biomechanics, Strength and Patient Reported Measures of Function.

4.1 Study Overview.

This study was a longitudinal prospective study, where recruitment of participants occurred via physiotherapy clinics within the Cardiff and Vale University Health Board. These included participants with ACL injury; those who had had ACL reconstruction (ACLR) and those who did not have surgical intervention (ACLD). These will be referred to as the ACL injured groups. We also recruited a healthy group (referred to as controls) of subjects from within Cardiff University.

The study data was collected across three data collection sessions in the ACL injured groups and one in the control group. Two of the data collection sessions (one for the control group), was a biomechanical assessment at the Research Centre for Clinical Kinesiology (RCCK) at the School of Healthcare Sciences, Cardiff University. Visit one to the RCCK included both ACLD and ACLR participants and the control group. A second visit was performed on a subset of those who attended visit one to the RCCK at a time point 12.9±1.8 months after their first visit.

A third data collection session was also performed on those patients who attended two visits to the RCCK, once consented they had an MRi scan of their injured knee at Cardiff University Brain Research Imaging Centre (CUBRIC). These scans were sequence matched to those scans performed on the ACL injured subjects in the Cardiff and Vale University Health Board following their injury. Both of these scans were used to document changes to knee structures indicative of degeneration within the tibiofemoral joint over time.

Outcome measures included in the assessment at the RCCK were measures of spatiotemporal, performance, kinematics and kinetics for three movements; level gait, jogging and single leg squatting (SLS). Other measurements included the strength of the quadriceps and hamstrings using isokinetic dynamometry and patient reported measures of knee function and fear of re-injury. Participants were assessed using patient reported questionnaires which were the International Knee Documentation

Committee (IKDC) knee function score (Appendix 2), the Cincinnati Knee Function Score (Appendix 3) and the Tampa Scale of Kinesiophobia (TSK) (Appendix 4).

MRi analysis to assess changes between the diagnostic scan performed in the NHS and the follow-up scan performed at CUBRIC included both quantitative (assessing regional cartilage thickness changes using a bespoke method (Chapter 4.17) and semi-quantitative scoring using an abridged version of the WORMS tool described by Peterfy et al. (2004) which assessed changes in articular features linked to the progression of OA using a visual scoring system (Chapter 4.16).

4.2 Recruitment.

Recruitment of participants was through the Acute Knee Screening Service (AKSS) and post-operative knee clinics within Cardiff and Vale University Health Board. Recruitment was undertaken by a research physiotherapist who works for both Cardiff and Vale University Health Board and Cardiff University. Recruitment was supported by NISHCR CRC (National Institute of Social and Health Care Research Clinical Research Centre) officers assigned to the project.

Individuals with an injured ACL and individuals whom had had an ACL reconstruction and were post rehabilitation, were recruited onto this study. In addition an age, gender and activity matched convenience sample of individuals with no knee injury was recruited as the control group..

The inclusion criteria for the ACLD and ACLR groups were:

- A full ACL rupture, with or without accompanying meniscal tear or collateral ligament sprain (Slauterbeck et al., 2009).
- No previous trauma that required clinical intervention, such as physiotherapy or investigative procedures, to either the affected or unaffected lower limb.
- Age 18 to 50 years.

The exclusion criteria were:

- Individuals suffering from neurological or other musculoskeletal pathology which affects their lower limb mobility.
- Inability to provide informed consent to participate.

This articular age range was chosen as biomechanical changes have been demonstrated to be related to age. Those over 50 are more likely to have associated changes relating

to knee pathology independent of ACL injury. This is also why this was a limiting factor in selecting the control participants (Hunter et al., 2009).

The inclusion criteria for the healthy control group were:

- No previous trauma that required clinical intervention or assistive devices to either limb including ankle knee and hip.
- Aged 18 to 50.

Exclusion criteria were:

- Any pathology or injury that impacts upon lower limb movement.

4.2.1 Recruitment Procedure.

Patients that met these inclusion criteria were given an information sheet (Appendix 5) on their visit to their physiotherapy appointment and a minimum of 48 hours to read the information. These were identified by either physiotherapist or research officers who were associated with the study form the physiotherapy departments NHS patient database. On their next physiotherapy appointment they were asked if they were willing to participate and written informed consent (Appendix 6) was obtained by the research physiotherapist or NISCHR CRC officer, after detailing the purpose and content of the research and answering any questions. They were then followed up to arrange an appointment date by the research team, with further confirmation on eligibility to take part in the study and further information regarding their participation was sent either via post or email.

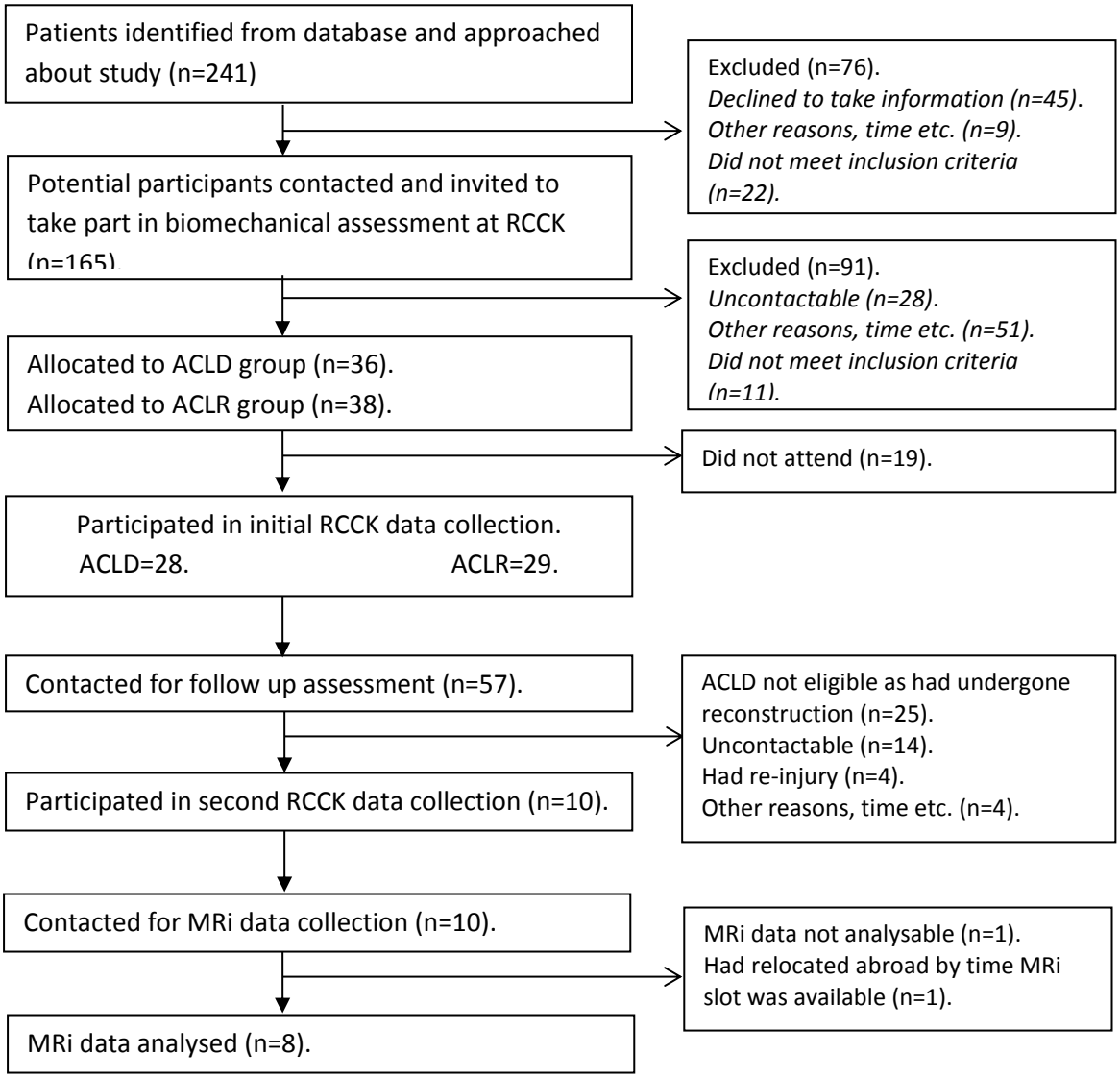


Figure 4.2.1 Recruitment process from Acute Knee Screening Service to MRi.

4.3 Sample Size Calculation.

Sample size calculation was undertaken using the following formula taken from Biau, Kernéis and Porcher, (2008). This proposed method uses previous literature in related studies to determine estimations of sample size.

$$n = \frac{2 \times (z_{1-\alpha/2} + z_{1-\beta})^2}{d_t^2} + 0.25 \times z_{1-\alpha/2}^2$$

Statistical significance was deemed at α=0.05, $Z_{1-\alpha/2}$=1.96, $Z_{1-\beta=}$1.28, β=0.10 (power of 90%), $l\mu_0-\mu_1 l$=0.06 (difference between group means), σ=0.085 (standard deviation of both groups), d_t=difference between means/standard deviation of both groups).

Values for the mean and standard deviations used in this formula were taken from Butler et al. (2009), who assessed gait mechanics in ACL injured participants; in particular the internal knee abductor moment was cited as an indicator of abnormal gait function that may lead to OA changes in the long term.

Transposing values into the above equation gives:

$$n = \frac{2 \times (1.96 + 1.28)2}{(\frac{0.06}{0.08})^2} + 0.25 \times 1.96^2$$

n= (20.99/0.75)+0.96= **28.94** participants in each group for a power of 90% at α=0.05.

For internal knee extensor moment figures were chosen from the paper by Bush-Joseph et al. (2001), who were the only study to assess kinetics in during jogging in ACLR participants.

Transposing values into the equation gives:

$$n = \frac{2 \times (1.96 + 1.28)2}{(\frac{3.1}{4.0})^2} + 0.25 \times 1.96^2$$

n= (20.99/0.6)+0.96=**35.94** participants in each group for a power of 90% at α=0.05.

4.4 Ethical Approval.

Ethical approval was given by the Research Ethics Committee for Wales (Reference: 10/MRE/09/28) on the 14th of October 2010. From November 2010 subjects were recruited under a multi-project ethical approval obtained for the Arthritis Research UK Biomechanics and Bioengineering Centre (ARUK BBC) based across several Schools at Cardiff University. This covered many aspects of the centres research including motion analysis and imaging (including MRi) used in this study.

4.5 Risk Assessment.

A Risk Assessment attempts to estimate the combined effect of the severity of an incident multiplied by the likelihood that incident will take place, therefore:

Risk = Severity x Likelihood

The practical significance of this is that even with high hazards, proper control measures can sufficiently reduce the likelihood of harm to adequately control the risk. Conversely, a relatively low hazard can become a substantial risk if not properly controlled. Risk was calculated for all tasks undertaken in the data collection session using Table 4.5 below.

Table 4.5 Likelihood and severity scores for calculating risk.

Likelihood	Severity
0 Zero to very low	0 No injury or illness
1 Very unlikely	1 First aid injury or illness
2 Unlikely	2 Minor injury or illness
3 Likely	3 “Three day” injury or illness
4 Very Likely	4 Major injury or illness
5 Almost certain	5 Fatality, disabling injury

Likelihood and severity scores for calculating risk associated with RCCK activities taken with permission from Cardiff University School of Healthcare Studies Research Ethics Handbook 2011/2012.

For each task the worst case severity was ranked 4, with major injury being the worst outcome of participating in this research for any patient, this would be an exacerbation of their knee symptoms (pain, swelling or giving way) during or following a data collection session. For walking the severity of injury was three but the likely hood of an injury occurring was categorised as zero giving an overall risk factor of 3x1=3

For jogging and SLS the likely hood of injury was greater as these activities place more demand on knee stability, and generated a likelihood score of two with a severity of three, giving an overall score of six.

Strength testing was also deemed as a likelihood of two and severity of three giving a score of six.

Even though the risk of injury is low for all tasks to further minimise the risk of injury, participants will only be allowed to perform activities that are considered safe following assessment of the participant's current knee function. Anyone experiencing increased knee symptoms was assessed in the AKSS and appropriate treatment given.

4.6 Informed Consent and Information Sheet.

The information sheets and consent forms for assessment in the RCCK and MRi at CUBRIC and participant information sheets can be found in Appendices 4-7.

4.6.1 Confidentiality of Data and Anonymity.

Individual participant codes were used on all data collection sheets and questionnaires. These were stored in a lockable filling cabinet in the School of Healthcare Sciences, Cardiff University. An excel database of participant names, contact details and research codes were stored on a computer in the School of Healthcare Sciences, Cardiff University. These databases are password protected and only accessible to the project researchers, who were responsible for scheduling the follow-up appointments on completion of rehabilitation and at two years post injury/surgery.

The video recordings of patients performing functional activities were used to extract biomechanical data. All the video tapes were stored in a lockable cabinet within School of Healthcare Sciences, Cardiff University. These tapes will be erased on completion of the research. No patients were identifiable in any reports, publications or presentations used to disseminate the results of the study.

All patient data will be maintained for 15 years according to Research Ethics Committee and Cardiff University Research Governance guidelines. During data collection participants were asked to wear tight fitting clothing. For patient privacy and confidentiality the laboratory data collection area was screened away from the view of other people and only the researchers linked to the study were permitted to enter the data collection area.

4.7 Pilot Studies.

During piloting for the study, key issues with technical equipment were raised. Firstly, the Kincom isokinetic dynamometer was problematic in terms of safely securing the

limb when testing isokinetic strength thus a new isokinetic dynamometer, the Biodex S4, was purchased.

The pilot study determined that it took approximately 1.5-2 hours per data collection session for assessment of walking, running, and SLS. Between three and eight valid trials of each activity were collected.

It was noted that the Vicon Nexus system was not accurately detecting the reflective markers within the required data collection volume. On further inspection of the motion analysis cameras it was apparent 2 lenses did not have the sufficient focal length to be able to pick up markers effectively which was creating severe 'flickering' of the markers meaning the system could not be calibrated.

This issue was rectified by acquiring new lenses for two cameras and a Vicon engineer attended to ensure proper installation, aimed the cameras and adjusted the intensity and sensitivity threshold of the lenses for the appropriate data collection volume. These were checked for appropriate level of error using the in-built Vicon Nexus calibration procedure which included the waving of a standardised 5 marker 'wand' with each camera having to register 1000 frames. The accepted level of image error for each camera in the system was <0.2mm and this was also the same standard for participant data collection sessions.

The Kistler Force platform (Model 9281C, Switzerland) had been calibrated in the factory and values for the sensitivity inputted into the Vicon Nexus system. During piloting and periodically throughout the data collection period the force platforms output through Vicon Nexus was assessed for accuracy using a standardised 20kg/191.1N weight. The Kistler Force platforms output through the Vicon Nexus was found to be within 0.5% (0.1N) of the calibration weight for within the Fz range of 0-10kN in which the data collection was undertaken.

Piloting also developed appropriate communication at key times as there was a requirement for the researchers to be doing different tasks that needed to be synchronised and also to accurately instruct the participant in the most effective way to perform the tasks .

4.8 Participant Information.

To clarify the multi-dimensionality of this study with respect to the groups of subjects participating. The flow chart (Figure 4.8) below represents the various cohorts undergoing data analysis.

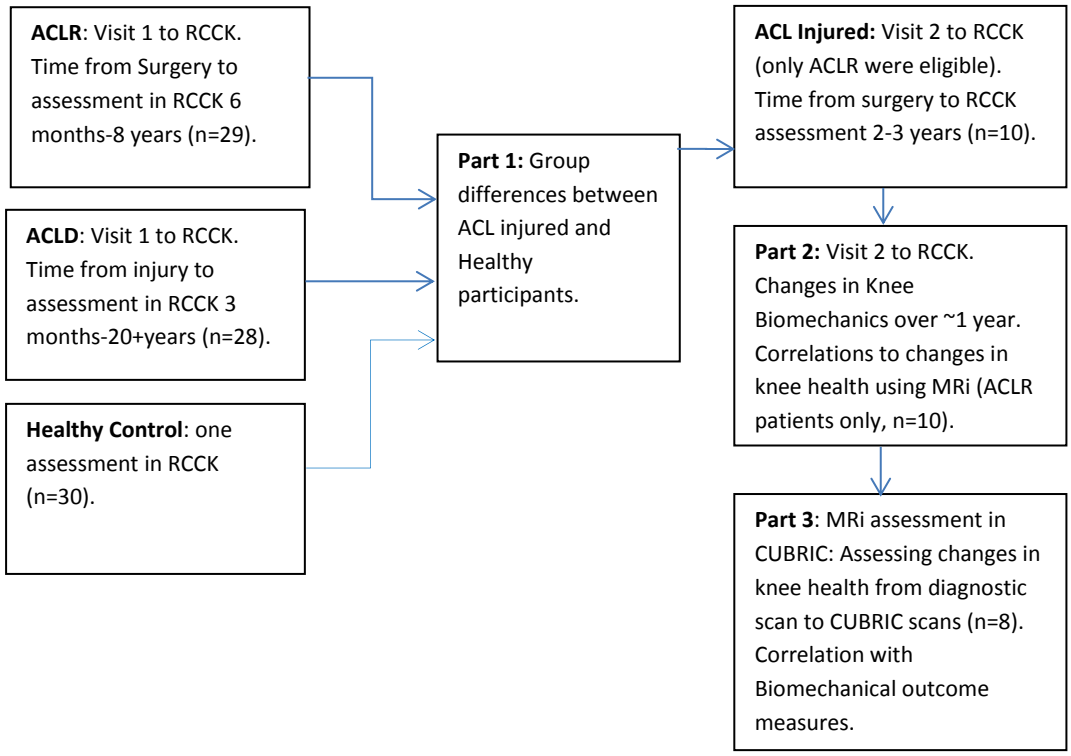


Figure 4.8 Flow chart of participant data collection journey.
Flow chart representing the data collection and analysis journey including participant numbers at each stage, from full group assessment at the RCCK to follow-up assessment in the RCCK and finally to MRi assessment.

4.9 Data collection Tools.

A detailed list of all data collection equipment, including manufacturer information, can be found in Appendix 9.

4.9.1 Questionnaires.

At the start of each visit to the RCCK participants completed validated questionnaires, the International Knee Documentation Committee (IKDC) functional knee outcome score, the Cincinnati knee score and the Tampa Scale of kinesiophobia (TSK). These questionnaires covered aspects such as pain, fear of re-injury and activity levels

4.9.1.1 IKDC Subjective Knee Form and Cincinnati Knee Score

The IKDC subjective knee score was developed by an international committee from both the American Orthopaedic Society for Sports Medicine (AOSSM) and the European Society for Sports Traumatology, Knee Surgery and Arthroscopy (ESSKA). These groups combined to form the International Knee Documentation Committee (IKDC) (Higgins et al., 2007).

The measurement tool was developed to assess knee function and consists of the measurement of symptoms including pain, stiffness, swelling, joint locking, and joint instability. Other items designed to measure knee function assess the ability to perform activities of daily living. The IKDC consists of 18 scored items and has been validated in several languages (Higgins et al., 2007).

Higgins et al. (2007) used an exploratory factor analysis and this demonstrated a two-factor solution, these were related to and defined as symptom and knee articulation (SKA) and activity level (AL). Both SKA and AL demonstrated good internal consistency (0.87 for SKA; 0.88 for AL). Both SKA and AL demonstrated statistically significant correlations to the SF-12 (short form 12 health questionnaire) total score, particularly to the physical component (Higgins et al., 2007).

Irrgang et al. (2001) state that the IKDC has shown an internal consistency coefficient (Cronbach's alpha) of 0.92 and test-retest reliability of 0.95. Validity of the IKDC subjective knee form was demonstrated through its relationship with the SF-36 physical function subscales (r=0.44-0.66). Analysis using Partial Credit Item Response Theory (PC-IRT) demonstrated that item responses correlated appropriately with levels of function. The analysis also demonstrated that the IKDC was appropriate in scoring knee function across different genders, age ranges and different diagnoses. Both the above studies state that the IKDC is a reliable and valid tool capable of assessing knee function across a wide variety of knee pathologies.

The first iteration of the Cincinnati knee rating system was undertaken to create an instrument that can be used across a number of knee pathologies (Barber-Westin et al., 1999). Barber-Westin et al. (1999) assessed the reliability of the tool on 100 hundred participants tested one week apart. Validity and responsiveness were assessed on a cohort of 250 participants with ACL reconstruction over a period of 2 years. The items on the questionnaire demonstrated high test-retest reliability (all intra-class correlation coefficients were 0.70 or above). In addition, the questionnaire demonstrated both good

content validity and construct validity. Importantly the tool was highly responsive to clinically and patient reported changes in knee function.

Risberg et al. (1999) assessed both the Cincinnati Knee score and IKDC to determine sensitivity over time, the relationship between the scores and the criterion validity of the IKDC score. The study included 120 participants having undergone ACL reconstruction with a follow up period of 3,6,12 and 24 months post-surgery. Data from these tools was compared to tests for knee joint laxity and functional tests. The Cincinnati Knee score was demonstrated to again be highly sensitive to change in function over time. The IKDC demonstrated high criterion validity, indicating that the tool is a good means of documenting clinical examination at one follow-up, but not of detecting changes over time. Importantly, Risberg et al. (1999) stated that individually these are important tests and are significant outcome measurements for patient reported knee function after ACL reconstruction. However, the limitations of each tool mean they should be combined for a thorough analysis of knee function over time.

4.9.1.2 TSK

The TSK was developed as it is widely recognised that not only functional outcomes, but psycho-social factors influence a person's return to their previous activity level following injury (Kvist et al., 2005). Houben et al. (2005) stated that a person who has thoughts about the vulnerability of their body and its susceptibility to injury is likely to be fearful of certain movement patterns and the chance of re-injury, especially if they are still experiencing pain. Houben et al. (2005) speculated that negative emotions towards movement are associated with increased muscular reactivity and avoidance and in the long term have the potential to negatively affect a patient's psychological and physiological wellbeing.

The TSK was developed to assess fear of movement in patients suffering with musculoskeletal pain, an idea adapted from the pain avoidance theory (Damsgard et al., 2007). In short, pain leads to fear which leads to avoidance of activities related to the cause of pain. The TSK is a 13 item questionnaire directed to assess the fear of movement and re-injury, each item is scored on a 4 point Likert scale from 'strongly agree' to 'strongly disagree' (Damsgard et al., 2007). Vlaeyen et al. (1995) demonstrated the TSK to be sufficiently reliable (Cronbach's Alpha=0.77). Kvist et al. (2005) employed the TSK in an ACL reconstructed cohort, to investigate if fear of injury was a factor influencing return to participation to a patient's pre-injury level.

After a time period of 3-4 years post-surgery only 53% of the patients had returned to their pre-injury activity level, with those with higher fear of re-injury demonstrating a lower activity levels and this was also correlated with a lower quality of life

4.9.2 Vicon Nexus.

3D motion capture is an established technique used to assess human movement and performance (McGinley et al., 2008; Schwartz et al., 2004). In order to assess the kinematics and kinetics of our participants the Vicon Nexus (UK) motion capture system with eight specially designed infra-red cameras was used.

Retroflective markers 12mm in diameter were placed at specific anatomical locations as designated by the Plug-in Gait full body model (see Figure 4.9.2.1a and 4.9.2.1b). The Plug-in Gait model is an automated biomechanical model which when created accurately gives patient specific kinematic and kinetic data including joint angles, forces and joint moments and powers, as well as spatiotemporal characteristics. Plug-in Gait is the Vicon implementation of the Conventional Gait Model (CGM) (Oxford Metrics, 2010).

The present study used the full body Plug-in Gait model for several reasons. Firstly it was ready to use immediately without the need for development of our own models; this had the advantage of allowing data collection to be undertaken almost immediately which was important for completion of the present study within a reasonable timeframe. Secondly, the data included in this thesis was part of a larger study that was interested in whole body compensations after ACL injury; therefore a full body model was required. This also allowed for the calculation of squat depth in the present study, which was calculated the vertical displacement of the participants centre of mass. Thirdly, compatibility of the Plug-in Gait model with Vicon's other software makes Plug-in Gait an adaptable data collection model that can easily be manipulated to allow for easier processing and analysis of data.

4.9.2.1 Plug-In Gait Marker Setup.

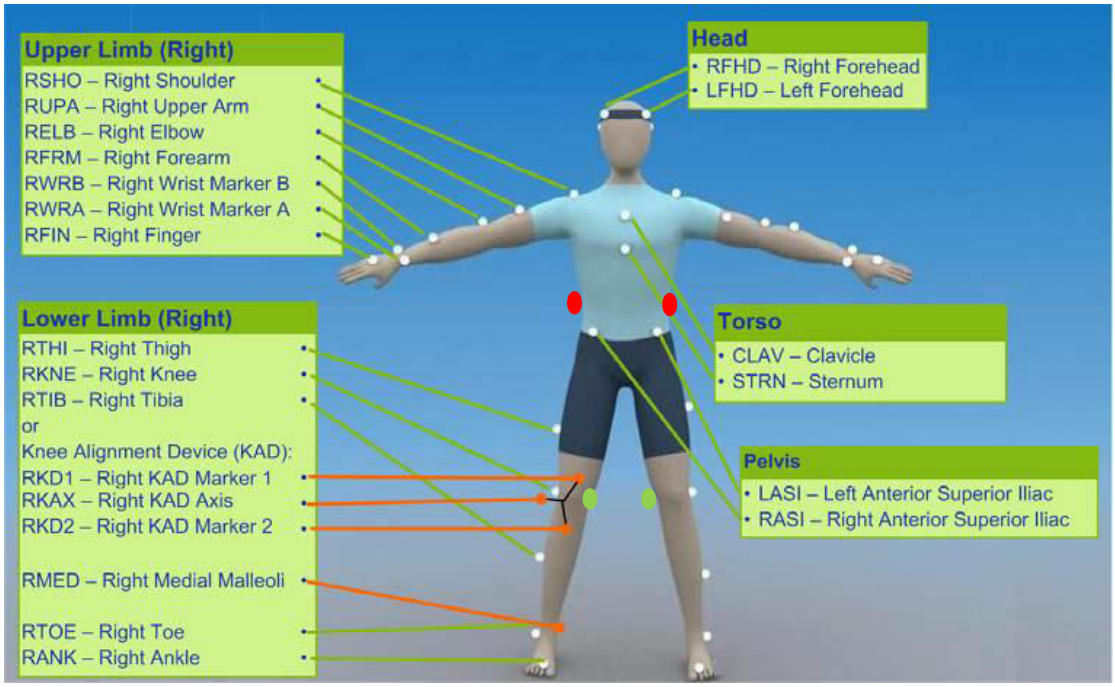


Figure 4.9.2.1a Plug-in Gait marker positioning, anterior view.
Note: The red dots on the hips represent the positioning of additional markers for recreating ASI markers using Plug-in Gait. Green dots on the medial side of the knee were used to aid with calibration and to more accurately measure knee alignment during calibration. The model was used without the addition of the optional KAD (Knee Alignment) device.

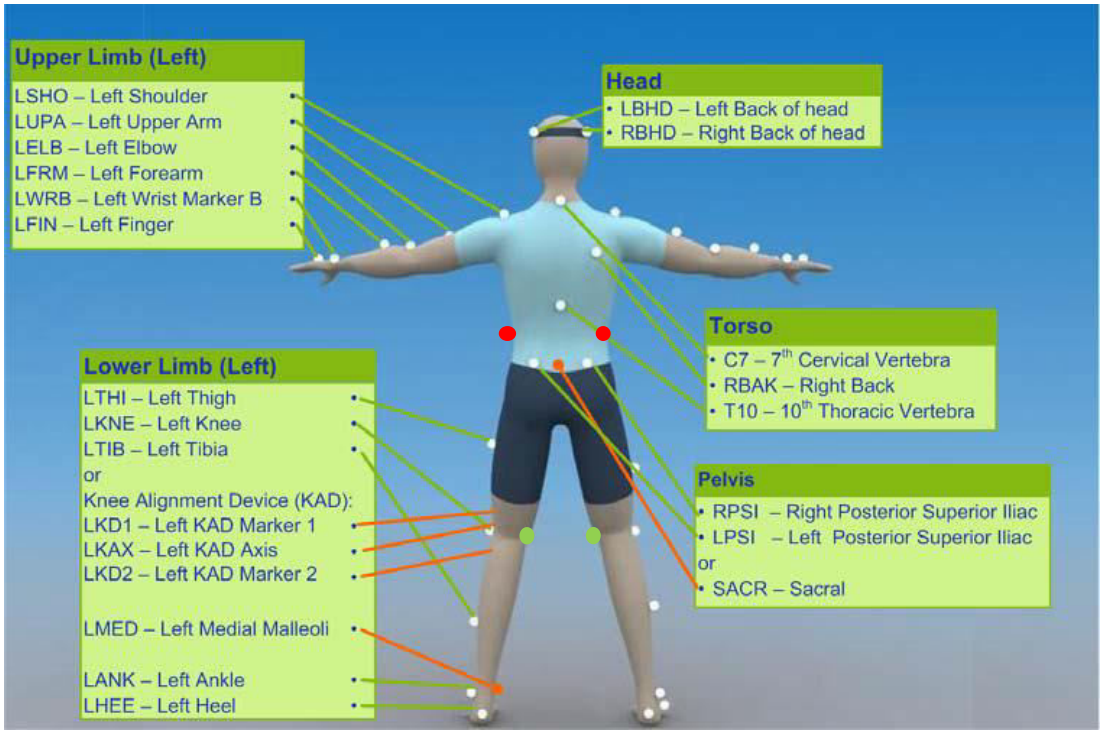


Figure 4.9.2.1b Plug-in Gait marker positioning, posterior view.
The model was used without the addition of the optional KAD device and SACR (sacroiliac) marker.

4.9.2.2 Coordinate Systems and Calculation of Joint Centres.

The direction of the subject walking in the global coordinate system is determined in Plug-in Gait by the Clinical Gait Model (CGM) applied to the lower limb. This uses the first and last valid position of the LASI marker. The x displacement is compared to the y displacement. If the x displacement is bigger, the subject is deemed to have been walking along the y axis either positively or negatively. Otherwise, the y axis is chosen. It is always assumed that the z axis is always vertical.

The Pelvic Coordinate System.

The pelvic coordinate system in the CGM is defined from the pelvic markers with the origin taken as the mid-way point between the ASIS markers. The dominant y axis is defined along the line from the right to left ASIS markers. The secondary y axis (pelvic tilt) is defined from the mean position of the two PSIS markers in relation to the ASIS markers. The vertical z axis is perpendicular to this plane and the x axis is perpendicular to both these planes in the forwards direction (Figure 4.9.2.2a).

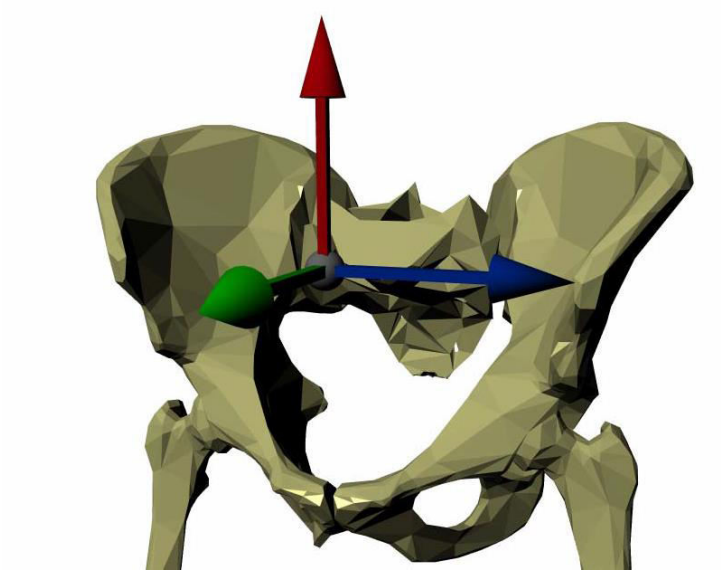


Figure 4.9.2.2a Pelvic Co-ordinate System.
Key: Green arrow represents x axis, blue arrow represents y axis and red arrow represents z axis.

The ASIS are also used to determine the lateral positions of the hip joint centres within the pelvis segment. These affect the determination of the femur segments, and thus influence both the hip and knee joint angles.

Calculating the Hip Joint Centres.

The Newington-Gage model is used to define the positions of the hip joint centres in the pelvis segment. A special vector in the pelvic coordinate system defines the hip joint centre using pelvis size and leg length as scaling factors (Davis, Õunpuu, Tyburski and Gage, 1991).

Calculating the Knee Joint Centres.

The knee joint centre is calculated in the same manner for both the static and dynamic models. The knee joint centre is determined using a modified chord function, calculated from the position of the hip joint centre, the thigh marker and the lateral knee marker, together with the knee offset (half of the width of the knee at the knee marker position) and thigh marker angle offset (Figure 4.9.2.2b). The anterior-posterior position of the

knee joint centre is determined by the position of the thigh marker and the value of the thigh marker offset was assumed to be zero.

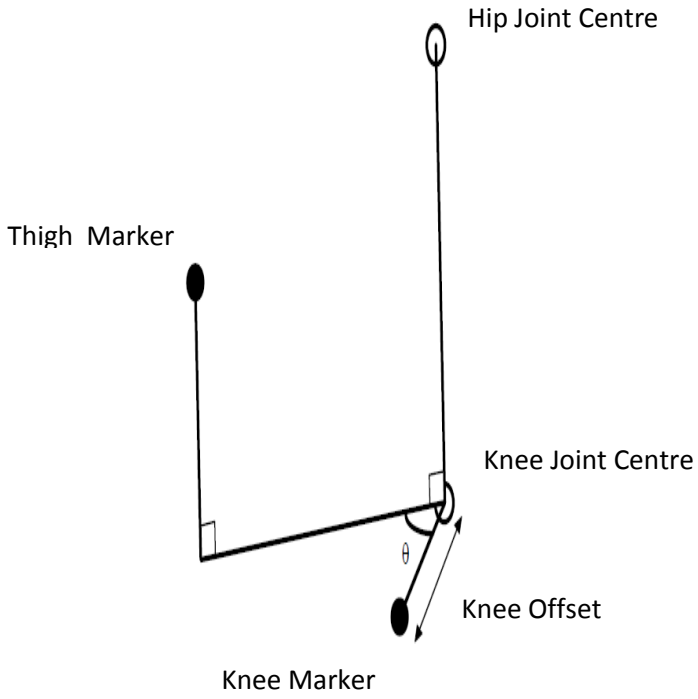


Figure 4.9.2.2b Using a Modified Chord Function to Determine Knee Joint Centre. Using the hip joint centre, thigh and knee markers together with knee offset measurement and thigh marker offset (Ø assumed to be zero).

The Femur Coordinate System.

The femur origin is taken as the knee joint centre. The z axis is taken from the knee joint centre to the hip joint centre. The secondary axis is taken parallel to the line from the knee joint centre to the knee marker and also directly gives the direction of the y axis. For both the left and the right femur, the y axis is directed towards the left of the subject. The x axis for both femurs is hence directed forwards from the knee. The lateral orientation is defined by the vertical orientation of the Z axis (the line joining the hip and knee joint centres). The y axis may pass either above or below the knee marker (Figure 4.9.2.2c).

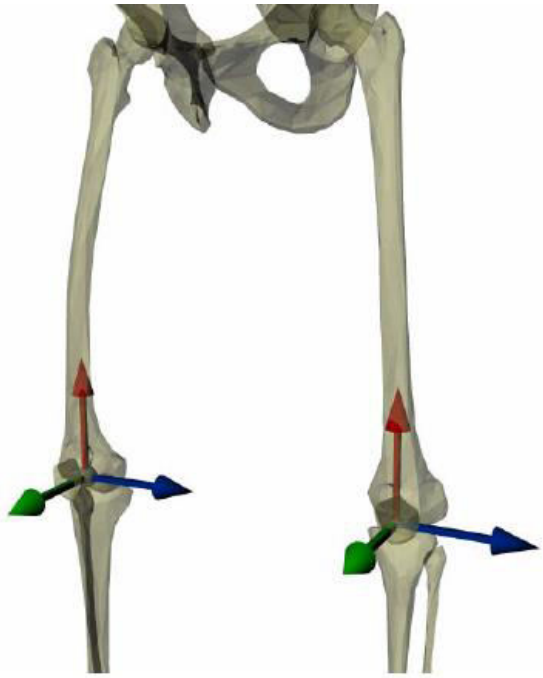


Figure 4.9.2.2c The Femur Coordinate system.
Key: Green arrow represents x axis, blue arrow represents y axis and red arrow represents z axis.

Calculating the Ankle Joint Centres.

The ankle joint centre is calculated in a similar manner to the knee joint centre. Using a modified chord function including the knee joint centre, tibia marker and ankle marker with the ankle offset (half of the ankle width) and tibia marker rotation offset. Thus the ankle joint centre is at a distance of ankle offset from the ankle marker, and the angle between the knee joint centre-ankle joint centre-ankle marker plane and the knee joint centre-ankle joint centre-tibia marker plane is equal to the tibia rotation offset.

The Foot Coordinate Systems.

The model effectively makes two foot segments. For both segments, the ankle joint centre is used as the origin. The first foot segment is constructed using the toe to heel marker line as the primary axis. The heel marker point is moved vertically (along the global z axis) to be at the same height as toe marker. This line is taken as the z axis, running forwards along the length of the foot. The direction of the y axis from the tibia is used to define the secondary y axis. The x axis thus points down, and the y axis to the left. A second foot segment is constructed, using the toe marker to ankle joint centre as

the primary axis, and again the Y axis of the tibia to define the perpendicular x axis and the foot y axis.

The Static offset angles (Plantar Flexion offset and Rotation offset) are then calculated from the 'yxz' Cardan angles between the two segments. This calculation is performed for each frame in the static trial, and the mean angles calculated. The static plantar-flexion offset is taken from the rotation round the y axis, and the rotation offset is the angle around the x axis. The angle around the z axis is ignored. The angle is measured between the line joining the heel and toe markers and the line joining the ankle centre and toe marker. A positive static foot rotation value corresponds to a foot vector internally rotated with respect to the line joining the ankle centre and toe marker.

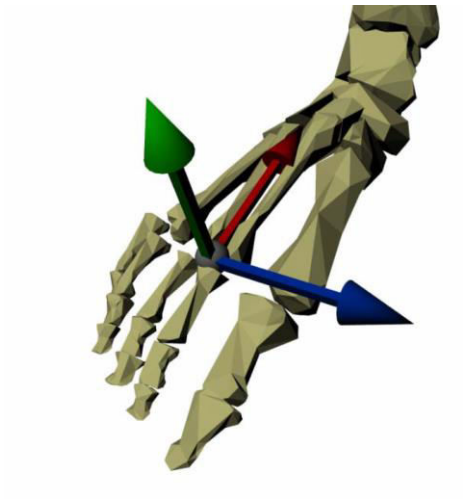


Figure 4.9.2.2d Foot Coordinate System.
Key: Green arrow represents x axis, blue arrow represents y axis and red arrow represents z axis.

Plug-In Gait Angle Outputs.

The output angles for all joints are calculated from the yxz Cardan angles derived from the relative orientations of the two segments. Knee angles are calculated from the femur and tibia segments. The ankle joint is calculated from the tibia and the foot segment.

4.9.2.3 Additional Modelling.

From initial piloting of data collection and processing it became apparent that as the Plug-in Gait model is specifically designed for gait that during the more dynamic activities, in particular SLS, certain markers around the pelvis (ASIS markers in Figure 4.9.2.1a) were missing throughout a large number of frames in the data with gaps up to 75 frames. This was found to be too large of a gap for the Vicon Nexus in-built gap

filling splines to accurately plot the missing ASIS trajectories. This method uses the trajectory of only one selected marker, subjectively selected to be of a comparable trajectory to the missing marker.

It was therefore necessary to add additional markers to the participant (red markers on Figures 4.9.2.1a and 4.9.2.1b) on the iliac crest. Vicon BodyBuilder software used these markers in combination with the remaining visible markers to more accurately recreate the position and trajectories of the missing ASIS marker (www.vicon.com/bodybuilder) throughout the entire movement in gaps larger than ten frames. This method was developed by a member of the research team (Dr PRH), who was experienced in the creation of motion analysis models. These extra markers were used solely for the purpose of recreating the missing ASIS markers and not incorporated into the gait model. This meant that the Plug-in Gait model could still be applied to the data without need for recalculation of the hip joint centres.

To check errors in this method, artificially created gaps of differing lengths were placed in a complete trial which had no gaps in the ASIS trajectory data, these gaps were then filled using the above method. The filled trajectories were then compared to the real trajectory data and errors were found to be less than 10mm in all planes, which although a notable error, appeared to have no discernible effect on peak knee moments.

Markers were also placed on the medial aspect of the knee (green markers on Figures 4.9.2.1a and 4.9.2.1b). This was necessary as early data showed much larger than expected frontal plane knee angles during the SLS activity. This was caused by the knee co-ordinate system being calculated during a static calibration trial where a participant's foot, and in turn lower limb position (which would be likely to be externally rotated in relation to the pelvis), gave a false frontal plane knee axis relative to the pelvic position. This error was not for a large part noticeable during gait and jogging (although was problematic in some participants), as frontal plane knee range of motion was small and the error in alignment was typically only a few degrees, but during SLS this error was amplified by the large range of motion at the knee in the frontal plane. The acute angle between the thigh, knee and ankle markers also increased sensitivity to changes in position of the lower limb outside of what would be expected during gait, for which this model was developed.

Therefore, the medial knee marker was added during the static calibration trial, and in conjunction with the existing lateral knee marker, allowed for a frontal plane knee

angle offset to be calculated in relation to the pelvic frontal plane coordinate system (Figure 4.9.2.3). This was also calculated using Vicon BodyBuilder (PRH).

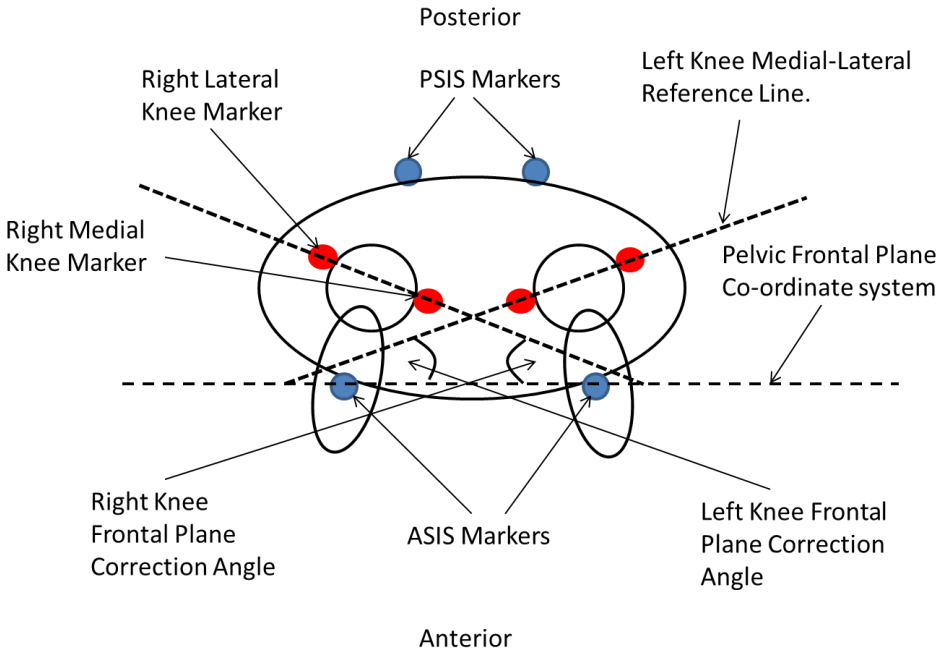


Figure 4.9.2.3 Technique for calculating frontal plane knee angle correction.
Key: Axial view of the pelvis and lower limb. Blue circles represent markers on the pelvis and red circles represent medial and lateral knee markers. Pelvic frontal plane co-ordinate system calculated from the pelvic markers. Due to external rotation of the feet/lower limb during calibration, using only the lateral knee marker created a 'false' knee frontal plane co-ordinate system. The addition of a medial knee marker allowed for a calculation of an offset to the frontal plane pelvic system co-ordinates. This was used to correct the knee co-ordinate system into a position that would be representative of its relationship to the pelvis during the activities where the foot and lower limb position would be less externally rotated than during relaxed standing.

This correction was then applied to the dynamic trials to adjust for the knee static alignment errors. Interestingly, testing of this correction performed by PRH had a profound effect on frontal plane knee angles, adjusting them to more appropriate values for the SLS, but this had no discernible effect on frontal plane moments. This shows that data from frontal plane kinetics can be treated with relative confidence; however frontal plane angles should be interpreted with caution.

4.9.2.4 Determining Data Collection Frequencies.

As the nature of a movement such as jogging includes rapid accelerations and decelerations, the highest possible frequency for the motion camera system was required to acquire as much useful data as possible for this task. This was achieved by optimising the frequency of camera collection with the ability for the markers to be distinguished for effective processing and analysis. After a process of trial and error using 100, 200, 250 and 500Hz, the maximum frequency for motion capture with ability to track marker trajectories with minimal flickering was 250Hz (which also was compatible with the frequency of the force platform at 1000Hz for synchronisation purposes) and this was used across all tasks performed for convenience. Force platform data was collected on a Kistler Force platform (Model 9281CA, Switzerland) at 1000Hz and synchronised to the motion capture data systems kinematic data in order to calculate knee kinetics.

4.9.3 Isokinetic Dynamometer.

Isokinetic dynamometry has shown to be highly accurate and reliable in making strength measurements by a number of studies (Drouin et al., 2004; Gleeson et al., 1992; Gross et al., 1991; Lund et al., 2005). Measuring knee extension and flexion torque, representing participants quadriceps and hamstring strength, has been demonstrated to be a safe measurement tool in both ACLD and ACLR populations across several time points from within weeks of injury (Dvir, 2004).

It was determined that isokinetic, concentric/concentric muscle strength of the knee flexors and extensors would be measured. Although eccentric strength of the knee flexors would be a useful measurement due to its proposed relationship with quadriceps avoidance strategy, piloting suggested it was a difficult measure to take using isokinetic dynamometry, with many participants not able to grasp the concept and apply force in the appropriate manner to be a reliable measurement.

Isokinetic motion was chosen over other modalities as peak torque would be identified throughout the entire ROM not isolated to the specific angle chosen in isometric contractions. Using data described in Dvir (2004) summarising several studies assessing the optimum speed to measure maximum strength, this appears to be in the range of 60-120°/s, therefore 90°/s was used for assessing our participants.

4.10 Laboratory Protocol.

The data collection area was cleared of items that may cause a potential trip hazard or cause reflective artefacts. Reflective artefacts are unwanted areas of reflection that are registered by the Vicon system. These can be masked out of the data collection volume, but this may interfere with the marker being located by the system if its trajectory passes through the masked area which will cause difficulties in data collection and post data model processing.

Before the participant arrived the Vicon Nexus system was calibrated following the appropriate guideline, a data collection session created for the participant using an individualised code to ensure anonymity. Synchronisation between the Vicon System cameras and force platform was checked visually by a researcher standing on the platforms and shifting their weight from one platform to the other. This also allowed for a check of the output from the force platform being an appropriate measure of force compared to the researcher's mass, measured using scientific scales (Seca 888, UK).

Before this took place the force platforms were zeroed using the control box reset buttons, this was also performed between each data collection trial.

The marker set and check list to ensure correct marker placement was prepared. The Biodex S4 isokinetic dynamometer system was calibrated and the assessment protocol selected. Other data collection tools such as questionnaires, trial sheets and the participant demographic data sheet were prepared (Appendix 10).

4.10.1 Participant Demographics for Motion Analysis Modelling.

Participant's anatomical measurements were inputted into the Vicon Nexus motion analysis system in order to create kinetic models. Measurements taken where in mm and were as follows:

Height, body mass and for both limbs, leg length, ankle width, knee width, hand thickness, wrist width, elbow width and distance from acromio-clavicular marker to centre of glenohumeral rotation.

4.10.2 Participant Preparation and Familiarisation.

Participants were required to wear suitable footwear, shorts and provided with a tight fitting vest, to ensure that markers placed on the torso were as close as possible to the skin whilst maintaining patient dignity. Reflective markers were placed by personnel trained by an experienced physiotherapist who had undertaken motion analysis research

(Dr KB) in identifying anatomical locations described by the Plug-In-Gait marker set (Oxford Metrics, 2010). The retroflective markers were attached using strong double sided tape. In areas prone to loosening micro-pore tape was used for extra fixation. The marker locations were checked and verified by at least one other researcher to ensure marker placement reliability. Activities of daily living and sport would be undertaken in the participant's own footwear. It was for this reason the participant's own footwear was chosen over standardised footwear as the research question was concerned with 'real world' loading's impact on the development of OA.

Each subject was familiarised with the laboratory and demonstration of the tasks to be completed. The markers were applied prior to the active trials for two reasons: firstly to identify areas were the markers did not fixate well and reinforced these points and secondly to instil confidence in the participant that the markers remain in place securely during movement to prevent the participant moving uncharacteristically which may have dislodged the markers.

4.10.3 Data Collection Task Description.

4.10.3.1 Calibration.

After the markers were attached and patient measurements entered into the system, the participant stood in the middle of the data collection volume with their arms in front of them, slightly bent at the elbows, with their thumbs pointing to the ceiling. A trial of approximately 5 seconds in length was collected.

Immediately, this trial was loaded into the Vicon Nexus system where a frame with each of the markers visible was identified. Each marker was then manually labelled according to the Plug-in Gait specification. The labelled model was then processed using the static Plug-in Gait calibration option, this allows the Vicon system to give real time feedback with the model attached, thus enabling the operator to see clearly the efficacy of the data in the live trials and to assess for any issues with marker placement or visibility and further ensure synchronisation with force platforms.

4.10.3.2 Walking.

Participants identified either the injured leg, or dominant leg in the control group, the dominant leg was defined as the limb with which they would feel most comfortable performing a single leg hop. Participants started from one end of the room and instructed with the command 'start' to walk at a self-selected speed across the platform to the other side of the room. Self-selected velocity was chosen to discern the 'real

world' kinematics and kinetics of ACL injured participants as standardised velocity may have disrupted normal gait patterns. Visual checking of individual participants data showed although there was a natural variation in gait velocity between trials, trials included for analysis were all of a comparable velocity.

They were instructed to look straight ahead and to not adjust their stride length to ensure contact with the force platform. They were instructed to walk until a researcher instructed them to 'stop and return to the start position'. A researcher made a mark of the starting position on the floor using tape; this was adjusted until the participant was consistently making contact with the platform in the correct locations, however the position of the force platforms was not directly indicated. The starting position was then used for the 'live' capture trials and adjusted if necessary. Five valid trials were collected and at least three valid trials were averaged to generate the outcome measure value.

4.10.3.3 Jogging.

Participants started from one end of the room and instructed with the command 'start' to jog at a self-selected speed across the platform to the other side of the room. They were instructed to look straight ahead and not to adjust their stride length to ensure contact with the force platform. They were instructed to jog until a researcher instructed them to 'stop and return to the start position'. A researcher made a note of the starting position and area of foot contact, when the participant was consistently making contact with the platform in the correct location. This starting position was marked on the floor with tape for future trials. As with gait five valid trials were collected of which at least three valid trials were averaged to generate the outcome measure values. As with gait, velocity was assessed for consistency within the subjects.

4.10.3.4 Single Leg Squat.

Participants were instructed to stand in front of the force platform and on command of the researcher to step into the middle of the force platform with the affected/dominant leg and hold their balance and then to squat as deeply as possible using only the affected/dominant limb. The participant was instructed to repeatedly squat until they completed eight repetitions, or feel they could no longer continue or maintain their balance by placing the non-standing leg on the ground. For analysis the four middle repetitions of the eight trials was analysed.

4.10.3.5 Isokinetics.

Participants were seated in a self-selected position on the isokinetic dynamometer and securely fastened into the seat using the machines restraints. The ankle pad was attached at a point as distal to the knee joint and above the lateral malleolus, in a position in which the participant felt comfortable and stable enough to generate maximum torque.

It was explained that they would then use the machine twice, on the first attempt they were told to 'push and pull as hard as possible' for 8 repetitions as a familiarisation with the task they were going to perform, and on the second attempt they were told they would be instructed to 'push and pull as hard as possible' until the isokinetic dynamometer protocol ended, This was undertaken for both limbs in both the control and ACL injured groups, with peak torques for both limbs noted for both group and limb to limb comparisons.

4.11 Data Processing and Analysis.

4.11.1 Vicon Data.

After data collection the Vicon Nexus data was processed using Vicon software. The calibration model was loaded into Nexus. Additionally to the static gait model which is used to determine the model parameters, the two bodybuilder models (one to replace ASIS markers using extra pelvis markers for when the ASIS were not visible, and the other responsible for the frontal knee plane correction) were applied to the calibration trial.

Next the data from each trial was loaded into Vicon Nexus. The model was reconstructed and markers checked for correct labelling and any markers that were incorrectly labelled were corrected. Smaller gaps in marker trajectories were filled using the gap filling spline tools available within Vicon Nexus. Larger gaps in the ASIS markers (greater than 10 frames), were filled using the bespoke bodybuilder code.

Once each trial was completed, the data was processed through an anatomical modelling protocol. Force platform data was filtered with a low pass filter at 25Hz as this was an adequate cut-off frequency to remove unwanted system noise but still maintain force platform output characteristics. Marker trajectories were filtered with a low pass filter at 12Hz which was found to be adequate for all tasks. This frequency

was high enough to remove unwanted marker trajectory noise (as these are at a relatively low frequency) without adveresly attenuating the marker trajectory data. Filtering at higher frequencies (closer to that of 25Hz used for force platforms) meant the output characteristic was too noisy to analyse. Finally, application of the knee alignment correction tool discussed previously was applied in order to get the kinematic and kinetic outcome files. Data was saved in a C3D format, which was then exported into Matlab 2010b for further analysis.

A bespoke analysis routine was written in Matlab to calculate the peak values for each trial for the outcome measures of interest (see Table 4.12). Gait and Jogging velocity were calculated from the mean horizontal centre of mass velocity from heel strike to toe off for each trial. Peak stance phase knee moments and angles for both the sagittal and frontal plane were calculated from heel strike to toe off for both gait and jogging. This time period was divided into two halves. Data for the first 50% of the stance phase was used to determine early stance internal extensor moment, internal peak knee abductor moment, peak knee flexion angle and peak adduction angle.

For gait and jogging the second 50% of the trial data was used to determine internal peak flexor moment, minimum knee flexion angle and for gait second peak internal knee abductor moment and second peak adduction angle.

Figure 4.11.1 shows a typical time series plot of knee flexion and adduction angles during the stance phase of gait, with peak values used for analysis annotated. Figure 4.11.2 shows a typical time series plot for non-normalised (absolute) internal knee moments; the peak values shown were normalised for analysis using participants mass and height data in Matlab.

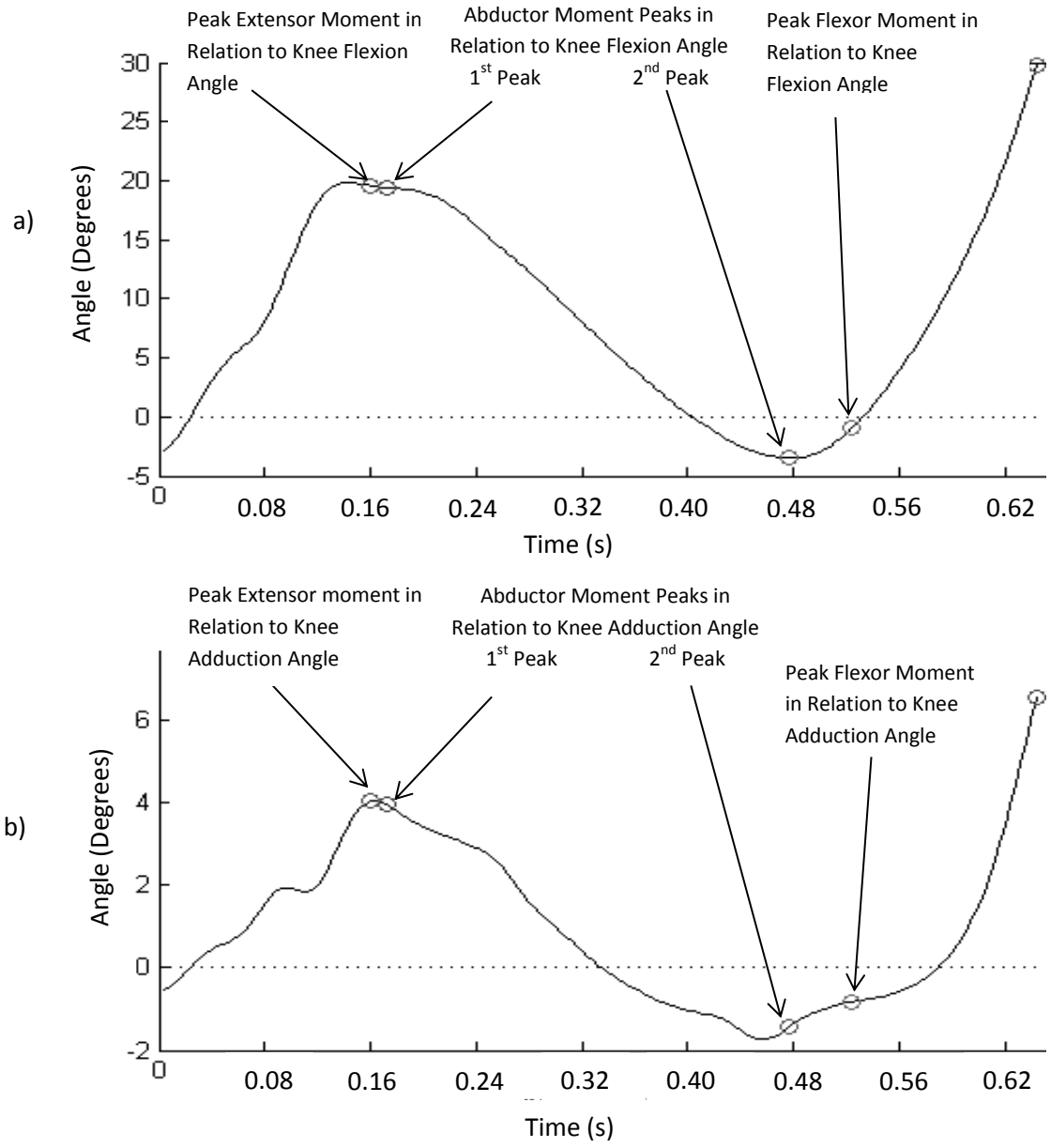


Figure 4.11.1 Typical time series plots of a) Knee flexion angles and b) Knee adduction angle during the stance phase of gait.

