The role of muscle dysfunction in patellofemoral pain: Influence of different treatment approaches

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Glossary

AD	Activation deficit
ADL	Activity of daily living
AKE	Active knee extension
AKP	Anterior knee pain
AKPS	Anterior knee pain scale
AMI	Arthrogenic muscle inhibition
AP	Action potential
ARV	Average rectified value
ASIS	Anterior superior iliac spine
CAR	Central activation ratio
CAST	Calibrated anatomical system technique
CCR	Co-contraction ratio
CI	Confidence Interval
CMC	Correlation of multiple coefficient
EMG	Electromyograpy
ER	External rotation
ES	Effect Size
ESP	Early stance phase
Ext	Extension
Flx	Flexion
FPI-6	6-item foot posture index
GMax	Gluteus maximus
GMed	Gluteus medius
GRF	Ground-reaction force
HG	Henrike Greuel (first reviewer)
HQ	High quality
H-Reflex	Hoffmann-reflex
HSR	Health Services Research
Hz	Hertz
ICC	Intra-class correlation coefficient
IN	Interneuron
IR	Internal rotation
ITB	Iliotibialis
ITT	Interpolation twitch technique
KAAI	knee adductor angular impulse
kg	Kilo gramm
KOOS	Knee injury and osteoarthritis outcome score
lat	Lateral
LH	Lee Herrington (third reviewer)
LHS	Left heel strike
LOFF	Left off

LON	Left on
LQ	Low quality
LSP	Late stance phase
LTO	Left toe off
mA	Milliampere
m	Meter
µs	Microsecond
mm	Millimeter
ms	Millisecond
MDD	Minimal detectable difference
med	Medial
MI	Muscle inhibition
MN	Motor neuron
MQ	Moderate quality
MRI	Magnetic resonance imaging
MSP	Mid stance phase
MUAP	Motor Unit Action Potential
MUAPTs	Motor Unit Action Potential trains
MVC	Maximal voluntary contraction
MVIC	Maximal isometric contraction
M-wave	Muscle response, evoked by the massed action potential of a muscle
Nm	Newton meter
NPRS	Numeric pain rating scale
PedRO	Physiotherapy Evidence Database
PFJ	Patellofemoral joint
PFP	Patellofemoral pain
PSIS	Posterior superior iliac spine
QOL	Quality of life
QTM	Qualisys track manager
RFD	Rate to force development
RJ	Richard Jones (second reviewer)
RHS	Right heel strike
RM	Repetition maximum
rms	Root mean square
ROFF	Right off
ROM	Range of motion
RON	Right on
RTO	Right toe off
RTT	Resting twitch torque
SD	Standard deviation
SEBT	Star excursion balance test
SEM	Standard error of the measurement
sEMG	Surface electromyograpy

SENIAM	Surface ElectroMyoGraphy for the Non-Invasive Assessment of muscles
SIB	Superimposition technique
SMD	Standardised mean differences
SPSS	Statistical Package for the Social Sciences
TNJ	Talonavicular joint
US	The United States
USA	The United States of America
VAS	Visual analogue scale
VGRF	Vertical ground-reaction force
VL	Vastus lateralis
VLL	Vastus lateralis longus
VM	Vastus medialis
WoS	Web of Science
2D	Two dimensional
3D movement analysis	Three dimensional movement analysis
°	degrees

ABSTRACT

Patellofemoral pain (PFP) is the most frequently diagnosed condition in patients with knee complaints and is particularly prevalent in young physically active individuals. Studies revealed that despite receiving treatment, the majority of individuals with PFP suffer from persistent complaints, indicating that current treatments fail to prevent the chronicity of symptoms. The failing long-term outcomes reflect the need to provide an update on the evidence of underlying muscular dysfunctional factors of PFP, as well as the investigation of different treatment approaches.

As part of this PhD, a literature and a systematic review were conducted, which discussed the definition, risk factors, prognosis, pathophysiology and treatment of PFP. The meta-analysis showed that the majority of studies analysed muscle strength or muscular activity. Whereas, muscular dysfunctional factors such as atrophy, muscular inhibition, fatigue and flexibility remained understudied in individuals with PFP.

