

**ASSESSING THE STABILITY AND ENHANCING THE FUNCTION OF THE
HUMAN KNEE**

By

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ABSTRACT

Knee instability has been the focus of a large number of studies over the last decade; however, a high incidence rate still exists. The aim of this thesis is to better understand knee joint stability assessment and enhancement of knee function through rehabilitation strategies. A mixed methods approach was used, incorporating both a systematic review of the literature and two experimental studies. Chapter 3 presents evidence that there is no consensus in the literature on a single technique to detect knee instability and provide return-to-play criteria. Chapter 4 demonstrates that the response rate of the anterior cruciate ligament-hamstring reflex is too low for it to be reliably used in a clinical setting, and thus it has limited value in assessing the return of neuromuscular function following knee injuries. Chapter 5 shows that peripheral electrical and magnetic stimulation can be used as an adjunct to resistance training. Overall, the research reported in this thesis provides further evidence that knee stability assessment depends on multiple factors rather than a single measure. In addition, peripheral stimulation may be efficacious to enhancing knee function and a guide to return-to-play following injuries. This thesis highlights important points for future studies on knee stability assessment and rehabilitation; the necessity of a sensorimotor assessment of knee stability and the promising role of peripheral stimulation in knee rehabilitation.

DEDICATION

I dedicate this thesis to my aunt, Ms. Najeeba Mousa Abualhasan, for her infinite support, encouragement and love. I pray that her soul rests in peace.

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LIST OF PUBLICATIONS

During the period of postgraduate study in the School of Sport, Exercise and Rehabilitation Sciences at the University of Birmingham, the following articles and conference abstracts have been accepted for publication and/or presentation at scientific meetings.

This thesis is comprised of the following three empirical papers:

Abulhasan, J.F., Snow, M.D., Anley, C.M., Bakhsh, M.M. and Grey, M.J. 2016. An Extensive Evaluation of Different Knee Stability Assessment Measures: A Systematic Review. *Journal of Functional Morphology and Kinesiology*, 1(2), 209-229.

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Abulhasan, J.F., Anley, C.M., Snow, M.D. and Grey, M.J. 2016. Hamstring stretch reflex: could it be a reproducible objective measure of functional knee stability? Poster presented at the First World Sports Physical Therapy Congress; Return to Play Conference, Bern, Switzerland, 20th - 21st November 2015.

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LIST OF ABBREVIATIONS

| | |
|--------------------|--|
| ACL | Anterior Cruciate Ligament |
| AP | Anterior-Posterior |
| CA | Cameron Anley |
| CI | Confidence Interval |
| CNS | Central nervous System |
| EMG | Electromyography |
| ICC | Intra-class Correlation Coefficient |
| IRAS | Integrated Research Approval System |
| ITB | Iliotibial band |
| JA | Jawad Abualhasan |
| LCL | Lateral Collateral Ligament |
| MB | Mohammad Bakhsh |
| MCL | Medial Collateral Ligament |
| MG | Michael Grey |
| MMS | Manual Muscle Force |
| MRI | Magnetic Resonance Image |
| ms | Milliseconds |
| MS | Martyn Snow |
| PCL | Posterior Cruciate Ligament |
| Y | Year |
| PI | Principal Investigator |
| PNS | Peripheral Nervous System |
| PRISMA | Preferred Reporting Items for Systematic Reviews and Meta-Analyses |
| QUADAS | Quality Assessment of Diagnostic Accuracy Studies |
| RM | Repetition Maximum |
| SD | Standard Deviation |
| CNS | Central nervous system |
| PNS | Peripheral nervous system |
| RFD _{max} | Maximum rate of force development |
| US | Ultrasound |
| USTEM | University of Birmingham Science, Technology, Engineering and Mathematics |

CHAPTER 1 - GENERAL INTRODUCTION

1.1 Assessment of knee stability

Joint instability is a problem that both athletes and non-athletes suffer from, and one source of instability is in the knee joint. Knee instability has a high incidence rate and has been extensively studied over the last decade. It affects a varied population, including professional athletes [Rahnama, Bambaiechi and Daneshjoo, 2009, Noya Salces et al., 2014], older adults, and recreational exercisers [Kellis et al., 2014]. A prospective cohort study conducted over seven consecutive professional football seasons found that injuries due to knee instability was second only to thigh strains (23%), and 18% of all injuries were sustained at the knee joint [Ekstrand, Häggglund and Waldén, 2011]. Such type of injuries are not limited to contact sports, as Johansen et al. [2015] concluded that the knee is the most commonly injured joint of the body (21%) in skiers. It is not only are professional athletes at risk of these injuries, as Loes, Dahlstedt and Thomée [2000] reported that knee injury accounts for 15% to 50% of injuries related to 12 different sports during a longitudinal seven year trial of recreational male and female exercisers. Similarly, it is not only the younger population that is affected, as those aged over 65 years also suffer from 1-3 incidences of falls due to several factors, included self-reported knee instability [Van Der Esch et al., 2014]. A large number of studies have tried to gain a better understanding of the risk factors [Everhart, Best and Flanigan, 2015], epidemiology [Esquivel et al., 2015], and assessment methods [Lam et al., 2009] for knee instability; however, these have yielded no robust solutions to this multifactorial problem.

The impact of knee instability can be severe, and may lead to an increased risk of falls [Van Der Esch et al., 2014] and a long period of rehabilitation [Bauer et al., 2014]. These consequences of knee instability increase the cost to health care

systems [Saltzman et al., 2015, Spetz, Brown and Aydin, 2015]. Loes, Dahlstedt and Thomée [2000] concluded that knee injuries accounted for a high proportion of the costs in the medical treatment of sport injuries. Many countries have health care systems focused on value-based care, which are systems focused on understanding the cost drivers and implementing high-value therapies [Lansky, Nwachukwu and Bozic, 2012]. Therefore, improving methods of knee instability assessment and rehabilitation would potentially reduce the health care costs associated with knee injury.

Despite the dynamic research into knee instability, it remains one of the most common problems in sport [Rahnama, Bambaiechi and Daneshjoo, 2009, Noya Salces et al., 2014, Ekstrand, Hägglund and Waldén, 2011]. Athletes damage their knees during sharp, sudden, and fast pivoting movements [Nordenvall et al., 2012], and acceleration and deceleration have also been associated with knee injury during both contact and non-contact sports [Mccall et al., 2015, Hughes, 2014]. A change in running speed results in enormous forces on the structures of the knee, which may result in knee injury [Sailors, Keskula and Perrin, 1995].

Many people participate in either recreational or competitive sport, and/or daily physical exercise. Sports-related injuries can lead to severe consequences, such as long periods of non-participation and possibly retirement from sport [Dekker et al., 2000]. Moreover, knee instability is usually associated with other knee injuries, such as meniscal tears and strains of the medial and lateral collateral ligaments [Hughes, 2014, Melnyk et al., 2007a, Héroux and Tremblay, 2006], which if not treated properly, result in further joint degeneration and additional injuries may occur. The early diagnosis of knee problems and the use of 'gold standard' assessment tools aid

in the better management of an injury. However, to the author's knowledge, there is currently no 'gold standard' technique for assessing knee stability within the clinical setting.

Previous studies have investigated several techniques for assessing knee stability [Melnyk and Gollhofer, 2007b, Van Eck et al., 2013, Malanga et al., 2003], while others have investigated techniques to improve knee function, such as examining the effect of lower extremity weight training on knee neuromuscular function [Hasan, 2015, Taradaj et al., 2013, Kyung-Min Kim, 2010, Bax, Staes and Verhagen, 2005, Fremerey et al., 2000]. The sport-related incidence rate of knee injuries in general, and knee instability in particular, are high compared to that for the hip and ankle, accounting for between 15% and 21%, respectively [Ekstrand, Hägglund and Waldén, 2011, Johansen et al., 2015, Rahnama, Bambaiechi and Daneshjoo, 2009]. To better understand this problem, researchers have investigated the risk factors for knee injury [Mccall et al., 2015, Hughes, 2014], and the sensitivity and validity of the available techniques for measuring knee instability [Barcellona, Christopher and Morrissey, 2013, Boyer et al., 2004].

However, as stated, previous research has not identified a 'gold standard' technique for clinically assessing knee instability. Some studies have used measures that are subjective rather than objective [Malanga et al., 2003], which could lead to assessment bias between clinicians, whilst the methodologies used in other studies are of low quality to confidently consider their conclusions to be robust. Many of the existing studies on diagnostic accuracy lack a reference standard to compare their results to [Fleming et al., 2002, Wroble et al., 1990], and in addition, many measurement methods and their inter-individual methodological variability has

resulted in the lack of a consensus regarding an appropriate measurement technique for knee instability [Hoshino et al., 2012, Malanga et al., 2003, Küpper et al., 2007, Lam et al., 2009, Campuzano Marín and Gómez-Castresana Bachiller, 2010, Lopomo, Zaffagnini and Amis, 2013, Leblanc et al., 2015].

1.2 Enhancement of knee stability

Unlike the literature on knee stability assessment measures, there is a consensus within the literature regarding the effectiveness of lower extremity weight training to enhance knee function and stability. A large number of studies have compared the effectiveness of different training strategies on knee function for both youth and adult populations [Barcellona et al., 2015, Mandelbaum et al., 2005, Perry et al., 2005, Seynnes, De Boer and Narici, 2007, Moezy et al., 2008, Zebis et al., 2008, Morrissey, Perry and King, 2009, Sanchez-Ramirez et al., 2013, Bieler et al., 2014, Akbari et al., 2015, Hasan, 2015, Sugimoto et al., 2015, Taylor et al., 2015, Paillard, 2008, Emery et al., 2015], while others have investigated the role of fatigue after weight training on knee proprioception and sport specific exercises [Fremerey et al., 2000, Kim et al., 2012, Melnyk and Gollhofer, 2007b, Wojtys, Wylie and Huston, 1996, Rozzi, Lephart and Fu, 1999, De Ste Croix et al., 2015]. However, although it is clear that lower extremity strength training does enhance knee stability, previous studies have used many different techniques to improve leg strength, hypertrophy and knee stability, but a consensus on an optimal strength training method has not been identified.

Barcellona et al. [2015] investigated the effects of 12 weeks of open-kinematic-chain knee extensor resistance training in three different groups with different training loads (high, low and standard training) on anterior knee stability in anterior cruciate ligament (ACL)-deficient knees. They showed a reduction in knee instability in all

groups, with a significant difference between only the low training group and the other groups. This result indicates that knee instability can be decreased by resistance training; however, a type 1 error (false positive) may have influenced the results, especially when considering the inter-individual baseline variability of the knee laxity of the three groups in the study protocol.

Gruber and Golhoffer [2004] showed that four weeks of sensorimotor training of the quadriceps muscle facilitated the afferent neural drive, which has a direct effect on joint stiffness during physical activity. They reported a significant increase in the maximum rate of force development (RFD_{max}) from 4.95 ± 0.48 N/ms before training to 6.58 ± 0.76 N/ms ($P < 0.05$) at the end of the protocol. Hence, they concluded that neural activation was of distinct relevance to enhancing joint stiffness within short time periods. However, their sample size was small ($n= 17$), which may have influenced the robustness of their conclusions.

Emery et al. [2015] in their systematic review and meta-analysis, evaluated the efficacy of various neuromuscular training strategies in youth team sports. In line with the conclusions of the previously mentioned studies, they revealed that neuromuscular training had a preventative effect for lower extremity injury. Although their results were not statistically significant, their point estimate suggested that neuromuscular training specifically reduced the risk of knee injury (IRR=0.74 (95% CI 0.51 to 1.07)). However, their conclusions are of limited use for sport-specific training programmes because each sport has specific movement requirements.

Although weight training protocols tend to enhance knee stability, a wide variety of training protocols have been utilised in studies on this topic. Consequently, it is not

yet possible to recommend a specific strength-training protocol as most effective for improving the stability of the knee.

1.3 Anatomy and physiology of knee stability

This section presents an overview of the structure and function of the knee. A comprehensive understanding of the anatomy and physiology of the structures of the knee is important in order to make accurate diagnoses and informed decisions regarding treatment plans. Additionally, an overview of the physiology of knee stability, mechanics, and hamstring stretch reflex will be presented. The aim of this section is to provide an overview on the structure and function of the knee joint, which will provide basic background knowledge to the experiments described in the subsequent chapters of this thesis.

1.3.1 Anatomy of knee stability

1.3.1.1 Bony structures

The knee is a modified hinge joint that permits flexion, extension, and rotation, yet maintains stability and control during a variety of loading situations. It consists of two bony articulations; the articulation between the femur and tibia bears most of the body weight, while the articulation between the patella and femur creates a frictionless transfer over the knee of the forces generated by contraction of the quadriceps femoris muscle [Whitesides, 2001]. The knee consists of two main joints: the femorotibial joint and the patellofemoral joint, which allow the knee to move in three different planes (sagittal, transverse and frontal). This offers a six degrees of freedom range of motion, including flexion, extension (sagittal planes), internal, external rotation (transverse plane), varus and valgus stress (frontal plane). The

position of the knee between the two longest lever arms of the body, the femur and tibia, and its role in weight bearing renders it susceptible to injuries.

1.3.1.2 Knee cartilage and ligaments

Two fibrocartilaginous menisci, medial and lateral, are positioned between the medial and lateral femoral condyles and the tibia, which accommodate changes in the shape of the articular surfaces during activity. These provide a good 'seat' on the tibial condyles for the corresponding femoral condyles. Articular cartilage covers both the femoral and tibial condyles and provides a frictionless surface that allows joint movement. These also act as shock absorbers for the body load and dynamic movements. The lateral meniscus is much more mobile than the medial meniscus, and this is reflected by the higher rate of medial side injuries [Hirschmann and Müller, 2015]. This may be due to the fixed meniscus being less able to compensate for joint forces and rotations during movement. Nonetheless, it provides greater restraint to anterior translation of the tibia on the femur. During rehabilitation, injury to the lateral meniscus is more devastating than a medial meniscus injury, leading to instability of the lateral side of the knee, and the rapid development of osteoarthritis [Haviv et al., 2016].

Ligaments are fibrous bands of tissue that connect bone to bone and provide support to joints. The knee is reinforced by two collateral ligaments, one on the medial side and another on the lateral side, as well as two stronger ligaments (the cruciate ligaments) that prevent excessive anterior, posterior, varus and valgus displacement of the tibia in relation to the femur. The patellar ligament attaches proximally to the apex of the patella and distally to the tibial tuberosity, and is the inferior continuation of the quadriceps femoris tendon. Other ligaments, such as the transverse, arcuate

popliteal, and oblique popliteal, all act as knee stabilisers. The intercondylar articular cavity of the knee is enclosed by a fibrous joint capsule.

1.3.1.3 Knee bursae, innervation and vascularity

The knee has approximately 12 bursae, which are soft tissue structures that facilitate movement of the tendons and skin over the joint. These are distributed around the whole joint in high-motion areas to ensure smooth, friction-free movement.

The knee is innervated by branches of the obturator, femoral, tibial, and common fibular nerves. Each structure within the knee is innervated by a shared or a specific nerve.

The vascular supply to the knee consists of a network of many arteries. The genicular branches of the femoral and popliteal arteries, the circumflex fibular arteries, and the recurrent branches of the anterior tibial artery, all supply blood to the knee.

1.3.1.4 Muscles acting on the knee joint

The majority of the muscles around the knee act to primarily mobilise and secondarily stabilise the knee. Some of these muscles have additional actions at the hip joint and the muscles acting on the knee can be categorised according to their position. The anterior aspect of the knee consists predominantly of the quadriceps muscles, namely the rectus femoris, vastus lateralis, vastus medialis, and vastus intermedius, and the primary function of these muscles is to extend the knee joint.

The posterior aspect of the knee consists of the biceps femoris, semimembranosus, and semitendinosus, which form the hamstring group of muscles which function as knee flexors. The plantaris muscle and the medial and lateral heads of the gastrocnemius muscle are also part of the posterior musculature of the knee. The

soleus muscle also resists anterior translation of the knee. These act primarily as plantar flexors and secondarily as knee flexors.

The medial musculature of the knee consists of the sartorius and gracilis muscles, which both aid in knee flexion. In addition, the semitendinosus acts as a medial rotator of the knee. Finally, the musculature of the lateral aspect of the knee consists of the iliotibial band and the popliteus muscles. The primary function of these muscles, along with the semimembranosus and semitendinosus, is to flex the knee, but these muscles also act as hip extensors. The biceps femoris acts as a lateral rotator of the knee, as does the semimembranosus muscle, whilst the tensor fasciae latae and iliotibial band acts as a lateral stabiliser of the knee, and the popliteus muscle rotates the knee both laterally and medially.

1.4 Physiology of knee stability

1.4.1 Terminology for describing knee instability

As Noyes, Grood & Torzilli [1989] reported in their review, in order to better understand the condition of a knee, it is important to clarify the definition of the terms commonly used to describe its motion. There is confusion within the literature over the terminology used to characterise knee instability, for example the terms instability, laxity, and disability, tend to be used incorrectly. Laxity is defined as excessive joint movement within the constraints of its ligaments, whilst knee instability is defined as the inability to maintain a single leg stance because the joint subluxes due to pathological laxity, and disability is defined as instability that

interferes with the required function of the knee. Thus, each of these terms describes a specific situation.

1.4.2 Muscular and ligamentous stabilisers of the knee

The knee is stabilised by both static stabilisers and dynamic stabilisers. Primary knee stabilisation is achieved through static stabilisers, while dynamic stabilisers play a secondary role, although both work congruently to help the knee function reliably.

This is achieved through involuntary work as some of the ligaments are connected to tendons in order to be dynamically reinforced and tightened during motion, which is when ligaments are at risk and need the assistance provided through muscular force.

1.4.2.1 Static stabilisers

The static stabilisers of the knee are the five main ligaments: the ACL, posterior cruciate ligament (PCL), medial collateral ligament (MCL), lateral collateral ligament (LCL) and popliteofibular ligament. All provide stability in a specific direction and play role in joint proprioception through their cutaneous receptors. The ACL primarily resists anterior and rotational displacement of the tibia relative to the femur, while the PCL prevents posterior displacement. The MCL provides stability to the medial aspect of the knee, preventing excessive valgus stress external rotation of the knee, becoming tight during extension and external rotation, and loose during flexion and internal rotation. The LCL runs from the femur to the fibula to stabilise the lateral aspect of the knee, preventing excessive varus stress and external rotation at all positions of knee flexion [Gollehon, Torzilli and Warren, 1987, Laprade and Wentorf, 2002]. The popliteofibular ligament acts as a static restraint to the external rotation of the tibia on the femur and to posterior tibial translation. There are additional small ligaments that surround the knee and aid in maintaining overall knee stability,

including the capsular ligament, anterolateral ligament, arcuate ligament, and posterior oblique ligament.

Part of this thesis comprises of work that assessed anterior-posterior and rotational knee laxity, which is mainly provided by the ACL. Hence, it is sensible to discuss this ligament in detail in order provide background to the work presented in Chapters 3 and 4. The ACL is considered the main stabiliser of the knee (85%) and provides controlled, smooth and stable flexion and rotation of the knee [Ellison and Berg, 1985]. It has been the major focus of studies in recent decades, and its importance and fundamental role in knee stability has led to a substantial body of work investigating its anatomy [Schutte et al., 1987, Arnoczky, 1983], physiology [Kennedy, Weinberg and Wilson, 1974, Hirschmann and Müller, 2015], biomechanics [Zlotnicki et al., 2016, Arms et al., 1984, Palmieri-Smith and Lepley, 2015], assessment [Lam et al., 2009, Schoene et al., 2009, Kiapour et al., 2014, Kostov, 2014, Rohman and Macalena, 2016], risks [De Ste Croix et al., 2015, Johnson et al., 2015] and rehabilitation [Gregory D. Myer, 2006, Hart et al., 2012, Cinar-Medeni et al., 2015, Failla et al., 2015, Grooms, Appelbaum and Onate, 2015]. The ACL is supplied by branches of the genicular artery, which consists of two bundles, the anteromedial and posterolateral. The anteromedial bundle forms the shortest band and are tense in flexion and lax in extension, while the posterolateral bundle is taut in extension and lax in flexion. The ACL experiences least strain between 20° to 30° under normal knee motion, consequently, assessment of the ACL at 20° to 30° of knee flexion is preferably in order to accurately assess the stiffness of the ligament [Goldblatt and Richmond, 2003]. During early rehabilitation of an ACL injury, knee

flexion should be set at 60° and beyond, as quadriceps muscle activity has its least degree of strain at 60° and beyond of knee flexion [Arms et al., 1984].

The ACL is supplied by branches of the tibial nerve, and Schutte et al. [1987] found three mechanoreceptors and nerve endings along the course of the ACL, each with a specific function. There are two Ruffini receptors which sub-serve speed and acceleration (sensitive to stretching) and one Pacinian receptor which signals motion. Furthermore, a small number of free nerve endings have been identified in the ACL that are responsible for pain.

1.4.2.2 Dynamic stabilisers

The dynamic stabilisers of the knee are all the muscles around the knee and were described in Section 1.3.1.4. Although their primary function is to produce motion for all the 6 degrees of freedom of the knee, they also interact with the neuromuscular system to control knee motion, and hence play a vital role in knee proprioception. A summary of the main primary and secondary stabilisers is presented in Table 1.1.

Table 1.1: Primary and secondary stabilisers in each direction of knee laxity and the innervation, origin, insertion and action of the main muscles and ligaments that restrict laxity

| Direction of laxity | Primary stabilisers (ligaments) | Secondary stabilisers (muscles) | Innervation | Origin | Insertion | Action |
|---------------------|---------------------------------|---------------------------------|--|---|--|---|
| Posterior-anterior | PCL | – | – | Anterior-lateral aspect of medial femoral condyle | Posterior slope of tibial plateau | Restrict PA translation of tibial on femur and tibial external rotation |
| | | Rectus femoris | Femoral nerve | Anterior inferior iliac spine | Patellar tendon Knee extension, hip flexion | Extends knee , flexes hip |
| | | Vastus lateralis | Femoral nerve | Greater trochanter, intertrochanteric line of femur | Patella and tibial tuberosity | Extends and stabilises knee |
| | | Vastus medialis | Femoral nerve | Medial side of femur | Quadriceps tendon | Extends legs |
| | | Vastus intermedius | Femoral nerve | Anterior-lateral femur | Quadriceps tendon | Extends knee |
| Anterior-posterior | ACL | – | – | Posterior-medial aspect of lateral femoral condyle | Anterior aspect of tibial plateau | Restrict AP translation and anterolateral rotation of tibial on femur |
| | | Biceps femoris | Long head: tibial nerve , Short head; common fibular nerve | Tuberosity of the ischium, femur | Head of fibula | Flexes knee, laterally rotates knee, extends hip |
| | | Semimembranosus | Sciatic nerve | Ischial tuberosity | Medial condyle of tibia | Flexes knee, extends hip |
| | | Semitendinosus | Sciatic nerve | Tuberosity of the ischium | Pes anserinus (tibia) | Flexes knee, extends hip |
| | | Plantaris | Tibial nerve | Lateral supracondylar ridge of femur | Tendo calcaneus | Planter flexes foot and flexes knee |
| | | Gastrocnemius | Tibial nerve | Lateral and medial condyle of femur | Calcaneus | Planter flexes foot, flexes knee |

| Direction of laxity | Primary stabilisers (ligaments) | Secondary stabilisers (muscles) | Innervation | Origin | Insertion | Action |
|--------------------------------|---------------------------------|---------------------------------|-----------------|------------------------------------|---|--|
| Varus and Valgus stress forces | | Soleus | Tibial nerve | Fibula, medial border of tibia | Calcaneus | planter flexes ankle, extends knee |
| | | Sartorius | Femoral nerve | Anterior superior iliac spine | Pes anserinus (tibia) | Flexes, abducts and laterally rotates hip, flexes knee |
| | MCL | – | – | Medial femoral epicondyle of femur | Periosteum of proximal tibia | Restrict valgus stress forces and anterior-medial rotation of tibia on femur |
| | LCL | – | – | Lateral femoral epicondyle | Posterior to anterior point of fibular head | Restricts varus stress forces and posterior-lateral rotation of tibia on femur |
| | | Gracilis | Obturator nerve | ischiopubic ramus | Pes anserinus (tibia) | Flexes, adducts and medially rotates hip Medially rotates tibia if femur fixed, laterally rotates femur if tibia is fixed |
| | | Popliteus | Tibial nerve | Lateral femoral epicondyle | Posterior surface of tibia | Flexes hip, medially and laterally rotates knee |
| | | Tensor fasciae latae | Gluteal nerve | Iliac crest | Iliotibial tract | |

Abbreviations:

ACL = anterior cruciate ligament, PCL = Posterior cruciate ligament, MCL = Medial collateral ligament, LCL = Lateral collateral ligament, AP = Anterior-posterior, PA = Posterior-anterior

1.4.3 Knee neuromuscular and proprioceptive control

1.4.3.1 Neuromuscular control

Human movement consists of both conscious and subconscious movements. In order for the body to move and function efficiently, the actions of the central nervous system (CNS), peripheral nervous system (PNS), and the neuromuscular system must be synchronised to function in a congruent manner [Winter, 2009].

Neuromuscular control relies on afferent sensory information sent from mechanoreceptors (Ruffini, Pacini, and Golgi-like receptors) within the muscles, ligaments, and tendons to the CNS (subconscious), in order to modulate conscious movements, the impulses for which descend through efferent motor neurons along the cortical spinal tract to the target muscle [Nyland et al., 1994]. The efferent motor and afferent sensory neurons also innervate the proprioceptive organs in the body. Consequently, a continuous neurofeedback loop develops between the CNS and the proprioceptive organ (e.g. Golgi tendon organ and muscle spindles), which augments muscle force generation and proprioceptive sensitivity. Increased neural drive leads to greater efficiency in neural transmission [Aagaard, 2003] and a reduction in the onset latency of muscle force production follows [Nyland et al., 1994].

As mentioned in Section 1.4.2, static, dynamic, and proprioceptive mechanisms all act to stabilise the knee. Research suggests that an ACL-hamstring reflex exists and plays a role in knee stability [Grüber, Wolter and Lierse, 1986, Tsuda et al., 2001].

Beard et al. [1993] showed that ACL-deficient knees had a longer hamstring contraction latency than non-injured knees (99 ms and 53 ms, respectively), yet Jennings and Seedhom [1994] when replicating the work of Beard et al. [1993] found no significant difference between hamstring contraction latency in ACL-deficient knees and non-injured knees. However, Jennings and Seedhom [1994] recruited

participants who had undergone arthroscopy sometime in the previous 10 years without reporting if the participants in the ACL-deficient knee group had undergone any proprioceptive training, while Beard et al. [1993] recruited participants within 18 months of arthroscopy and none of their participants had received any proprioceptive training. This difference in participant populations may have resulted in the disparity in the results obtained from these two studies, as sensorimotor training may enhance neural drive and subsequently improve joint proprioception [Fremerey et al., 2000, Cooper, Taylor and Feller, 2005, Moezy et al., 2008], thereby reducing the delayed onset of the ACL-hamstring reflex.