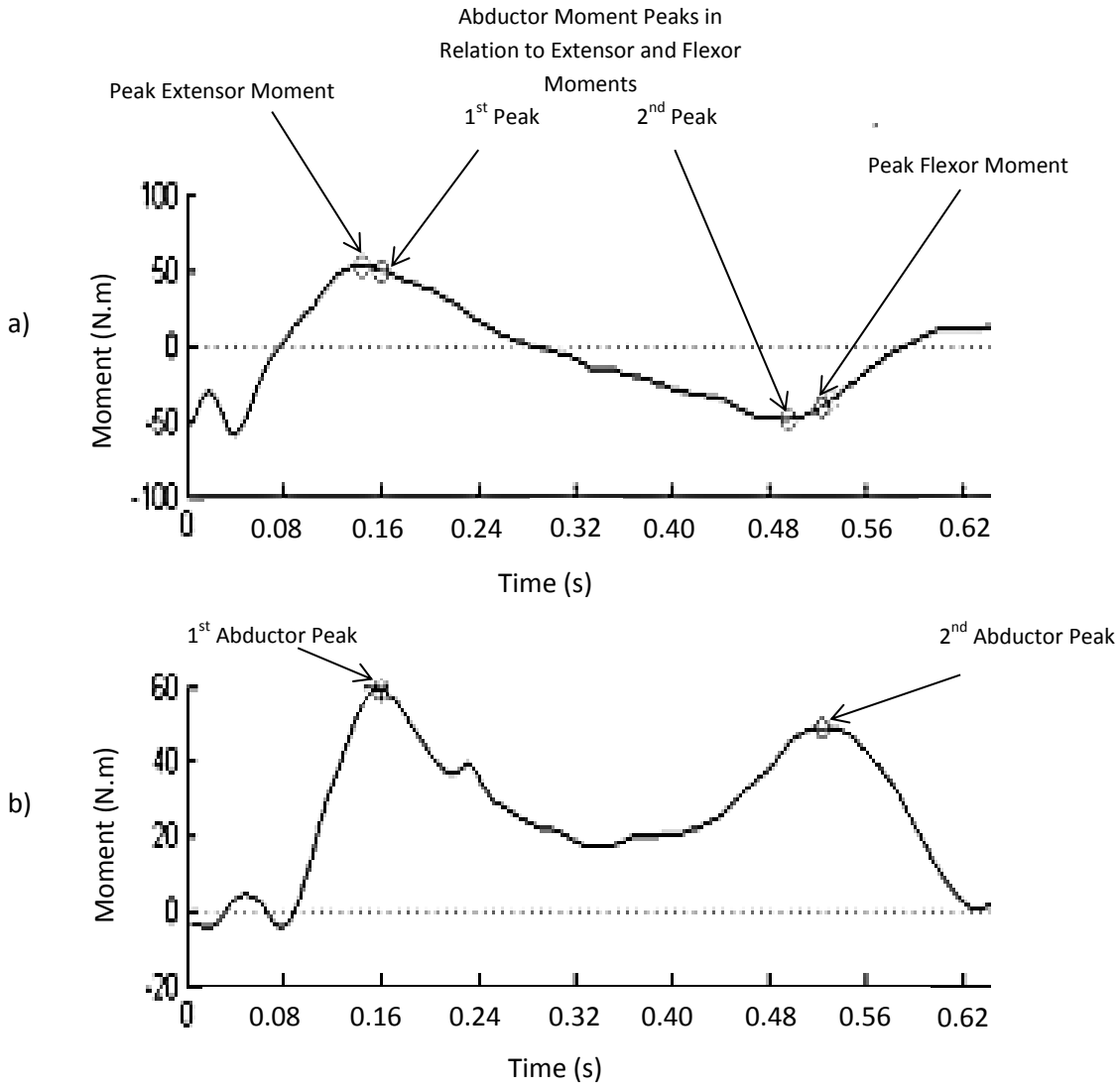


Figure 4.11.2 Typical time series plots of a) Internal knee extensor and flexor moment and b) Internal knee abductor moment during the stance phase of gait.

Figure 4.11.3 shows a typical time series plot of knee flexion angle during the stance phase of jogging, with peak values used for analysis annotated. Figure 4.11.4 shows a typical time series plot for non-normalised (absolute) internal knee moments; the peak values shown were normalised for analysis using participants mass and height data in Matlab

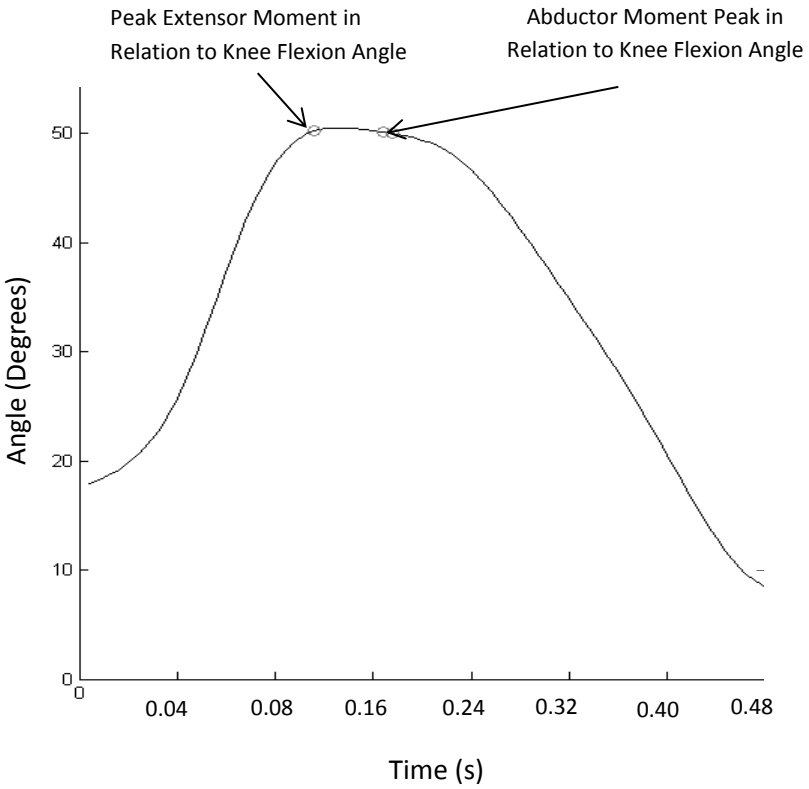


Figure 4.11.3 Typical time series plots of knee flexion angles during the stance phase of jogging.

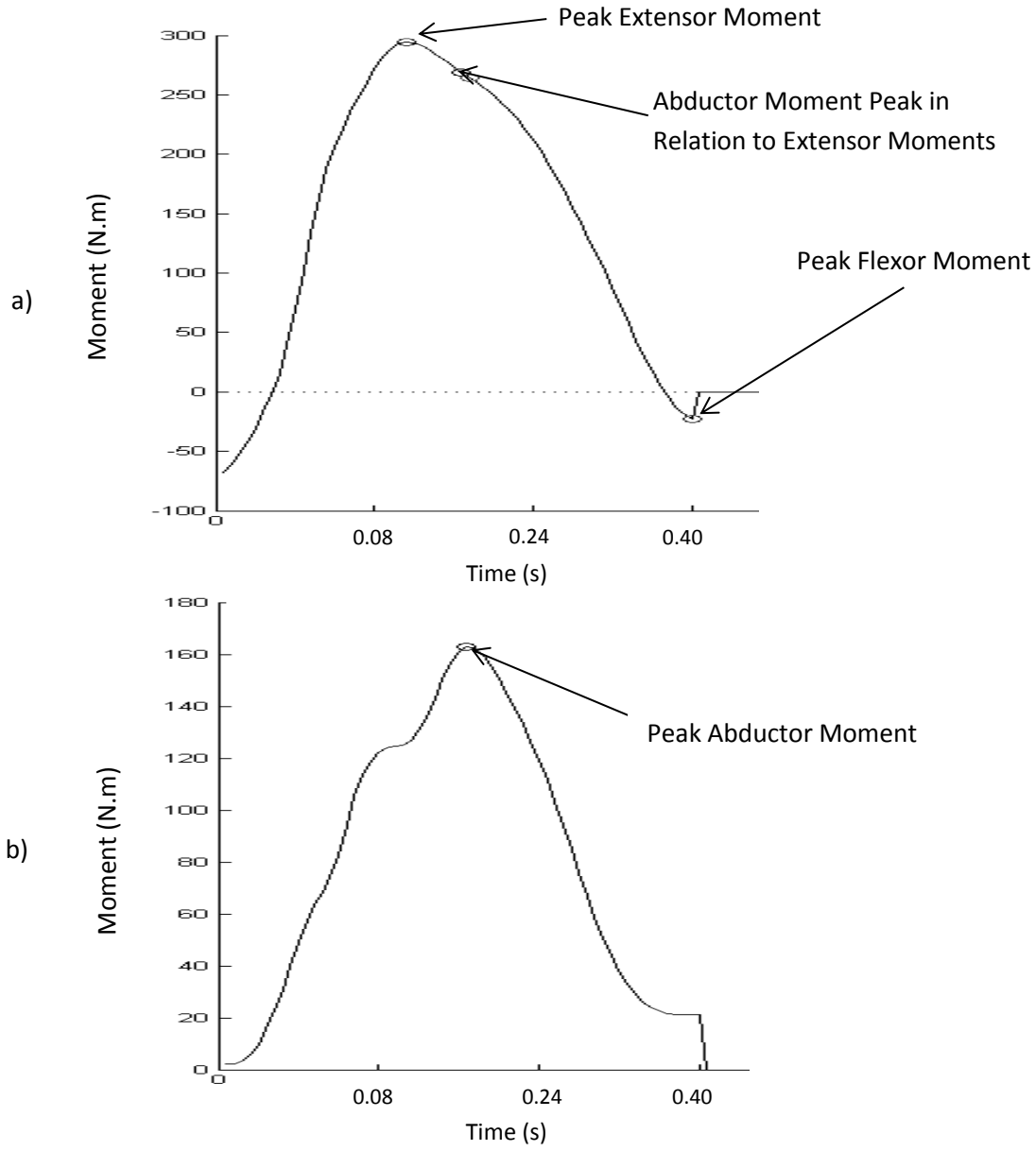


Figure 4.11.4 Typical time series plots of a) Internal knee extensor and flexor moment and b) Internal knee abductor moment during the stance phase of jogging

The start and stop of each repetition for analysis during the SLS was defined by the finding the lowest and highest vertical position of the centre of mass. When the centre of mass crossed a threshold on the descent of 5% of the total vertical distance, the repetition start was registered. On the ascent of each squat when 95% of the vertical distance was covered each repetition stop point was registered. If 95% of this position was not reached in subsequent repetitions (if the participant was not returning to near full extension) this percentage was adjusted in the analysis routine to be appropriate for

the individual. Subsequent values were determined from data between the start and stop positions.

SLS squat depth was calculated using the vertical displacement of the centre of mass, ascent and descent velocity was calculated using the average of the instantaneous centre of mass velocities throughout each repetition calculated using a differentiation algorithm. Internal peak knee extensor and abductor moments, peak knee flexion and adduction angles and sagittal and frontal plane range of motion were calculated for each of the previously defined repetition periods. Figure 4.11.5 shows a typical time series plot of knee flexion angles for the SLS with peak values used for analysis shown.

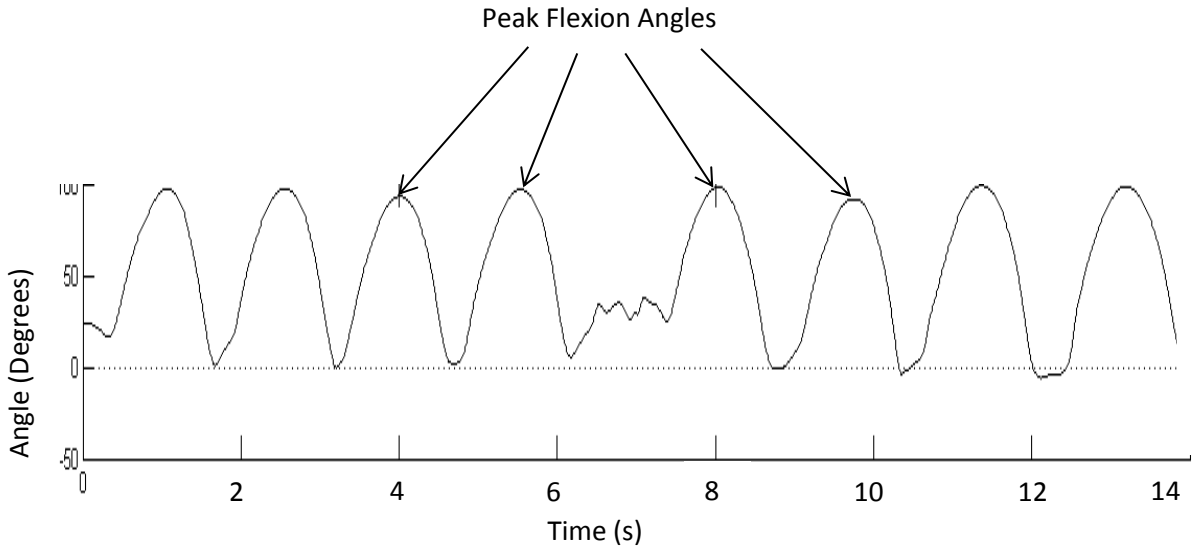


Figure 4.11.5 Typical time series plots of knee flexion angle during the SLS.

Typical time series plots are shown for non-normalised (absolute) internal knee moments during SLS below in Figure 4.11.5. The values shown were normalised for analysis using participants mass and height data in Matlab.

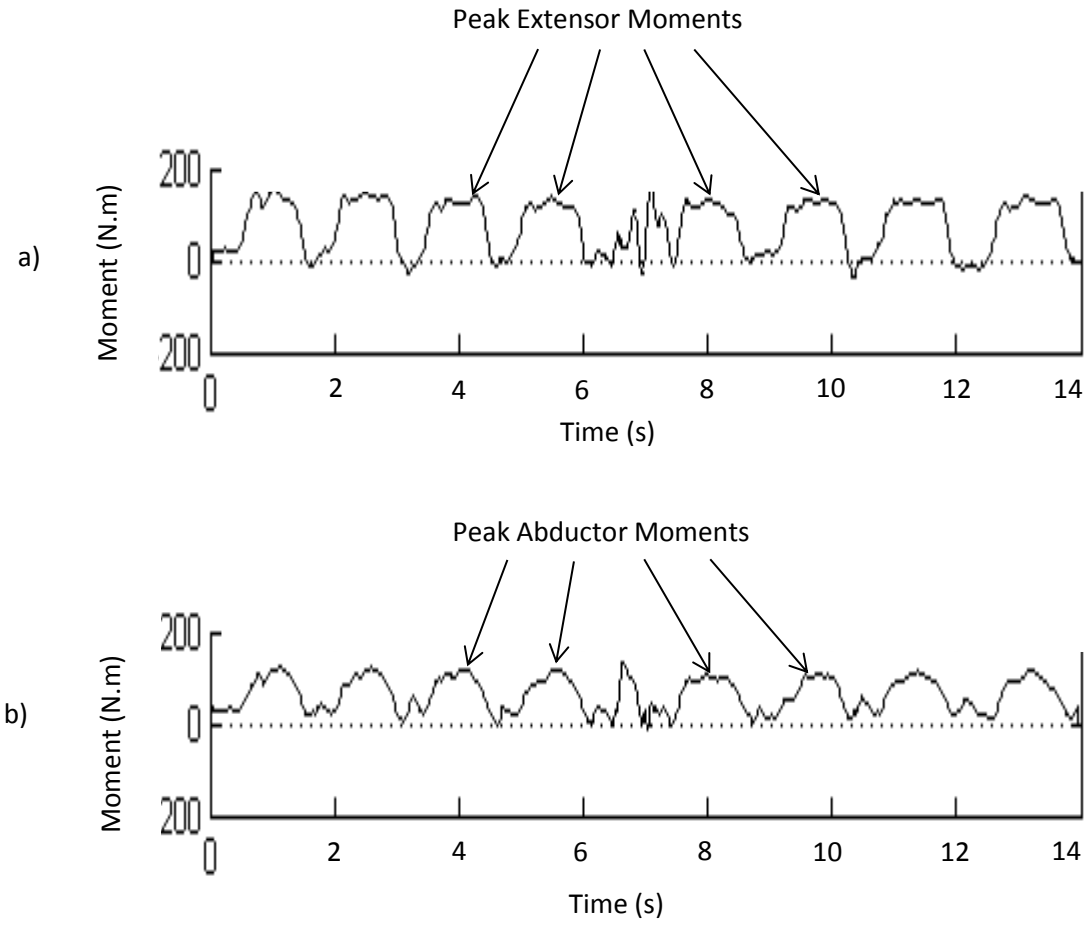


Figure 4.11.6 Typical time series plots of a) Internal knee extensor and flexor moment and b) Internal knee abductor moment during the SLS.

Joint moments at the knee were expressed as both absolute values in N.m, and normalised to both height and body mass (N.m/Kg.m) using Matlab 2010b. Knee angles are given in absolute values in degrees. This data was then exported into Microsoft Excel™ 2007 for manual checking of the data to check for anomalies in peak values. Spatiotemporal, kinematic and kinetic outcome values for each trial were averaged for at least three trials for gait, three trials for jogging and four repetitions of SLS. This gave the value used for statistical analysis.

Analysis was undertaken on the injured limb of the ACL injured participants to compare to the dominant limb of the controls. The opportunity to detect OA related changes in ACL injured participants using MRi was only on the injured limb, therefore

to explore if kinematic and kinetic outcome measures were associated with degenerative knee changes, these outcomes were analysed on the injured limb.

4.11.2 Isokinetic Data and Questionnaires.

Each participant's maximum torque registered during the protocol was recorded from the feedback screen on the Biodex S4. Scores were recorded for both legs for both the hamstrings and quadriceps. Data for maximum strength for both the injured and uninjured limb was recorded for hamstrings and quadriceps. From this side to side differences, the ratio of quadriceps to hamstring strength and peak torque/body mass values were calculated. These have been shown to be key parameters when identifying pathological muscle strength deficits using isokinetic dynamometry (Dvir, 2004). All data was inputted into an Excel document for data storage and analysis.

Each questionnaire was scored according to the methods prescribed (Higgins et al., 2007; Damsgard et al., 2007) and Microsoft Excel^{TM} automatically summated the scores

4.12 Statistical Analysis.

Scoring of questionnaires was undertaken in Microsoft Excel using the appropriate method defined for each measurement tool. Data for isokinetic measurements were read manually from the systems computer screen and inputted into excel for data storage and analysis.

Data from biomechanical outcomes calculated in Matlab 2010b was also written to and stored in Microsoft Excel spreadsheets.

All data was exported from Microsoft Excel^{TM} into Predictive Analytics Software, PASW version 18 for Windows (IBM, 2009). Descriptive data (means and standard deviations) will be given for all outcome measures.

For visit one group differences will be assessed using a One-Way Analysis of Variance tests (ANOVA) or Analysis of Co-variance test (ANCOVA) if related outcome measures were found to be different between groups. All values were deemed significant at a level of $p<0.05$. If significant group differences were found these would be explored using a post hoc Bonferroni test to determine the significance values between each participant group.

ANOVA and ANCOVA will be used to assess between groups differences under the assumption that the data is normally distributed across all groups. Tests for normality included visual inspection of histograms and both P-P and Q-Q plots, as well as assessing the Kolmogorov-Smirnov test for normality (Field, 2005).

At this juncture a non-parametric, independent samples Kruksal-Wallis test may be used to assess the distribution of the relevant outcome measure across the Control, ACLR and ACLD groups. However, it has been demonstrated that ANOVA may be an appropriate analysis technique, depending on assumptions of the normality of the data from a researchers perspective, the decision making process for statistical analysis is described in Figure 4.12 (Skovlund and Fenstad, 2001; Osborn, 2013).

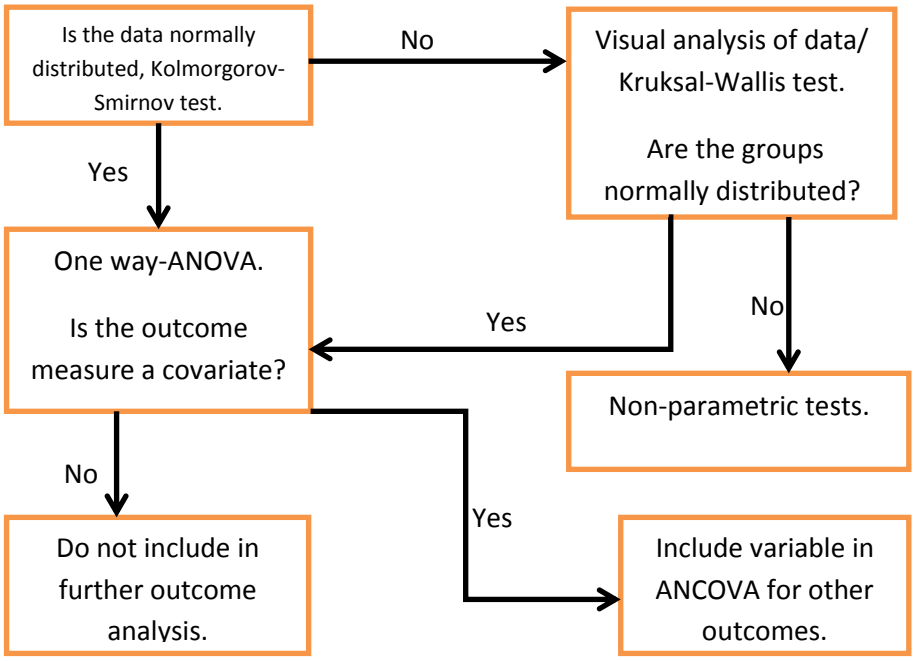


Figure 4.12 Overview of statistical analysis.
Flow chart for selecting statistical analysis procedures for group differences between Control, ACLR and ACLD groups for part one of the study.

Differences between groups for the outcome parameters listed in Table 4.12 were measured using one way ANOVA/ANCOVA with post hoc testing were appropriate. This was undertaken for all group comparisons with the exception of the IKDC and

Cincinnati Knee score, which was analysed using an independent t-test to measure differences between ACLD and ACLR participants. Longitudinal changes within the ACLR2 were also measured using a dependent t-test for the variables of interest (Hurley et al., 2010).

Table 4.12 Biomechanical and clinical outcome measures.

		Outcome measures	**Results Chapter/Page number**
Clinical Questionnaires		IKDC. Cincinnati Knee Score. TSK.	Chapter 5.2/Page 137
Isokinetics		Peak Quadriceps Torque Peak Hamstring Torque	Chapter 5.3/Page 139
Biomechanics	Stance Phase of Gait	Gait Velocity. Cadence. Stride Length. Peak Knee Extension Angle. Minimum Knee Flexion Angle. Peak Adduction angles. Peak Extensor Moment. Peak Flexor Moment. Peak Abductor Moments.	Chapter 5.4/Page 141
	Stance Phase of Jogging	Jogging Velocity. Peak Knee Extension Angle. Minimum Knee Flexion Angle. Peak Adduction angle. Peak Extensor Moment. Peak Flexor Moment Peak Abductor Moment.	Chapter 5.5/Page 154
	SLS	Ascent Velocity. Decent Velocity. Squat Depth. Peak Knee Flexion Angle. Sagittal Knee ROM. Peak Adduction Angle. Frontal Plane ROM. Peak Extensor Moment. Peak Abductor Moment.	Chapter 5.6/Page 165

The above table shows the main areas of analysis including clinical questionnaires, isokinetics and biomechanics, the associated outcome measures and the chapter heading and page numbers at which the relevant results can be seen.

Chapter 4 (Part 2) Methods: MRi Analysis.

4.13 Introduction to MRI Methods.

The primary aim of this part of the study was to map changes in knee structures, over time, using the participant's clinical diagnostic scan following their ACL injury and a follow-up scan undertaken at Cardiff University Brain Research Imaging Centre (CUBRIC), using the same clinical imaging sequences described below in Chapter 4.14.1. These sequences were validated by a Consultant Radiologist specialising in musculoskeletal imaging, Dr. Kathleen Lyons (KL) (MB BCh, BAO, FRCR).

The cohort included in this exploratory study, were recruited from those participants who had visited the RCCK for assessment on two occasions, as described in the data collection flow chart above. This part of the study incorporated 2 methodologies to map this potential change, both of which aimed to quantify, on some level, the articular features within the affected knee of the participants.

Method 1 was a quantitative approach in which a semi-automated segmentation of six MRI slices (three from the medial compartment and three from the lateral compartment) using a bespoke analysis routine developed by Dr. PRH using Matlab. This was used to define cartilage and bone boundaries and these features were used to calculate cartilage thicknesses (see Chapter 4.17 below). Cartilage thickness was mapped across several anatomical locations of the knee. These areas related to sections of the bone-cartilage which are commonly loaded in activities of daily living and sport (Koo et al., 2005; Li et al., 2005).

Method 2 used a semi-quantitative approach to compare the 2 scans. This method incorporated assessment of 3 key anatomical features that have been demonstrated to show degenerative changes associated with OA (Bennell et al., 2011; Hunter et al., 2006; Hernandez-Molina et al., 2008). This assessment was performed by a relevantly qualified and experienced Consultant Radiologist for all scans (KL). The three key anatomical features, cartilage morphology, bone marrow lesions and meniscal integrity were scored across multiple locations throughout the tibiofemoral joint adapted from

the WORMS system (Peterfy et al., 2004) and are described in greater detail in Chapter 4.17.

4.14 Participant Information.

A majority of the ACLD cohort (n=25) had undergone hamstring graft reconstructive surgery after the initial assessment in the RCCK or could not be contacted for follow up or declined to take part (n=3). This meant biomechanical data could not be collected on two separate occasions at a period of 12 months apart as this fell outside a reasonable time frame for completion of the PhD study. Therefore, the MRi cohort was recruited from the ACLR participants who were able to attend for a second visit to the RCCK (ACLR2) and given an information sheet (Appendix 7) on attendance. The ACLR2 group contained ten participants of which, nine subjects agreed to take part in the MRi aspect of the study and signed relevant consent forms prior to MRi (Appendix 8), however one was not available for assessment. This sub-cohort of ACLR participants with two visits to the RCCK and MRiwas named the Anterior Cruciate Ligament MRi group (ACLM) (n=8), which will be the acronym used throughout this thesis. Each ACLM participant was required under NHS Wales's procedures to give consent to access and download their NHS clinical MRi scans for analysis. This was obtained for each participant (Appendix 11).

Semi-quantitative scoring of MRi scans requires the imaging of several articular features in order to get a cumulative score for these features across several regions. These features and the regions of the tibiofemoral joint to be assessed are described in greater depth below in Chapter 4.16. This requires several sets of images covering the knee in both the axial, coronal and sagittal plane, as each articular surface is more accurately visualised depending on not only the orientation of the MRi image slices but also the sequence used. The specific sequence used can more accurately focus upon the features of interest, be that bone, cartilage, ligaments and menisci etc., in order to thoroughly assess the integrity of these features for accurate scoring (Peterfy et al., 2004). The imaging sequences used for clinical, semi-quantitative MRi scoring is in Chapter 4.15.1.

Quantitative MRi based methods generally require slices in one plane and are either combined to create whole knee models or each slice assessed individually to typically assess cartilage thickness (Conaghan et al., 2006; Dam et al., 2007), therefore a

sequence is chosen that best delineates the bone and cartilage edges for further and more accurate segmentation (Eckstein et al., 2000; Hunter et al., 2009). In the current study, as we were limited to the protocol of the initial NHS clinical scans, which was then matched, as described previously, in CUBRIC to make an appropriate comparisons both quantitatively and semi-quantitatively. Using the literature and consultation with relevant clinicians it was determined which scanning sequence to use which would best delineate bone and cartilage from one sequence, in order to assess cartilage thickness, and this is documented below in Chapter 4.15.2.

4.14.1 Imaging Sequences used for Semi-Quantitative Clinical Scoring Method.

Semi-quantitative assessment requires multiple imaging sequences. The WORMS tool was chosen to be used to assess articular features in the present study (see Chapter 4.16 for rationale). Imaging sequences included in the initial protocol to assess WORMS were defined by Peterfy et al. (2004) as;

a) Axial T1-weighted spin-echo (SE), 20 cm field of view [FOV], 5 mm/1 mm (slice thickness/inter-slice gap), 256×192 matrix, frequency encoding (FE) anterior-posterior, one excitation.
b) Coronal T1-weighted SE, 16 cm FOV, 4 mm/0.5 mm, 256×192, FE superior-inferior, two excitations averaged.
c) Sagittal T1-weighted SE, 16 cm FOV, 4 mm/0.5 mm, 256×192, FE anterior-posterior, two excitations averaged.
d) Sagittal T2-weighted fast spin echo, (FSE), 14 cm FOV, 4 mm/0 mm, 256×192, FE superior-inferior, two excitation averaged with fat suppression.
e) Sagittal fat suppressed T1-weighted three dimensional (3D) spoiled gradient echo (FS-3DSPGR), 14 cm FOV, 256×128 matrix, 60 contiguous 2-mm slices covering all articular cartilage plates in the knee, FE superior-inferior, one excitation.

The differences between the clinical NHS diagnostic scans and the matched CUBRIC scans with the scans described by Peterfy et al. (2004) for use with WORMS were related not to the scanning sequences, field of view or plane of scanning, but to slice spacing and thickness. The NHS and CUBRIC scans had a slice thickness of 3mm with 0.3mm spacing compared to 4mm with 0 spacing for scanning sequences ‘a’, ‘b’ and ‘c’. The CUBRIC scanning sequences did not include ‘d’ from above, however a

similar fat-supressed imaging sequence was used in the sagittal plane, giving 35 slices with a thickness of 3mm.

The total time required for MRi at CUBRIC, including patient set up, was 60 minutes, this was comparable to the time taken for the scanning sequence described by Peterfy et al. (2004).

4.14.2 Imaging Sequences used for Quantitative Cartilage Modelling Methods.

From reviewing the literature and analysis of available imaging sequences above, the sequence which was most able to provide a clear image of the bone and cartilage interface was chosen. It was important that the sequence provided clarity across the regions of the knee associated with degenerative knee changes and typically loaded in activities of daily living. The sagittal fat suppressed T1-weighted three dimensional (3D) spoiled gradient echo sequence was chosen. This was chosen as it was the scanning sequence available which was deemed to show the features needed to define bone/cartilage boundaries, in areas of the knee that were of interest with the most clarity.

4.15 Semi-Quantitative Methods.

4.15.1 Methodological Development.

Several features were identified as having key degenerative changes in those with existing OA by Bennell et al. (2011). They noted that the features of bone marrow lesion size, cartilage morphology and meniscal integrity to be important in the progression of OA. The scoring system used by Bennell et al. (2011) was adapted from the WORMS tool (Peterfy et al., 2004), and this was deemed appropriate to be used in the present study as it is a reliable (Table 4.15.1.1) and well described method for assessing structural changes in the tibiofemoral joint. WORMS is described in Chapter 4.15.2.

4.15.1.1 WORMS: A Summary of Reliability, Sensitivity and Validity.

The WORMS tool was developed by Peterfy et al. (2004) to identify and score key features relating to OA changes in the knee. These key features, discussed more broadly in the literature review, are summarised below.

Hunter et al. (2006) demonstrated a link between meniscal integrity and cartilage degeneration. Hernandez-Molina et al. (2008) and Hunter et al. (2006) also demonstrated a link between BMA and associated cartilage loss. Lynch et al. (2010)

found the WORMS BMA score predicted cartilage score change more strongly than the BLOKS BMA variable.

Peterfy et al. (2004) assessed the reliability of the WORMS score on 19 patients with radiographic OA. Reliability was assessed independently by 2 trained radiologists. Inter-observer agreement was based on the exact rating of each feature, not just the presence or absence of each feature, and expressed as inter-class correlation coefficients (ICC) by treating the data as a continuous variable. All values for inter-rater assessment demonstrated excellent agreement (Table 4.15.1.1) for the medial (MFTJ), lateral (LFTJ) and patella (PFJ) areas of the tibiofemoral joint.

Table 4.15.1.1 Inter-rater assessment ICC's for the WORMS score for the articular features across each knee region.

	MFTJ	LFTJ	PFJ	S-Region	Total
Cartilage	0.98	0.99	0.98		0.99
Marrow Abnormality	0.90	0.96	0.82	1.0	0.74
Bone Cysts	0.98	0.95	0.73	1.0	0.94
Osteophytes	0.93	0.94	0.98		0.97
Compartment Total	**0.97**	**0.98**	**0.99**		
Menisci	0.94	0.81			0.87
Ligaments					1.0
Synovitis					0.74
Total					0.98

Key: MFTJ=medial tibio-femoral compartment of the knee, LFTJ=lateral tibiofemoral compartment of the knee, PFJ= patella-femoral joint, 'S' region is the region under the tibial spine. Recreated with permission from Peterfy et al., *Whole-Organ Magnetic Resonance Imaging Score (WORMS) of the knee in osteoarthritis*. Osteoarthritis and Cartilage (2004) 12, 177–190.

High reliability is shown for those features identified and used by Bennell et al. (2011) as key features for mapping degenerative knee changes in OA and thus selected for this current study. For these features Peterfy et al. (2004) calculated ICC scores for cartilage morphology in the MFTJ=0.99 and LFTJ=0.99, bone marrow abnormality in the MFTJ=0.90, LFTJ=0.96, TS=1 and meniscus for the MFTJ=0.94 and LFTJ=0.81.

The abridged version of WORMS used in the current study was in line with Bennell et al. (2011) and was chosen due to time constraints placed upon the clinical expert to

complete the task. Therefore the outcomes had to be developed to be as focused as possible, firstly on the features that were to be assessed, and secondly on the regions and sub regions of the knee being evaluated. The amended scoring protocol for the specific regions and articular features of interest are explained fully in Chapter 4.15.3.

4.15.1.2 Clinical Assessment and Scoring.

All scans were assessed by an experienced Consultant Radiologist (KL) from the radiology department and University Hospital of Wales, Cardiff. KL was blinded as to the participant, although blinding as to order of the scan (clinical scans vs CUBRIC scans) was impossible due to the fact that scans were taken pre and post reconstructive surgery.

4.15.2 Analysis Protocol.

4.15.2.1 Defining Regions for Scoring.

As described previously scores were applied to measures of cartilage quality, bone marrow abnormality and meniscal integrity for the tibiofemoral joint. The tibiofemoral joint is divided into separate regions as defined in Figure 4.15.2.1a below. Each region was scored separately for cartilage morphology and bone marrow abnormality, with the menisci integrity being scored for the anterior, posterior and body of the lateral and medial meniscus.

The femur and tibia were divided into M (medial) and L (lateral) regions (right image of Figure 4.15.2.1a), with the trochlear groove of the femur considered part of the M region. Region S represents the portion of the tibia beneath the tibial spines. The femoral and tibial surfaces were further subdivided into anterior (A), central (C) and posterior (P) regions (left image in Figure 4.15.2.1a). A schematic view of all the regions of the knee to be scored individually is shown below in Figure 4.15.2.1b.

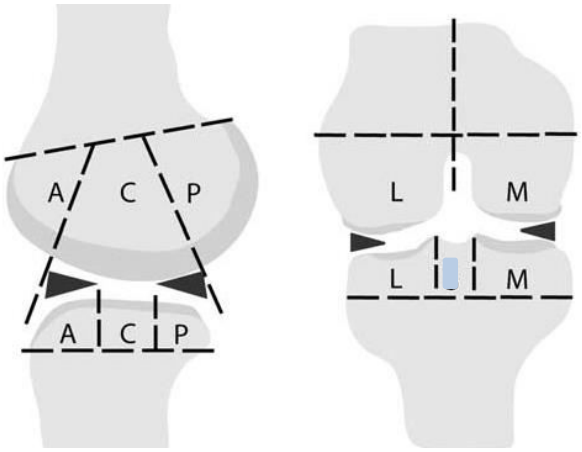


Figure 4.15.2.1a Regions of the tibiofemoral joint to be scored.
Key: A=anterior, C=Central, P=Posterior, L=Lateral and M=Medial. Reproduced with permission from Peterfy et al. (2004).

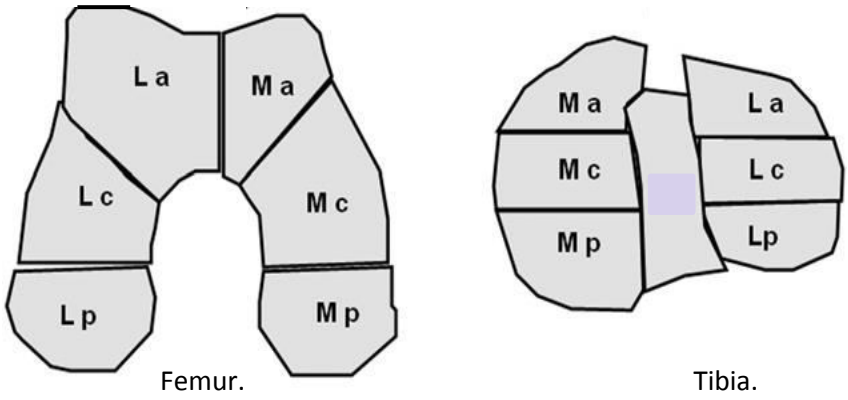


Figure 4.15.2.1b Schematic view of regions of the knee.
Key: LAF/MAF=Lateral/Medial anterior femur, LCF/MCF=Lateral/Medial Central Femur, LPF/MPF=Lateral/Medial Posterior Femur, LAT/MAT=Lateral/Medial Anterior Tibia, LCT/MCT=Lateral/Medial Central Tibia, LPT/MPT=Lateral/Medial Tibia. Reproduced with permission from Peterfy et al. (2004).

4.15.2.2 Cartilage Morphology.

This was scored using fat supressed T2 weighted Fast Spin Echo (FSE) and Spoiled Gradient Recalled (SPGR) imaging sequences. Figure 4.15.2.2 demonstrates the visual scoring scale for cartilage morphology, for each region of the knee.

Figure 4.15.2.2 Cartilage morphology scoring scale.
Key: 0=normal thickness and signal. 1=normal thickness. 2= partial thickness defect <1cm in greatest width. 2.5= full thickness defect <1cm in greatest width. 3= multiple areas of partial thickness intermixed with normal cartilage or a grade 2 defect > than 1cm but less than 75% of the cartilage area. 4=≥ 75% of the region having partial thickness loss. 5= multiple areas of full thickness loss or a grade 2.5 lesion wider than 1cm but <75% of the region. 6=>75% of the cartilage in the region have full thickness loss. Reproduced with permission from Peterfy et al. (2004).

For each region of the knee as defined in Figure 4.15.2.1b the following scoring sheet was completed for all participants, Table 4.15.2.2 This was used to compare scores for each individual region as well as compartmental and total scores.

Table 4.15.2.2 Scoring table for cartilage morphology.

	LAF	LCF	LPF	MAF	MCF	MPF	LAT	LCT	LPT	MAT	MCT	MPT	TOTAL
Cartilage score													
Compartment Score													

Key: LAF/MAF=Lateral/Medial anterior femur, LCF/MCF=Lateral/Medial Central Femur, LPF/MPF=Lateral/Medial Posterior Femur, LAT/MAT=Lateral/Medial Anterior Tibia, LCT/MCT=Lateral/Medial Central Tibia, LPT/MPT=Lateral/Medial Tibia.

4.15.2.3 Bone Marrow Abnormality

Bone marrow abnormality (BMA) is defined as areas with increased signal intensity in the Fat suppressed T2-weighted FSE images. This feature was scored for the 12 articular surface regions as defined in Figure 4.15.2.1b. The following guide (Figure 4.15.2.3) defines the level of abnormality.

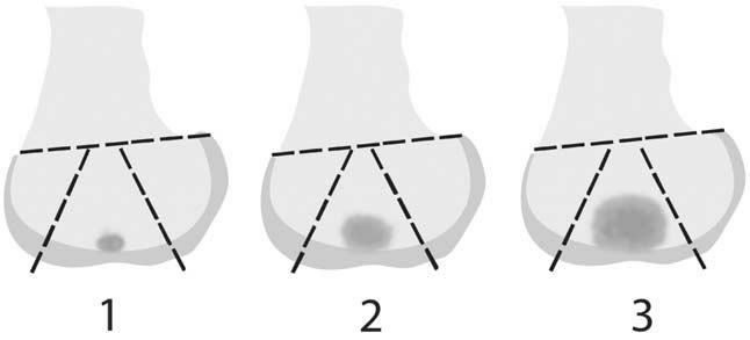


Figure 4.15.2.3 BMA lesion score guide.
Score is based on level of regional involvement from 0-3. 0=none, 1=<25% of the region, 2=25-50% of the region, 3=>50% of the region. Reproduced with permission from Peterfy et al. (2004).

Table 4.15.2.3 Scoring table for BMA.

	LAF	LCF	LPF	MAF	MCF	MPF	LAT	LCT	LPT	MAT	MCT	MPT	TOTAL
Bone marrow score													
Compartment Score													

Key: LAF/MAF=Lateral/Medial anterior femur, LCF/MCF=Lateral/Medial Central Femur, LPF/MPF=Lateral/Medial Posterior Femur, LAT/MAT=Lateral/Medial Anterior Tibia, LCT/MCT=Lateral/Medial Central Tibia, LPT/MPT=Lateral/Medial Tibia.

4.15.2.4 Menisci.

The menisci regions are defined as the anterior horn, body segment and posterior horn of the medial and lateral menisci, these are not clearly defined but subjectively assessed by KL. These were graded separately from 0 to 4 based on both the sagittal and coronal images using the following scoring system;

0=intact.
1=minor radial tear or parrot-beak tear.
2=non-displaced tear or prior surgical repair.
3=displaced tear or partial resection.
4=complete maceration/destruction or complete resection.

Table 4.15.2.4a Scoring table for meniscal damage.

Region	Lant	Lbody	Lpost	Mant	Mbody	Mpost	
Meniscus Score							Total Meniscus Score
Cumulative Regional score							

Key: Lant/Mant=Lateral/Medial anterior horn, Lbody/Mbody=Body of Lateral/Medial Menisci, Lpost/Mpost= Lateral/Medial posterior horn.

An overall grade for the lateral and medial meniscus regions is determined using the scheme shown in the Table 4.15.2.4b below.

This conversion was needed in order to adjust for nonlinearity among the regional grades, which could lead to inconsistencies if the grades were simply summed. For example, if a meniscus had a grade-2 tear in the body and posterior horn, simply summing these regional grades would yield the same total score (4) as for a meniscus that was completely missing its posterior horn, even though the latter abnormality would be a far greater biomechanical deficit to the knee. The corresponding scores derived with the conversion algorithm, however, would be 3 and 5, respectively.

Table 4.15.2.4b Scheme for cumulative scoring for the medial and lateral meniscus.

Score	Grades (Regions: Ant, Body and Post)
0	All 0
1	At least one 1, but no >1
2	2 in only one region
3	2 in more than one region
4	3 in one or more region
5	4 in only one region
6	4 in more than one region

Reproduced with permission from Peterfy et al. (2004).

4.16 Quantitative MRi Method.

4.16.1 Overview of Quantitative Method.

Our group developed a bespoke method to analyse cartilage thickness across several anatomical regions across the knee. This study aimed to use clinical scans (see Chapter 4.14.1 for details) to segment and analyse cartilage and this enabled us to retrospectively assess the cartilage thickness across the regions of the knee.

These regions were defined using the method described below in Chapter 4.16.3. These regions were chosen as they were demonstrated in other studies (Eckstein et al., 2010; Andriacchi et al., 2006) to be the load bearing regions of the knee, and those areas deemed to be most susceptible to degenerative changes in cartilage in situations of abnormal loading.

Three consecutive MRi slices from the medial and three from the lateral compartment were chosen for analysis; these were selected by the operator (PR) from a selection of MRi slices for the MRi sequence described below. PR chose slices from the central portion of the medial and lateral condyle with the most appropriate slices to accurately delineate between cartilage and bone edges, without artefact or other structural interference. The selected slices were analysed using a bespoke analysis routine developed using Matlab 2010b, further details are described in Chapter 4.16.4.

4.16.2 Scanning Sequence.

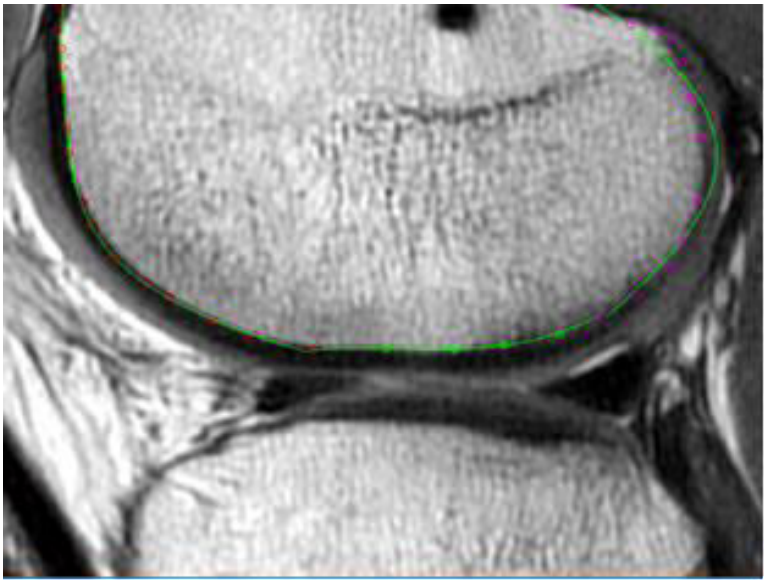
The scanning sequences available for analysis were as described above in Chapter 4.14.1. From these available sequences and after consulting with radiologists and engineers regarding the most appropriate methodology with which to best segment and delineate cartilage from bone (Chapter 4.16.4), it was decided the most appropriate scanning sequence available for quantitative cartilage modelling was a sagittal fat suppressed T1-weighted three dimensional (3D) spoiled gradient echo sequence described above.

4.16.3 Segmentation Information.

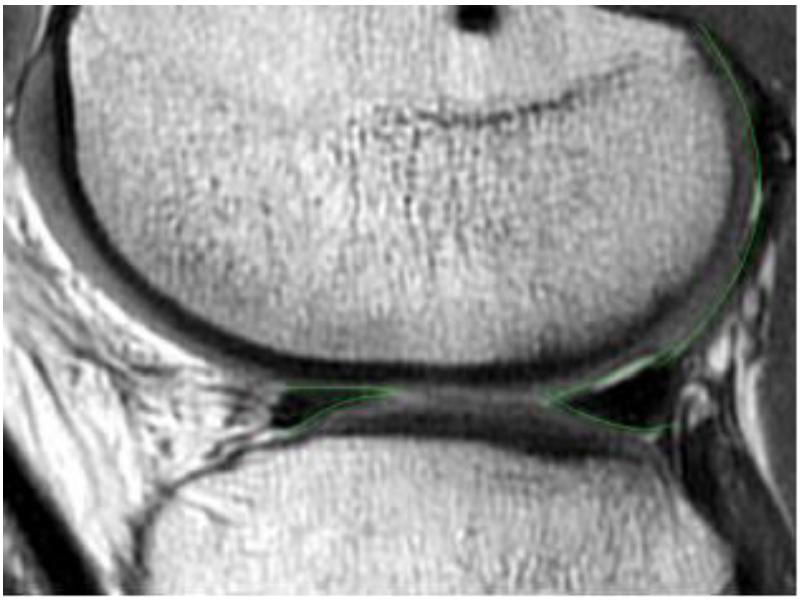
Segmentation was carried out by one operator (PR) for both scans from the NHS and CUBRIC (See Chapter 4.17 for reliability assessment of the MRi analysis sequence).

Segmentation was undertaken by selecting a series of points around the femur, tibia and meniscus at the bone and cartilage edges. A spline was then constructed for the selected data points for anterior (red circles in Figure 4.16.3.1a), medial (green circles in Figure

4.16.3.1a) and posterior (purple circles in Figure 4.16.3.1a) aspects of the structure with PR choosing an appropriate spline 'order' to create a line of best fit through the data points (Figure 4.16.3.1).



a)



b)

Figure 4.16.3.1 Example of operator selection for outlining bone and meniscus.a) Example of operator selected data points for femur with corresponding splines (green line), red circles for anterior portion of femur, green circles for medial portion of femur and purple circles for posterior portion of femur. b) Green lines showing the spline delineating the menisci and articular cartilage.

The analysis routine used this spline around the relevant feature to define a region of interest to systematically search around spline for contrast differences between pixels with a threshold for bone/cartilage edge. Once the analysis had been completed data points could be adjusted creating the final segmented image (Figure 4.16.3.2).

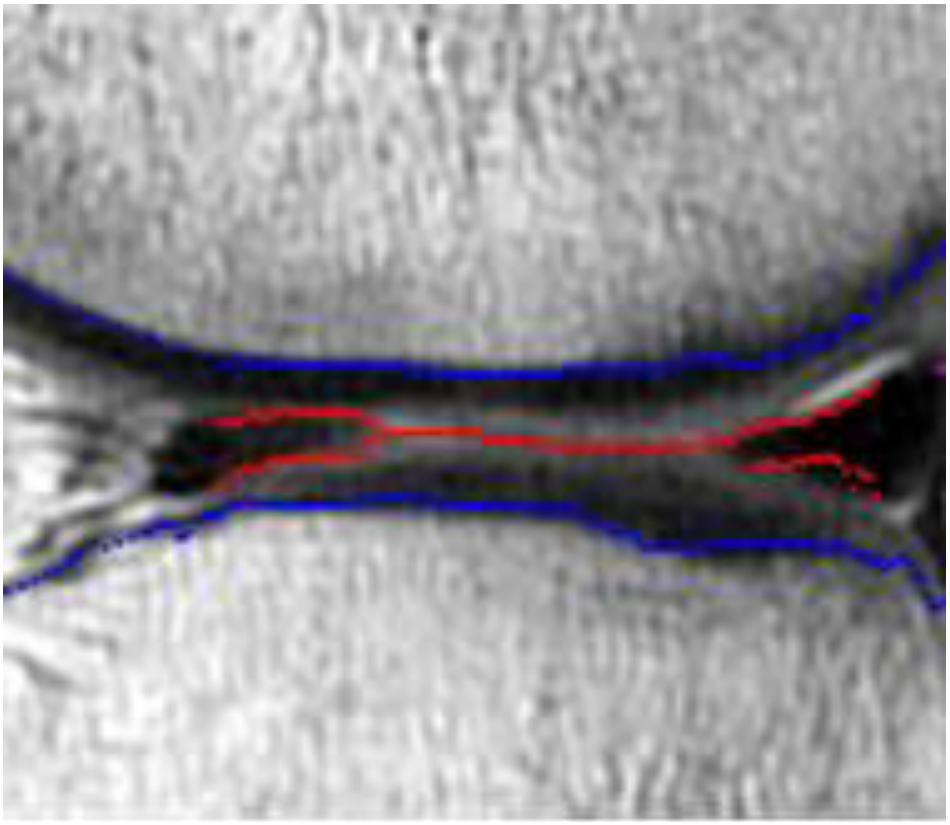


Figure 4.16.3.2 Example segmentation of the tibiofemoral joint.
Blue pixels represent the bone/cartilage interface, red pixels represent the cartilage edges.

4.16.4 Defining Regions of the Knee to be Analysed.

4.16.4.1 Femur.

This was defined by selecting the most inward points of the anterior and posterior of the meniscus and creating a Meniscal reference line (Mref) between these points shown in Figure 4.16.4.1a. Next we created three points of equal distance between them along the 'Mref' line.

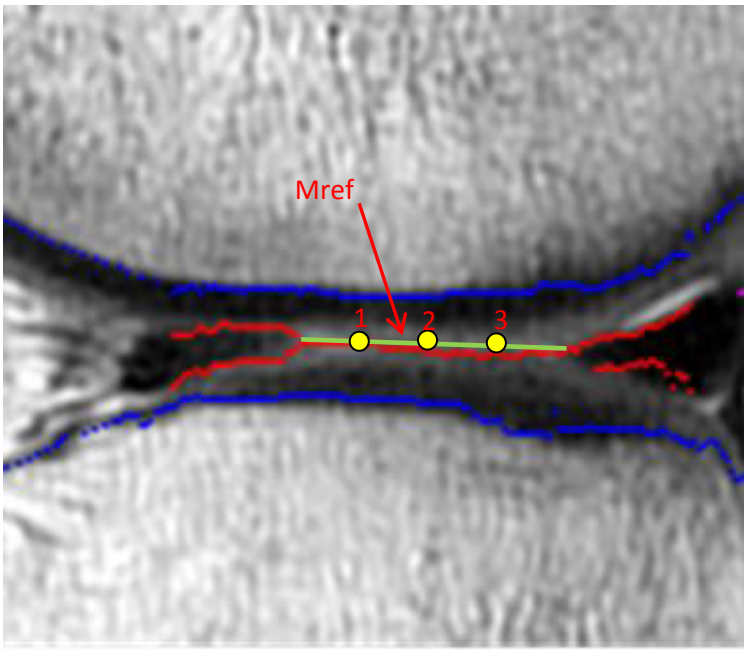


Figure 4.16.4.1a Defining the femoral sub-regions.
Key: Mref=Meniscal reference line, with the 3 points equally distanced along Mref, noted by numbers 1, 2 and 3 shown with yellow circles.

From the most inward points of the anterior and posterior meniscus, as well as the pixels at points, 1, 2 and 3, we constructed a line perpendicular to the Mref line at these points to the femoral bone edge, using the following method.

Firstly the slope of the Mref line was calculated using the x,y coordinate matrix for the MRi slice, given as a change in magnitude in the 'x' direction divided by the change in magnitude of 'y', from the first (A) to last (B) pixel on the 'Mref' line, given as:

$$slope = \frac{Ay - By}{Ax - Bx}$$

A line perpendicular to this slope and in turn 'Mref' (Pslope) is given by the formula:

$$Pslope = -\frac{1}{slope}$$

The Matlab routine then searched the bone edge vector (Fy and Fx) in order to find the point where:

$$\frac{Ay - Fy}{Ax - Fx} = Pslope$$

Therefore:

$$\frac{Ay - Fy}{Ax - Fx} - Pslope = 0$$

From this a minimisation function was applied to find the optimum line perpendicular from Mref to the available bone edge pixels, to select the appropriate image pixel to define the start of each region. This step was undertaken for the points defined above in Figure 4.16.4.1a creating four regions on the femur for analysis of cartilage thickness (1, 2, 3 and 4 Figure 4.16.4.1b).

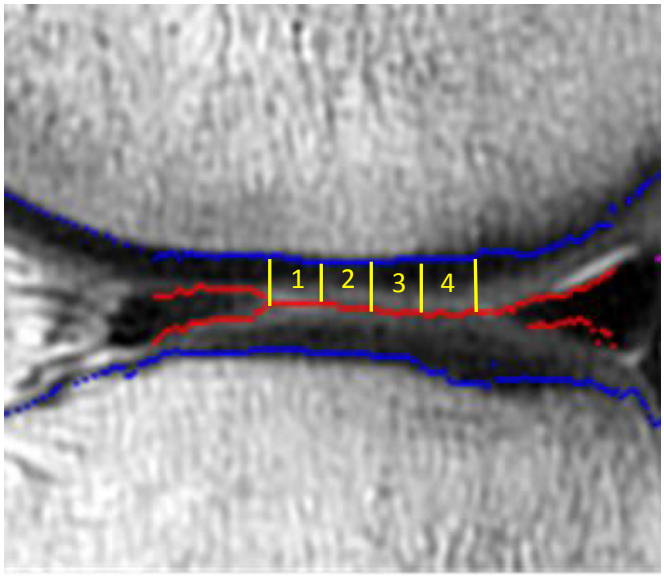


Figure 4.16.4.1b Defining regions for one slice, part of the central lateral femur sub-region for analysis.
Key: 1, 2, 3, 4 Four regions for mean cartilage thickness to be measured, these are combined to give a total mean cartilage thickness for each MRi slice. These were initially defined as four separate regions to enable easier checking for errors in data.

4.16.4.2 Tibia.

As with the femoral protocol three points of equal distance between them along the Mref line were created. From these points a perpendicular line again was constructed as per the described method above, to the tibial bone edge, defining the tibia regions (A, B, C and D) for further cartilage thickness analysis (Figure 4.16.4.2).

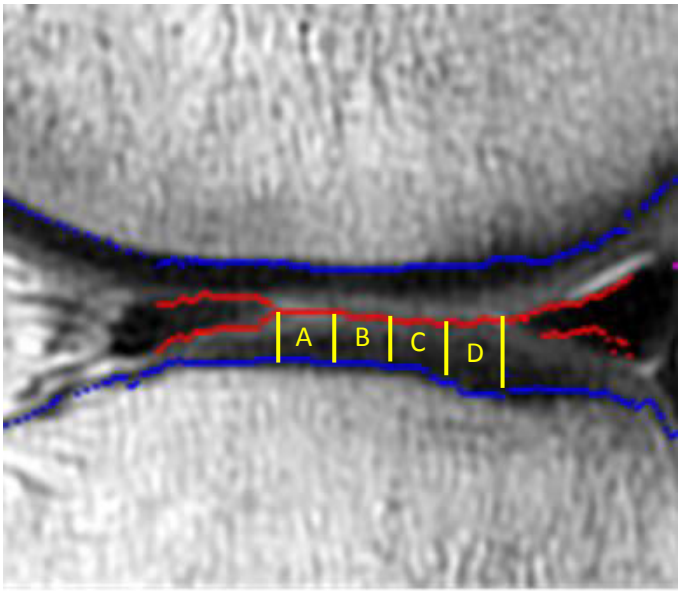


Figure 4.16.4.2 Defining regions for one slice, part of the central lateral tibia sub-region for analysis.
Key: A, B, C, D Four regions for mean cartilage thickness to be measured, these are combined to give a total mean cartilage thickness for each MRi slice. These were initially defined as four separate regions to enable easier checking for errors in data.