To develop a robust and reliable test protocol for the investigation of muscular dysfunctional factors in individuals with PFP, a reliability study was performed, which enabled the development of a protocol that was applied in the following studies of the thesis. Knee braces are recommended in the acute phase of PFP. However, research on knee braces analysing the effect on stabilising the sagittal and coronal plane of the knee joint demonstrated conflicting results. Thus, the effect on lower limb biomechanics and pain of the Powers^{TM} strap was investigated in 24 individuals with PFP and 22 healthy individuals and revealed that the Powers^{TM} strap reduced pain and was able to modify lower limb biomechanics during functional tasks. Furthermore, a six week exercise programme for individuals with PFP was developed and investigated in 25 individuals with PFP. It could be shown that the treatment was effective to reduce pain, improve function and the functional performance of individuals with PFP. The final study of this PhD focused on the influence of acute pain on the functional performance, strength and quadriceps inhibition in 21 individuals with PFP. It was found that acute pain caused an increase of quadriceps inhibition in individuals with PFP, but did not affect functional performance or quadriceps strength.

Thus, this thesis investigated the role of muscle dysfunction in PFP, explored the link to pain and showed how different treatment approaches were able to influence muscle dysfunction in individuals with PFP.

Chapter 1: Introduction

The terms patellofemoral pain (PFP) and anterior knee pain (AKP) are usually used synonymously and describe a syndrome with aching or diffusing pain in the peripatellar or retropatella regions (Farzin, Reza, & Tohid, 2013; Roush & Curtis Bay, 2012; Witvrouw, Callaghan, Stefanik, Noehren, Bazett-Jones, Willson, Earl-Boehm, Davis, Powers, McConnell, & Crossley, 2014). Commonly, the pain is aggravated during loaded knee flexion, such as ascending and descending stairs, squatting and/ or prolonged sitting (Nunes, Stapait, Kirsten, de Noronha, & Santos, 2013; Thomee, Augustsson, & Karlsson, 1999).

PFP is the most frequently diagnosed condition in individuals with knee complaints and is prevalent in 7%-19% of the general population (Boling, Padua, Marshall, Guskiewicz, Pyne, & Beutler 2010; Wilson, Masterson, & Seagrave, 2012). In particular young and physically active people are affected (Powers, Bolgla, Callaghan, Collins, & Sheehan, 2012). Roush and colleagues (2012), reported PFP symptoms in 12-13% of young females (aged 18 - 35 years), which might cause limitation in physical activity or even lead to sport cessation (Myer, Ford, Barber Foss, Goodman, Ceasar, Rauh, Divine & Hewett, 2010; Rathleff, Skuldbol, Rasch, Roos, Rasmussen, & Olesen 2013).

To date, the underlying mechanisms in PFP are unknown and the pathophysiological processes associated with PFP can be compared with a complex mosaic (Collado & Fredericson, 2010; Powers, Bolgla, Callaghan, Collins, & Sheehan, 2012). It is believed that patellofemoral malalignment and maltracking play an important role in PFP, which might be caused by poor neuromuscular control of the trunk or the lower extremities, weakness or abnormal muscular activation (Earl, Hertel, & Denegar, 2005; Lankhorst, Bierma-Zeinstra, & van Middelkoop, 2013; Powers et al., 2012; Thomee, Augustsson, & Karlsson, 1999; Witvrouw, et al., 2014). Several factors have been postulated to contribute to malalignment and maltracking of the patella, including quadriceps weakness, quadriceps muscle imbalances, excessive soft tissue tightness, gluteal muscle weakness and altered foot posture (Baldon, Nakagawa, Muniz, Amorim, Maciel, & Serrao, 2009; Bolgla, Malone, Umberger, & Uhl, 2008; Cheung, Ng, & Chen, 2006; Collins, Bierma-Zeinstra, Crossley, van Linschoten, Vicenzino, & van Middelkoop, 2013; Cowan, Bennell, Crossley, Hodges, & McConnell, 2002; Dierks, Manal, Hamill, & Davis, 2008; Fagan & Delahunt, 2008; Ferber, Farr, & Kendall, 2010; Fukuda, Rossetto, Magalhaes, Bryk, Lucareli, & de Almeida Carvalho, 2010;

Halabchi, Mazaheri, & Seif-Barghi, 2013; Khayambashi, Mohammadkhani, Ghaznavi, Lyle, & Powers, 2012; Kwon, Yun, & Lee, 2014; Lankhorst, Bierma-Zeinstra, & van Middelkoop, 2012; Laprade, 2000; Nakagawa, Baldon, Muniz, & Serrao, 2011; Pappas & Wong-Tom, 2012; Powers et al., 2012; Song, Lin, Jan, & Lin, 2011; Van Cant, Pineux, Pitance, & Feipel, 2014; Waryasz & McDermott, 2008; Weiss & Whatman, 2015). Although pathophysiological muscular factors in individuals with PFP have been addressed in several studies, important underlying factors, such as arthrogenic muscle inhibition (AMI) and the break phenomenon appear to be relatively understudied. AMI and break phenomenon describe the neurological decline in quadriceps muscle activation, which results in the inability to recruit the motor-neuron pool fully during a maximal voluntary contraction (Drover, Forand, & Herzog, 2004; Hopkins & Ingersoll, 2000; Hurley & Newham, 1993; Palmieri-Smith, Villwock, Downie, Hecht, & Zernicke, 2013; Suter, Herzog, De Souza, & Bray, 1998). Thus, an investigation of AMI and the break phenomenon might enable insights into quadriceps weakness and a further understanding of these factors might even lead to an amendment of the current treatment scheme.