1.4.3.2 Proprioceptive control

Another crucial element of knee stability is the proprioceptive control of the joint. All of the previously mentioned ligaments and muscles consists of proprioceptive fibres (mechanoreceptors) [Mccloskey et al., 1983]. These proprioceptive fibres, together with the ligaments and muscles, combine to create reflex arcs that play a vital role in knee stability [Tsuda et al., 2001, Grüber, Wolter and Lierse, 1986] by providing feedback between the CNS and the joint. The CNS (cerebellum) receives neurologic input from joint position sensors, muscles spindles, and the joint capsule, and this generates neurological feedback from the cerebellum in response to joint movement which aids in maintaining joint stability [Mccloskey et al., 1983]. However, this protective mechanism can fail during movements that exceed the structural limits of the joint. For example, an external traumatic force or sudden unpredicted movements can exceed the ability of the proprioceptive arc to respond, and consequently, injury may occur. The resistance of the knee to injury depends on the strength of both its

static and dynamic stabilisers, and the proprioceptive efficiency of the structures around the knee [Solomonow et al., 1987].

Several studies have tackled knee instability with respect to various aspects, for example some have focused on techniques for assessing knee instability [Markolf, Graff-Radford and Amstutz, 1978, Cannon, 2002, Lam et al., 2009, Malanga et al., 2003], while others have focused on rehabilitation strategies [Fremerey et al., 2000, Gregory D. Myer, 2006, Imoto et al., 2011, Hart et al., 2012, Ardern et al., 2014]. In addition, a substantial body of work has focused on knee injury prevention programmes [Bizzini and Dvorak, 2015, Sugimoto et al., 2015], injury predictors [Everhart, Best and Flanigan, 2015], and risk factors [Mccall et al., 2015]. However, knee injuries are evident during sport participation and/or activities of daily living, and routine knee stability assessments for high risk, highly active populations reduces the risk of knee injury [Michaelidis and Koumantakis, 2014, Mccall et al., 2015]. Hence, accurate monitoring and profiling of knee stability using valid and sensitive measures is vital during both injury assessment and rehabilitation [Ter Stege et al., 2014].

Figure 1.1 summarises the most important factors that contribute to knee stability.

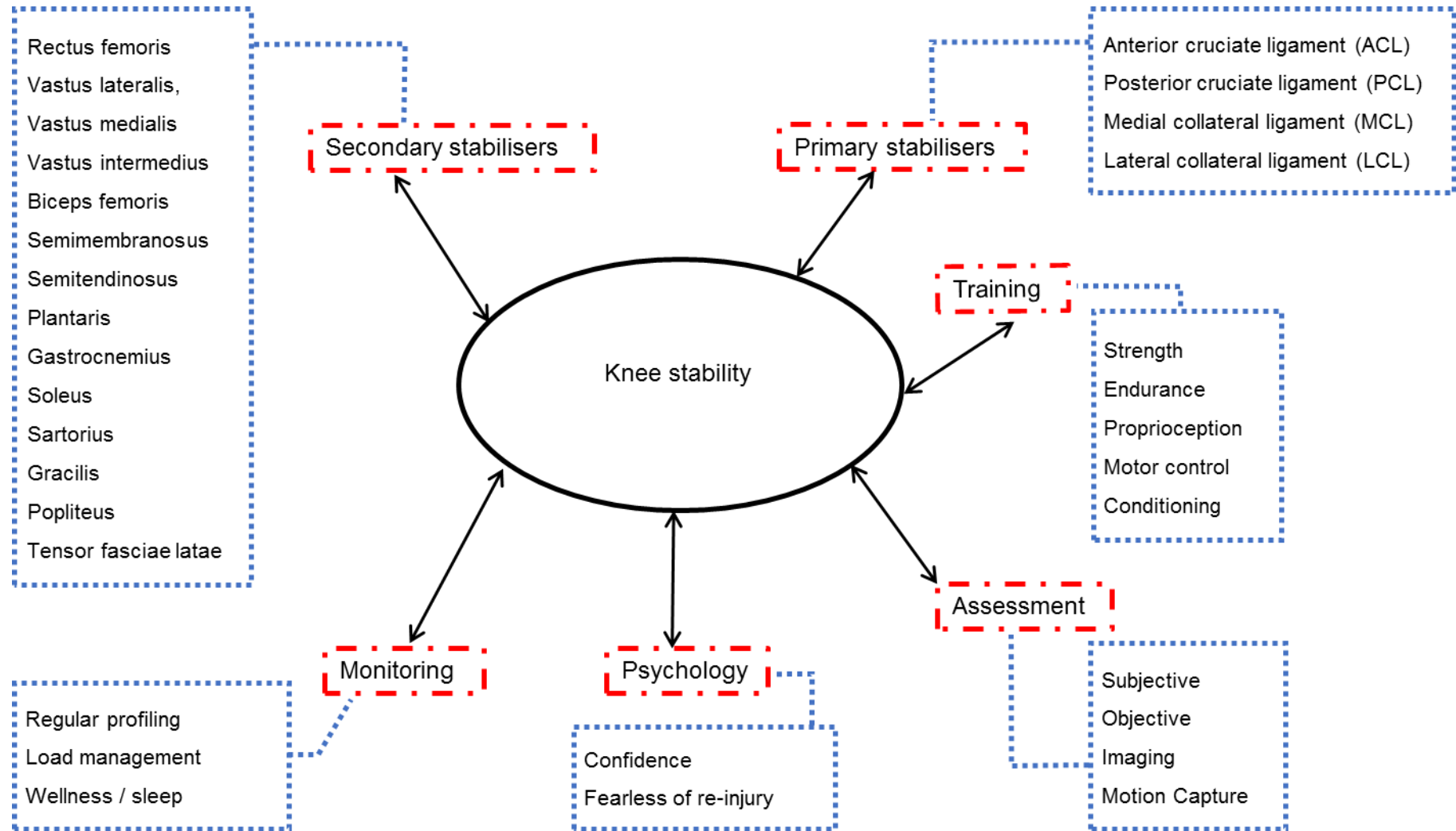


Figure 1.1: Schematic showing the most important factors that contribute to knee stability

1.5 Research gaps in the related literature

Previous research has suggested a variety of actions that can be taken to reduce the toll of knee injuries in terms of epidemiology [Sugimoto et al., 2015], economic cost [Saltzman et al., 2015], and return-to-play considerations [Bauer et al., 2014]. Two specific suggestions for future research that were presented in several reports on knee injury were: (1) an emphasis on the use of valid and reliable measures for the assessment and prevention of knee instability [Küpper et al., 2007, Pugh et al., 2009]; and (2) the enhancement of knee strength training protocols [Eklund et al., 2015, Hasan, 2015, Sugimoto et al., 2015]. These are the areas that are addressed in the work presented in this thesis.

1.5.1 Assessment of knee stability

The primary focus of this work was the assessment of knee stability and function, which is only a single part of a holistic knee joint rehabilitation and injury prevention protocol. Several techniques for measuring knee stability have been previously investigated. Some of these, such as clinical examination tests, have been studied in depth [Küpper et al., 2007, Malanga et al., 2003, Barcellona, Christopher and Morrissey, 2013], while others, such as the use of stretch reflex onset delay as a measure of knee stability, have only more recently been investigated [Schoene et al., 2009, Friemert et al., 2005a]. A diversity of views for each test has been published within the literature, yet no consensus has been reached regarding a 'gold standard' measure. An extensive overview of knee stability measures will be presented in chapter 3 in order to systematically review the related literature.

The results of previous studies suggest that the hamstring stretch reflex may be a useful measure of knee stability. However, none of these studies have used a clinically relevant technique to measure the ACL-hamstring reflex [Tsuda et al., 2001,

Friemert et al., 2005a, Schoene et al., 2009]. For example, Schoene et al. [2009] assessed the reliability of the ACL-hamstring reflex as an objective measure of functional knee instability; however, they used a laboratory-based instrument (rig) rather than clinical apparatus, thus limiting the utility of their technique for clinical settings.

To allow the hamstring stretch reflex to be used widely within the clinical setting, it should be reliably measurable using commonly available instrumentation. There is a consensus in the literature that the KT-1000 arthrometer is one of the most commonly used objective anterior-posterior knee stability measures [Highgenboten, Jackson and Meske, 1989, Wroble et al., 1990, Jardin et al., 1999, Feller, Hoser and Webster, 2000, Boyer et al., 2004, Isberg et al., 2006]. In addition, Van Eck et al. [2013] reported that measurements made using the KT-2000 arthrometer (MEDmetric Corp, San Diego, California, USA) during the maximum manual force technique, were more sensitive (0.93) and specific (0.93) than all the other measurements of knee stability. Hence, the KT-2000 arthrometer with the maximum manual force technique was chosen for use in study 1 (chapter 4) as this is a commonly used and suggested clinical measure of knee stability.

1.5.2 Enhancement of knee stability

Previous studies suggest that high intensity training results in an increased speed and magnitude of muscle force production [Bieler et al., 2014, Seynnes, De Boer and Narici, 2007]. The rate of force development can be measured by the slope of the force-time curve [Aagaard, 2003], and in knee injury prevention strategies, the rate of force is as important as the muscle strength itself [Gruber and Gollhofer, 2004, Hughes, 2014, Mccall et al., 2015, Ter Stege et al., 2014]. For example, during voluntary muscle contraction the muscle takes approximately 300 ms to attain peak

contraction force [Aagaard et al., 2002], while in explosive movements, such as during on-field sports participation (involuntary), the maximum force occurs 50–250 ms after initial ground contact [Aagaard et al., 2002]. Hence, a fast muscle response is a critical component of knee stability during physical activity. Ideally, both muscle strength and muscle response time should be optimised to provide knee stability, and both are critical to injury prevention during participation in sports. In general, the earlier the onset of force production around the knee, the more stable the joint [Gruber and Gollhofer, 2004, Cowling and Steele, 2001].

A substantial amount of work has been conducted to develop evidence-based exercises to improve knee stability, and protocols have been developed using resistance training [Bieler et al., 2014], isometric training [Del Balso and Cafarelli, 2007], and the application of electrical muscle stimulation [Taylor et al., 2015]. In addition, researchers studying knee rehabilitation programmes have gone beyond the assessment of the outcome of training programmes and have also investigated other factors that affect knee stability. For example, Rozzi, Lephart and Fu [1999] studied knee stability after muscle fatigue and found that both male and female participants exhibited decrements in their proprioceptive ability and altered muscle activity when fatigued, which suggests that muscular fatigue decreases knee stability. Similarly, Wojtys, Wylie and Huston [1996] concluded that fatigue may play a role in the pathomechanics of knee injuries during physically demanding sports.

Previous studies have also examined the effects of agility training on knee stability [Abaza, 2015, Araujo, Cohen and Hayes, 2015, Vaithianadane, Patel and Vakhariya, 2014]. Sailors, Keskula and Perrin [1995] examined changes in anterior knee laxity in normal and ACL-reconstructed (patellar tendon graft) knees before and after 30

minutes of running. They found that anterior knee stability did not significantly differ ($p = 0.40$) between the ACL-reconstructed knees (6.5 mm) and normal knees (5.7 mm), which suggested that running does not alter knee stability. However, their sample size was small ($n = 7$) and they only recruited female participants, thus limiting the generalisability of their results

A systematic review by Cooper, Tayler and Feller [2005] on the effects of neuromuscular training interventions on knee and ACL injuries, showed a reduction in the incidence of repeat injuries in female athletes. Five of the six interventions reviewed showed that strength, balance, and core stability training can induce neuromuscular changes and potentially prevent injuries in female athletes. However, their review included studies comparing participants who had undergone surgical ACL reconstruction with those who had ACL-deficient knees, even though the rehabilitation programmes for these groups differ. Because of these differences in the rehabilitation programmes, caution should be exercised when comparing such groups and more rigorous inclusion criteria should be used to produce more conclusive results.

Recent research has shown that neuroplasticity training through the integration of visual-motor training approaches into current knee injury management protocols may improve the results of rehabilitation programmes [Grooms, Appelbaum and Onate, 2015]. However, analyses of visual-motor training tend to yield inconclusive results owing to the subjective nature of the technique. Nevertheless, Grooms, Appelbaum and Onate [2015] acknowledged that enhancement of current rehabilitation protocols may lead to more positive results. Whole-body vibration and balance training have similarly been suggested as effective means of enhancing knee stability [Akbari et

al., 2015, Moezy et al., 2008]. In general, there is a consensus that resistance training of the core and/or thigh muscles improves knee and/or body stability [Cinar-Medeni et al., 2015, Maria et al., 2015]. Additional rigorous longitudinal and controlled trials and an exploration of novel neuromuscular re-education techniques are warranted to further improve current methods of knee injury rehabilitation and prevention.

The effects of neuromuscular electrical stimulation on knee function have been extensively studied. This technique has been used after surgery [Stevens, Mizner and Snyder-Mackler, 2004, Kho et al., 2015, Eriksson and Häggmark, 1979, Morf et al., 2015], within trauma units [Howlett et al., 2015, Deley et al., 2015, Kho et al., 2015], at sports rehabilitation institutions [Taylor et al., 2015], to treat immobilised patients [Morrissey et al., 1985], and following a stroke [Bauer et al., 2015, Howlett et al., 2015]. All of these studies reported the positive effect of electrical muscular stimulation and recommended its use. Recent reports have concluded that functional electrical stimulation improved the gait cycle in cerebral palsy [Khamis et al., 2015] and multiple sclerosis [Coote et al., 2015] patients. In addition, a recent systematic review revealed that electrical muscular stimulation was the most effective means of reducing pain in osteoarthritic knees [Zeng et al., 2015].

Like electrical stimulation, the use of peripheral magnetic stimulation as a means of rehabilitation has also been investigated in similar populations [Szecsi, Straube and Fornusek, 2014, Atzori et al., 2013, Kim et al., 2012, Tsai, Chiang and Jiang, 2004, Smania et al., 2003], and beneficial effects have been reported in both recreational exercisers [Atzori et al., 2013] and patients [Smania et al., 2003]. Smania et al. [2003] showed that peripheral magnetic stimulation may have positive short- and

medium-term therapeutic effects on myofascial pain. Han, Shin & Kim, [2006] compared the effects of magnetic versus electrical muscle stimulation on pain level, and showed that magnetic stimulation of the quadriceps muscle produced less pain at the same level of isometric peak torque than did electrical stimulation. Although both electrical and magnetic muscle stimulation have been investigated in different rehabilitation strategies, to the author's knowledge none of the previous studies have tested the effects of these techniques on muscle failure during resistance training. Previous studies have applied the two stimulation techniques from the first repetition of a weight training set [Kubiak Jr, Whitman and Johnston, 1987, Szecsi, Straube and Fornusek, 2014, Bauer et al., 2015], but it may be that hypertrophy is better induced by applying the stimulation at the time of failure in order to overcome muscle fatigue. This may allow more repetitions to be performed than would be possible without the stimulation and thus enhance muscle strength, hypertrophy, and perhaps, knee stability.

In the human body, fatigue is centrally regulated through the CNS and peripherally through the PNS. Both systems contribute to the perception of, and performance decrements associated with, fatigue during exercise. There is a consensus within the literature that both electrical and magnetic stimulation act directly on the motor units within the muscle and thus bypass involuntary regulation by the CNS. Increased stimulation intensity and resistance load will lead to greater strength [Campos et al., 2002], and stimulation at the onset of muscle fatigue may produce more muscle contractions and thus enhance performance [Kremenec et al., 2009]. The promising effects of peripheral magnetic stimulation have been reported in different rehabilitation fields, yet the literature lacks evidence as to its usefulness as an

adjunct to already implemented strength training protocols, and no previous research has compared the effects of electrical and magnetic stimulation following muscle failure. Hence, in study 2 of this thesis (chapter5), an investigation into the effects of electrical and magnetic muscle stimulation after fatigue-induced muscle failure is reported.

1.6 Summary of the literature in areas pertinent to this thesis

The literature highlights the need for a 'gold standard' measure of knee stability, and for better techniques for enhancing neuromuscular control of the knee, both of which would improve knee injury rehabilitation and prevention protocols. As discussed earlier, knee stability is not solely dependent upon the muscles and ligaments acting on the knee, as proprioception also plays an important role in knee stability. The current clinical techniques for measuring knee stability focus solely on assessing the integrity of the ligaments that stabilise the knee, while assessment of the proprioceptive part of knee stability has been limited to intraoperative assessments [Friemert et al., 2005a]. Thus, an investigation of the ACL-hamstring stretch reflex as an objective clinical measure may provide a clinically useful means of assessing the sensorimotor integrity of the knee.

As mentioned previously, the research suggests that better muscle strength and rapid muscular force generation around the knee will improve knee stability [Cinar-Medeni et al., 2015]. Moreover, the addition of electrical muscle stimulation and peripheral magnetic stimulation to strength and hypertrophy training protocols has yielded promising results [Szecsi, Straube and Fornusek, 2014, Kubiak Jr, Whitman and Johnston, 1987, Taradaj et al., 2013, Doix et al., 2014]. However, these studies have utilised different techniques and protocols, for example, some have applied either electrical or magnetic stimulation from the first repetition of a weight training set

[Taradaj et al., 2013], while others have utilised electrical stimulation as an independent treatment arm and compared this with control and isometric quadriceps training groups [Kubiak Jr, Whitman and Johnston, 1987]. It may be that muscle strength, hypertrophy and knee stability are better enhanced by applying the stimulation at the time of fatigue-induced muscle failure in order to facilitate more repetitions. Potentially, this would increase the total stimulation intensity, rate of force, and resistance load of an exercise protocol, and may lead to enhanced strength, hypertrophy and knee stability.

These gaps in the literature led to the two studies that are described in this thesis. In the first study, the hamstring stretch reflex was tested as a measure of knee stability, while in the second study, electrical and magnetic stimulation was compared at the point of muscle failure as a means of increasing thigh strength, hypertrophy and decrease anterior knee laxity.

1.7 Scope of this thesis

Figure 1.2 is a schematic showing the chapters in this thesis. This thesis consists of an overview of the assessment methods used in the studies reported in this thesis (chapter 2), an extensive systematic review of the literature on knee stability measures (chapter 3), two experimental studies (chapter 4 and chapter 5) and a general Discussion section (chapter 6). The first study examined the usefulness of a novel technique for assessing knee stability by quantifying the ACL-hamstring stretch reflex using a KT-2000 arthrometer. It was hypothesised that this reflex may be a reproducible and objective method for assessing the neuromuscular function of the ACL using a KT-2000 arthrometer as a clinical tool. The second study aimed to: (1) determine the ability of electrical muscle stimulation and peripheral magnetic stimulation at the time of fatigue-induced muscle failure to stimulate more repetitions

during muscle hypertrophy training; and (2) to compare the effects of electrical and magnetic muscle stimulation on mean quadriceps strength and hypertrophy, as well as anterior-posterior knee laxity. It was hypothesised that magnetic stimulation would induce more repetitions after perceived muscle failure than electrical muscle stimulation. In addition, it was hypothesised that the addition of electrical muscle stimulation and peripheral magnetic stimulation to a weight-training protocol would boost muscle strength, increase quadriceps hypertrophy, and improve anterior-posterior knee laxity after a 3-week training programme.

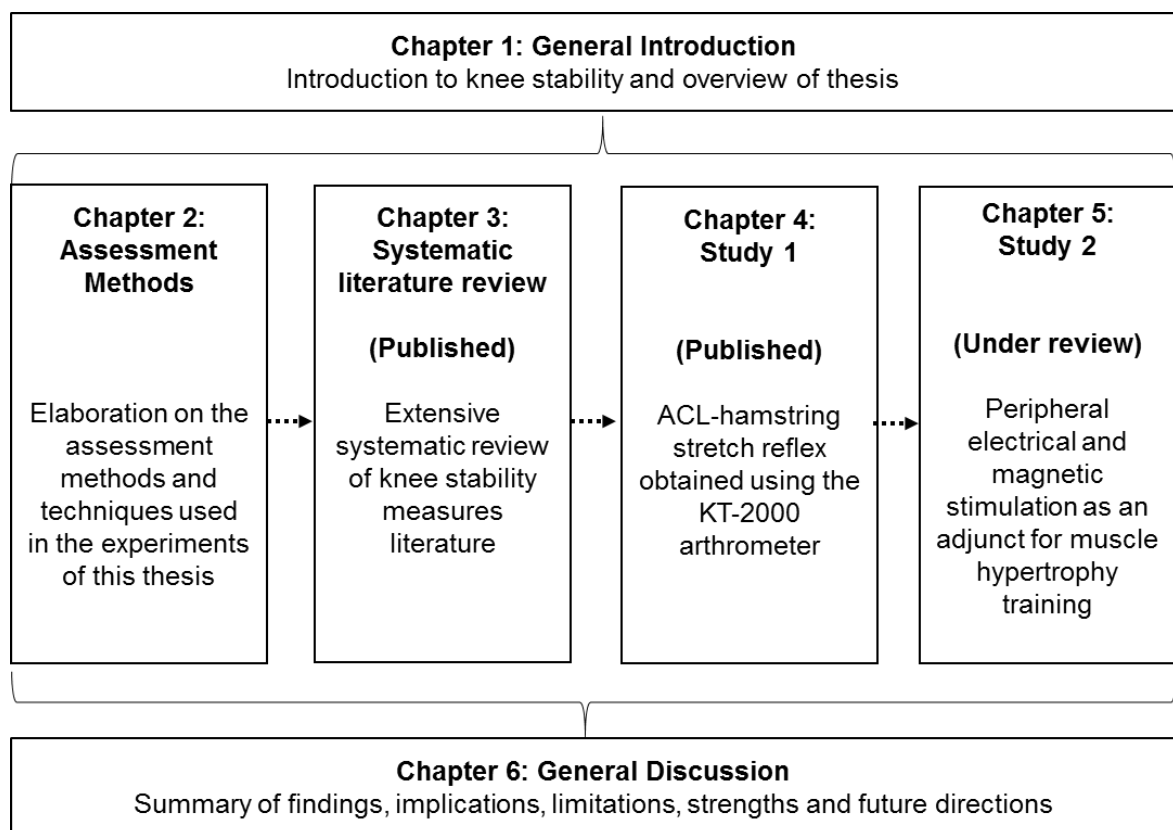


Figure 1.2 Schematic showing the chapters in this thesis

CHAPTER 2 - ASSESSMENT METHODS

This chapter elaborates on the assessment methods and techniques used for each study described in this thesis. In addition, an overview on the utility and applicability of each technique is provided.

2.1 Electromyography

Electromyography (EMG) is a diagnostic tool that is commonly used to gather information on how efficiently muscles can generate force, produce movement, and function. Similar to any physiological measurement tool, it has both advantages and limitations. The access and application of EMG must be scientifically based rather than trial and error based [De Luca and Van Dyk, 1975], and because EMG is easy to use, it is therefore also easy to abuse [De Luca, 1997]. Static and dynamic EMG has three main uses: measuring the activation timing of the tested muscle; assessing the force/EMG signal relationship; and as a fatigue index [De Luca, 1997]. The most important technical considerations related to study 1 of this thesis (chapter 4) for recording EMG in order to measure onset latency are discussed in this chapter. Thereafter, a guide to all practitioners in the proper uses of EMG as a measure of onset latency, including recommendations and application problems, is provided.

2.1.1 Factors affecting the EMG signal

Several independent factors affect the detected EMG signal, and consequently the data produced by the tested muscle; one of these factors is the amplitude of the signal after being rectified and smoothed. The detected signal is a result of numerous physiological, anatomical, and technical elements grouped together, and while some of these elements can be managed by consistent and appropriate application, others cannot [De Luca et al., 2006]. As a general guideline, understanding the anatomy and physiology of the tested region of the body will increase the likelihood of achieving the highest possible signal fidelity. Other factors that can affect the EMG signal include: ii) the area and shape of the electrodes; iii) the location of the electrodes; iv) the space between each electrode; and v) the orientation of the

detection surfaces with respect to the muscle fibres [De Luca, 1997, De Luca et al., 2012].

In addition, several other extrinsic and intrinsic factors contribute to the EMG signal quality, and one example of an extrinsic factor is the shape and size of the electrode itself. These parameters play a vital role in determining the number of active motor units being recruited, and thus activated [Koh and Grabiner, 1993]. Another example of an extrinsic factor is the orientation of the detection surfaces with respect to the orientation of the muscle fibres, which affects the conduction velocity of the detected action potentials [De Luca et al., 2012].

Intrinsic factors, which cannot be controlled or modified, include the anatomical and physiological individualities of the muscle. For example, the number of active motor units at the time of contraction and the fibre type composition of the muscle are intrinsic factors [Taylor and De Luca, 1997]. Blood flow in the tested muscle, fibre diameter, depth and location of the active fibres [Herda et al., 2015], and amount of soft tissue between the surface of the muscle and the electrode are all also intrinsic factors that affect the EMG signal fidelity and amount of crosstalk [Winter, Fuglevand and Archer, 1994]. Similarly, there are technical factors that can be modified to improve the EMG signal. Band-pass filtering of the electrode [Potvin and Brown, 2004] and crosstalk from nearby muscles can also affect the EMG signal [Nawab, Chang and De Luca, 2010] and there are two important factors that affect the characteristics of the detected signal. First, is the relative movement of the electrode during the contraction [De Luca et al., 2010], which can change the number of active motor units and the detection volume, and second, are changes in the spatial filtering

characteristics of the signal detection arrangement which can affect the amplitude and frequency of action potentials [De Luca, 1997].

2.1.2 Electrode placement

Two surface electrodes need to be placed to measure muscle activity; the active electrode and the reference electrode. The reference electrode plays an important role in determining the EMG signal fidelity by providing a common reference for the differential input of the preamplifier in the electrode [Clancy, Morin and Merletti, 2002]. This must remain in very good contact with the skin and conductive gels are always useful in ensuring this. In addition, the reference electrode should be placed as far as possible from the active electrode [Stegeman et al., 2000], which should be placed with respect to the motor points in the muscle; the nearer the electrode is placed to the motor points, the higher the amplitude and frequency of the detected signal [De Luca, 1997].

2.1.3 Digital sampling

All EMG signals must be converted from analogue to digital format for analysis because computers can only process the signal after digitisation into discrete numbers. This conversion procedure is known as digital sampling and this generates a sequence of numbers that vary in amplitude throughout their range. Each number represents the amplitude of a signal at a specific point in time [Clancy, Morin and Merletti, 2002]. The outcome signal is called the digital signal, which is a sampled version of the analogue signal.