4.16.4.3 Calculating Mean Cartilage Thickness.

For each region of interest the first pixel on the bone-cartilage interface was defined starting at the left furthermost pixel on the bone edge, we then used four pixels either side (if available) that had been defined as bone (blue pixels), then optimised a line of best fit between these points. A line perpendicular to this, (orange line) was constructed to cross the cartilage edge (red pixels), and its length calculated (Figure 4.16.4.3a). The analysis was then performed on the next pixel and repeated until this measurement had been taken for each pixel within the region.

Thickness ‘T’ was calculated using the following method. The x,y coordinate matrix for the MRi can be used to form a right angled triangle making ‘T’ the hypotenuse. The number of pixels in both horizontal and vertical directions can be measured and multiplied by the pixel height in the vertical direction to give ‘dy’ and pixel width in the horizontal direction to give ‘dx’, then using Pythagoras, ‘T’, which is representative of the length being measured, was calculated as part of the Matlab image analysis code. Below an example is given for the tibia for one data point on the bone surface (Figure 4.16.4.3a).

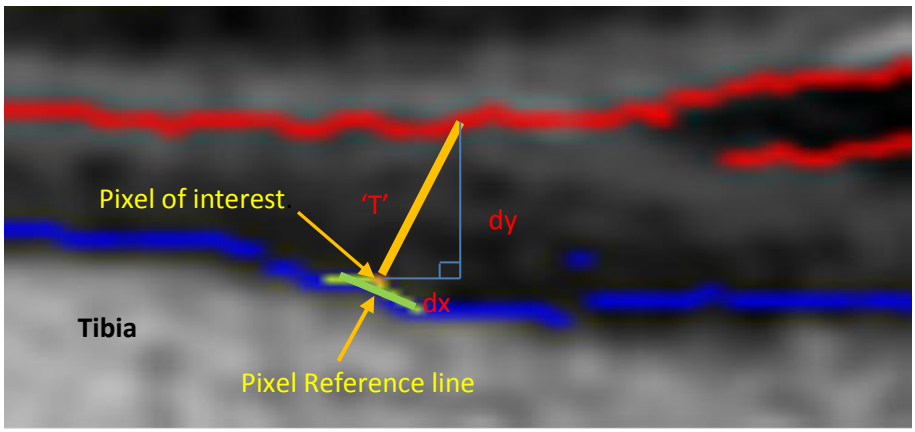


Figure 4.16.4.3a Using Pythagoras ($T = \sqrt{dy^2 + dx^2}$) to measure cartilage thickness. Key: dx=horizontal component of right angle triangle, dy=vertical component of right angled triangle, T=hypotenuse, representative of cartilage thickness perpendicular to the pixel reference line, here showing measurement for a single pixel point on the tibial bone edge.

The mean of the distances measured within a region was calculated to measure average cartilage thickness within it. This was repeated to measure the average thickness across all eight regions (four femur, four tibia) across the six selected slices three medial compartment, 3 lateral compartment, defined above in the tibiofemoral joint. A schematic view of the regions of the knee where average cartilage thicknesses were measured is shown in Figure 4.16.4.3b.

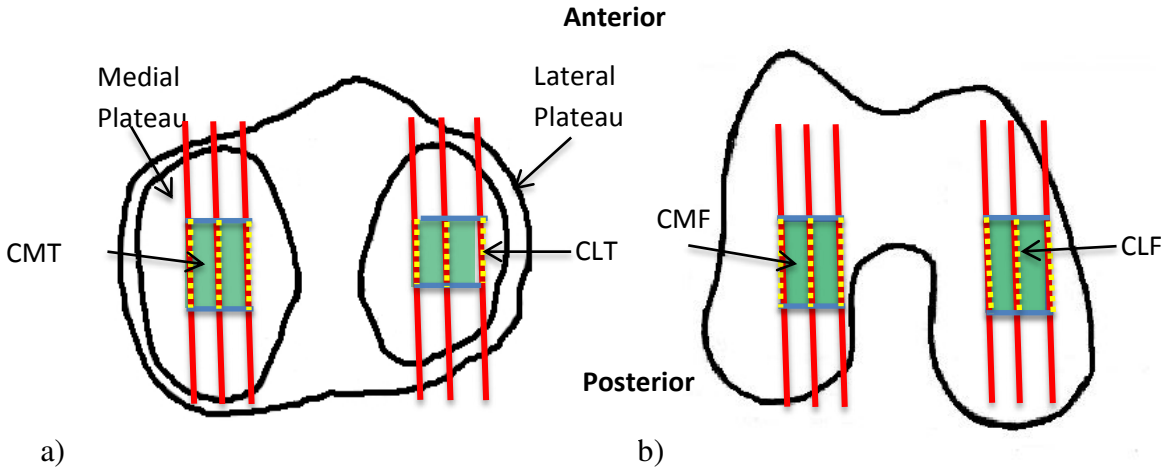


Figure 4.16.4.3b Schematic view of the regions of the tibia and femur that are to be assessed for mean cartilage thickness.
a) Shows the outline of the tibia and the medial and lateral plateaus and b) the medial and lateral femoral condyles, the red lines represent the MRi slices used for assessment (3 medial, 3 lateral). Blue lines represent the anterior and posterior borders of the region to be measured. Yellow dotted lines represent the line along which cartilage thicknesses were measured for each pixel and the green areas indicate the regions over which mean cartilage thickness was calculated, CMT= Central medial tibia region, CLT=Central lateral tibia region, CMF=Central medial femoral region and CLF=Central lateral femoral region. Our outcome measurements for each region (mCMT, mCLT, mCMF, mCLF) would represent the mean of the measurements for cartilage thicknesses along the 3 yellow dotted lines in each central region.

4.16.5 MRi Limitations.

The aim of comparing the NHS diagnostic scan to the matched follow scans up at CUBRIC was to assess for any evidence of degenerative changes within the TF joint. The limitations described below stem from the fact that these scanning sequences were designed to diagnose ACL injury and other associated injuries such as meniscal tears and fractures. Therefore, the scanning sequence was used to give an overview of all structures within the knee and not primarily designed to quantify cartilage thickness or quality specifically, which is typically the outcome variable of interest in studies assessing cartilage change in those with degenerative disorders of the knee.

4.16.5.1 Slice alignment.

As these scans are diagnostic scans, and MRi scans can be aligned in 3 planes independently of each other, the MRi operator is primarily concerned with aligning the

scans in a way that best evaluates the ACL. This is conducted using an axial view of the knee and using the femoral condylar notch for alignment of the sagittal plane slices and the posterior aspects of the femoral condyles for coronal slices (Figure 4.16.5.1).

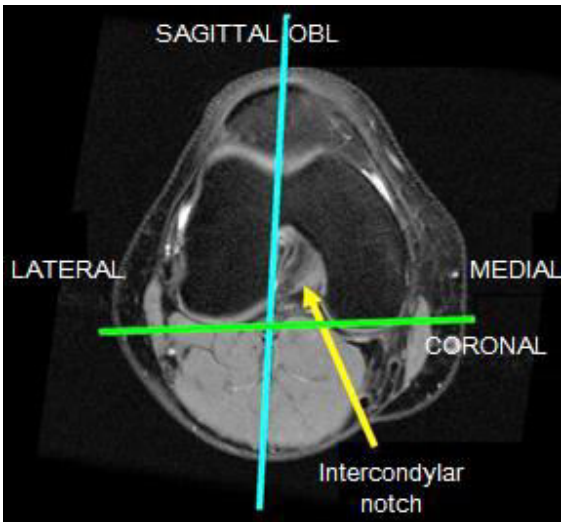


Figure 4.16.5.1 Operator alignment procedure for sagittal and coronal plane MRi slices. MRi operator alignment of the Sagittal (blue line) and coronal plane (green line) MRi slices using the intercondylar notch and posterior points of femoral condyles as reference points.

MRi alignment is completed in a subjective manner by the MRi operator determining the sagittal slice placements using the guidelines above. Within our study, we assessed 3 consecutive slices from the medial and lateral compartments of the knee. This again was subjective as the MRi analysis operator (PR) had to determine which three slices gave the best quality image to segment for the most accurate result.

This primary issue this creates is that the MRi scanning operator alignment means that even if the slice number of the MRi in their diagnostic and follow up scans is the same, the anatomical position of the cartilage being measured will be different, so comparing these points directly is difficult as cartilage is not uniformly distributed across the tibiofemoral joint. This is difficult to be adjusted for, as stated earlier; the positioning of the patient's knee and the orientation of the slices in multiple planes can be determined independently and is done so subjectively by the MRi operator. Unfortunately, although details can be procured relating to the position and orientation

of each MRi slice for comparison, this does not relate to where the anatomy appears on each slice. This is due to the fact that this is irrelevant to the operator for diagnostic scans as they are not concerned with exact alignment within every patient, as the aim of scans in these instances is visualisation of the relevant anatomical structures.

4.16.5.2 Voxel Size.

A voxel is a three dimensional pixel. When an MRi slice is viewed, each image pixel seen on a 2D slice is representative of the signal present in the entire voxel in the 'through plane' direction. Voxel size is influenced by the position of the scanning planes (as demonstrated below in Figure 4.16.5.2. Consequently, if the sagittal plane images between two scans were aligned precisely, the images may still appear different as they would be affected by the interaction of the axial and coronal plane alignment,

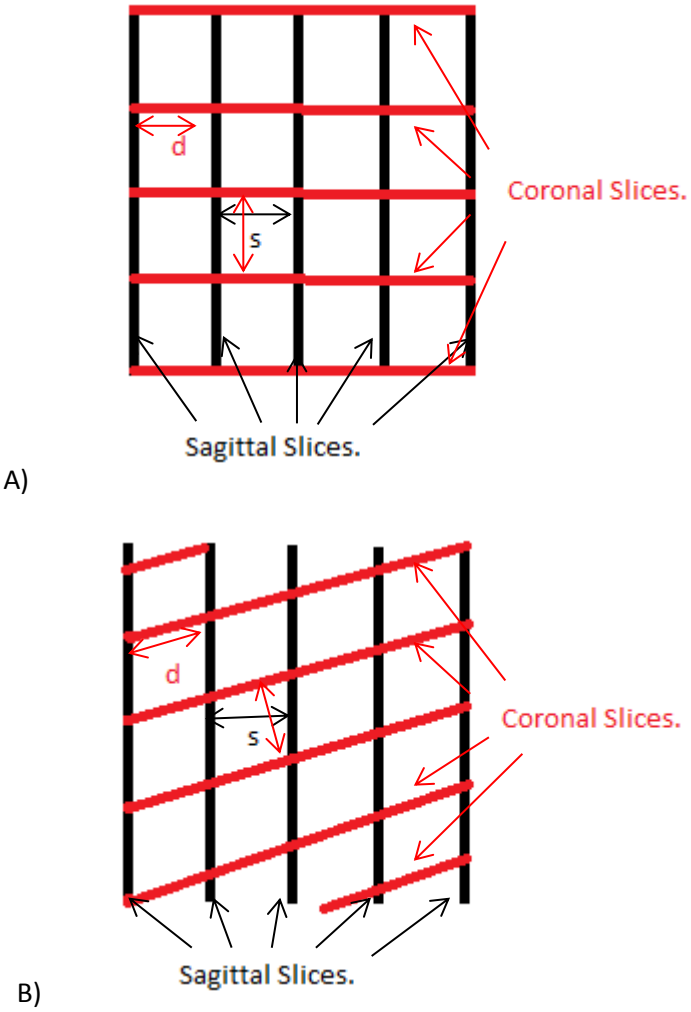


Figure 4.16.6.2 The effect of MRi slice alignment on voxel depth.
Key: d=voxel depth, s=slice spacing. Top image (A) demonstrates an isotropic scanning sequence meaning the coronal and sagittal scanning planes run perpendicular to each other where 's'='d'. The bottom image (B) shows the same sagittal plane alignment however the coronal plane alignment is more acute increasing voxel depth 'd'. A change in alignment angle between planes, even when sagittal and coronal slice spacing 's' remains the same, this changes 'd' and influences the image pixel contrast.

As a subsequence if the voxel depth was different by alignment, either increasing or decreased the through plane dimension between scans, then the pixel colour in the 2D slice, which is representative of the signal through the entire voxel, may demonstrate colour variation between different scans even if the pixel was aligned perfectly in the sagittal plane. Thus when using clinical imaging sequences to differentiate between bone and cartilage using contrast to define these two features can become problematic as one slice may be more bone like, with the corresponding one with a different planar

alignment may be more cartilage like. It is therefore important to acknowledge these limitations when using modelling techniques derived from clinical MRi scanning protocols, concerned with assessing anatomical features in the clinical environment.

These limitations were countered as far as possible by using multiple pixel analysis and averaging cartilage thickness across regions of the tibiofemoral joint. Multiple measurements in an area may limit measurement error due the principle of 'regression towards the mean', which is a more solid method of measurement, where measurement errors may be particularly common, than looking at simple points of maximum and minimum thickness in this instance (Bland and Altman, 1994).

4.17 Reliability Analysis.

Intra-rater reliability testing was undertaken by a single rater (PR) who analysed six slices of the same MRi scan chosen at random from both the CUBRIC and NHS clinical scans. The variables of interest were the mean thicknesses of the CMT (Central medial tibia region), CLT (Central lateral tibial region), CMF (Central medial femoral region) and CLF (Central lateral femoral region).

Analysis of reliability was performed using the Intra-class Correlation (ICC), this test was deemed to be most suitable for the data set according to as the ICC reflects both degree of consistency and agreement among ratings, however as this is only a measurement of the agreement between measurements (Chinn et al., 1991) on a scale of 0-1 (with 1 being absolute agreement), and does not directly measure the difference between measures, therefore the standardised error of measurement (SEM) was also reported. The SEM is a measure of absolute reliability and is expressed in the actual units of measurement, making it easy to interpret, with the smaller the SEM, the greater the reliability, this will be used to give a more accurate depiction of the measurement error for each of the regions defined above.

Another important measure for analysis is the Minimum Detectable Change (MDC). This measure allows a measure of the minimum amount of change (in this case regional cartilage thickness change) in the units being measure before a change between individual scans can be considered notable (Field, 2005). This is a function of the SEM and given by the formula:

$$MDC = 1.96 \times SEM \times \sqrt{2}$$

Table 4.17.1 Mean values and standard deviation for regions of the knee for assessment 1 and 2 with Intra-rater ICC, SEM and MDC.

Region	Assessment 1 (mm)	Assessment 2 (mm)	Single measure ICC	SEM (mm)	MDC (mm)
CMT	2.90±0.53	3.37±0.88	0.970	0.77	2.13
CLT	3.76±0.74	3.81±0.85	0.976	0.25	0.98
CMF	2.85±0.64	3.26±0.60	0.993	0.08	0.22
CLF	2.96±0.29	3.07±0.33	0.976	0.03	0.08

Key: mm=Mean compartment cartilage thickness in for 4 sub-regional measurements of CMT= Central medial tibia region, CLT=Central lateral tibia region, CMF=Central medial femoral region and CLF=Central lateral femoral region.

All values for intra-rater reliability ICC were deemed to be excellent with all values being over 0.97 (Field, 2005). SEM and MDC values showed smaller values in the femur than in the tibia, and between compartments the SEM and MDC was lower for both the tibia and femur in the lateral compartment. For the CMT region the SEM represented an error relating to approximately 21.2% of the cartilage thickness in this region, corresponding values for the CLT, CMF and CLF were 6.4%, 2.5% and 0.9%.

Inter-rater reliability testing was undertaken by three raters, each rater analysed six slices of the same MRi scan chosen at random from both the available CUBRIC and NHS clinical scans (Table 4.17.2).

Table 4.17.2 Inter-rater reliability measurement performed using ICC.

Region	Rater 1 Average thickness (mm)	Rater 2 Average thickness (mm)	Rater 3 Average thickness (mm)	Single measure ICC
Medial femur	2.63±0.25	2.58±0.26	2.59±0.26	0.964
Medial tibia	2.76±0.22	2.89±0.29	2.80±0.26	0.857
Lateral femur	2.68±0.62	2.66±0.58	2.68±0.60	0.992
Lateral tibia	5.07±0.73	5.22±0.65	5.16±0.70	0.990

For each rater, the average compartment cartilage thickness in mm and standard deviation for 12 sub-regional measurements is shown alongside the single measures ICC.

All values for inter-rater reliability ICC were deemed good to excellent with only medial tibia falling below 0.9 (0.857).

The full ACLM cohort cartilage regional thickness data will give a more thorough analysis of the validity of this measurement tool, as comparing a dataset accounting for some of the individual variation in cartilage thickness to those in the literature, will be more favourable than a single individual scan who may not be representative of the full group data. The validity of the present study's quantitative MRi analysis tool and comparison of its findings with other study's will be discussed in greater depth in the discussion Chapter 7.

4.18 MRi Statistical Analysis.

Data for cartilage thickness measurements from the bespoke Matlab routine for quantitative assessment was stored in Microsoft Excel™. Data was then checked for anomalies, average cartilage thickness for the CMT, CLT, CMF and CLF was calculated using Excel™ and exported into SPSS for further analysis. Differences between initial diagnostic scans and follow-up were undertaken using a non-parametric independent Wilcoxon signed-rank test.

For the semi-quantitative method described, the scores were uploaded into SPSS and analysis was undertaken for the total score for the three assessed features in all regions using the non-parametric Wilcoxon signed-rank test. Descriptive mapping was also undertaken for each feature in each region defined in Chapter 4.15.3 for both the diagnostic scan and follow-up MRi. Descriptive mapping include the cumulative score (the total score for all participants for the given feature in each defined region) and the prevalence of this feature (the number of participants that had demonstrated an abnormality in each region).

Due to the small number of participants an in depth analysis was undertaken in a case series format for each participant, including their semi-quantitative scores of cartilage, BMA and meniscus as well as quantitative cartilage thickness measures and the participant specific demographic, biomechanical, strength and clinical measurements. This was undertaken using a ranking system with each participant ranked from 1-9 with 1 being the lowest value and 9 being the highest. This was undertaken to evaluate if any features were associated with changes in MRi indicators of progression of OA in order to identify features that may be used to generate future research questions. MRi outcome measures are shown below in Table 4.18 with the corresponding result chapter and page numbers

Table 4.18 MRi outcome measures.

	Outcome measures	**Results Chapter/Page number**
Semi- Quantitative Method	Total score change. Regional mapping of: BMA score. Cartilage Morphology Score. Meniscal Integrity Score.	Chapter 6.2/Page 178
Quantitative Method	Change in thickness of: mCMT mCLT mCMF mCLF	Chapter 6.3/Page 190

The above table shows the main areas of analysis for MRi methods, the associated outcome measures and the chapter heading and page numbers at which the relevant results can be seen.

Chapter 5 Results: Kinematic, Kinetic and Patient Reported Measures.

5.1 Introduction to Results.

The primary objective of this chapter is to examine if patient reported measures of knee function and biomechanical differences exist between groups of ACL injured groups and controls. Kinematic and kinetic analysis took place across a number of functional tasks, increasing in demand on the knee from gait, jogging and finally the SLS. Longitudinal analysis was undertaken on a sub-cohort of ACLR with two biomechanical assessments (ACLR2), to determine if any changes occurred longitudinally in kinematic and kinetic outcomes. This was undertaken to answer the first study aim, assessing if alterations in spatiotemporal, kinematics and kinetics may alter loading at the knee, which may be associated with the development of early OA.

The ACLR, ACLD and Control participants that performed gait analysis at the RCCK then were assessed for the tasks of jogging and SLS where possible. For jogging and then SLS there was a reduction in participant numbers for each group, this loss in participant numbers was due to factors such as the obscuration of markers, either completely or for a large number of frames, which could not then be recreated reliably and some participants not being able to complete activities due to restraints placed upon them by their injury. For this reason the following chapter describes the demographic parameters for each group for each activity, to identify any appropriate confounding factors that may require further investigation or inclusion as covariates for further analysis of the activity.

For initial assessment of the three groups differences were assessed using a one-way ANOVA or ANCOVA where confounding variables that had been identified were included using covariates from group differences discovered in demographics and performance. If ANOVA and ANCOVA were deemed significant at $p<0.05$, Bonferroni post-hoc analysis was undertaken and significance values were corrected for the three groups to a level of $p<0.017$. Longitudinal changes in our ACLR group were assessed using a paired t-test.

The Null hypotheses' to be tested in this chapter include:

1. ACL injured participants will show no differences in subjective measures of knee function when compared to controls.

2. ACL injured participants will also demonstrate no significant differences in hamstring or quadriceps strength when compared to controls.

3. No change will occur in knee function or strength measurement between first and second assessments.

4. ACL injured participants will show no differences in kinematics or kinetics when compared controls across functional tasks.

5. At a 1 year follow up no significant changes will take place in the ACL injured groups' kinematics and kinetics during functional tasks.

6. No significant differences in kinematics and kinetics regardless of demand of activity.

7. The will be no changes in participants kinematics and kinetics between first and second assessment.

The following chapter will start with patient reported measures of knee function and assessment of strength of the quadriceps and hamstrings using isokinetic dynamometry. The biomechanical assessment of the functional tasks described in the method will then follow, starting with the perceived least demanding activity gait, then jogging and finally on to the perceived most demanding activity, the SLS.

5.2 Patient Reported Function: The IKDC, Cincinnati Knee score and TSK.

Clinical measures of function through patient reported questionnaires are an important and often used measure to determine success of patient rehabilitation. These IKDC and Cincinnati knee score have been designed to subjectively score pathology in the knee joint both directly and indirectly associated with ACL injury and OA (Barber-Westin et al., 1999; Irrgang et al., 2001). Fear of injury may also influence participant function either in conjunction with or separate to physiological impairments, this was measured using the Tampa Scale of Kinesiophobia (TSK) (Houben et al., 2005).

Data for the IKDC, Cincinnati knee score and TSK were collected for the ACLD and ACLR groups. Data was found to be normally distributed for the IKDC and Cincinnati knee score (Kolmogorov-Smirnov, p=0.191 and p=0.200 respectively), however, the TSK was not (p=0.04). Sub-group analysis of TSK scores demonstrated this was due to

a wider distribution of scores in the ACLR group (p<0.001). It has been demonstrated that even in non-normal distributions both the t-test and ANOVA are robust enough to be acceptable tools for statistical analysis (Skovlund and Fenstad, 2000; Osborn, 2013). Group comparisons were performed with an independent t-test for clinical scores (two groups) and one way ANOVA for muscle strength measurement (three Groups), with group differences deemed significant at a level of p<0.05.

Table 5.2.1 Scores for the International Knee Documentation Committee score (IKDC), Cincinnati knee function score and Tampa Scale of Kinesiophobia (TSK) (means±S.D).

Variable	**Participant Group.**			
	ACLR	**ACLD**	***t Value***	***P* value**
IKDC	82.02±14.46	61.91±11.90	4.918	*<0.001
Cincinnati	481.86±64.07	391.36±58.46	4.349	*<0.001
TSK	32±7.42	41.06±55.09	-3.496	*<0.001

Key: ACLR=ACL reconstructed group, ACLD=ACL deficient group. High scores on the IKDC and Cincinnati knee function score relate to higher perceived levels of knee function and a high TSK score relates to a large fear of injury. *Signifies group differences at a level of p<0.05.

There was a significant difference in the IKDC and Cincinnati (p<0.001) knee function scores between the participant groups with the ACLD groups demonstrating significantly reduced levels of subjective knee function compared to the ACLR participants. For the TSK the ACLD showed an increased 'fear of injury' compared to the ACLR participants (p<0.001).

The ACLR2 cohort was assessed longitudinally for changes in the clinical outcomes described above. Differences in clinical scores (TSK, IKDC and Cincinnati knee score) were analysed using a paired t-test with significance level being determined at p<0.05. Table 5.2.2 shows the means±S.D for the clinical outcome measurements at visit one and visit two to the RCCK.

Table 5.2.2 Scores for the International Knee Documentation Committee score (IKDC), Cincinnati knee function score and Tampa Scale of Kinesiophobia (TSK) (means±S.D) for ACLR2.

Variable	Visit 1	Visit 2	*T value*	*P* value
IKDC	90.46±6.73	89.08±14.94	0.2	0.786
Cincinnati	524.30±34.57	527.60±566.60	-0.117	0.909
TSK	31.3±5.73	29.0±5.61	2.226	0.053

Participants demonstrated no differences in the IKDC between visit one and visit two (p=0.786). This was also evident for the Cincinnati knee score with (p=0.909). The TSK also demonstrated a non-significant difference between visit one and visit two (p=0.053).

5.3 Isokinetic Strength Measurement.

Knee strength is an important consideration and primary objective for rehabilitation in those suffering with an ACL injury (Bush-Joseph et al., 2001; Dvir, 2004). Strength measurement has been associated with both biomechanical and performance deficits in those with pathology in the knee joint (Bush-Joseph et al., 2001; Dvir, 2004).

Peak strength was measured (as peak torque in N.m) for both the quadriceps and hamstrings during a continuous maximal effort knee extension and flexion task. Using the Kolmogorov-Smirnov test (p=0.200 for all variables), data was found to be normally distributed for both quadriceps and hamstring strength, in both the involved and uninvolved side. Group differences were analysed using ANOVA (α level of <0.05).

Table 5.3.1 Strength measurements as peak moment normalised to body mass and height (means±S.D).

Variable	Participant Group.			*F Value*	*P* value
	Control	ACLR	ACLD		
Peak Quadriceps Strength Injured/Dominant (N.m/kg.m)	1.92±0.50	1.79±0.71	1.71±0.51	0.475	0.366
Peak Hamstring Strength Injured/Dominant (N.m/kg.m)	1.17±0.34	1.14±0.39	1.16±0.31	0.134	0.950
Peak Quadriceps Strength Non-Injured/Non-Dominant (N.m/kg.m)	1.92±0.5	2.10±0.63	2.00±0.60	0.379	0.689
Peak Hamstring Strength Non-Injured/Non-Dominant (N.m/kg.m)	1.17±0.34	1.23±0.33	1.20±0.34	0.136	0.931

Key: N.m/kg.m=Normalised moment, equating to peak moment in Newton.metres divided by the product of a participant's height and body mass.

No significant differences were observed for any outcome measures between groups for strength measurement, for the uninjured/dominant limb normalised quadriceps moment (p=0.366), for the injured/dominant limb normalised hamstring moment (p=0.950). In the non-injured/non-dominant limb normalised quadriceps strength (p=0.689) and for the non-injured/non-dominant limb normalised hamstring strength (p=0.931).

Normalised Quadriceps and hamstrings strength was again assessed at a follow-up visit approximately 12 months after visit one. Data was analysed for group differences using a within subjects, paired t-test, group differences were determined at a level of $p<0.05$ and shown in Table 5.3.2 below.

Table 5.3.2 Strength measurement given as normalised peak moment (means±S.D) for ACLR2.

Variable	Visit 1	Visit 2	*T* Value	*P* Value
Peak Quadriceps Strength (N.m/kg.m) need to normalise	1.22±0.29	1.41±0.39	-1.901	0.090
Peak Hamstring Strength (N.m/kg.m) need to normalise	0.72±0.14	0.84±0.21	-2.346	***0.044**

Key: N.m/kg.m=Normalised moment, equating to peak moment in Newton.metres divided by the product of a participants height and body mass *Signifies group differences at a level of p=0.05.

Participants demonstrated no significant differences in peak quadriceps strength on the injured limb between visit 1 and visit 2 (p=0.087). Peak hamstring strength in the injured limb did however demonstrated a significant increase between visit one and visit two (p=0.043).

5.4 Gait Analysis.

Gait is an important task to evaluate after ACL injury as alterations in gait mechanics would then subject the knee joint to altered loading countless times over the course of days, weeks, months and years. The cumulative effect of these alterations has been stated as a potential causal mechanism in the initiation, progression and development of OA.

Group demographics were assessed to check for matching between groups and identify potential confounding variables for further analysis. Spatiotemporal characteristics during gait were also assessed for covariate potential, as adaptations in performance may be a strategy to reduce loading at the knee may be evident, which will influence the analysis of kinematic and kinetic factors.

Participant demographics included age, height, body mass, gender, activity level both pre and post injury (taken from the 'Sports Activity Scale' component of the Cincinnati Knee score, details of this are given in Appendix 3, page 288) and time from injury in ACLD participants and time from surgery in ACLR. Table 5.4.1 shows the demographic data for the cohorts included in gait analysis including their means, standard deviations and analysis for group differences.

Table 5.4.1 Gait group demographics (means±S.D) including age, height body mass, activity level pre and post injury and time from injury/surgery. Analysis of group differences is also reported.

Variable	Participant Group.			*(df) F Value*	*P* value
	Control (n=30)	ACLR (n=29)	ACLD (n=28)		
Age (years)	27.9±6.8	30.7±9.8	31.0±7.8	(2,84)1.317	0.337
Height (m)	1.7±0.1	1.7±0.1	1.8±0.1	(2,84)3.147	**0.048***
Body mass (kg)	72.7±16.6	79.6±10.7	81.2±14.8	(2,84)3.328	**0.041***
Male/Female	21/9	20/9	22/6	NA	NA
Activity Level Pre Injury	82.8±18.9	90.2±12.4	93.6±7.3	(2,84)4.062	**0.017***
Current Activity Level	82.8±18.9	85.9±14.9	72.7±18.4	(2,84)4.435	**0.015***
Time from Injury in ACLD or Surgery in ACLR (months)	NA	12.0±7.7	32.3±69.4	NA	NA

Key: m=metres, kg=Kilogram.* Signifies group differences at a level of p=0.05.

Age was demonstrated to be normally distributed when assessing groups individually using Kolmogorov-Smirnov (Control: p=0.126, ACLR: p=0.074, ACLD: p$\geq$0.200), therefore parametric analysis undertaken using ANOVA to compare groups.

Height and body mass were also found to be normally distributed (Kolmogorov-Smirnov, p$\geq$0.200). One-way ANOVA between groups demonstrated that there were significant differences between the three groups in terms of height (p=0.048) and body mass (p=0.041). Post hoc testing showed that no differences existed individually between groups for height, however ACLD was near significance (p=0.051) when compared to Controls. For mass a significant difference existed between Controls and ACLD (p=0.047), therefore body mass was chosen as a single covariate for ANCOVA.

Activity level, measured using the activity level component of the Cincinnati Knee score, was significantly different between groups in both the pre-injury (p=0.017) and post injury (p=0.015) conditions. Pre injury post hoc analysis showed group differences existed between the ACLD and Control participants (p=0.023), with the ACLD demonstrating significantly higher levels of activity. At the post injury time of assessment post hoc analysis also demonstrated that differences existed between the

ACLD and Controls (p=0.017), however in this instance the ACLD group were significantly less active than Controls.

As there were differences in activity level between groups, and placed in the context of the proposed importance activity level is stated as having on influencing loading from the literature this was investigated appropriately in a more thorough analysis in Table 5.4.6. Table 5.4.7 also includes analysis of another proposed key factor influencing gait kinematics and kinetics, time from injury/surgery.

Table 5.4.2 shows the individual group means and standard deviations for spatiotemporal performance characteristics alongside analysis for group differences. Results analysed were gait velocity, cadence and stride length.

Table 5.4.2 Gait performance and spatiotemporal outcome measures (means±S.D), with between group differences.

Variable	Participant Group.			*(df) F* value	*P* Value
	Control (n=30)	ACLR (n=29)	ACLD (n=28)		
Gait Velocity (m/s)	1.5±0.2	1.5±0.2	1.5±0.2	(2,83) 0.009	0.991
Cadence (step/min)	116.2±9.5	113.2±8.7	113.9±14.8	(2,83) 0.405	0.156
Stride Length (m)	1.29±0.1	1.39±0.2	1.39±0.2	(2,83) 3.063	0.053

Key: m/s=velocity in metres per second, step/min= steps taken per minute, m=metres.

All outcome parameters demonstrated assumptions for normal distribution were met using Kolmogorov-Smirnov tests ($p\geq$0.200 for gait velocity, $p\geq$0.200 for cadence and p≥0.200 for stride length). ANOVA demonstrated no significant differences between groups with regard to gait velocity (p=0.991), cadence (p=0.156) and stride length (p=0.053).

Key kinematic parameters investigated for gait included early stance maximum knee flexion and adduction angle and late stance minimum knee flexion angles and second peak adduction angle. Body mass was included as a covariate for analysis. All outcome parameters were found to be normally distributed using the Kolmogorov-Smirnov test ($p\geq$0.200 maximum knee flexion angle, $p\geq$0.200 minimum knee flexion angle, $p\geq$0.200

first peak adduction angle, p=0.064 second peak adduction angle). Therefore, ANCOVA was used to assess group differences between these kinematic outcomes. Table 5.4.3 shows the individual group means and standard deviations for kinematics in the sagittal and frontal plane alongside group differences.

Table 5.4.3 Gait sagittal and frontal plane knee angles (means±S.D) with between group differences.

Variable	**Participant Group.**			**(*df*) *F* Value**	***P* value**
	Control (n=30)	**ACLR (n=29)**	**ACLD (n=28)**		
Peak Knee Flexion Angle(°)	17.5±6.4	16.1±6.4	17.1±6.7	(2,83) 0.186	0.905
Minimum Knee Flexion Angle(°)	-0.7±4.7	1.3±4.1	1.4±5.7	(2,83) 1.599	0.195
1st Peak Knee Adduction Angle(°)	5.0±3.3	5.4±4.2	4.0±4.0	(2,83) 1.096	0.355
2nd Peak Knee Adduction Angle(°)	0.3±3.5	-0.3±4.5	-0.6±3.4	(2,83) 0.459	0.711

Key: °=Angle in degrees.

In the sagittal plane ANCOVA demonstrated no significant differences between groups with regard to peak knee flexion angle (p=0.905) and minimum knee flexion angle (p=0.195). ANCOVA demonstrated no significant differences between groups with regard to the frontal plane kinematics, first peak knee adduction angle (p=0.355) and second peak knee adduction angle (p=0.355).

Normalised kinetics were calculated using the participants' peak moment, divided by the product of the participants' height in metres and their mass in kilograms and given as N.m/kg.m. Normalised kinetic outcome measures were developed in order to adjust for individual variance in height and mass as this makes comparison with other literature easier as this is standard practice. In the present study both of these variables were significantly different between groups when demographics were assessed, therefore creating a normalised outcome variable which did not require covariate analysis, gives a more complete insight when comparing ACL injured and Control groups.

Table 5.4.4 shows the means and standard deviations for normalised kinetic parameters investigated for gait, these included normalised early stance (0-50% of stance) peak internal knee extensor and abductor moment and late stance (50-100% of stance) flexor moments and second peak knee abductor moment.

Table 5.4.4 Gait normalised sagittal and frontal plane knee moments (means±S.D) with between group differences.

Variable	**Participant Group.**			***(df)F value***	***P* value**
	Control (n=30)	**ACLR (n=29)**	**ACLD (n=28)**		
Norm. Peak Knee Extensor Moment (N.m/kg.m)	0.40±0.2	0.40±0.2	0.33±0.2	(2,84) 0.920	0.403
Norm. Peak Knee Flexor Moment (N.m/kg.m)	-0.20±0.1	-0.17±0.1	-0.18±0.2	(2,84) 0.698	0.500
Norm. 1st Peak Knee Abductor moment (N.m/kg.m)	0.38±0.1	0.34±0.1	0.36±0.1	(2,84) 0.659	0.520
Norm. 2nd Peak Knee Abductor moment (N.m/kg.m)	0.23±0.1	0.21±0.1	0.19±0.1	(2,84) 1.945	0.149

Key: N.m/kg.m=Normalised knee moment.

Kolmogorov-Smirnov analysis for distributions showed that normalised extension moment ($p \geq 0.200$) and normalised second peak abductor moment ($p \geq 0.200$) were normally distributed. For peak normalised peak flexor moment exploration of individual group distributions using Kolmogorov-Smirnov found groups were distributed normally (Control $p=0.191$, ACLR $p \geq 0.200$ and ACLD $p \geq 0.200$).

Investigation of group distributions for normalised first peak knee abductor moment using Kolmogorov-Smirnov showed the ACLR ($p = \geq 0.200$) and ACLD ($p \geq 0.200$) group had normal distributions. The Control participants did not ($p=0.05$). It was determined that as two groups showed normal distributions and considering the robustness of the ANOVA (described by Osborn, 2013), that ANOVA was still appropriate to perform statistical analysis.

ANOVA demonstrated no significant differences in both the normalised peak internal knee extensor and flexor moments (p=0.403 and p=0.500 respectively). There was also no significant difference between either the first or second internal knee abductor moments between groups (p=0.520 and p=0.149 respectively).

As the longitudinal aspect of the study aims to explore relationships between biomechanical adaptations and their association with changes evident on MRI scans, the absolute kinetics (the peak non-normalised calculated knee moment) for knee extensor and flexor moments, alongside the two abductor moments, provide an indication of the net loading across the various biological tissues. Table 5.4.5 shows the absolute kinetic outcomes for each group with means and standard deviations and statistical analysis for group differences.

Table 5.4.5 Gait sagittal and frontal plane peak knee moments (means±S.D) with between group differences.

Variable	**Participant Group.**			***(df) F* Value**	***P* value**
	Control (n=30)	**ACLR (n=29)**	**ACLD (n=28)**		
Peak Knee Extensor Moment (N.m)	48.5±22.3	47.3±21.4	46.0±25.6	(2,83) 0.754	0.523
Peak Knee Flexor Moment (N.m)	-24.6±11.9	-22.9±10.7	-30.6±35.15	(2,83) 0.566	0.639
1st Peak Knee Abductor moment (N.m)	47.1±21.5	47.1±22.1	49.7±17.8	(2,83) 0.298	0.827
2nd Peak Knee Abductor moment (N.m)	29.0±12.8	28.7±14.6	26.3±11.0	(2,83) 1.576	0.201

Key: N.m= Knee moment in Newton.metres.

Overall distributions for the generalised population of all three participant groups were considered to be normal for second peak knee abductor moment (p=0.072). Peak internal knee extensor moment was found to be normally distributed for the Control (p=0.152) and ACLD participants ($p \geq 0.200$), however ACLR was not (p=0.009).

Further investigation using assessing of residuals, demonstrated normal distributed using Kolmogorov-Smirnov (p=0.185) so data was treated as parametric in nature.

Further investigation of peak internal knee flexor moment distributions found it to be normally distributed for the Control (p=0.127) and ACLR groups ($p\geq$0.200), however ACLD group was not (p<0.001). Removal of an outlier in the ACLD group demonstrated that data was normally distributed ($p\geq$0.200).

Further examination of distributions of first peak internal knee abductor moment was found to be normally distributed for the ACLR ($p\geq$0.200) and ACLD participants ($p\geq$0.200), however Controls were not (p=0.007). Residual analysis of peak internal knee abductor moment showed that groups were normally distributed using Kolmogorov-Smirnov was normally distributed (p=0.099), therefore all variables for absolute kinetics were treated as parametric in nature and analysed using ANCOVA (Table 5.4.5).

Body mass was again included as a covariate as height and mass where not accounted for with absolute kinetics in ANCOVA and demonstrated that there were no significant differences between groups with regard to peak internal knee extensor and flexor moments (p=0.523 and p=0.639 respectively). ANCOVA demonstrated that there were also no significant differences between groups with regard to first and second peak internal knee abductor moments (p=0.827 and p=0.201 respectively).

This chapter will assess correlations between our participants groups for both current activity level and time from injury. Time from injury data will give deeper insight as to how the ACL injured cohorts sit in relation to the timeframe from injury framework developed from the literature and allow deeper insight into the time dependant recovery after ACL injury.

Evaluation of biomechanics in relation to activity level data, will allow a more thorough understanding of how different levels of function create more or less demand mechanically on the knee, which may influence long term knee health

Key parameters to be analysed were related to selected spatiotemporal, kinematic and kinetic outcomes. Gait velocity was chosen as it was deemed to be the most important indicator of performance and encompasses components of both stride length and cadence as an outcome measure. Kinematic and kinetic outcomes for correlation analysis were targeted in consideration of proposed adaptations evident in literature

assessing ACL injured groups and in the context of the present studies research questions, with which parameters investigated having been cited as being potential outcomes in the progression of OA in ACL injured cohorts (Butler et al., 2009; Gao et al., 2010; Andriacchi and Dyrby 2005). Kinetic outcomes were limited to normalised moments as these take in to consideration both individual and group variations in height and body mass.

Table 5.4.6 shows the kinematic and kinetic outcome measures with the appropriate Pearson's correlations (r) values alongside significance levels for current activity level for each group.

Table 5.4.6 Pearson's correlations (*r)* between current activity level and performance, kinematic and kinetic outcome measures during gait.

	Variable	Control (n=30)		ACLR (n=29)		ACLD (n=28)	
		***r* value**	***P* value**	***r* value**	***P* value**	***r* value**	***P* value**
Performance	Gait velocity (m/s)	0.503	***0.005**	0.198	0.302	0.183	0.352
Kinematics	Peak Knee Flexion Angle (°)	0.132	0.248	0.069	0.362	-0.036	0.428
	Min. Knee Flexion Angle (°)	-0.255	0.091	0.023	0.453	-0.003	0.494
Normalised Kinetics	Norm. Peak Extensor Moment (N.m/kg.m)	0.377	***0.022**	0.194	0.157	0.313	0.052
	Norm. Peak 1 Abductor Moment (N.m/kg.m)	0.088	0.326	0.201	0.148	-0.172	0.190

Key: m/s=velocity in metres per second, °=Angle in degrees, N.m/kg.m=Normalised knee moment. *Denotes significance at $p<0.05$.

No significant correlations existed between current activity level and the key parameters with the exception of Control participants normalised peak extensor moments and gait velocity.

For gait velocity and current activity level the adjusted r^2 value was found to be 0.225 for the Control group demonstrating that activity level accounted for approximately

22% of the variation in gait velocity within this group. For normalised knee extensor moment and current activity level the adjusted r^2 value was found to be 0.111 for the Control group demonstrating that activity level accounted for 11% of the variation in normalised knee extensor moment within this group.

Table 5.4.7 displays the kinematic and kinetic outcome measures with the appropriate Pearson's correlations (r) values alongside significance levels for time from injury/surgery for each group.

Table 5.4.7 Pearson's correlations (r) between time from injury/surgery and performance, kinematic and kinetic outcome measures during gait.

	Variable	ACLR (n=29)		ACLD (n=28)	
		***r* value**	***P* value**	***r* value**	***P* value**
Performance	Gait Velocity (m/s)	-0.161	0.413	-0.283	0.144
Kinematics	Peak Knee Flexion Angle (°)	-0.340	***0.038**	0.183	0.175
	Min. Knee Flexion Angle (°)	-0.255	0.095	0.255	0.095
Normalised Kinetics.	Norm. Peak Extensor Moment (N.m/kg.m)	-0.063	0.375	-0.190	0.167
	Norm. Peak 1 Abductor Moment (N.m/kg.m)	0.005	0.491	-0.042	0.416

Key: m/s=velocity in metres per second, °=Angle in degrees, N.m/kg.m=Normalised moment equating to peak moment in Newton.metres divided by the product of a participants height and body mass. *Denotes significance at $p<0.05$.

No significant correlations existed between time from injury/surgery and the key outcome parameters, with the exception peak knee flexion angles in ACLR which showed a negative association.

5.4.1 Longitudinal Gait Analysis.

Data was collected longitudinally on the ACLR cohort in the RCCK to assess changes in gait biomechanics over time. Table 5.4.8 shows the group means and standard deviations for the overall ACLR cohort and the ten participants who had a second

assessment, named from this point on in the thesis as ACLR2. For the following demographic comparisons these participants were classified as ACLR2a to denote the ACLR2 group at the time of first visit assessment and ACLR2b to denote the ACLR2 group at the time of a second, follow-up, assessment. This analysis was undertaken to compare demographics between groups to assess how representative the ACLR2 participants are when compared to the whole ACLR group, at both time points. Both time points were assessed as ACLR2b would detect any changes in demographics such as activity level or body mass that may have occurred between visit one and visit two. ACLR2a was also included to assess data at the first time point so that any bias that would be directly influenced by time, such as age and time from injury would be removed when comparing groups. Statistical analysis of differences between these groups was performed using an ANOVA.

Table 5.4.8 Group means and standard deviations for our ACLR cohort, ACLR2a and ACLR2b groups for demographic parameters during gait.

Variable	**Participant Group.**			***(df) F Value***	***P* value**
	ACLR (n=28)	**ACLR2a (n=10)**	**ACLR2b (n=10)**		
Age (years)	30.7±9.8	28.7±8.6	30.2±8.7	(2,45) 0.176	0.912
Height (m)	1.73±0.1	1.77±0.1	1.77±0.1	(2,45) 1.246	0.302
Body mass (kg)	79.6±10.7	81.4±9.3	79.9±9.3	(2,45) 0 .048	0.986
Male/Female	20/9	9/1	9/1	NA	NA
Activity Level at Time of Assessment	85.9±14.9	90.5±8.3	86.5±17.6	(2,45) 0.311	0.817

Key: m=metres, kg=Kilogram.* Signifies group differences at a level of p=0.05

Table 5.4.8 shows that no significant differences existed between groups for demographics measurements at a level of p>0.05, this demonstrates that our ACLR2 was representative of our initial ACLR from a demographic perspective at both first and second visit to the RCCK.

Statistical analysis to compare the ten ACLR2 participants' changes in outcome measures over time was undertaken using a paired t-test. Presented below in Table

5.4.9 is the data for the participants, for the output parameters described above relating to gait spatiotemporal characteristics, kinematics and both absolute and normalised knee kinetics.

Table 5.4.9 Gait analysis data for visit one and visit two for ACLR2 (means±S.D).

	Variable	Visit 1	Visit 2	*(df) t* Value	*p* Value
Spatio-Temporal	Gait Velocity (m/s)	1.5±0.2	1.5±0.1	(9) 0.463	.654
	Cadence (steps/min)	112.3±5.0	112.0±4.8	(9) 0.154	.881
	Stride Length (m)	1.3±0.2	1.2±0.1	(9) 2.977	***.021**
Kinematics	Peak Knee Flexion Angle (°)	17.6±7.6	17.8±4.3	(9) -0.72	.945
	Min. Knee Flexion Angle (°)	2.2±3.4	0.2±2.3	(9) 1.617	.140
	Peak 1 Adduction Angle (°)	5.6±3.1	5.9±3.2	(9) -0.374	.717
	Peak 2 Adduction Angle(°)	0.6±3.3	0.6±4.2	(9) 0.009	.993
Absolute Kinetics	Peak Extensor Moment (N.m)	48.9±22.1	48.9±22.1	(9) 1.086	.306
	Peak Flexor Moment (N.m)	-27.0±9.8	-27.0±8.4	(9) 0.003	.998
	Peak 1 Abductor Moment (N.m)	49.6±22.3	49.0±14.0	(9) 0.078	.940
	Peak 2 Abductor Moment (N.m)	30.4±13.9	29.3±11.7	(9) 0.281	.785
Normalised Kinetics.	Norm. Peak Extensor Moment (N.m/Kg.m)	0.3±0.2	0.3±0.1	(9) 0.93	.377
	Norm. Peak Flexor Moment (N.m/kg.m)	-0.2±0.1	-0.2±0.1	() 0.28	.840
	Norm. Peak 1 Abductor Moment (N.m/kg.m)	0.3±0.1	0.3±0.1	-0.172	.867
	Norm. Peak 2 Abductor Moment (N.m/kg.m)	0.2±0.1	0.2±0.1	0.189	.854

Key: m/s=velocity in metres per second, step/min= steps taken per minute, m=metres, °=Angle in degrees, N.m= Knee moment in Newton.metres, N.m/kg.m=Normalised knee moment.

Between visit one and visit two participants demonstrated no significant differences in gait spatiotemporal, kinematic and kinetic outcome measures.

It can be seen that the above analysis agrees with the model developed from knee extensor moments for gait described from the literature (Figure 5.4.1). The current full ACLR group knee extensor moments are represented by the solid purple line with the group mean time from injury are represented with a purple dot. The longitudinal analysis of the ACLR2 group, represented by the dashed purple line, supports the idea that once returned to normal, loading level are maintained after ACL reconstruction, however this timeframe is still relative close to the time of surgical intervention. More longitudinal data would be required to confirm if these parameters were maintained in the long term of 2.5+ years post-surgery.

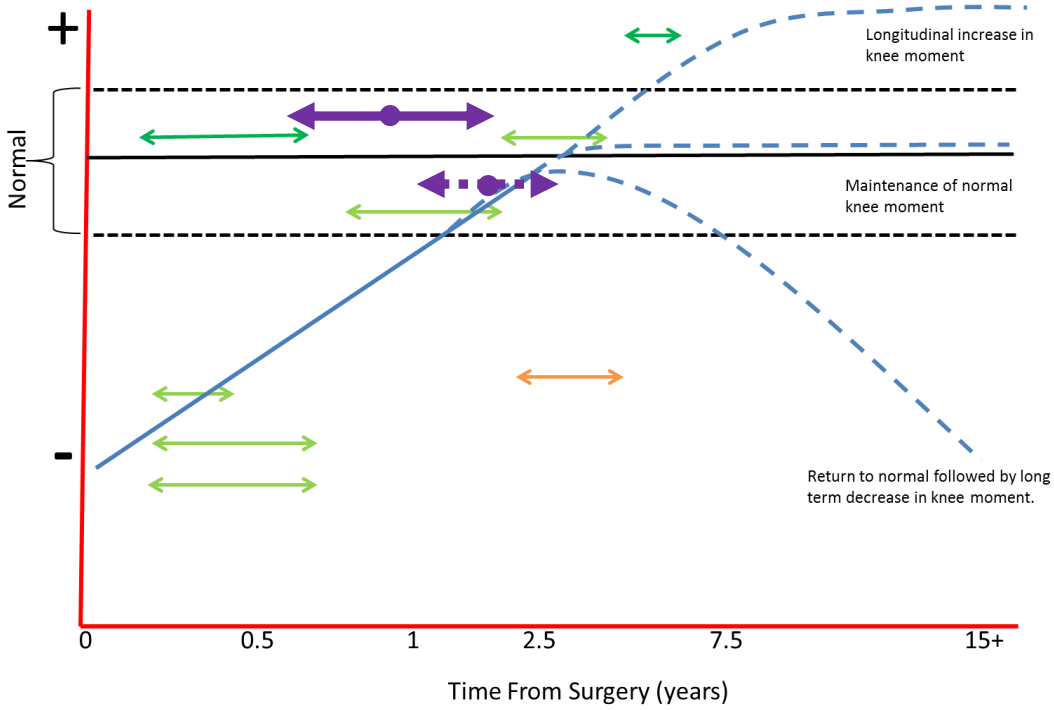


Figure 5.4.1 The current study's knee extensor moments data (ACLR=Solid purple lines, ACLR2 dashed purple lines, purple dot =group mean time from surgery) plotted in the context of the developed framework and models for predicting future adaptations in ACLR after surgery.
Key: Light green line=Gait studies on ACLR, horizontal length represents the time frame at which the study's participants were assessed since surgery. Dark green lines=Abductor moment during gait, horizontal length represents time frame from surgery at which assessment took place. Orange lines= Jogging studies on ACLR, horizontal length represents the time frame at which the study's participants were assessed since surgery. +=Reported significant increase in internal knee extensor moment from control values. -=Reported decrease in internal knee extensor moment from control values. Continuous blue line= Model best fitting internal knee extensor moments ACLD post-injury adaptation trajectory data. Dashed blue line=potential direction for future adaptations.

Contrary to the literature the internal knee abductor moment in the present study was not different to the control group at a similar time-frame. The ACLD group had also returned to normal knee moments, which was in line with other studies at a similar time frame. The current studies ACLD group are represented by the solid purple line in Figure 5.4.2. The ACLD group had a large standard deviation of time from injury therefore the mean value is highlighted with a purple circle.

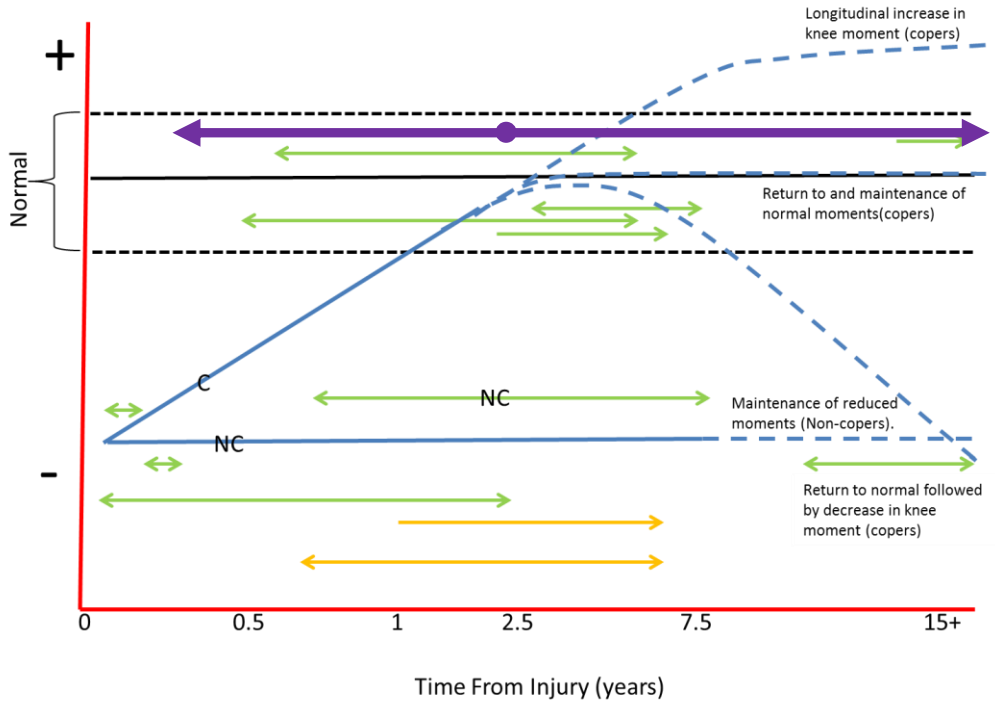


Figure 5.4.2 The current study's knee extensor moments data for gait (ACLD=Solid purple lines) plotted in the context of the developed framework and models for predicting future adaptations in ACLD after injury.
Key: Light green line=Gait studies on ACLD, horizontal length represents the time frame at which the study's participants were assessed since injury. Orange lines= Jogging studies on ACLD, horizontal length represents the time frame at which the study's participants were assessed since injury. +=Reported significant increase in internal knee extensor moment from control values. -=Reported decrease in internal knee extensor moment from control values. Continuous blue line= Model best fitting internal knee extensor moments ACLD post-injury adaptation trajectory data. Dashed blue line=potential direction for future adaptations. C=adaption line for copers. NC=adaptation line for Non-copers.

5.5 Jogging Analysis.

Jogging is an important task to assess as it is more demanding on the knee, creating greater accelerations and having only a single leg weight transference phase (Karinikas et al., 2009). It is also an activity commonly performed in these active populations, therefore deficits in mechanics may cause repeated bouts of abnormal loading or be indicative of incomplete rehabilitation which may place the knee at risk of re-injury or additional trauma.

Some of the participants who performed gait analysis were not able to perform the jogging activity; this demonstrates in part the aforementioned increase in demand placed on the knee causing a reduction in participants capable of completing the task.

Jogging performance, kinematic and kinetic outcome measures was analysed for 28 Controls (two Controls were lost due to markers being obscured throughout the trial), 27 ACLR and 27 ACLD, this compared to 30 healthy Controls, 29 ACLR and 28 ACLD who completed gait analysis. Table 5.5.1 shows the means and standard deviations of demographic parameters alongside ANOVA to assess differences between groups.

Table 5.5.1 Jogging participant demographic characteristics (means±S.D) with between group differences.

Variable	**Participant Group.**			***(df) F* value**	***P* value**
	Control (n=28)	**ACLR (n=27)**	**ACLD (n=27)**		
Age (years)	28.1±6.9	30.0±10.0	30.7±7.7	(2,79) 0.692	0.504
Height (m)	1.7±0.1	1.7±0.1	1.8±0.1	(2,79) 2.484	0.09
Body mass (kg)	72.6±17.0	80.4±10.3	81.7±15.0	(2,79)3.216	***0.045**
Male/Female	20M/8F	21M/6F	21M/6F	NA	NA
Activity Level Pre Injury	83.9±17.9	90.8±12.9	94.1±7.2	(2,79) 4.063	***0.021**
Current Activity Level	83.9±17.9	86.7±15.6	73.3±18.4	(2,79) 4.451	***0.015**
Time from Injuryin ACLD or Surgery in ACLR (months)	NA	11.96±7.0	28.8±12.2	NA	NA

Key: m=metres, kg=Kilogram.* Signifies group differences at a level of $p<0.05$.

For age distribution analysis using Kolmogorov-Smirnov found groups were normally distributed for Control ($p\geq0.200$) and ACLD ($p\geq0.200$), however ACLR ($p=0.033$) was not. Despite the non-normality of the Control group, the robustness of the ANOVA and the normal, as described by Osborn (2013), and as two groups showed normal distributions, it was determined that ANOVA would be used to undertake statistical analysis.

Height and body mass were deemed to be normally distributed using Kolmogorov-Smirnov test for normality ($p \geq 0.200$ and $p \geq 0.200$ respectively). As with Gait, activity level pre injury was significantly different between groups (p=0.21) with post hoc analysis using Bonferroni demonstrated that the Control group was significantly less active than the ACLD cohort (p=0.02) with no other group differences existing. Post injury activity levels were significantly different (p=0.015). However, post-hoc analysis demonstrated a significant between ACLD and ACLR (p=0.018), with the ACLD having significantly reduced activity level after injury.

ANOVA demonstrated significant differences between the 3 groups in terms of body mass (p=0.045) but not age (p=0.507) and height (p=0.090). Bonferroni post-hoc analysis demonstrated that there was a significant difference between ACLD participants' and Control participants' body mass (p=0.020) with the ACLD participants' being significantly heavier. No other group differences were discovered. As before, mass was therefore used as a covariate in ANCOVA for kinematic and kinetic parameters analysed below.