Beside pathophysiological factors, pain is believed to play a crucial role in the aetiology and progression of PFP (Bazett-Jones, 2011; Collins et al., 2013; Rathleff, Rathleff, Olesen, Rasmussen, & Roos, 2015; Wyndow, Collins, Vicenzino, Tucker, & Crossley, 2016). Previous studies reported a link of pain to several factors, such as the alterations of lower limb biomechanics and muscular coordination, quadriceps strength deficits, gluteal strength deficits, knee instability, irregularities in the quadriceps torque curve and AMI (Dvir & Halperin, 1992; Dvir, Halperin, Shklar, & Robinson, 1991; Guney, Yuksel, Kaya, & Doral, 2015; Hart, Collins, Ackland, Cowan, & Crossley, 2015; Khayambashi et al., 2012; Long-Rossi & Salsich, 2010; Nakagawa, Serrao, Maciel, & Powers, 2013; Noehren, Sanchez, Cunningham, & McKeon, 2012; Riddle & Stratford, 2011; Silva, Briani, Pazzinatto, Ferrari, Aragao, & de Azevedo, 2015; Yilmaz, Baltaci, Bayrakci Tunay, & Atay, 2015). Research has been conducted in individuals with PFP and analysed the influence of pain intensity on functional performance and strength. However, this exclusive focus on functional performance and strength did not enable the analysis of AMI in individuals with PFP nor the direct link of AMI to pain. Furthermore, none of the existing studies have investigated the direct influence of pain in individuals with PFP by comparing the pain condition with the baseline results of the same participants performing the tasks without having acute pain.

The conservative intervention and management in individuals with PFP varies, however, an expert consensus published high-quality guidelines on the treatment of PFP (Barton, Lack, Hemmings, Tufail, & Morrissey, 2015; Crossley, van Middelkoop, Callaghan, Collins, Rathleff, & Barton, 2016). These guidelines summarised the findings of a high-quality systematic reviews and combined them with clinical reasoning of an international consensus panel of PFP investigators. The developed guidelines advise to combine passive and active interventions, whereby passive interventions are recommended to reduce pain and active interventions are recommended to improve function in individuals with PFP.

Passive interventions such as knee braces are relatively inexpensive and can be applied during sport and recreational activities to reduce pain especially in the short term (Aminaka & Gribble, 2005; Barton, Balachandar, Lack, & Morrissey, 2014; Barton et al., 2015; Barton, Munteanu, Menz, & Crossley, 2010; Bolgla & Boling, 2011; Callaghan & Selfe, 2012; Crossley, Bennell, Green, & McConnell, 2001; Crossley, Cowan, Bennell, & McConnell, 2000; Crossley et al., 2016b). Knee braces and straps have been shown to be effective in pain reduction, but demonstrated heterogeneous findings in the modification of lower limb biomechanics in individuals with PFP (Denton, Willson, Ballantyne, & Davis, 2005; Devita, Hunter, & Skelly, 1992; McCall, Galen, Callaghan, Chapman, Liu, & Jones, 2014; Powers, Ward, Chen, Chan, & Terk, 2004a; Richards, Chohan, Janssen, & Selfe, 2015; Theoret & Lamontagne, 2006). A commonly observed biomechanical abnormality in individuals with PFP is the dynamic knee valgus, which is characterised by an excessive pronation of the foot, an increased femoral adduction and internal rotation and an increased tibial external rotation (Levinger & Gilleard, 2007; Nakagawa, Maciel, & Serrao, 2015; Nakagawa, Moriya, Maciel, & Serrao, 2012; Nakagawa et al., 2013; Powers, 2003; Willson, Binder-Macleod, & Davis, 2008; Willson & Davis, 2008). To date research focuses on knee braces and straps that aim to stabilise the knee joint locally. However, there is still a paucity of research that aims to reduce the dynamic knee valgus. The analysis of a knee brace or strap that addresses the reduction of an excessive hip internal rotation and thereby achieves the reduction of the dynamic knee valgus might have a strong potential to not only reduce pain, but also to modify lower limb biomechanics and to decrease the dynamic knee valgus in individuals with PFP.