An EMG signal can be digitised at several sampling frequencies, which is crucial for generating an accurate and reproducible sampled signal. To create a reproducible and accurate digital signal, the sampling frequency must obtain data from all of the amplitudes of the analogue signal [De Luca et al., 2006], and this can be achieved by

sampling at a frequency that produces sinusoids that shield all of the signal amplitudes at each point of time along the acquired signal [De Luca, 1997]. If the sampling frequency is too low, the digital signal will be under-sampled causing aliasing. To ensure that the digital signal contains sufficient samples to avoid aliasing, the Nyquist Theorem rule should be implemented, which states that digital sampling at no less than twice the signal frequency is necessary to produce an acceptable sampling rate [De Luca, 1997]. The EMG signal bandwidth spans up to 500 Hz; therefore, all EMG sampling should by default be performed at a minimum sampling rate of 1024 Hz [De Luca and Van Dyk, 1975].

2.1.4 Muscle activation time measurement and onset latency of the stretch reflex

How to best implement EMG for practical and clinical experiments is discussed in this section. De Luca [1997] recommended that the full activation time should be measured for all types of muscle contractions, as this will allow a full overview of the amplitude variability along the entire contraction time.

Electromyographic activity of muscles can be used to evaluate the stretch reflex through the measure of muscle onset latency. The onset latency of a reflex is defined as the time delay from the onset of muscle activity to the onset of the first major deflection in the reflex of the tested muscle. To detect the onset latency of a stretch reflex response, a time window of a 20—50 ms should be defined after the stretch onset, which incorporates the physiological range for the onset of a reflex [Friemert et al., 2005b]. Within this window, the onset of the reflex can be determined through visual inspection by comparing the magnitude of the response with the background EMG of the tested muscle. In conclusion, EMG is a useful technique for use in biomechanical studies where it can be used to gather information on muscle

activation, especially onset latency. The consensus in the literature on the utility of EMG led to the use of this tool in the work conducted in study 1 (chapter 4).

2.2 Motion capture system

2.2.1 Classification of the motion capture system

The capture of a moving object, a human walking, using cine film was first reported in the 1940s and 1950s in California, USA [Inman, Ralston and Todd, 1981]. In the late 1970s and 1980s, infra-red and video-based cameras were industrialised, and at that point tracking systems were developed and refined over time. Tracking systems can be classified as non-visual (inertial based), visual (marker based), or a combination of both [Zhou and Hu, 2008]. More recently, 3D motion capture systems have been developed, such as the Quick Mag (Ouyoukeisoku, Kenkyusyo, Japan), Video Locus (Anima Co. Ltd., Japan), Peak 5 (Peak Performance Technologies Inc., Colorado, USA), Vicon 370 (Oxford Metrics Co. Ltd., Oxford, UK), Elite (Bioengineering Technology & Systems, Milan, Italy), and Optotrack 3020 (Northern Digital Inc., Ontario Canada). Such systems made the process of recoding and analysing motion far easier and faster, and the integration of these advanced technologies with basic science knowledge has enhanced the utility of motion capture system techniques. In addition, a thorough understanding of the biomechanics of human movement is essential for data interpretation and the analysis of human motion. The use of such techniques during laboratory-based experiments has helped scientists and researchers gain a better understanding of human kinesiology [Coutts, 1999, Wren et al., 2011]. They have also been widely used for clinical decision making and the evaluation of therapeutic outcomes [Chung et al., 2011b].

Human motion tracking for rehabilitation purposes has been an active research topic since the 1980s, and has been used during stroke rehabilitation to assess, rectify,

and monitor movement patterns [Zhou and Hu, 2008]. Motion capture systems generate real-time data that dynamically represent the human body at pose changes [Beth et al., 2003]. Specifically, motion capture systems can measure a range of motion and the starting position of a joint together with the acceleration of a limb segment [Coutts, 1999].

The validity and reliability of such systems has also been investigated [Chung and Ng, 2012, Fonda, Sarabon and Li, 2014, Williams et al., 2009, Robert, Michele and Gordon, 2005]. Williams et al. [2009] compared observational data from 30 healthcare providers with captured and video recorded locomotion clips. They reported low accuracy (30% to 50% inaccuracy) and high variability between the observers, even with experienced observational analysers, and concluded that their results support the need for the objective quantification of human movements. Ehara et al. [1995] compared the measurement accuracy and data processing times of different motion capture systems. The Optotrack 3020 was found to have the shortest processing time (5 s) and the smallest measurement errors (1 mm). They concluded that the interface software and data processing time of each system plays an important role when deciding which motion capture system to use.

The accuracy and precision of motion capture systems have also been investigated [Charlton et al., 2004, Windolf, Götzen and Morlock, 2008, Chung et al., 2011a, Chung et al., 2011b]. Chung et al. [2011a] evaluated the within- and between-sessions variability of the Vicon system when capturing fencing lunges. They found a moderate to high repeatability; the within-session coefficient of multiple correlations ranged from 0.70 to 1.00, and for between-sessions ranged from 0.69 to 0.99. In addition, Chung et al. [2011b] compared the validity of the Vicon system against the

XSENS (Xsens Technologies 2007) inertial tracking sensors for upper limb fast joint motions of the shoulder, elbow, and wrist. They found good agreement in all three joints, for example, the Pearson's correlations for the wrist joint ranged from 0.76 to 0.84.

One widespread use of motion capture systems during assessment and rehabilitation is to measure the reaction times of moving joints or body parts. The majority of previous research has focused upon the upper limbs and gait [Dawson, Bryan and Kelly, 2015, Ehara et al., 1995, Davis et al., 1991, Greenberg et al., 1996, Bonnechère et al., 2015]. However, these findings cannot be replicated for knee displacement measures because of the differences in the kinetics and kinematics between upper and lower limbs [Christou and Rodriguez, 2008]. Consequently, Chung and Ng [2012] investigated the reliability of the Vicon system for measuring the motor reaction time of the knee during extension. They reported good reliabilities for both measurements (intra-class correlation coefficients ranged from 0.72 to 0.822) with a mean onset time of 8 milliseconds for the Vicon system, which was faster than that measured with an accelerometer. Likewise, Everaert et al. [1999] determined the accuracy of a 3D motion analysis system to measure small linear displacements of predefined objects. They tested the repeatability of the motion capture system using between-trials comparisons, and in 810 trials, the mean standard deviation (SD) and 99% confidence interval (99% CI) inter-trials was 0.47 mm (99% CI: ± 0.121 mm) and for intra-trials was 0.30 mm (99% CI: ± 0.077). They

concluded that motion analysis allows measurement with high accuracy for applications in rehabilitation research.

Although motion capture systems are costly, they provide an abundance of excellent information on the detailed characteristics of any activity. Nonetheless, these systems have not yet been designed to provide patient-oriented therapy, and therefore cannot be used within the home environment. There is a consensus in the literature that motion capture systems can support various rehabilitation settings and the delivery of training [Bonnechère et al., 2015, Dawson, Bryan and Kelly, 2015, Fonda, Sarabon and Li, 2014, Coutts, 1999, Sandau et al., 2014]. However, there is evidence within the literature that the use of human motion systems is complicated and an experienced operator is required to reduce errors and avoid pitfalls [Wren et al., 2011]. Despite these drawbacks, 3D motion analysis technology, such as that used by the Vicon system, is regarded as the gold standard for the analysis of human movement [Mcginley et al., 2009].

2.2.2 The Vicon motion capture system

The Vicon motion capture system has been used in the animation market and for biomechanics and ergonomics for the last 30 years. The Vicon uses multiple cameras, each emitting a beam of infrared light, with small reflective markers placed on the object to be tracked, and infrared light flashes are picked up again by the cameras. Several 2D data trajectories from the active cameras are then combined to determine the 3D position of the reflective target. A series of predefined calculations are performed by the system software and 3D kinetic, kinematic, and spatiotemporal parameters are then calculated to measure the outcome of the trial.

The Vicon system has been used to analyse different human movements, such as whole body vibration [Robert, Michele and Gordon, 2005], gait analysis [Davis et al.,

1991], bike fitting [Fonda, Sarabon and Li, 2014], and ankle joint assessment [Nair et al., 2010]. The motion capture system provides quantified kinematic, kinetics and timing data that can help clinicians and researchers assess patients, monitor injuries, and guide rehabilitation strategies [Wren et al., 2011]. Moreover, Windolf et al. [2008] concluded that with careful configuration, the Vicon-460 system provides a powerful measuring method for biomechanical applications. In addition, students and staff at the School of Sport, Exercise and Rehabilitation Sciences at the University of Birmingham, United Kingdom, have had the opportunity to use the Vicon system for research purposes. Based on the reasons described above, the Vicon 460 was used in study 1 (chapter 4) as a reference standard for the EMG parameters when measuring the onset (ms) and magnitude (mm) of tibial translation.

2.3 Ultrasonography

Several imaging techniques have been developed for, or applied to, medical applications, including plain X-ray, magnetic resonance imaging (MRI), telos stress radiography, and ultrasonography (US). Each imaging modality has advantages and limitations, and their frequency of use and applications vary. Plain X-rays are useful for examining bone fractures, while MRI provides better information on knee ligaments and cartilage injuries [Lee and Bouffard, 2001]. US of the musculoskeletal system is a clinical tool that is easy to access, and the ease of use, ready accessibility, low cost, and rapid evaluation of soft tissues of the knee make it a quicker assessment tool than MRI [Friedman, Finlay and Jurriaans, 2001].

2.3.1 History and definition of US

Ultra means 'beyond', hence ultrasound refers to sound waves beyond the level of human hearing, which is 20,000 or more vibrations per second [Otto, 2000]. US is used in a variety of imaging tools and the first article on medical US was published by

Karl Dussik [1942]. Then, in 1958, Donald, Macvicar and Brown [1958] were the first to report the practical application of an ultrasound machine as a diagnostic tool for abdominal masses.

US devices consist of a transducer that is connected to a monitor display, along with a central processing unit. The probe transducer attached to the ultrasound machine gives off sound waves that are then reflected back from organs or tissues [Dussik, 1942], and this reflection provides an instantaneous image of what is inside the body and is displayed on the ultrasound machine. The transducer acts like a speaker that generates sound waves, then a microphone that receives the sound waves constructs the US image on the machine monitor, and finally, this image is used to analyse and diagnose potential problems or defects [Donald, Macvicar and Brown, 1958]. The wavelength and frequency of the ultrasound device are inversely related, that is a high frequency US has a low wavelength and vice versa, and medical ultrasound devices utilise sound waves ranging from 1 to 20 MHz [Chan and Perlas, 2011]. The selection of an appropriate transducer is a key step in obtaining an appropriate image; higher frequency transducers are more appropriate for superficial body structures because their signals are more attenuated than low frequency transducers, while low frequency transducers are more appropriate for deep body structures, such as lumbar neuraxial structures [Lawrence, 2007]. A baseline frequency of 7.5 MHz is commonly used to evaluate musculoskeletal structures [Grobbelaar and Bouffard, 2000].

2.3.2 Advantages, disadvantages and applications of US

Ultrasound devices are portable, pose no radiation risk, and are relatively inexpensive compared to other imaging techniques, such as MRI [Chan and Perlas, 2011, Jacobson and Van Holsbeeck, 1998]. Therefore, US is widely used in many

medical clinics for various applications, including abdominal scans [Donald, Macvicar and Brown, 1958], muscle injuries [Paczesny and Kruczyński, 2011], and bladder problems [Chan and Perlas, 2011]. In addition, US is widely used in sports medicine clinics and on-site at athletic events by radiologists and non-radiologist medical practitioners [Hall and Mautner, 2015]. Despite being commonly used, US devices are operator-dependent, meaning that they rely on the experience of the examiner [Lin et al., 2000]. Moreover, the image quality is sensitive to the amount of pressure applied to the transducer by the examiner, and different amounts of pressure create different imaging outcomes that can affect the diagnosis of an existing issue [Jacobson, 1999]. However, ongoing development and image improvements over the last 10 years have helped to minimise these problems through the development of Doppler and 3-D imaging ultrasound [Kurjak, 2000]. Despite these and other recent advances in US devices, the well-documented US anisotropy artefact remains, and this occurs when the US transducer is not perpendicular to the examined structure. This is a major problem of which all examiners must be aware [Grobbelaar and Bouffard, 2000], as when the transducer is perpendicular to the examined structure, all of the sound waves will be reflected back to the transducer. However, when the transducer is at any angle other than 90°, a portion of the waves will be reflected away from the transducer, producing a blackish image that is barely readable [Chhem and Cardinal, 1999, Grobbelaar and Bouffard, 2000].

2.3.3 Applicability of US

The sensitivity and specificity of US have been investigated in many studies over the recent decade and the accuracy of US for assessing different anatomical structures, such as the ACL of the knee [Skovgaard Larsen and Rasmussen, 2000], bony foot structures [Wright et al., 2015], and the cartilage around the knee [Paczesny and

Kruczyński, 2011], have been reported. The sensitivity (range: 70–100%) and specificity (range: 75–100%) of US at the intercondylar notch of the knee for diagnosing acute ACL injuries are high, but do not reach the levels achieved with MRI [Skovgaard Larsen and Rasmussen, 2000]. Although high sensitivities and specificities have been reported as being achieved in the analysis of US, generally speaking, the methodological quality of these studies has been questioned. Low sample sizes, a lack of appropriate blinding of the examiner to the participant's knee injury, and the use of subjective tests as reference standards are all noted limitations. For example, arthroscopy may be an appropriate tool for use as a reference standard. Wright et al. [2015] reviewed the literature reporting US for the diagnosis of lower extremity stress fractures and found the sensitivity ranged from 43% to 99%, and the specificity from 13% to 79%. The ranges of the reported sensitivities and specificities of US are different when it is used to diagnose knee injuries and stress fractures. Problems with the knee meniscus can be diagnosed by US with reasonable sensitivity (range: 60%–90%) [Azzoni and Cabitza, 2002] and specificity (range: 21%–83%) [Park et al., 2008], but caution is needed when evaluating US as a useful diagnostic tool for different knee injuries and subsequent knee instability. General conclusions based on low quality studies and non-constructive critical evaluations should be avoided. Despite the variability in US sensitivity and specificity reported in the literature, several authors [Lee and Bouffard, 2001, Paczesny and Kruczyński, 2011, Hall and Mautner, 2015, De Maeseneer et al., 2014] have recommended that US is a versatile tool for diagnosing several common knee pathologies. However, this recommendation is subject to the condition that the examiner should be aware of the standard US pitfalls, have sufficient knowledge of

the examined region's anatomy and physiology, and should select an appropriate transducer frequency. US is best used for a fast and initial diagnosis before requesting more expensive tools, such as arthroscopy or MRI.

The advantages of US as mentioned above and its availability within the laboratory led to its use in study 2 (chapter 5), where it was used to measure muscle layer thickness.

**CHAPTER 3 - AN EXTENSIVE EVALUATION OF DIFFERENT KNEE
STABILITY ASSESSMENT MEASURES: A SYSTEMATIC
LITERATURE REVIEW**

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3.1 Abstract

Re-injury to a recently rehabilitated or operated knee is a common occurrence that can result in significant loss of function. Knee stability measures have been used to diagnose and assess knee stability before and after rehabilitation interventions. Here, we systematically review the literature and evaluate the different anterior-posterior and rotational knee stability measures currently in use. A computer-assisted literature search of the Medline, CINAHL, EMBASE, PubMed and Cochrane databases was conducted using keywords related to knee stability measures. In a second step, we conducted a manual search of the references cited in these articles to capture any studies that may have been missed in the searched databases. The literature search strategy identified a total of 574 potential studies. After revisiting the titles and abstracts, 34 full-text articles met the inclusion criteria and were included in this review. Most articles compared knee stability measures, whilst other studies assessed their sensitivity and specificity. Several techniques and devices used to measure knee stability are reported in the literature. However, there are only a limited number of quality studies where these techniques and/or devices have been evaluated. Further development and investigation with high quality study designs is necessary to robustly evaluate the existing devices/techniques

Keywords: anterior cruciate ligament; physical examination; diagnostic; instability

3.2 Introduction

Knee stability is critical for many sports, and decreased stability is strongly associated with risk of injury [Mccall et al., 2015, Ter Stege et al., 2014]. The 'giving way' phenomenon associated with knee joint instability has been shown to result from injury to mechanical constraints and associated neuromuscular impairment [Melnik et al., 2007a]. At present, an objective and universally-accepted measure of knee joint stability does not exist. It is therefore difficult to sufficiently quantify when an injured knee has recovered and when an individual may safely return to sport. Despite a large number of preventative rehabilitation protocols proposed to reduce knee injuries [Gilchrist et al., 2008, Mandelbaum et al., 2005], the incidence of knee injury remains high, with one study suggesting it accounts for nearly a quarter of all injuries sustained in professional football [Ekstrand, Hägglund and Waldén, 2011]. For example, Prodromos et al. [2007] reviewed the incidence rates of Anterior Cruciate Ligament (ACL) injury, which is the most common knee stabiliser that is injured. They noted that collegiate soccer players had an incidence of 0.32, basketball players 0.29 and recreational alpine skiers 0.63 per 1000 exposures. A key element to reduce recurrent knee injuries following treatment is the integration of subjective examination techniques, objective instrumented devices and imaging techniques for diagnosis and guidance in return-to-play [Pugh et al., 2009, Leblanc et al., 2015]. Several studies [Barcellona, Christopher and Matthew, 2013, Schoene et al., 2009, Wiertsema et al., 2008, Kostov, 2014] have investigated the usefulness of different knee stability measures to diagnose knee injuries and to provide additional information on return-to-play or return-to-work decisions. Although the diagnostic

accuracy of knee stability measures has previously been evaluated, as yet, a gold standard measure has not been synthesised.

Surgery for the correction of knee instability has increased over the last two decades. Nevertheless, return to competitive sport has been reported as low as 55% [Ardern et al., 2014]. This inconsistency together with the high cost of such surgeries [Saltzman et al., 2015] highlights the need for better clinical pre- and post-surgical measures of knee instability. The use of better clinical assessments is likely to improve surgical case selection and post-surgical rehabilitation. Previous reviews suggested that further research is needed to truly understand the clinical relevance inherent in new device designs [Leblanc et al., 2015, Van Eck et al., 2013]. Therefore, the objective of this study was to conduct an extensive systematic review of the literature to describe and evaluate knee stability measures used for diagnosis and assessment for return-to-play after instability-related knee injury/surgery.

3.3 Materials and methods

3.3.1 Search strategy

Medline, CINAHL, EMBASE, PubMed and Cochrane databases were searched electronically for English-language studies published up to December 2015 independently by (JA and CA). All databases were searched using the Index Medicus Medical Subject Headings (MeSH), such as 'anterior cruciate ligament' and 'arthrometry' (see

Table 3.1 for the full search details). A manual search was also performed by (JA) to check reference list of each of the included articles in order to capture articles that might not have been listed on the databases. Differences of opinion were resolved through discussion with the third author (MB). This review used the Preferred

Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for the search and reporting phases of the study.

Table 3.1: Search terms used in the databases Medline, CINHAL, EMBASE, PubMed and Cochrane from 1900 to 2015

| Medline, CINHAL, EMBASE, PubMed and Cochrane |
|---|
| “Knee laxity” |
| KT-1000 |
| KT-2000 |
| ACL and stability |
| “Laxity testing” and knee |
| “Physical examination” and knee |
| “Instrumented devices” and knee |
| “Stability testing” and knee |
| Instability and knee |
| Imaging and knee |
| Lachman |
| Genucome |
| Rolimeter |
| “Pivot shift” |
| “Anterior drawer” |

3.3.2 Inclusion and exclusion criteria

Articles examining knee stability measures were eligible if they met all of the following criteria: (1) full-text published articles in peer-reviewed journal and articles in press (grey literature); (2) assessed anterior-posterior and rotational knee stability; and (3) written in English. Studies were excluded from the review if they: (1) recruited participants with systematic disease; (2) used non-human subjects; (3) assessed cadavers.

3.3.3 Data extraction

One reviewer independently extracted the data and information regarding the examined knee stability measure, study population, age, sensitivity and specificity

(JA). Any possible disagreement was resolved during a scheduled meeting. Both quantitative data and qualitative data were extracted from the included studies by (JA). The quantitative outcome measures extracted from each study were: (1) 'test sensitivity', which was defined as the percentage of people who test positive for a specific pathology among a group of people who have the pathology; (2) 'test specificity', which was defined as the percentage of people who test negative for a specific pathology among a group of people who do not have the pathology. The qualitative data were the applicability of the measures.

3.3.4 Risk of bias / quality assessment

Two authors independently assessed the quality of the articles that met the inclusion criteria (JA + CA). Study quality was assessed with the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool [Whiting et al., 2003]. QUADAS is a validated clinometric tool used to assess the overall quality of diagnostic accuracy studies through individual quality component questions. Any possible disagreement was planned to be resolved during a scheduled meeting. Based on similar published reviews, any study with a QUADAS score ≥ 10 was stratified as 'high quality/low risk of bias', and any study scoring < 10 was considered 'low quality/high risk of bias' [Hegedus et al., 2008].

3.3.5 Synthesis of the results

It was not appropriate to combine studies for meta-analysis due to the heterogeneity of the included studies and the variable reference standard. For example, subjective measures as oppose to objective measures were utilised in few studies thus making it difficult to compare. Also, time between injury and experiment were variant among the studies hence participants could have different post-injury conditions. Therefore,

the results were tabulated for semi-quantitative comparison of the sensitivity and specificity variables. The qualitative data were descriptively discussed.

3.4 Results

3.4.1 Selection of studies

The systematic literature search strategy through the selected databases identified a total of 571 potential abstracts. Three additional abstracts were handpicked through manual search. Duplicate entries were removed from the two databases, leaving 105 abstracts to be assessed for eligibility. After revisiting the titles, abstracts and full text articles, 34 full-text articles met the criteria for inclusion in this review (Figure 3.1).

This review included a total of 2133 participants investigating eight different knee

stability measures. The sample size of the studies ranged from five to 401 participants.

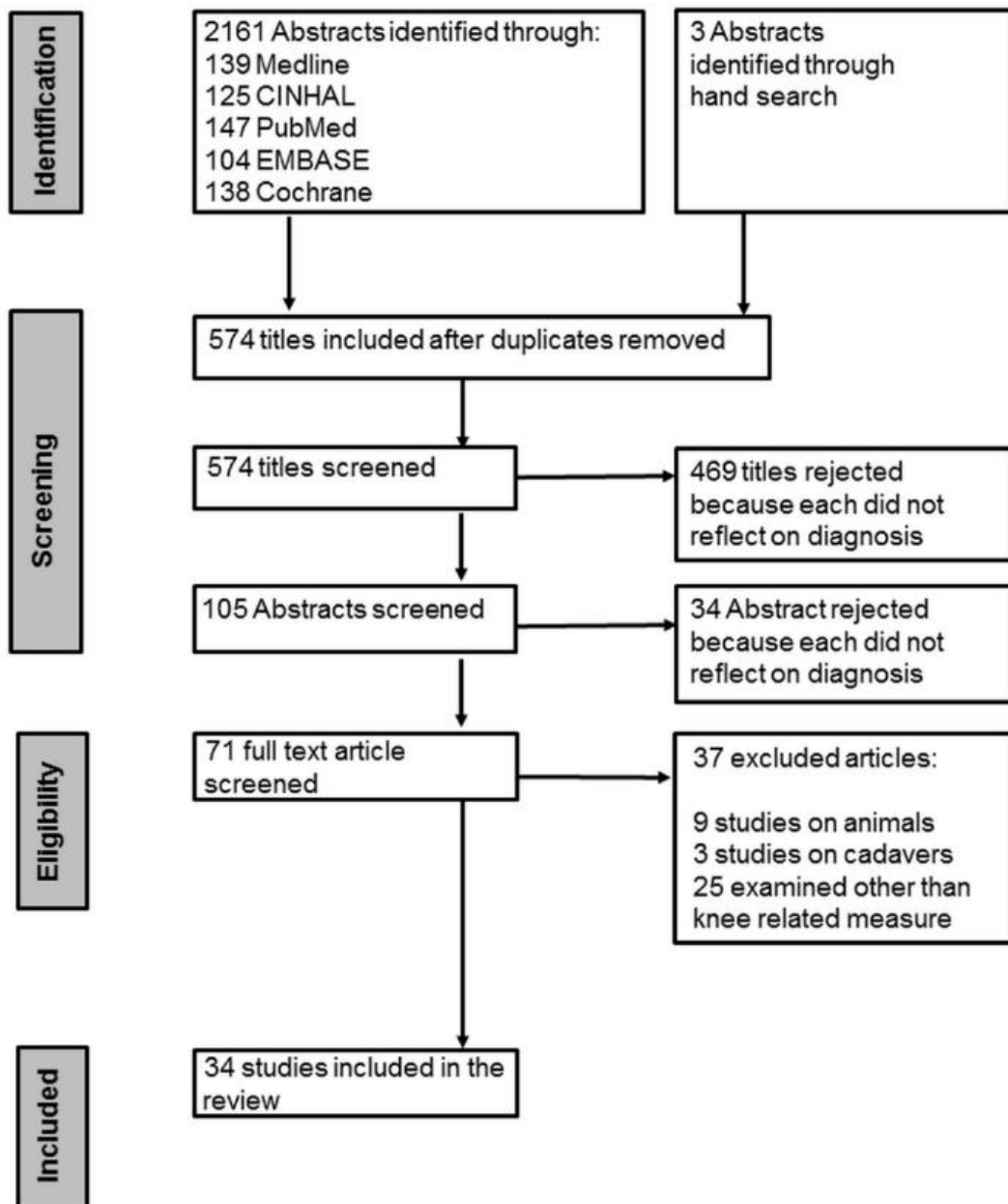


Figure 3.1: Flow diagram of the search strategy and the study selection

3.4.2 Quality scores

Table 3.2 provides the overall risk of bias score; fourteen studies demonstrated high quality/low risk of bias and 20 demonstrated low quality/high risk of bias.

3.4.3 Pooled results from the individual knee stability measures

3.4.3.1 Quantitative data

Fifteen studies investigated the KT-1000 arthrometer; three studies investigated the Lachman test; nine studies investigated the pivot shift test; seven studies investigated the anterior drawer test; three studies investigated a navigation system; five studies investigated the Genucom arthrometer; five studies investigated the rolimeter; two studies investigated Telos radiography; and five studies investigated the ACL-hamstring reflex arc. Table. 3.3 reports which tests each study investigated and the sensitivity and specificity of each test, as well as the sample size, participants age, quality score and effect size of each study.