Performance was assessed by calculation of average jogging velocity, which was found to be normally distributed amongst all participants (Kolmogorov-Smirnov, $p \geq 0.200$). Jogging velocity demonstrated no significant differences between participant groups (p=0.730). ACLR, ACLD and Controls descriptive data and analysis can be seen in Table 5.5.2.

Table 5.5.2 Jogging performance, sagittal and frontal plane knee angles (means±S.D) with between group differences.

Variable	**Participant Group.**			***(df) F* value**	***P* value**
	Control (n=28)	**ACLR (n=27)**	**ACLD (n=27)**		
Jogging Velocity (m/s)	2.8±0.4	2.8±0.5	2.7±0.5	(2,78) 0.316	0.730
Peak Knee Flexion Angle(°)	39.0±5.8	34.1±9.0	33.1±7.2	(2,78) 3.340	***0.041**
Minimum Knee Flexion Angle(°)	11.4±8.3	9.4±6.8	8.3±5.5	(2,77) 1.146	0.323
Peak Knee Adduction Angle(°)	10.0±4.6	12.1±11.4	13.9±6.9	(2,78) 1.304	0.277

Key: m/s=velocity in metres per second, ° =angle in degrees. *denotes group differences at p=0.05 using ANCOVA for knee angles and ANOVA for velocity.

Jogging kinematic parameters included sagittal plane maximum and minimum knee flexion angle and peak adduction angle in the frontal plane.

Kinematic outcome parameters were tested for normal distributions (Kolmogorov-Smirnov test). Values reported were: maximum knee adduction angle $p \geq 0.200$, peak knee flexion angle $p \geq 0.200$ and minimum knee flexion angle $p=0.000$. Distribution analysis demonstrated that at a group level, groups were normally distributed for ACLR ($p \geq 0.200$) and ACLD ($p \geq 0.200$), however Control ($p=0.001$) was not. Residual analysis also showed a non-normal distribution for all participants ($p=0.001$). Despite the non-normality of the Control group it was decided that because of the robustness of ANOVA, as described by Osborn (2013), and as two groups showed normal distributions, that ANCOVA would be used to undertake statistical analysis.

In the sagittal plane there was a significant difference with regard to peak knee flexion angle ($p=0.041$). Post hoc testing demonstrated no significant difference between each cohort, when using a corrected p value (Bonferroni adjustment, $p=0.052$). ANCOVA also demonstrated no significant differences between groups with regard to minimum knee flexion angle ($p=0.323$) and peak adduction angle ($p=0.277$).

Kinetic parameters investigated in jogging included sagittal plane normalised peak internal knee extensor and flexor moments and peak internal abductor moment. Unlike gait this typically presents itself as one discreet peak, not the two peaks noted for gait.

Table 5.5.3 Jogging normalised sagittal and frontal plane knee moments (means±S.D) with between group differences.

Variable	**Participant Group.**			***(df) F* Value**	***P* value**
	Control (n=28)	**ACLR (n=27)**	**ACLD (n=27)**		
Norm. Peak Knee Extensor Moment (N.m/kg.m)	1.16±0.3	0.83±0.4	0.7±0.4	(2,79) 11.155	*<0.001
Norm. Peak Knee Flexor Moment (N.m/kg.m)	-0.19±0.1	-0.24±0.2	-0.20±0.1	(2,79) 1.234	0.297
Norm. Peak Knee Abductor moment (N.m/kg.m)	0.88±0.3	0.84±0.4	0.83±0.4	(2,79) 0.167	0.847

Key: N.m/kg.m=Normalised knee moment.

Normalised peak internal knee extensor moment and peak knee abductor moment were demonstrated to be normally distributed (Kolmogorov-Smirnov test) (p=0.200 and p=0.180 respectively). Peak internal knee flexor moment was deemed to be not normally distributed (p=0.001), however after visual inspection of histograms, Q-Q and P-P plots this data was deemed to meet assumptions for normality. As knee moments were normalised to include both body mass and height, this factor was not used as covariates in analysis of sagittal and frontal plane knee kinetics, therefore ANOVA was an appropriate statistical tool.

ANOVA demonstrated a significant difference in peak knee extensor moment between groups ($p<0.001$), post hoc analysis (Bonferroni) showed a significant reduction in peak knee extensor moment in both the ACLR (p=0.004) and ACLD ($p<0.001$) cohorts compared to the Controls. There was no significant difference between either internal peak knee flexor moment (p=0.297) or peak knee abductor moment (p=0.847) for all groups.

Absolute values for kinetics were also calculated for knee extensor and flexor moments and the peak abductor moment during the jogging activity. The data for internal peak knee extensor, flexor and abductor moments were all demonstrated to be normally distributed ($p \geq 0.200$, p=0.179 and $p \geq 0.200$ respectively, Kolmogorov-Smirnov).

Table 5.5.4 Sagittal and frontal plane absolute knee moments for jogging (means±S.D), with between group differences.

Variable	**Participant Group.**			***(df) F* value**	***p* value**
	Control (n=28)	**ACLR (n=27)**	**ACLD (n=27)**		
Peak Knee Extensor Moment (N.m)	146.5±55.4	114.8±59.0	98.4±52.4	(2,79) 8.524	***<0.001**
Peak Knee Flexor Moment (N.m)	-25.1±19.1	-33.1±21.1	-28.8±15.2	(2,79) 0.686	0.506
Peak Knee Abductor moment (N.m)	110.2±40.6	117.8±57.0	114.6±44.9	(2,79)0.079	0.924

Key: N.m=Knee moment given in Newton.metres.* Signifies group differences at a level of p=0.05.

Mass was included as a covariate in ANCOVA and a significant difference between groups with regard to peak internal knee extensor moment (p<0.001) was noted with peak internal knee flexor moment and abductor moment demonstration no significant differences between groups (p=0.506 and p=0.924 respectively). Post hoc analysis of the internal knee extensor moment (Bonferroni) showed that both ACLR (p=0.018) and ACLD (p<0.001) had a significantly reduced knee extensor moment when compared to healthy Controls.

From analysis of kinematics and kinetics during jogging there were observed significant differences between ACL injured participants when compared to the Control group. As the individuals in our ACL injured groups were assessed across a spectrum of times from injury or surgery, assessment of correlations will take place between the participants groups for jogging biomechanics and time from injury or surgery. Correlations will also be performed with activity level to determine if a return to higher activity levels is accompanied by a corresponding return to more normal jogging biomechanics.

Key parameters to be analysed were related to selected spatiotemporal, kinematics and kinetic outcomes that were comparable to gait. Such as jogging velocity, peak knee flexion angle, minimum knee flexion angle, normalised peak knee extensor and normalised peak knee abductor moments.

Table 5.5.5 shows the kinematic and kinetic outcome measures with the appropriate Pearson's correlations (r) values alongside significance levels for current activity level for each group.

Table 5.5.5 Pearson's correlations (r) between current activity level and performance, kinematic and kinetic outcome measures during jogging.

	Variable	Control (n=28)		ACLR (n=27)		ACLD (n=27)	
		***r* value**	***P* value**	***r* value**	***P* value**	***r* value**	***P* value**
Performance	Jogging velocity (m/s)	0.657	***<0.001**	0.375	***0.027**	0.394	***0.026**
Kinematics	Peak Knee Flexion Angle (°)	-0.094	0.321	0.543	***0.002**	0.282	0.077
	Min. Knee Flexion Angle (°)	-0.473	***0.007**	0.116	0.282	0.169	0.199
Normalised Kinetics	Norm. Peak Extensor Moment (N.m/kg.m)	0.145	0.235	0.417	***0.015**	0.420	***0.015**
	Norm. Peak Abductor Moment (N.m/kg.m)	0.179	0.186	0.422	***0.014**	0.136	0.249

Key: m/s=velocity in metres per second, °=Angle in degrees, N.m/kg.m=Normalised knee moment. *Denotes significance at $p<0.05$.

For jogging velocity and current activity level the adjusted r^2 value was found to be 0.409 for the Control group, 0.106 for ACLR and 0.119 for ACLD groups, demonstrating that current activity level accounted for 41% (Control), 11% (ACLR) and 12 % (ACLD) of the variation in jogging velocity within these groups.

There was a positive correlation between peak knee flexion angle and current activity level, the adjusted r^2 value was found to be 0.267 for the ACLR group demonstrating that current activity level accounted for about 27% of the variation in peak knee flexion angle.

There was a negative correlation between minimum knee flexion angle and current activity level, with ACL groups showing the opposite, a positive but non-significant relationship. The adjusted r^2 value was found to be 0.191 for the Control group demonstrating that current activity level accounted for 19% of the minimum knee flexion angle within this group.

Normalised peak knee extensor moment and current activity level the adjuster r^2 value was found to be 0.141 for the ACLR and 0.143 in the ACLD group demonstrating that current activity level accounted for 14% in the ACLR and 14% in the ACLD groups of the variation in the

Normalised peak internal knee abductor moment and current activity level adjusted the r^2 value was found to be 0.145 for the ACLR group demonstrating that current activity level accounted for 15% of the variation in normalised peak knee abductor moment within this group. Table 5.5.6 displays the kinematic and kinetic outcome measures with the appropriate Pearson's correlations (r) values alongside significance levels for time from injury/surgery for each group.

Table 5.5.6 Pearson's correlations (r) between time from injury/surgery and performance, kinematic and kinetic outcome measures during jogging.

	Variable	ACLR		*ACLD*	
		***r* value**	***P* value**	***r* value**	***P* value**
Performance	Jogging Velocity (m/s)	0.091	0.333	0.001	0.498
Kinematics	Peak Knee Flexion Angle (°)	0.181	0.193	0.573	***0.001**
	Min. Knee Flexion Angle (°)	0.077	0.356	0.199	0.164
Normalised Kinetics.	Norm. Peak Extensor Moment (N.m/kg.m)	0.338	***0.049**	0.238	0.121
	Norm. Peak Abductor Moment (N.m/kg.m)	-0.041	0.424	0.272	***0.089*

Key: m/s=velocity in metres per second, °=Angle in degrees, N.m/kg.m=Normalised knee moment. *Denotes significance at $p<0.05$.

Significant correlations existed between time from injury/surgery with both normalised peak extensor moment (in ACLR) and peak knee flexion angle (in ACLD).

For peak flexion angle the adjusted r^2 value was found to be 0.308 for the ACLD group demonstrating that time from surgery accounted for 30% of the variation in peak knee flexion angle.

For normalised peak internal knee extensor moment, adjusted the r^2 value was found to be 0.075 for the ACLR group demonstrating that time from surgery had a positive

relationship with time from surgery, this accounted for 8% of the variation in peak knee extensor moment.

5.5.1 Longitudinal Jogging Analysis.

Data was collected longitudinally for the ACLR2 cohort to assess changes in biomechanics over a time period of 12.9±1.8 months (range 11-17 months) between visit one and visit two. Statistical analysis was again performed using a paired t-test. Table 5.5.7 presents the data for the ten ACLR2 for jogging spatiotemporal parameters, kinematics and both absolute and normalised knee kinetics. As the same participants were followed up for gait (and SLS) no significant differences existed between demographics from visits one to visit two.

Table 5.5.7 Jogging analysis data for visit one versus visit two for the ACLR2 (means±S.D).

	Variable	Visit 1	Visit 2	*(df) t* Value	*p* Value
	Jogging Velocity (m/s)	3.0±0.3	2.9±0.4	(9) 0.839	0.425
Kinematics	Peak Knee Flexion Angle (°)	39.8±5.7	39.2±6.7	(9) 0.285	0.782
	Min. Knee Flexion Angle (°)	14.5±5.2	12.0±4.1	(9) 2.410	**0.042***
	Peak Adduction Angle (°)	10.4±7.1	9.2±5.2	(9) 0.409	0.693
Absolute Kinetics	Peak Extensor Moment (N.m)	164.6±34.4	163.0±49.0	(9) 0.092	0.928
	Peak Flexor Moment (N.m)	-27.3±13.3	-26.1±11.1	(9) 0.455	0.660
	Peak Abductor Moment (N.m)	122.9±55.3	106.6±48.5	(9) 0.860	0.414
Normalised Kinetics.	Norm. Peak Extensor Moment (N.m/kg.m)	1.1±0.2	1.1±0.3	(9) 0.005	0.996
	Norm. Peak Flexor Moment (N.m/kg.m)	-0.2±0.1	-0.2±0.1	(9) 0.483	0.642
	Norm. Peak Abductor Moment (N.m/kg.m)	0.8±0.3	0.7±0.3	(9) 0.839	0.425

Key: m/s=velocity in metres per second, step/min= steps taken per minute, m=metres, °=Angle in degrees, N.m= Knee moment in Newton.metres, N.m/kg.m=Normalised knee moment.* Signifies group differences were reported at a level of $p<0.05$.

Between visit one and visit two participants demonstrated no significant differences in any of the outcomes other than minimum knee flexion angle which was significantly reduced between visit one and visit two (p=0.042).

It can be seen that the above analysis agrees with the model developed from knee extensor moments for jogging described from the literature (Figure 5.5.1). The current full ACLR group internal knee extensor moments are represented by the solid purple line with the group mean time from injury are represented with a purple dot. The longitudinal analysis of the ACLR2 group, represented by the dashed purple line, supports the idea that loading levels are maintained after ACL reconstruction.

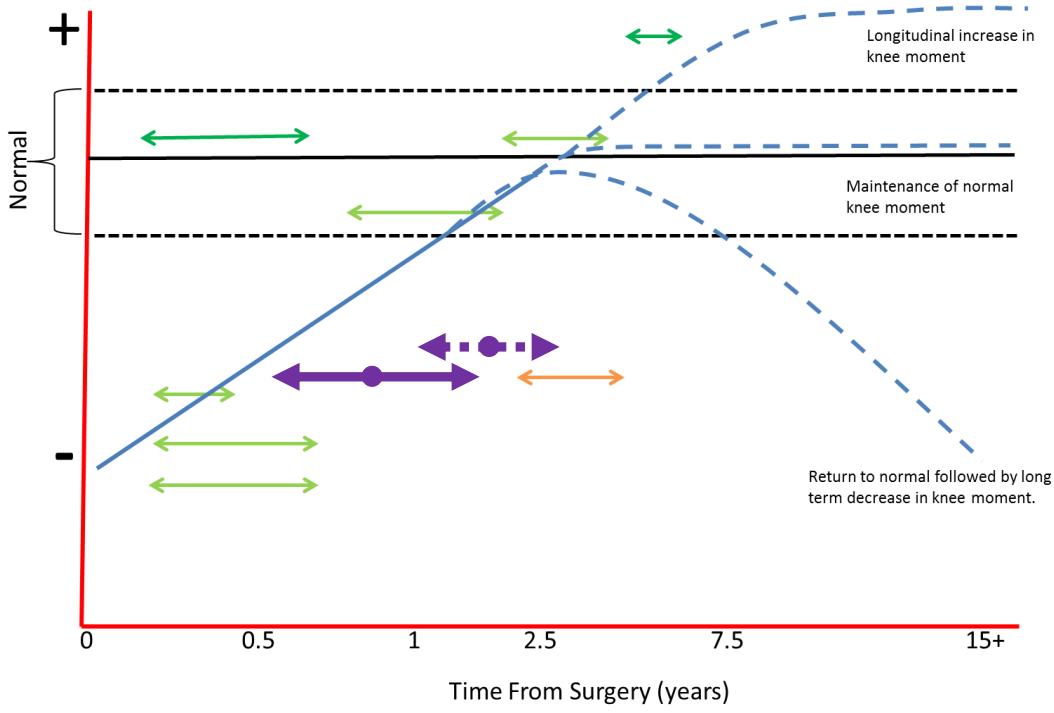


Figure 5.5.1 The current study's knee extensor moments data for jogging (ACLR=Solid purple lines, ACLR2 dashed purple lines, purple dot =group mean time from surgery) plotted in the context of the developed framework and models for predicting future adaptations in ACLR after surgery.
Key: Light green line=Gait studies on ACLR, horizontal length represents the time frame at which the study's participants were assessed since surgery. Dark green lines=Abductor moment during gait, horizontal length represents time frame from surgery at which assessment took place. Orange lines= Jogging studies on ACLR, horizontal length represents the time frame at which the study's participants were assessed since surgery. +=Reported significant increase in internal knee extensor moment from control values. -=Reported decrease in internal knee extensor moment from control values. Continuous blue line= Model best fitting internal knee extensor moments ACLD post-injury adaptation trajectory data. Dashed blue line=potential direction for future adaptations.

Longitudinally only one parameter, minimum knee flexion angle, was significantly different between visit one and visit 2, this may suggest that adaptations do take place in the long term after surgery however these timeframes may have been outside of the scope of the study.

The ACLD group had also a reduction in internal peak knee extensor moment which was in line with the other studies at a similar time frame. The current studies ACLD group are represented by the solid purple line in Figure 5.5.2. The ACLD group had a large standard deviation of time from injury therefore the mean value is highlighted with a purple circle.

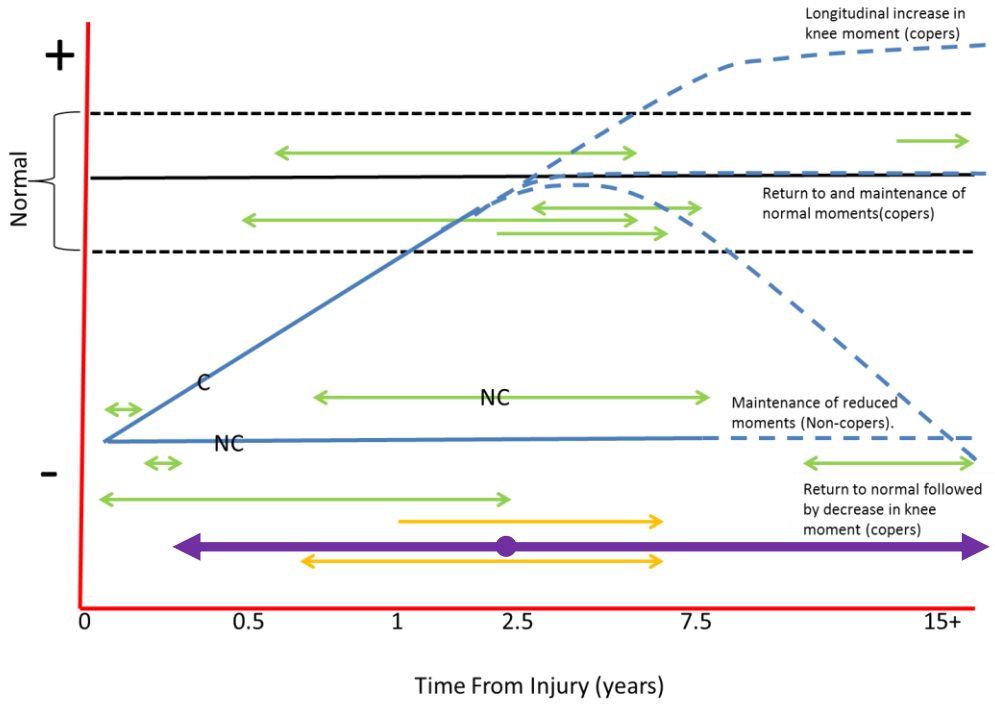


Figure 5.5.2 The current study's knee extensor moments data for jogging (ACLD=Solid purple lines) plotted in the context of the developed framework and models for predicting future adaptations in ACLD after injury.
Key: Light green line=Gait studies on ACLD, horizontal length represents the time frame at which the study's participants were assessed since injury. Orange lines= Jogging studies on ACLD, horizontal length represents the time frame at which the study's participants were assessed since injury. +=Reported significant increase in internal knee extensor moment from control values. -=Reported decrease in internal knee extensor moment from control values. Continuous blue line= Model best fitting internal knee extensor moments ACLD post-injury adaptation trajectory data. Dashed blue line=potential direction for future adaptations. C=adaption line for copers. NC=adaptation line for Non-copers.

The following chapter analyses the most demanding of the three activities SLS. With the hypotheses stating this should demonstrate the greatest number of biomechanical differences within bot ACLR and ACLD when compared to controls.

5.6 Single Leg Squat Analysis.

After the assessment of gait then the more demanding activity of jogging, reflected in the increased velocity, knee flexion angles and knee moments. The SLS was deemed to be the most challenging activity performed by the participants, although having lower accelerations at the knee, the need for the participants to control the large range of motion and knee flexion angles in order to perform the squat to the participant's maximum depth makes this potentially more challenging.

As with gait and jogging, participant groups' demographics were assessed initially to check for matching between groups and also potential covariates for further analysis. This group consisted of 26 Controls, 23 ACLR and 20 ACLD, this compared to 30 Controls, 29 ACLR and 28 ACLD who completed gait analysis and 28 Controls, 27 ACLR and 27 ACLD who were analysed for jogging.

This decrease in numbers in ACLD was due primarily with participants feeling incapable of performing the movement (n=5) and occasionally issues with the quality of the data for some participants (n=2).

Reduction in numbers for the ACLR was principally due to errors in data collection (n=3) and not related to the participants injury (n=1). Four Controls were missing from SLS analysis. These had missing markers throughout or for large portions of the trial making data unreliable for analysis.

The data in the following table (Table 5.6.1) shows the participants who could not complete the SLS task due to injury key outcome measure including time from injury/surgery, Cincinnati Knee score, velocity for gait and jogging, peak knee flexion angle for both gait and jogging and normalised knee extensor moment for both gait and jogging alongside the means for these outcomes from the full ACL injured groups.

Table 5.6.1 Comparison of key demographic, performance, kinematic and kinetic outcome measures for gait and jogging in those who could not complete the SLS due to impaired function vs. the full group means for each outcome.

Group	ACLR 1	ACLD 1	ACLD 2	ACLD 3	ACLD 4	ACLD 5	Total Group Mean (S.D) for ACLR/ACLD
Time from injury/Surgery (months)	32	18	6	9	12	4	12.0±7.7/32.3±69.4
Cincinnati Knee score	324	278	357	371	333	366	481.9±64.1/391.4±58.5
Quadriceps Strength (N.m/kg.m)		0.37	0.55	1.28	0.88	1.12	1.79±0.71/1.71±0.51
Hamstring Strength (N.m/kg.m)		0.44	0.58	0.74	0.54	0.51	1.14±0.39/1.16±0.31
Gait Velocity (m/s)	0.89	1.33	1.22	1.72	1.31	1.3	1.45±0.21/1.47±0.17
Jogging Velocity (m/s)		1.94	2.16	2.70	2.53	2.11	2.82±0.48/2.72±0.47
Gait Peak Knee Flexion Angle (°)	2.4	18.9	15.22	5.81	14.11	6	16.1±6.4/17.1±6.7
Jogging Peak Knee Flexion Angle (°)		23.3	26.6	25.6	38.33	23.1	34.1±9.0/33.1±7.2
Gait Norm. Peak Knee Extensor Moment (N.m/kg.m)	0.01	0.14	0.19	0.19	0.12	-0.01	0.35±0.17/0.33±0.21
Jogging Norm. Peak Knee Extensor Moment (N.m/kg.m)		-0.08	0.57	0.17	0.14	0.17	0.83±0.41/0.70±0.40

Key: m/s=velocity in metres per second, °=Angles in degrees, N.m/kg.m= Normalised knee moment.

Table 5.6.1 shows that for subjective measures of knee function using the Cincinnati knee score that all participants, regardless of group were below the mean score for the respective full group data.

Strength measurement was not available for ACLR1 as they did not feel confident to safely perform the activity. For the ACLD participants all five demonstrated markedly less quadriceps strength and hamstring strength when compared to the group mean. For both quadriceps and hamstring strength 3/5 participants had less than 50% of the full group mean strength.

Analysis of gait parameters showed that the one ACLR participant had markedly reduced gait velocity, peak knee flexion angle and normalised knee extensor moments when compared to the ACLR full group data. This participant could also not perform the jogging activity, which again shows this participant was not functioning at a level that would be expected of those after ACL reconstruction, especially in consideration of the time from injury, which should have allowed ample time for recovery as this was much greater than the group mean.

Four out of the five ACLD had noticeably lower gait velocities than the full group data; this was also the case for jogging velocity. For kinematics 2/5 had noticeably lower peak knee flexion angles for gait, however for the more demanding activity of jogging, 4/5 had lower peak knee flexion angles. With regard to normalised peak knee extensor moment, the most direct measure of loading at the knee, all 5 participants had markedly reduced moments when compared to the full group data; this was evident for both gait and jogging.

For those included in the SLS activity, age data demonstrated a normal distribution using Kolmogorov-Smirnov (Control, $p \geq 0.200$; ACLR, $p=0.072$; ACLD, $p \geq 0.200$). Height and body mass were also deemed to be normally distributed using Kolmogorov-Smirnov test for normality ($p \geq 0.200$ and $p \geq 0.200$ respectively). ANOVA demonstrated significant differences between the three groups in terms of body mass ($p=0.042$) but not age ($p=0.614$) and height ($p=0.074$). Mass was again employed as a covariate used for analysis of other performance, kinematic and kinetic parameters. Bonferroni post-hoc analysis noted that there was a significant difference between ACLD and Controls ($p=0.045$) with the ACLD being significantly heavier. No other group differences were discovered. Table 5.6.2 shows the participant demographic characteristics for those participating in SLS (means±S.D) and statistical analysis outcomes using ANOVA.

Table 5.6.2 SLS participant demographic characteristics (means±S.D) and group differences.

Variable	Participant Group.			*(df) F* value	*P* value
	Control (n=26)	ACLR (n=23)	ACLD (n=20)		
Age (years)	28.4±6.9	30.6±9.9	30.1±6.9	(2,66) 0.491	0.614
Height (m)	1.72±0.11	1.75±0.09	1.79±0.07	(2,66) 2.714	0.074
Body mass (kg)	73.8±17.5	80.6±11.0	84.3±12.4	(2,66) 3.325	***0.042**
Male/Female	18M/8F	16M/7F	15M/5F	NA	NA
Activity Level Pre Injury	84.0±17.6	90.0±13.5	93.5±17.2	(2,65) 2.729	0.073
Current Activity Level	84.0±17.6	86.5±12.9	75.2±17.9	(2,64) 2.615	0.081
Time from Injuryin ACLD or Surgery in ACLR (months)	NA	12.3±37.8	21.5±7.9	NA	NA

Key: m=metres, kg=Kilogram.* Signifies group differences at a level of p=0.05.

Unlike gait and jogging, activity level pre and post injury was not significantly different between groups (p=0.081 and p=0.073 respectively). This suggests that the ACLD included in the SLS had a higher level of function than the participants from gait and jogging.

This is reflected in the descriptive data from Table 5.6.1, which shows that the participants who could not perform the SLS activity were also typically lower functioning, both subjectively and from biomechanical analysis of gait and jogging when compared to the full group data.

SLS performance was assessed by measuring squat depth and peak velocity during the descent and ascent, all of which were found to be normally distributed (Kolmogorov-Smirnov, $p \geq 0.200$ for all variables). Table 5.6.3 shows the performance characteristics for the SLS groups (means±S.D) and statistical analysis outcomes using ANCOVA.

Table 5.6.3 SLS performance measures (means±S.D) with between group differences.

Variable	Participant Group.			*(df) F* value	*P* value
	Control (n=26)	ACLR (n=23)	ACLD (n=20)		
Squat Depth (m)	0.28±0.08	0.25±0.09	0.24±0.06	(2,66) 2.782	0.069
Descent Velocity (m/s)	0.58±0.16	0.55±0.18	0.53±0.15	(2,66) 1.305	0.278
Ascent Velocity (m/s)	0.52±0.16	0.49±0.16	0.49±0.15	(2,66) 0.877	0.421

Key: m=distance in metres measured using vertical change in centre of mass position, m/s=velocity in metres per second.

ANCOVA demonstrated no significant differences between groups with regard to the performance measures of squat depth (p=0.069), descent velocity (p=0.278) and ascent velocity (p=0.412).

SLS kinematic parameters included sagittal plane maximum knee flexion angle and sagittal plane knee range of motion (ROM). The inclusion of ROM reflects strongly the peak flexion angle, but also incorporates the full angle travelled during the SLS which also includes the early part of the SLS near full extension so gives a more complete picture of changes in angles in the sagittal plane.

In the frontal plane peak adduction angle and frontal plane ROM were also assessed. ROM was assessed in the frontal plane as this reflects control of the knee in this plane. The measure of peak adduction angle alone may not reflect full movement at the knee, as the SLS movement pattern is not as clearly defined as in gait and jogging. As the SLS is more likely to demonstrate a number of different strategies to control motion in the SLS, frontal plane ROM allows assessing full motion at the knee giving a more complete picture.

Table 5.6.4 shows the kinematic results (means±S.D) and statistical analysis results using ANCOVA. Kinematic outcome parameters were tested for normal distributions using Kolmogorov-Smirnov, values reported were: Peak knee flexion angle $p \geq 0.200$, maximum knee adduction angle $p \geq 0.200$. ROM values in the sagittal plane (p=0.028) and frontal plane (p=0.022) were found to be not normally distributed for all participants. Further analysis for each participant group found that Controls, ACLR and ACLD were normally distributed for both sagittal plane ROM ($p \geq 0.200$, p=0.057 and

$p \geq 0.200$ respectively) and frontal plane ROM (p=0.181, $p \geq 0.200$ and p=0.125 respectively).

Table 5.6.4 SLS sagittal and frontal plane kinematics (means±S.D) with between group differences.

Variable	Participant Group.			*(df) F* Value	*P* value
	Control (n=26)	ACLR (n=23)	ACLD (n=20)		
Peak Knee Flexion Angle (°)	77.8±11.5	70.8±14.7	66.8±7.7	(2,66) 3.905	***0.025**
Sagittal Plane Knee ROM (°)	72.5±12.9	63.1±13.7	58.1±7.5	(2,66) 7.350	***0.001**
Peak Knee Adduction Angle (°)	14.0±14.6	19.5±17.4	23.6±12.6	(2,66) 0.517	0.599
Frontal Plane Knee ROM (°)	12.0±15.4	18.5±16.3	23.6±11.2	(2,66) 1.178	0.314

Key: °=Angle in degrees. *denotes significant differences between groups at p<0.05.

In the sagittal plane there were significant differences with regard to peak flexion angle (p=0.025) and ROM (p=0.001). Post hoc Bonferroni analysis showed that at a group level, significant differences existed between ACLD and Controls for both peak flexion angle (p=0.024) and ROM (p=0.001). ACLR also had a significant difference when compared to Controls for sagittal knee ROM (p=0.036).

However adjustment to the Bonferroni analysis due to the number of comparisons (n=3) reduces the significance value from p<0.05 to 0.05*(1/3)=**0.017.** Meaning that for ACLD peak knee flexion angle and ACLR knee ROM these demonstrated no significant differences.

Kinetic parameters investigated in SLS included normalised peak internal knee extensor and normalised peak internal abductor moment. Alongside this absolute peak extensor and abductor moment were also analysed. These variables were shown to be normally distributed using Kolmogorov-Smirnov (normalised peak internal knee extensor moment p=0.199, normalised peak internal abductor moment p=0.200, absolute peak knee extensor moment p=0.200 and absolute peak knee abductor moment p=0.200). Statistical analysis for outcomes is shown in Table 5.6.5. This was performed using ANOVA for normalised moments and ANCOVA (using body mass as

a covariate) for absolute moments. Group means and standard deviations are also given.

Table 5.6.5 SLS normalised and absolute sagittal and frontal plane knee moments (means±S.D) with between group differences.

Variable	Participant Group.			*(df) F* Value	*P* value
	Control (n=26)	ACLR (n=23)	ACLD (n=20)		
Norm. Peak Knee Extensor Moment (N.m/kg.m)	0.57±0.2	0.52±0.2	0.49±0.1	(2,66) 1.177	0.315
Norm. Peak Knee Abductor Moment (N.m/kg.m)	0.49±0.2	0.41±0.2	0.44±0.2	(2,66) 0.509	0.603
Peak Knee Extensor moment (N.m)	73.5±31.0	72.0±30.7	73.6±21.4	(2,66) 0.797	0.455
Peak Knee Abductor moment (N.m)	59.1±25.7	59.3±26.1	63.6±19.7	(2,66) 0.463	0.630

Key: N.m=knee moment given in Newton.metres, N.m/kg.m=Normalised knee moment.

Key parameters to be analysed for relationships with activity level and time from injury/surgery included squat depth, peak knee flexion angle, minimum knee flexion angle, normalised internal peak knee extensor and abductor moments.

Table 5.6.6 Pearson's correlations (r) between current activity level and performance, kinematic and kinetic outcome measures during SLS.

	Variable	Control (n=26)		ACLR (n=23)		ACLD (n=20)	
		***r* value**	***P* value**	***r* value**	***P* value**	***r* value**	***P* value**
Performance	Squat Depth (m)	0.556	***0.004**	0.394	0.063	0.133	0.576
Kinematics	Peak Knee Flexion Angle (°)	0.351	0.085	0.517	***0.011**	0.024	0.920
	Knee Flexion ROM(°)	0.409	***0.043**	0.456	***0.029**	-0.121	0.611
Normalised Kinetics	Norm. Peak Extensor Moment (N.m/kg.m)	0.140	0.503	0.243	0.264	-0.219	0.353
	Norm. Peak Abductor Moment (N.m/kg.m)	0.276	0.181	0.302	0.161	0.153	0.520

Key: m=squat depth in metres, °=Angle in degrees, N.m/kg.m=Normalised knee moment.

Significant correlations existed between current activity level and peak knee flexion angle and knee flexion ROM.

There was a positive correlation between squat depth and current activity level with the adjusted r^2 value was found to be 0.279 for the Controls demonstrating that current activity level accounted for 28% of the variation in SLS depth within these groups.

Peak knee flexion angle and current activity level were positively correlated, the adjusted r^2 value was found to be 0.373 for the ACLR, demonstrating that current activity level accounted for 37% of the variation in peak knee flexion angle.

There was a positive correlation between minimum knee flexion angle and current activity level, the adjusted r^2 value was found to be 0.204 for the ACLR. The controls showed a negative correlation with an adjusted r^2 value of 0.131. This demonstrated that current activity level accounted for 20% and 13 % of the variation in minimum knee flexion angle within these groups during the SLS.

Table 5.6.7 displays the kinematic and kinetic outcome measures with the appropriate Pearson's correlations (r) values alongside significance levels for time from injury/surgery for each group for the SLS.

Table 5.6.7 Pearson's correlations (*r*) between time from injury/surgery and performance, kinematic and kinetic outcome measures during SLS.

	Variable	ACLR (n=23)		ACLD (n=20)	
		***r* value**	***P* value**	***r* value**	***P* value**
Performance	Squat Depth (m)	-0.106	0.638	0.025	0.918
Kinematics	Peak Knee Flexion Angle (°)	0.200	0.371	-0.223	0.359
	Knee Flexion ROM (°)	0.209	0.350	-0.189	0.439
Normalised Kinetics.	Norm. Peak Extensor Moment (N.m/kg.m)	0.181	0.421	-0.440	0.059
	Norm. Peak Abductor Moment (N.m/kg.m)	-0.117	0.603	-0.093	0.704

Key: m=squat depth in metres, °=Angle in degrees, N.m/kg.m=Normalised knee moment.

No significant correlations existed between time from injury/surgery and performance, kinematic and kinetic parameters investigated for the SLS.

5.6.1 Longitudinal SLS Analysis.

As the same participants were followed up for all activities, no significant differences existed between demographics from visit one to visit two in the ACLR2.

Table 5.6.8 SLS analysis data for visit 1 versus visit 2 for the ACLR2 (means±S.D).

	Variable	Visit 1	Visit 2	*(df) t* Value	*p* Value
Performance	Squat depth (m)	0.27±0.1	0.28±0.1	(9) -0.861	0.414
	Descent Velocity (m/s)	0.60±0.1	0.65±0.1	(9) 1.504	0.171
	Ascent Velocity (m/s)	0.52±0.1	0.57±0.1	(9) -1.514	0.168
Kinematics	Peak Knee Flexion Angle (°)	76.8±11.7	76.7±9.5	(9) 0.042	0.968
	Sagittal Knee ROM (°)	67.8±12.0	69.7±12.7	(9) -0.551	0.599
	Peak Adduction Angle (°)	26.7±13.8	22.2±9.3	(9) 1.019	0.338
	Frontal Plane Knee ROM (°)	24.2±12.1	18.8±9.1	(9) 1.116	0.301
Absolute Kinetics	Peak Extensor Moment (N.m)	82.0±37.9	90.6±29.3	(9) -0.517	0.621
	Peak Abductor Moment (N.m)	68.4±23.2	61.6±29.6	(9) 1.117	0.301
Normalised Kinetics.	Norm. Peak Extensor Moment (N.m/kg.m)	0.58±0.27	0.63±0.2	(9) -0.441	0.673
	Norm. Peak Abductor Moment (N.m/Kg.m)	0.64±0.25	0.41±0.2	(9) 2.033	0.082

Key: m/s=velocity in metres per second, m=metres, °=Angle in degrees, N.m= Knee moment in Newton metres, N.m/kg.m=Normalised knee moment.

With regards to performance parameters, participants demonstrated no significant differences in squat depth (p=0.414), descent velocity (p=0.171) and ascent velocity (p=0.168) between visit one and visit two.

Between visit one and visit two participants demonstrated no significant differences with regard to peak knee flexion angle (p=0.968), sagittal knee ROM (p=0.599), peak adduction angle (p=0.338) and frontal plane ROM (p=0.301).

For absolute kinetics participants demonstrated no significant differences in peak knee extensor moment (p=0.621) and peak knee abductor moment (p=0.301). Normalised kinetic assessment of participants also demonstrated no significant differences in peak knee extensor moment (p=0.673) and peak knee abductor moment (p=0.082) between visit one and visit two.

5.7 Results Summary: Kinematic, Kinetic and Patient Reported Measures.

For the patient reported measures of function the null hypothesis was rejected as there was a predicted significant decrease in patient reported measures of knee function between the ACLD and ACLR groups alongside those with ACLD demonstrating an increased fear of re-injury compared to the ACLR group.

Our second major hypothesis relating to muscle strength demonstrated acceptance of the null hypothesis as no differences in strength of the quadriceps and hamstring was revealed between the Control and ACL injured groups. Interestingly longitudinal analysis showed significant increases in hamstrings and non-significant trends towards increases in quadriceps strength were evident in ACLR2.
This may highlight that the control group, who were less active than the ACL injured groups in the pre-injury condition were potentially weaker, therefore although not fully recovered at time of first assessment the ACL injured groups were recovered enough to match the strength of the less active controls.

The null hypothesis that ACL injured participants will show no differences in kinematics or kinetics when compared to controls across functional tasks was accepted for a majority of outcome measures. However the null hypothesis was rejected for sagittal plane kinetics during jogging and kinematics in the SLS. However the expected increase in differences as activity demand also increased was proposed to increase was only partially evident.

Finally, at follow up no significant changes took place in the ACLR2 kinematics and kinetics during functional tasks with the exception of minimum knee flexion angle during jogging and stride length during gait, suggesting that for a majority of parameters the ACLR group levels of performance, kinematics and kinetics were maintained longitudinally. The potential impact some of the discovered deficits may have on long term knee health will be deliberated in the discussion chapter.

Chapter 6 Results: MRi Outcomes and Case Series Analysis.

6.1 Introduction.

The following chapter describes the results for the ACLR who had undertaken assessment with MRi, coded ACLM. The demographics for the ACLM are described below in Table 6.1.1. Analysis of changes in MRi using both the quantitative (cartilage thickness regional changes) and semi-quantitative methods (scoring of the meniscus, cartilage and BMA) are described in Chapters 6.2 and 6.3.

The final chapter (Chapter 6.4) will describe the participants in the context of a case series analysis. This will explore each participant's quantitative and semi-quantitative MRi outcome measurements as well as kinematic, kinetic, strength measurement and patients self-reported measures of knee function. This was performed to give an insight into which of the previously identified risk factors for OA were associated with degenerative changes to hopefully to identify those who are at greater risk after ACL injury. This could eventually inform rehabilitation to target the delay or prevention of the progression of OA in these at risk individuals. Table 6.1 gives the demographics for the ACLR, ACLR2 and the ACLM groups (those with two visits to the RCCK and having undergone MRi analysis), these were compared to see how representative each sub-group was when compared to the overall ACLR groups.

Table 6.1.1 Demographics for the ACLM and comparison with ACLR and ACLR2 at time of first assessment.

Variable	Participant Group.			*(df) F Value*	*P* value
	ACLR (n=29)	ACLR2 (n=10)	ACLM (n=8)		
Age (years)	30.7±9.8	28.7±8.6	26.3±6.8	(2,44) 0 .747	0.480
Height (m)	1.70±0.1	1.77±0.1	1.76±0.1	(2,44) 0.857	0.431
Body mass (kg)	79.6±10.7	81.4±9.3	78.1±6.5	(2,44) 0 .271	0.764
Male/Female	20/9	9/1	7/1	NA	NA
Activity Level at Time of Assessment	85.9±14.9	90.5±8.3	83.8±19.8	(2,44) 0.581	0.564
Time from Surgery to Assessment (months)	12.0±7.7	14.1±9.1	15.1±10.0	(2,44) 0.381	0.685

Key: m=metres, kg=Kilogram.

Table 6.1.1 shows that no significant differences existed between groups for demographics measurements between the three ACLR groups. This demonstrates that the eight ACLM participants remained reasonably representative of the initial ACLR and ACLR2 groups from a demographic perspective.

For the eight ACLM participants Table 6.1.2 below shows each individuals demographics and additional variables of interest including differences in time of day the scanning took place, the time from injury to both diagnostic scan (1st MRi) and time from diagnostic scan to follow up at CUBRIC (2nd MRi), time from 1st MRi to surgery and time from surgery to 2nd MRi. These factors were also analysed as these have been shown to influence both the extent of cartilage loss in those with existing knee OA (Le Graverand et al., 2010; Raynauld et al., 2006) and also short term daily changes in cartilage morphology (Waterton et al., 2000).

Table 6.1.2 Demographics for the eight ACLM participants analysed for regional cartilage thickness change, including group means and standard deviations.

	Age (years)	Gender	Mass (Kg)	Height (m)	Current Activity Level	Time of day scan 1	Time of day scan 2	Time from Injury to 1st MRi (months)	Time from 1st MRi to Surgery (months)	Time from Surgery to 2nd MRi (months)	Time between 1st and 2nd MRi (months)
1	27	Male	66.6	1.62	80	18:00	11:00	1	4	20	27
2	27	Male	82.0	1.77	100	11:00	10:00	10	16	33	39
3	38	Male	77.8	1.75	80	17:30	11:30	1	21	50	24
4	21	Male	76.2	1.70	40	9:00	10:00	64	4	24	27
5	20	Male	82.4	1.80	100	9:00	12:00	1	1	24	47
6	49	Male	99.8	1.77	80	13:45	20:00	4	0	36	36
7	27	Male	88.4	1.77	95	15:30	13:00	11	5	21	8
8	34	Female	73.4	1.76	95	15:00	8:30	2	11	37	22
Mean	26.6		78.1	1.76	83.8	13:40	12:10	11.75	8.25	30.6	27.0
S.D	6.5		6.5	0.1	19.8	3.3	2.2	21.5	7.0	10.3	11.7

Key: m=metres, kg=kilogrammes, hrs=hours, S.D=Standard deviation.

Table 6.1.2 shows that the range of scanning time from injury date to first diagnostic scan undertaken in the NHS had a large standard deviation when compared to the mean (11.75±21.5months) and a broad range of times (1-64 months).

The time between 1st and 2nd MRi scans (mean=27, S.D=11.7, range 8-47 months), time from 1st MRi to surgery (mean=8.25, S.D=7.0, range 0-21 months) and time from surgery to 2nd MRi (mean=30.6, S.D=11.7, range 15-47 months) showed less deviation than time from injury date to diagnostic scan but still encompassed a wide range of times.

Considering the nature of the recruitment process that had to be employed in the present study, it was problematic ensuring all participants were at the same point along their rehabilitation and recovery time frame. This would be expected due to the different path ways under which patients enter the NHS system after ACL injury. For example those with an ACL rupture that may not have sought emergency treatment in the immediate period after injury or attended GP clinics as opposed to the emergency trauma clinic would affect the time at which referrals to the AKSS and further diagnostic confirmation of rupture using MRi took place.

After the point of diagnostic MRi it appears that for the present studies ACLM, once confirmation of the rupture had taken place the timeline for surgery, rehabilitation and follow up assessment at CUBRIC deviated less from the group mean. This demonstrates a more structured common pathway to surgery and entering into the study after diagnosis from MRi had been confirmed.

6.2 Semi-Quantitative Results of the MRi Analysis.

Semi-quantitative scoring used the features cited as most important for the indication of OA and included cartilage morphology score, BMA score and meniscal integrity score. Comparison between clinical diagnostic MRi and follow up at MRi CUBRIC was undertaken using the non-parametric Wilcoxon signed-rank test (Chapter 6.4.1). For feature assessed, mapping also undertaken to show the distribution of scores within each of the regions for the tibia and femur and how these changed between scans. This chapter will test the hypothesis that the semi-quantitative method will show significant degenerative changes in the articular features described above.

6.2.1 Total Knee Score Change.

Table 6.2.1 shows the ACLM participants total score for clinical diagnostic MRi and follow up at CUBRIC with group means and standard deviations. The total score refers to the sum of the scores encompassing all regions of the knee described in Figure 4.15.2.1b for BMA, cartilage morphology and meniscal integrity scores.

Table 6.2.1 Total semi-quantitative score for first and second visit MRi for ACLM with group means, standard deviations and related samples Wilcoxon signed-rank test result. Highlighted red boxes demonstrate an increase and green a decrease in total knee score between visit one and visit two.

	Total SQ score MRi 1	Total SQ score MRi 2
1	19	4
2	7	4
3	25	11
4	8	15
5	20.5	9
6	11	1
7	16.5	13.5
8	11	5
Mean	14.8	7.8
SD	6.5	5.1
***P* Value**		***0.038**

Total score for all regions of the knee for BMA, Cartilage morphology and meniscal integrity at diagnostic MRi assessment (MRi1) and follow up MRi (MRi2).*signifies group differences at a level of $p<0.05$

Significant differences existed between the total knee score clinical diagnostic MRi scan and the follow up scan at CUBRIC, with a significant positive improvement i.e. a reduction in total score of features normally associated with development of knee OA ($p<0.05$). Thus there was an acceptance of the null hypothesis that the semi-quantitative method did not show evidence of significant worsening.

Due to the variation observed between ACLM participants with regard to the length of time from injury to follow up MRi assessment (2nd MRi), to give insight into the impact this may have on changes in knee health score (Figure 6.2.1). This was then compared

to the framework developed in Figure 3.7.3 to put the current ACLM groups' data into context of the previously developed models of recovery and/or injury progression

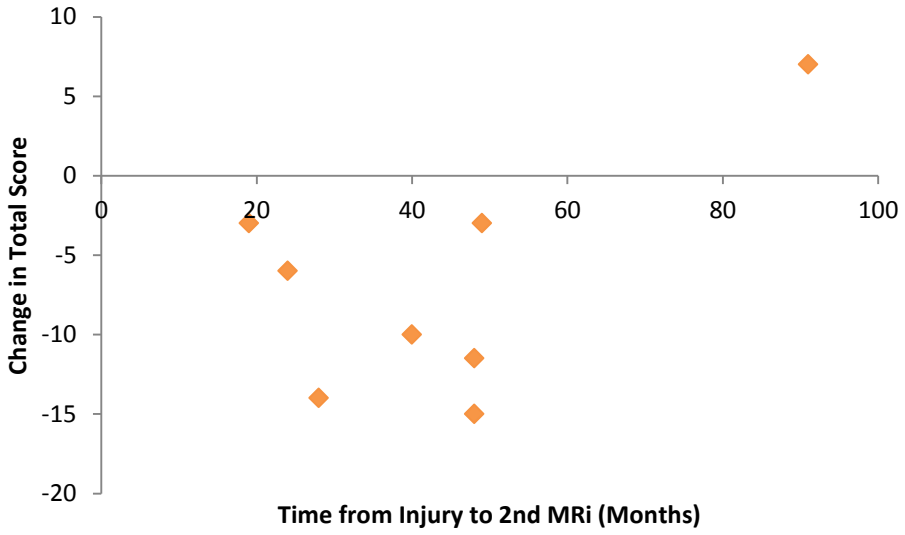


Figure 6.2.1 Total semi-quantitative score change between first and second MRi scan plotted against time from injury to second MRi for the ACLM participants.

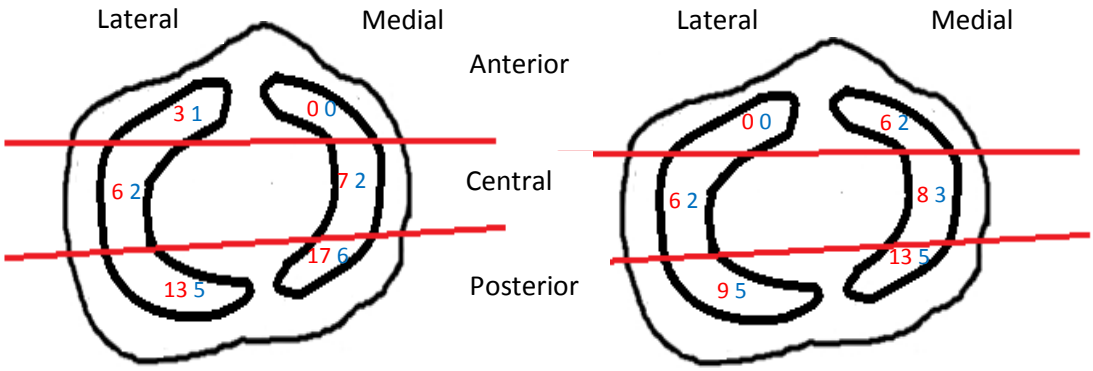
The only participant demonstrating worsening in total knee score between first and second MRi assessment was interestingly also the furthest time from injury to assessment at 91 months. However assessing the distribution of the change score for the remaining ACLM participants, no discernible pattern was evident that suggested a common model of recovery after ACL injury. Although this data hints at the possibility of a model of an initial period of recovery after injury followed by a worsening of knee condition.

Overall improvement in score was mainly due to large improvements in BMA score (Chapter 6.2.4). However there is a possibility that meniscal and cartilage score may have worsened and the areas of worsening may have also been region specific. Therefore further analysis took place assessing distributions and prevalence of abnormalities on a tibiofemoral 'map' and is described below for each feature in Chapter 6.2.2-6.2.4, alongside plots relating to score changes versus time from injury to 2nd MRi to be described in the context of the proposed framework (Figure 3.7.3).

6.2.2 Meniscal Mapping.

For the meniscus distributions, prevalence and total score of abnormality is shown for the anterior, central and posterior regions of both the medial and lateral meniscus as described in Chapter 4.16.3.1. This was undertaken at both time points and the results are shown in Figure 6.2.2.1 data in red represents the cumulative score in each region for the grade of meniscal tear including all ACLM participants. With 0=intact, 1=minor radial tear or parrot-beak tear, 2=non-displaced tear or prior surgical repair, 3=displaced tear or partial resection, 4=complete maceration/destruction or complete resection. Giving a total possible score for each region of 8x4=32; the sum for all subjects together.

Blue represents the number of participants that showed meniscal abnormalities out of the eight ACLM participants with a total score possible of eight.



a) b)

Figure 6.2.2.1 Distributions of meniscal tears at time of injury and follow-up.
Key: red numbers= cumulative grading of tears type within each region, blue numbers=total number of ACLM demonstrating abnormality in this region for a) the diagnostic MRi scan and b) the follow up assessment.

For the diagnostic scan it appears that for both the cumulative scores and the total number of ACLM participants that the posterior regions of the meniscus had the highest prevalence and severity; this was followed by the central regions and finally the anterior regions. This was also true in the follow up scan. The medial meniscus in the

diagnostic scan demonstrated a marginally higher cumulative score for each region with the exception of the anterior region; in the follow up scan this was evident for the anterior, central and posterior regions of the knee. Only one participant demonstrated no abnormality of the meniscus at both MRi assessments.

Comparing the MRi scores for each region it was apparent that in the lateral meniscus the anterior and posterior regions improved (reduced score) with the central region of the lateral meniscus remaining the same with regard to both cumulative score and number of ACLM participants demonstrating tears with in these regions. In the medial meniscus there was an improvement in the posterior region in terms of both cumulative score and total number of ACLM participants showing meniscal tears. However for both the central and anterior regions of the medial meniscus there appeared to be an increase in the cumulative scores for meniscal tears and the prevalence of tears in these regions in the ACLM participants.

Figure 6.2.2.2 shows the ACLM participants change in meniscal score in relation to their time from injury to 2nd MRi scan. This was performed to evaluate if changes in the meniscus could be understood in the context of the developed framework for time related changes in structures in the knee that may be indicative of degenerative change.

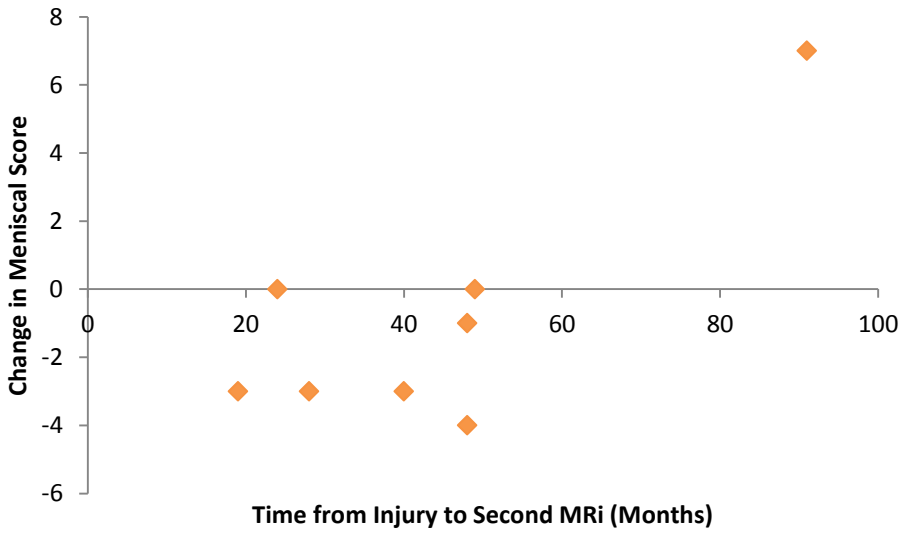


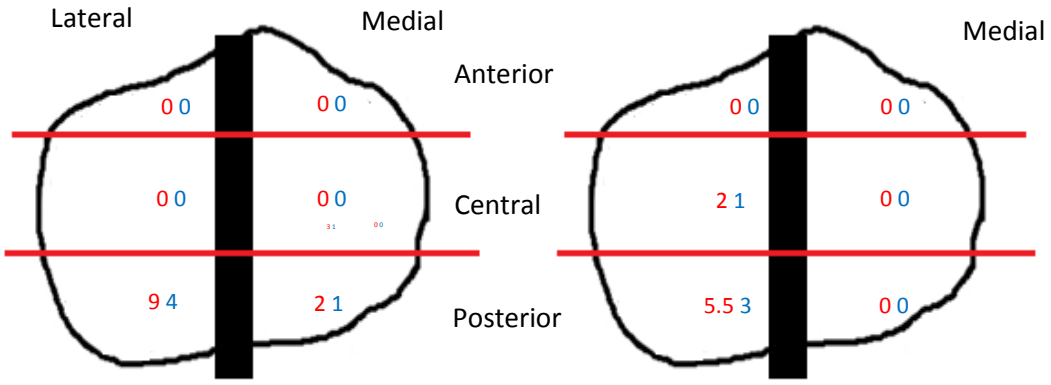
Figure 6.2.2.2 Total meniscal score change between first and second MRi scan plotted against time from injury to second MRi for the ACLM participants.

As with total knee score, the participant with signs of overall worsening of meniscal integrity score was also the furthest from injury and showed a marked increase in score (+7). In the context of the developed framework, the above data again suggests the potential for an initial improvement in meniscal health after injury, followed by a period of worsening. However the remaining ACLM did not appear to have a discernible pattern of worsening or improvement in relation to time from injury.

6.2.3 Cartilage Mapping.

As cartilage is the most direct measure of the three features assessed for indicators of osteoarthritic change, the following chapter mapped the scoring for cartilage morphology for the anterior, central and posterior regions of both the medial and lateral compartment of both the tibia and femur. This was undertaken at both time points; data in red represents the cumulative score in each region for the cartilage morphology assessment score for all ACLM participants. Scores are 0=normal thickness and signal, 1=normal thickness, 2= partial thickness defect <1cm in greatest width, 2.5= full thickness defect <1cm in greatest width, 3= multiple areas of partial thickness intermixed with normal cartilage or a grade 2 defect > than 1cm but less than 75% of the cartilage area, 4=> 75% of the region having partial thickness loss, 5= multiple areas of full thickness loss or a grade 2.5 lesion wider than 1cm but <75% of the region, 6=>75% of the cartilage in the region have full thickness loss. This would lead to a total possible score for each region of 6 x 8 (number of participants) = 48.

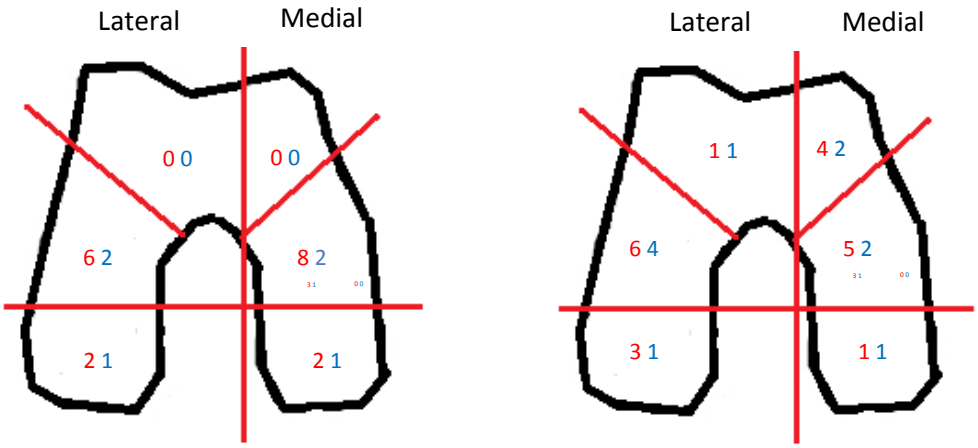
Blue again represents the number of participants that showed cartilage morphology abnormalities within each region out of the eight ACLM participants.



a) b)

Figure 6.2.3.1 Distributions of cartilage morphology scores at time of injury and follow-up for the tibia.
Key: red=cumulative grading of cartilage morphology within each region of the tibia, blue=total number of ACLM demonstrating abnormality in this region for a) the diagnostic MRi scan and b) the follow up assessment.