Secondly, the guidelines recommend active interventions to improve function and pain in the long term. The guidelines include detailed information of how an exercise treatment should

be structured to ensure an improvement of function and a decrease of pain in the long-term in individuals with PFP. Since these guidelines are very recent, no studies developed and tested an exercise programme that is based on the recommendations of these high-quality guidelines.

In summary, the pathophysiology of PFP appears to be complex and although much research in this field has been published specific factors such as, AMI, as well as the influence of pain itself remain understudied. Since the guidelines for conservative treatments in PFP have been published, these guidelines need to be practically applied and their effect on PFP should be investigated.

1.1. Thesis aims

The aim of this thesis is to provide a multifaceted investigation of the effect of current recommended treatment approaches on muscular and biomechanical factors in individuals with PFP.

Therefore the current literature related to Patellofemoral Pain (PFP) was reviewed, including the definition, the risk factors, the pathophysiology of PFP and the treatment of PFP (chapter 2).

To establish the confidence in data quality a test and re-test reliability study was performed on biomechanical data (gained by 3D motion analysis) and surface EMG data of the quadriceps and hamstrings muscles during running, the single leg squat and the step down task. Furthermore, a repeatability analysis of the patella position, foot posture, muscle flexibility, muscle strength and quadriceps inhibition measures was carried out. Thereby the aim of chapter 3 was to create the main research study design.

The aim of chapter 4 was to investigate the effect of the Powers^{TM} strap on lower limb biomechanics and the sEMG activity of the quadriceps and hamstrings in individuals with and without PFP during functional tasks.

The aim of chapter 5 was the development of a 6-week intervention programme based on the current guidelines and the investigation of the effect of this 6-week intervention programme on muscular dysfunction and functional performance in individuals with PFP.

The aim of the last study was to analyse link of pain to muscular dysfunction in individuals with PFP (Chapter 6).

Chapter 7-8 highlights the findings of this thesis and discusses the future work..

Chapter 2: Literature review and meta-analysis

2.1. Introduction

This chapter investigated the definition of patellofemoral pain (PFP), the prognosis of PFP, the risk factors of PFP, the pathophysiological factors which might lead to PFP and the treatment of PFP.

2.2. Patellofemoral pain definition and prevalence

There is no clear consensus on the definition of patellofemoral pain (PFP), also known as anterior knee pain, or commonly known as the runner's knee (Crossley, Callaghan, & Linschoten, 2016; Cutbill, Ladly, Bray, Thorne, & Verhoef, 1997; Thomee et al., 1999). Literature describes patellofemoral pain (PFP) as a diffuse pain in the peripatellar region and unrelated to a trauma (Crossley et al., 2016a). However, the definition of patellofemoral pain still remains vague. To find a consensus on the terminology and definition of PFP, investigators who attended the patellofemoral pain research retreat in 2016 worked together on a consensus statement (Crossley, Stefanik, et al., 2016). This consensus statement names two core criteria to define patellofemoral pain, which are:

1) Pain around or behind the patella.

2) Pain by at least one activity that loads the patellofemoral joint, such as hiking, squatting, stair ambulation, jogging/ running and hopping/ jumping (Crossley, Stefanik, et al., 2016).

Although PFP is the most frequently diagnosed condition in individuals with knee complaints, current epidemiological evidence for the incidence of PFP is lacking (Wilson Masterson, & Seagrave, 2012; Wood, Muller, & Peat, 2011). One reason for the lack of knowledge about the exact incidence of PFP is that most studies recruited the PFP population from sports medicine or military settings and thus the results are not transferable to the general population (Callaghan & Selfe, 2007). Glaviano et al. (2015) investigated the occurrence of PFP in the United States of America (USA) over a period of five years based on a national database containing orthopaedic patient records. They reported an incidence rate of PFP of approximately 1.5 to 7.3% of all orthopaedic visits (Glaviano, Kew, Hart, & Saliba, 2015). Wilson et al. (2012) examined medical records of individuals seen for knee

injuries from a multisite, urban-based hospital in the USA over a period of thirteen years and showed that PFP was the most prevalent diagnosis in every age group. Wood et al. (2011) investigated the epidemiology of PFP in adulthood by analysing data from eight general practices in the UK and confirmed that PFP was the most prevalent diagnosis.

In conclusion, PFP is a common overuse injury and particularly young and physically active people are affected, which might cause limitation in physical activity or even lead to sport cessation (Myer et al., 2010; Powers et al., 2012; Wilson et al., 2012). Although PFP is a frequently diagnosed condition, the core criteria to define PFP, which have been defined within a consensus meeting, still reamin vague still. Furthermore, the knowledge about the incidence of PFP is still lacking.