Table 3.2: Quality Assessment of Diagnostic Accuracy Studies (QUADAS) quality assessment scores of the included studies

| Authors | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | Total |
|---|---|---|---|---|---|---|---|---|---|-----|----|----|----|----|-------|
| [Anderson and Lipscomb [1989] | Y | Y | Y | Y | Y | N | Y | N | Y | U | Y | Y | Y | N | 10 |
| [Anderson et al., 1992] | Y | Y | Y | N | Y | N | Y | Y | N | N | Y | Y | Y | N | 9 |
| [Balasch et al., 1999] | Y | Y | Y | Y | U | N | Y | Y | Y | U | Y | Y | N | N | 9 |
| [Beard et al., 1993] | Y | Y | Y | Y | Y | Y | Y | Y | N | N/A | Y | Y | N | N | 10 |
| [Bach Jr et al., 1990] | Y | Y | Y | N | Y | Y | Y | Y | N | N | Y | Y | N | U | 9 |
| [Fleming et al., 2002] | Y | Y | Y | Y | N | Y | Y | Y | Y | N | U | Y | N | N | 9 |
| [Forster, Warren-Smith and Tew, 1989] | Y | Y | Y | U | U | N | Y | Y | Y | Y | Y | U | N | U | 8 |
| [Friemert et al., 2005b] | Y | Y | Y | Y | N | Y | Y | Y | Y | U | U | Y | Y | Y | 11 |
| [Ganko, Engebretsen and Ozer, 2000] | Y | Y | Y | Y | Y | N | Y | Y | Y | U | U | Y | N | U | 9 |
| [Graham et al., 1991] | Y | U | Y | Y | Y | Y | N | N | N | U | U | Y | Y | U | 7 |
| [Hanten and Pace, 1987] | Y | Y | Y | U | U | Y | Y | Y | Y | N | U | Y | N | U | 8 |
| [Highgenboten, Jackson and Meske, 1989] | Y | Y | Y | U | U | Y | Y | N | N | U | U | Y | N | U | 6 |
| [Hoshino et al., 2012] | Y | N | Y | U | U | Y | Y | Y | N | U | Y | U | U | U | 6 |
| [Küpper et al., 2007] | Y | N | Y | U | U | U | U | Y | N | Y | U | Y | U | U | 5 |
| [Kuroda et al., 2008] | N | N | Y | U | U | Y | U | Y | U | U | Y | Y | U | U | 5 |
| [Kuroda et al., 2012] | Y | N | Y | U | U | Y | U | Y | U | U | Y | Y | U | U | 6 |
| [Liu et al., 1995] | Y | N | Y | Y | Y | Y | Y | N | N | Y | Y | Y | N | Y | 10 |
| [Lopomo et al., 2010] | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | U | U | 12 |
| [Lopomo, Zaffagnini and Amis, 2013] | Y | Y | Y | Y | N | Y | Y | Y | Y | U | Y | U | Y | U | 10 |
| [Melnyk and Gollhofer, 2007b] | Y | Y | Y | Y | N | Y | Y | Y | Y | Y | Y | Y | U | U | 11 |
| [Mitsou and Vallianatos, 1988] | Y | Y | N | N | N | U | U | Y | U | N | N | N | N | N | 3 |
| [Mulligan, Harwell and Robertson, 2011] | Y | Y | Y | Y | U | U | Y | Y | U | Y | Y | Y | Y | Y | 11 |
| [Panisset et al., 2012] | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | U | U | 12 |
| [Pugh et al., 2009] | Y | N | Y | U | U | U | U | Y | N | Y | Y | Y | U | U | 6 |
| [Schoene et al., 2009] | Y | Y | Y | U | U | Y | Y | Y | Y | Y | U | Y | Y | U | 10 |
| [Sernert et al., 2001] | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | U | Y | Y | U | 12 |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|
| [Steiner et al., 1990] | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | U | Y | U | U | 11 |
| [Tsuda et al., 2001] | Y | Y | Y | U | U | Y | Y | U | Y | Y | Y | Y | U | U | 9 |
| [Wroble et al., 1990] | Y | N | Y | Y | N | N | U | N | N | N | Y | Y | U | U | 5 |
| [Barcellona, Christopher and Matthew, 2013] | Y | N | Y | Y | N | Y | Y | N | N | U | U | Y | N | N | 6 |
| [Van Eck et al., 2013] | Y | Y | Y | Y | U | Y | Y | Y | U | Y | Y | Y | Y | Y | 12 |
| [Monaco et al., 2009] | Y | U | Y | Y | N | Y | Y | Y | N | Y | U | Y | U | U | 8 |
| [Kopf et al., 2012] | Y | N | Y | U | N | U | N | Y | N | U | U | Y | Y | U | 5 |
| [Leblanc et al., 2015] | Y | Y | Y | U | Y | Y | Y | Y | Y | N | U | Y | Y | Y | 11 |

Y = Yes; N = No; U = Unclear; NA = Not Applicable; grey highlight = high quality studies.

1 = was the spectrum of participants representative of the patients who will receive the test in practice;

2 = were selection criteria clearly described;

3 = was the reference standard likely to classify the target condition correctly;

4 = was the period between the performance of the reference standard and the index test short enough to be reasonably sure that the target condition did not change between the two tests;

5 = did the whole sample or a random selection of the sample receive verification using the reference standard;

6 = did participants receive the same reference standard regardless of the index test result;

7 = was the reference standard independent of the index test (that is, the index test did not form part of the reference standard);

8 = was the execution of the index test described in sufficient detail to permit its replication;

9 = was the execution of the reference standard described in sufficient detail to permit its replication;

10 = were the index test results interpreted without knowledge of the results of the reference standard;

11 = were the reference standard results interpreted without knowledge of the results of the index test;

12 = were the same clinical data available when the test results were interpreted as would be available when the test is used in practice;

13 = were uninterpretable, indeterminate or intermediate test results reported;

14 = were withdrawals from the study explained.

Table 3.3: Summary of articles reporting on the accuracy of different anterior-posterior and rotational knee laxity measures

| Authors | Devices/ Technique Studied | Sample Size | Age, Mean | Sensitivity/ Specificity $p < 0.05$ | Conclusions | QUADAS Quality Score | Effect Size |
|---|---|-------------------|---------------|--|--|----------------------|-------------|
| [Anderson and Lipscomb, 1989] | KT-1000, Lachman test, anterior drawer, pivot shift | 50 | 19.8 | N/A | Clinical examination by an experienced examiner is the most accurate method to determine ACL integrity; however, instrumented testing was beneficial | 10 | N/A |
| [Anderson et al., 1992] | KT-1000, Genucom, Acufex, Dyonics dynamic cruciate tester | 100 | 26 | N/A | This study establishes that anterior knee laxity measurements cannot be generalised from one device to another in both normal and ACL-injured participants | 9 | 0.2 |
| [Bach Jr et al., 1990] | KT-1000 | 401 | Not mentioned | At manual maximum force (MMF), sensitivity = 79%, specificity = 77%; at 89 Newton, sensitivity = 75%, specificity = 83% | KT-1000 is a helpful knee laxity measure adjunct to a careful history and physical examination of ACL-injured patients | 9 | 0.0 |
| [Balasch et al., 1999] | Rolimeter | 60 | 33.6 | N/A | Rolimeter provides an economic, exact and simple operating device for quantifying anterior knee joint instability | 9 | N/A |
| [Barcellona, Christopher and Matthew, 2013] | KT-2000 | 3 KT-Arthrometers | N/A | N/A | KT-2000 knee joint arthrometers overestimates anterior displacement with a predictable relative systematic error | 6 | N/A |
| [Beard et al., 1993] | Reflex Hamstring Contraction Latency (RHCL) | 30 | 24.8 | N/A | The reflex hamstring contraction latency is a measure of proprioception and can be used to provide objective data for the management of patients with ACL deficiency | 10 | 1.46 |
| [Van Eck et al., 2013] | KT-1000, Genucom, anterior drawer | Review article | N/A | Sensitivity of KT-1000 = 0.93, anterior drawer = 0.74; Genucom = 0.76; specificity of KT-1000 = 0.93, anterior drawer = 0.82; Genucom = 0.76 | The KT arthrometer performed with maximum manual force has the highest sensitivity, specificity and accuracy for diagnosing ACL rupture | 12 | N/A |
| [Fleming et al., 2002] | KT-1000, planer stress radiography, RSA | 15 | 34 | N/A | KT-1000 and RSA document temporal changes in anterior-posterior knee laxity following ACL reconstruction that were not documented by planer stress radiography | 9 | 0.42 |
| [Forster, Warren-Smith and Tew, 1989] | KT-1000 | 10 | 30 | N/A | The KT-1000 was not capable of overcoming result variation and providing reliable and reproducible measurement of laxity of the ACL | 8 | 0.8 |
| [Friemert et al., 2005b] | Reflex Hamstring Contraction Latency (RHCL) | 13 | 24.6 ± 5.5 | N/A | Short and medium latency responses of the hamstring stretch reflex exist after an ACL stimulation during isometric hamstring contraction | 11 | 0.15 |

| Authors | Devices/ Technique Studied | Sample Size | Age, Mean | Sensitivity/ Specificity $p < 0.05$ | Conclusions | QUADAS Quality Score | Effect Size |
|---|--|----------------|---------------|--|---|----------------------|-------------|
| [Ganko, Engbretsen and Ozer, 2000] | Rolimeter | 38 | 27.4 | Sensitivity = 89%, specificity = 95% | The rolimeter, when compared to the KT-1000, provides a valid measure of anterior knee laxity | 9 | 0.6 |
| [Graham et al., 1991] | Lachman test, anterior drawer, KT-1000 | 21 | Not mentioned | N/A | Anterior drawer and the Lachman test were found to be the most accurate indicators of ACL deficiency; the KT-1000 was found to be totally inaccurate | 7 | N/A |
| [Hanten and Pace, 1987] | KT-1000 | 43 | 18.5 | N/A | Our results indicated relatively high reliability of KT-1000 and clinician can use such tool to get objective and reliable AP knee laxity measurements | 8 | N/A |
| [Highgenboten, Jackson and Meske, 1989] | Genucom, KT-1000, Stryker | 30 | Not mentioned | N/A | All devices can provide reproducible quantitative measurements of knee laxity; however, due to differences in device sensitivities and design, numerical results from one device cannot be generalised to another device | 6 | 0.6 |
| [Hoshino et al., 2012] | Quantitative pivot shift test | 5 | Not mentioned | N/A | The sudden shift of the lateral compartment of the knee joint was successfully detected by the newly-developed image analysis measurement method | 6 | 0 |
| [Küpper et al., 2007] | KT-1000, Genucom, Stryker, rolimeter | Review article | N/A | N/A | The development of theoretical models that accurately represent knee joint laxity in combination with more precise and repeatable clinical assessment of ACL injuries should lead to an improved understanding of joint laxity and the factors associated with acute injury and genetic pathologies that affect joint stability | 5 | N/A |
| [Kuroda et al., 2008] | Pivot shift test | 30 | 21.2 | N/A | The new non-invasive measurement system enables monitoring instantaneous 3D position displacement of the knee by using an electromagnetic sensor; these measurements can be used for quantified evaluation of dynamic instability demonstrated by the pivot shift test | 5 | N/A |
| [Hoshino et al., 2012] | Quantitative pivot shift test | Review article | N/A | N/A | Accumulative biomechanical and clinical evidence have shown the usefulness of quantitative assessment of the pivot shift test | 6 | N/A |

| Authors | Devices/ Technique Studied | Sample Size | Age, Mean | Sensitivity/ Specificity $p < 0.05$ | Conclusions | QUADAS Quality Score | Effect Size |
|---|---|----------------|-----------------|---|--|----------------------|-------------|
| [Liu et al., 1995] | MRI, KT-1000, Lachman test, anterior drawer, pivot shift | 38 | 26 | KT-1000 sensitivity = 97%, Lachman test sensitivity = 95%, MRI sensitivity = 97%; specificity for all measure was not mentioned | No significant differences between the results of the Lachman test and the KT-1000, but these were significantly better than MRI and anterior drawer; it has been shown that inexpensive tests can allow treatment to proceed rapidly and in the most economical manner without the routine use of MRI | 10 | N/A |
| [Lopomo et al., 2010] | Pivot shift test | 18 | 33 | The PS test was reliable in identifying the surgical reconstruction. Correlation analysis showed good coefficients both for pre- ($r = 0.7$; $p < 0.05$) and postoperative ($r = 0.9$; $p < 0.05$) values | The new quantification method of the pivot shift test could be helpful in characterising patient-specific knee laxity, thus quantifying the clinical relevance of the test | 12 | N/A |
| [Lopomo, Zaffagnini and Amis, 2013] | Quantitative pivot shift test | Review article | N/A | N/A | Several methodologies have been identified to quantify the pivot shift test; clinicians are still lacking the "gold standard" method of the quantitative pivot shift test | 11 | N/A |
| [Melnyk and Gollhofer, 2007b] | Submaximal fatigue exercises of hamstring | 15 | 25 ± 2.6 | N/A | Submaximal hamstring fatigue is associated with a mechanical loss of knee stability; this instability might explain at least in part a higher risk of ACL injury | 11 | 1 |
| [Mitsou and Vallianatos, 1988] | Lachman test, anterior drawer | 144 | Not mentioned | Not mentioned | The diagnostic accuracy of the Lachman test in recent ruptures when the patient is examined without general anaesthetic is superior to that of the anterior drawer test, while in chronic cases with third-degree instability, the two tests are equally reliable | 3 | N/A |
| [Mulligan, Harwell and Robertson, 2011] | Lachman test | 52 | 34 | Sensitivity = 70%, specificity = 97% | The prone Lachman test is a reliable technique that can be used to confirm the presence of an ACL tear | 11 | N/A |
| [Panisset et al., 2012] | Telos, rolimeter, clinical examination | 177 | 30.2 ± 11.7 | Sensitivity of Telos combined with CE = 88%, sensitivity of rolimeter combined with CE = 72.7; specificity of Telos combined with CE = 94.6%, specificity of rolimeter combined with CE = 92.4 | The combination of clinical examination with telos was more accurate than with rolimeter | 12 | 0.49 |
| [Pugh et al., 2009] | KT-1000, rolimeter, Telos, Genucom, Acufex, Dyonics dynamics cruciate tester, UCLA, Vermont | Review article | N/A | N/A | The KT-1000 knee arthrometer and the rolimeter provide the best results when testing anterior laxity at the knee, whereas the Telos device is superior for the assessment of posterior laxity | 6 | N/A |

| Authors | Devices/ Technique Studied | Sample Size | Age, Mean | Sensitivity/ Specificity $p < 0.05$ | Conclusions | QUADAS Quality Score | Effect Size |
|------------------------|---|----------------|---------------------------|--|--|----------------------|-------------|
| [Schoene et al., 2009] | Reflex Hamstring Contraction Latency (RHCL) | 34 | 20 | N/A | The study has demonstrated that the investigated method of measuring the ACL-hamstring reflex is both reliable and reproducible | 10 | 0.7 |
| [Sernert et al., 2001] | KT-1000 | 40 | 29 | Control group; sensitivity = 50%, specificity = 70% ; experimental group; sensitivity = 60%, specificity = 70% | The reproducibility of the KT-1000 measurements of anterior knee laxity between two experienced examiners was considered as fair | 12 | 0.1 |
| [Steiner et al., 1990] | KT-1000, Stryker, Genucom, Acufex | 28 | 25 | Sensitivity of Acufex = 90%, KT-1000 = 80%; Stryker = 85%;Genucom = 60%; specificity of Acufex = 85%, KT-1000 = 70%. Stryker = 70%, Genucom = 65% | We recommend the use of Acufex, KT-1000 and Stryker, as they had more reproducible measurements than Genucom, as it tended to report greater differences in displacement between the right and left knees of normal participants | 11 | 0.2 |
| [Tsuda et al., 2001] | Reflex Hamstring Contraction Latency (RHCL) | 9 | 30 | N/A | ACL-hamstring reflex arc exists after an isometric hamstring contraction | 9 | N/A |
| [Wroble et al., 1990] | KT-1000 | 6 | 26 | N/A | KT-1000 standard evaluation should report paired differences rather than individual knee measurements and should be supplemented by clinical examination | 5 | N/A |
| [Monaco et al., 2009] | KT-1000, navigation system | 30 | 29 (range 19 to 39) | N/A | This study validates the accuracy of the KT-1000 to exactly calculate anterior-posterior (AP) translation of the tibia, in comparison with the more accurate measurements obtained using a navigation system | 8 | 0.13 |
| [Kopf et al., 2012] | Pivot shift test | 20 | 27.8 (range 23.2 to 32.4) | N/A | Quantification of the pivot shift test is practicable when inertial sensors are used | 5 | N/A |
| [Leblanc et al., 2015] | Lachamn, pivot shift, anterior drawer and MRI | Review article | | Lachman, all ruptures type 89%, complete rupture 96%, partial rupture 68%; pivot shift, all rupture types 79%, complete rupture 86%, practical rupture 67%; no data for other measures | Decreased sensitivity of Lachman and pivot shift tests for partial ACL rupture cases and for awake patients raised suspicions regarding the accuracy of these tests for the diagnosis of ACL insufficiency | 11 | N/A |

Abbreviations: MMT = Manual Muscle Testing; STSD = Side-To-Side-Difference; MMF = manual maximum force; CE = Clinical Examination; PS = Pivot Shift; RSA = Roentgen Stereophotogrammetric Analysis; AP = anterior-posterior; MRI = Magnetic Resonance Image; N/A = Not Applicable; grey highlight = high quality studies

3.4.3.2 Qualitative data

Lachman test

The Lachman test is used widely in clinical setting as it is fast and easy to perform for assessing the instability of the knee [Gurtler, Stine and Torg, 1987]. The test is performed with the patient supine and the knee relaxed at 20° to 30° of flexion. The examiner places one hand on the distal end of the thigh and the other hand behind the proximal end of the tibia. The tibia is then translated anteriorly on the femur, and the endpoint is assessed as firm (intact ACL) or soft (injured ACL). An injured ACL should be graded either I < 2 mm, II 2 to 5 mm, III > 5 mm.

The literature lacks consensus on the usefulness of the Lachman test as a measure of anterior knee stability. Its reliability and validity range from 87% to 97% and 91% to 97%, respectively [Graham et al., 1991, Wiertsema et al., 2008, Torg, Conrad and Kalen, 1976]. One of the disadvantages of the Lachman test is the difficulty for examiners with smaller hands to perform it properly. It is restricted to examiners with larger hands to properly perform it [Rebman, 1988, Draper and Schulthies, 1993], as it needs a firm gripping of the femur to displace the tibia anteriorly. As a result, conducting the test in a prone position has been proposed and yielded a positive alternative to the Lachman test [Mulligan, Harwell and Robertson, 2011]. Moreover, Muller et al. [2015] examined the proficiency in performing the prone Lachman test as opposed to the classic Lachman. They showed that prone Lachman yielded 78% of positive predictive value while the classic Lachman 28%. The prone Lachman test uses gravity to pull down the femur, which will let the examiner grip and displace the tibia in both hands [Floyd, Peery and Andrews, 2008]. Consequently, the size of the

knee may be an important factor in deciding which knee instability measure should be used to assess knee stability.

Pivot shift test

Galway, Beaupre and MacIntosh [1972] initially described the pivot shift test as an examination tool of functional knee instability. This is performed with the patient supine with the examiner standing lateral to the patient holding the knee and ankle in 20° of internal rotation, with the patient's hip flexed to 30°. A valgus force is applied to the proximal tibia, to create impingement of the plateau on the femur. The knee is then flexed and assessed for a clunk due to the reduction of the displaced tibia on the femur, which normally occurs between 20° and 30°. The motion is then graded as: 0 = no clunk, I = glide, II = clunk and III = gross clunk with locking. A false negative may be obtained in patients with Iliotibial Band (ITB) pathology, medial collateral ligament injury, a bucket handle meniscus tear or a flexion contracture. A false positive pivot shift may be present in a patient with increased laxity.

Comparison with the uninjured knee should always be undertaken.

There is a controversy in the literature on the usefulness of the pivot shift test. The controversy surrounds the various techniques used by clinicians when performing the pivot shift test. Variations exist particularly in the degree of knee flexion, hip flexion and tibial internal rotation [Hoshino et al., 2012]. It is difficult to assess the effect on the test outcome of associated injuries to the knee and the limited range of motion in knees with injured meniscus [Kong et al., 1994]. Similarly, the subjectivity on the amount of the applied valgus force whilst doing the test leads to difficulties in replicating the test for confirmation [Kuroda et al., 2008]. The specificity of the pivot shift test has been shown to be dependent on whether or not the patient is

anaesthetised [Hoshino et al., 2013]. It ranges from 32% without to 85% with anaesthesia; this result was confirmed by Kuroda et al. [Kuroda et al., 2012], who theorised that muscular resistance can suppress the pivot shift manoeuvre.

Anterior drawer test

The anterior drawer test specifically assesses the anterior stability of the knee [Jonsson et al., 1982]. Several studies reported that clinicians use it widely in both clinics and operation theatres [Van Eck et al., 2013, Mitsou and Vallianatos, 1988, Galway, 1972, Colombet et al., 2012, Cannon, 2002]. It is performed in a supine position, with the knee at 90° flexion and the hip at 45° flexion. The examiner sits on the patient's tested foot and with one or both hands grasping the proximal end of the leg aligning the thumb(s) with the anterior joint line. The tibia is then pulled anteriorly, and an assessment is made of the relative translation of the tibia on the femur. The tibia should displace within a similar range to the sound knee. If an excessive displacement occurs in the injured knee compared to the sound knee and a soft endpoint is felt, it is assumed that there is an ACL injury yet to be confirmed with an objective knee instability measure.

The anterior drawer test has an agreement in the literature regarding its usefulness [Mitsou and Vallianatos, 1988, Scholten et al., 2003]. Mitsou and Vallianatos [1988] highlighted the difficulty in performing the anterior drawer test at the acute stage following a suspected ACL injury. In addition, they reported specificity ranged from 78% to 99% when patients were examined under general anaesthesia. On the other hand, Scholten et al. [2003] concluded that such a test is of unproven value. It has

been shown that failure to quantify the amount of displacement of the tibia on the femur and inability to use it in the acute stage of injury were weaknesses of this test.

The rolimeter

The rolimeter (Aircast Europa, Neubeuern, Germany) is a portable knee arthrometer used to measure anterior-posterior displacement of the tibia on the femur while performing the Lachman test [Balasch et al., 1999]. It is performed whilst the patient is positioned supine with 30° flexion of the tested knee. Next, a proximal convex pad is placed over the patella and a distal pad placed over the tibia with a strap. The two pads are connected a few inches above the limb by a steel bar. A feeler should be placed over the tibial tubercle; the Lachman test is performed after the device has been zeroed. To that end, the anteroposterior displacement of the tibia on the femur is measured in increments of 2 mm by the marks on the feeler. A difference of 4 mm or greater, in comparison with the uninjured knee, is suggestive of an ACL injury [Cannon, 2002].

The rolimeter provides an economic, exact and simple device for quantifying anterior knee joint instability [Balasch et al., 1999]. Among 20 healthy participants and 18 patients with chronic ACL injury, Ganko et al. [2000] assessed the reliability of the rolimeter as opposed to the KT-1000. In the mean knee displacement, both devices showed strong correlation ($r = 0.73$, $p < 0.001$) for the injured knees, while there was no significant correlation in their uninjured knees ($r = 0.32$, $p > 0.10$). Hence, they concluded that, with experienced examiners, the rolimeter is a valid method to assess anterior knee instability. However, its specificity as a standalone measure of knee stability (84.3) was questioned when compared to its results alongside clinical examination (92.4) [Panisset et al., 2012]. This was justified based on the fact that

the rolimeter does only measure the anterior-posterior stability rather than the rotational stability of the knee [Ganko, Engebretsen and Ozer, 2000]. The use of the rolimeter as a standalone measure can give false negative results with the notion that knee stability is maintained by both anterior-posterior and rotational mechanical stability [Hirschmann and Müller, 2015].

Navigation systems

This is a computerised navigation system designed to assist surgeons during knee ligament reconstructions and arthroplasty surgery [Klos et al., 1998]. It uses kinematic measurements along with bone-morphing technology to determine data on alignment, kinematics and morphologic characteristics of the knee [Lopomo et al., 2009]. Pins are placed within the tibia and femur; attached to these pins are markers, which are detected by the computer sensors and registered relative to predefined anatomical locations. Based on the movement of these markers relative to each other, small displacements can be detected and used to quantify knee joint stability during surgery [Lopomo et al., 2009, Colombet et al., 2007].

The navigation system remains the gold standard for the measure of anterior-posterior knee laxity due to its precision, validity and accuracy [Lopomo et al., 2010, Monaco et al., 2009, Lopomo et al., 2009, Colombet et al., 2007, Pearle et al., 2007]. Pearls et al. [2007] investigated the reliability and repeatability of using a knee navigation system in knee instability examination by comparing the navigation system to a robotic testing system. Intra-class Correlation Coefficients (ICC) were used to assess the correlation between the two systems. The authors reported that the surgical navigation system is a precise intraoperative tool to quantify translational and rotational knee instability. The ICCs were all statistically significant at $p < 0.01$,

and the overall ICC was 0.9976. Continuous developments to the knee navigation system have provided the ability to measure rotational knee stability in addition to the translational stability [Degenhart, 2004]. Nevertheless, it is strictly used in connection with surgery. The use of navigation systems is limited to surgical procedures; it is expensive, invasive and requires surgical experience, due to the need for accurate fixation of sensors in the femur and tibia [Lopomo et al., 2009]. Thus, it is a good research and clinical tool; however, it cannot be used on-field or within a clinical setting to aid in decision making [Colombet et al., 2007].

The Genucom knee analysis system

The Genucom knee analysis system (FARO Medical Technologies Inc., Montreal, QC, Canada) is a computerised device developed in the 1980s to objectively measure knee stability in different planes (e.g., sagittal and frontal planes) [Cannon, 2002].

The participant's tested knee is positioned in 20° flexion and the thigh secured with restraints. An electro-goniometer is attached to the thigh, with anatomical markers placed on the medial and lateral femoral condyle, patella and tibial crest. The markers are digitised, and then, the relative displacement of the knee is recorded in addition to the distance between the markers [Highgenboten, Jackson and Meske, 1989].

The genucom knee analysis system is the only objective instrument to provide a multiplanar measure of knee stability, but it is more complicated and time consuming to use compared to other measures [Highgenboten, Jackson and Meske, 1989, Mcquade, Sidles and Larson, 1989]. Furthermore, it has poor sensitivity, and its cost-

effectiveness has been questioned [Steiner et al., 1990]. As a result, it has fallen out of common use.

The KT-1000/KT-2000 arthrometer

The KT-1000 knee ligament arthrometer (MEDmetric Corp, San Diego, CA, USA) is the most commonly-used arthrometer in both a clinical and research setting [Küpper et al., 2007]. It is an objective device that measures anterior-posterior translation of the tibia on the femur in millimetres [Daniel et al., 1985]. The patient should remain in a supine position on the examination bed with the tested knee supported at 30° of flexion using a goniometer. The thigh strap, thigh support platform and foot support should be placed on and attached to the patient. The KT-1000 arthrometer is secured over the participant's leg in the ideal position with reference to the knee joint line. The Lachman and anterior drawer tests can then be performed with the KT-1000.

Its reliability has been tested in several studies. The side-to-side difference is the recommended measure to use for assessment of anterior knee stability [Isberg et al., 2006]. The experience of the examiners plays an important role in the result of the test [Anderson and Lipscomb, 1989, Jardin et al., 1999]. The KT-2000 has the same method of use as the KT-1000 with the added feature of graphic documentation via an X-Y plotter. It produces data regarding the amount of knee displacement and the magnitude of the applied force.