For the tibial plateau in the initial diagnostic scans, cartilage morphology abnormalities were found only in the posterior region and in four participants, with greater cumulative morphology score and participant numbers being evident in the lateral portion of the tibia. This tendency for increased cumulative cartilage score in the lateral and posterior region of the knee was also evident at follow-up. At follow up there was a greater cartilage morphology score in the lateral compartment in the central region, corresponding to one participant registering this score.



a) b)

Figure 6.2.3.2 Distributions of cartilage morphology scores at time of injury and follow-up for the femur.
Key: red=cumulative grading of cartilage morphology within each region of the tibia, blue=total number of ACLM demonstrating abnormality in this region for a) the diagnostic MRi scan and b) the follow up assessment.

In the femur at the time of the diagnostic scan the central region had both the highest prevalence and cumulative cartilage morphology score, which was also observed in the follow-up scan, this was followed by the posterior and anterior regions of the knee. At initial scanning the central medial region had the highest score, at follow up this region demonstrated a reduced score which is consistent with an improvement in health of this feature. The central lateral region was the region with the highest cumulative and prevalence scores at follow-up, this had also increased in score and prevalence when compared to the diagnostic scan. The posterior lateral region had also worsened but in the same participants, as well as the anterior medial region, with which two participants were now showing cartilage abnormalities and in one participant worsening in the anterior lateral region of the knee. Only the central and posterior regions in the medial compartment showed reduction in cartilage morphology score.

Figure 6.2.3.3 shows the ACLM participants change in total cartilage morphology score between 1st and 2nd MRi in relation to their time from injury to 2nd MRi scan, this was performed to evaluate if total changes in cartilage morphology can be placed in the context of the framework previously developed for time related changes in structures in the knee for the most direct measure of OA related changes in the knee.

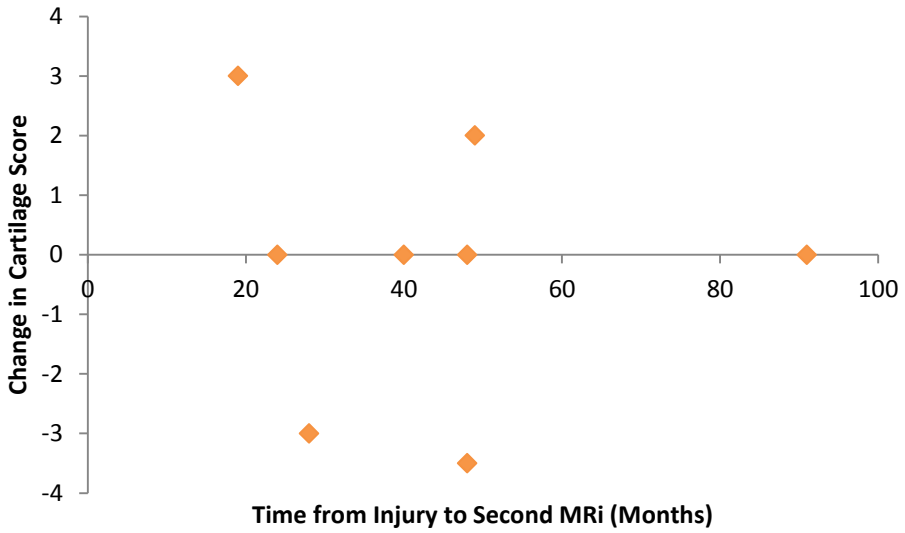


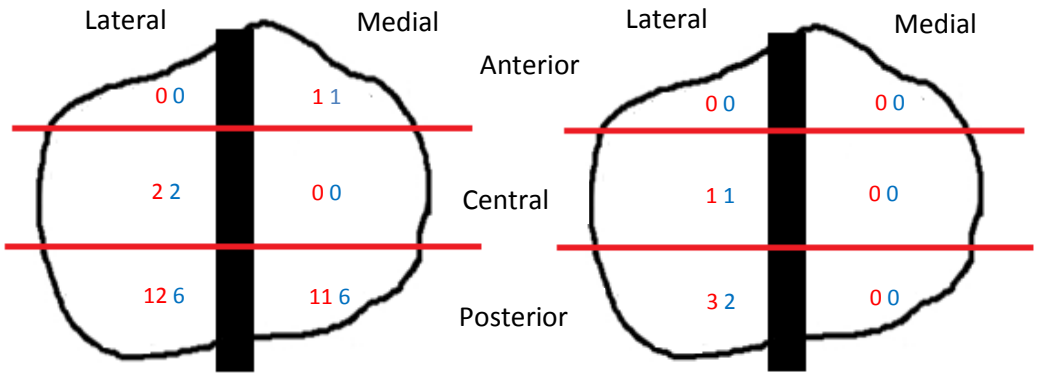
Figure 6.2.3.3 Total cartilage score change between first and second MRi scan plotted against time from injury to second MRi for the ACLM participants.

Of the eight ACLM participants two showed total cartilage score worsening, the distribution of this data shows that the participant with the greatest degree of worsening was the closest to injury, the other participant with worsening was the 6th longest in terms of time from injury to follow-up. Unlike what was demonstrated for total score and meniscal score, it appears that degenerative changes in cartilage occurs independently of these features and that even in the early stages after injury degenerative changes can take place. However due to the distributions in such a small group of data it appears that no discernible patterns exist pertaining to the models developed from the framework. This hints that other mechanisms are at play influencing the rate of degenerative changes in certain individuals. For this reason the case series analysis (Chapter 6.4.3) assessed an individual's risk factors identified for development of OA in conjunction with both semi-quantitative and quantitative assessment of knee structures.

6.2.4 Bone Marrow Abnormality Mapping.

Mapping of the scoring for BMA was undertaken for the anterior, central and posterior regions of both the medial and lateral compartment of both the tibia and femur as described in Figure 4.15.2.1b. Numbers in red represents the cumulative score in each region for the BMA assessment score for all ACLM participants with a score based up on level of regional involvement from 0-3. 0=none, 1=<25% of the region, 2=25-50%

of the region, 3=>50% of the region. Blue represents the number of participants that showed BMA abnormalities out of the eight ACLM participants, giving a total possible score of 24 for each region.

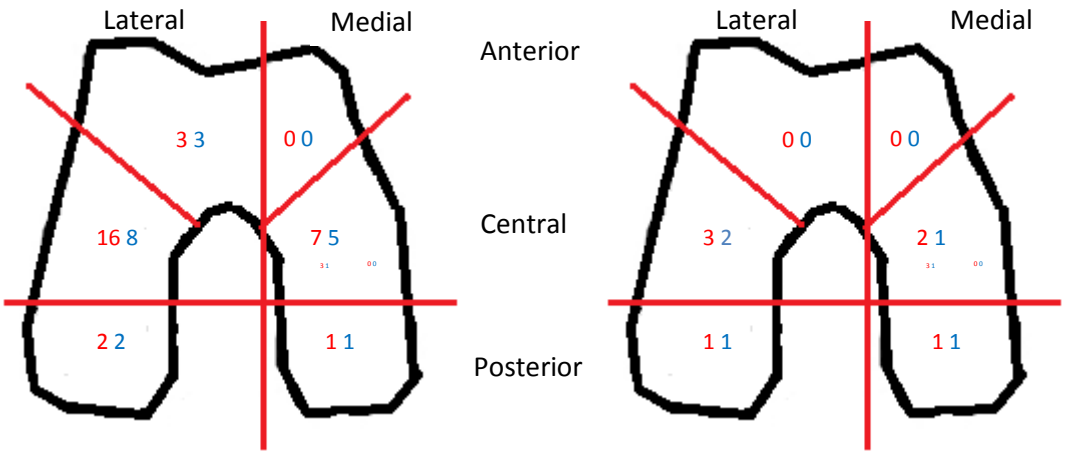


a) b)

Figure 6.2.4.1 Distributions of Bone Marrow Abnormality scores at time of injury and follow-up for the tibia.
Key: red=cumulative grading of BMA within each region of the tibia, blue=total number of ACLM demonstrating abnormality in this region for a) the diagnostic MRi scan and b) the follow up assessment.

On the tibia plateau at both time of diagnostic scan and follow-up scan the posterior region had the highest prevalence and cumulative score of BMA, only one participant showed no BMA at diagnostic scan. This was more evident in both time points in the lateral side of the knee. The central region had the second highest prevalence and cumulative score, again at both time points this was more evident in the lateral compartment. In the anterior region of the knee however, only only participant demonstrated a BMA, in the medial aspect of the knee at time of diagnostic MRi.

For the rest of the regions there was a reduction in BMA score in both the medial and lateral compartment, with evidence of BMA existing in only the central and posterior lateral regions of the tibia, whereas at the time of diagnosis every region defined with the exception of the anterior lateral compartment had evidence of a BMA.



a) b)

Figure 6.2.4.2 Distributions of BMA scores at time of injury and follow-up for the femur.
Key: red=cumulative grading of BMA within each region of the femur, blue=total number of ACLM demonstrating abnormality in this region for a) the diagnostic MRi scan and b) the follow up assessment.

The area of greatest prevalence and cumulative BMA score in the femur was, as with the tibia, in the lateral compartment, however the central region demonstrated the greatest prevalence followed by the anterior and posterior regions. At the diagnostic scan only the anterior region in the medial compartment showed no BMA score. At the follow-up scan the central region, in both the lateral and medial compartment showed a noticeable reduction in BMA score and prevalence, which was more marked on the medial side. All other regions that had shown BMA in the diagnostic scan had reduced in score and prevalence with the exception of the posterior region of the medial compartment.

Figure 6.2.4.3 shows the ACLM participants change in total BMA score between 1st and 2nd MRi plotted against their time from injury to 2nd MRi scan. This was performed to evaluate if BMA change could be placed in the context of the previously described framework of potential time related changes in structures in the knee, which may be indicative of degenerative knee health.

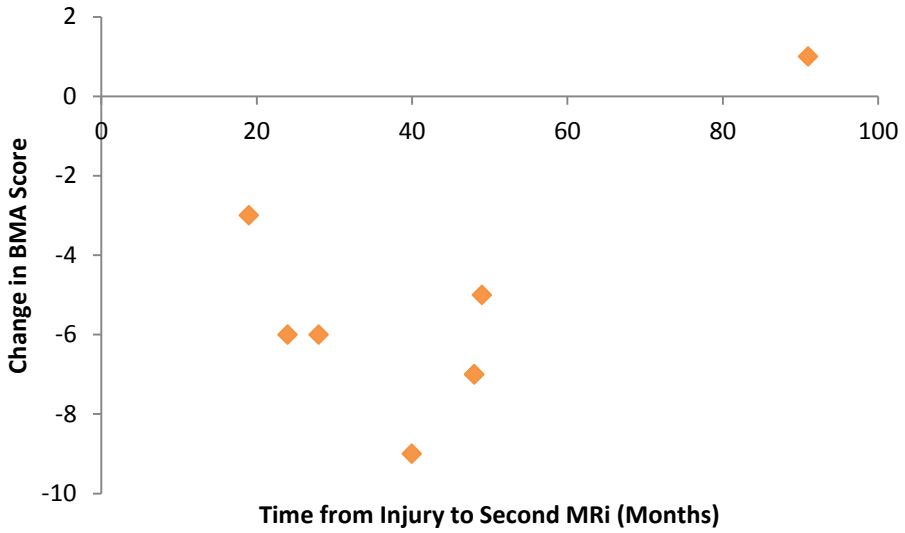


Figure 6.2.4.3 Total BMA score change between first and second MRi scan plotted against time from injury to second MRi for the ACLM participants.

BMA showed an improvement in score in seven of the eight ACLM participants, as with meniscal score and total score there is an indication that after an initial recovery period that a worsening of score may take place. However due to the small sample size in the present study, it was always going to be challenging to accurately determine a model for structural changes after ACL injury. It appears that a majority of the participants in the study were in a recovery phase after injury suggesting that in order to detect degenerative changes using this type of scoring may need longer term follow ups.

From the evidence presented thus far it appears that degenerative changes have manifested themselves in some participants, particularly in cartilage. As the physiological response in cartilage in the short term after ACL injury (and the early stages of OA) is unknown, a quantitative method for assessing regional cartilage thickness change was employed to give further insight into these changes, as this is the most direct indicator of degenerative OA change.

6.3 Quantitative Results of MRi Analysis.

Quantitative analysis was undertaken with regard to cartilage thickness changes in the CMF, CMT, CLF and CLT. Each regional thickness given below comprised the mean of 12 measurements. Each of these measurements was in turn the average cartilage thickness for every image data point in the four defined sub-regions of the tibia/femur, across the three MRi slices that were used to assess either the medial or lateral compartment (Figure 4.16.4.3b). This chapter will target the hypothesis that quantitative assessment of mean cartilage thickness will show significant changes between diagnostic scan and follow-up MRi and this will be more evident in the medial compartment of the knee.

Data was analysed for differences between the clinical MRi and follow-up MRi using the non-parametric independent Wilcoxon signed-rank test. This test was chosen as the small sample size meant that data could not be assumed to be normally distributed, the statistical analysis was also to be undertaken within the same participants at two separate time points, the Wilcoxon signed-rank test was therefore the most suitable test to achieve this (Field, 2005).

Table 6.3 Regional mean cartilage thickness for first and second visit MRi for ACLM. Group means, standard deviations and independent Wilcoxon signed-rank test results are also shown. Highlighted red boxes demonstrate a decrease and green an increase, in mean regional cartilage thickness between visit one and visit two.

	mCMF Scan 1 (mm)	mCMF Scan2 (mm)	mCMT Scan 1 (mm)	mCMT Scan 2 (mm)	mCLF Scan 1 (mm)	mCLF Scan 2 (mm)	mCLT Scan 1 (mm)	mCLT Scan 2 (mm)
1	3.13	3.73^	3.08	3.86	3.17	3.32^	4.36	5.23^
2	3.24	3.46	3.07	3.34	3.38	3.52^	3.62	3.80
3	2.06	3.51^	2.87	4.54	2.41	3.66^	2.53	3.29^
4	2.60	2.55	2.07	2.03	2.85	2.77	3.39	3.36
5	2.20	3.32^	2.63	3.33	2.95	2.86^	3.92	3.33
6	4.06	4.18	3.90	4.43	3.10	3.28^	4.59	3.27^
7	2.83	2.58	3.10	2.76	2.85	2.69^	4.57	5.07
8	2.67	2.74	2.50	2.62	2.92	2.86	3.10	3.14
Mean	2.85	3.26	2.90	3.37	2.95	3.10	3.76	3.81
SD	0.64	0.59	0.54	0.88	0.29	0.33	0.74	0.85
***P* Value**		0.093		0.069		1.000		0.575

Key: mm=millimetres, mCMF=Mean central medial femoral compartment thickness, mCMT= Mean central medial tibia compartment thickness, mCLF= Mean central lateral femur compartment thickness, mCLT= Mean central lateral tibia thickness.
^Denotes an individual change greater than the Minimum Detectable Change.

There were no significant differences in mean cartilage thicknesses between scan one and scan two for the CMF region (p=0.093), CMT region (p=0.069), CLF (p=1.000) and CLT region (p=0.575). .

In the CMF region six of eight participants demonstrated a thicker cartilage at follow up, giving an average increase from 2.85± 0.64mm at scan one to 3.26±2.85mm at scan two (14.3%). This was also evident in the CMT region, with average increase from 2.90±0.54mm at scan one to 3.37± 0.88 at scan 2 (16.2%).

In the CLF region four of the participants showed a comparatively smaller increase in average cartilage thickness from 2.95±0.29mm at scan1 to 3.10±0.33mm at scan 2 (5.1%). This increase was also evident in five participants in the CLT region with an increase from 3.76±0.74mm at scan one to 3.8±0.85mm at scan two (0.3%).

For the CMF region three of eight participants showed an increase in thickness greater than the minimum detectable change (MDC) of 0.22mm, this was also evident in 4/8 participants in the CLF region (with two showing decreases), however for the CLF region, with the exception of one participant, these values were close to the MDC value (0.08mm), so should be treated cautiously. The CLT region showed two participants increase in cartilage thickness greater than the MDC of 0.69mm, with one decreasing. The only region to show no changes greater than the MDC (2.13mm) was the CMT region.

These results demonstrate that we have to accept the null hypothesis that quantitative assessment of mean cartilage thickness did not demonstrate significant changes between diagnostic scan and follow-up MRi. Non-significant trends in the medial compartment of both the tibia and femur existed, which were hypothesised to be the expected region within which the greatest change would occur, however this was in a direction not expected with an increases in thickness being more evident.

The current data for each of the participants regional thickness change was plotted against the time from injury to 2nd MRi scan at CUBRIC (Figures 6.3.1-6.3.4), this was undertaken as time from injury to follow up MRi (2nd MRi) was not homogeneous within the ACLM group, to give an insight into the time related changes that may take place in cartilage thickness after ACL injury, that can be discussed in the context of the previously developed framework (Figure 3.7.1).

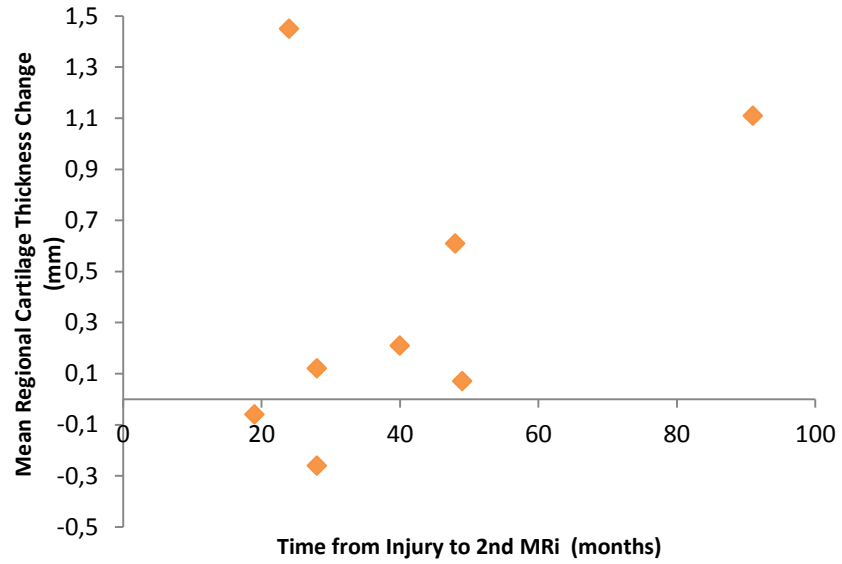


Figure 6.3.1 Change in CMF region mean cartilage thickness between first and second MRi, plotted against time from injury to second MRi for the ACLM participants.

ACLM one, three and five demonstrated increases in cartilage thickness greater than the MDC, participants were in the middle range of time from injury, with all other participants showing no changes outside of the MDC range.

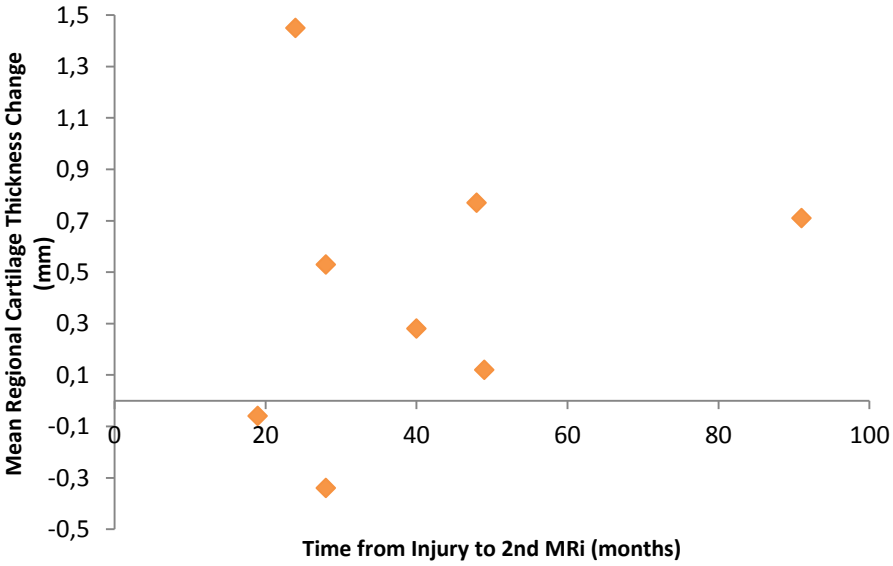


Figure 6.3.2 Change in CMT region mean cartilage thickness between first and second MRi, plotted against time from injury to second MRi for the ACLM participants.

For the CMT region despite one participant showing a large increase in cartilage thickness and three others demonstrating sizeable increases in thickness, the large MDC discovered for this region meant that none of the participants had an increase in cartilage thickness greater than the MDC.

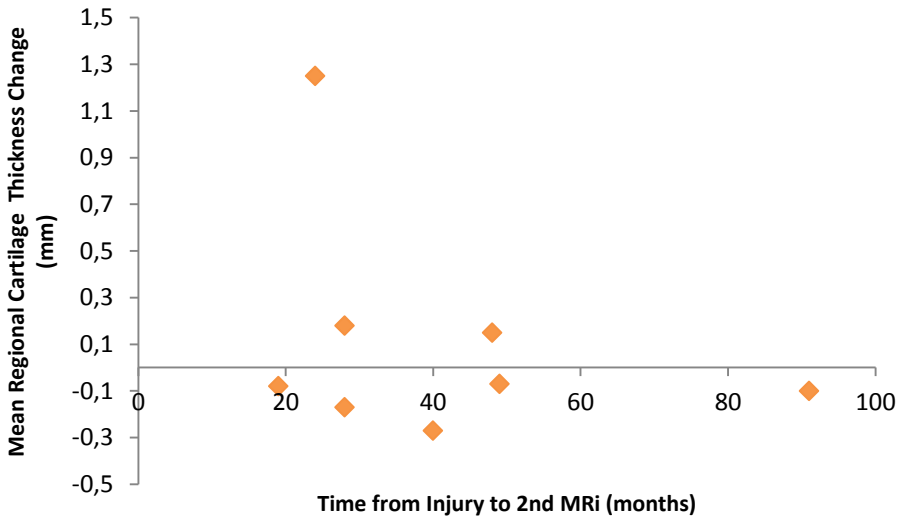


Figure 6.3.3 Change in CLF region mean cartilage thickness between first and second MRi, plotted against time from injury to second MRi for the ACLM participants.

The CLF region demonstrated the greatest number of participants with a change in thickness greater than the MDC (ACLM, 1,2,3 and 6) and also decreases relative to the MDC (ACLM 5 and 7). The small MDC for this region derived from reliability testing (0.08mm) meaning even subtle changes in thickness may be deemed as significant. This does however point to one participant demonstrating significant changes in cartilage thickness much greater than the MDC within this region.

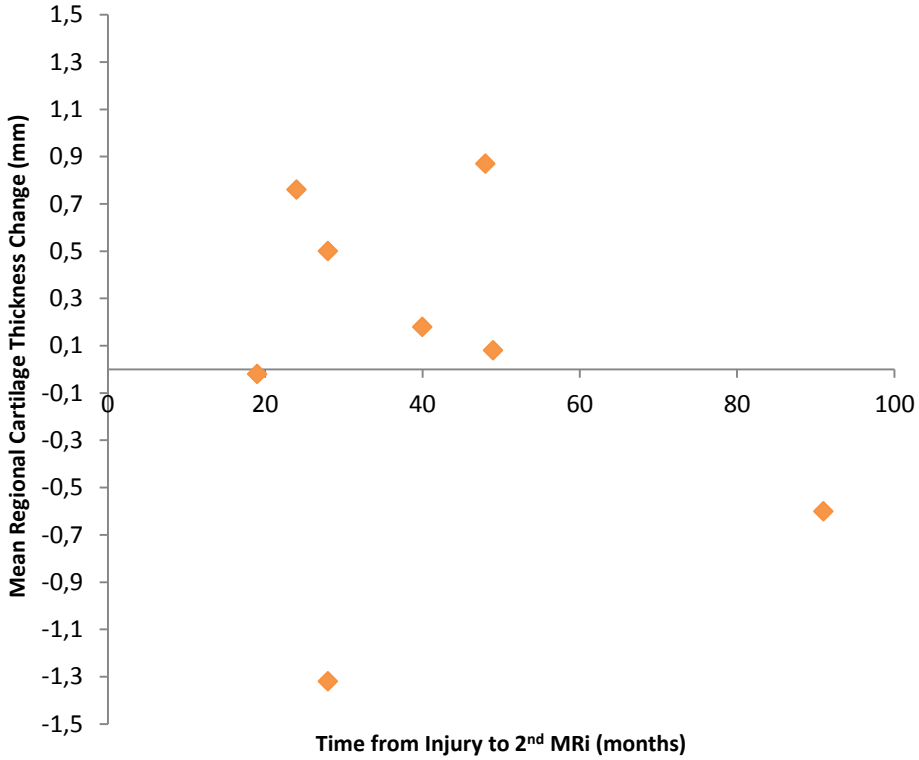


Figure 6.3.4 Change in CLT region mean cartilage thickness between first and second MRi, plotted against time from injury to second MRi for the ACLM participants.

For the CMT region ACLM one and three showed increases greater than the MDC with ACLM6 showing a reduction greater than the MDC. As with the other regions of the knee there appears to be no distinct pattern relating to changes in cartilage thickness and time from injury.

Time from injury has shown potential associations with changes in semi-quantitative features however others, alongside quantitative regional measurements, did not. However with such a small sample size it is difficult to put into the context of the developed framework and draw any firm conclusions on the physiological responses to knee structures after ACL injury.

Changes in cartilage in particular seemed to be independent of time from injury and this highlights that other risk factors may be at play including key demographic, kinematic and kinetic outcomes. These outcomes will be investigated in Chapter 6.4 in a case series style of analysis, giving a deeper insight into how these variables may be

associated with each other within individual participants. This will be used to identify if any common themes emerge, that can lead to more targeted outcomes for future research, with which to help identify those at risk of developing OA.

6.4 Case Series Analysis.

6.4.1. Introduction.

Due to the small sample size included in the present study the use of inferential statistics was limited therefore a more descriptive style of analysis was applied. Within this chapter the participants who undertook MRi assessment will be evaluated in the context of the results from each part of the study, these include the results for both the quantitative and semi-quantitative MRi analysis, the participants demographics, subjective assessment of knee function using both the IKDC and Cincinnati Knee score strength measurement and biomechanics. This was undertaken to identify if any common themes existed between changes in articular structures of the knee using both the quantitative and semi-quantitative methods and demographic, subjective measures of function and kinematics and kinetics at the knee in ACL injured participants.

Chapter 6.4.2 demonstrates the ACLM participants' biomechanics within the context of the overall group to evaluate how this group of ACLM is representative of the full ACLR group (Table 6.4.2). Data used was from visit one for a more direct comparison.

6.4.2 ACLM Participants Outcome Measures in the Context of the Full ACLR group.

Table 6.4.2 below shows mean values for the ACLM participants in comparison with the full ACLR group for key spatiotemporal, kinematic and kinetic outcome measures assessed during their first RCCK visit. Assessment of group differences was also being undertaken for each outcome measure using an independent sample t-test, with equal variances not assumed.

Table 6.4.2 Comparison of spatiotemporal, kinematic and kinetic outcomes between ACLR and ACLM.

	ACLR	ACLM	*t* Value	P Value
Gait Velocity (m/s)	1.45±0.21	1.50±0.19	-0.582	0.582
Jogging Velocity (m/s)	2.82±0.48	2.96±0.36	-0.879	0.393
Squat Depth (m)	0.25±0.09	0.27±0.11	-0.369	0.720
Gait Peak Knee Flexion Angle (°)	16.1±6.4	16.4±7.4	-0.086	0.933
Jogging Peak Knee Flexion Angle (°)	34.1±9.0	35.7±9.0	-0.439	0.699
SLS Peak Knee Flexion Angle (°)	70.8±14.7	74.4±9.9	-0.769	0.451
Gait Normalised Internal Peak Knee Extensor Moment (N.m/kg.m)	0.40±0.2	0.39±0.2	1.058	0.308
Jogging Normalised Internal Peak Knee Extensor Moment (N.m/kg.m)	0.83±0.4	0.98±0.5	1.131	0.201
SLS Normalised Internal Peak Knee Extensor Moment (N.m/kg.m)	0.52±0.2	0.64±0.27	-1.147	0.277
Gait Normalised Internal Peak Knee Abductor Moment (N.m/kg.m)	0.34±0.1	0.38±0.01	-0.696	0.498
Jogging Normalised Internal Peak Knee Abductor Moment (N.m/kg.m)	0.84±0.4	0.79±0.3	0.385	0.706
SLS Normalised Internal Peak Knee Abductor Moment (N.m/kg.m)	0.41±0.2	0.38±0.1	0.541	0.597

Key: m/s=Velocity in metres per second, °=Angle in degrees, N.m/kg.m=Normalised knee moment.

This demonstrates that spatiotemporal, kinematic and kinetic parameters our ACLM group was comparable to the full ACLR group.

6.4.3 Individual ACLM Participant Analysis.

The following chapter will assess each individual participant within the ACLM group. Table 6.4.3 at the end of the chapter shows the actual value for each of the outcome measures described for the participants with their associated rank in brackets.

The following figures (Figure 6.4.3.1-6.4.3.8) show an individual's outcomes from the semi-quantitative method including total BMA, total cartilage score and total meniscal score, and are shown for the clinical diagnostic MRi and at follow up. These outcomes are given in their *absolute* value in order to assess not only the magnitude of change,

but also what abnormalities and to what extent these were evident at both time points. Graphical representations are also shown with the rank of the participant within the ACLM group for outcome measures including age, mass, peak knee flexion angles for and peak internal knee extensor and abductor moments for all activities. Each outcome measure is ranked from lowest value numerically to highest, for example the youngest and lightest would be ranked one with the oldest and lightest ranked eight.

The final chapter within the MRi results (6.4.4) shows a summary of the main findings from the case series analysis. This identifies those participants which were noted as having signs of degenerative changes from MRi assessment and will attempt place them in the context of other outcome measures/risks for OA described above to identify if themes existed. Discussion of how these outcomes may play a role in the development of early OA in those with ACL injury will take place in Chapter 7.

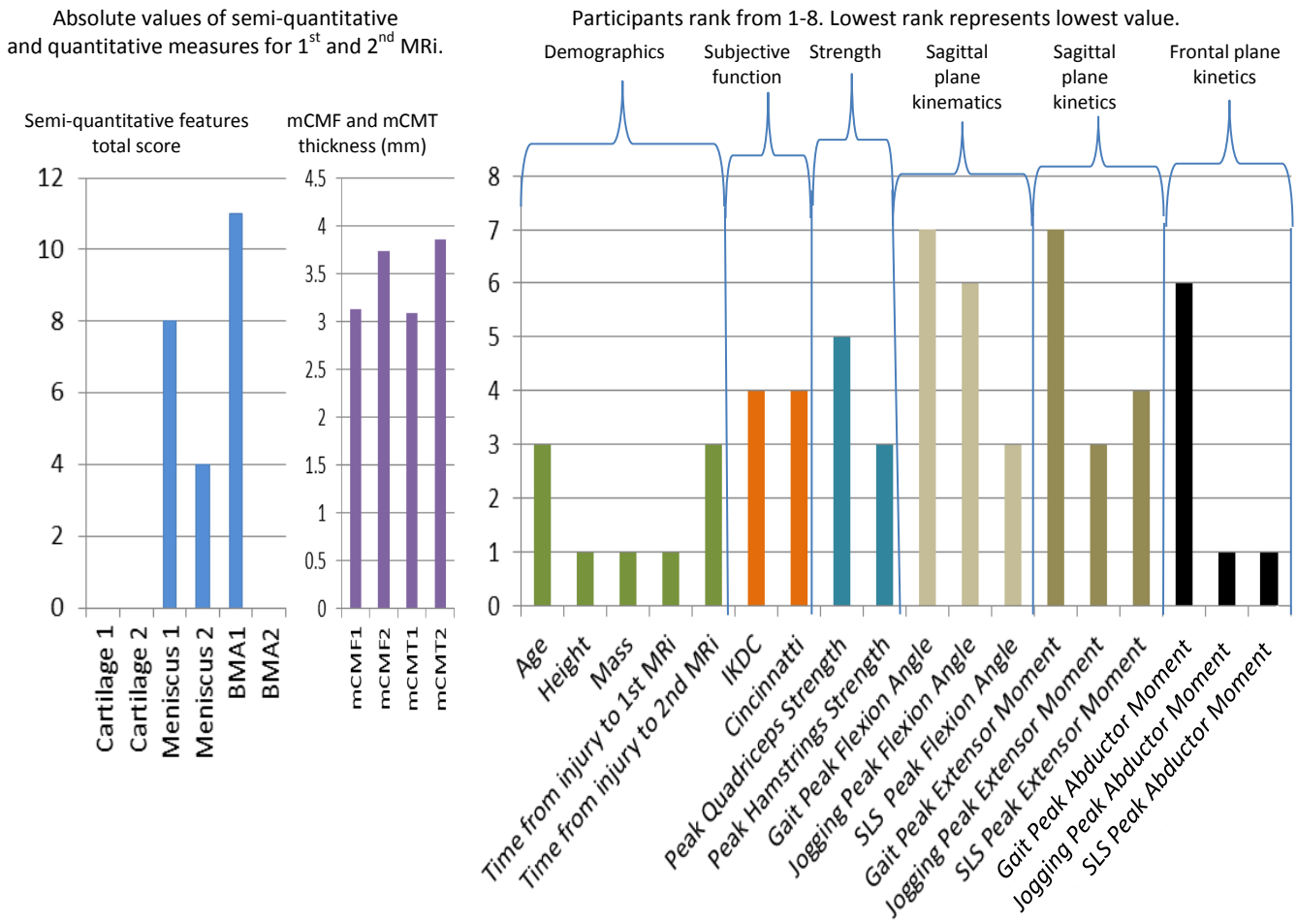


Figure 6.4.3.1 ACLM1 Total scores for semi-quantitative features (far left, blue bars), mean cartilage thickness measurement (second from left, purple bars) in the medial compartment of the femur and tibia and ranking from 1-8 for demographic (green bars), subjective measures of knee function (orange bars), strength (turquoise bars), kinematics and kinetics (light grey, khaki and black bars) for gait, jogging and SLS.

Description of Results: ACLM1 showed increase thickness greater than the minimal detectable change using the quantitative measurement of mean cartilage thickness in the CMF (3.13vs. 3.73mm), CLF (3.17 vs.3.32mm) and CLT (4.36 vs 5.23mm) regions of the knee.

This did not correspond with increased in score in any of the features scored semi-quantitatively. Cartilage remained healthy with a score of 0 at both time points, whilst meniscal abnormality improved by 4 points, however some meniscal abnormalities remained. BMA showed the most marked improvement showing a score of 11 which returned to a normal knee having no abnormalities detected at follow up.

For the demographic parameters ACLM1 was the lightest and shortest participant, and was the 3rd longest time from injury to follow up scan at 28 months, meaning changes between scans were discovered over a period of 27 months as initial diagnostic scan was taken only one month post injury.

Subjective measures of function placed ACLM1 ranked in the middle of the ACLM group with a rank of four for both the IKDC and Cincinnati Knee Scores. Measurements of quadriceps and hamstring strength also placed ACLM1 in the middle portion of the group ranking 5th and 3rd respectively.

For kinematic and kinetic parameters outcome measures, peak knee flexion angle and extensor moment during gait were of note, ranking second highest for both these outcomes (21.7°, 53.7N.m), for jogging and SLS ACLM1 were ranked in the middle portion of the group (between three and six), for all other kinematic and kinetic outcomes with the exception of jogging and SLS internal peak knee abductor moment where they had the lowest moments.

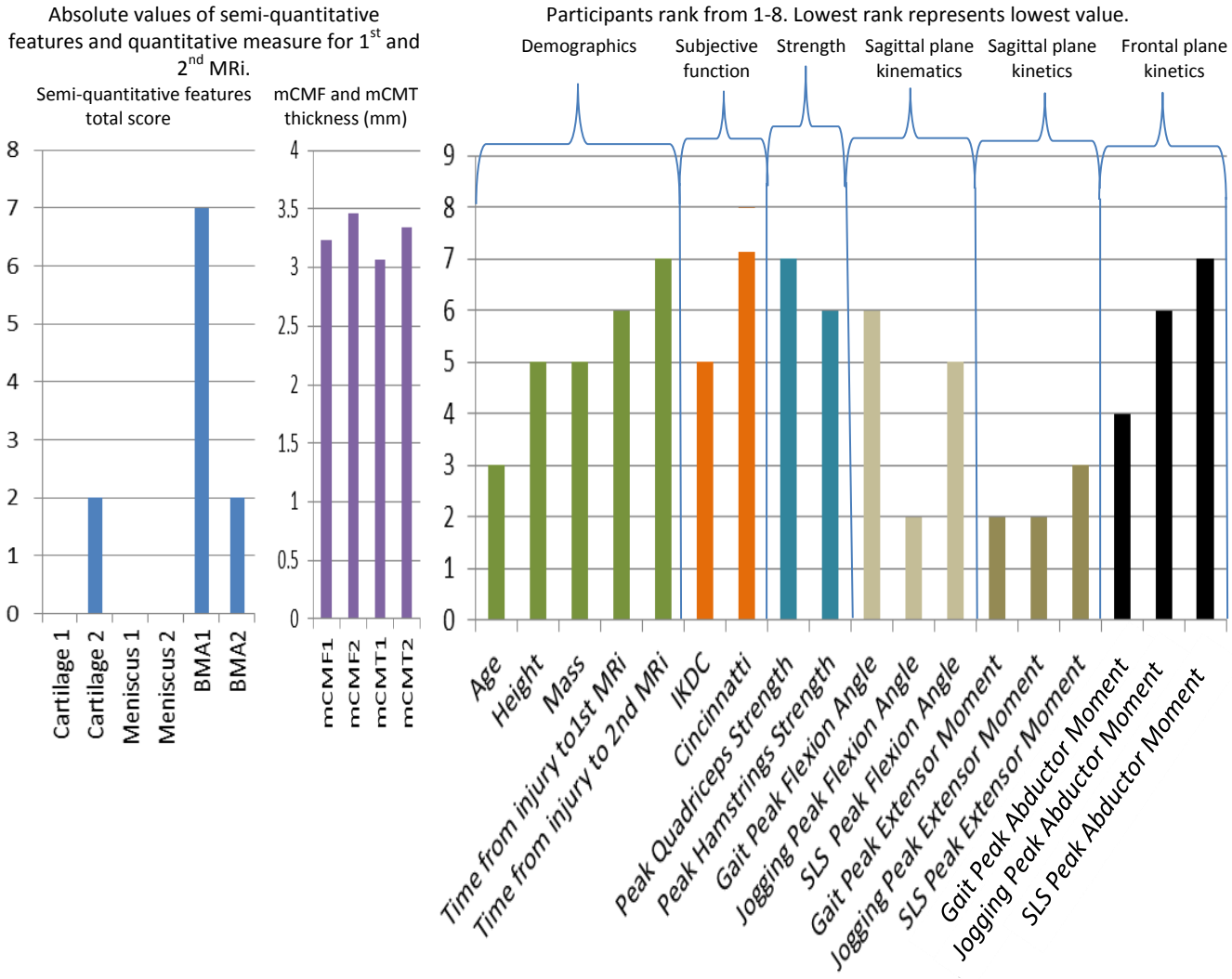


Figure 6.4.3.2 ACLM2 Total scores for semi-quantitative features (far left, blue bars), mean cartilage thickness measurement (second from left, purple bars) in the medial compartment of the femur and tibia and ranking from 1-8 for demographic (green bars), subjective measures of knee function (orange bars), strength (turquoise bars), kinematics and kinetics (light grey, khaki and black bars) for gait, jogging and SLS.

Description of Results: ACLM2 showed increases in mean cartilage thickness greater than the MDC in only the CLF region of the knee increasing from 3.38 to 3.52mm using the quantitative method. An increase in cartilage score was also noted using the semi-quantitative method, which took place over a period of 42 months and at a time point of 49months from injury, the second longest time from injury. For other demographic parameters ACLM2 ranged between three and six. Interestingly the increase in cartilage score took place in the central portion of the lateral femur coinciding of the area of increased cartilage thickness.

For subjective measures of knee function ACLM2 ranked the second highest for the Cincinnati Knee Score (570) but only 4th highest for the IKDC. The high level of function reported by the IKDC was reflected in the measurements of strength ranking 7th and 8th for quadriceps and hamstring strength.

For kinematic and kinetic outcomes ACLM2 ranked the 2nd lowest for flexion angle during jogging and peak knee extensor moment for both gait and jogging and 3rd for SLS knee flexion angle and knee extensor moment. For all other gait parameters ACLM2 ranked in the middle range of the ranking.

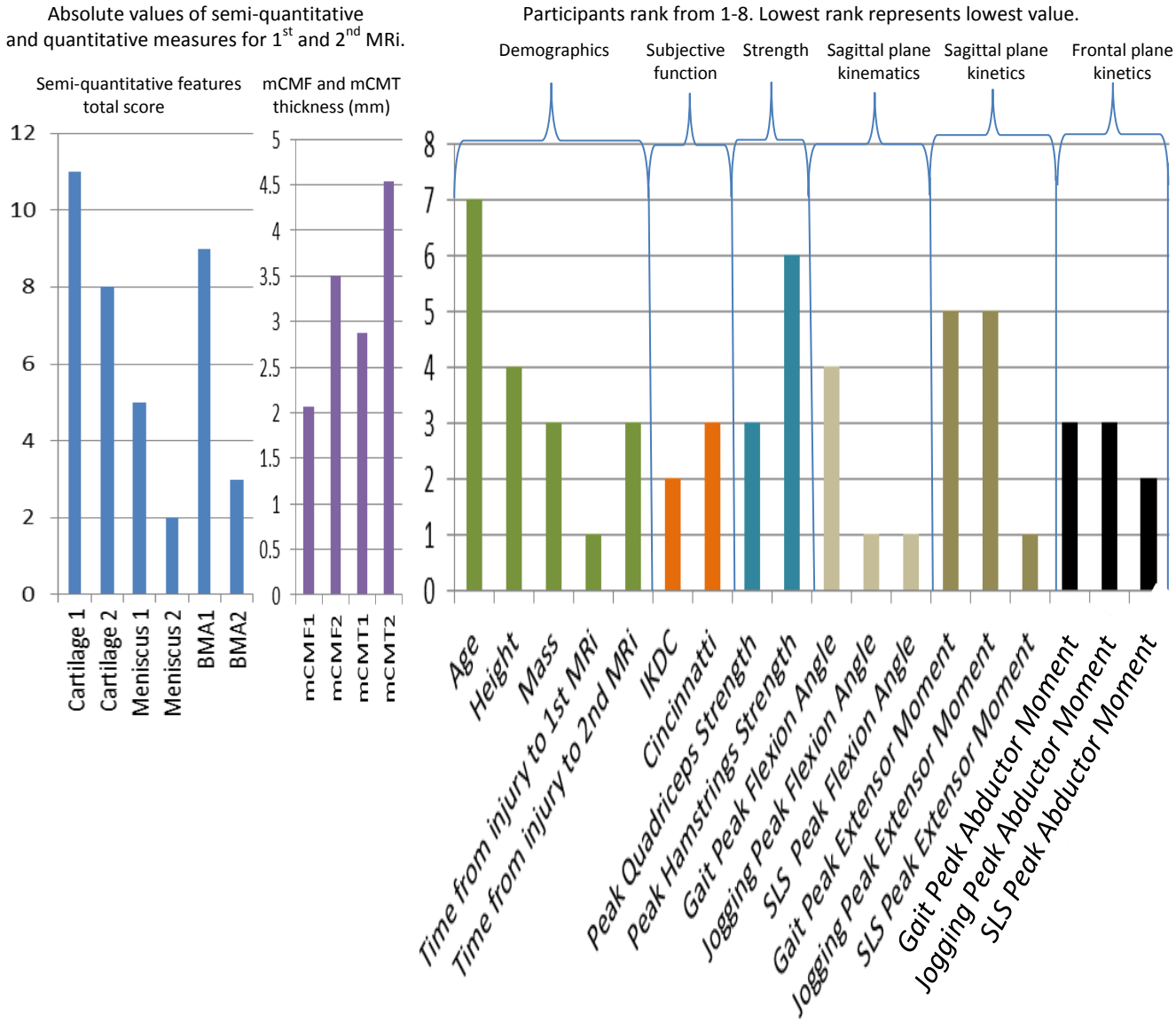


Figure 6.4.3.3 ACLM3 Total scores for semi-quantitative features (far left, blue bars), mean cartilage thickness measurement (second from left, purple bars) in the medial compartment of the femur and tibia and ranking from 1-8 for demographic (green bars), subjective measures of knee function (orange bars), strength (turquoise bars), kinematics and kinetics (light grey, khaki and black bars) for gait, jogging and SLS.

Description of Results: ACLM3 showed increases in mean cartilage thickness across three regions of the knee including the CMF (2.06 to 3.51mm), CLF (2.41 to 3.66mm) and the CLT (2.53 to 3.29mm). As with ACLM1, despite demonstrating these increases in thickness all the features scored using the semi-quantitative method showed improvement, however slight abnormalities existed in the meniscus and in BMA score. Despite improvements in cartilage score, the remaining score of seven, having shown worsening in the anterior CLF and anterior CMF regions combined with remaining

abnormalities in both BMA and meniscus may be of importance for long term monitoring.

This participant was ranked 3rd at a time of injury to follow-up MRi of 28 months and was the 2nd oldest at 38 years for all other demographic outcomes ACLM3 ranked between three and six. For subjective measures of function ACLM3 ranked 2nd and 3rd lowest for the IKDC and Cincinnati Knee Score respectively and measurement of strength was ranked 3rd for quadriceps and 6th for hamstring strength.

Kinematic and kinetic outcome measures of note were peak flexion angle for jogging and SLS were ACLM3 had the lowest ranked value. They also had the lowest peak extensor and 2nd lowest peak abductor moment during the SLS. All other outcomes were ranked in the middle range of rankings between three and six.

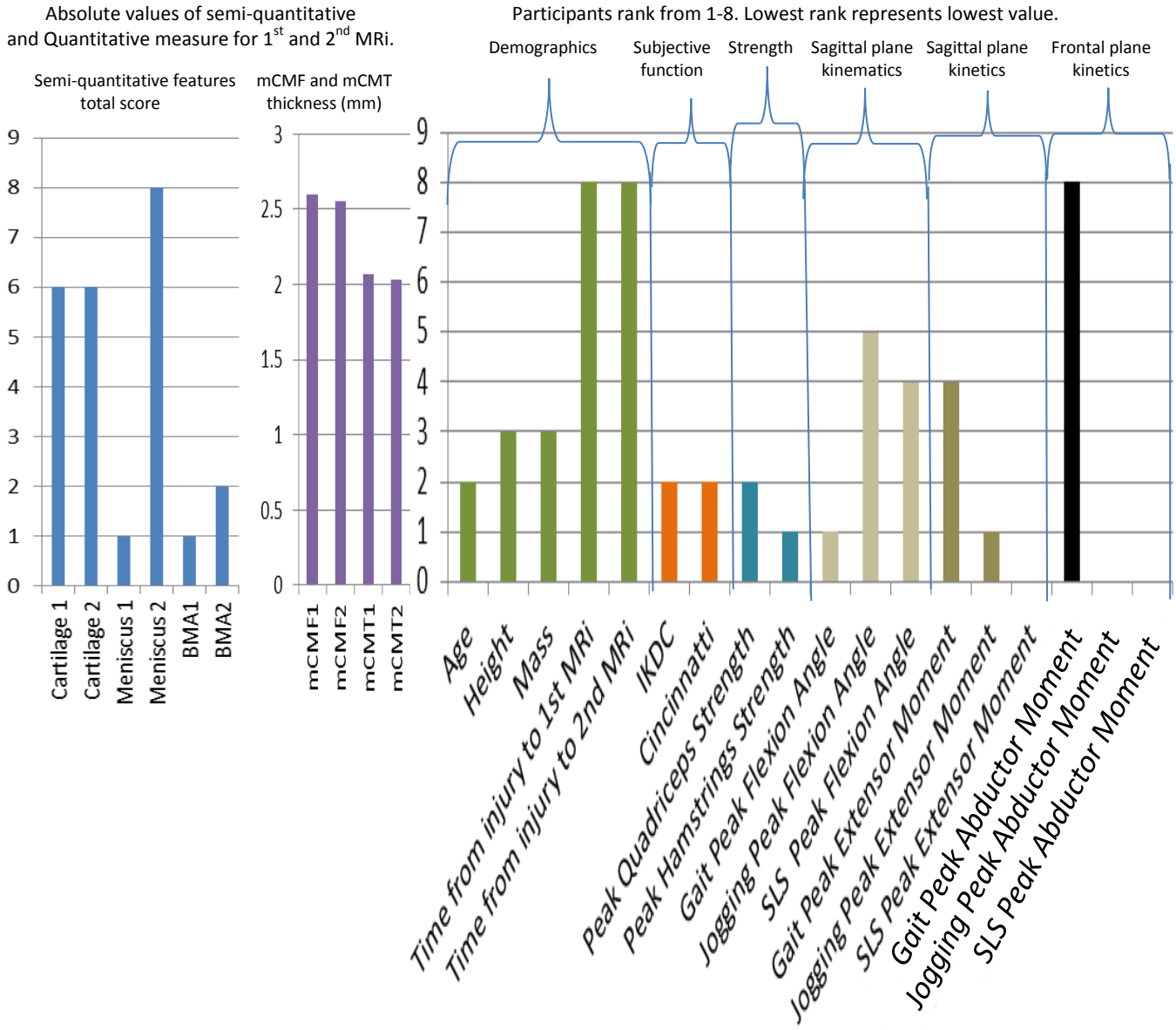


Figure 6.4.3.4 ACLM4 Total scores for semi-quantitative features (far left, blue bars), mean cartilage thickness measurement (second from left, purple bars) in the medial compartment of the femur and tibia and ranking from 1-8 for demographic (green bars), subjective measures of knee function (orange bars), strength (turquoise bars), kinematics and kinetics (light grey, khaki and black bars) for gait, jogging and SLS.

Description of Results: ACLM4 showed no changes in cartilage thickness across any of the defined regions using the quantitative methods. The semi-quantitative method showed worsening in both meniscus and BMA score with cartilage score remaining the same and was the only participant demonstrating overall worsening using this method.

Interestingly this participant was the furthest from time of injury to both 1st and 2nd MRi at 64 and 91 months respectively and had the second lowest subjective

measurement of function for both the IKDC and Cincinnati Knee Score, and was in the bottom two for the quadriceps and hamstring strength.

These results would be surprising as ACLM4 was the 2nd youngest participant so might be expected to be more active, however the low rankings in clinical measures of function and strength are reflected in low rankings for flexion angle during gait (1st) and peak extensor moment during jogging (1st), being markedly lower than all other participants at 8.7N.m. However peak abductor moment during gait was the highest value, unfortunately no data was available for SLS and jogging abductor moments.

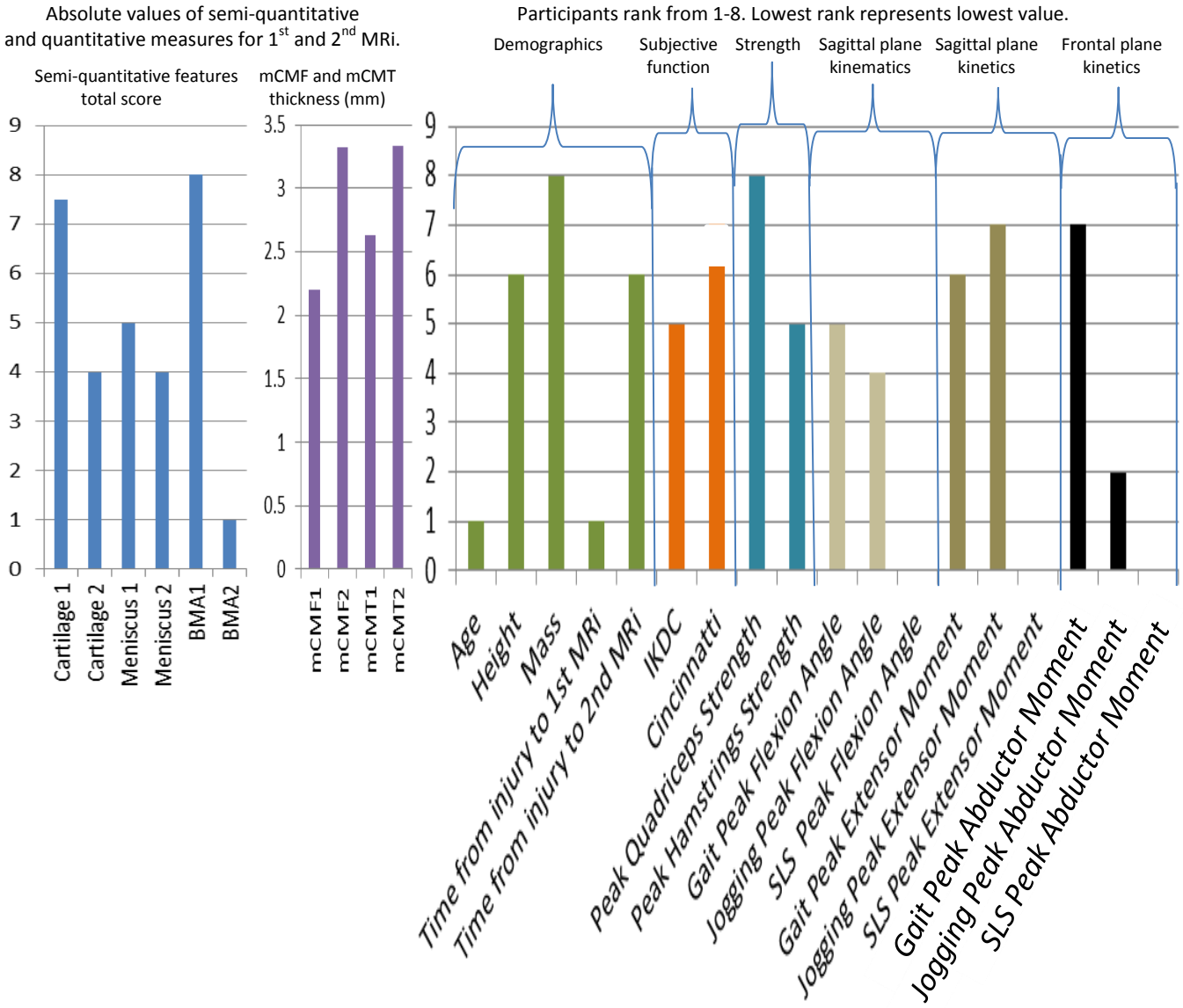


Figure 6.4.3.5 ACLM5 Total scores for semi-quantitative features (far left, blue bars), mean cartilage thickness measurement (second from left, purple bars) in the medial compartment of the femur and tibia and ranking from 1-8 for demographic (green bars), subjective measures of knee function (orange bars), strength (turquoise bars), kinematics and kinetics (light grey, khaki and black bars) for gait, jogging and SLS.

Description of Results: ACLM5 demonstrated increase in thickness using the quantitative method in only the CMF region (2.20 to 3.32mm) with a significant decrease found in the CLF region (2.95 to 2.86mm) when compared to the MDC.

Improvements were found for all features in the semi-quantitative scoring methods, however all features still had evidence of abnormality most noticeably the cartilage and

meniscus, cartilage score worsened in only one region, the posterior region of the CLF, with meniscus worsening in only the central region of the lateral meniscus.

ACLM5 was the youngest participant in the ACLM cohort at 19 years of age, and was the tallest of the cohort. For subjective measures of function ACLM 5 had the third largest Cincinnati knee score and also had the strongest quadriceps.

Unfortunately no data was available to assess kinematics and kinetics for the SLS. For gait and jogging the only kinematic and kinetic variables that were ranked outside the ranks of three to six were peak abductor moment for gait (ranked 7^{th} and jogging (ranked 2^{nd}) with knee extensor moment for jogging ranked 7^{th}.

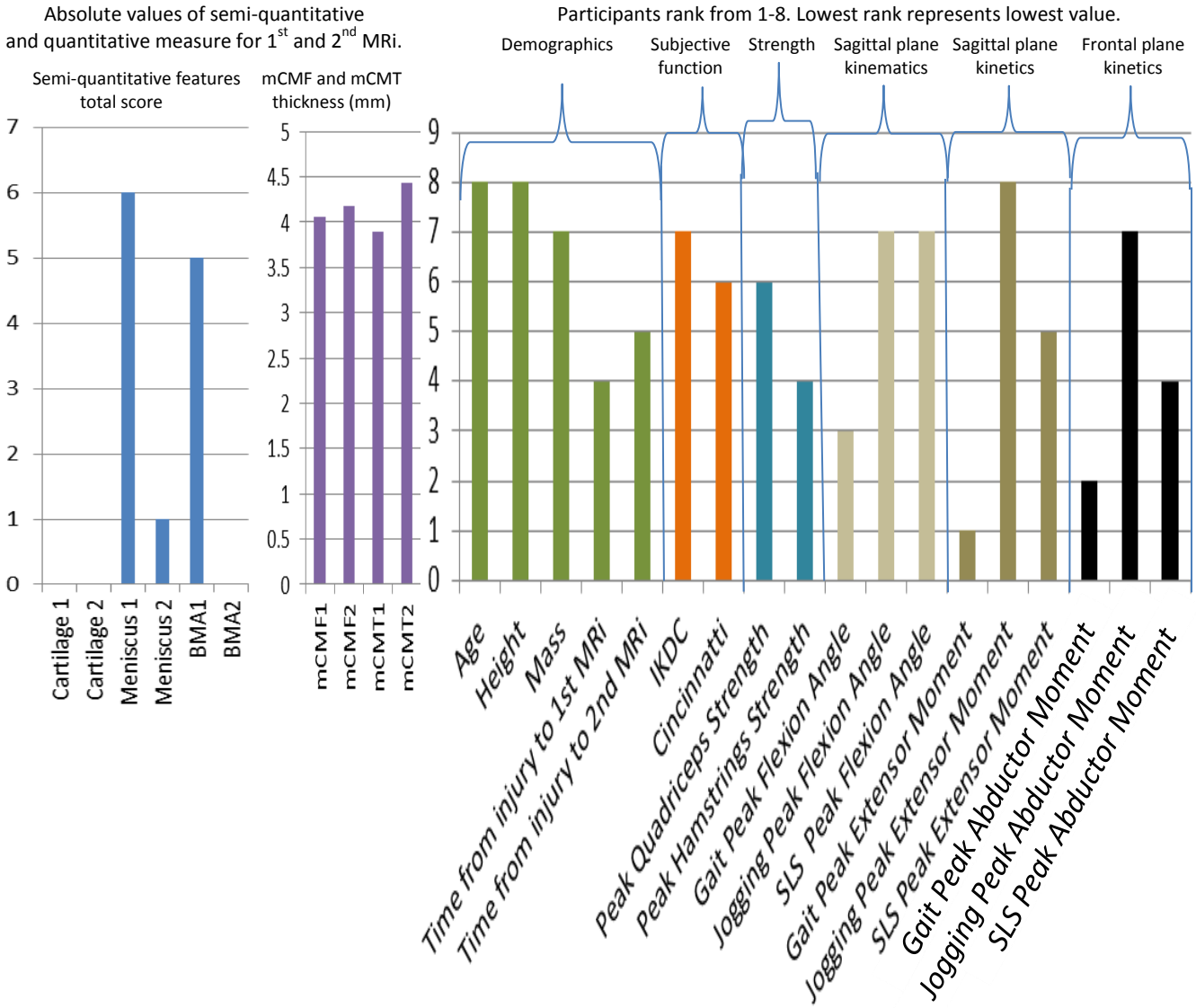


Figure 6.4.3.6 ACLM6 Total scores for semi-quantitative features (far left, blue bars), mean cartilage thickness measurement (second from left, purple bars) in the medial compartment of the femur and tibia and ranking from 1-8 for demographic (green bars), subjective measures of knee function (orange bars), strength (turquoise bars), kinematics and kinetics (light grey, khaki and black bars) for gait, jogging and SLS.

Description of Results: ACLM6 demonstrated an increase in cartilage thickness in the CLF but a decrease in the CLT region of the knee, greater than the MDC. Despite being the oldest and heaviest participant, two of the main risk factors cited for development of structural changes within the knee, and at a time point of 40months from injury, of the semi-quantitative scoring features cartilage showed no abnormalities at both 1st and 2nd MRi, with both meniscus and BMA score showing marked improvement, with

virtually no abnormality shown at follow up. Only the meniscus had a score of one at time of 2nd MRi.

Both internal peak knee extensor and abductor moments for gait were ranked 2nd lowest, which is surprising considering the much higher ranked body mass, however for jogging ACLM6 ranked 7th for peak flexion angle, peak internal knee extensor and abductor moment during jogging.

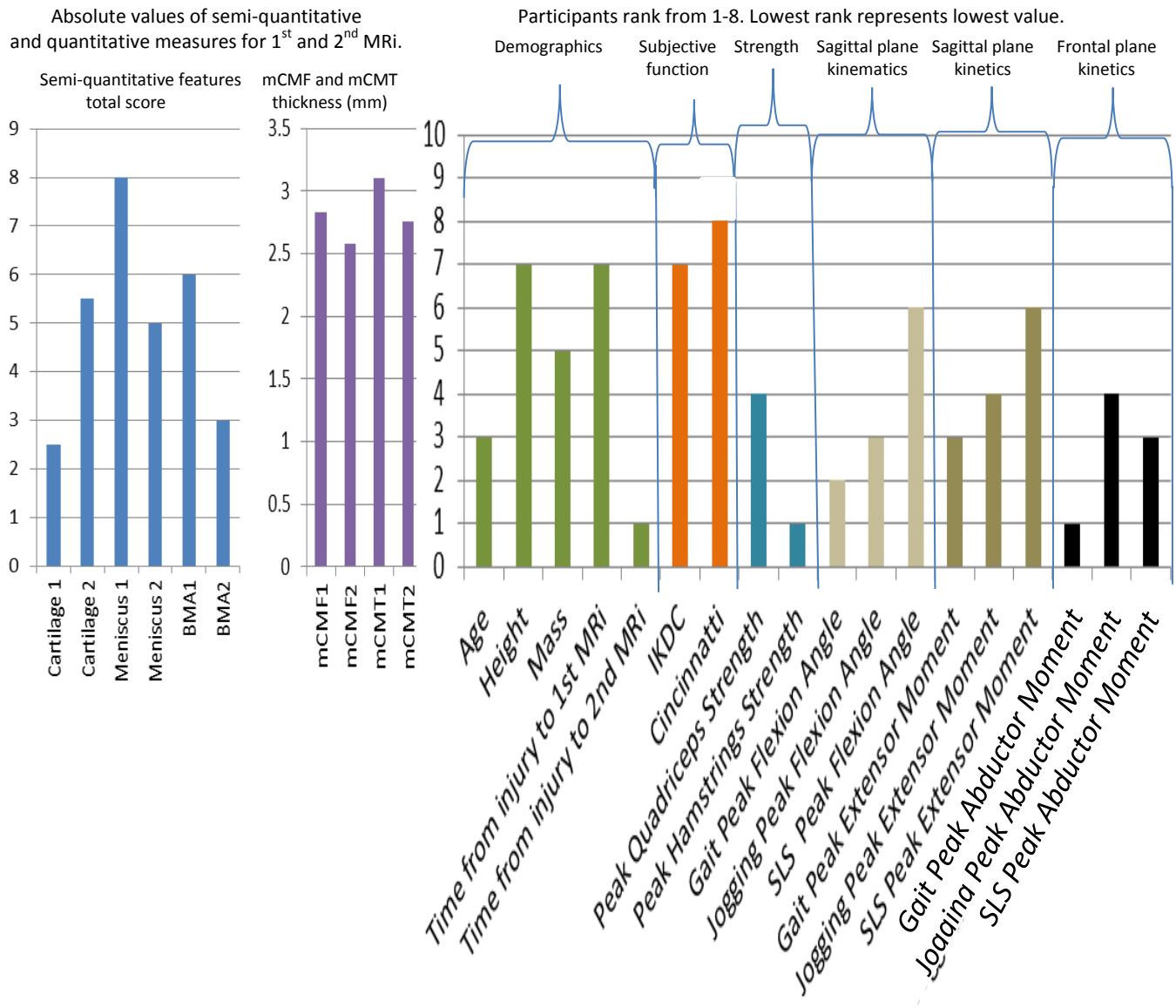


Figure 6.4.3.7 ACLM7 Total scores for semi-quantitative features (far left, blue bars), mean cartilage thickness measurement (second from left, purple bars) in the medial compartment of the femur and tibia and ranking from 1-8 for demographic (green bars), subjective measures of knee function (orange bars), strength (turquoise bars), kinematics and kinetics (light grey, khaki and black bars) for gait, jogging and SLS.

Description of Results: ACLM7 showed a change in cartilage thickness greater than the MDC, demonstrating a decrease in the CLF region from 2.85 to 2.69mm. Although meniscal and BMA score showed improvement some abnormalities still remained. The cartilage score worsened between 1st and 2nd MRi over a period of only 8 months and at

a time period of 19 months from injury, which was the shortest time from injury to follow in the ACLM group. Worsening in cartilage score took place in the central region of the lateral femur (0 to 1) and the central region of the lateral tibia (0 to 2).

ACLM7 was the second heaviest participant in the ACLM group and had the highest level of function on the Cincinnati and second highest on the IKDC. All other outcome measures were within the middle rankings of the group (from 3-6) with the exception of peak knee flexion angle during gait (ranked 2nd) and gait peak abductor moment (ranked 1st).

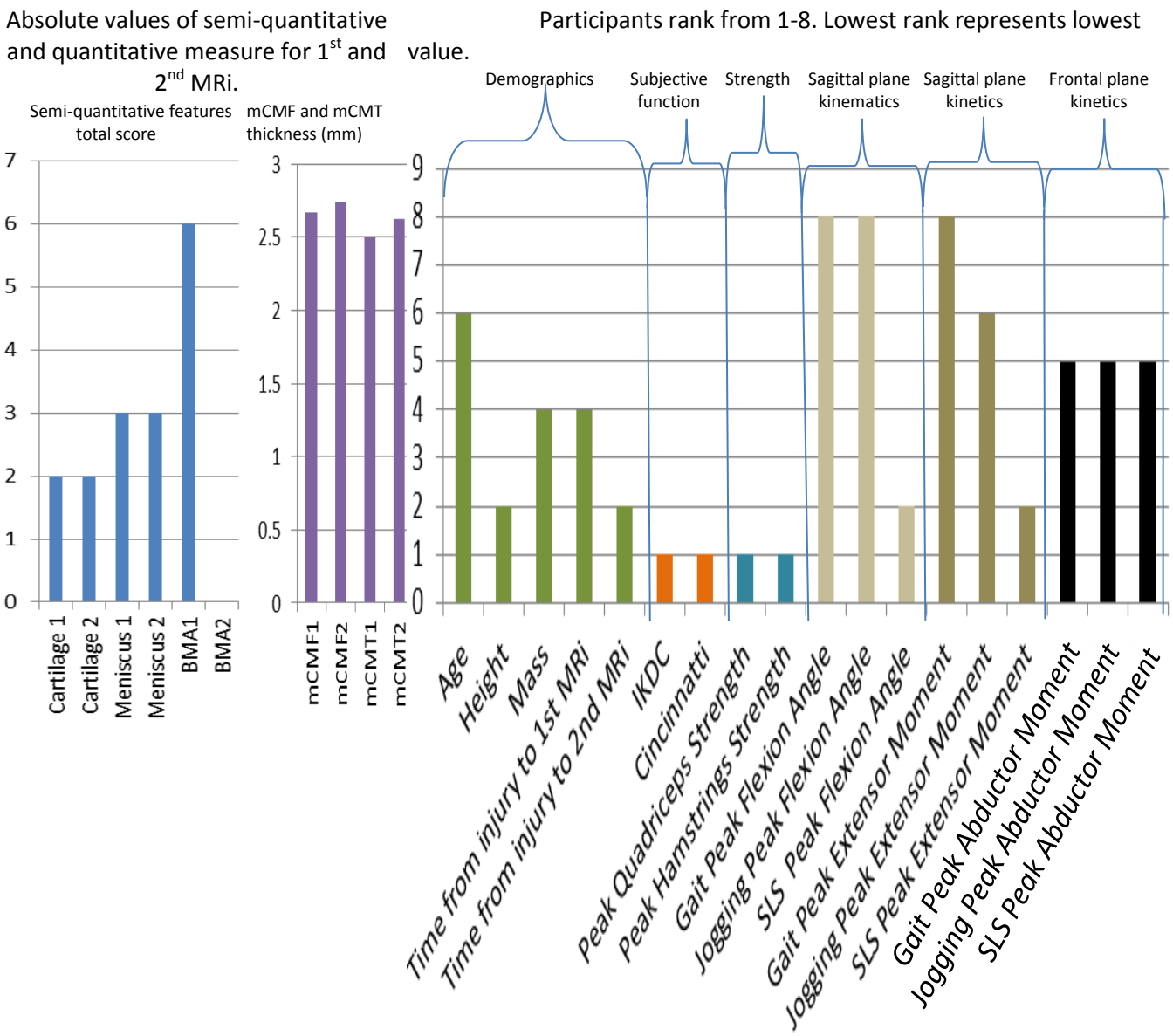


Figure 6.4.3.8 ACLM8 Total scores for semi-quantitative features (far left, blue bars), mean cartilage thickness measurement (second from left, purple bars) in the medial compartment of the femur and tibia and ranking from 1-8 for demographic (green bars), subjective measures of knee function (orange bars), strength (turquoise bars), kinematics and kinetics (light grey, khaki and black bars) for gait, jogging and SLS.

Description of Results: ACLM8 showed no changes in mean cartilage thickness greater than the MDC. No changes in either cartilage score or meniscal score were noted although abnormalities still remained at follow up, however BMA showed a large reduction in score, demonstrating no abnormalities at follow up MRi 24 months after injury.

Despite showing no indication of degenerative change, ACLM8 was the lowest functioning from subjective perspective ranking lowest on both the IKDC and Cincinnati Knee Scores and also strength of the quadriceps and the hamstrings.

ACLM8 had the highest ranking for peak flexion angle for gait and jogging but the second lowest for SLS, this was reflected in the highest knee extensor moment during gait and 3rd highest during jogging, with SLS having the second lowest knee extensor moment corresponding with the reduced knee flexion angle.

Table 6.4.3 Values for each of the outcome measures investigated for the ACLM. This shows the change in scores for BMA (Bone Marrow Abnormality) Meniscal score and cartilage morphology score between MRi 1 and MRi 2 as well as regional cartilage thickness change for the cMF and CMT region of the knee. Values for the participants' demographics, subjective measures of knee function, strength of quadriceps and hamstrings and kinematic and kinetic outcomes. Each value is followed by the participants rank in brackets, with the smallest value equating to the lowest rank.

	ACLM1	ACLM2	ACLM3	ACLM4	ACLM5	ACLM6	ACLM7	ACLM8
BMA Change	-7	-5	-6	+1	-7	-9	-3	-6
Meniscus Change	-4	0	-3	+7	-1	-3	-3	0
Cartilage Change	0	+2	-3	0	-3.5	0	+3	0
mCMF Thickness Change (mm)	+0.60	+0.22	+1.45	+0.05	+1.12	+0.12	+0.25	+0.07
mCMT Thickness Change (mm)	+0.78	+0.27	+1.67	-0.04	+0.70	+0.53	-0.34	+0.12
Age (years)	27(3)	27(3)	38(7)	20(2)	19(1)	49(8)	27(3)	34(6)
Mass (kg)	66.6(1)	82.0(5)	77.8(4)	76.2(3)	82.4(6)	99.9(8)	88.4(7)	73.4(2)
Height (m)	1.62 (1)	1.77(5)	1.75(3)	1.70(2)	1.80(8)	1.77(7)	1.77(5)	1.76(4)
Time from injury to scan 1 (Months)	1(1)	7(6)	1(1)	64(8)	1(1)	4(4)	11(7)	4(4)
Time from injury to scan 2 (Months)	28(3)	49(7)	28 (3)	91(8)	48(6)	40(5)	19(1)	24(2)
IKDC score	95.4(4)	97.5(5)	90.8(2)	90.8(2)	97.7(5)	100(7)	100(7)	50.6(1)
Cincinnati Score	550(4)	570(7)	538(3)	502(2)	569(6)	555(5)	599(8)	352(1)
Peak Quads. Strength (N.m)	167(5)	201(7)	140(3)	103(2)	226(8)	192(6)	164(4)	95(1)
Peak Hams Strength (N.m)	77 (3)	151(8)	146(6)	68(1)	123 (5)	100(4)	123(5)	71(2)
Peak Flexion Angle Gait (°)	21.7(7)	19.5(6)	16.0(4)	12.7(1)	18.4(5)	15.8(3)	13.1(2)	27.1(8)
Peak Flexion Angle Jogging (°)	41.1(6)	33.7(2)	27.6(1)	40.6 (5)	39.2(4)	43.0(7)	37.6(3)	52.4(8)
Peak Flexion Angle SLS (°)	68.5(3)	76.4(5)	62.84(1)	74.0(4)	NA	90.8(7)	82.2(6)	66.8(2)
Peak ext. moment Gait (N.m)	53.7(7)	23.3(2)	45.8 (5)	38.0(4)	51.9 (6)	20.33(1)	32.7(3)	67.8(8)
Peak ext. moment Jogging (N.m)	143.3(3)	140.1(2)	161.3(5)	8.7 (1)	192.1(7)	199.5(8)	155.4(4)	188.2(6)
Peak ext. moment SLS (N.m)	101.7(4)	64.0(3)	46.0(1)	NA	NA	102.8 (5)	125.3(6)	17.6(2)
Peak abd. moment Gait (N.m)	49.5 (6)	46.3(4)	44.5(3)	62.5(8)	52.8(7)	42.0(2)	34.9(1)	47.3(5)
Peak abd. moment Jogging (N.m)	30.1 (1)	141.5(6)	63.8(3)	NA	50.5(2)	165.2(7)	101.1(4)	134.9(5)
Peak abd. moment SLS (N.m)	17 (1)	101.7 (5)	26.3(2)	NA	NA	78.3(4)	62.2(3)	118.4(6)

Key: mm=Thickness in millimetres °=Angle in degrees, N.m=Force in Newton metres.

6.4.4 Case Series Summary.

Despite no significant differences in changes in thickness as full group data, all participants bar two demonstrated changes greater than the MDC in at least one region of the knee using the quantitative method. The region with the greatest number of participants showing a change larger than the MDC was the CLF (6/8), however caution must be aired due to the small MDC found in this region, meaning that only small changes may be deemed significant. Further evaluation of reliability with greater numbers and repeated measurements would help identify the true nature of these changes.

These results are however supported as the semi-quantitative scoring of cartilage showed worsening of score in a comparative region in four of the six participants. Of the four participants that demonstrated changes in both MRi methods for risk factors identified from the literature two of the four participants were ranked seven and eight for time from injury to 2nd MRi. Of the remaining demographics parameters of interest one was the 2nd oldest at 38 years For patient reported measures of function using the IKDC and Cincinnati knee score showed no demonstrable themes, neither did kinematics or kinetics with participants showing a variety of rankings and values.

Of the ACLM two participants were of particular interest ACLM4 and ACLM7. ACLM4 was at a much larger time from injury than the rest of the ACLM group, at 64 months for first MRi and 91 months at 2nd MRi with the participant with the next highest value being 49 months from injury to 2nd MRi. This highlights the need for more long term monitoring in order to discern a time frame at which changes may take place as it could be hypothesised that a majority of this cohort were at too early a time frame to detect significant changes, particularly as ACLM4 also demonstrated worsening in both meniscal score and BMA and the only participant to demonstrate worsening in total semi-quantitative scoring.

This overall worsening also highlights other parameters that require further investigation, having low rankings in strength (ranked 2nd for quadriceps and 1st for hamstrings) and patient reported measures of knee function (IKDC and Cincinnati both ranked 2nd). Peak internal knee extensor moment during jogging was also significantly lower than all other participants, with the 2nd highest abductor moment during gait.

ACLM7 was of interest due to the short time frame under which changes took place (eight months) and also cartilage score worsened in another region, the lateral tibia. Of

the key risk factors identified from the literature ACLM7 was the second heaviest participant, interestingly this did not increase loading at the knee and in fact ranked lowest in knee abductor moment during gait (a key risk factor identified for the progression of OA). There was also a corresponding reduction in knee flexion angle, however this was the opposite of ACLM4. ACLM7 also had some of the highest levels of function for the IKDC (ranked 8) and Cincinnati (ranked 7) knee scores showing that patient reported function may not be reflective of structural changes in the early stages of OA.

Of the other regions of the knee and associated outcomes no discernible patterns emerged, of the remaining participants ACLM8 was of interest as this was the only participant who showed no marked changes in cartilage thickness across region and improvements in all features of the semi-quantitative method to low levels of abnormality.

This was despite ACLM8 functioning at a lower level in terms of both subjective function (ranking 1st for IKDC and Cincinnati Scores) and strength (1st for quadriceps and 2nd for hamstrings) and having the highest ranking for peak flexion angle for gait and jogging but the second lowest for SLS, this was reflected in the highest knee extensor moment during gait and 3rd highest during jogging, with SLS having the second lowest knee moment corresponding with the reduced knee flexion angle.

It may be that these conflicting results point to other factors that lead to degenerative changes, or that time dependant adaptations take place in function and loading that require greater participant numbers, across a broader range of time frames, to uncover these potential pathways towards degenerative change.

The following discussion chapter will aim to place the findings from MRi analysis above in the context of the findings from the full group kinematic and kinetic analysis from Chapter 5. It will also endeavour to discuss the implications of the findings, from all parts of the present study, might have in the initiation and progression of OA.

Chapter 7 Discussion of Results.

7.1 Introduction to Discussion.

The primary aim of the study was to investigate if biomechanics in those with ACL injury are associated with changes in structures within the knee that are related to OA changes. The following discussion will focus initially around the key kinetic outcome measures that have been theoretically implicated in changes in loading at the knee that potentially can influence structural changes and how these fitted into the context of the other literature (Chapter 7.2.2 and 7.2.3).

For kinetic outcomes there were no significant differences between groups for gait or SLS, however for jogging both the ACLR and ACLD groups demonstrated a significant reduction in both their normalised and absolute internal peak knee extensor moments during jogging when compared to the controls. Despite the suggestion that the SLS was the most difficult activity to perform, evidence from the present study suggests that loading at the knee was greatest during jogging and demonstrated differences with controls, however the SLS did show kinematic differences. It is also of note that the drop out in participants able to perform the SLS hints at the prospect of the SLS being a more challenging activity especially in the ACLD group. These kinematic (Chapter 7.3) and kinetic outcomes (Chapter 7.2.2) will be explored in the following chapter and discussed in the context of their potential impact on degenerative changes in the tibiofemoral joint (Chapter 7.2.3).

MRi analysis showed a significant change in semi-quantitative score however this demonstrated an improvement of score indicative of improvement of knee health. Three participants from the ACLM (2, 4 and 7) group demonstrated a worsening of at least one feature associated with the development of OA and where of particular interest for further investigation of kinematics, kinetics and other risk factors for development of OA. Quantitative measurements of regional cartilage thickness showed no significant changes between diagnostic scan and follow-up for any regions. Despite a hypothesised thinning of cartilage expected as a sign of degenerative change two regions, the CMF and CMT, showed a non-significant trend towards thickening.

For all activities there were no significant differences in spatiotemporal measures between groups. Kinematic assessment also showed no significant differences between

groups for gait, however for jogging there was a significant difference, although group analysis showed only the ACLD group had a non-significant trend towards a reduction on knee flexion angle. For SLS the ACLR also showed a non-significant trend towards a reduction in sagittal plane knee ROM, with the ACLD group showing a non-significant trend towards reduction in peak knee flexion angle and significantly reduced sagittal plane knee ROM.

Chapter 7.4 will then deliberate the effect of two main areas that were identified as having a key influence on how the results of the present study are interpreted in the context of other studies on ACL injured groups and also on the findings presented for MRi; the time from injury at which the participants were assessed and their level of activity. Finally Chapter 7.5 will then discuss other risk factors for the development of OA identified from the literature in participants from the ACLM group who either showed degenerative changes or had demographics that would put them at increased risk of OA.

7.2 Discussion of Key Outcome Measures: Kinetics and MRi Changes.

7.2.2 Discussion of Kinetics.

The most widely reported outcome measure in the literature relating to adaptations in those having ACL injury was that of a reduction in internal peak knee extensor moment. It was for this reason the framework for adaptations after ACL injury was constructed using this outcome in order to help place the current study's data in the context of other studies. A reduction in knee extensor moment is cited as an important adaptation in ACL injured groups. Devita et al. (1998) and Karinikas et al. (2009) state that a reduction in knee extensor moment in the earlier stages after injury/surgery may be a strategy to prevent stressing the newly reconstructed ligament and protect against further injury to the ACL and other structures, avoid pain and/or also allow other structures to adapt and compensate after ACL injury and subsequent reconstruction. Other strategies from the literature employed by ACL injured groups include reduction of knee moment coinciding with a reduction in flexion angles indicative of co-contraction of the hamstrings with the quadriceps, to stabilise the knee in a more favourable position to maintain stability (Andriacchi and Dyrby, 2005; Alkjaer et al. 2003; Von Porat et al. 2006; Knoll et al. 2004).

Frontal plane moments were also identified as a key target for investigation as they have been demonstrated to influence knee loading patterns, which have been

considered a significant indicator of OA progression with each 1% increase of internal knee abductor moment showing an increased risk of OA progression of 6.46 times (Miyazaki et al., 2002). It is theorised that increases in internal knee abductor moment increases loading in medial compartment, which is cited as a potential initiator in the development and progression of OA. However literature on this outcome in ACL injured groups is scarce, therefore internal knee abductor moment was deemed a key outcome measure for assessment (Butler et al. 2009). Kinetic analysis therefore included internal peak knee extensor and flexor moments and internal peak knee abductor moments for gait, jogging and SLS.

Gait is an important task to evaluate after ACL injury as alterations in gait mechanics would then subject the knee joint to altered loading countless times over the course of days, weeks, months and years. The cumulative effect of these alterations, even if small, has been stated as a potential mechanism for accelerating the initiation, progression and development of OA (Gao et al., 2010). For the current study's ACLR and ACLD groups there were no significant differences between groups with regards to either absolute or normalised kinetics during gait. The longitudinal analysis of the ACLR2 group demonstrated no significant changes in both absolute and normalised internal peak knee extensor moment. This supports the model that once returned to normal loading levels are maintained after ACL reconstruction. However the timeframe at which the ACLR2 were assessed was still within a time from surgery at which other studies had demonstrated a return to normal extensor moments, therefore longer term adaptations may not have had an appropriate amount of time to manifest themselves.

The results of the present study's ACLR group are in agreement with Bush-Joseph et al. (2001) who demonstrated that no differences in knee kinetics occurred in their ACLR group and state that adaptations may be time dependant resulting in no observed differences at the time point at which this study was undertaken. This theory is supported by the work of Karinikas et al. (2009) who demonstrated a time dependant return to normal gait mechanics.

Contrary to this Devita et al. (1998) demonstrated a significantly decreased internal peak knee extensor moment, however the ACLR group studied by Devita et al. (1998) was assessed at only six months post-surgery and this could be one potential factor influencing the difference in results in comparison to the present and other studies. The

investigation of how time from injury influenced biomechanics in the present study is discussed in Chapter 7.4.

For the ACLD group in the current study the data is in contrast to the majority of studies which have demonstrated changes in sagittal plane kinetics. Hurd and Snyder-Mackler (2007), Andriacchi and Dyrby (2005), Alkjaer et al. (2003) and Wexler et al. (1998) all demonstrated that their ACLD group had a reduced internal peak knee extensor moment when compared to their respective control condition. This has been proposed to be a strategy to limit anterior translation of the tibia on the femur in the absence of the ACL, to reduce shearing forces within the knee for which cartilage is poorly adapted for, as it typically is evolved structurally to cope with compressive forces (Andriacchi and Dyrby, 2005). This suggests that within the present ACLD group time dependent adaptations have taken place in other structures that allow for a return to more normal knee kinetics, including an increase in muscle strength and muscle activation patterns. However within the constraints of the data from the present study it is not known what the impact this more normal return to function has on the compressive and shear forces within the knee and whether this is therefore a positive situation for long term knee health.

There are several differences between the present study and the aforementioned ones that may influence the discrepancy in findings. The study by Andriacchi and Dyrby (2005) took place on average over ten years from injury, a much greater time point than the present study. This could potentially mean that more long term adaptations take place even after an initial return to normal knee kinetics demonstrated in the present study as is demonstrated in the model from Figure 3.6.1 showing after initial recovery of extensor moment a further decrease in moment in the long term. This may be a more long term protective adaptation to maintain knee health or may be caused by structural changes that require the knee to protect against normal loading which may now be deemed excessive if other structures (ligaments and muscles) or cartilage ill adapted to loading can no longer sustain these loads. This idea is supported by Wexler et al. (1998) who assessed time dependant differences by subdividing the ACLD into groups of early, intermediate and chronic participants. Wexler et al. (1998) demonstrated that peak internal knee extensor moment was significantly decreased in the early and chronic stages, but not in the intermediate phase when compared to the control group. The intermediate group's time frame of 2.5-7.5 years would be the most comparable with the ACLD group in the present study, thus findings were in line with the present

study. Whereas the ACLD group analysed by Hurd and Snyder-Mackler (2007) had a mean time from injury to assessment of 11.4 weeks, which was a much shorter time frame than the present study and therefore provides a possible explanation for the differences with the present study.

The internal peak knee abductor moment in the present study, for both normalised and absolute values, was not significantly different between groups, therefore there was acceptance of the null hypothesis that no differences in knee abductor moment existed between groups. Data suggests that internal abductor moment was maintained longitudinally with no significant differences between visit one and two in the ACLR2 for both absolute and normalised knee abductor moment.

Contrary to the findings of the present study Butler et al. (2009) demonstrated that ACLR had a significantly increased peak internal knee abductor moment when compared to the controls. This increase in abductor moment was claimed to be a potential causal factor in the initiation of early OA in ACL injured groups due to increased medial compartment loading. Webster et al. (2011), in conjunction with the present study, have shown no differences in frontal plane kinetics in either the first or second abductor moment peaks. Differences between the above studies may have been caused by a number of factors; gender biases may be an important factor to explain the differences between studies. Webster et al. (2011) although finding no differences overall between ACLR and controls, did find a significant difference in peak knee abductor moment between the ACLR males (n=18) and females (n=18), with females demonstrating a significantly increased peak abductor moment. This increase in abductor moment was stated to not be related to gender in healthy populations but no explanation was offered as to why this would be the case in ACL injured groups. The author suggests this could in part be due to the increase in 'Q' angle (the angle formed by a line drawn from the anterior superior iliac spine through the centre of the patella and a line drawn from the centre of the patella to the centre of the tibial tubercle) demonstrated in women that has been shown to influence frontal plane knee loading and has been cited as a risk factor for ACL injury (Sutton et al. 2013). Webster et al. (2011) did not investigate the effect of gender differences within the control group and state more investigation was required to evaluate if the increased abductor moment is directly associated to gender differences in mechanics and deemed normal or adaptations in movement after ACL injury may be amplified in females putting them at increased risk of OA. The current study also has a high percentage of males at 61%,

whereas Butler et al. (2009) consisted of a smaller group of 17 participants 76% of which were female. However exploratory analysis of gender data for the ACLR within the present study found that there was no significant difference in normalised internal peak knee extensor moment between the males and female groups demonstrating that within the present study this was not likely to influence the outcome of the analysis markedly.

The effect of the time from surgery, at which these studies were undertaken, may be linked to the different findings and in turn the interpretation these studies draw on the influence of ACL reconstruction on gait mechanics and the implications these may have for long term knee health. Butler et al's. (2009) study were on average 5.3±4.4 years from surgery when assessed, whereas the present study's ACLR findings at average 14.1±9.1 months from surgery were in line with Webster et al. (2011) whose ACLR females and ACLR males to were 19.8±11.6 and 20.3±11.4 months from injury respectively. It appears that if there is time related adaptations after ACL surgery as demonstrated by Karinikas et al. (2009), that due to the comparative times of assessment between the present study and Webster et al. (2009) this would not be a causal factor that would explain the difference in results between these studies.

Differences between the studies can also potentially be explained by a number of other factors. Surgical technique and skill may have differed between groups alongside the variation between studies in terms of time for, appropriateness and intensity of rehabilitation. For example Butler et al. (2009) gave no details of the rehabilitation or surgical procedure their group undertook whereas Webster et al. (2011) gave a detailed analysis of surgical technique and rehabilitation methods. Surgical technique was an anatomical reconstruction using the hamstring tendon and comparable surgical technique was performed in the present study using a double bundle anatomical reconstruction using the hamstring tendon. However due to the inherent variation in health care practitioners treatment approach and the efficacy with which patients adhere to rehabilitation protocols, comparison between studies in this context is always challenging.

It appears that the present study's ACLR group had returned to normal kinetic values, implying that loading levels are not increased or decreased within this group. Despite the return to normal knee loading implying the restraining properties of the ACL have been returned, it is unknown at the time of writing as to how successful this procedure

is at returning the knee to pre-injury loading patterns and if the areas of cartilage being loaded, if different, are well enough adapted to cope with new loading levels (Gao et al. 2010; Andriacchi and Dyrby, 2005). For this reason analysis of regional MRi changes using quantitative and quantitative methods was combined with patient specific biomechanical data for the ACLM group. This enables exploration of those with worsening of structures of the knee associated with OA to identify if trends in the data exist that support the hypothesis of changes in loading causing degenerative change or if other factors may be at play.

Gait is also a low demand activity on the knee, higher demand activities with which a majority of this participant group would have returned to according to their activity level scores may demonstrate significant kinetic differences. Jogging and SLS are task that require greater knee flexion angles, greater velocities and therefore increased knee moments and loading when compared to gait as was demonstrated in the comparison of these tasks shown in Table 6.4.2. As jogging and SLS require a greater demand on the knee, it was hypothesised that if abnormal kinetics were demonstrated in these activities and considering the relative frequency with which these activities would occur, that it may be during these higher demand activities that frequent abnormal loading may influence long-term knee health.

The SLS activity, in terms of loading at the knee, was found to be an intermediate activity between gait and jogging in the present study. Button et al. (2014) also state that the SLS is a safer way to assess knee function at higher degrees of knee flexion in ACL injured groups than more demanding activities such as hopping. However, as with gait, no significant differences were found between groups with regard to knee extensor moment and this was in part due to adaptations in kinematics that potentially maintained knee loading within normal levels and this concept is discussed further in Chapter 7.3. It is worth considering that the volitional nature of the SLS allows a level of control that would not be possible in the sporting environment, to which a majority of the ACLR and ACLD participants within this group had returned according to their activity level (Chapter 7.4). This could mean that if there was a requirement for increased knee flexion angles during exercise or sport, that loading would be increased beyond normal expected levels and be a risk factor for further injury and potentially in the initiation and progression of OA in those who do not modify their activity level accordingly after ACL injury.

For the more demanding activity of jogging the present study demonstrated a reduction in knee extensor moment for both ACLR and ACLD groups. This was in line with other studies (Bush-Joseph et al. 2001; Berchuk et al. 1990; Patel et al. 2003) which would, on face value, be unsupportive of the hypothesis of increased loading causing initiation and progression of OA in ACL injured groups. This may be indicative of a quadriceps avoidance strategy described by (Berchuk et al., 1990). It is however worth noting that a reduction in knee moment is the summation of opposing moments. These opposing moments could be high in the case of muscle co-contractions, especially eccentric contraction of the hamstrings, which have been described as a mechanism to stabilise the knee joint after ACL injury (Andriacchi and Dyrby, 2005; Alkjaer et al. 2003; Von Porat et al. 2006; Knoll et al. 2004). This could however lead to increased compressive forces within the knee, which if excessively abnormal or loading areas of cartilage not capable of handling increased loads may initiate degenerative change after repeated cycles of this abnormal loading.

Devita et al. (1998) and Karinikas et al. (2009) provide a possible explanation for a reduction in knee moment, as knee extensor moments have been shown to be representative of stress within the ACL in the earlier stages after injury avoidance of extensor moment may be a strategy to prevent stressing the newly reconstructed ligament and protect against further injury to the ACL and other structures, avoid pain and/or also allow other structures to adapt and compensate after ACL injury and subsequent surgery. The author suggests this explanation is in part unsatisfactory, in that greater demand is placed on the ACL in other activities such as hopping and jump landings which a majority of these participants would have returned to undertaking with a mean activity level score of 86.7±15.6 relating to taking part in sports 1-3 days a week including jumping, hard pivoting, and cutting such as basketball, volleyball, gymnastics and football. The author proposes that the reduction in knee extensor moment and potentially knee loading, may be related to adaptations in movement or performance that would under normal circumstances be tolerated but after ACL injury places the knee in specific positions of weakness, loading areas of the knee that are not accustomed (particularly if associated damage to the cartilage or meniscus were present) or that there are in specific positions that the 'new' ACL is not able to handle the stress in the same way as the original. To consider the relationship between knee extensor moments and degenerative changes in the knee, the ACLM participants who

demonstrated evidence of structural changes in the knee indicative of degenerative changes were investigated in the context of their kinetic outcomes across all activities.

ACLM4 was the only participant who showed overall worsening in total semi-quantitative score, relating to an increase of meniscal and BMA score. ACLM4 demonstrated two main kinetic variables of interest, peak internal extensor moment in jogging, in which the subject demonstrated the lowest extensor moment and internal peak knee abductor moment during gait which was the highest of the participants. Reduction in peak extensor moment has been associated with a protective strategy to reduce load on the knee in the sagittal plane (Berchuck et al., 1990; Devita et al., 1998) however if corresponding increases in abductor moment are evident this could load the knee in a manner that has been associated with degenerative OA changes (Butler et al., 2009; Webster et al., 2011). This could be a further area of investigation and generates the research question to investigate if different types of loading are associated with different structural changes within the knee and in which compartments of the knee these changes take place. Increases in shear, axial and compressive loading may impact knee structures differently. Tibiofemoral cartilage is stated as being poorly adapted to shear and axial loads, but well adapted to compressive loading (Andriacchi et al., 2006; Andriacchi et al. 2004). However, once knee OA is present progression of OA may well also be enhanced by compressive loading (Andriacchi et al., 2004).
The meniscus is also a key load distributing structure in the knee, helping protect cartilage from damage and is adapted to resist axial and compressive loading (Hunter et al. 2006). Injuries to the meniscus have been strongly linked to the development and progression of OA (Hunter et al., 2011). Slauterbeck et al. (2009) found that meniscal injury was present in 52% of ACL injured patients in the lateral portion and 22% of ACL injured patients in the medial portion. Hunter et al. (2006) state that if a meniscal tear is present it is less effective at resisting axial loading, this will increase the loading of other tissues such as bone (potentially leading to increased BMA) and cartilage (leading to cartilage thickness or morphology changes) in the same compartment.

ACLM4 showed notable worsening of the meniscus in equal amounts of both the lateral and medial meniscus, therefore degenerative patterns associated with the increased internal peak knee abductor moment could not be ascertained. Interestingly on investigation of those who had symptomatic OA Von Porat et al. (2006) found that five of six participants demonstrated knee extensor weakness, which was associated

with a reduction in internal knee extensor moment. As this group were at a time from injury of approximately 16 years, knee extensor weakness particularly if persisting in the long term may be a potential indicator for symptomatic OA. However, it is difficult to interpret if this is a causal effect of OA or a result of OA changes that have occurred that may have caused pain or impingement of function and in turn a reduction in knee extensor moments.

Two other participants ACLM2 and ACLM7 also showed worsening in semi-quantitative assessment, demonstrating an increase in cartilage morphology. This corresponded with ACLM2 and ACLM7 both demonstrating increases in cartilage thickness measurement greater than the MDC in the CLF region of the knee increasing from 3.38 to 3.52mm and 2.85 to 2.69mm respectively. ACLM2 and ACLM7, in a similar manner to ACLM4 had two of the lowest internal peak knee extensor moment values during gait, for abductor moment this was in the middle of values for the group rankings for ACLM2 and the lowest for ACLM7. For jogging and SLS ACLM7 was ranked in the middle grouping of participants for both peak internal extensor and abductor moments. Despite the hypothesis that those who have higher levels of knee loading (represented by larger moments) showing increased signs of structural changes this was not strongly supported within this group. It is worth noting that the ACLM group as a whole were functioning at a higher level of performance and higher moments than the full ACLR group. Within this group only one participant presented data which was exceptionally different from the rest of the group showing a marked reduction in knee extensor moment during jogging, ACLM4.
However discerning the interactions of the study's demographic, biomechanical and subjective functional outcomes with changes in knee structures in a small number of participant's demonstrating relatively homogeneous biomechanics was improbable. The current study's data does however demonstrate the complex nature of interactions between different risk factors in patient populations that may be used to investigate predisposition or initial development of early OA. Considering the complex yet undiscovered nature of the relationships of biomechanical, demographic and subjective measures of function and how this influences degenerative structural change is remains to be seen.

For the present study's biomechanical data we have discovered that both ACLD and ACLR groups showed a significant reduction in internal peak knee extensor moment in

jogging, this was returned to normal loading levels in the SLS. This suggests that ACL injured patients are attempting strategies to lower levels of loading at the knee to keep them within normal limits or reduce them as far as is possible within the demands of the activity. These findings would not fit into the idea that increased loading in the sagittal or frontal planes would initiate degenerative changes. However the ACLM recruited from the full ACLR were functioning in general with higher knee moments, greater levels of performance and kinematic values even when compared to the control group. This could be hypothesised to be a more at risk group for degenerative change if indeed the biomechanical model is a contributing mechanism in the development of early onset OA.

7.2.3 Discussion of MRi Results.

Analysis of regional cartilage thickness changes in the ACLM for the CMF, CMT, CLF and CLT demonstrated no significant changes in cartilage thickness. In concurrence with Andreisek et al. (2009) the current study demonstrated no significant differences in cartilage thickness across the femoral and tibia regions of the knee. The current studies participants were assessed at a time point generally closer to injury with a range of time of injury to follow up scan of 19-91 months with an average time of 38.75±23.9 months. This contrasted with Andreisek et al. (2009) whose ACL injured participants had a mean time between injury and follow-up MRi of approximately 96 months. It could be hypothesised that as Andreisek et al. (2009) demonstrated no changes in cartilage thickness, at an average follow up of a time frame over double that of the present study that the present study would have found a similar result.

However the CMF and CMT regions demonstrated a non-significant trend. Interestingly this was towards an increase in cartilage thickness between diagnostic scan and follow up was evident in the CMF and CMT in six participants. In the CLF and CLT region 50% (n=4) of the participants demonstrated an increase in cartilage thickness. For the CMF region the mean cartilage thickness value increased from 2.85±0.64mm to 3.26±0.59mm and in the CMT region 2.90±0.54mm to 3.37±0.88mm. This represents an average increase of 0.41mm for the CMF and 0.47mm in the CMT region. This increase is only important in the context of the errors that have been induced both systematically and by the operator (Koo et al. 2005). The SEM discovered in the previous analysis of reliability for the CMF and CMT was 0.08mm and 0.77mm respectively. This means that increases discovered in the CMT must be treated with

caution due to the errors introduced in the analysis, whereas increases in other regions, greater than that of the SEM could be interpreted as being more convincing.

Although several studies investigating changes in participants with long term OA have shown a reduction in regional cartilage thickness (Eckstein et al., 2010; Dam et al. 2009; Hellio le Graverand et al. 2010: Hunter et al. 2009; Bruyere et al. 2006) further insight was required as to why the CMF region in particular showed several increases in cartilage thickness greater than would be expected due to systematic errors. An additional search of the literature found studies that had demonstrated an increase in cartilage thickness in the early stages of OA (Frobell et al. 2010; Hellio Le Graverand et al. 2009). These results indicate that studies need to be undertaken to help clarify how cartilage responds in the different phases of OA and also in a post injury condition when cartilage may have been adversely affected.

In studies that have demonstrated thickening of cartilage this has taken place primarily in the central portion of the medial femur, coinciding with the weight bearing portion of the knee (Frobell et al. 2010; Hellio Le Graverand et al. 2009). This is comparable to that of the regions of the knee that showed a non-significant trend towards thickening in the present study. The study by Frobell et al. (2009) demonstrated that in ACL participants assessed for regional cartilage thickness changes of a period up to a year after injury, also demonstrated an increased thickness in the central portion of the medial femoral condyle with no changes in the other compartments.

The present study was at a time frame from injury much further than that of Frobell et al. (2009). This might suggest that after an initial period of swelling that a majority of the participants had returned to a more normal level. However the current study's participants first scan was at a time period on average of 11.5±21.5 months it is therefore possible that at this time point that if initial swelling had taken place would suggest that cartilage had maintained. Interestingly the three participants that showed an increase in cartilage thickness greater than the MDC, ACLM1, ACLM3 and ACLM5 all had a time from injury to first assessment of one month, suggesting that the above theory holds some weight as these participants were assessed early enough before longitudinal increases in cartilage thickness had manifested. Unfortunately no comparable data in line with the current study is available to assess how long swelling is maintained for after this initial period and what happens to the structure of cartilage after this point. Frobell et al. (2009) state that the significance of increasing cartilage

thickness in the early stages after injury is unknown, although animal models have suggested an initial swelling of cartilage precedes cartilage breakdown. This suggests that the CMF region should be carefully monitored over to give deeper insight into how cartilage responds in the short, medium and longer term after injury. Data from the present study for the CMF region suggests that in the context of the framework developed for cartilage thickness change after time from injury/surgery that the model depicting an initial swelling of cartilage in the early time period after injury seems most appropriate. However not enough data points were observed to determine what happens after this initial period of swelling in these participants, whether there was a return to comparable cartilage thickness as the diagnostic scan that was maintained longitudinally, suggesting that cartilage integrity is maintained, or if after a reduction in swelling to normal levels that a further breakdown of cartilage takes place indicative of OA changes.

Despite the lack of group significance it can be seen that a majority of participants in the ACLM group demonstrated a change in cartilage thickness in at least one region greater than the MDC (6/8) and all participants also presented evidence of remaining structural abnormality in other features suggesting that changes are taking place within this sub-group of ACLR who demonstrated typically higher knee moments and levels of function. However due to the as yet unknown pathological timeline of the initiation and progression of OA it is unknown what the identified changes mean for long term knee health. The challenge for future research is to define what can be considered a normal physiological response to ACL injury and what factors are indicative of degenerative change. This analysis needs to be undertaken in larger samples with a more targeted battery of outcomes, some of which have been identified in the present study, to give a more complete picture of what is occurring in the knee of those after ACL injury in the short, medium and long term.

The absence of significant cartilage change described by Andreisek et al. (2009) and the current study may also be due to a reduction in meniscectomies which have been associated with OA in other ACL studies (Neuman et al., 2008; Øiestad et al., 2010). Interestingly the four participants in Andreisek et al. (2009) study that had meniscectomies demonstrated significant cartilage thickness loss. It is worth noting that Andreisek et al. (2009) discovered significant changes in both sub-chondral bone area and femur shape after ACL injury despite the absence of degeneration of cartilage. It may be that changes in both bone and/or meniscus precede cartilage loss in those

suffering with ACL injury (Neuman et al., 2008; Øiestad et al., 2010; Andreisek et al., 2009).

ACLM4 was the only participant who demonstrated worsening in total knee score using the prescribed semi-quantitative method and this reflected an increase in score for both BMA and meniscal abnormality, however cartilage morphology score remained the same throughout. This was also found in regard to the quantitative method ACLM4 demonstrated no evidence of changes in cartilage greater than the MDC in any of the four defined regions of the knee. This shows that degeneration in other structures may take place before cartilage changes. Whether these changes occur independently of each other or that if structural changes to load bearing structures like the meniscus precede changes in cartilage morphology and cartilage thickness changes is yet to be fully understood. However, meniscal damage has shown to have a strong association with the development OA (Neuman et al., 2008; Slauterbeck et al., 2009; Hunter et al., 2006) and in the case of this participant showing noticeable degeneration should be a warning signal to clinicians to monitor long-term knee health and consider measures to protect the knee from further damage.

Therefore the present study targeted changes in both the total score for the combination of these features, alongside analysis of each feature in a descriptive manner to evaluate firstly how these structures change over time and secondly to determine which of these features has the biggest influence on changes in scoring over time. At the time of diagnostic assessment the mean total score was 14.8±6.5 and at follow up this was significantly reduced to 7.8±5.1. This demonstrates that a marked improvement in features associated with OA was observed. From the framework developed from literature the data for cumulative scoring of all features demonstrates the model that after initial injury abnormalities demonstrate a return to more normal levels; however a remaining average total score of 7.8±5.1 may be of concern if remaining structural abnormalities within individuals have been identified as risk factors for degenerative changes (Neuman et al., 2008; Slauterbeck et al., 2009; Hunter et al., 2006; Felson et al., 2003; Hunter et al., 2008; Neogi et al., 2012). It is also possible that even in healthy knees a certain level of abnormality would be expected due to natural age related changes however this data was not available in the literature for comparison.

Meniscal integrity is an important factor for preserving long term knee health (Slauterbeck et al., 2009; Hunter et al., 2006) and was the feature that showed the most

evidence of abnormality at follow up and degenerative change and least improvement in the present study. At the time of the initial diagnostic scan damage was reported in 6/8 (75%) participants in the medial compartment and 6/8 (75%) in the lateral compartment, with all participants demonstrating some evidence of damage to the meniscus. At follow up scan this was improved slightly with 4/8 (50%) participants showing meniscal damage in the medial meniscus and 5/8 (62%) showing damage in the lateral compartment.

To date Slauterbeck et al. (2009) presents the most thorough documentation of prevalence of meniscal abnormalities in those suffering ACL injuries. This study was undertaken in 1104 patients with meniscal injuries being confirmed from arthroscopic investigation. It was discovered that the lateral meniscus was injured in 378 patients (52%) and the medial meniscus in 157 patients (22%). The results from the present study demonstrated an increased prevalence of meniscal abnormalities in both the medial and lateral compartment when compared to Slauterbeck et al. (2009) however with the small sample size in the present study this comparison is made tentatively. In contrast to Slauterbeck et al. (2009) the present study also demonstrated a similar prevalence of meniscal injuries in the medial and lateral meniscus at time of diagnostic scan, however this patterns was comparable to that of Slauterbeck et al. (2009) at follow up scan with an increased prevalence in the lateral compartment.

The differences in prevalence of meniscal injuries in the present study could also be attributed to the method of analysis. The present study used MRi to evaluate meniscal integrity, making it possible to evaluate MRi signal abnormalities included in the scoring of the meniscus whereas Slauterbeck et al. (2009) only used visual feedback from arthroscopy. The grading of MRi abnormalities in the present study was adapted from WORMS (Peterfy et al., 2004) which used a system based around signal intensity changes in MRi. These would not be detectable to the naked eye during arthroscopy and therefore it might be expected that a lower prevalence would be discovered using visual methods.

Slauterbeck et al. (2009) also suggest that meniscal abnormalities were associated with a greater time from injury, however it is difficult to compare data between the present study and Slauterbeck et al. (2009) as no specific times from injury to assessment was given.

In the present study the data for ACLM4 aligned with this idea as a notable worsening in meniscal score was found in the participant furthest from injury to follow up scan. However the lack of association between time from injury and change in score in other participants potentially indicates that a majority of the current study's ACLM were not at a time point where degenerative changes have been manifested.

Slauterbeck et al. (2009) also found an association with gender and meniscal injury with only 29% of males without meniscal injury and an increased incidence in injuries in the medial compartment. As 7/8 of the present studies' participants were male this may have influenced both the prevalence and distribution of meniscal injuries. When assessing the regional distribution for both the cumulative scores and total number of ACLM that demonstrated meniscal damage, the posterior region of both the medial and lateral meniscus had the highest prevalence; this was followed by the central region and finally the anterior region. This was also true in the follow up scan; these findings were comparable for the distributions discovered by Slauterbeck et al., (2009).
Comparing the MRi scores for each region it was shown that in the lateral meniscus the anterior and posterior regions improved in score with the central region of the lateral meniscus remaining the same, with regard to both cumulative score and number of ACLM demonstrating tears in these regions. In the medial meniscus there was an improvement in the posterior region in terms of both cumulative score and total number of ACLM showing meniscal tears. However for both the central and anterior regions of the medial meniscus there appeared to be an increase in the cumulative scores and prevalence for meniscal tears.

As the meniscus has a limited ability to self-repair and surgical intervention would have attempted to restore meniscal integrity, improvements in score would be expected with the grading system used in WORMS. However remaining evidence of meniscal damage even in situations where there has been no further deterioration may be of concern due to the function the meniscus plays in load distribution and normal articular knee motion (Hunter et al., 2006). Hunter et al. (2006) state that the structure of the menisci consists of circumferentially oriented collagen fibres woven together with radial fibres, which act like tension rods to maintain shape and structure under physiological loading conditions. It has been demonstrated in mechanical testing that if the meniscus does not cover the articular surface that it is designed to protect, due to a change in position or if a tear leaves it unable to resist axial loading, it will not

effectively perform this role and increases in loading of other tissues such as bone and cartilage in the same compartment will occur. Hunter et al. (2006), using the scoring system in WORMS, demonstrated a significant association between level of meniscal damage and disease progression in those with OA. This would add support for the idea that the extent of meniscal injury reduces the capacity for distributing loads within the knee leading to OA.

For all the features assessed the one with the largest degree of change was BMA. This would be expected as other studies have demonstrated that from assessment at time of trauma to follow up at a period of within a year, BMA decreased significantly in ACL injured participants (Frobell et al., 2009). In the present study at time of diagnostic scan 7/8 (87%) participants had evidence of a BMA in the medial compartment in both the tibia and femur. In the lateral compartment 8/8 participants (100%) had evidence of BMA. At the follow up scan this was reduced to 2/8 (25%) participants in the medial compartment and 3/8 (38%) participants in the lateral compartment. BMA showed the biggest change in total score when compared to meniscus integrity and cartilage morphology scores with a reduction of total BMA score for all participants (65 to 12). It is important to note that because BMA has a large weighting and influence on total score, that using solely total summative scores for all features to assess improvement in knee health may be flawed as worsening in other features may be 'washed out' by the dramatic improvements in BMA score.

Distributions of BMA on the bone area of the tibial plateau at both time of diagnostic scan and follow-up scan was found to be greatest in the posterior region which had both the highest prevalence and cumulative score for BMA. This was more evident at both time points in the lateral compartment of the knee. The central region had the second highest prevalence and cumulative score, again at both time points this was more evident in the lateral compartment. In the anterior region of the knee at both time points only one participant demonstrated an increase in BMA score, this was in the medial aspect of the knee and was consistent between the diagnostic and follow-up MRi. For the rest of the regions there was a marked reduction in BMA score in both the medial and lateral compartment with evidence of BMA existing in only the central and posterior lateral regions of the tibia, whereas at the time of diagnosis every region with the exception of the anterior lateral compartment had evidence of a BMA.

The area of greatest prevalence and cumulative BMA score in the femur was (as with the tibia) in the lateral compartment, with the central region of the lateral femur demonstrating the greatest prevalence followed by the anterior and posterior regions. At diagnostic scan only the anterior region in the medial compartment showed no BMA. At follow-up scan the central region, in both the lateral and medial compartment showed a noticeable reduction in BMA score and prevalence which was more marked in the medial compartment. All other regions that had demonstrated BMA showed a reduction in score and prevalence with the exception of the posterior region of the medial compartment.

Although dramatic improvements were noted in BMA score a key question remains. As participants were still demonstrating BMA at follow up does this still have potential negative connotations for long term knee health, or do these remaining BMA features improve even further over time. What are also unknown are reference values for healthy populations of a comparable age. Therefore would a level of BMA be expected to be evident in those with healthy knees, related to natural processes of aging and remodelling that are dissociated with biomechanical or physiological changes associated with ACL injury?

BMA in those participants already suffering with OA has been associated with narrowing of joint space and an indicator of increasing degenerative changes. Bone marrow lesions within each compartment have also been correlated with degenerative change in the corresponding region (Felson et al., 2003). Despite the relationship between BMA and progression of OA (Felson et al., 2003; Hunter et al., 2008; Neogi et al., 2012) little is known about the underlying mechanisms which cause this process. Therefore more long term studies are also required to identify how BMA's change over time and if the rate of change in BMA is associated with changes in the cartilage. How loading conditions as well as other clinical and demographic factors may also influence progression or regression of BMA's also needs to be investigated thoroughly, to give deeper understanding of the mechanisms at work to make the interpretation of results more concrete.

Hunter et al. (2008) proposes a possible explanation for the negative relationship between BMA and OA stating that cartilage integrity may be influenced by the structural mechanical properties of the underlying bone. Thick dense bone is thought to be incapable of dissipating the forces which may lead to cartilage breakdown. It also potentially inhibits nutritional flow from the marrow space to the joint cartilage

inhibiting reparative processes. Another possibility is that structural changes in bone and cartilage occur independently of each other and are caused by changes in mechanical loading in the relevant compartment of the knee.

Cartilage morphology score is a direct measure of cartilage change from healthy cartilage to that typically demonstrated in OA. It was found that the scoring system used in the present study showed low cumulative scores when compared to injuries that are more commonly prevalent in combination with ACL injury such as BMA and meniscal injury. This might be expected considering the previously described small annual changes that are noted in cartilage in those with pre-existing OA (Eckstein et al., 2010; Dam et al., 2009; Hellio le Graverand et al., 2010, Hunter et al., 2009; Bruyere et al., 2006).

At first assessment 2/8 (25%) participants demonstrated a level of cartilage damage in the medial compartment totalling a score of 12; in the lateral compartment 5/8 (63%) participants had evidence of cartilage damage with a total score of 19. Slauterbeck et al. (2009) demonstrated femoral articular cartilage injuries were identified in 43% of patients with a majority of these in the medial compartment. The femoral cartilage with the present study showed abnormalities were found in 3/8(38%) participants showing values for prevalence in our study are in line with that noted by Slauterbeck et al. (2009).
However 2/8 (22%) participants showed abnormality in the medial femur and 1/8 (12%) in the lateral femur showing a reverse pattern of distribution compared to Slauterbeck et al. (2009). Interestingly at follow up scan this pattern was reversed with 5/8(63%) participants showing abnormalities in the lateral femur with medial compartment abnormality remaining the same. This highlights the importance of the time from injury at which those with ACL injuries knee health is assessed, as this could strongly influence the results and inferences of the impact that ACL injury has on long term knee health.

On the tibial plateau in the initial diagnostic scans cartilage morphology abnormalities were found only in the posterior region with greater cumulative morphology score and prevalence being evident in the lateral portion of the tibia. This tendency for increased cumulative cartilage score in the lateral and posterior region of the knee was also evident at follow-up. At follow up there was a greater cartilage morphology score in

both the medial and lateral compartment in the central region, the anterior portion of the medial compartment of the tibia also demonstrated an increase cumulative cartilage morphology score.

In the femur at the time of the diagnostic scan the central region had the highest prevalence and cumulative cartilage morphology score and this was also observed in the follow-up assessment. This was followed by the posterior and anterior regions of the knee. At initial scanning the central medial region had the highest scores, at follow-up this region showed a reduction in score with the central lateral region now being the region with the highest cumulative and prevalence scores. The posterior lateral region had also worsened alongside the anterior medial region and anterior lateral region of the knee. Only the central and posterior regions in the medial compartment showed reduction in cartilage morphology score. It is of note that despite other features typically showing improvement the most direct measure associated with OA change showed worsening in five of the 12 regions assessed. This emphasises the importance of assessing features individually (and by sub-regions) separated from total scoring of all features to avoid potentially omitting important data for mapping the complex factors involved in the initiation and progression of OA.