Despite the large number of KT-1000/2000 studies in the literature, there is no consensus on its sensitivity and specificity in measuring anterior-posterior knee laxity. Its sensitivity ranged from 0.50 [Bach Jr et al., 1990] to 0.97 [Van Eck et al., 2013], and its specificity ranged from 0.70 [Steiner et al., 1990] to 0.93 [Van Eck et al., 2013]. The wide range in the sensitivity and specificity was justified based on the

quality of the conducted studies, the experience of the examiner and the amount of force being utilised in each test [Wroble et al., 1990]. Regardless of the controversy regarding the sensitivity and specificity of the KT-1000 arthrometer, it is commonly used in research rather than in a clinical setting [Pugh et al., 2009]. However, the majority of the available literature supports the KT-1000 arthrometer as being at least equal to other available knee stability measures [Van Eck et al., 2013, Bach Jr et al., 1990, Hanten and Pace, 1987, Steiner et al., 1990].

The Telos stress radiography device

The Telos stress radiograph (Telos GmbH, Laubscher, Holstein, Switzerland) is a device that can measure knee stability by utilising stress forces with high quality radiographic images [Fleming et al., 2002]. It was originally described by Staubli and Jacob [1991]. The test involves the application of an anterior stress to the injured knee; the subsequent displacement is measured on a lateral X-ray. The displacement is described relative to the opposite “normal” side.

The two included articles in this review that investigated the usefulness of the Telos as a measure of knee stability showed that its sensitivity ranged from 0.72 to 0.88 and it had a specificity of 0.82 [Panisset et al., 2012]. Similarly, Jardin et al. [1999] compared the KT-1000 to Telos after ACL reconstruction. They recommended Telos instead of KT-1000 to assess knee stability after ACL reconstruction. The widespread range in the sensitivity and specificity was vindicated based on the variation in the quality of the X-rays obtained, the experience of the radiographer and the experience of the radiologist in reading such radiographs [Stäubli and Jakob, 1991, Wright et al., 2015]. Nevertheless, imaging techniques (e.g., Telos) are an established tool to confirm the diagnosis of suspected knee instability, to assess the ACL reconstruction

outcome and to rule out injuries to other soft tissue structures [Panisset et al., 2012, Jardin et al., 1999].

ACL-hamstring stretch reflex

This is designed to measure the onset latency of biceps femoris muscle. Hence, it is not designed *per se* as a test of knee stabilisation. It uses electromyography (EMG) to record muscle activity produced by a stretch reflex elicited by the application of anterior-posterior translation of the knee joint. The latency of the biceps femoris stretch reflex is then calculated and used as an indicator of knee stability and neuromuscular function [Beard et al., 1993].

It has been evaluated in several studies to assess muscle fatigue, knee stability [Melnyk and Gollhofer, 2007b] and knee proprioception [Jennings and Seedhom, 1994]. It is used in operative theatres through a direct pull of the ACL to differentiate short and long latencies [Friemert et al., 2005a]. The reflex has been investigated intra-operatively by direct traction under arthroscopic visualisation and in a research setting by instrumenting a laboratory-based rig [Schoene et al., 2009]; thus, its clinical usefulness is doubtful. Three studies by Schoene et al. [2009], Friemert et al. [2005b] and Melnyk and Gollhofer [2007b] revealed that the ACL-hamstring reflex measurement could be elicited, specifically for injured ACLs. Previous work by Friemert et al. [2005b] has shown that a prolonged reflex was present in patients with a ruptured ACL. The longer reflexes corresponded with patients who had instability symptoms even though mechanical testing with the KT-1000 showed no difference. On the other hand, Melnyk and Gollhofer [2007b] concluded that it was hamstring muscle fatigue during submaximal isometric exercises that was the reason behind the longer latencies of the hamstring stretch reflex and not the existing ACL injury.

Despite the argument in the literature on its usefulness for detecting the aforementioned variables, the authors suggested that this technique has room for improvement in terms of its applicability in a clinical setting to guide rehabilitation protocols [Melnyk et al., 2007a, Schoene et al., 2009, Jennings and Seedhom, 1994].

3.5 Discussion

This present paper systematically reviewed a broad spectrum of knee measures designed to assess anterior and rotational stability. Similar to others used in the hip [Reiman et al., 2012], ankle [Rosen, Ko and Brown, 2015] and hamstring injuries [Reiman, Loudon and Goode, 2013], the existing tests for knee stability assessment are deficient in relation to diagnosis, surgical outcome assessment and clinical decisions on return-to-play following injury or surgery.

The subjective tests demonstrated variability in sensitivity and specificity of each test thus questioning their clinical usefulness as stand-alone measures. As with any subjective test, comparing the outcome of tests is difficult due to the subjective nature of the grading system. On the other hand, objective tests can be quantitatively compared to each other in terms of their sensitivity and specificity. For example, the sensitivity and specificity of the Genucom knee analysis system have been reported to be low, at 60% and 65%, respectively [Steiner et al., 1990]. On the other hand, the KT-1000 sensitivity at maximum manual force is 93%, and it has a specificity of approximately 93% [Van Eck et al., 2013]. Despite the existing studies on the use of the hamstring-stretch reflex [Friemert et al., 2005b, Melnyk and Gollhofer, 2007b, Jennings and Seedhom, 1994, Friemert et al., 2005a], the literature lacks evidence on whether the reflex latency can be a valid objective clinical knee stability measure. Mitsou and Valiianatos et al. [1988] showed that the anterior drawer test is reliable when used for chronic knee cases. On the contrary, a review by Van Eck et al. [2013]

suggests that the anterior drawer test is less sensitive (0.74) than the KT-1000 arthrometer (0.93). The literature disagreement is based on the difference of knee conditions being examined and the quality of the studies conducted. However, the anterior drawer test has been used in a clinical setting and in-the-field as a quick and early assessment technique of ACL injury.

The specificity of the pivot shift test ranged from 32% without to 85% with anaesthesia. Muller et al. [2015] reported an ICC for intra-tester reliability ranging from 0.913 to 0.999 (95% CI range: 0.319 to 1.000) and ICC for inter-tester reliability of 0.949 (95% CI: 0.542 to 1.000) for iPad software (The PIVOT software, iOS, programming language Objective-C) designed specifically for quantifying the pivot shift test. Nevertheless, Hoshino et al. [2013] did quantify the pivot shift test using an iPad tablet (Apple Inc., Cupertino, CA, USA). They concluded that pivot shift measurements using an iPad did provide quantification of rotational stability for ACL-deficient knees. However, the limitation of their study was the use of subjective clinical grading as a reference standard to the quantified iPad results. This produced bias in the notion that the same tester performed the subjective grading and the quantitative measurements. The quantification of the pivot shift test using the iPad technique needs to be investigated further to assess its robustness on a larger and cross-sectional population. Due to the intra-examiner variation in the technique being used for the assessment of knee stability, subjective tests need to be tough and applied in a standardised fashion. These differences make comparisons between the reported results in the literature difficult because of the inability to accurately and

systematically compare two different techniques [Musahl et al., 2012]. Hence, a better evaluation of each test needs to be conducted.

In spite of the accuracy of the navigation system when compared to a robotic testing system (ICC was 0.9976) [Pearle et al., 2007], its use is limited to surgical procedures; it is expensive and requires surgical experience, thus limiting its use in clinical practice. Unlike the navigation and genucom knee analysis systems, the rolimeter has superiority as a lightweight device and can be used in clinical, surgical and in-the-field settings. The inability to quantify the magnitude of the pulling force and the difficulty of assessing the functional instability of ACL reconstructed knees are disadvantages of this device [Küpper et al., 2007]. Consequently, using the rolimeter adjacent to physical examination and imaging techniques would be preferable.

Telos stress radiography has the advantage of measuring knee stability in a number of planes (sagittal, frontal and horizontal) [Panisset et al., 2012]; unlike other devices, which only measure the laxity in one direction (anterior-posterior) or two directions (anterior-posterior and rotational movement) [Pugh et al., 2009]. The Telos system is unable to measure rotational instability and also has the disadvantage of radiation exposure when participants/patients are being tested; thus, it should be used judiciously.

There are a number of reasons for the poor clinical usefulness of the reviewed knee stability measures and the challenges in reviewing them. Firstly, is the different pathomechanics between injured knees [Musahl et al., 2012, Rozzi et al., 1999], as well as inter-individual variations in patient outcome during rehabilitation programmes [Rozzi et al., 1999]. Secondly, the majority of the knee stability measures for anterior

and rotational instability were highly sensitive, but had lower specificity (Table. 3.3). Consequently, a positive test means little in the diagnosis of rotational instability, since the same test will also be positive in anterior instability. Thirdly, there is a risk that lower quality studies fail to fully discriminate the true usefulness of the various knee stability measures. Fourthly, limitations in experiment design affect the interpretability and generalisability of these measures.

The quality assessment of the studies included in this review indicates that many of the studies in this area lack scientific rigour. The median QUADAS score was nine, and 20 of the 34 studies reviewed had a score of less than 10. The studies we reviewed were typically underpowered; they failed to report important study details (see the QUADAS scoring details in Table 3.2) or failed to compare to a reference standard (see Question 5 in Table 3.2). Only twelve of the 34 studies used a reference standard, whilst most studies had a sample size greater than 30 participants (range: five to 401), nearly half of the studies had a low effect size ($d < 0.3$), with five studies reporting a medium effect ($0.3 < d < 0.8$) and only three studies reporting a large effect size ($d \geq 0.8$). As a result, it is difficult to draw strong conclusions from much of the reported data. In almost half of the reviewed studies ($n = 15$), the selection criteria of their samples were not clearly described (see Question 2 in Table 3.2), and some studies did not adequately describe participant withdrawals (see Question 14 in Table 3.2). In two studies, the sex of the recruited sample was not described [Panisset et al., 2012, Tsuda et al., 2001], and several studies [Liu et al., 1995, Wroble et al., 1990, Kopf et al., 2012, Lopomo et al., 2009] recruited a

mixture of males and females without accounting for the known increased knee instability of females compared to males [Waldén et al., 2011].

The use of a reference standard in the testing diagnostic apparatus is critical for an understanding of accuracy and reproducibility [Whiting et al., 2003]. Whilst only twelve studies in the present review used a reference standard, eight studies did not use a reference standard, and the remaining thirteen studies did not clarify if a reference standard was used or not (see Question 5 in Table 3.2). Of the studies that used a reference standard, two studies used the KT-2000 arthrometer [Ganko, Engebretsen and Ozer, 2000, Graham et al., 1991]; one study used both the genucom and the KT-2000 [Anderson et al., 1992]; five studies used knee arthroscopy [Anderson and Lipscomb, 1989, Beard et al., 1993, Lopomo et al., 2010, Steiner et al., 1990, Kopf et al., 2012]; two studies used both physical examination and arthroscopy [Bach Jr et al., 1990, Sernert et al., 2001]; and two studies used Magnetic Resonance Imagery (MRI) [Leblanc et al., 2015, Liu et al., 1995]. Although knee arthroscopy was used in five studies, such a procedure is not cost effective [Marsh et al., 2016]. Additionally, the ability to assess and diagnose patients in a clinic with simpler diagnostic tests allows rehabilitation to proceed rapidly and economically. Unlike the KT-2000 arthrometer, the magnetic resonance scan is not a knee stability measure. The MRI only shows the integrity of the knee structures in a static position [Grobbelaar and Bouffard, 2000], rather than measuring the displacement of the tibia relative to the femur. These results highlight the lack of a robust gold standard knee stability measure. Hence, the lack of an accepted reference standard leads to biased estimates of the tested instruments and reconstruction techniques. Table 3.4 illustrates a literature overview/summary of the

most common knee stability test/technique used, what stability provider is being assessment (mechanical vs sensorimotor) and the situations they are being used in (i.e. laboratory or clinical).

Table 3.4 Shows the most common knee stability test/technique used in the literature, what stability provider being assessed and in what situations they are being used.

| Measure | Type of test | Target assessment | Commonality |
|--------------------------------------|--|---|---|
| Lachman test | Subjective | Mechanical stability (ligaments) | Less in laboratory; common in clinical settings |
| Pivot sheft | Subjective but there is preliminary work by Hoshino et al. 2013 to make it objective | Mechanical stability (ligaments) | Less in laboratory; common in clinical settings |
| KT-2000 | Objective | Mechanical stability (ligaments) | Common in laboratory; less in clinical settings |
| Navigation system | Objective | Mechanical stability (ligaments) | Restricted to surgery |
| ACL-hamstring stretch reflex latency | Objective | Sensirimotor stability (proprioception receptors) | Common in laboratory; less in clinical settings |

3.6 Conclusions

We have reviewed a broad spectrum of knee stability measures designed to detect anterior-posterior and rotational knee instability. Whilst there is a wide variety in diagnostic accuracy, many of the studies lack scientific rigour. Despite the importance of such measures, there is no consensus in the literature on a single gold standard measure of knee instability. As a result, there is a need for high-quality randomised control trials, which are sufficiently powered, in order to move closer to a gold standard knee stability measure. In the meantime, clinicians must consider the

limited capacity of the reviewed knee stability measures in making a definite clinical decision on the severity of an injury and/or return-to-play. However, the use of the most common tests/techniques (subjective, objective) (Table 3.4) will provide better diagnosis and guide return-to-play decision.

**CHAPTER 4 - HAMSTRING STRETCH REFLEX: COULD IT BE A
REPRODUCIBLE OBJECTIVE MEASURE OF FUNCTIONAL KNEE
STABILITY?**

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Journal of Experimental Orthopaedics, 3(1), 1-8.

4.1 Abstract

The ACL plays an important role in anterior knee stability by preventing anterior translation of the tibia on the femur. Rapid translation of the tibia with respect to the femur produces an ACL-hamstring stretch reflex which may provide an objective measure of neuromuscular function following ACL injury or reconstruction. The aim of this study was to determine if the ACL-hamstring stretch reflex could be reliably and consistently obtained using the KT-2000 arthrometer. A KT-2000 arthrometer was used to translate the tibia on the femur while recording the EMG over the biceps femoris muscle in 20 participants, all with intact ACLs. In addition, a sub-group comprising 4 patients undergoing a knee arthroscopy for meniscal pathology, were tested before and after anaesthetic and with direct traction on the ACL during arthroscopy. The remaining 16 participants underwent testing to elicit the reflex using the KT-2000 only. A total number of 182 trials were performed from which 70 trials elicited stretch reflex (38.5%). The mean onset latency of the hamstring stretch reflexes was 58.9 ± 17.9 ms. The average pull force was 195 ± 47 N, stretch velocity 48 ± 35 mm/s and rate of force 19.7 ± 6.4 N/s. Based on these results, we concluded that the response rate of the ACL -hamstring reflex is too low for it to be reliably used in a clinical setting, and thus would have limited value in assessing the return of neuromuscular function following ACL injuries.

Keywords: Anterior Cruciate Ligament, ACL, Hamstring Activity, Short-latency response, Instability

4.2 Introduction

The goal of rehabilitation following knee injury is to restore stability and function, allowing patients to return to their maximum level of function [Gregory D. Myer, 2006, Bizzini and Dvorak, 2015]. The return to normal activity following injury is usually determined by an amalgamation of medical history, examination, combined with subjective physical assessment [Malanga et al., 2003] and sometimes instrumented testing devices and/or imaging [Campuzano Marín and Gómez-Castresana Bachiller, 2010].

Numerous protocols have been advocated for return to sport participation following knee injury; however, there remains a lack of consensus in the literature as to the appropriate criteria on which to base this decision. In a recent review, Arden et al. [2014] concluded that following ACL reconstruction, 82% of patients return to some type of sport participation, 63% return to pre-injury level of participation, and only 44% return to competitive sport, despite their observation that 90% were assessed as having normal or near normal function based on knee stability and lower limb strength testing. This discrepancy between return to sport participation and clinical findings highlights the possibility that additional factors that may not be assessed could be contributing to rehabilitation efficacy.

Ideally, knee neuromuscular function should be assessed in addition to mechanical stability assessment. Few studies have been conducted to better understand the applicability of an assessment of proprioception in the return to play decision [Beard et al., 1993, Friemert et al., 2005a, Schoene et al., 2009, Tsuda et al., 2001].

Schoene et al. [2009] noted that both the mechanical and functional (sensorimotor) components of the knee play a role in the subjective feeling of instability following ACL reconstruction. They defined functional instability as a feeling of instability due to

muscular dysfunction, which is caused by impaired neuromuscular function. This highlights the important role that proprioception plays in regulating the function of the muscles surrounding the knee. Various authors have noted that deficits in proprioception, balance, strength and neuromuscular control may persist for months following an injury or surgery [Lam et al., 2009, Torg, Conrad and Kalen, 1976, Tsuda et al., 2001]. Therefore, assessment of these factors may be critical for the return to play decision. Assessing these components in clinical practice can be challenging. As a result, there is a need for clinic-based objective measures of neuromuscular function to aid the return to play decision.

Whilst these researchers have suggested this reflex could be used as a measure of knee stability, it has not been implemented as a clinical-related measure. To allow the reflex to be used widely in a clinical setting, it would need to be obtained reliably with commonly available instrumentation, the most common of which is the KT-2000 arthrometer. Therefore, the aim of the present study was to investigate the efficacy of the KT-2000 to evoke the ACL-hamstrings reflex, thus providing an objective measure of neuromuscular function in a clinical setting.

4.3 Methods

Our study sample was comprised of two groups. Eighteen healthy male participants (mean age 30 ± 6.6 y, range 24–46 y) were recruited as a sample of convenience from the student population of the University of Birmingham. There is a consensus in the literature that females have more tendency of knee laxity than males [Rozzi, Lephart and Fu, 1999, De Ste Croix et al., 2015, Boguszewski et al., 2015], therefore; we recruited only male participants to reduce the inter-individual variabilities of the baseline laxity of the recruited sample. A subset of six of these participants were also tested with the Vicon motion analysis system to better elucidate the movement of the

tibia with respect to the femur. In addition, a set of 6 participants (5 ♂, 1 ♀; mean age 39.5 ± 13.8 y, range 20–51 y) were recruited to the study from the Royal Orthopaedic Hospital Birmingham, UK. These participants were patients undergoing arthroscopic meniscectomy or diagnostic arthroscopy, all of whom had intact and healthy ACL. In all cases the participants were healthy adults with no history of knee instability.

Participants were excluded from the study if they had any neurological condition or impairment of the involved limb, inability to give informed consent, history of ACL reconstruction, ligamentous instability, previous knee surgery or fracture, and clinical or radiological evidence of osteoarthritis.

All participants provided written informed consent and the study was conducted according to the Declaration of Helsinki. Ethical approval for the laboratory-based component of the study was obtained from the University of Birmingham Science, Technology, Engineering and Mathematics (STEM) Ethics Committee (ERN_13-0290) and approval for the clinical component was obtained from the Integrated Research Approval System (IRAS project ID 13-0164).

All trials were conducted by a physiotherapist (JA) experienced with the KT-2000 arthrometer (MEDmetric Corp, San Diego, CA, USA). Surface EMG (Biometrics, Ltd., Newport, UK) electrodes were placed on the belly of the biceps femoris muscle in accordance with SENIAM guidelines [Hermens et al., 2000]. The position and force outputs from the KT-2000 were connected to the data acquisition system. These analogue traces were bandpass filtered at 20–500 Hz and sampled at 5 kHz. All data were stored on an encrypted computer for offline analysis.

In order to elicit a stretch reflex, the force of the pull and subsequent stretch velocity of the tibial translation must be sufficient to activate the proprioceptors. The velocity

of the pulls was generated as fast as possible by the tester (JA). For the force magnitude, Friemert et al [2005b] demonstrated that a force of ≥ 140 N and stretch velocity of 30 mm/s would increase the chance to elicit stretch reflex to 100%. In a pilot experiment, the force of pull on the handle of the KT-2000 measured using a strain gauge. The force output of the KT-2000 was determined statically with calibration weights within the range of forces expected to be generated by the user. Similarly, the position output of the KT-2000 was calibrated using ceramic test gauge blocks.

The KT-2000 arthrometer was used with the Lachman test [Daniel et al., 1985] in which the assessor produces an anterior displacement of the tibia with respect to the femur. The participant remained relaxed in a supine position on the examination bed with the dominant knee supported at 30° of flexion. A goniometer was used to ensure the knee was placed in 30° flexion. The KT-2000 was secured over the participant's leg in the ideal position with reference to the knee joint line. Both knees were supported on a firm comfortable platform placed proximal to the popliteal space. In addition, a foot support, was used to position the leg symmetrically and avoid external rotation of the tibia. Next, a Lachman test was performed by pulling rapidly on the handle of the KT-2000. Each participant underwent 3 trials, with 3 attempts in each trial to elicit hamstring stretch reflex. Furthermore, to determine the onset and magnitude of the tibial translation, a control experiment was performed with six participants using a high-speed 3D motion analysis system (Vicon MX Nexus system, Vicon Motion Systems Limited, Oxford Metrics Ltd., Oxford, UK). Retro-reflective markers were fixed to the skin using double-sided adhesive tape over the lateral femoral epicondyle, 3 cm above the lateral femoral epicondyle, 3 cm below the lateral

tibial epicondyle and on the apex of the patellae. Three dimensional movement was capture by six cameras, calibrated with a residual error less than 1 mm and a sampling rate of 500 Hz.

In addition, to specifically confirm that the muscle activity traces were indeed the ACL/Hamstring reflex rather than movement artefacts, we compared the responses elicited with the KT-2000 to responses elicited from direct traction on the ACL during arthroscopy [Friemert et al., 2005a]. In this control experiment, four participants scheduled for an arthroscopic meniscectomy were recruited to the study. Reflexes were initially elicited with the KT-2000 inside the operating theatre using a very similar procedure described by Friemert et al. [2005a] Whilst we could not specifically control the force from direct traction in the same manner, we did ensure the force was greater than that of Friemert et al. [2005a]. Furthermore, precautions were taken to replicate the same procedure in our laboratory-based experiments: 1) the knee angle was maintained at 30°, 2) the placement of the EMG electrodes was standardised for all participants, 3) participants were placed in the same position, 4) the technique used for the pulling force was similar in the laboratory and arthroscopic procedures (Figure 4.1). Reflexes were elicited initially with the patients awake and again following anaesthesia. Patients were then placed under general anaesthesia using propofol and sevoflurane, it is unlikely that the excitability of the monosynaptic reflex arc or neuromuscular function were affected by the dosage of drugs used (see Kerz et al., [2001]. Sterile surface markers and leads were then placed over the hamstrings in order to eliminate contamination of the operative site. All arthroscopies were performed by a single consultant orthopedic surgeon (MS). During arthroscopy direct anterior traction was placed on the ACL using an arthroscopic probe, and the

subsequent electromyographic activity measured within the hamstrings as described by Friemert et al. [2005a].

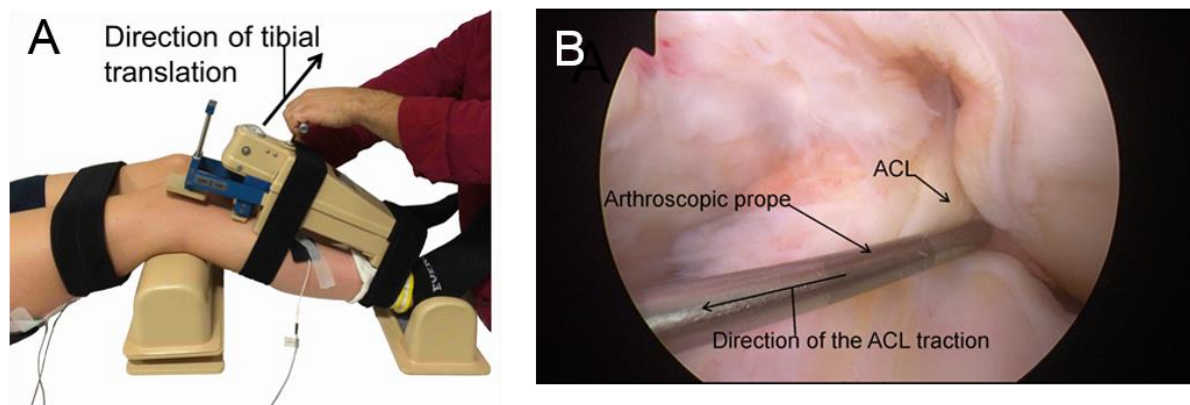


Figure 4.1: A. The experimental procedure of the KT-2000 arthrometer and the position of the knee joint, placement of the examiner hands and the direction of the tibial pull illustrated. B. shows the position of the arthroscopic probe and the direction of the ACL pull by the examiner. The tibial translation with the KT-2000 and, by inference, the ligament movement is similar to that of the direct ACL pull reported by Friemert et al. [2005a]. This does not mean to imply that the reflex onset latency between the two methods is the same.

Mean \pm SD of the stretch reflexes responses was calculated to produce a percentage of reflex across all participants. Moreover, a t-test was executed to assess the difference between the onset latencies of the laboratory group and the sub-set of the camera group. All calculations were made using SPSS Statistics Software Version 21 (IBM Corporation, New York, USA).

The force of the pull was calculated for each trial. The presence of a stretch reflex in response a pull was calculated to produce a percentage of reflex across all participants. Reflex onset latency was determined from all traces. To detect the onset latency of the stretch reflex response, a time window was defined in a 20—50 ms after the stretch onset; which incorporates the physiological range for the onset of a

reflex [Friemert et al., 2005b]. Within this window, the onset of the reflex was determined by visual inspection comparing the magnitude of the response with the background EMG. The onset latency of the reflex was defined as the time delay from the onset of tibial translation to onset of the first major deflection in the reflex (Figure 4.2).