Therefore the author suggests that analysis of the individual components that make up the score should be undertaken to give greater insight in to underlying structural changes as physiological and biomechanical processes can change scoring of some of these features to a greater extent and rate than others. For this reason imaging data which identified the changes in cartilage morphology (which worsened overall in two participants) was combined with the individual's outcome measures that were considered risk factors for the development of OA including kinematics, demographics and subjective measures of function. The following chapter discusses the performance and kinematic adaptations evident from the present study that might be employed to control loading at the knee. These adaptations have the potential to have an association with degenerative changes or help protect the knee from further damage due to their impact on kinetics at the knee. This was again discussed in the context of those ACLM showing degenerative changes in the knee.

7.3 Discussion of Spatiotemporal and Kinematic Outcomes.

Altered spatiotemporal and kinematic outcome measures can have a marked effect on the calculation of knee moment as they impact on the accelerations and lever arms involved around the joint (McGinnis, 2013). As mentioned earlier for the SLS, there is the possibility that strategies are employed by ACL injured subjects to maintain loading at the knee, this may also be the case for gait. For jogging it appears that both ACLD and ACLR group employed strategies to reduce loading levels when compared to controls. Therefore the present study evaluated key performance and kinematics to further investigate strategies that may be used to control knee moments.

No significant differences were found in any of the gait performance measures, the only measure nearing significance was that of stride length. The near significance of stride length between groups would be expected, as height was significantly different between the three groups. This would be likely as taller people would have longer leg lengths and in turn a longer stride length. Pearson's correlation showed that there was a significant relationship between height and stride length when evaluating all of the groups. These results suggest that the performance of the ACLR and ACLD groups was not having a marked influence on the kinetic outcomes discussed for gait.

The results for the current study's performance measures during gait for the ACLR group were comparable to that with other studies assessing gait performance parameters in those with ACLR. The results for gait velocity are in agreement with Bush-Joseph et al. (2001), Georgoulis et al. (2003), Webster and Feller (2011) and Butler et al. (2009) who all demonstrated no significant differences in gait velocity between ACLR and controls. Georgoulis et al. (2003) was the only study to assess other performance outcomes in ACLR as with the present study Georgoulis et al. (2003) demonstrated no significant differences in cadence between ACLR and controls.

The ACLD performance data was again consistent with several other studies that had assessed a variety of gait spatiotemporal outcomes (Button et al. 2006; Von Porat et al. 2006; Fuentes et al. 2011; Lindstrom et al. 2010; Roberts et al. 1999; Alkjaer et al. 2003 and Georgoulis et al., 2003). Contrary to the present study Gao et al. (2010) discovered a step length when comparing an ACLD group to controls. The study by Gao et al. (2010) and the present study differed in one key area. The ACLD group assessed by Gao et al. (2010) was on average only three months from injury, whereas the ACLD group in the present study were 32.3±69.4 months from injury. Considering

the differences in time from injury to assessment between the studies and the time dependent recovery of gait performance outcomes described in those suffering ACL injury (Button et al. 2006), this could be a factor in the discrepancy between the gait performance results of the present study and that of Gao et al. (2010). Nevertheless Button et al. (2006) demonstrated that performance of normal step length in ACLD took approximately one month to recover regardless of functional group (copers, non-copers and adapters). It would then be expected that the ACLD group studied by Gao et al. (2010) would have returned to normal step lengths. It is difficult to ascertain the reasons for this, there are many possible influences on recovery that were not discussed in enough depth within each paper, including the type and amount of rehabilitation that took place and adherence to the rehabilitation program.

Longitudinal analysis of performance outcomes for gait showed no significant changes within the ACLR2, with the exception of stride length which was significantly shortened from visit one from 1.37±0.2m to 1.19±0.1m at follow up. Control values for stride length were 1.29±0.1m, showing that the stride length in the ACLR2 was initially larger (and was representative of the full ACLR which had a stride length of 1.39±0.2m) but then had a big swing towards a reduction in stride length. This was the only variable that showed a significant change over time in the ACLR2 for any of the performance, kinematic and kinetic outcome measures. It is difficult to ascertain the reasons why stride length would be impacted and not the other gait performance and kinematic variables. Stride lengths may be affected by factors associated with data analysis limitations and learning effects by the group. Of the ACLR2, two participants had a marked reduction in stride-length (1.60 to 1.23m and 1.73 to 1.36) that had a marked impact on the significance level; removal of these participant's moved the outcome to non-significance. It is possible that having already undertaken analysis at first visit some participant's would be familiar with the location of the force platforms. This could have potentially influenced them to adjust stride lengths accordingly to target the platforms. The location would have become evident as part of the verbal instructions to the participant in order to perform activities such as the SLS at the first assessment at the RCCK.

This idea of a reduction in performance in jogging, represented by a lower jogging velocity, would mean lower accelerations and could provide in part an explanation for the lower knee moments demonstrated in ACLD and ACLR groups. However, the present study's ACLD and ACLR groups demonstrated no significant differences when

compared to controls. In other studies that have assessed jogging performance in ACLR groups this was standardised by Karinikas et al. (2009) and Tashman et al. (2004), both selecting a standardised jogging velocity of 2.5m/s. Bush-Joseph et al. (2001) when comparing ACLR and controls used a participants self-selected jogging velocity which allowed for a more direct comparison of results with the present study. As with Bush-Joseph et al. (2001) the present study found no significant differences between the ACLR group and controls jogging velocities, with jogging velocities found to be on average 2.7m/s for the ACLR and 2.58m/s for the controls, these values were comparable to the present study's ACLR group (2.82±0.5m/s) and controls (2.78±0.4m/s). Thus further discussion comparing results between studies can be undertaken with a degree of confidence that the ACLR group were performing in a similar manner.

Although it was hypothesised that there may be performance deficits within the present study's ACLR group, it is worth considering that the present study, and that of Bush-Joseph et al. (2001), assessed ACLR participant's at a time from surgery on average greater than 12 months. Karinikas et al. (2009) noted that gait deficits in performance may be time dependent and therefore only evident in the early stages following reconstruction. By 12+ months full recovery of normal mechanics or adaptations in kinematics and kinetics, may have taken place that allow recovery of performance. Data from the ACLR2 also suggests that once performance is returned to the level of controls in ACLR that this is maintained longitudinally. The ACLR2 group's gait velocity was 3.0±0.3m/s at visit one and 2.9±0.4m/s at visit two this was comparable to the full ACLR group's volitional jogging velocity at 2.8±0.5.

It might be expected that due to the higher demands placed on the knee during jogging and in consideration of the mechanical deficits those with ACLD are proposed to suffer in the absence of the ACL, that the ACLD group would be hypothesised to be more likely than the ACLR to show performance deficits when compared to controls. Contrary to this hypothesis the ACLD group showed no significant differences with the controls with regard to jogging velocity. This was in agreement with observations by Patel et al. (2003) and Berchuk et al. (1990). The respective jogging velocities of the ACLD investigated by Patel et al. (2003) and Berchuk et al. (1990) were on average velocity of 2.6m/s and 2.8m/s respectively, this was in line with the current investigation (2.72±0.5m/s). Rudolph et al. (2001) who analysed ACLD participants in two sub-groups, copers and non-copers, found no differences in jogging velocity

between these groups, however when compared to the controls these were both significantly slower.

Comparison of these studies is difficult as Rudolph et al. (2001) used a normalised jogging velocity per participant's leg length whereas other studies have used standardised jogging velocity or group 'absolute' self-selected velocity. Differences in results between ACLD groups could be explained by observing the time from injury to assessment. Patel et al.'s (2003) ACLD group had an average time from injury of 21±31 months, which was comparable to the present study's assessment time from injury at 28.8±12.2 months. Rudolph et al. (2001) gave no specific information on time from injury to assessment of their ACLD group, and only stated that it consisted of eight copers more than a year from injury and ten non-copers, assessed within eight months since injury.

For the measure of squat depth during the SLS there were no significant differences between participant groups. SLS descent velocity and ascent velocity also demonstrated no significant differences between groups. This was in opposition to the findings of Yamazaki et al. (2009) who demonstrated a significant reduction in squat depth in the ACLD group when compared to the controls. Differences between the present study and that of Yamazaki et al. (2009) may be explained by methodological and demographic differences. Demographic differences could be related to the participant's levels of function and the time from injury at which the assessment took place. Yamazaki et al.'s (2009) ACLD group appear to be low functioning as the squat ROM was limited to ensure successful completion of the task, whereas in the present study the ACLD group had to be able to complete the task to their perceived maximum depths. This caused a number of ACLD participants (n=5) in the present study to withdraw as they did not feel they could accomplish this. The removal of these participants increased the overall functional capacity in the ACLD group, reflected by a marked increase group activity level score, which was significantly lower than controls during gait and jogging, yet returned to non-significance for SLS. Therefore the remaining ACLD SLS group managed to perform similar to controls, although this tendency towards impaired performance was reflected in their SLS squat depth, the primary performance outcome.

The current study's ACLD group were also much further in terms of times from injury than the ACLD group of Yamazaki et al. (2009), whose participants had a time from

injury of 3.5±1.8 months for male patients and 3.0±1.7 months for female patients, compared to 21.5±7.9 months for the SLS ACLD group. Time from injury has been demonstrated to influence biomechanics in ACL injured groups (Button et al. 2006; Wexler et al., 1998; Karinikas et al., 2009). The combined factors of time from injury and activity level of the ACLD in the present study compared to that of Yamazaki et al. (2009) would influence the differences in results between these studies.

The ACLD in Yamazaki et al.'s (2009) study were also instructed on how to perform the SLS. They were instructed to cross their arms over their chest and to perform a half squat whilst keeping proper balance. This differed to the current study which allowed participants to use any strategy to stabilise the body including arm movement, which would have reflected how assessment would be undertaken within the NHS rehabilitation setting. The capacity for ACLD to use the trunk/arms as part of the balancing strategy may have allowed for greater knee control. The non-significant differences in squat depth could also be influenced by compensation strategies at the hip and/or ankle. Within the present study biomechanics at the hip and ankle were not investigated as the research question was focussed upon investigating the outcomes that would directly affect loading at the knee that may influence long term knee health. These outcomes alongside the multitude of MRi based outcomes developed for detecting changes in long term knee health, meant that outcomes had to remain focussed on the primary study aim and although investigation of strategies at the hip and ankle are important to see how these impact on knee biomechanics, these are indirect factors that were decided to not be within the remit of the current study's research aim.

It appears that within the current study that spatiotemporal measures during gait did not influence knee moments. In particular jogging velocity would not account for the decreased internal and absolute knee extensor moments discovered in ACLD and ACLR groups. For the SLS the non-significant trend towards a decrease in squat depth may in part account for the maintenance of knee moments. It was for these reasons that analysis of kinematics was undertaken to further investigate mechanisms by which ACL injured groups maintained or in the case of jogging reduced knee extensor moments.

For ACLM2, ACLM4 and ACLM7 who demonstrated evidence of degenerative changes, ACLM 2 had a corresponding low flexion angle for gait and jogging

corresponding to a lower ranking of internal knee extensor moment, suggesting this participant employed a kinematic strategy to reduce loading at the knee. ACLM7 also had a pattern associating knee flexion angle ranking to extensor moment ranking. However ACLM4 who had the lowest extensor moment for jogging by some margin had rankings in the middle of the spectrum for jogging knee flexion angle. Despite the expected relationship between knee flexion angles and knee moments as described in the literature, it appears that other strategies, such as directing loading to the hip and/or ankle are employed in certain individuals to reduce loading at the knee.

For gait the measurements of knee flexion and extension angles in the present study's ACLR group demonstrated a return to kinematic parameters similar to the controls, which is in agreement with Devita et al. (1998), Karinikas et al. (2009), Bush-Joseph et al. (2001), Georgoulis et al. (2003) and Webster et al. (2011). Contrary to these findings Gao et al. (2010) discovered that the ACLR group had a higher value of minimum knee flexion (less extension).

The assessment of ACLR participants by Gao et al. (2010) took place at a time from surgery that was defined loosely as 'typically within 12 months and no earlier than three months post-surgery'. Without accurate measurement of time since surgery to assessment it is difficult to compare the results of the present to that of Gao et al. (2010) especially in consideration of other studies that have shown time dependant recovery after injury/surgery (Karinikas et al. 2009). Adaptations in knee extension angles were also discovered by Karinikas et al. (2009), however this was at a time point of 3-6 months post-surgery. At 6-12 months some kinematic differences still existed but at the 12+ month assessment all kinematic values for knee flexion and extension angles had returned to being non-significant compared to the uninjured leg. This again demonstrates the importance of time since surgery when considering potential adaptations in ACLR. For kinematic measurements in the frontal plane the current study's ACLR was in concurrence with Georgoulis et al. (2003), Butler et al. (2009) and Webster et al. (2011), who also found no significant differences existed between peak knee adduction angles during the stance phase of gait when compared to the control condition. The ACLD group in the present study also demonstrated no significant differences in frontal plane kinematics.

Injury to the ACL and the development and progression of OA has previously been associated with increases in knee adduction angles and internal knee abductor moments

(Butler et al. 2009; Miyazaki et al., 2002). The absence of frontal plane kinematic and kinetic differences across all activities in both ACL injured groups may suggest that, within the current study's timeframe, these groups were not at increased risk of re-injury or development of OA when focussing on frontal plane knee kinematic and kinetic outcome measures.

The present study conflicts with a number of studies that have shown that differences in peak knee flexion angles exist in those with ACL deficiency compared to control conditions. Hurd and Snyder-Mackler (2007) and Beard et al. (1996) reported that during mid-stance a significant increase in peak knee flexion angle in their ACLD group was observed compared to the control condition. However other studies have demonstrated the opposite adaptation, Berchuk et al. (1990) stated that the ACLD demonstrated a significant decrease in peak mid-stance knee flexion angle compared to healthy controls but not when compared to the contra-lateral limb. With regards to minimum knee flexion angles Gao et al. (2010) demonstrated that their ACLD group were significantly less extended (more flexed) at the knee during a majority of mid-stance. This finding also concurs with the findings of Muneta et al. (1998), Fuentes et al. (2011) also discovered significantly less knee extension during terminal stance. Interestingly, Roberts et al.'s (1999) ACLD group had increased knee extension angle when compared to controls.

The frontal plane kinematics for gait in the present study concurred with those of Georgoulis et al. (2003) and Roberts et al. (1999) who demonstrated no significant differences in peak knee adduction angles in ACLD groups when compared to controls. In contrast Gao et al. (2010) found a significant increase in knee adduction angle in ACLD when compared to controls during the stance phase of gait. Differences between the current study's results with the aforementioned studies could be due to a number of key factors. Time from injury again appears to be a deciding factor when assessing differences between studies with Gao et al. (2010) and Muneta et al. (1998) group being assessed relatively close to injury at a time period of approximately 3-6 months, whereas Roberts et al. (1999) who found the contrary result of an increased extension angle, when compared to both the current study and that of Gao et al. (2010) and Muneta et al. (1998), had a time from injury on average of over 47 months. It could be hypothesised that the present study's ACLD group were at a stage where an increasing of knee extension over time from the point of injury had returned knee extension angles

to a level comparable to the controls at time of assessment, with an average time from injury of 32.3±69.4 months.

Comparison of adduction angles between studies must be treated with caution due to limitations in the Plug-in Gait marker system, which in its original form found adduction angle measurement to be erratic (for reasons described in Chapter 4.9.2.3), particularly at higher degrees or knee flexion, thus requiring the development of the frontal plane correction tool. However, investigation of internal knee abductor moments in the present study was shown to be consistent, despite the correction required for knee adduction angles. Therefore interpretation of internal knee abductor moments in the present study can be done so with a degree of confidence.

For jogging there was evidence that a reduction in knee angles may help explain the reduction in internal knee extensor moment, as there was a significant difference between groups with regard to a reduction in early stance peak knee flexion angle with no other differences for sagittal and frontal plane outcome measures. A reduction in knee flexion angle would have directly impacted on knee extensor moments. However, further investigation of peak knee flexion angle demonstrated that both ACLR and ACLD groups had no significant differences with the controls.

The current study's data for the ACLR group agreed with that of Karinikas et al. (2009) who demonstrated ACLR returned to more normal knee flexion angle values as time progressed toward 12 months post injury. Tashman et al. (2004) and Bush-Joseph et al. (2004) also discovered no significant differences between limbs with regard to flexion and extension angles when using the uninjured limb as a control during jogging activity. The current study's ACLR group included in the jogging analysis were on average 11.96±7.0 month's post-surgery, meaning the current study's results are comparable with regard to time from injury. It is of interest that despite this change in kinematics for jogging towards that of controls, at the time of first assessment the ACLR2 were functioning with increased mean peak knee flexion angles when compared to the main group of ACLR and more in line with controls for gait (ACLR2=17.6±7.6°, ACLR=16.1±6.4°, Control=17.5±6.4°), jogging (ACLR2=39.8±5°, ACLR= 34.1±9.0°, Control=39.0±5.8°) and SLS (ACLR2=76.8±11.7°, ACLR 70.8±14.7°, Control=77.8±11.5°).

The increases in both peak knee flexion angles (in all activities) and minimum knee flexion angle during jogging when compared to the full ACLR group, suggest the

ACLR2 were not representative of the full ACLR from a kinematic perspective. Minimum knee flexion angle was the only parameter to significantly change between visit one and visit two, showing a significant reduction from 14.5±5.2° to 12.0±4.1°. This was in the direction of controls (11.4±8.3°) but still higher than the full ACLR (9.4±6.8°).

The increased minimum knee flexion angle (equating to less extension) demonstrated in the ACLR2 may be representative of a strategy to avoid extending the knee maximally in the late stance phase; which has been cited as a protective strategy to increase knee stability. In the latter part of stance an increase in minimum knee flexion angle may place the knee in a more favourable position to increase eccentric hamstring activation and in turn increase knee stability. It has also been suggested by Rudolph et al. (2001) that an increase in minimum knee flexion angle places the knee in a less vulnerable position than when approaching full extension, were there can be large shear forces acting on the knee. The significant reduction in minimum knee flexion angle over time might be considered a return to more normal function, related to time dependant adaptations in the ACLR2.

The jogging data for the ACLD group showed a non-significant trend towards a reduction of peak knee flexion angle. In the early stages of recovery this reduction in peak flexion angle has been hypothesised to be a protective strategy in the absence of the ACL. Fuentes et al. (2011) state that knee stability is dependent on the remaining structures in the knee, both the remaining passive structures such as the ligaments and menisci alongside active muscular control. These passive structures may also have been injured or take time to compensate for the loss of the ACL, therefore in the earlier stages after injury a reduction in knee flexion may reduce loading at the knee to reduce vulnerability to further injury. This is investigated in greater depth in Chapter 7.4.

Hurd and Snyder-Mackler (2007) and Rudolph et al. (2001) proposed the reduction in knee flexion angle could be a stiffening strategy linked to a co-contraction of the quadriceps and hamstrings. Hurd and Snyder-Mackler (2007) state that these co-contractions could result in higher knee forces to stabilise the knee, but also potentially overload the knee cartilage. However it remains to be seen if the adaptation strategies observed in ACLD during the early phases after injury are protective or may initiate further damage to structures within the knee which are indicative of degeneration of knee health, before long term adaptations (which may also have potential detrimental

effects) or reconstructive surgery to stabilise the knee can take place.
Despite a significant reduction in internal peak knee extensor moments there was no corresponding adaptation in performance or kinematics in ACLR. In the ACLD group there was an indication of a potential kinematic strategy to reduce knee moments however this was not supported statistically. This suggests that other adaptations in biomechanics have taken place at the hip and ankle to maintain performance and knee kinematics but with a reduction in knee moment. There are important biomechanical outcomes to investigate adaptations at the hip and ankle in those with ACL injuries; however the remit of the present study was to investigate a potential biomechanical link as to how ACL injury leads to OA. Therefore the variables of interest in the present study were targeted primarily to investigate this question and focussed around the knee.

For the SLS the ACLD group had a non-significant trend towards a reduced knee flexion angle and the ACLR group a non-significant trend towards a reduction in knee ROM with the ACLD group demonstrating a significantly reduced knee ROM, yet interestingly had a similar knee moment when compared to the controls. It could be hypothesised that the reduction in knee flexion and ROM may be an adaptation strategy to keep loading close to or slightly reduced compared to a normal healthy knee in order to preserve stability, reduce pain or reduce further susceptibility to damage. Further damage may be caused if increased knee flexion angles pushed the knee outside normal boundaries of loading and stability, creating excessive stress on structures of the knee. The more the knee is flexed the centre of mass moves further away from the knee centre of rotation, increasing the lever arm and in turn increasing loading at the knee (McGinnis, 2013). The author suggests that this strategy of reducing knee flexion in those with ACLD will decrease the external moment acting on the knee, reducing the amount of external loading to a level that muscle contraction/co-contraction and other passive structures can control the movement whilst maintaining a stable knee position.

Yamazaki et al. (2009) demonstrated that those participants with increased knee flexion angles demonstrated less hip flexion, if this was demonstrated in the present study, this would support the idea of an inter-relationship between a reduction in knee flexion angle with a corresponding increase in hip flexion angles in order to achieve a ‘feeling’ of greater squat depth. This would impact on interpretation of squat depth as a measure of knee function (therefore knee flexion angle was also included in analysis). Squat depth values were 0.28±0.08m for controls, ACLR 0.25±0.09m and ACLD

0.24±0.06m. Peak flexion angle also demonstrated the same order with controls (77.8±11.5°) showing the greatest knee flexion followed by ACLR (70.8±14.7°) and ACLD (66.8±7.7°). Correlation between squat depth and knee flexion angle was significant for all groups, however the *r* value for ACLD (r=0.558, p=0.005) was lower than the control (r=0.673, p<0.001) and ACLR (r=0.746, p<0.001). This suggests that other strategies at the hip or ankle must be taking place to ensure that squat depth (vertical centre of mass displacement) was adapted to just within normal levels.

The present study's results for sagittal plane peak knee flexion angles were in line with that of Yamazaki et al. (2009) who also demonstrated similar knee flexion angles in their control and ACLD group, with the present study demonstrating 77.8±11.5° of knee flexion for the controls and a significant reduction in angle to 66.8±7.7° in the ACLD group, this was comparable to Yamazaki et al. (2009) who showed 74.3±13.6° and 64.7±19° for the control and ACLD groups respectively.

Contrary to the current study, which showed no significant differences in peak adduction angle or frontal plane knee ROM, Yamazaki et al. (2009) demonstrated frontal plane kinematic changes in ACLD with increases in knee adduction angle when compared to controls. However, the measurement of frontal plane angles needs to be treated with caution due to the previously stated issues with alignment of the frontal plane and calculation of adduction angles using the Plug-in Gait model, which required for the development of the frontal plane knee alignment correction tool (Chapter 4.9.2.3).

Another difference between the studies is the use as mass as a covariate in the present study and the use of normalisation, whereas Yamazaki et al. (2009) did not. Analysis without inclusion of potential covariates may have led to different findings, as in this case the influence of body mass on frontal plane kinematics may cause statistical differences. It could be hypothesised that heavier body mass leads to increased external joint moments and a greater requirement for larger internal muscle forces to control these moments. When body mass was factored in to the calculation any differences in kinetics would have been removed. For this reason body mass was identified as a key demographic outcome and a key risk factor to be investigated in the ACLM for the development of early OA due to its direct impact on knee loading (see Chapter 7.5).

It appears that for gait the present study's ACLD and ACLR groups are capable of returning to normal gait spatiotemporal, kinematics and kinetics within the time frame

of the present study. This was also the case for jogging velocity and kinematics despite evidence of kinetic adaptations. The SLS activity interestingly showed maintenance of kinetics and squat depth at normal levels but adjusted kinematics. This demonstrated, as hypothesised, that as activity demand increased, differences compared to controls were more evident. This emphasises the need to assess tasks that involve a large single leg stance component as these place more demand on the injured knee, thus requiring greater amounts of muscle contraction/co-contractions and proprioceptive response to control the movement that may not yet have fully recovered (or may never fully recover). This highlights that assessment of gait alone in those suffering ACL injury, particularly in those who have apparently recovered appropriately post injury/surgery, may not be sufficiently challenging to evaluate movement deficits and in turn knee loading that may influence long term knee health. It is also unknown that this return to normal knee mechanics in ACLD is a desired outcome after ACL injury for long term knee health and function, if as other studies have suggested that unstable non-copers have shown more normal knee kinematics. This again raises the importance of using individual analysis to explore the idiosyncrasies of how a patient's level of function, biomechanics and demographics in combination may impact on long term knee health.

Both the present study's ACLD and ACLR groups could be categorised as typically being in the short to medium term post injury. It might be that there are time dependant adaptations in movement and structural changes that take place in ACL injured groups that have been described in the literature. It is also possible that those with higher activity levels subject the knee to more repeated bouts of loading that if abnormal or creating stresses on other tissues influence the development OA. Therefore the following chapter will discuss two main areas that may influence the findings from both the biomechanical and MRi analysis and differences in findings to the literature; time from injury and activity level.

7.4 Discussion of the Impact of Time from Injury and Activity Level on Biomechanics.

7.4.1 Discussion of the Impact of Time from Injury/Surgery to Assessment on Spatiotemporal, Kinematic and Kinetic Outcomes.

The framework developed from internal knee extensor moments from other studies assessing gait showed a time dependant return to normal levels during gait. This was also demonstrated within the present study's ACLD and ACLR groups at a comparable

timeframe. However, also in line with other studies jogging knee extensor moments were significantly reduced. It was hypothesised that this may take longer to recover being a more demanding activity than gait, however longitudinal assessment of jogging showed no changes in kinetics in the ACLR2 suggesting that jogging mechanics were maintained.

It is of note that the ACLR2 group were higher functioning, being more in line with controls for kinetics at visit one and therefore ascertaining long term kinetic changes in this group would not give insight into the full ACLR and ACLD groups. To give further insight into the proposed time dependant adaptations described from literature, the present study investigated the relationship between time from injury and kinetics, alongside kinematic and performance outcomes for all activities.

Despite the proposed time dependant adaptations further investigation of time from surgery and kinetics showed no significant correlations in the ACLR for gait. However as the range of time of participant data collection was 3-36 months, with 23 of the 29 participants falling within a timeframe of 6-18 months, as the ACLR were relatively tightly grouped around the mean producing a small standard deviation thus this finding might be expected. Therefore a wider range of time from surgery values, and more participants, would be required to thoroughly evaluate time related changes in internal knee extensor moments during gait.

Within the present study the range of time from injury to assessment in the ACLD group was larger, from 4-288 months; this provided an opportunity to explore the relationship of the time from injury with kinetic outcomes for gait in the ACLD. As with the ACLR participants no correlations existed between kinetic parameters and time from injury. This may suggest that time dependant adaptations may not exist in ACLD participants. Intuitively this may seem at loggerheads with the expected avoidance of loading on the injured knee due to pain and effusion in the early stages after rupture or surgery in the case of the ACLR. However data was only collected from a minimum of four months. Button et al. (2006) showed a return to normal gait characteristics in ACLD within a period of three months; it might be that the present study's ACL injured groups were all at a time at which a majority would have recovered normal gait mechanics.

The idea that jogging takes longer to recover biomechanics than gait due to the higher demand on the knee and would therefore be more likely show associations with time

from injury/surgery in the present cohort, was supported in the ACLR group with time from injury/surgery being associated with internal peak knee extensor moment. However despite this association in ACLR the ACLD groups did not display this relationship. It is possible that the grouping of time from injury may impact the findings between groups, however as with gait a majority (18 of 27) of the ACLR group included in the jogging task were between three and 12 months post-surgery, and 16 of the 27 ACLD jogging group were within the same frame post- injury. The remaining participants in both the ACLR and ACLD groups had a wide variability but tended to be at a much greater time from injury/surgery in the ACLD group than the ACLR. The positive correlation for knee extensor moment in ACLR, albeit just significant, must be treated with caution for several reasons. Firstly, all other jogging outcomes did not result in any significant relationships with time from injury/surgery for both ACLR and ACLD groups which might be expected. Secondly the SLS data also showed no associations of time from injury with kinetics, kinematics and performance outcomes.

It is probable that although time from injury would be expected to be related with kinetics, that in the initial period of recovery after injury/surgery, where there is increase amounts of swelling, pain and a reduction of knee ROM, the present study had limited data. It is also important to consider that after initial recovery that it is the level of activity to which a patient returns that is the more direct influence on knee function, biomechanics and amount and type of loading that knee structures are subjected to that will influence long term knee health. For this reason activity level and it's associations with kinetic outcomes was investigated in both ACLD and ACLR groups and discussed in Chapter 7.4.2.

It has been stated that knee moments may be impacted by changes in spatiotemporal characteristics and kinematics (McGinnis, 2013). Performance showed no associations with time from injury/surgery for both ACLD and ACLR groups for all activities and of kinematic outcomes only peak flexion during gait in ACLR and jogging in ACLD were of interest. As with extensor moment during jogging in ACLR, there is a chance for the reasons described previously that this relationship was by chance. However, the highly significant relationship in the ACLD group is more intriguing, this suggests a time dependant return to normal knee flexion angles which would be in line with the literature for gait.

It might be expected that with kinematics being so closely related to kinetics, that a significant relationship with kinematics might also be demonstrated. However, as with the full group data a significant difference in knee moments was not associated with a corresponding difference in kinematic, suggesting other adaptations are at play to maintain or reduce knee moments. To investigate this idea further the ten ACLD who were over 12 months from injury and impacted the time from injury data by increasing the mean time from injury markedly to 28.8±12.2 were removed from the analysis of peak knee flexion angle. The seventeen ACLD under twelve months demonstrated that there was a significant reduction in peak knee flexion angle when compared to the controls. This exhibits the importance of a participant's time since injury when assessing potential adaptations in those with ACL injuries. There was nevertheless no correlation between time from surgery and peak knee flexion angle in the ACLR group. The author suggests that the close grouping of the ACLR time from surgery demographics means that finding well supported and consistent associations of time from surgery with biomechanics within the present study was unlikely, although this is likely to exist from assessing the weight of evidence from the literature. This also demonstrates that reconstruction helps a quicker return to knee kinematics, as this was not significantly different to controls at a comparable time frame of the abridged ACLD group.

There is limited knowledge about the structural changes that take place after injury in those with ACL injury. The lack of significant findings from MRi assessment may be caused by the assessment taking place at a time period in which degenerative changes had not yet manifested. Interestingly ACLM4, who was the only participant to show worsening of total knee score, was assessed at a time point the furthest from time of injury to follow up at a period of 91 months. This may mean that initial improvement in knee abnormalities (demonstrated in the other ACLM) had been made followed by a second period of worsening that took place up to the time at which the current study assessed ACLM4 at follow-up scan, following a model described in the framework of potential structural adaptations after ACL injury (Figure 3.7.3).

Considering the diagnostic scan for ACLM4 took place at 64 months after suspected ACL injury, which was further from injury than every other participant at their follow-up scan, it might be expected that the score at this time frame would be low as improvements in BMA and meniscus would have been evident at a time frame more in line with follow up in the other participants. This view is supported as at the time of the

diagnostic scan ACLM4 score was low when compared to the other participants, scoring only eight when other participants totalled at least a score of 11 (with the exception of one participant who scored seven) and was more in line with the follow up scan of other participants who demonstrated a mean of 7.8±7.1.

However contrary to this, the other ACLM's of interest who demonstrated worsening of cartilage score, were ACLM2 who had the fifth longest time period to follow-up scan at 40 months and ACLM7 who had the shortest time from injury at 19 months. This would be in contrast to the idea that degenerative changes may start to take place at a time period outside of which a majority of the participants included in the present study were assessed at follow-up. However the changes in total cartilage score of two and three respectively were relatively small in comparison to the total possible score available of 72 (12 regions each with a maximum score of six), more long term analysis may be required to determine more noticeable changes in cartilage morphology within these participants and as a group as a whole.

It may also be due to as only a percentage of those with ACL injury, and subsequent repair, develop signs of early OA within the time scale of the present study, with more longer term studies (at around 15 years post injury) showing rates of between 16 and 80% (Neuman et al. 2008; Øiestad et al., 2010; Neuman et al. 2008), that finding only one participant with significant degenerative changes in the knee from a small cohort might be expected especially within the relatively short time frame from injury at which the ACLM group were assessed. More research is required to identify those who show evidence of degenerative changes and at what time points these changes typically start to present themselves. This is essential in order to investigate more thoroughly if it is those who adapt and reduce knee loading who are at risk of developing OA or if it those with higher levels of loading and function (discussed in the following chapter) that are at risk of further degenerative change.

7.4.2 Discussion of the Impact of Activity Level and Function on Spatiotemporal, Kinematic and Kinetic outcomes.

Despite no differences between ACLD and ACLR biomechanics for gait and jogging, the notion that ACLR returns those with ACL injury to more normal levels of function was supported as the ACLD group demonstrated a significant reduction in activity level when compared to controls which was not evident in ACLR. The ACLD group also

demonstrated a significantly worse score on both the complete Cincinnati knee and IKDC subjective knee function scores when compared to the ACLR group. This was also true for a measure of fear of re-injury (the TSK) being significantly increased in the ACLD group suggesting other factors such as an innate feeling of instability, lack of strength and/or pain may be influencing biomechanics and/or a return to more normal levels of activity that were evident in the pre-injury condition, with ACLR scoring 90.2±12.4 and ACLD scoring 93.6±7.3.

Despite the hypothesis that activity level would be associated with kinematic and kinetic outcomes for gait, no significant relationships existed between activity and any of the gait outcome measure in either the ACLD and ACLR groups. However this might be expected as gait is a low demand activity (Button et al. 2014), so even those with lower levels of function may successfully have returned to normal gait mechanics. This needs to be considered in the context of the distribution of the activity levels within the group; three participants scored 0-40, four scored 41-61, 13 scored 61-80 and 8 scored 81-100. This demonstrates that participant scores were distributed towards higher activity levels.

The range of activity level score for the control group was 40–100; this was the same range as the ACLR group. The control group had 22/29 participants with a score of 75 or over and the ACLR group had 27/29 participants in this range. This demonstrates that there was not a large enough number of participants in the lower functioning categories to resolve the impact activity level may have on kinetics for gait. This lack of association between kinetic parameters with both activity level and time from injury/surgery during gait, emphasises the importance of including analysis of activities that place more demand on the knee that may take longer to recover biomechanics as was demonstrated in jogging and SLS.

Interestingly current activity level was positively correlated with jogging velocity in all groups within the present study, suggesting that this outcome measure may be independent of ACL injury. Despite all groups showing a relationship between activity level and performance it is of note that only ACLD and ACLR groups had a positive relationship with kinetics and activity level, suggesting that this outcome is influenced more directly by ACL injury and performance can be maintained using other strategies. Despite no significant differences between ACL injured groups and controls for kinematics in jogging there was an association with activity level in ACLR and a non-

significant trend in ACLD, which would be expected due to the proposed relationships between knee extensor moments and knee flexion angles.

It remains to be seen if it is the participant's adherence to rehabilitation that allows higher levels of activity by increasing muscle strength, proprioceptive response and therefore allowing the knee to be placed in greater degrees of flexion, or if a premature return to higher activity levels places the knee in these positions and places the knee in a more vulnerable position that is detrimental to long term knee health. It might be expected that activity level would therefore show correlations with outcomes from SLS as this is also a more demanding activity than gait and showed kinematic differences to controls. This was in part supported as ACLR showed a significant relationship of activity level with peak knee flexion angle and sagittal plane knee ROM. Interestingly there were no significant findings for any of the outcomes for ACLD.

It is of note that the activity level for the ACLD group who completed both gait and jogging were significantly lower than the controls. There was an increase in the activity level closer to that of controls in the ACLD group who performed the SLS. This was caused by a reduction in ACLD group numbers who could complete each activity from 28 in gait, 27 in jogging to 20 for the SLS. The participants who could not perform the SLS activity due to inability to complete the task successfully or unable to take part (n=5) were typically on the lower end of function. When compared to the respective full group means 4/5 had lower gait and jogging velocities. For kinematics 2/5 had noticeably lower peak knee flexion angles for gait, however for the more demanding activity of jogging, 4/5 had lower peak knee flexion angles. With regard to normalised peak knee extensor moment, the most direct measure of loading at the knee, all five participants had markedly reduced moments when compared to the full group data; this was evident for both gait and jogging. This reduction in scores at the lower end of activity would have influence the relationships with ACLD biomechanics and explain a lack of associations with activity level for SLS outcomes, due to the increased levels of activity in the ACLD participants who could successfully perform the activity.

The presence of a range of activity level scores for gait and jogging adds some credence that there is an association between activity level and performance, kinematic and kinetic parameters as activity demand increases. Although caution must be aired as a small number of extreme values at the lower end of the score may cause leverage

towards a correlation, therefore more participants within the lower range of scores would be required in order to more firmly confirm the nature of these relationships.

It can be hypothesised that if participants had higher levels of activity this would expose the knee to greater amounts of loading. If this loading was outside the limits at which cartilage or other structures could successfully manage this may lead to degenerative change. It might also be that in certain individuals increases in muscle strength, proprioception and other adaptations creates stabilisation around the knee and protects the knee from structural damage and degeneration, enabling a safe return to higher levels of activity. These ideas were explored in the ACLM data.

Of those showing signs of degenerative change (ACLM2, ACLM4 and ACLM7) ACLM2 demonstrated a high level of function on the Cincinnati Knee Score (ranked 7th), this was also demonstrated by ACLM7 having the second highest level of function on both the Cincinnati and highest on the IKDC. This might add credence to the idea that increased activity exposes the knee to repeated bouts of abnormal loading that causes degenerative changes; however ACLM4 who showed the greatest amount of degenerative changes had the second lowest level of function for both IKDC and Cincinnati Knee score.

A point of interest is that both ACLM2 and ACLM7 showed only degenerative changes in cartilage and ACLM4 did not, demonstrating worsening of meniscal score and BMA. It is possible that activity level and other biomechanical outcomes may influence degenerative changes in different ways after ACL injury, dependant on the nature of associated injuries, the success of the surgical procedure and the person's willingness to regain range of motion and muscle strength. This suggests that OA can be seen as an end point, but the journey to this point may initiated by different mechanisms and be amplified by other risk factors such as age, body mass and the length of time the person has been subjected to these risk factors.

7.5 Discussion of Demographics and their Associations with Changes on MRi.

Within the present study key demographic risk factors identified as being an important influence for the development of OA were age and body mass (Louboutin et al., 2009). These were explored in the ACLM group to see if any associations existed with those demonstrating signs of degenerative change.

Both ACLM2 and ACLM7 were 27 years of age and joint ranked 3rd youngest, ACLM4 was also the youngest at 20 years of age, suggesting that age at least within this typically young cohort (six of eight less than 30 years of age) that age was not an associated risk factor for degenerative change. However due to the small number of participants over 30 it is impossible to ascertain how age may influence degenerative change or interact with other outcomes. Of the remaining participants ACLM6 was a participant of interest as they were the oldest participant at 49 years of age. However ACLM6 demonstrated improvement of meniscal and BMA score and had no cartilage morphology abnormality at either time point, they did however demonstrate an increase cartilage thickness in the CLF but a decrease in the CLT region knee greater than the MDC. As the majority of the group were under the age of 30 it is difficult to ascertain the influence of age on degenerative changes in the knee.

Interestingly ACLM6 also had another key risk factor for OA being the heaviest participant, as might be expected this meant having the largest internal extensor moment during jogging, however this was not the case for gait or SLS. ACLM7 despite being the second heaviest also did not demonstrate increased loading at the knee and in fact ranked lowest in peak internal knee extensor moment during gait, corresponding with a reduction in knee flexion angle, suggesting that knee moment can be reduced or maintained within normal levels; however this again hints that increases in kinetic outcomes values are not an appropriate predictor of those who show signs of degenerative change. This lack of association with body mass and degenerative change was emphasised as ACLM4 and ACLM2 were 3rd and 4th lightest respectively, therefore it could be hypothesised that changes observed in cartilage, BMA and meniscus were not associated with typical age and demographic risk factors that have been identified in those with onset of OA (Louboutin et al., 2009).

Despite kinetic outcomes showing limited associations with OA, which have been predicted in other studies, it is important to note that kinetics is an outcome of opposing forces and, although related, is not directly a measure of loading of structures inside the knee (McKinnis, 2013 and Perry and Burnfield, 2010). Therefore in order to fully uncover if there is a model of OA related to changes in loading, methods involving accurate measurement of degenerative change combined with accurate models of knee loading needs to be employed. This limitation of the present study and others will be discussed in the following chapter.

7.6 Study Limitations and Recommendations.

Within the present study limitations existed with regard to both the collection of 3D motion analysis data and the analysis of MRi data. The following chapter will discuss the study limitations and recommendations for future studies.

In relation to motion capture data the first limitation was related to the Plug-in gait marker system. In participants that have excessive body fat levels covering the bony prominences on the pelvis where the markers should be placed. This has the potential to create inaccuracies in the calculation of the hip joint centres. This will have had knock on effects on calculation of joint centres and calculation of angles and moments across the various segments.

Marker position, particularly of the thigh marker, highlighted another limitation of using skin based markers. The acute angle between the thigh, knee and ankle markers increased sensitivity to changes in position of the lower limb leading to abnormally high knee adduction angles. This led to the development of the frontal knee correction tool described in Chapter 4.9.2.3.

Despite the large reduction in knee adduction angles towards more expected levels when using the frontal plane knee correction tool (especially during the SLS), this had a negligible effect on knee moments. This suggests that adduction angle data should be treated with caution – However knee moment data can be used in a more robust manner.

A major limitation within the present study was the lack of test-retest reliability on marker positioning. This means that there may have been issues with both inter-and intra-rater reliability. However, as discovered when assessing the gap filling tool for recreating missing ASIS markers, errors in positioning of up to 10mm did not have a marked impact on knee moments. This creates another potential limitation as the Plug-in gait model may not be sensitive enough to detect subtle changes in movement related to dysfunction.

Aside from the previously aforementioned limitations relating to the use of external marker systems to determine joint centres and in turn joint loading. Walter et al. (2010) found that internal knee abductor moment was not associated with medial compartment contact forces assessed using a force measuring implant, although this was only in a single participant. This does however suggests that caution must be used when

interpreting the effect of kinetic data derived from external markers on internal forces within the knee.

There were several other possible limitations identified related particularly to the use of MRi to identify structural changes. Firstly, there is the potential for the tendency of increasing thickness between scans demonstrated in the present study may have been caused by errors induced into the MRi procedure due to a number of factors including differing MRi scanning locations and MRi operators under which the scanning took place. However these increases are unlikely to be caused by the scanning being undertaken in different geographical locations as sequences were matched by an experienced radiographer. It might also be expected that if the clarity or location of the image was affecting analysis that increases would be found across both compartments for a majority of the scan, this was not the case.

Scanning sequences used in the literature to assess cartilage change are specifically designed to do this with a high degree of accuracy and sensitivity. The slice thicknesses developed for specific modelling of the knee discovered in the literature are reduced compared to typical clinical scans like those in the present study. This creates more slices and therefore more data points for accurate reconstruction. This coupled with a smaller more focused field of view and higher resolution will enable a more accurate recreation of cartilage volume and thickness models than would be possible using clinical diagnostic scanning sequences.

This however means that the clinical applicability of modelling sequences for cartilage that use optimised imaging techniques is limited to answering research questions from the time of development of the imaging method. This was the deciding factor when developing and refining the current study's methodology, as using clinical scans created a unique opportunity to be able to retrospectively use the participant's diagnostic scan to map longitudinal changes. The use of clinical scanning sequences also enables the present study to use clinical scoring systems in conjunction with quantitative assessment in order to give a more complete view of structural changes that may occur that may be indicators of early degenerative knee changes. The present study's methodology for thickness measurement used a large number of sampling locations to determine a regional value to help reduce measurement error alongside a thorough visual assessment of the data, in order to inspect for unexpected values and potential errors.

Reliability analysis was undertaken using the ICC and SEM analysis (Chinn et al., 1991). As MRi analysis was undertaken by one reader (PR), who analysed 8 scans chosen at random from the available diagnostic and CUBRIC scans, it was the intra-rater reliability that was most important to the reliability of the study. PR demonstrated that for all regions the ICC showed excellent intra-rater reliability (Field, 2005). The SEM values demonstrated that the tibia had higher SEM values than the femur and this was greater in the medial compartment when compared to the lateral.

Another important outcome described within the assessment of reliability was that of the Minimum Detectable Change (MDC). This representation is the minimum change in regional cartilage thickness that is required to identify a notable change and was a particularly important tool with which to analyse individual data in the case series analysis to evaluate if changes in regional cartilage thickness were meaningful in the context of the MDC. There are several potential reasons as to why the SEM and in turn the MDC were markedly higher in the CMT (CMF=0.22mm, CLF=0.08mm, CLT= 0.69mm and CMT=2.13mm). However, pinpointing the cause of these differences is difficult. It is potentially due to the curvature that is evident in the medial compartment of the tibia. The fitting of pixels that are inherently straight edged to curves that have rapid changes in gradient, may mean that errors are more likely to take place by the operator when selecting data points. The greyscale for imaging at the bone/cartilage interface within this region was sometimes blurred and heavily graded making it difficult to accurately identify these borders. As each pixel side represents a length of 0.274mm, an error of 3 pixels between scans would be possible and could account for this error. As the operator then tended to follow this subjective greyscale 'line' this error once introduced would be evident for the full region in the slice. It might be expected that if this was a causal mechanism for the higher SEM and MDC in the CMT regions, it might also be expected to find greater SEM in measurements of the femur due to its curvature. However due to the relatively large size of the femur the gradient of the curve in this central portion was reduced, compared to the more anterior and posterior regions.

Validity and the accuracy of the above tool are difficult to assess as no direct precise measurements of the cartilage are available for the observed participants for comparison with the reported method. Other studies have developed cartilage modelling techniques and validated them using either cadavers or model knees, where the cadaveric knee underwent an MRi scan, then measurements from the segmentation

was compared to a 'hands on' measurement ex vivo. Another common method for assessing validity of MRi segmentation and analysis techniques is to compare the findings with that of more refined imaging techniques such as computerised tomography (CT) scanning (Eckstein, 2000; Gandy et al. 2002; Li et al. 2005). This type of validation was not undertaken in the present study due to the time constraints placed upon it. Therefore, validation could only be performed within the context of values for cartilage thickness measurements performed in similar regions in other studies for comparison. We acknowledge this does not directly validate the accuracy of the measurement however gives a guideline as to whether these are comparable.

Data presented below in Table 7.6 shows the cartilage thickness measurements for the regions described in the current study with the comparative regional thickness measurements from key studies that have measured regional cartilage thickness.

Table 7.6 Regional cartilage thickness measurement for the present and key studies from the literature.

	CMF (mm)	CMT (mm)	CLF (mm)	CLT (mm)
Present Study	2.85-3.26	2.90-3.37	2.96-3.07	3.76-3.81
Andriacchi et al. (2006)	2-3.5	2-5	2-4	2.5-5
Andreisek et al. (2009)	2.4	2.6	2.3	3.6
Li et al. (2005)	2-2.2	1.8-2.5	2.3-2.9	2.8-3.2

The approximate thicknesses in mm (millimetres) discovered in the CMF (Central Medial Femur), CMT (Central Medial Tibia), CLF (Central Lateral Femur) and CLT (Central Lateral Tibia) regions of the knee for the present study and key papers.

The results of the current studies ACLM cohort showed that average medial femoral thickness ranged from 2.85±0.64 to 3.26±0.60mm between reliability assessments. Andreisek et al. (2009) found that in an ACLR cohort of 52 participants approximately seven years post-surgery a cartilage thickness in the same region was on average 2.37mm. The average medial tibia thickness in the current cohort (2.90±0.53 to 3.37±0.88mm) was again higher than that of Andreisek et al. (2009) who showed an average thickness of 2.56mm. In the lateral compartment Andreisek et al. (2009) demonstrated femoral thickness of 2.31mm and tibia thickness of 3.58mm; these were

again lower than the values reported by this study, with the lateral femur showing values of 2.96±0.29 to 3.07±0.33mm and 3.76±0.74 to 3.81±0.85mm for the lateral tibia.

The lower value reported by Andreisek et al. (2009) is potentially due to the ACLM demographics being different to that of the participants in the study by Andreisek et al. (2009). Body mass was on average 78.1±6.5kg and 1.76±0.1m tall in the present study, whereas Andreisek et al. (2009) group were on average 75.6kg with no details given for height. A greater proportion of the Andreisek et al. (2009) study was female (24/52) compared in the present study (1/8). These differences in mass and gender may mean that participants in Andreisek et al. (2009) study had a tendency for smaller joints and therefore expectancy for smaller cartilage volumes and thicknesses.

In agreement with the studies in Table 7.6 our data showed greater overall cartilage thickness in the lateral compartment of the knee compared to the medial compartment. It has been hypothesised that the regions of the knee where cartilage is thickest are those most greatly loaded, which is contrary to the findings from biomechanics studies using external marker systems which would expect to load the medial compartment of the knee, as the typical gait pattern produces an internal abductor moment which is proposed to load the medial side at greater levels than the lateral side (Georgoulis et al. 2003; Butler et al. 2009; Webster et al. 2011). This may demonstrate a limitation of external marker systems in predicting internal knee motion discovered using MRi and modelling techniques.

Loading of the lateral compartment may be achieved internally by the recruitment of both passive and active knee structures to counteract the internal abductor moment. It could be hypothesised that if knee moments (and in turn loading) are increased or at a level that active and passive structures cannot maintain normal knee loading, that the that the medial compartment may be loaded outside of its normal limits, on areas that are ill adapted for loading, initiating degenerative cartilage changes (Li et al. 2005; Andriacchi et al. 2006).

As no significant differences between time points were discovered in any locations for cartilage thickness change, it is possible that quantitative assessment may not have been sensitive enough to detect potentially small annual changes (Koo et al., 2005). Quantitative assessment of structures in the knee joint, particularly cartilage, in investigations in those with or likely to develop OA is dependent on the accuracy and

reliability of the scanning image. Accurate techniques for segmentation of the structures in the knee either manually or automatically is of huge importance, this allows for an accurate reconstruction of these segments to create cartilage models to detect what are potentially small changes in cartilage morphology between scans; this is also vital for the validity of the interpretation of results (Koo et al., 2005).

It is also possible that significant differences were not found due to the small sample size which is a key limitation of the study for both MRi methods. Therefore a case series style of analysis was performed to explore the relationships between MRi data, biomechanics and patient reported measures of function in greater depth, as the low numbers did not provide sufficient power for inferential statistics. It is worth noting that using individual biomechanical data is not a practiced technique in the motion analysis community. Group data is often used to reduce the influence that errors in measurement, most likely introduced by the operator misplacing markers or markers on clothing moving which may influence angles and moment. Therefore using this type of analysis on individual patients must be interpreted with caution.

Another limitation of the MRi aspect of the study was the absence of analysis of the patellofemoral joint with studies showing OA changes can manifest themselves in this region (Hunter et al.,2011). Unfortunately within the present study, the image sequences used for quantitative analysis did not clearly image this region with enough clarity to segment and map thickness changes. We acknowledge there was an opportunity to assess the patellofemoral joint using the semi-quantitative measurement; however in the initial development of the study the focus was to identify regions of cartilage that could be compared using both of the MRi methods. Patellofemoral assessment using both MRi methods would be an outcome that future research into the development of OA could focus up on, assuming appropriate imaging of the patellofemoral joint was available. This also emphasises the aforementioned need for more long term studies to use more specialist imaging sequences for quantitative assessment, to allow for accurate assessment of all the regions in the knee.

To improve future research using the current methodology, data for MRi must be collected in larger sample sizes, over extended periods of time, so that changes in MRi can be grouped in the context of other outcome measures including biomechanics, demographics and subjective functional, with enough power to draw firmer conclusions. The addition of other outcomes, such as assessment of the patellofemoral

joint and calculation of the knee adduction angular impulse (which allows for both the magnitude and duration of loading of internal knee abductor moment), can potentially give a deeper insight into the mechanisms by which degenerative changes take place after ACL injury and subsequent reconstruction.

The addition of other methods such as EMG, to assess muscle activation patterns in the lower limb and fluoroscopy, to image the knee during motion, could be combined with motion analysis and more detailed imaging and segmentation models of the knee joint. This would lead to more accurate patient specific model to investigate the effect of knee loading patterns on long term knee health after ACL injury.

Chapter 8 Conclusions.

The overall aim of this study was to investigate if evidence existed of degenerative changes to knee structures in participants after ACL injury and if these changes were associated with biomechanical outcome measures cited as a potential causal mechanism in the development of early OA (Andriacchi et al, 2004; Chaudhari et al., 2008; Hosseini et al., 2012). This was undertaken in 3 distinct steps; firstly biomechanical assessment was undertaken to assess performance, kinematic and kinetic differences when compared to healthy control participants. Secondly structural changes in the knee were investigated using a bespoke quantitative and semi quantitative MRi analysis. Finally, a case series analysis which combined outcomes from the first two parts of the study in order to explore if associations existed between structural changes in the knee with demographic, biomechanical and patient reported measures of functions.

Performance of both ACL injured groups appears to return to normal in a time period of greater than 12 months for all of the functional tasks performed within the present study and analysis of the ACLR2 group suggests that performance is maintained longitudinally in ACLR participants. However, it is worth noting that due to reduction in size of the ACLD group in the SLS activity, due to some participant's inability to perform the activity safely, that this could be interpreted as a deficiency in a portion of ACLD population. Therefore this suggests that a proportion of the ACLD are not fully rehabilitated, and those who cannot perform the SLS activity would not be returning to normal activity and require either further rehabilitation or surgical intervention. Surgical intervention improved patient reported measures of function and activity levels, and should therefore be recommended to those who have an ACL injury who cannot complete tasks relevant to sport and wish to return to this level of activity.

Data from the present study was in line with that used to create a framework for kinetic adaptations after ACL injury. As the analysis moved to a deeper level of kinematics and kinetics the ACL injured group's demonstrated increasing evidence of differences with controls. Despite gait returning to normal levels jogging showed a reduction in knee extensor moment in both ACL injured groups, both of which were in line with previous literature on ACL injured groups at a comparable timeframe. This reduction in internal knee extensor moment during more demanding activities has been cited as a protective strategy for reducing excessive loading on the ACL graft or to reduce

general knee loading in the absence of the ACL (Hurd and Snyder-Mackler, 2007; Andriacchi and Dyrby, 2005; Alkjaer et al., 2003; Wexler et al., 1998). Despite the SLS showing no differences in performance and kinetics compared to controls, both ACL injured groups showed sagittal plane kinematic differences, relating to a reduction in knee flexion angles. This was hypothesised to help maintain knee moments and in turn loading within normal levels, to help protect the knee from further injury and/or abnormal loading.

Abnormal loading has been suggested to be a potential causal mechanism in the development and progression of OA (Andriacchi et al, 2004; Chaudhari et al., 2008; Hosseini et al., 2012). This link was investigated by combining MRi analysis (measuring changes in regional cartilage thickness and scoring of articular features), with indicators of knee loading such as kinematics and kinetics. Interestingly despite the ACLR group showing a reduction in extensor moment during jogging the ACLM cohort were functioning at a level more comparable to the controls. This enabled insight into a key question of the study, 'does a return to more normal kinematics and kinetics have implications for degenerative knee change?' perhaps indicating that the reduction in knee moments demonstrated in the ACLR and ACLD groups may be protective of degenerative changes.

Using the quantitative MRi method we had to accept the null hypothesis that there were no changes in regional cartilage thickness between diagnostic scanning and follow up. This could be explained due to time frame at which the MRi evaluation took place, as the expected small annual changes demonstrated even in those with pre-existing OA would not have manifested themselves to a great enough extent to be detected by the current studies bespoke method. There was however mild changes towards significance in the CMF and CMT regions with an increase in cartilage thickness. Other studies have also demonstrated thickening of cartilage after ACL injury as a result of swelling, and this has taken place primarily in the central portion of the medial femur. It is hypothesised that after initial swelling a cascade of reactions can take place from the inflammatory response which can lead to cartilage breakdown and development of OA (Frobell et al., 2010; Hellio Le Graverand et al., 2009). However time related changes in cartilage after ACL injury and even in those with pre-existing OA, have yet to be documented in enough detail to determine where the current study's data falls in the context of a framework for the development of OA after ACL injury.

Regional cartilage variations suggest that areas of the knee with the thickest cartilage would have the greatest loading. This was demonstrated to be in the lateral compartment by the present and other studies (Kurz et al. 2005; Li et al. 2013; Andriacchi et al., 2009). This is an area for future research to see if external marker systems (which suggest the medial compartment is loaded to a greater extent) are representative of actual internal joint contact forces. It is also possible that the thinner cartilage in the medial compartment is more sensitive to changes in contact mechanics leading to degenerative change.

The underlying challenge in using the measurement of cartilage thickness to identify the onset and progression of OA is that cartilage changes in the early stages of OA are poorly understood, especially in populations who have suffered knee trauma which may initiate the development of OA. This combined with the lack of definitive conclusions on joint contact mechanics is an area that requires deeper investigation in order to more thoroughly understand the complex inter relationships between external marker systems, internal joint contact forces and cartilage formation and loading which may help uncover the biomechanical mechanisms under which OA is initiated and progresses after ACL injury.

The semi-quantitative method showed an overall improvement in score, corresponding to an improvement in knee health. However meniscus and cartilage showed worsening in some regions of the knee. Therefore the author suggests that analysis of the individual components that make up the score should be undertaken to give greater insight into the underlying structural changes that are taking place, particularly in longitudinal studies where physiological processes can change scoring of these features at a greater rate than others. This means scoring systems may need to be revised to avoid any excessive influence individual components (such as BMA) may have on total scoring when other, potentially more important features may be degenerating. The current evidence from changes in cartilage and meniscus shows that a proportion of those with an ACL injury are showing signs of negative change in key risk factors for the development of OA. This supports the hypothesis that despite reconstruction and a return to what would be considered more normal levels of function and loading, the ACLM group demonstrated worsening of specific knee structures cited as risk factors for development of OA.

Deeper insight into the ACLM participant's individual data was performed to explore if patterns existed between those with evidence of degenerative change and potential risk factors including demographics, level of function and indicators of knee loading. From those that showed degenerative changes in knee structures there appeared to be some indication of association with identified risk factors; however this was not consistent within other participants. In the key area of this study's investigation, the proposed link between knee loading and degenerative knee changes, available evidence did not support this theory or identify key parameters. However this group typically had higher levels of loading, therefore discerning the interactions of the study's outcomes with changes in knee structures in a small number of participant's demonstrating relatively homogeneous biomechanics was challenging.

Within this group only one participant presented kinetic data which was exceptionally different from the rest of the group showing a marked reduction in knee extensor moment during jogging, more in line with the full ACLR group. This participant had the greatest evidence of degenerative change (the only participant with an increase in total semi-quantitative score), hinting that a reduction in knee moment does not equate with a decreased risk of degenerative change. However it remains to be seen if a reduction in knee moment is associated with degenerative changes or if degenerative changes occur independently of participant kinetics. If key outcomes could be identified, this has the potential to serve as sign posts to identify those as risk of development of OA after ACL injury. Once identified participants could be targeted for the development of strategies with which to reduce the impact of these risk factors through rehabilitation and activity modification.

In summary this study has attempted to give insight into one of the key theoretical pathways by which ACL injury influences the development of early OA. In the context of the current study's ACLM group this degeneration appears to be independent of risk factors associated with demographics, levels of function and knee loading. It also appears that evidence of degeneration in structures is not consistent within participants. This combined with the lack of identifiable patterns with any of the study's outcomes or identified risk factors, suggests that OA might be viewed as an end point, but there may be many different pathways that exist either independently or in combination with other mechanisms/risk factors to reach this point. Therefore more research in this field needs to be undertaken with larger sample sizes across a wide range of time frames to

define the potential mechanisms and risk factors that are associated with structural changes in the short, medium and long term after ACL injury.

WORD COUNT: 79,802

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Chapter 10: Appendices.

Appendix 1: Literature Search Strategy.

Literature search took place using Medline/PubMed/EMBASE.

1	(Anterior Cruciate Ligament OR ACL) AND (Rupture OR Injury)
2	1 AND Biomechanics OR Kinematics OR Kinetics OR Motion Analysis
3	2 AND GAIT
4	2 AND Jogging OR Running
5	2 AND Squatting
6	3 AND 4 AND 5
7	Knee Osteoarthritis OR Knee OA OR OA
8	1 AND 7
9	Epidemiology
11	1 AND 9
12	7 AND 9
13	MRI OR Magnetic Resonance Imaging OR Imaging
14	Knee OR Tibiofemoral Joint OR Knee Cartilage
15	13 AND 14
16	7 AND 15
17	2 AND 15
18	6 AND 8 AND 11 AND 12 AND 16 AND 17
19	Limit 18 to 1990-2014
20	Limit 19 to English Language

Appendix 2: International Knee Documentation Score.

2000 IKDC SUBJECTIVE KNEE EVALUATION FORM

Your Full Name_____

Today's Date: _____/_____/_____ (Day / Month / Year) Date of Injury: _____/_____/_____ (Day / Month / Year)

SYMPTOMS*:
*Grade symptoms at the highest activity level at which you think you could function without significant symptoms, even if you are not actually performing activities at this level.

1. What is the highest level of activity that you can perform without significant knee pain?

   4 ☐ Very strenuous activities like jumping or pivoting as in basketball or soccer
   3 ☐ Strenuous activities like heavy physical work, skiing or tennis
   2 ☐ Moderate activities like moderate physical work, running or jogging
   1 ☐ Light activities like walking, housework or yard work
   0 ☐ Unable to perform any of the above activities due to knee pain

2. During the past 4 weeks, or since your injury, how often have you had pain?

Never	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	8 ☐	9 ☐	10 ☐	Constant

3. If you have pain, how severe is it?

No pain	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	8 ☐	9 ☐	10 ☐	Worst pain imaginable

4. During the past 4 weeks, or since your injury, how stiff or swollen was your knee?

   4 ☐ Not at all
   3 ☐ Mildly
   2 ☐ Moderately
   1 ☐ Very
   0 ☐ Extremely

5. What is the highest level of activity you can perform without significant swelling in your knee?

   4 ☐ Very strenuous activities like jumping or pivoting as in basketball or soccer
   3 ☐ Strenuous activities like heavy physical work, skiing or tennis
   2 ☐ Moderate activities like moderate physical work, running or jogging
   1 ☐ Light activities like walking, housework, or yard work
   0 ☐ Unable to perform any of the above activities due to knee swelling

6. During the past 4 weeks, or since your injury, did your knee lock or catch?

   0 ☐ Yes 1 ☐ No

7. What is the highest level of activity you can perform without significant giving way in your knee?

   4 ☐ Very strenuous activities like jumping or pivoting as in basketball or soccer
   3 ☐ Strenuous activities like heavy physical work, skiing or tennis
   2 ☐ Moderate activities like moderate physical work, running or jogging
   1 ☐ Light activities like walking, housework or yard work
   0 ☐ Unable to perform any of the above activities due to giving way of the knee

SPORTS ACTIVITIES:

8. What is the highest level of activity you can participate in on a regular basis?

   4 ☐ Very strenuous activities like jumping or pivoting as in basketball or soccer
   3 ☐ Strenuous activities like heavy physical work, skiing or tennis
   2 ☐ Moderate activities like moderate physical work, running or jogging
   1 ☐ Light activities like walking, housework or yard work
   0 ☐ Unable to perform any of the above activities due to knee

9. How does your knee affect your ability to:

		Not difficult at all	Minimally difficult	Moderately Difficult	Extremely difficult	Unable to do
a.	Go up stairs	4 ☐	3 ☐	2 ☐	1 ☐	0 ☐
b.	Go down stairs	4 ☐	3 ☐	2 ☐	1 ☐	0 ☐
c.	Kneel on the front of your knee	4 ☐	3 ☐	2 ☐	1 ☐	0 ☐
d.	Squat	4 ☐	3 ☐	2 ☐	1 ☐	0 ☐
e.	Sit with your knee bent	4 ☐	3 ☐	2 ☐	1 ☐	0 ☐
f.	Rise from a chair	4 ☐	3 ☐	2 ☐	1 ☐	0 ☐
g.	Run straight ahead	4 ☐	3 ☐	2 ☐	1 ☐	0 ☐
h.	Jump and land on your involved leg	4 ☐	3 ☐	2 ☐	1 ☐	0 ☐
i.	Stop and start quickly	4 ☐	3 ☐	2 ☐	1 ☐	0 ☐

FUNCTION:

10. How would you rate the function of your knee on a scale of 0 to 10 with 10 being normal, excellent function and 0 being the inability to perform any of your usual daily activities which may include sports?

FUNCTION PRIOR TO YOUR KNEE INJURY:

Couldn't perform daily activities	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	8 ☐	9 ☐	10 ☐	No limitation in daily activities

CURRENT FUNCTION OF YOUR KNEE:

Can't perform daily activities	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	8 ☐	9 ☐	10 ☐	No limitation in daily activities

Knee Rehabilitation Model, Version 1 January 2010
Participant Code: Date Completed: Visit No:

Cincinnati Knee Rating System: Symptom Rating Scales, Patient Perception Scale

1. Directions: Using the key below, circle the appropriate boxes on the four scales below which indicate the highest level you can reach without having symptoms.

Scale	Description
10	Normal knee, able to do strenuous work/sports with jumping, hard pivoting
8	Able to do moderate work/sports with running, turning, and twisting: symptoms with strenuous work/sports
6	Able to do light work/sports no running, twisting or jumping: symptoms with moderate work/sports
4	Able to do activities of daily living alone: symptoms with light work/sports
2	Moderate symptoms (frequent, limiting) with activities of daily living
0	Severe symptoms (constant, not relieved) with activities of daily living

1. Pain

10 — 8 — 6 — 4 — 2 — 0

2. Swelling (actual fluid in the knee; obvious puffiness)

10 — 8 — 6 — 4 — 2 — 0

3. Partial Giving-Way (partial knee collapse, no fall to the ground)

10 — 8 — 6 — 4 — 2 — 0

4. Full Giving-Way (knee collapse occurs with actual falling to the ground)

10 — 8 — 6 — 4 — 2 — 0

2. Patient grade: Rate the overall condition of your knee at the present time. Circle one number below, using the scale below.

1	2	3	4	5	6	7	8	9	10
	poor		fair		good				normal

Poor – I have significant limitations that affect activities of daily living.
Fair – I have moderate limitations that affect activities of daily living, no sports possible.
Good – I have some limitations with sports but I can participate, I compensate.
Normal/excellent – I am able to do whatever I wish (any sport) with no problems.

1

Knee Rehabilitation Model, Version 1, January 2010
Participant Code: Date Completed: Visit No

Cincinnati Knee Rating System:
Sports Activity Scale, Activities of Daily Living Function Scales,
Sports Function Scales

3. Sports Activity Scale

Select a level based on the frequency that you exercise. Within that level circle a number that corresponds to the statement that best summarises the activities you currently participate in.

Level 1 (participates 4-7 days/week)

100 Jumping, hard pivoting, cutting (basketball, volleyball, football, gymnastics, soccer)

95 Running, twisting, turning (tennis, racquetball, handball, ice hockey, field hockey, skiing, wrestling)

90 No running, twisting, jumping (cycling, swimming)

Level 2 (participates 1-3 days/week)

85 Jumping, hard pivoting, cutting (basketball, volleyball, football, gymnastics, soccer)

80 Running, twisting, turning (tennis, racquetball, handball, ice hockey, field hockey, skiing, wrestling)

75 No running, twisting, jumping (cycling, swimming)

Level 3 (participates 1-3 times/month)

65 Jumping, hard pivoting, cutting (basketball, volleyball, football, gymnastics, soccer)

60 Running, twisting, turning (tennis, racquetball, handball, ice hockey, field hockey, skiing, wrestling)

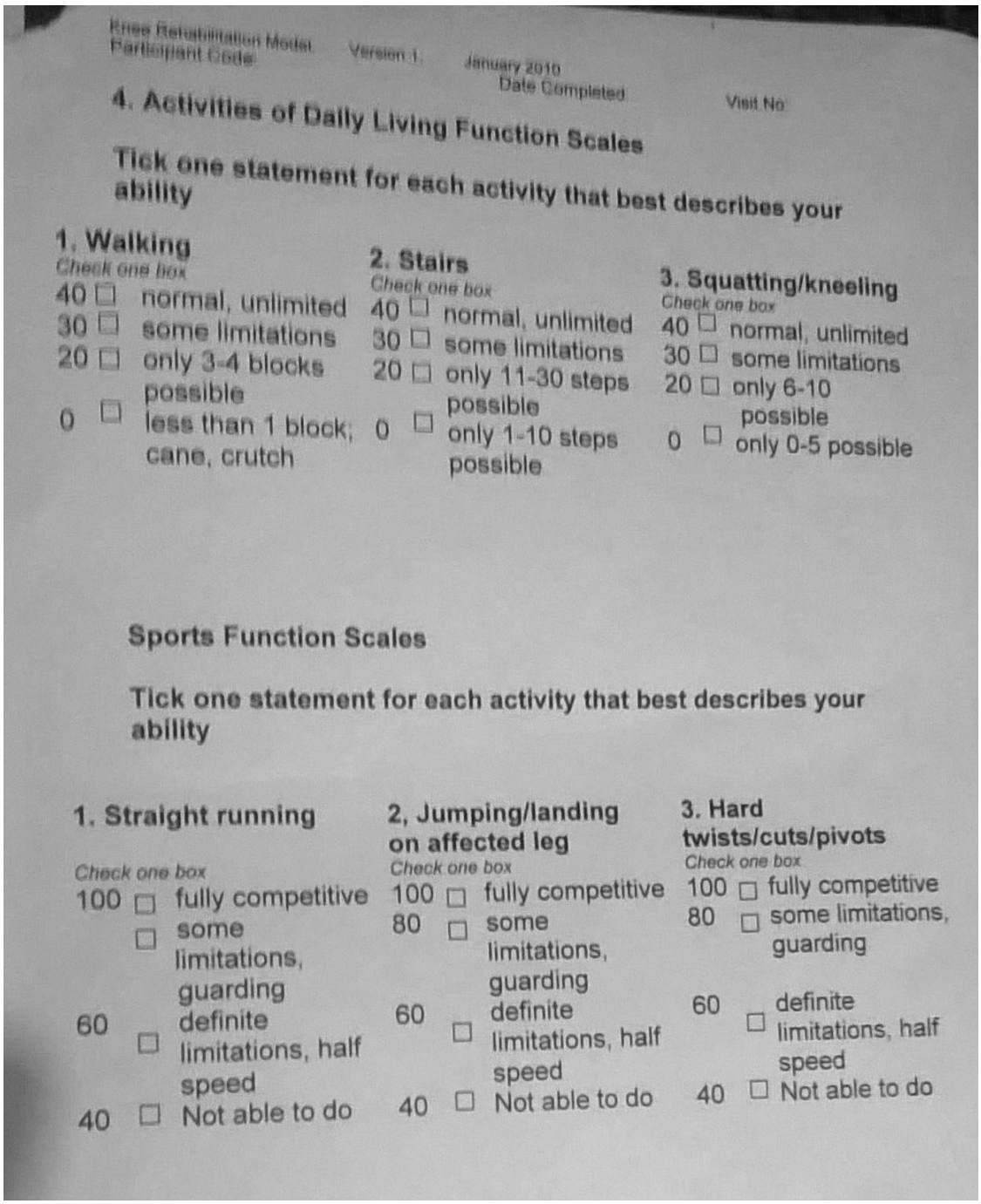
55 No running, twisting, jumping (cycling, swimming)

Level 4 (no sports)

40 I perform activities of daily living without problems

20 I have moderate problems with activities of daily living

0 I have severe problems with activities of daily living: on crutches, full disability



Knee Rehabilitation Model Version 1. January 2010
Participant Code: Date Completed: Visit No:

4. Activities of Daily Living Function Scales

Tick one statement for each activity that best describes your ability

1. Walking
Check one box

- 40 ☐ normal, unlimited
- 30 ☐ some limitations
- 20 ☐ only 3-4 blocks possible
- 0 ☐ less than 1 block; cane, crutch

2. Stairs
Check one box

- 40 ☐ normal, unlimited
- 30 ☐ some limitations
- 20 ☐ only 11-30 steps possible
- 0 ☐ only 1-10 steps possible

3. Squatting/kneeling
Check one box

- 40 ☐ normal, unlimited
- 30 ☐ some limitations
- 20 ☐ only 6-10 possible
- 0 ☐ only 0-5 possible

Sports Function Scales

Tick one statement for each activity that best describes your ability

1. Straight running
Check one box

- 100 ☐ fully competitive
- ☐ some limitations, guarding
- 60 ☐ definite limitations, half speed
- 40 ☐ Not able to do

2, Jumping/landing on affected leg
Check one box

- 100 ☐ fully competitive
- 80 ☐ some limitations, guarding
- 60 ☐ definite limitations, half speed
- 40 ☐ Not able to do

3. Hard twists/cuts/pivots
Check one box

- 100 ☐ fully competitive
- 80 ☐ some limitations, guarding
- 60 ☐ definite limitations, half speed
- 40 ☐ Not able to do

Appendix 4: Tampa Scale of Kinesiophobia.

TSK questionnaire

Please answer below whether you either 'strongly disagree', 'disagree', 'agree', or 'strongly agree' with the given statements.

	Strongly disagree	Disagree	Agree	Strongly agree
1. I'm afraid that I might injure myself if I exercise.	○	○	○	○
2. If I were to try to overcome it, my pain would increase.	○	○	○	○
3. My body is telling me I have something dangerously wrong.	○	○	○	○
4. My knee trouble would probably be relieved if I were to exercise.	○	○	○	○
5. People aren't taking my medical condition seriously enough.	○	○	○	○
6. My accident has put my body at risk for the rest of my life.	○	○	○	○
7. Pain always means I have injured my body.	○	○	○	○
8. Just because something aggravates my knee trouble does not mean it is dangerous.	○	○	○	○
9. I am afraid that I might injure myself accidentally.	○	○	○	○
10. Simply being careful that I do not make any unnecessary movements is the safest thing I can do to prevent my injured leg from worsening.	○	○	○	○
11. I wouldn't have this much trouble if there weren't something potentially dangerous going on in my body.	○	○	○	○

12. Although I have injured my knee, I would be better off if I were physically active.	○	○	○	○
13. Pain lets me know when to stop exercising so that I don't injure myself.	○	○	○	○
14. It's really not safe for a person with a condition like mine to be physically active.	○	○	○	○
15. I can't do all the things normal people do because it's too easy for me to get injured again.	○	○	○	○
16. Even though my injured knee is causing me a lot of pain, I don't think it's actually dangerous.	○	○	○	○
17. No one should have to exercise when he/she gets injured.	○	○	○	○

Appendix 5: Joint Function Patient Information Sheet.

Dr Helen Roberts / Dr Andrea Longman
Research Coordinators
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CARDIFF UNIVERSITY
PRIFYSGOL CAERDYDD

PATIENT INFORMATION SHEET

Assessment of joint function in patients with joint problems using three dimensional motion analysis techniques

Part one

You are being invited to take part in a research study with Cardiff University's Arthritis Research UK Biomechanics and Bioengineering Centre. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. One of our team will go through the information sheet with you. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to participate. Part 1 tells you about the purpose of this study and what will happen to you if you take part. Part 2 gives you more detailed information about the conduct of the study.

What is the purpose of this trial?
The aim of the trial is to investigate the function of joints for people with joint problems and people with healthy joints. The data can be used to develop new treatments, improve the design of joint replacements, improve rehabilitation and improve the way that motion is analysed clinically.

The study is designed to examine the effects of joint problems and any subsequent operation or other treatment (where appropriate), on the joints ability to perform daily tasks (such as walking, lifting a cup etc).

Do I have to take part?
It is up to you to whether or not to take part. If you do decide to take part you will be given this information sheet to keep and after you have had enough time to read through it, be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time or without giving a reason. A decision not to take part or to withdraw at any time will not affect the standard of care you receive. Should you decide not to take part, you do not have to provide a reason for this decision.

What will happen to me if I take part?
You have been asked to take part in this as you have a problem with your joint that we are interested in looking at with this technique. It will allow us further insight into the nature of joint function and pain that people with your joint problem encounter. You may also been asked to take part so we can examine a non affected joint so we can compare it to the joint problem.

If you wish to take part you will assessed either in the Cardiff University School of Engineering, Human Motion Analysis Laboratory or in the Cardiff University School of Healthcare studies (SOHCS) Research Centre for Clinical Kinaesiology (RCCK) or in the relevant clinical settings. The number of times we would ask you to attend would depend on the joint problem; we will discuss this with you when going through this information sheet. Each session will last a maximum of three hours.

Data will be kept securely for a minimum of 15 years in accordance with good research practice and data protection regulations imposed by Cardiff University in accordance with the Data Protection Act 1998. All data obtained during the study will remain confidential. Access to data will only be available to the investigators attached to the Arthritis Research UK Biomechanics and Bioengineering Centre at Cardiff University.

If new information becomes available, we may invite you to take part in a follow-up study in the future, please indicate on the consent sheet if you do not mind us contacting you.

What will I have to do?
Before your first assessment you will be asked to sign a patient consent form which includes the following clause: I understand that I may withdraw from the study at any time without it affecting my ongoing treatment in any way.

All participants will be sent a map and directions to the place of assessment and travel expenses can be reimbursed on production of a receipt for journeys to the assessment venue.

At the beginning of your visit, we will explain the study in full and ask for your consent, bearing in mind that you are free to withdraw at any time.

We will ask you to complete questionnaires that will ask you questions about how the problem affects your activities of daily living.

Prior to the start of the assessment, you may be asked to change into appropriate clothing depending on the joint we want to examine (for example shorts for knee, well fitting vest, sports bra or swimming costume for shoulder and spine, etc). This process will be conducted with the upmost professionalism and a screened off area is provided for changing. During laboratory sessions, access to the laboratory is limited and a sign is placed on the door advising other staff not to enter whilst the trial is in progress.

You will have a number of very light polystyrene or cork round markers attached to the skin and the locations of the markers will be dependent on the joint type under examination.

You will be asked to perform a range of activities of daily living as appropriate (such as walking, standing, climbing stairs, combing hair, taking hand to mouth). You will be free to stop for a break at any time. The position of the markers on the skin will provide a series of recordings by using cameras that record the position of the markers.

When appropriate to the joint under study, muscle activity and joint strength may also be determined during these sessions. This will involve placement of electromyography (EMG) electrodes onto the surface of the skin to record muscle activity during joint movement. The locations of the electrodes will be dependent on the muscle groups under examination. Particularly hairy skin may sometimes need a small patch shaving for the sensors to attach (approximately 2x2cm).

Throughout the sessions your joint movement will be recorded using standard audiovisual equipment. The recordings will be used for data verification post processing. Your face will be digitally masked from these files so that nobody can identify you from the videos. All data files, including audiovisual files will be stored in encrypted folders on Cardiff University password protected computers. Cardiff University and NHS members of staff who are directly involved with the study will have access to the files.

Regular rest and toilet breaks will be provided as often as you need them to assure maximum comfort.

Are there any risks in participating in this trial?
The measurements taken during the trial involve the placement of very light polystyrene or cork round markers onto the skin or EMG electrodes in various places of the body depending on what joint we will be examining. The markers/electrodes are placed with sticky tape which may cause some mild discomfort when it is being removed, similar to removing a small sticking plaster.

Are there any benefits in participating in this trial?
We hope to be able to better understand how joint problems affect the motion of the joint. There is no intended clinical benefit to the participant from taking part in the study. The information we get from this study may help us to provide future patients who have joint disease or injury with improved treatment options.

If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making a decision.

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PATIENT INFORMATION SHEET

Assessment of joint function in patients using three dimensional motion analysis techniques

Part Two

What if new information becomes available?
Sometimes during the course of a research project, new information becomes available about the investigation. If you decide to withdraw, it will not affect your any care in the NHS. If you decide to continue, you will be asked to sign an updated consent form.

What will happen if I do not want to carry on with the study?
If you withdraw from the study, we will erase all identifiable material, but we will need to use the data collected up to your withdrawal.

What if something goes wrong?
If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms should be available to you.

Will my taking part in this study be kept confidential?
All information which is collected about you during the course of the research will be kept strictly confidential. Any information about you which leaves the Cardiff University or the University Hospital of Wales will have your name and address removed so that you cannot be recognised from it.

Will my GP be informed of my involvement in the study?
With your permission, we will send a letter to your General Practitioner informing him or her of your involvement in the study.

What will happen to the results of the research study?
The measurements taken will provide information about the movement of your joint. The results of the study will be presented at meetings of orthopaedic surgeons, clinical scientists, physiotherapists and engineers, and if accepted, published in medical and engineering journals. If interested, a copy of the published article can be made available to you. You will not be identified in any report/publication.

Version 2 28/09/2010

Who is organising and funding the research?
Research staff at the Arthritis Research UK Biomechanics and Bioengineering Centre at Cardiff University and Consultant Orthopaedic Surgeons at the University Hospital of Wales are carrying out the study. The study is part of the Arthritis Research UK Biomechanics and Bioengineering Centre at Cardiff University; it is not funded by commercial sources and runs alongside research in the Cardiff Gait and Motion Analysis Laboratory at Cardiff University School of Engineering and Research Centre for Clinical Kinaesiology at Cardiff University School of Healthcare Studies.

Who has reviewed the study?
This study has been reviewed by the Research Ethics Committee (REC) for Wales.

What if I wish to lodge a complaint?
If you wish to make a minor complaint regarding the way you were approached or treated during the trial, please contact the Arthritis Research UK Biomechanics and Bioengineering Centre Research Coordinator at the contact details below or you can contact the Cardiff University Research Governance Team on 029 208 79277.

Contact for further information
Research Coordinator
Arthritis Research UK Biomechanics and Bioengineering Centre
Cardiff School of Biosciences
Cardiff University
Cardiff
CF10 3AX
Tel: 029 2087 5419
Email: Robertshc@cf.ac.uk or Longmanaj@cf.ac.uk

This completes Part 2. Thank you for reading this information sheet.

If you agree to take part in this study then you will be given a copy of the information sheet and a signed consent form to keep.

Appendix 6: Joint Function Consent Form.

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PATIENT CONSENT FORM

Assessment of joint function in patients with joint problems using three dimensional motion analysis techniques

Study Number
Patient Identification Number for this trial:

You DO NOT have to sign this document. Please DO NOT sign this document unless you fully understand it. If there is ANYTHING which you do not understand please do not hesitate to ask for a full explanation.

To confirm agreement with each of the statements below, please initial each box:

1. I confirm that I have read and understand the information sheet dated 11/04//2012 (Version 5) for the above study and have had the opportunity to ask questions. ☐

2. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care or legal rights being affected. ☐

3. You may contact me in the future to take part in other research projects or surveys. ☐

4. I agree to my hospital number being used to track my data on your secure system. ☐

5. I agree to my GP being informed of my participation in the study. ☐

6. I agree to take part in the above study. ☐

Name of Patient: _____
(Please print)

Signature: _____ Date: _____

Appendix 7: Joint Imaging Information Sheet.

Dr Helen Roberts / Dr Andrea Longman
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PATIENT INFORMATION SHEET

Joint imaging in patients with musculoskeletal disease and healthy people

Part One

You are being invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Part 1 tells you about the purpose of this study and what will happen to you if you take part. Part 2 gives you more detailed information about the conduct of the study. Ask us if there is anything that is not clear or if you would like more information. Please take time to decide whether or not you wish to take part.

What is the purpose of this study?
Close work between orthopaedic surgeons, physiotherapists, scientists and engineers is improving the tools available for patient's assessment and diagnosis. Patients can clearly benefit from better diagnosis, thus promoting increased confidence in their medical care.

With improved clinical assessment for this common disease, surgical input to relieve the painful and functionally disabling symptoms could be more effectively tailored to suit patients.

The purpose of this study is to use magnetic resonance imaging (MRI) to take pictures of your joints to help understand joint disease or injury.

This study is for research purposes only and you would receive no therapeutic benefits for taking part.

Why have I been asked to take part in this study?
You have been asked to take part in this study as you may have a problem with your joint that we are interested in looking at with this technique. It will allow us to gain further insight into the nature of the pain that people with a problem with their joint in the same joint as you face. Your clinician has been informed that you have been invited to take part in this study and has agreed that it is OK for you to do so.

Do I have to take part?
It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time, without giving a reason.

Version 3 24/08/2011

A decision not to take part or to withdraw at any time will not affect the standard of care that you receive. Should you decide not to take part, you do not have to provide a reason for this decision.

Am I able to take part?
Before you take part in this study, we will give you a questionnaire to identify potential health reasons which you know about that suggest you should not participate in this study. This is aimed at ensuring your safety. If you would prefer not to reveal any information about your health, please do not participate.

You should not take part if you:

- have now or have had in the past cardiac (heart), vascular (blood vessel) or respiratory/pulmonary (breathing/lung) conditions, including high blood pressure
- have now or have had in the past a neurological (brain or nerve) disease
- experience dizziness or fainting
- have a pacemaker
- suffer from either asthma or diabetes mellitus
- are pregnant or have given birth in the last 6 weeks
- have a history of drug dependency
- have taken illicit drugs in the last 4 weeks
- have been involved in any drug trials (scientific studies involving you taking a drug) in the last 4 weeks

If you are unsure about any of these items affecting your participation you can discuss it with one of the medical doctors associated with the study when you come for your initial screening session.

What will happen if I agree to take part?
With your permission your GP will be notified of your participation in this study. After attendance at the session you will be reimbursed for reasonable travel expenses.

You will be asked to visit the Cardiff University Brain Research Imaging Centre (CUBRIC) on 1 or 2 occasions.

During the visit, you would have your joint scanned using the MRI scanner at CUBRIC. You will be asked to lie as still as possible in the scanner while pictures of your joint are taken.

In some cases, we will ask you to perform a task, which will induce pain similar to that induced by your activities of daily living. The level of pain will always be acceptable to you. The task may consist of joint manipulation, loading or compression. You will be free to stop the task at any time during the experiments. These imaging techniques will measure your joint while the movements are being applied. A single visit to CUBRIC will typically last 2 hours.

We may also ask to do a further 30 minute scan to measure the metabolites (certain molecules) present within your joint.

What will I have to do before these visits?
You do not have to do anything specific in preparation for this study.

Expenses
You will be reimbursed for reasonable travel expenses.

What are the benefits of taking part?
This study involves taking pictures of your joint. It is not therapeutic and there is no intended clinical benefit to the patient from taking part in the study. We hope that the information we get from this study may help us to develop more effective treatments for the pain experienced by people with conditions such as yours.

What happened if you find something unusual on my scan?
The researchers involved do not have experience in medical diagnosis using MRI or MRS, as they are imaging scientists. The person conducting your scan will not be able to comment on the results of your scan. You should not regard these research scans as a medical screening procedure. Occasionally when we image healthy participants, the researchers may be concerned that a potential abnormality may exist on the scan. In such cases, we will ask an appropriate consultant with appropriate expertise to examine the scans. If the specialist radiologist feels it to be appropriate, a report can be forwarded to your GP, so that he/she may arrange to further investigate any potential abnormality.

In most cases, an orthopaedic consultant will not look at images of your joint. It is important that you realise that these scans are not intended to provide any information that may help in the diagnosis of any medical condition.

Are there any risks in participating in this study?
Some people find that being in the scanner makes them feel uncomfortable or claustrophobic because they have to keep still for a long time and the scanner can be noisy while pictures are being taken.

The activities that we may ask you to perform or loading device that we use to apply stretching and compression to your joint may cause some discomfort. The discomfort you feel should not be over and above the discomfort caused by activities of daily living.

What will happen if I do not want to carry on with they study?
If you withdraw from the study, we will erase all identifiable material, but we will need to use the data collected up to your withdrawal.

What if something goes wrong?
If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for legal action, but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanism should be available to you.

Will my taking part in this study be kept confidential?
All information which is collected about you during the course of the research will be kept strictly confidential. We may share the data we collect with researchers at other institutions including Universities and commercial research organisations. However, any information that leaves the Centre will be anonymised. It will have your name and address removed so that you cannot be recognised from it. In any sort of report we might publish, we will not include information that will make it possible for other people to know your name or identify you in any way. You will simply be referred to by your gender, age, the affected joint and possibly some characteristic such as left or right handedness. If you join the study, some parts of your records and the data collected for the study may be looked at by authorised persons from the University, hospital where you are being treated, or research ethics committee, for the purposes of monitoring and auditing.

Data will be kept securely for a minimum of 15 years in accordance with good research practice and data protection regulations imposed by Cardiff University in accordance with the Data Protection Act 1998.

Will my general practitioner (GP) be notified of my participation in this research?
With your permission your GP may be notified of your participation in this study. For this reason we ask you to bring details (name and address) of the GP with whom you are registered.

What will happen to the results of the research study?
We hope to publish the results of this study in a scientific journal. We may also present the results at a scientific conference or a seminar in a university. We may also publish results on our website. We would be happy to discuss the results of the study with you and send you a copy of the published results. It will not be possible to identify you or images of your joint in any report or publication.

Who is organising and funding the research?
Research staff at the University of Wales, Cardiff School of Engineering and Orthopaedic Consultant Surgeons and Physiotherapists at the University Hospital of Wales are carrying out the study. Principal investigators are Mr Chris Wilson, who is a Senior Consultant Orthopaedic Surgeon at the University Hospital of Wales and Honorary Visiting Professor at Cardiff University, Dr. Deborah Mason, Senior Lecturer at the Cardiff University School or Biosciences and Dr. Cathy Holt, Senior Lecturer at Cardiff School of Engineering, Cardiff University. The study is part of the Arthritis Research UK Biomechanics and Bioengineering Centre at Cardiff University; it is not funded by commercial sources and runs alongside research in the Cardiff Gait and motion Analysis Laboratory at Cardiff University School of Engineering and Research Centre for Clinical Kinaesiology at Cardiff University School of Healthcare Studies. Where appropriate, the sponsors of this study will pay Cardiff and Vale University Health Board, Radiology Directorate.

Version 3 24/08/2011

Who has reviewed the study?
This study has been reviewed by the Research Ethics Committee (REC) for Wales.

What if new information becomes available during the course of this research?
If the new information pertains specifically to your health as the participant, you will be informed and continued inclusion in the research will be discussed with you.

What if I wish to lodge a complaint?
If you wish to make a minor complaint regarding the way you were approached or treated during the trial, please contact the Arthritis Research UK Biomechanics and Bioengineering Centre Research Coordinator at the contact details below or you can contact the Cardiff University Research Governance Team on 029 208 79277.

Contact for further information
Research Coordinator
Cardiff School of Biosciences
Cardiff University
Cardiff
CF10 3AX
Tel: 029 20875419
Email: Robertshc@cardiff.ac.uk / Longmanaj@cardiff.ac.uk

Contact for MRI
Ann Harvey
Cardiff Academic Fellow
Cardiff School of Medicine
Cardiff University
Cardiff
CF14 4XN
Tel: 029 20687324
Email: HarveyAK@cardiff.ac.uk

If you agree to take part in this study then you will be given a copy of the information sheet and a signed consent form to keep.

CARDIFF UNIVERSITY
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PATIENT INFORMATION SHEET

Joint imaging in patients with musculoskeletal disease and healthy people

Part Two - The Visits

At the beginning of your first visit, we will explain the full study to you and ask for your consent, bearing in mind that you are free to withdraw at any time. A questionnaire checking for contraindications to magnetic resonance imaging (MRI) and / or magnetic resonance spectroscopy (MRS) will be performed. This makes sure that you do not have any metal in your body (see below) and that it is safe for you to enter the scanner. We will also ask you questions about your joint and loading or movement of your joint. Based upon the results, you would either be included or excluded from the study. All data obtained during the study would remain confidential. Access to data would be available to the investigators attached to the project at the Arthritis Research UK BBC.

During this and subsequent visits you would be asked to undergo MRI and / or MRS scanning.

The MRI scanner is a large box with a tube running through the middle, where the participant lies. For some people, being inside the scanner can induce feelings of claustrophobia. The MRS scanning also uses the MRI scanner but instead of measuring the water signal to produce an image, it will measure other components present. MRS does not cause any additional risk to the participant.

During the visit, you would have your joint scanned using the MRI scanner at CUBRIC. You would lie on the bed of the MRI scanner, which moves you into the centre of the tube, and a device will be placed around the joint being imaged. You will be given ear plugs to protect your hearing but, you will still be able to hear the researcher when spoken to over the intercom.

You would also be given a call button to hold throughout the scan. You can use this to get the attention of the researcher who will be on the other side of a window just outside the scanner room. You can speak to the researcher via a microphone from inside the scanner. It is very important that you keep still during the scans and try not to move your joint at all. We would make sure that you were comfortable by providing cushions around the head and under the legs and a blanket if necessary.

We may ask you to perform certain tasks, which involve loading or compressing your joint, to try to understand the pain you are experiencing in arthritis. If you find any task too uncomfortable, you can ask for the scan to stop by pressing the call button at any time. We may also ask you to wear several monitoring devices. These may include a plastic probe on your finger to monitor blood oxygen levels, a flexible belt around your chest/abdomen to

monitor your breathing; and a cuff around your arm/finger that tightens to measure blood pressure.

MRI / MRS

Magnetic resonance imaging (MRI) is a well-established technique for imaging the body and brain using strong magnetic fields and low energy radio waves to make pictures of the inside of the human body non-invasively. Magnetic resonance spectroscopy (MRS) uses the same scanner as MRI. However, instead of producing an image it produces a profile of the other components present. NONE of these non-invasive techniques use ionizing radiation (X-rays).

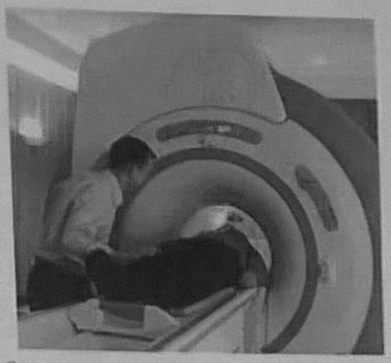


Figure: Photograph of a volunteer in the CUBRIC MRI scanner

What does MRI / MRS involve?

We will need you to lie in the MRI scanner for up to 1.5 hours and you will be given the opportunity to have a break at anytime.

In preparation for the MRI / MRS scan, you will first be asked a set of safety questions to make sure that you don't have anything in your body that might be affected by the scans, such as a pacemakers and other implanted devices, or metal in your body (e.g. shrapnel from war injuries). You will be asked to remove all metal objects from your person including keys, coins, jewellery and watches and will need to remove credit cards and travel-cards, belts and under-wired bras. Your valuables will then be locked away for security reasons. If you are wearing make-up you may be asked to remove this as well.

Although MRI / MRS is not known to affect the unborn child, we exclude subjects who may be pregnant just to be on the safe side.

Wear soft, loose but warm clothing which preferably has no metal fixings.

While the scanner is acquiring images it can be very noisy, so you will be given earplugs and/or ear defenders to wear.

What are the possible disadvantages and risks of MRI / MRS?

MRI and MRS involve minimal risk. No serious side effects of being in an MRI scanner have been reported despite millions of scans having been worldwide. Although the possibility of long-term effects cannot be completely ruled out, the weight of experience and opinion is against this.

Some people find being inside an MRI scanner claustrophobic although this is less so with the more compact systems like those used in CUBRIC. The scanner also makes quite loud noises for which we provide ear plugs. The radiofrequency waves we use to create the MR scans and profiles can cause your head and body to warm up slightly. This is not a problem, and you usually won't notice it, as your blood flow will increase slightly to take the heat away; we also keep the scanner room quite cool so that you always remain comfortable.

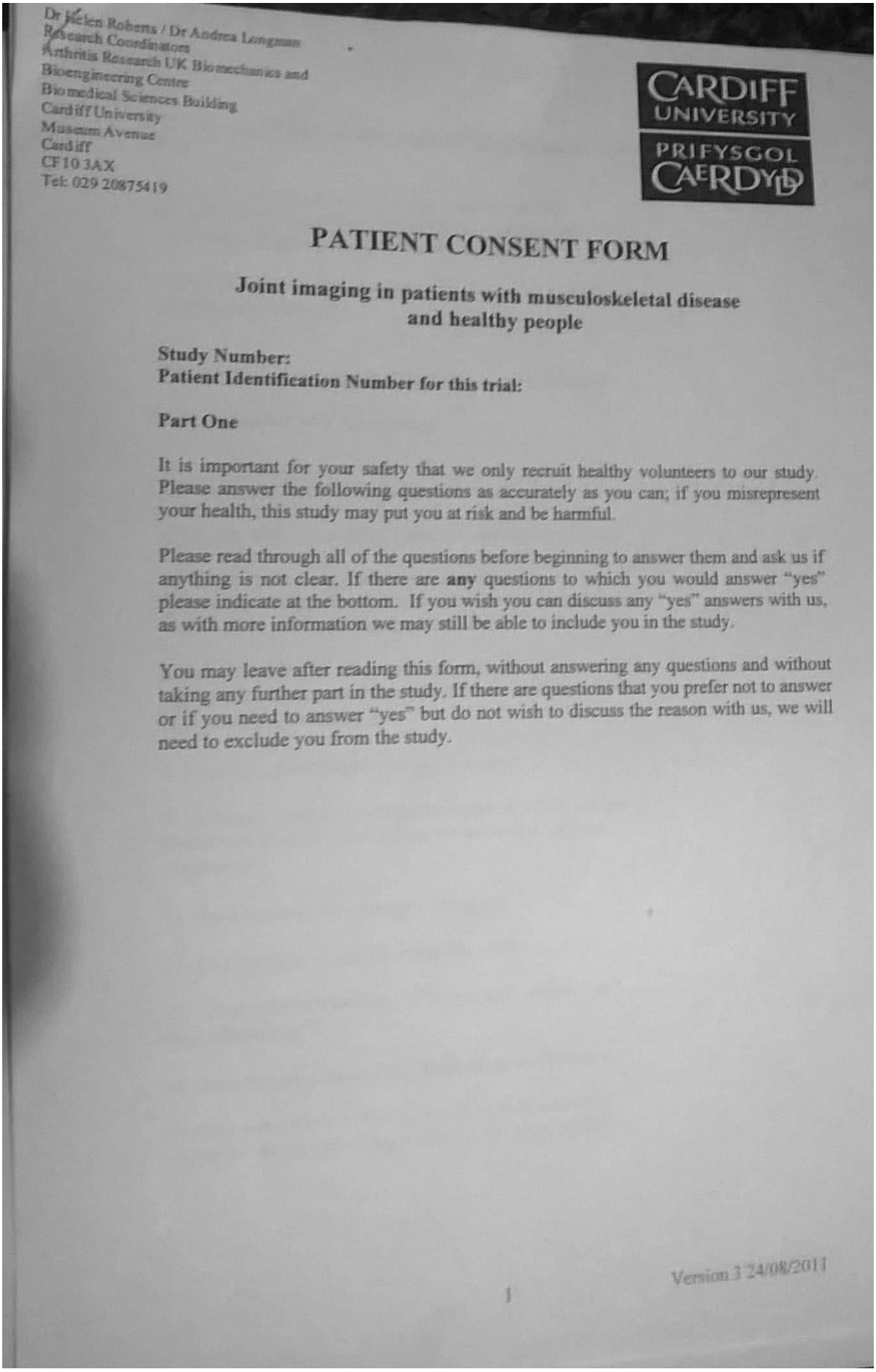
A few people have reported minor side effects including dizziness, mild nausea, a metallic taste in the mouth, and the sensation of seeing flashing lights. These side effects, if experienced, go away soon after you leave the magnet. If you experience any of these or others please let us know as soon as possible.

If you find the experience in the scanner unpleasant, just let us know straight away and we will stop and take you out of the scanner.

This completes Part 2 - Thank you for reading this information sheet.

If you agree to take part you will be given a copy of the information sheet and a signed consent form to keep.

Appendix 8: Joint Imaging Consent Form.



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CARDIFF UNIVERSITY
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PATIENT CONSENT FORM

Joint imaging in patients with musculoskeletal disease and healthy people

Study Number:
Patient Identification Number for this trial:

Part One

It is important for your safety that we only recruit healthy volunteers to our study. Please answer the following questions as accurately as you can; if you misrepresent your health, this study may put you at risk and be harmful.

Please read through all of the questions before beginning to answer them and ask us if anything is not clear. If there are **any** questions to which you would answer "yes" please indicate at the bottom. If you wish you can discuss any "yes" answers with us, as with more information we may still be able to include you in the study.

You may leave after reading this form, without answering any questions and without taking any further part in the study. If there are questions that you prefer not to answer or if you need to answer "yes" but do not wish to discuss the reason with us, we will need to exclude you from the study.

Version 3 24/08/2011

Please answer YES or NO to the following questions by ticking the appropriate box.

	YES	NO
1. Do you currently have any cardiac (heart), vascular (blood vessel) or respiratory/pulmonary (breathing/lung) conditions, including known high blood pressure?	☐	☐
2. Do you have a past history of cardiac, vascular, respiratory or pulmonary disease?	☐	☐
3. Do you have any neurological (brain or nerve) disease?	☐	☐
4. Do you suffer with palpitations?	☐	☐
5. Do you experience dizziness or fainting?	☐	☐
6. Do you suffer from either asthma or diabetes mellitus?	☐	☐
7. Are you taking any prescribed medication? We are especially interested in medication that alters heart, blood vessel and breathing characteristics.	☐	☐
8. Are you taking an un-prescribed medication e.g. over the counter herbal medications or medication to help performance during sport?	☐	☐
9. Have you given birth in the last 6 weeks?	☐	☐
10. Is there a chance you might be pregnant, i.e. if you are female and have not been taking precautions to prevent pregnancy?	☐	☐
11. Have you recently undergone surgery?	☐	☐
12. Have you had a cold/flu in the last week?	☐	☐
13. Are you drug dependent, or do you have a history of drug dependency?	☐	☐
14. Have you taken any illegal drugs in the last 4 weeks?	☐	☐
15. Have you been involved in any drug trials (scientific studies involving you taking a drug) in the last 4 weeks?	☐	☐

...berts / Dr Andrea Longman
Coordinators
...esearch UK Biomechanics and
...ering Centre
...l Sciences Building
...iversity
...venue

...0875419

CARDIFF UNIVERSITY
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PATIENT CONSENT FORM

Joint imaging in patients with musculoskeletal disease and healthy people

Study Number:
Patient Identification Number for this trial:

Part Two

You DO NOT have to sign this document. Please DO NOT sign this document unless you fully understand it. If there is ANYTHING which you do not understand please do not hesitate to ask for a full explanation.

To confirm agreement with each of the statements below, please initial the box:

1. I confirm that I have read and understand the information sheet dated 24/08/2011 (Version 3) for the above study and have had the opportunity to ask questions. ☐

2. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care or legal rights being affected. ☐

3. You may contact me in the future to take part in other research projects or surveys. ☐

4. I agree to my hospital number being used to track my tissue on your secure system. ☐

5. I agree for my GP to be contacted. ☐

6. I agree to take part in the MRI part of the study. ☐

8. I agree to take part in the joint loading part of the study. ☐

9. I agree to take part in the MRS part of the study. ☐

Name of Patient:

_____

Signature: _____ Date: _____

I confirm that I have fully explained the experimental protocol and purpose of the study

Name of Researcher:

_____

Signature: _____ Date: _____

Name of person taking consent:

_____

(If different from researcher)

Signature: _____ Date: _____

1 copy for the patient; 1 copy for the researcher

Appendix 9: Equipment List.

Anthropometer: VAPC Caliper, Seattle Systems. Washington: USA.

Force Platforms: Piezo-Instrumentation, Kistler 9281CA. Winterhur: Switzerland.

Height measure: Seca 222, Seca Limited. Birmingham: UK.

Isokinetic Dynamometer: Biodex S4, IPRS Mediquipe. Suffolk:UK.

Motion and MRi Analysis Software: Matlab 2010b, The MathWorks Inc. Massachusetts: USA

MRi Scanner: MR750, General Electric Healthcare. Buckinghamshire: UK.

Spreadsheet Software: Microsoft Excel 2010, Microsoft Corporation. Washington: USA.

Statistics Sofware: IBM SPSS Statistics 20, IBM. New York: USA.

Tape measure: SKF Services LTD. West Sussex: UK.

Vicon Bodybuilder Software: Oxford Metrics limited. Oxford: UK.

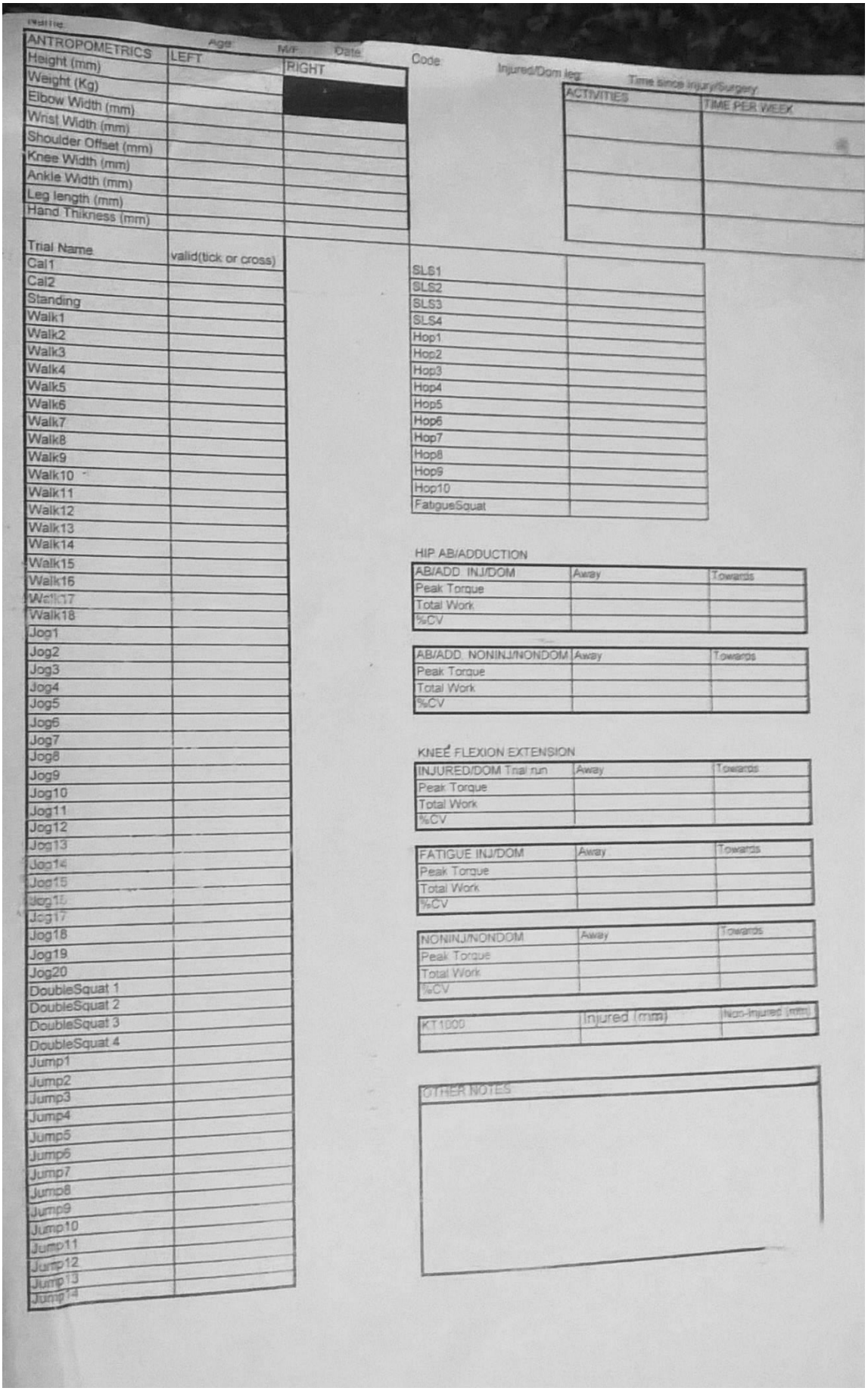
Vicon Mx Cameras: Oxford Metrics limited. Oxford: UK.

Vicon Nexus Software: Oxford Metrics limited. Oxford: UK.

Weighing Scales: Seca 888, Seca Limited. Birmingham: UK.

Word processing Software: Microsoft Word 2010, Microsoft Corporation. Washington: USA.

Appendix 10: Data Collection Trial Sheet.



Name: Age: M/F Date: Code:

Injured/Dom leg: Time since injury/Surgery:

ANTROPOMETRICS	LEFT	RIGHT
Height (mm)		
Weight (Kg)		
Elbow Width (mm)		
Wrist Width (mm)		
Shoulder Offset (mm)		
Knee Width (mm)		
Ankle Width (mm)		
Leg length (mm)		
Hand Thikness (mm)		

Trial Name	valid(tick or cross)
Cal1	
Cal2	
Standing	
Walk1	
Walk2	
Walk3	
Walk4	
Walk5	
Walk6	
Walk7	
Walk8	
Walk9	
Walk10	
Walk11	
Walk12	
Walk13	
Walk14	
Walk15	
Walk16	
Walk17	
Walk18	
Jog1	
Jog2	
Jog3	
Jog4	
Jog5	
Jog6	
Jog7	
Jog8	
Jog9	
Jog10	
Jog11	
Jog12	
Jog13	
Jog14	
Jog15	
Jog16	
Jog17	
Jog18	
Jog19	
Jog20	
DoubleSquat 1	
DoubleSquat 2	
DoubleSquat 3	
DoubleSquat 4	
Jump1	
Jump2	
Jump3	
Jump4	
Jump5	
Jump6	
Jump7	
Jump8	
Jump9	
Jump10	
Jump11	
Jump12	
Jump13	
Jump14	

ACTIVITIES	TIME PER WEEK

SLS1	
SLS2	
SLS3	
SLS4	
Hop1	
Hop2	
Hop3	
Hop4	
Hop5	
Hop6	
Hop7	
Hop8	
Hop9	
Hop10	
FatigueSquat	

HIP AB/ADDUCTION

AB/ADD INJ/DOM	Away	Towards
Peak Torque		
Total Work		
%CV		

AB/ADD NONINJ/NONDOM	Away	Towards
Peak Torque		
Total Work		
%CV		

KNEE FLEXION EXTENSION

INJURED/DOM Trial run	Away	Towards
Peak Torque		
Total Work		
%CV		

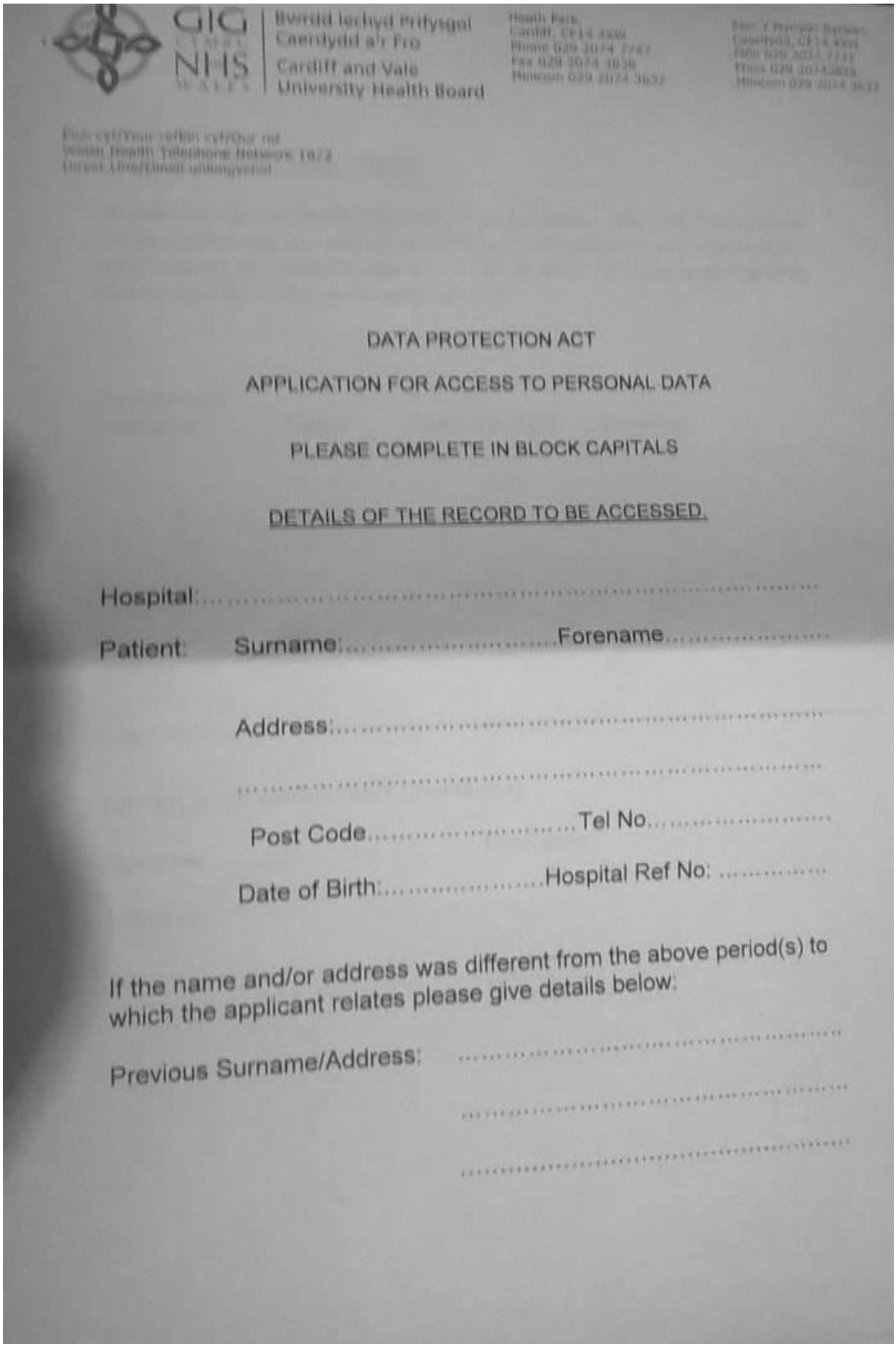
FATIGUE INJ/DOM	Away	Towards
Peak Torque		
Total Work		
%CV		

NONINJ/NONDOM	Away	Towards
Peak Torque		
Total Work		
%CV		

KT1000	Injured (mm)	Non-Injured (mm)

OTHER NOTES

Appendix 11: NHS Data Access Form.



GIG CYMRU NHS WALES
Bwrdd Iechyd Prifysgol Caerdydd a'r Fro
Cardiff and Vale University Health Board

DATA PROTECTION ACT

APPLICATION FOR ACCESS TO PERSONAL DATA

PLEASE COMPLETE IN BLOCK CAPITALS

DETAILS OF THE RECORD TO BE ACCESSED.

Hospital:.....

Patient: Surname:.....Forename.....

Address:.....

.....

Post Code.....Tel No.....

Date of Birth:.....Hospital Ref No: .....

If the name and/or address was different from the above period(s) to which the applicant relates please give details below:

Previous Surname/Address: .....

.....

.....

PATIENT'S HOSPITAL VISITS

Please provide as much information as possible. Give full details of all the examinations you are interested in, and if you only wish to receive data relating to a specific aspect of one or other of these examinations please specify in the comments section.

Department Attended	Dates	Consultant/GP	Comments

DETAILS OF APPLICANT (if different)

Surname: ..... Forename: .....

Address: .....

.....

DECLARATION

I declare that the information given by me is correct to the best of my knowledge and that I am entitled to apply for access to the Health Record referred to above under the terms of the Data Protection Act.

Please tick	YES	NO
1. I am the patient	☐	☐
2. I have been asked to act by the patient and attach the patient's written permission.	☐	☐
3. I am acting in locoparentis and the patient is incapable to understanding the request	☐	☐
4. I am the patients personal representative and attach confirmation of my appointment	☐	☐

Signed:..... Date:.....

Note: This section must be signed in the presence of the person who countersigns your application.