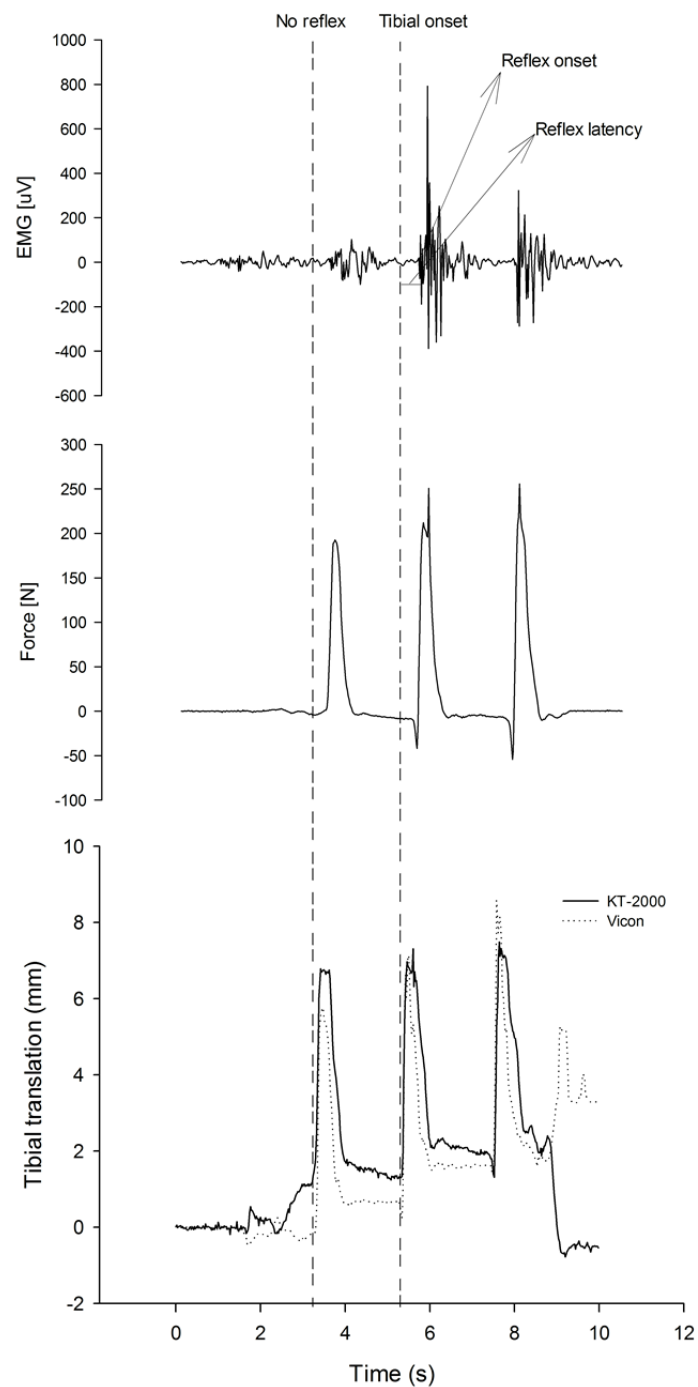


Figure 4.2: Example of a participant's EMG recorded from the biceps femoris muscle which shows the responses obtained after a single trial with three attempts to elicit a reflex using the KT-2000. EMG, force and position measured with the KT-2000 and Vicon system, respectively, are illustrated. The onset of tibial translation and onset latency of the reflex are illustrated. Reflex responses are observed with the second and third pulls, but not the first pull.

4.4 Results

Tibial translation (mm) with the KT-2000 is similar to that elicited when the tendon is directly pulled (Figure 4.3). On average, the force (195 ± 47 N), stretch velocity (48 ± 35 mm/s) and rate of force (19.7 ± 6.4 N/s) of pull that elicited stretch reflexes in the present study were not significantly different from those perturbations that did not elicited stretch reflexes 202 ± 42 N ($p = 0.32$), 50 ± 28 mm/s ($p = 0.76$) and 18.3 ± 6.0 N/s ($p = 0.16$) respectively. On average, 38.5% of the trials elicited a stretch reflex. In the laboratory group 41% of the trials elicited a stretch reflex. In the arthroscopy group, there was no difference in the percentage of reflexes elicited with the KT-2000 before anaesthesia (30%) and after anaesthesia (29%), or with direct traction on the ACL (42%) (Figure 4.4). The mean onset latency of the hamstring reflex across all trials was 58.9 ± 17.9 ms. The mean onset latency of the hamstring reflex laboratory group (61.7 ± 17.4 ms) and the sub-set of the camera group (58.7 ± 18.9 ms) were not statistically different ($p = 0.472$). A correlation analysis reveals that age was not correlated with either the number of reflexes $r(68) = 0.074$; $p = 0.527$; 95% CI (-3.793 to 0.917).) or the onset latency $r(68) = 0.078$; $p = 0.622$; 95% CI (-0.735 to 0.330).

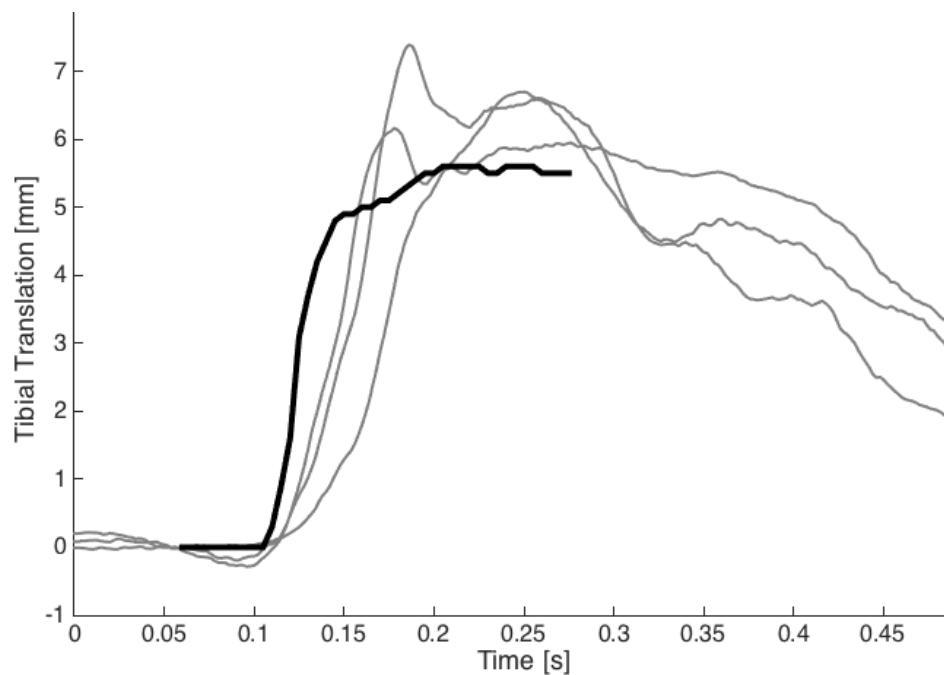


Figure 4.3 A comparison of the tibial translation acquired by direct tendon pull Friemert et al. [2005a] (black line) and the tibial translation from a single trial with three translations elicited with the KT-2000 (grey lines). The tibial translation (mm) induced with the KT-2000 and, by inference, the ligament movement is similar to that of the direct tendon pull reported by Friemert et al.[2005a]. This does not mean to imply that the reflex onset latency between the two methods is the same. It is likely that the ACL does not take up the stretch immediately when the tibia is translated as this would explain the longer latency in our findings (58.9 ± 17.9) compared with Friemert et al. [2005a].

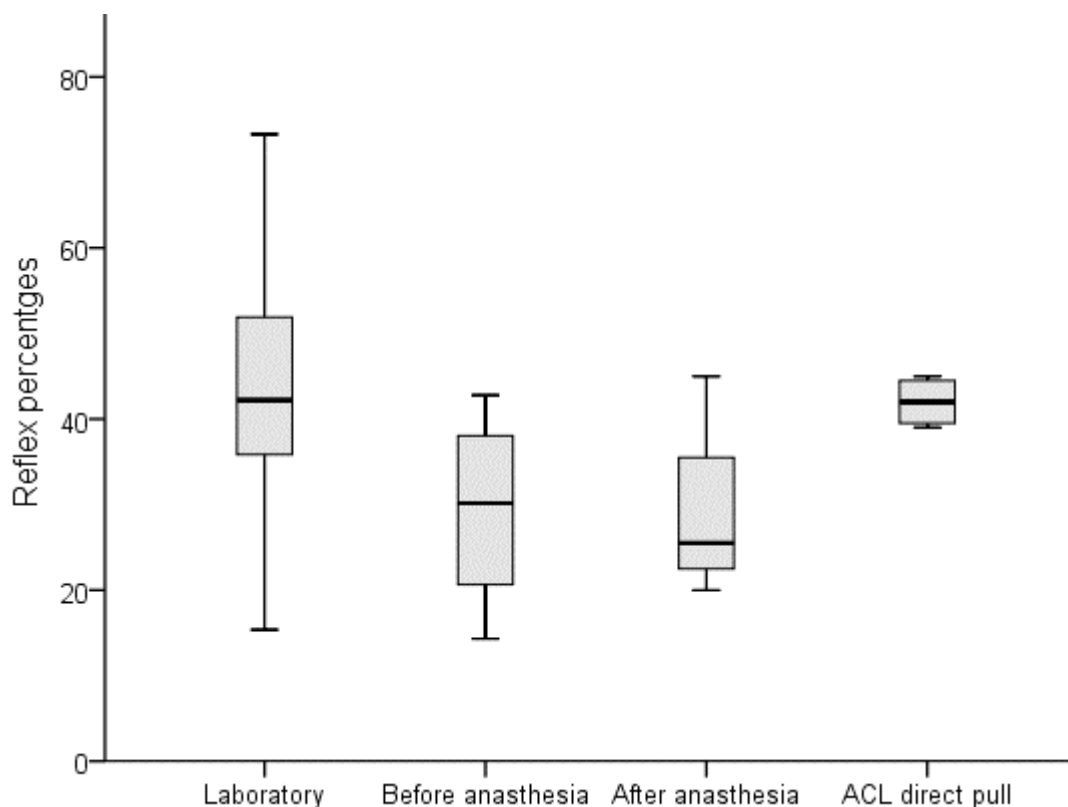


Figure 4.4: Box plot of hamstring stretch reflex percentages in all testing conditions. The laboratory group consists of 16 participants 41% while the arthroscopic group consists of 4 participants; 30% before anaesthesia, 29% after anaesthesia and 42% with a direct pull. The low percentages represent the lack of reproducibility of the hamstring stretch reflex when used as an objective measure of knee functional stability.

4.5 Discussion

The aim of this study was to determine if the ACL hamstring stretch reflex could provide a reproducible objective clinical measure to assess the neuromuscular functional stability of the knee. Hence, we aimed to quantify the robustness of ACL hamstring stretch reflex that could be generated using the KT-2000. The tibial translation (mm) induced with the KT-2000 and, by inference, the ligament movement is similar to that of the direct ligament pull reported by Friemert et al. [2005a]. Whilst

the force of the pull (195 ± 47 N), rate of force (19.7 ± 6.4 N/s) and the velocity of tibial translation (49 ± 35 mm/s) were sufficient to elicit a reflex, only 38.5 % of the trials elicited a stretch reflex. As a result, we must conclude that the ACL-hamstring stretch reflex elicited with the KT-2000 arthrometer is not sufficiently reproducible to provide a reliable clinical measure.

The ACL -hamstring reflex has been proposed as an objective measure of the neuromuscular state of knee both arthroscopically [Friemert et al., 2005a] and clinically [Schoene et al., 2009]. In both cases, the ACL-hamstring reflex was suggested to be clinically useful. Schoene et al.'s [2009] investigated the reliability of such technique on the bases of intra-individual reproducibility, inter-examiner reliability, fatigue, weight, height and physical fitness. Their protocol involved participants standing with the knees flexed at 30° , the feet externally rotated to 5° and the patella against a supporting plate. Posterior–anterior tibial translation is induced by a 300 N force applied via a pneumatic cylinder and piston, 10 cm below the popliteal fossa and parallel to the tibial plateau. Only the inter-tester reliability showed a significant difference between examiners. On the other hand, all the remaining factors showed no significant differences. This study concluded that none of the above-mentioned factors had a relevant influence on the reflex responses. Schoene et al. [2009] suggested that their method may assist in establishing a clinically relevant testing system for the functional stability of the knee. However, their protocol is fairly complex and requires specific equipment not commonly available in a clinical scenario.

The force of the perturbation in the present study was less than that reported by Friemert et al., (2005) (300 N compared with approximately 200 N in the present

study). However, in a pilot study undertaken on 10 participants, Freimert et al. [2005b] demonstrated that below 50 N no reliable response could be obtained, but the response rate increased to 80% at 90 N and 100% over 140 N. These results are similar to those shown by Jennings and Seedhom [1994], who used a 140 N force in their study as they could not demonstrate contraction of the hamstrings below 100 N. In line with their conclusion that the higher perturbation forces the higher chance of eliciting the stretch reflex, our method of eliciting the stretch reflex used the strongest and fastest perturbation possible. The mean rate of force and stretch velocity in the present study was 19.7 ± 6.4 N/s and 49 ± 35 mm/s respectively, which exceeded the minimum velocity (30 mm/s) recommended by Friemert et al. [2005b] to obtain a reliable reflex response. On the contrary, Bedingham et al. [1984] reported that stretch reflex latency being independent of force when tested on Monkeys. However, consistency of our methodological procedure was maintained by trying to have the same experienced user perform the procedure through the study. Force, rate of force and stretch velocity was recorded and examined from all trials. No trials were eliminated for the possibility that the force was not strong enough. This is illustrated in Figure 4.2 which showed an example of data of a single trial with the amount of force for each of the three pulls.

Although not reported in all studies, Tsuda et al. [2001] demonstrated that the elicited rate of the hamstring stretch reflex through a direct electrical stimulation of the ACL was 8/9 for the biceps femoris and 5/9 for the semitendinosus muscles. With direct traction on the ACL, Freimert et al. [2005b] demonstrated the median latency response aspect of the reflex 10/10 times in the medial hamstrings and 8/8 times in the lateral hamstrings. Unlike invasive studies, the specific rate of acquisition of

stretch reflexes at non-invasive studies has not been reported [Schoene et al., 2009, Melnyk and Gollhofer, 2007b, Friemert et al., 2010]. This is however important when considering the reproducibility and applicability of such a method in clinical settings. In a sub-group of our sample, the arthroscopy group, a battery of trials was performed after anaesthesia to exclude artefacts and confirm that the reflexes obtained were in fact related to the ACL-hamstring reflex. Although small, the reflexes in this group were seen as the gold standard against which the remainder of the tests were compared ($30 \pm 12\%$ before anaesthesia and $29 \pm 11\%$ after anaesthesia, or $42 \pm 3\%$ with direct traction on the ACL). The rate at which the stretch reflex was obtained was similar to the laboratory group. Therefore, in contrast with Friemert et al. [2005a], the inability to obtain consistent stretch reflex percentages during the four different situations shows why the hamstring stretch reflex cannot be used as an objective measure of knee functional stability. Although we tried to replicate Friemert et al.'s [2005a] work (Figure 4.3), we could not reproduce their results in the arthroscopic tests of our study. Whilst they used a well-defined perturbation with a force of 300 N to elicit stretch reflexes while we used the strongest and fastest possible manual perturbation done by the surgeon's hand. Furthermore, the manual technique using the KT-2000 produces a faster stretch velocity (49 ± 35 mm/s) and higher rate of force (19.7 ± 6.4 N/s) and this would increase the likelihood of eliciting stretch reflexes. Nonetheless, our results showed that the mean onset latency of the stretch reflexes were 58.7 ± 18.9 ms compared to [Friemert et al., 2005a] who reported 23.9 ± 1.7 ms. The tibial translation (mm) with the KT-2000 and, by inference, the ligament movement is similar to that of the direct ACL pull reported by Friemert et al. [2005a]. It is likely that the ACL does not take up

the stretch immediately when the tibia is translated with respect to the femur. This would explain the longer latency in our findings compared with Friemert et al. [2005a] who used a direct pull on the tendon.

In the laboratory group, the rate of reflexes was slightly, but not significantly, higher ($41 \pm 11\%$). Although a reflex was obtained in every patient (range of 44.9), the reflexes were not consistently elicited. Accordingly, in our study, we were unable to reproducibly elicit the ACL-hamstring reflex using the KT-2000 arthrometer. Based on the inconsistent nature of the reflex, we feel that the reflex elicited by the KT-2000 could not be used in clinical practice as a measure of knee functional stability.

The lack of standardisation of force used to induce tibial translation with the KT-2000 arthrometer is a weakness of our study. Although the lack of standardisation can be considered as a weakness, it does however represent the intra-individual variability that exists in human clinical-related practice, and is therefore relevant to the application of such techniques in clinical settings. In addition, we acknowledge that we assessed the reflex in a small number of intraoperative cases, which was however used only to confirm the characteristics of a gold standard reflex to be used as a reference standard for our laboratory testing. To minimise variability, all tests were by the same investigator, who was familiar with the KT-2000 arthrometer.

4.6 Conclusion

Although it was possible to elicit the ACL -hamstring stretch reflex with direct traction on the ACL intraoperatively and with the KT-2000 device in every participant in the present study, the reflexes could not be evoked consistently. We therefore conclude that the ACL -hamstring stretch reflex cannot be elicited with the KT-2000 reliably in a clinical setting. It would therefore have limited value in assessing the return of

neuromuscular function following ACL injury. Further studies need to be conducted to investigate other robust ways to objectively measure knee neuromuscular stability.

**CHAPTER 5 - PERIPHERAL ELECTRICAL AND MAGNETIC
STIMULATION AS AN ADJUNCT FOR MUSCLE HYPERTROPHY
TRAINING**

This paper has been submitted for publication and currently in press:

Abulhasan, J. F., Rumble, Y. L., Morgan, E.R., Slatter, W.H., Grey, M.J. 2016 (In press). Peripheral electrical and magnetic stimulation as an adjunct for muscle hypertrophy training. *Journal of Functional Morphology and Kinesiology*

5.1 Abstract

Electrical (ES) and magnetic stimulation (MS) applied peripherally may be used to elicit muscle contraction for strength training, enhance knee laxity and rehabilitation following injury. We examined the effect of a 3-week exercise programme designed to induce muscle hypertrophy augmented by peripheral electrical or magnetic stimulation. We hypothesised that the addition of peripheral stimulation to a weight-training protocol would induce more repetitions and increase thigh circumference, muscle layer thickness, and quadriceps strength, whilst decreasing knee laxity. Thirty healthy participants were divided randomly into ES, MS or control groups. Five hypertrophy training sessions were carried out, consisting of four sets of quadriceps extensions. The first three sets were restricted to eight repetitions and on the last set the participant was instructed to perform the movement until failure. The MS and ES groups continued to exercise with the augmentation of peripheral stimulation to facilitate additional repetitions. Quadriceps strength (1 repetition maximum), thigh circumference, muscle layer thickness and knee laxity were assessed at baseline (day 1) and at the end of the protocol (day 21). All participants tolerated the stimulation, and on average, 4 ± 2 and 7 ± 6 additional repetitions were facilitated through the application of ES and MS, respectively. Following the training, significant increases were observed for both 1RM ($p = 0.005$) and muscle layer thickness ($p = 0.031$) and no change in thigh circumference ($p = 0.365$). Knee laxity was observed to decrease ($p = 0.005$). However, there were no changes for the stimulation groups compared to the control group for any of the measurements; 1RM ($p = 0.415$), muscle layer thickness ($p = 0.712$), thigh circumference ($p = 0.364$) and laxity ($p = 0.300$). The additional repetitions elicited by stimulation after the point of voluntary failure suggest that peripheral ES and/or MS may be useful as an adjunct for

hypertrophy training. However, as an effect on hypertrophy was not shown in the present study such training on muscle hypertrophy, strength and knee laxity may be small. Further research with a larger sample size is required to investigate if such training will be efficacious.

Key words: Electrical stimulation, magnetic stimulation, strength

5.2 Introduction

Weight training is frequently used to facilitate muscle hypertrophy, strength and knee stability. Electrical stimulation (ES) and magnetic stimulation (MS) have been used as an adjunct to athletic training [Szecsi, Straube and Fornusek, 2014, Laughman et al., 1983, Kubiak Jr, Whitman and Johnston, 1987], although it is more commonly used as a rehabilitation therapy to promote quadriceps strength after surgery [Kyung-Min Kim, 2010, Imoto et al., 2011, Draper and Ballard, 1991, Taradaj et al., 2013], quadriceps hypertrophy [Barcellona et al., 2015], to investigate different types of muscle fatigue [Millet et al., 2012], daily functional activities after stroke [Howlett et al., 2015], and osteoarthritis patients [Negm, Lorbergs and Macintyre, 2013, Hasan, 2015]. However, the evidence concerning the usefulness of peripheral stimulations as an adjunct to training programmes for enhancing muscle hypertrophy, strength, knee laxity and training healthy people is not conclusive. One reason for the inconsistency effects reported in the literature is the methods by which stimulation is applied.

Kyung-Min et al. [2010] systematically reviewed the literature assessing the effect of ES on quadriceps strength and functional performance following knee surgery. They reported significant effect sizes of quadriceps isometric and isotonic torque (ranging from -0.74 to 3.81) at 6 weeks post-operatively, in contrast, the effect sizes of the lateral step-up test and functional reach test were not significant (ranging from 0.07 to 0.64). The authors concluded that ES with exercise may be more effective in enhancing quadriceps strength than exercise alone. In a more recent systematic review, Howlett et al. [2015] examined the ability of ES to improve walking speed, wrist extension and ankle dorsiflexion, and investigated whether it is more effective than training alone. They showed that ES had a mean moderate effect (0.40 , 0.09 -

0.72; 95% CI) on activity compared to no or a placebo intervention. In addition, the stimulation group showed a mean large effect on upper limb activity (0.69, 0.33 -1.05; 95% CI) and a small effect on walking speed (0.08 m/s, 0.02 -0.15; 95% CI) compared to the control group. Their findings suggest that ES could be used in patients after traumatic injuries where functions have been affected.

Taradaj et al. [2013] assessed if anterior cruciate ligament (ACL)-reconstructed male football players (n=40) benefited from ES as an adjunct to their regular protocol after knee ACL reconstruction. To the author's knowledge, this study design had the shortest protocol for their experiment (1 month), and both the intervention and control groups received three sessions weekly consisting of the same exercise programme. The intervention group received ES on both right and left quadriceps three times daily, three days a week. The comparison of post-training measures showed a significant difference in favour of the stimulation group in the quadriceps extension (30.1% versus 4.6%, $P = 0.002$) and thigh circumference (1.4% versus 0.6%, $P = 0.04$). The authors concluded that there is evidence of the benefit of peripheral ES in restoring quadriceps muscle mass and strength in football players. Barcellona et al. [2014] investigated the effect of two sets of 20-RM (LOW group) and 20 sets of 2-RM (HIGH group) quadriceps open kinetic chain resistance training on anterior knee laxity. Unlike the HIGH and control groups, the LOW group demonstrated a mean reduction of 5 cm in anterior knee laxity after a twelve-week training protocol. The authors concluded that knee extensor open kinetic chain resistance training at the corrected dose may lead to a reduction in anterior knee laxity of the ACL-injured

knee. To the author's knowledge, this study is the only one that has investigated the effect of quadriceps hypertrophy training on anterior-posterior knee laxity.

In addition to its clinical use, the effect of peripheral stimulation as an adjunct to weight training has been investigated in healthy people. Kubiak et al. [1987] compared quadriceps strength torque in control (n= 9), isometric exercise (n= 10) and ES (n=10) groups before and after a five week training protocol consisting of three sessions per week. The quadriceps of the stimulation group received 15-second long stimulation contractions with a 50-sec rest period between each contraction. All the participants tolerated a stimulation intensity which ranged between 75% - 134% of the MVIC, and significant strength increases ($p < 0.05$) were seen for all in both the electrical and isometric exercise groups. Szecsi et al. [2014] evaluated the mechanical power generated by healthy participants during MS or ES induced ergometer training conditions; MS produced more mechanical power (23.8 ± 9.1 W) and longer cycling exercise compared to ES (11.3 ± 11.3 W). Bax et al. [2005] systematically reviewed the literature that investigated the effect of ES as an adjunct to training on the quadriceps femoris muscle strength for both healthy and ACL-reconstructed participants. The authors suggested that the application of ES for both injured and non-injured participants did not show a trivial difference between the traditional weight training and volitional training protocols (overall pooled point estimate is -11.51 Nm (95% CI $-22.94, -0.08$)). Importantly, they highlighted the fact that the literature in this field lacks high quality studies. Moreover, their meta-analysis indicated that publication bias may be present in the literature regarding whether the

included studies represent the full spectrum of trials performed in actual research practice.

Recently, peripheral MS has been trialled as an alternative to ES [Millet et al., 2012, Atzori et al., 2013]. As this technique is novel, there is a dearth of literature examining its efficacy as an adjunct to training programmes for quadriceps circumference, muscle layer thickness, strength and knee laxity. Previously, peripheral MS has been restricted to the study of fatigue [Kim et al., 2012] and it has been reported that peripheral stimulation might minimise the effect of muscle fatigue and shorten the time spent in recovery [Kim et al., 2012, Szecsi, Straube and Fornusek, 2014, Taradaj et al., 2013]. In addition, peripheral stimulation alongside weight training may be preferred by patients and athletes as it is characterised by portability (ES) and less pain (MS) compared to alternative methods, such as stretching, massage and cold water immersion [Negm, Lorbergs and Macintyre, 2013, Thakral et al., 2013]. Moreover, the application of peripheral ES and MS will bypass CNS fatigue, and therefore it may be more efficacious if applied at the point of voluntary muscle failure in order to induce additional repetitions. Nevertheless, studies that showed a positive effect of peripheral stimulation used subjective outcome measures (e.g. pain), which increase the chances of false positive results [Doix et al., 2014, Green, Robinson and Wallis, 2014].

We aimed to determine whether peripheral ES and MS applied at the point of muscle failure following voluntary exercise could induce greater hypertrophy, strength and less anterior knee laxity than voluntary muscle activity alone. We hypothesised that a three-week training protocol using peripheral ES or MS applied at the point of voluntary muscle failure would induce more repetitions, and increase thigh

circumference, muscle layer thickness, quadriceps strength, whilst decreasing anterior knee laxity compared to the controls.

5.3 Methods

5.3.1 Participants

Thirty healthy participants (16 females, mean age 20 ± 4 SD years, range = 18–37; and 14 males, mean age 19 years ± 1 SD, range = 18–20) were recruited. All the participants were undergraduate university students who performed active regular exercise of not less than 30 minutes of physical activity at least five times per week. Participants were screened for previous knee injuries and neuromuscular conditions, and agreed not to undergo any additional leg strength training during the three weeks of this study. All participants provided written informed consent prior to participating in the study. The experimental procedures were conducted in accordance to the Declaration of Helsinki and were approved by the ethical committee of the University of Birmingham Science, Technology, Engineering and Mathematics (STEM) committee (ethics approval code: ERN-14-0188).

5.3.2 Study design

The study was carried out over 21 days and had a between-participant design with four dependent variables: girth measurement of the thigh muscle, quadriceps muscle layer thickness, knee anterior-posterior laxity measure, and maximum weight lift of the quadriceps extension. Those four variables were chosen because they measure muscle hypertrophy, strength and knee laxity which all link to knee stability in the notion that bigger muscle size recruits more muscle fibers hence enhance neural activity. Also, strong muscle increases rate of force development thus enhance knee stability during exercise. All Participants were randomly assigned to one of the three study groups: strength training only (control), strength training with electrical

stimulation (ES), or strength training with magnetic nerve stimulation (MS). The study had two independent variables: time (pre vs. post) and group (electrical vs. magnetic vs. control). The study protocol started with baseline testing and a weight training session on day one, followed by two rest days, which were also provided between each subsequent training session. After the final training session all the participants rested for a week to ensure no peripheral fatigue existed as a result of the training protocol. Finally, on day 21, post-experimental testing was conducted (Figure 5.1). All measurements were carried out on the participant’s dominant leg in an non-fatigued state.

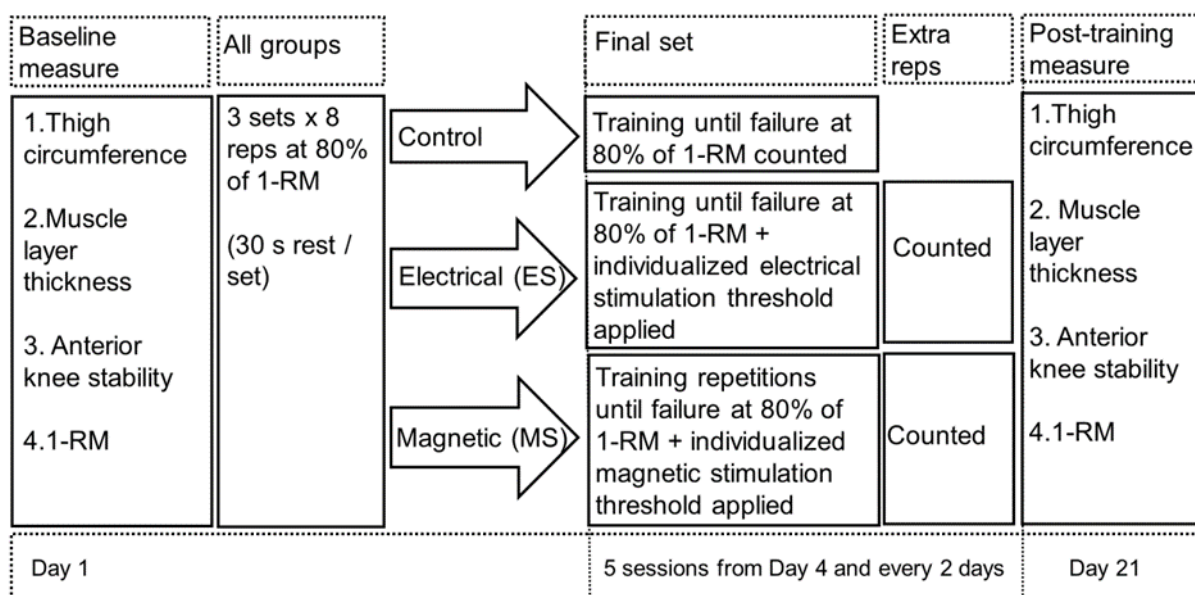


Figure 5.1: Flow diagram of the weight training protocol for the three groups. All performed a baseline measure before any weight training followed by four sets of resistance quadriceps weight training. The first three were standardised to eight repetitions only at 80% of 1-RM, while the fourth set was aimed to reach the maximum number of repetitions a participant could perform. The intervention groups received stimulation by either ES or MS to assess whether extra repetitions could be induced or not at the point of muscle failure. ES = electrical stimulation; MS = magnetic stimulation; reps = repetitions; 1-RM = 1- repetition maximum; s = second.

5.3.3 Procedures

The study training protocol aimed to focus on hypertrophy rather than strength. Previous research has suggested that optimum hypertrophy gains in healthy individuals are best obtained when performing eight repetitions at 85% of 1-repetition maximum (1-RM) [Thornton and Potteiger, 2002]. It has also been shown that training with higher intensities lead to better results [Poehlman, 1998, Thornton and Potteiger, 2002]. Therefore, each participant performed the weight training programme at 80% of their 1-RM with a 30-second rest between each set (Figure 5.1).

Muscle failure was determined as the point at which a participant could not voluntarily contract their quadriceps to fully extend their legs against the tibia pad of the Cybex VR3, (Cybex International Inc, MA, USA). In all groups, the first three sets were restricted to eight repetitions only in order to focus on hypertrophy rather than strength. During the fourth set, voluntary muscle failure marked the end of the training session for the control group, whereas for the ES and MS groups, voluntary effort was then augmented with peripheral stimulation until no further repetitions could be made. Stimulation was delivered to the motor point of the quadriceps femoris muscle. Electrical stimuli were delivered through self-adhesive surface stimulating electrodes (Compex Easy Snap, Compex Global) using the Mi Compex 3, Professional, (Compex Global, United Kingdom), with a pulse duration of 400 μ s and a pulse frequency of 50 Hz utilised during every training session. The participants were then asked to slowly increase the stimulus intensity until an individualised stimulation tolerance was felt, and this intensity was recorded as their maximum threshold (range 30 Hz - 50 Hz). The range of intensity were all within the

recommended parameters [Glaviano and Saliba, 2016] as to create large positive effects. Magnetic stimuli were delivered to identify the motor point via magnetic stimulation (MagPro X100, MagVenture, Denmark), and a low frequency single pulse stimulus was applied over the bulk of the muscle until the largest twitch was observed; this was marked as the motor point. To identify the magnetic threshold, 2-second duration pulses were used to stimulate the motor point, beginning at 5% intensity and increasing slowly until an individualised tolerable stimulation was felt, and the highest tolerable intensity was recorded as the magnetic threshold for each participant (range 39% - 60% of their highest intensity).

5.3.4 Assessment methods

All testing and weight training sessions were supervised by a certified strength and conditioning coach (WS). Post-testing was carried out by an experimenter who had remained blinded throughout the data collection sessions to avoid bias when reading the follow up results (JA). Post-training measurements were carried out at roughly the same time of day (± 2 hrs) to reduce the effect of circadian fluctuations [Kong et al., 1995, Coldwells, Atkinson and Reilly, 1994]. All measures were taken from the participant dominant leg.

Thigh circumference

Thigh circumference was measured with the participant lying supine position on a plinth. The measurement was taken at the midpoint between the anterior superior iliac spine (ASIS) and the lateral epicondyle of the femur, and the position was marked with a permanent marker. Three measures of thigh circumference were

made with a medical tape recording to the nearest millimetre, from which a median value was calculated for use in the statistical analysis.

Muscle layer thickness

With the participant in the same position as for the circumference measure, rectus femoris (RF) muscle layer thickness (MLT) was obtained using a Phillip Sonos D2 5500 ultrasound (US) with an 11-3L probe at an image depth of 7 cm. Measurements were made using the ultrasound's calliper function. Rectus femoris MLT measures were repeated three times to the nearest millimetre, from which a median value was calculated for use in the statistical analysis (Figure 5.2).

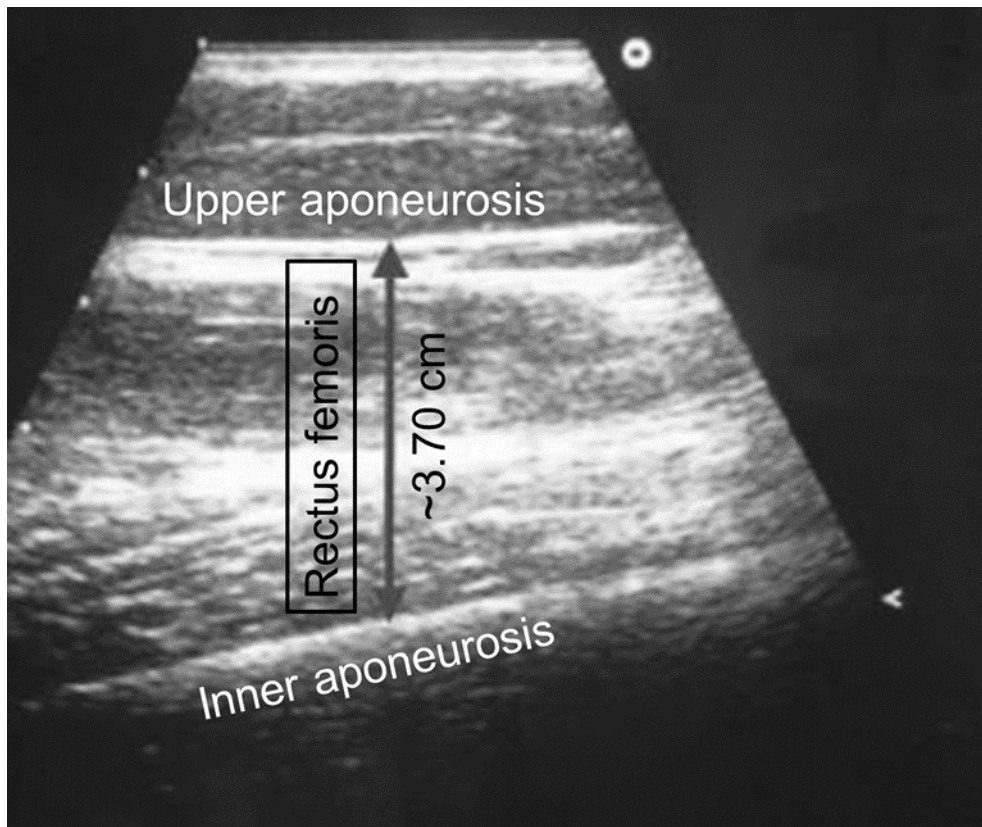


Figure 5.2: Illustration of how the muscle layer thickness was measured using the ultrasound image for every participant. The distance between the upper layer and lower layer of the rectus femoris muscle image was measured using the integrated US arrow. The US gives the exact distance between the two heads of the arrow

which corresponds to the thickness of the measured muscle

Maximal leg extension

Knee extension strength was measured with a Cybex VR3, Cybex International Inc, MA, USA (Figure 5.3). The participant was seated with the back support and tibia pad adjusted to fit the individual's height, and these seating adjustments were recorded in order to replicate the participant's position in all tests. Each participant sat with the hips straight and in line with each other, knees at 90 degrees, the back in a comfortable position and toes dorsiflexed. Following a short warm-up, participants were instructed to perform two repetitions at increasing weight and were challenged with ensuring that their legs reached full extension in a controlled manner. Also, motivation during exercise and sport participation enhance physical activity outcome [Frederick, Morrison and Manning, 1996], hence, all participants were continuously motivated verbally throughout every single repetition and set to encourage them to

reach their maximum weight/repetition. Once the participant could not complete a second repetition, this weight was recorded as their one-repetition maximum (1-RM).



Figure 5.3: Voluntary leg extension setup and participant in the starting position of the weight training programme. The participant was instructed to fully extend their lower limbs with a slow and controlled movement and then return to the starting point. This cycle was counted as one successfully completed repetition.

Knee anterior-posterior laxity test

A KT-2000 knee arthrometer (MEDmetric Corp, San Diego, CA, USA) was used to measure the anteroposterior displacement of the femur on the tibia. This measure

was used because 1) it is the most commonly used portable objective measure to assess anterior-posterior knee laxity and 2) it has the highest sensitivity and specificity compared to all other objective anterior-posterior knee laxity measures (see Table 3.3). For this measure the participant remained relaxed in a supine position on the plinth with their dominant knee supported at 30° of flexion as measured using a goniometer. Initially, the KT-2000 device was secured over the participant's leg in the ideal position with reference to the knee joint line. Both knees were supported on a firm, comfortable platform placed proximal to the popliteal space. In addition, a foot support, supplied in the KT-2000 arthrometer kit, was used to position the leg symmetrically and to avoid external rotation of the tibia. Next, the Lachman test, forced anterior displacement of the tibia with respect to the femur, was performed by holding the femur and pulling on the handle of the KT-2000. Anterior displacement was measured to the nearest millimetre. Three trials were conducted, with the median calculated for use in the statistical analysis.

5.3.5 Statistical analysis

An independent t-test was used to compare the additional number of repetitions elicited with ES or MS augmentation after voluntary failure. One-way analyses of variance (ANOVA) tests were used to compare the number of repetitions induced in each group during the final set before stimulation. In addition, two-way (ANOVA) tests were used to examine the time effect (pre and post) and the group effects in the three different study groups (control, ES and MS) for each of the four dependent variables. The normality of the data was assessed using the Kolmogorov-Smirnov test and there were equal variances of the dependent variables, which were assessed using the Levene's test, across all levels of the independent variables. The level of significance was set at $p \leq 0.05$ for all measures. If significance was

achieved, then a Tukey post-hoc test was planned to be performed. All the statistical analyses of the data were executed using SPSS Statistics 22 Software (IBM, New York, USA).

5.4 Results

All the participants completed the study successfully and tolerated the stimulation comfortably. At the end of the three week training protocol, the maximum number of repetitions in the final set was 8 ± 2 , 9 ± 1 and 10 ± 1 for the control, ES and MS groups, respectively. A one-way ANOVA indicated that there was no significant difference in the mean number of repetitions during the final set between the groups ($p = 0.538$) (Figure 5.4).

All the participants exposed to stimulation were able to complete additional repetitions; ES = 4 ± 2 and MS = 7 ± 6 , range (1-20). No significant difference between the number of additional repetitions for the ES and MS groups were observed ($p = 0.187$) (Figure 5.4). Participants in the ES group showed more confidence and comfort than the MS group during stimulation. This may be because the ES group had the ability to self-control the intensity of the stimulation as opposed to the MS group, where the intensity of the stimulation was controlled by the experimenter.

Following the training, significant time-effect increases were observed for both 1RM ($p = 0.005$) and muscle layer thickness ($p = 0.031$), whilst no change in thigh circumference ($p = 0.365$) was noted, and knee laxity was observed to decrease ($p = 0.005$). However, there were no group-effect changes for the stimulation groups compared to the control group for any of the measurements: 1-RM $F(2,27) = 0.90$, $p = 0.415$, partial $\eta^2 = 0.03$ (Figure 5.5c), muscle layer thickness $F(2,27) = 0.34$, $p = 0.712$, partial $\eta^2 = 0.01$ (Figure 5.5b), thigh circumference $F(2,27) = 2.10$, $p = 0.132$, partial $\eta^2 = 0.01$ (Figure 5.5a), and anterior knee laxity, $F(2,27) = 1.23$, $p = 0.300$,

partial $n^2 = 0.40$ (Figure 5.5d)

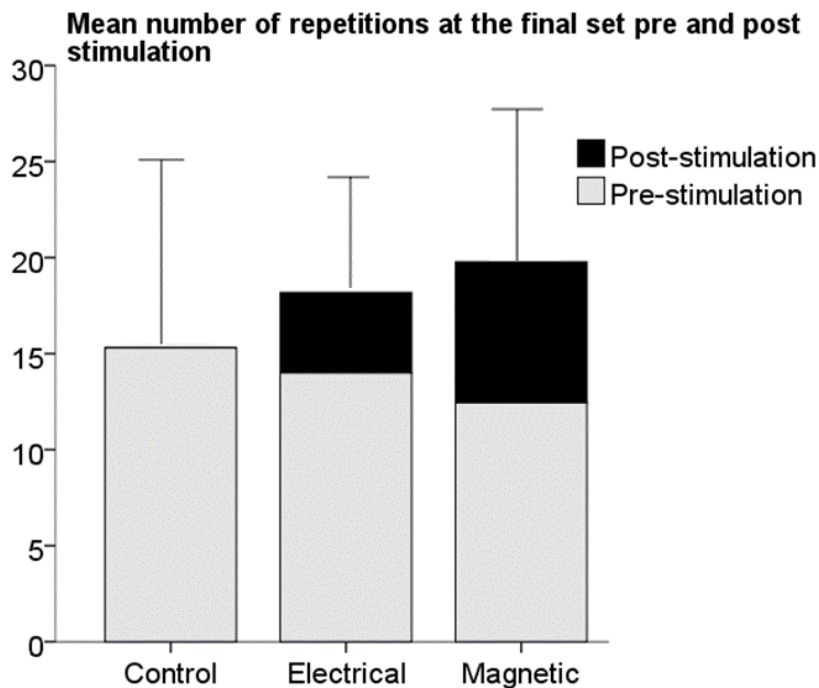


Figure 5.4: Bar plot of the mean number of repetitions each group performed during the final set before the addition of stimulation at the point of failure and the extra number of repetitions induced after muscle failure had been reached during the last training set in the two intervention groups. No significant difference in the mean of the extra repetition numbers was observed between the two intervention groups. Data are expressed as mean \pm standard deviation. ES = Electrical stimulation group, MS = magnetic stimulation group.

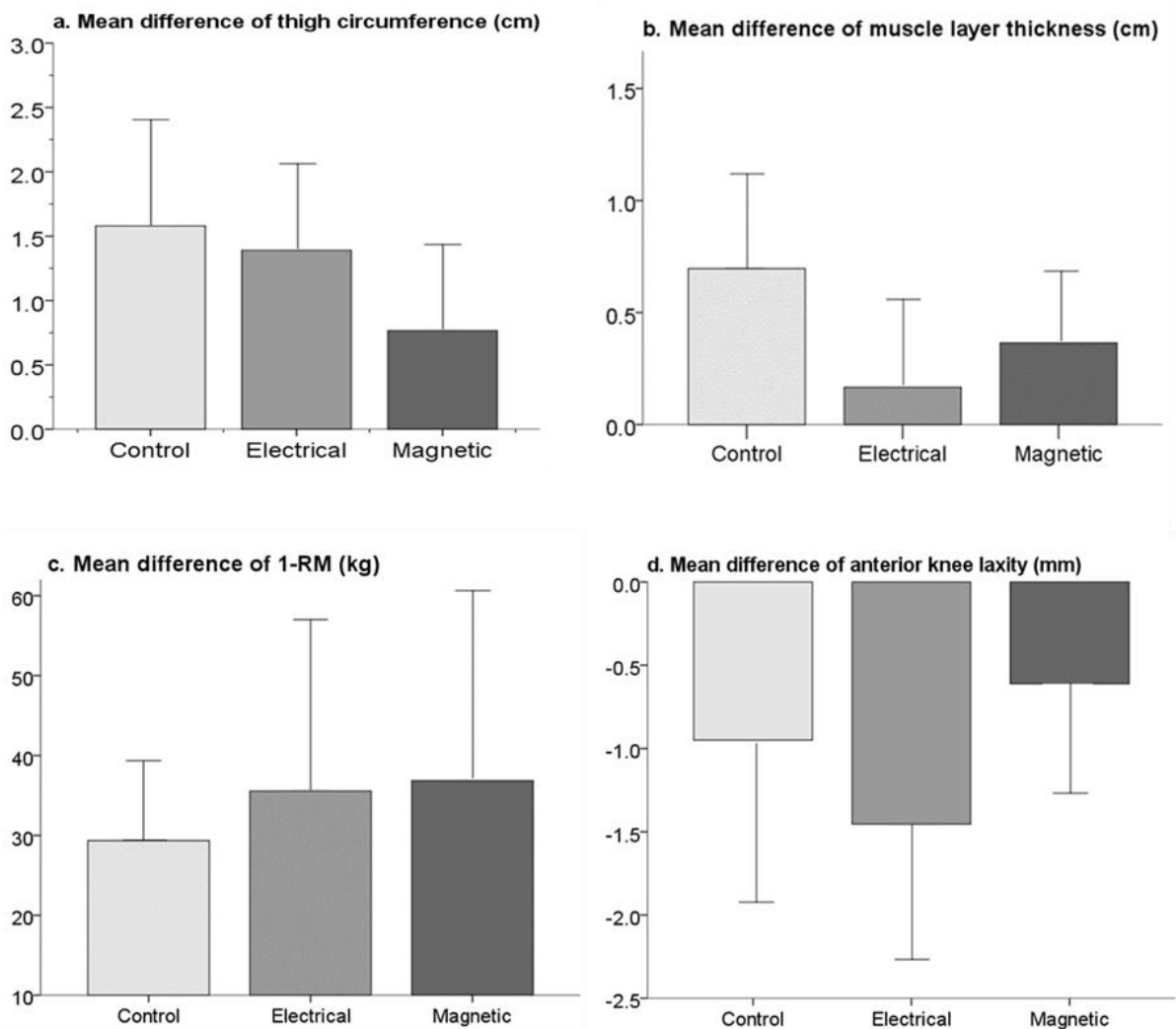


Figure 5.5: Bar plots of the means of the difference between baseline and post-training measures for all three groups for a) thigh circumference, b) muscle layer thickness, c) 1-repetition maximum and d) anterior-posterior knee laxity. No significant difference was observed between the three groups. Data are expressed as mean \pm standard deviation.

5.5 Discussion

The aim of this study was to determine if peripheral ES or MS applied at the point of muscle failure following voluntary exercise could induce greater hypertrophy, strength and less anterior knee laxity than voluntary muscle activity alone. Both peripheral ES

and MS elicited additional repetitions following voluntary muscle failure. However, as applied in the present study, the effect of such training on muscle hypertrophy, strength and anterior knee laxity was not significantly different from voluntary training alone; hence the effect may be small.

Within the literature different approaches have been utilised to evaluate muscle strength, such as hand-held dynamometer, isokinetic machines, 1-RM and maximal voluntary contraction technique. There is a consensus in the literature that the 1-RM is a reliable and relatively cost-effective technique, as it requires non-laboratory equipment and consequently is considered one of the most commonly used techniques to assess muscle strength in non-laboratory situations [Phillips et al., 2004, Levinger et al., 2009, Abdul-Hameed et al., 2012, Kraemer et al., 1995, Fleck and Kraemer, 2014]; therefore this measure was used to assess quadriceps muscle strength in this study. The number of extra repetitions for each participant in the final set was widespread (range, ES ; 2 - 8; MS = 1 - 20). Despite the fact that a firm procedure was used, in this study, to establish a participant's 1-RM, several factors may have affected the outcome and there remains the possibility that the participants who executed a higher number of repetitions had not in fact exercised at their 1-RM. This may be due to both neural and psychological supraspinal drive inhibition operating on the muscle motor units [Ikai and Steinhaus, 1961]. Belanger and McComas [1981] reported that 50% of participants did not reach their 1-RM even when they were asked to exert force with their maximal volition. Therefore, this study shows that our developed 1-RM technique can better ensure that maximum weight is reached. This could be achieved by overtaking the neural inhibition through the use of peripheral stimulation. Thus, the results of this study show that the use of ES and

MS alongside the traditional 1-RM technique can help better predict the actual 1-RM for the quadriceps muscle. This novel technique could be a useful tool to accurately measure the maximum voluntary contraction of patients after injury and/or athletes during training. Thus, our novel technique could help guide the return-to-play decision as maximum strength and hypertrophy is warranted for safe return-to-play [Peterson, Rhea and Alvar, 2004, Cinar-Medeni et al., 2015, Palmieri-Smith and Lepley, 2015].

Although the effect of weight training on muscle hypertrophy has been investigated in numerous studies, there is no information, to our knowledge, regarding the effect of ES and MS applied at the point of muscle failure following voluntary exercise on hypertrophy. Even though previous investigations have used ES or MS as standalone study arms to enhance hypertrophy [Gorgey and Khalil, 2015, Sillen et al., 2013, Hasegawa et al., 2011], no study has investigated if stimulation applied at the point of muscle failure following voluntary exercise could induce greater hypertrophic changes than voluntary muscle activity alone. Our results indicate that there was no significant hypertrophic difference in the thigh circumference $F(2,27) = 2.10$, $p = 0.132$, partial $\eta^2 = 0.01$ (Figure 5.5a) or muscle layer thickness $F(2,27) = 0.34$, $p = 0.712$, partial $\eta^2 = 0.01$ (Figure 5.5b) following the application of ES or MS between the study groups. This may be due to fat loss [Krishnan and Williams, 2010] or non-hypertrophic adaptation of the neuromuscular system in response to static resistance training [Billot et al., 2014], rather than a change within the quadriceps circumference. In line with the above, Carolan and Cafarelli, [1992] reported that after the first week of their training protocol the quadriceps extension antagonist muscle (hamstring) showed a decrease in muscle co-activation by 20%. This non-

hypertrophic adaptation of the neuromuscular system resulted in a reduction of thigh circumference post-training.

The results of the presented study showed no significant difference in strength, although there was a trend for the stimulated groups to be greater than the controls (Figure 5.5). In addition, our results showed a small trend towards a decrease in muscle size as determined by thigh circumference (Figure 5.5a) and muscle layer thickness (Figure 5.5b). This is seemingly paradoxical, but Brook et al. [2015] in his recent review concluded that the adaptations of muscle mass and strength to resistance-type training are as yet unclear. Previous literature has shown inconsistent results in the effect of resistance-type exercises on muscle mass and strength. Farup et al., [2012] reported a significant increase in quadriceps muscle mass ($p = 0.001$) and strength [Brook et al., 2015, Ribeiro et al., 2015, Farup et al., 2012] during a 10-week resistance training. In contrast, following a 12-week programme of leg press resistance training, McBride et al. [2003] reported a significant quadriceps strength gain ($p < 0.005$) yet a non-significant lean muscle mass gain ($p > 0.005$) between the intervention and control groups. The controversy in the literature regarding the relationship between strength and hypertrophy gains after resistance training may be justified by the insensitivity of the muscle lean mass measures and differences in muscle-fibre types [Viitasalo, Saukkonen and Komi, 1979]. Magnetic resonance scanning, dual-energy X-ray absorptiometry (DXA), and computed tomography (CT) are considered the gold standards for providing sensitive muscle measures [Mitsiopoulos et al., 1998, Heymsfield et al., 1990] but they are not cost-effective. US is a commonly used, cost-effective, portable and quick device with which to quantify hypertrophy [Jacobson and Van Holsbeeck, 1998, Chhem and

Cardinal, 1999, De Maeseneer et al., 2014]. Unlike Farup et al., [2012], Seynnes, De Boer and Narici [2007] and Defreitas et al., [2011] who used DXA, MRI and CT, respectively, as a measure of lean muscle mass and reported significant hypertrophic changes, we used US to measure hypertrophic changes. It is crucial to shed light on the notion that the existing literature on 'changes' in lean muscle mass in response to resistance training depends upon the method chosen to detect muscle hypertrophy [Heymsfield et al., 1997]. Hence, experience of the principle investigator in performing the US procedure and the insensitivity of the US device may have played a role in the outcome of our study. Consequently, more studies are needed in order to confirm if peripheral ES and MS applied at the point of muscle failure following voluntary exercise can induce significant hypertrophic changes more than voluntary muscle activity alone in terms of the use of sensitive measures of hypertrophic muscle changes.

Although the baseline measures differed between participants in the three groups, the tendency to a positive change of quadriceps strength as measured by the 1-RM (Figure 5.5c) in all groups is promising, despite the non-significant difference between the groups (CONT = 29.30 ± 10 kg, ES = 35.55 ± 21.38 kg, MS = 36.85 ± 23.61 kg). Previous studies have found a significant effect of ES on muscle strength versus a control group [Taradaj et al., 2013], and over periods as short as five weeks [Kubiak Jr, Whitman and Johnston, 1987, Hasan, 2015, Laughman et al., 1983]. However, no studies have investigated if peripheral ES and MS applied at the point of muscle failure following voluntary exercise could induce greater strength changes than voluntary muscle activity alone. Hence, it is worth emphasising that the present study showed that the positive change in the ES and MS groups were bigger than in

the control group. The findings of this study suggest that regardless of the non-significant results, a direct comparison between the two experimental groups revealed that MS induced more repetitions (7 ± 6) than ES (4 ± 2). Consequently, extra repetitions at 1-RM means extra strength gain [Campos et al., 2002]. Thus, the use of this novel protocol in traumatised patients will perhaps reduce quadriceps wasting in the early stages of return-to-play rehabilitation programmes. Also, we accept that applying ES and MS to injured/older or sedentary population as oppose to healthy sample may not have similar effects, perhaps yielding promising results. There is a consensus in the literature that strength training enhances knee stability [Tsarouhas et al., 2015, Stojanovic and Ostojic, 2012, Cinar-Medeni et al., 2015, Herring, 2015, Häkkinen et al., 2001]. However, the present study showed mixed results in anterior-posterior knee laxity measurements. Although the majority of the participants (25/30) showed a reduction in their anterior laxity post-training, some (5/30) demonstrated an increase. A possible justification as to why anterior-posterior knee laxity had increased after quadriceps weight training is the relaxed state of the hamstrings muscles during the anterior-posterior laxity measurement. Several studies have shown that lateral hamstring activity during the knee laxity test reduces anterior-posterior laxity [Barcellona et al., 2014, Markolf, Graff-Radford and Amstutz, 1978, Iversen et al., 1989]. In contrast, in the present study the procedure for the knee laxity test adhered to the guidelines for use of the KT-2000 arthrometer [Daniel et al., 1985], and the participants ensured that their hamstrings remained fully relaxed during the knee laxity testing. Barcellona et al.[2014] reported a non-linear relationship between hamstrings muscle activity and anterior-posterior knee laxity measured by the KT-2000 for a maximal manual technique. They reported that 2% of

EMG activity of the lateral hamstring caused an approximately 45% laxity reduction in anterior-posterior laxity. Moreover, Markolf, Graff-Radford and Amstutz [1978] reported that contraction of the hamstrings muscles reduces knee laxity to 25% - 50% of the normal values.

Whilst there was no measure of the participants daily activity during the 21 days of the study protocol rather than restriction to lower leg training, we acknowledge that there was no way of ensuring that the participants did not do further activity which might have influenced our results. To summarise, there is controversy in the literature as to whether the hamstrings muscles should be activated or should remain fully relaxed during an anterior-posterior knee laxity test. The aim of the test could determine which method is recommended, as an anterior-posterior knee laxity test with relaxed hamstrings shows the displacement of the tibia on the femur in a static state, while conducting a knee laxity test with activation of the hamstrings correlates better with the actual status of the knee during exercise. Therefore, questions arise regarding which test condition replicates the actual kinematics and kinetics of the knee. This debate may be better directed towards a more robust test that can replicate the dynamic condition of the knee during exercise. Therefore this favours the argument that knee laxity is better measured through activation of the hamstrings in order to replicate the actual condition of the knee during sport participation. Additionally, whilst there is an agreement in the literature that the ACL is one of the most injured ligament in the knee forcing long absences by athletes [Ekstrand, Hägglund and Waldén, 2011, Prodromos et al., 2007, Roi et al., 2006, Waldén et al., 2011], future work might be directed towards monitoring hamstrings activity during an anterior posterior knee laxity test in order to potentially improve the chances of

detecting a possible ACL injury as both ligaments (primary) alongside muscle activity around the knee (secondary) are required for knee stability.

5.6 Conclusion

Both interventions suggested a beneficial trend during weight training by inducing extra repetitions at the point of muscle failure. Magnetic muscle stimulation is able to produce similar effects on muscle strength, hypertrophy and anterior-posterior knee laxity when compared to electrical muscle stimulation. In addition, the use of such stimulations will, perhaps, offset muscle atrophy, facilitate early rehabilitation, and enhance resistance training protocols, especially when used for acute cases.

Specifically, traumatised patients and athletes who aim for a faster return-to-play might benefit from the use of peripheral stimulation as an adjunct to weight training.

Exactly how robust peripheral stimulation applied at the point of muscle failure following voluntary exercise has an effect on quadriceps strength, hypertrophy and knee stability warrants further investigations. Future research should investigate the aforementioned positive trends with a larger sample size and longer training protocols.

CHAPTER 6 - GENERAL DISCUSSION

The overreaching aims of the work presented in this thesis were to examine the opportunity to support sport medicine clinicians in potentially using a better measurement of knee joint stability during assessments and to improve knee function through the enhancement of existing weight training protocols. These aims were accomplished by implementing two approaches: 1) a comprehensive systematic literature review on the existing measures that can be used to assess or diagnose knee instability; and 2) two original, experimental studies. This chapter presents a general discussion on the findings of this thesis and the impact that have on their respective areas. The direction of future research is also discussed.

6.1 Summary of the results

The aim of the systematic literature review presented in chapter 3 was to summarise and evaluate the current body of literature on the diagnostic usefulness of knee stability measures to sport related injuries and pathologies. This review has been published as a systematic literature review which utilised the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines for search and reporting phases. Unfortunately, it revealed that few of the current studies are of good enough quality to help in clinical decision making. However, the KT-2000 arthrometer was identified from the data as a valid, specific, portable, clinically-attainable knee stability measure. Further studies implementing a high quality design are warranted to fully examine the value of the current knee stability measures for patients with knee instability.

The aim of study 1 (chapter 4) was to investigate whether the ACL -hamstring stretch reflex could be reliably and consistently obtained using the KT-2000 arthrometer. The KT-2000 arthrometer was used to translate the tibia on the femur while recording the EMG of the biceps femoris muscle for 20 participants, all with intact ACLs. However,

the response size of the ACL-hamstring stretch reflex was too small for it to be reliably used in clinical settings. Consequently, it has inadequate value in evaluating the return of neuromuscular function following knee instability.

Chapter 5 (study 2) aimed to examine the effect of a three week protocol of peripheral MS or ES and resistance training on the capability to complete further repetitions at the point of muscle failure, and the effect this has on quadriceps muscle strength, hypertrophy and knee stability. Thirty healthy participants were divided randomly into MS, ES or control groups, and all the participants followed a three week protocol consisting of five training sessions, each for four sets of eight repetitions. On the last set, all the groups continued to voluntary failure, at which point MS, ES or no stimulation was applied. The additional repetitions elicited by the stimulation after the point of voluntary failure suggests that peripheral ES and/or MS may be useful as an adjunct for resistance training. However, as an effect on hypertrophy was not shown in the present study, such training on muscle hypertrophy, strength and knee laxity may be small.

6.2 Implications

The incidence of knee instability has led thousands of studies to be conducted over the last century aimed at addressing this issue. However, their main focus has been on injury prevention strategies [Michaelidis and Koumantakis, 2014], the implications that assessment measures have on injury rate reduction [Van Eck et al., 2013] and safe return-to play [Ardern et al., 2014]. Until recently, this focus has, by implication, been regarded as limited, but more recent research has emerged from several distinct sports medicine fields, such as biomechanical aspects of knee instability [Gollehon, Torzilli and Warren, 1987, Lam et al., 2009, Zlotnicki et al., 2016] and strategies to enhance knee function [Hart et al., 2012, Jang et al., 2014, Hirschmann

and Müller, 2015, Palmieri-Smith and Lepley, 2015], which have aimed to aid knee stability. Each field of study appears to be aware of the others, which are all working towards similar targets and arriving at similar conclusions, yet no robust, single clinical knee stability measure is used for knee stability assessments and safe return-to-play criteria. The findings of this thesis resonate with the results emerging from a wide range of knee injury assessment and prevention endeavours.

6.2.1 Assessment of knee stability

It has been advocated that specific and sensitive assessment measures play a vital role in the result of assessment outcomes, and hence the robustness of assessment decisions [Altman and Bland, 1994]. One of the main aims of this thesis was to better understand the stability assessment and function enhancement of the human knee joint, and this was achieved by implementing a systematic literature review that further evaluated the existing knee stability measures (chapter 3), which aided in the testing of a better assessment method (chapter 4). In addition, the possibility to further improve existing weight training protocols for the knee muscles to better enhance knee stability and function was also examined (chapter 5). The results from the work of this thesis provide supportive evidence that clinicians need more robust and clinically objective knee stability measures. This was suggested because the body of related literature lacks a clinically objective, a gold-standard knee measure. As revealed in the systematic review presented, the literature contains low quality studies that cannot be used to form solid conclusions regarding a gold standard for a knee stability measure to be used for assessment and return-to-play criteria.

It is widely accepted that knee stability is maintained through the integrity of several stability directions, i.e. anterior-posterior, posterior-anterior and rotational stability [Hirschmann and Müller, 2015]. In addition, the sensorimotor part of stability also

plays a major role [Solomonow and Krogsgaard, 2001]. The results from study 1 (chapter 4) indicated that the ACL-hamstring stretch reflex exists when a strong and rapid anterior-posterior translation of the tibia on the femur was applied. This result is in-line with Solomonow and Krogsgaard [2001], who reported that the sensorimotor part of the knee plays a key role in aiding knee stability throughout an involuntary stretch reflex, and Friemert et al. [2005a] reported that the ACL-hamstring stretch reflex can be elicited intraoperatively through a direct pull at the ACL. However, the results of study 1 (chapter 4) indicated that the ACL-hamstring stretch reflex cannot be used as a valid objective knee stability measure within clinical settings. Despite replicating the work of Friemert et al. [2005a], the average stretch response size was small (38.5%), and this technique was not sufficiently reproducible to be considered reliable. The only difference between the study by Friemert et al. [2005a] and study 1 (chapter 4) was the amount of force applied to elicit the reflex. They used a fixed force of 300 N, while in study 1 (chapter 4) the pull force was utilised through a maximum manual pull performed by the principle investigator using the KT-2000 arthrometer, and a direct ACL pull during arthroscopy. These forces were comparable (200 N–300N) to the findings of Friemert et al. [2005a] (300 N). Another factor that might justify the small response size of the reflex was the involuntary change of the knee angle, which resulted from the pull of the KT-2000 arthrometer. It has been reported that to elicit an ACL-hamstring stretch reflex, the ACL should be in its relaxed state [Gurtler, Stine and Torg, 1987] and that different knee angles have different levels of knee stiffness [Boguszewski et al., 2015, Markolf, Graff-Radford and Amstutz, 1978]. In spite of the 30° knee flexion position of the participants, which led to a relaxed ACL, changes of the angle during the pull

were observed during testing. Consequently, this could have led to the ACL being taut, which reduced the possibility of obtaining a reflex. This limitation could potentially have been overcome by designing an electronic force generator to pull the tibia onto the femur to ensure that the knee angle is fixed in its pre-pull angle.

Nonetheless, its usefulness at clinical settings might be questioned.

To elicit a stretch reflex, the stretch needs to elongate the ligament for as long as possible in order to trigger the ligamentous mechanoreceptors [Solomonow and Krogsgaard, 2001]. Previous research has shown that people differ in their knee laxity measurements, even without any knee injury [Mouton et al., 2014]. Therefore, hyper-lax ligaments could not be elicited easily. It may be that some participants in the study were hyper-lax, which could be another reason why the response sizes were small. However, one of the selection criteria that was implemented was to recruit participants with no previous knee injuries. Nevertheless, there is a possibility that the tested participants may be hyper-lax by nature. In order to neutralise this possibility, a pre-measurement of the participants' ACL laxity could be utilised prior to stretch reflex measurements.

One of the rules of the KT-2000 arthrometer procedure, which was used to translate the tibia on the femur in study 1 (chapter 4), was that the hamstring of the tested knee should be fully relaxed [Daniel et al., 1985]. In spite of asking the participant to be fully relaxed to minimise any movement of the tested knee and the investigator making sure via a clinical palpation that the hamstring was relaxed, there was a possibility that the participant involuntarily contracted their hamstring as a protective mechanism during the forceful translating of the tibia on the femur. Consequently, this would restrict the translation which, in turn would constrain the elicitation of the

stretch reflex, and this could be another factor as to why the response sizes ($41 \pm 11\%$) were small and not reproducible. To offset this likelihood, further testing was performed, while patients were fully anaesthetised through a controlled experiment. However, no robust differences were observed in the stretch response sizes of the direct ACL-traction group ($42 \pm 3\%$). To better solve this problem, implementing a specific design of an EMG continuous acquisition setting would potentially instantaneously show the relaxed state of the hamstring of the tested knee, which could guide the investigator and provide biofeedback regarding the relaxation state of the tested hamstring.

The evidence suggests that the hamstring muscle plays an important role in knee stability. Fiebert et al. [2001] showed that the lateral hamstring (biceps femoris muscle) contributes to 60% of the thigh musculature EMG activity, as opposed to the medial hamstring (40%). In addition, Logan et al. [2004] showed that the lateral compartment of the knee contributes to the anterior translation of the tibia to a greater extent than the medial compartment. Thus, contraction of the biceps femoris could lead to a greater reduction in anterior knee translation, hence reducing anterior knee instability. Moreover, Barcellona et al. [2014] concluded that the biceps femoris muscle must be monitored during knee stability testing. Therefore, we tested the ACL-hamstring reflex through EMG monitoring of the biceps femoris muscle to investigate whether it could be reliably used as an objective measure of knee stability. However, the integrity of the biceps femoris muscle of the participants in study 1 (chapter 4) was not profiled. Opar et al. [2013] showed that previously strained muscles decrease the neural drive, rate of torque and EMG activity. Thus, it seems that such a confounding factor may have played a role in the results of study

1 (chapter 4), as participants may have had a history of biceps femoris strain. To rectify this factor, future work could include a history of biceps strain as an experimental exclusion criterion.

6.2.2 Enhancement of knee function and stability

It has previously been proposed that weight training shows a positive trend towards the enhancement of knee stability and function following knee injury [Perry et al., 2005, Keays et al., 2006]. One of the main aims of this thesis was to further test this theory, which was achieved using the adjunct of ES and MS for quadriceps weight training with stimulation applied at the point of muscle failure (chapter 5). The results from this study provide supportive evidence that the augment of ES and MS to quadriceps weight training improves muscle hypertrophy and knee stability. However, no statistically significant effect was observed.

It is widely accepted that the development of knee stability and muscle hypertrophy requires both the integrity of the neuromuscular system [Emery et al., 2015] and a constructively-designed training protocol [Eklund et al., 2015, Grooms, Appelbaum and Onate, 2015, Sugimoto et al., 2015]. The results of study 2 (chapter 5) revealed that three weeks of a total of five training sessions were associated with a positive, but not significant, trend towards increased quadriceps-thigh circumference, rectus femoris layer thickness, quadriceps strength and decreased knee laxity, further adding to the argument that a weight training protocol design is appropriate and frequent training sessions should be undertaken. Recently, Barcellona et al. [2015] showed that open kinetic chain resistance training can reduce anterior knee instability, and the results of study 2 (chapter 5) support these findings by showing that ES, as an adjunct to quadriceps weight training, showed a reduction of anterior knee instability of $(-1.5 \text{ mm} \pm 1.2)$, compared to weight training alone (-0.95 ± 1.3) .

Likewise, the results also showed a reduction of (-0.61 ± 0.8) when MS was applied as an adjunct to the same weight training of the ES group. However, these improvements in knee stability and function may be influenced by other confounding factors. Heterogeneity in the baseline data for each group was observed for the participants of study 2 (chapter 5); thus, the amount of change between baseline testing and post-training cannot be robustly compared. These data are reconciled with numerous studies, showing no consensus in the literature on the effect of weight on anterior knee stability, quadriceps hypertrophy and strength [Barcellona et al., 2015, Perry et al., 2005, Keays et al., 2006, Beard et al., 1994, Morrissey, Perry and King, 2009]. Training dosage has been a controversial issue for a few decades and remains unsolved to date.

Previous research has used both subjective [Beard et al., 1994] and objective [Keays et al., 2006] knee stability measures to assess the effect of weight training on anterior knee stability. Because knee stability measures have debatable issues in terms of their sensitivity and specificity [Malanga et al., 2003, Kiapour et al., 2014], clinicians need to be more careful when choosing a knee stability measure that is commonly used to address the effect of weight training on anterior knee stability in future studies. This adheres with the results of systematic literature review presented in chapter 3, which concluded that the literature lacks high quality studies to robustly suggest the gold standard measure of knee stability. Thus, it is not surprising that even the results of the effect of weight training on anterior knee stability are inconclusive in the literature. This is due to the variety of experimental procedures used, the uncertainty of the knee stability measures, and the diversity of training dosages applied in the studies; however, those concerns should not prevent future

studies from assessing such an effect. Most importantly, studies have to focus on what weight training protocol should be recommended and how knee stability should be measured. Hence, better clinical decisions and robust evidence-based practice can be suggested.

Like the findings of Taradaj et al. [2013] and Hart et al. [2012], the results of study 2 (chapter 5) showed a positive trend for the use of ES and MS as an adjunct to quadriceps weight training for the enhancement of knee function. Previous studies have also investigated the use of peripheral stimulation for pain management [Zeng et al., 2015], stroke [Howlett et al., 2015, Chen et al., 2016], knee osteoarthritis [Hasan, 2015, De Oliveira Melo, Aragão and Vaz, 2013, Negm, Lorbergs and Macintyre, 2013, Laprade et al., 2015], fatigue management [Millet et al., 2012, Deley et al., 2015], and healthy athletes to enhance training [Kubiak Jr, Whitman and Johnston, 1987, Szecsi, Straube and Fornusek, 2014]. Mixed results were reported in the literature, which consisted of a broad number of studies that assessed the usefulness and validity of ES and MS in different diseases / dysfunctions. In line with our conclusion from study 2 (chapter 5), caution needs to be undertaken when recommending ES and/or MS as a robust adjunct to weight training. Further investigations with a larger sample size and longer training protocol (> 12 weeks) should be implemented to better assess the usefulness and validity of such techniques as an adjunct to weight training.

6.3 Limitations

The research presented in this thesis is not without limitations and this section focuses on the general limitations of the thesis as a whole, as individual limitations regarding each study have been discussed in-depth in the discussion sections of each of the empirical chapters. The small sample sizes tested in the laboratory

studies (Chapters 4 & 5) could be regarded as a limitation; however, a power calculation revealed a sample size of 377 for such experiments, which is considered an unfeasible number. Thus, the sample sizes for both study 1 (chapter 4) ($n = 20$) and study 2 (chapter 5) ($n = 30$) were decided based upon similar numbers of participants in previous related literature; diagnostic accuracy studies where the sample size ranged between 10–105 [Reiman et al., 2012] and stimulation studies where the sample size ranged between 10–55 [Kyung-Min Kim, 2010]. Another limitation is that the findings for the ACL-hamstring reflex study (chapter 4) could have been influenced by other confounders. For instance, the participants may have involuntarily contracted their hamstring muscle during the forceful and rapid tibial translations. A probable explanation for this is the human protective reaction that might have involuntarily influenced the onset of the ACL-hamstring reflexes. In addition, there are concerns about generalisation. Study 1 (chapter 4) recruited only male participants because females tend to be more lax than males [Rozzi, Lephart and Fu, 1999, Boguszewski et al., 2015]. Therefore, recruitment was focused on males to rectify this confounding variable. Finally, it remains possible that the findings of this thesis could, to an extent, arise from other unmeasured variables [Sanchez-Ramirez et al., 2013]; however, all studies were adjusted for several potential confounders.

6.4 Strengths

There are also a number of strengths to the research presented in this thesis. Firstly, the systematic literature review (chapter 3) extracted both objective and subjective data from the literature, which provided larger coverage of the existing knee stability measures, and enabled the certainty of each test and the scrutiny of the testing procedures to be constructively criticised. Secondly, study 1 (chapter 4) included two

additional control experiments which were conducted to reinforce the main conclusion of the study and to reduce the effect of any confounding factors, where possible. Having results from healthy participants, patients and arthroscopic data further strengthens the findings. Thirdly, participant age was carefully selected in each experimental study. Study 1 (chapter) 4 recruited a slightly wider range of ages (20–51 years), as the proposed assessment technique planned to be used for both young return-to-play athletes and older individuals who were at risk of falls. In contrast, the participant age range (18–37 years) in study 2 (chapter 5) was selected to better sample active exercisers, in order to match the target population who use such training. Fourthly, and perhaps the biggest strength, is the investigation of the reliability of a knee stability measure to assess the sensorimotor part of knee stability (chapter 4). Functional knee stability relies not solely on the dynamic and static mechanical stabilisers but also on the proprioceptive part of the knee joint; therefore, the assessment of the sensorimotor part is very important [Solomonow and Krogsgaard, 2001]. Unlike most of the existing studies within the literature that have focused on the assessment of the mechanical part of knee stability, study 1 presented in chapter 4 examined the less-researched part of knee stability (sensorimotor), which plays a vital role in preserving the stability of the knee joint. The use of an objective clinical measure to assess the sensorimotor part of knee stability is very limited within the literature, and the vast majority of the measures (clinical examination and objective) were implemented to assess the mechanical part of knee stability. Fifthly, the combination of investigations to both knee stability assessment and knee function enhancement in a single thesis provides a complete and holistic outcome towards both patient and athlete assessment and training

directions. Finally, study 2 (chapter 5) provides preliminary information towards the use of ES and MS as adjuncts to weight training, which showed promising trends to enhancing knee stability and function. This is a novel technique that can be used to better improve knee stability and function.

6.5 Future directions

There are a number of ways future research could build upon the work presented in this thesis and a few will be highlighted in this section. Future research should focus on further testing as to whether the ACL-hamstring stretch reflex can be a valid and reproducible functional knee stability measure using an instrumented, portable and clinical based tool. Future work can also be directed towards the redesign of the KT-2000 arthrometer to provide better feedback to the practitioner. The ideal tool should have the ability to standardise and quantify the force used to elicit reflex to eliminate human error. The work in study 1 (chapter 4) demonstrates the applicability of the ACL-hamstring stretch reflex using the KT-2000 arthrometer; however, the methodology of the experiment was based on human input to facilitate each knee perturbation. Study 1 does not demonstrate that an ACL-hamstring stretch reflex can be elicited without human input, and a possible way to test this is would be to build a tool (e.g. rig) that automatically produces knee perturbations without human input. For example, collaboration with a mechanical engineer to build a rig that could accurately and precisely displace the tibia on the femur to elicit ACL-hamstring stretch reflex is warranted, as previous researchers have built instruments to elicit the ACL-hamstring stretch reflex [Beard et al., 1993, Friemert et al., 2005b, Schoene et al., 2009]. Nonetheless, these all lack portability and were implemented and designed for a research setting, rather than a clinical based setting. Another possible development could be improving the cushioning of the device, as this will allow for

better padding of the KT-2000 arthrometer, thus reducing scratches to the participant's skin during data collection procedures. The design of a portable and clinically applicable tool, will, perhaps, allow clinicians to reliably and objectively assess functional knee stability and therefore guide them to a return-to-play decision. Future research could usefully incorporate peripheral stimulation as an adjunct to weight training. The results of study 2 (chapter 5) showed an improvement in knee anterior laxity and quadriceps strength after the use of ES and MS as adjuncts to quadriceps weight training. Building upon the previous work in terms of the role of the rate of force development and torque measurements could further assess the usability and applicability of peripheral stimulation as an adjunct to weight training. Finally, studying the association between certain genetic features and knee stability may help better understand the extent to which knee injury risks can be identified and reduced. There is a consensus in the literature on the role of gender in knee stability and previous research has shown that females have an increased risk of knee instability and injuries compared to males [Boguszewski et al., 2015, Hewett, Myer and Ford, 2005, De Ste Croix et al., 2015, Rozzi et al., 1999]. This consensus raises an interesting question as to whether this trend exists or not, and if the expression of different genes influences knee stability. Potential candidate genes which may possibly be related to knee instability include Collagen type 1 (COL1), which is of particular interest given its relationship to ACL [Frank, 2004] and the possible connection between ACL genotype and knee instability. A second gene is Collagen type 5 (COL5), which has been associated with a higher risk of injury in females [Posthumus et al., 2009], while the matrix metalloproteinase (MMP) gene, has shown significantly higher 5A allele frequencies in ACL tear patients participating in contact

sports than in noncontact sports [Malila et al., 2011]. Figure 6.1 presents a brief summary of the outcomes of the presented work in this thesis alongside suggestions for future directions.

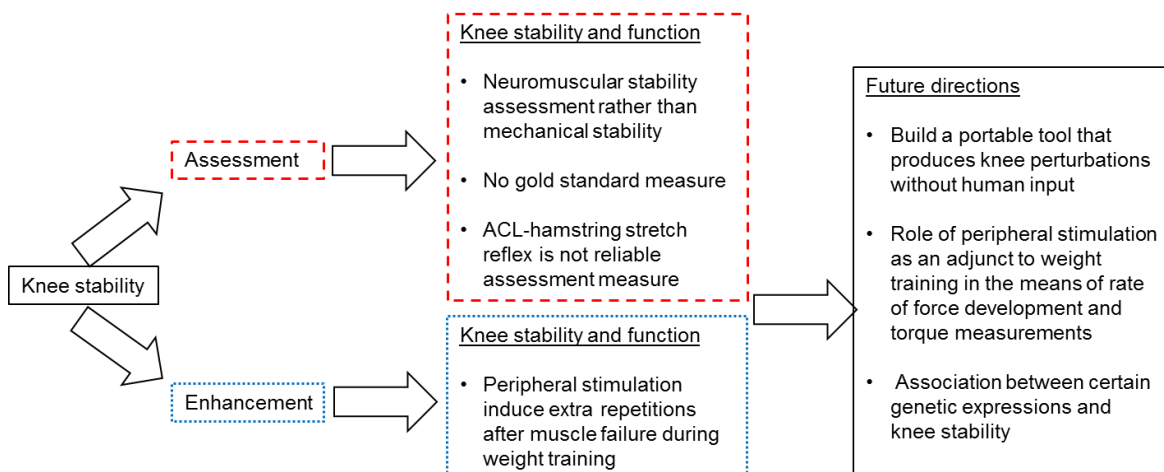


Figure 6.1: Schematic summary of the work undertaken and the results that may play a role in the assessment and enhancement of knee stability together with suggested future directions

6.6 Conclusions

In conclusion, the presented thesis has used a mixed method approach of secondary analysis of previously published research related to knee stability measures and two laboratory based studies. It was proposed and later confirmed that the existing literature lacks quality studies that have proper reporting and rigorous scientific designs. Consequently, clinicians are far from being confident in the use of existing knee stability measures with regards to reliability, sensitivity and specificity. Thus, the aim of establishing a clinically objective knee stability measure is crucial. It was also confirmed that despite the fact that the ACL-hamstring stretch reflex can be elicited in every participant, this reflex was not reproducible or reliable. Finally, it was shown that the adjunct of peripheral ES and MS to a weight training protocol produces more

repetitions, hence enhancing the quadriceps muscle strength, hypertrophy and reduce anterior-posterior knee laxity. This thesis provides further evidence that knee stability is attributed to multiple factors. Using the information presented in this thesis and current dynamic research in the related field, along with more than 40 years of research investigating factors that influence knee stability, it is perhaps fitting to conclude that knee stability assessment and enhancement is far from being conclusive.

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