2.3. The risk factors of patellofemoral pain

Risk factors are described as the factors which create a predisposition for the development of PFP (Dixit, DiFiori, Burton, & Mines, 2007). The risk factors of PFP have been described in various studies and have been shown to be multifactorial and closely linked to the pathophysiology of PFP (Lankhorst et al., 2012). PFP is associated with intrinsic as well as extrinsic factors (Witvrouw, Lysens, Bellemans, Cambier, & Vanderstraeten, 2000). Intrinsic factors are related to the physical and psychological characteristics of the individual (Witvrouw et al., 2000). Whereas extrinsic factors refer to the factors outside the human body, such as sport activities or the environmental conditions (Witvrouw et al., 2000).

2.3.1. Intrinsic risk factors

Intrinsic risk factors are predisposing factors and determined by the physical and psychological characteristics of the human body, such as age, body structure, physical condition, joint alignment, quality and quantity of joint motion, muscle strength, walking style or gait pattern etc. (Hewett, Briem, & Bahr, 2007; Witvrouw et al., 2000).

One of the main intrinsic factors for PFP is the abnormal patellofemoral joint alignment, maltracking and an abnormal trochlear morphology (Crossley, Stefanik, et al., 2016; Song et al., 2011; Waryasz & McDermott, 2008). Two studies showed that beside the patellar

tracking increased medial patellar mobility seemed to be significantly related to the development of PFP (Dixit et al., 2007; Witvrouw et al., 2000). However, these findings are not consistent across all studies and thus, patellar maltracking may not be a universial findings in individuals with PFP (Powers, Witvrouw, Davis, & Crossley, 2017).

In addition, abnormal biomechanics have been shown to be an important risk factor for the development of PFP (Crossley, Stefanik, et al., 2016; Holden, Boreham, Doherty, & Delahunt, 2017; Weiss & Whatman, 2015; Witvrouw, et al., 2014). Holden et al. (2017) revealed that knee valgus displacement was a predictor factor for the development of PFP. Furthermore, it could be shown that an increased abduction loading, a shallow knee flexion angle and an increased hip flexion angle are associated risk factors for PFP (Boling, 2008; Boling, Padua, Marshall, Guskiewicz, Pyne, & Beutler, 2009; Powers, et al., 2017; Weiss & Whatman, 2015). Other studies showed that lower internal knee extension moments and internal hip external rotation moments were risk factors for the development of PFP (Boling, et al., 2009; Fok, Schache, Crossley, Lin, & Pandy, 2013). Although many studies discussed the importance of the Q-angle in PFP, it was found that the Q-angle is not a risk factor for PFP (Duffey, Martin, Cannon, Craven, & Messier, 2000; Messier, Davis, Curl, Lowery, & Pack, 1991; Witvrouw, et al., 2014; Witvrouw et al., 2000).

Several studies showed that a reduced knee extensor strength is associated with a higher risk for future PFP (Boling, 2008; Boling, et al., 2009; Crossley, Callaghan et al., 2016; Dixit et al., 2007; Halabchi et al., 2013; Lankhorst et al., 2012; Waryasz & McDermott, 2008). In addition, it has been shown that individuals with future PFP were more prone to have a delayed onset of the vastus medialis (VM) in relation to the vastus lateralis (VL) (Briani, de Oliveira Silva, Pazzinatto, Ferreira, Ferrari, & de Azevedo, 2016; Cavazzuti, Merlo, Orlandi, & Campanini, 2010; Chen, Chien, Wu, Liau, & Jan, 2012; Chester, Smith, Sweeting, Dixon, Wood, & Song, 2008; Cowan, Bennell, Hodges, Crossley, & McConnell, 2001; Kim & Chang Ho, 2012) and a slower reflex response time of the VM and VL muscle of the quadriceps (Lankhorst et al., 2012; Waryasz & McDermott, 2008; Witvrouw et al., 2000). However, due to a high heterogeneity in studies assessing the quadriceps timing, it remains unknown if the delayed onset of the VM in relation to the VL is a risk factor for PFP (Lankhorst et al., 2012). Gluteus minimus and medius weakness has been well documented and is believed to be associated with the increased risk for the development of PFP (Boling, et al., 2009; Crossley, Callaghan et al., 2016). However, longitudinal studies on hip muscle

weakness are lacking and thus the association of gluteal muscle weakness as a risk factor could not be proven (Crossley, Callaghan et al., 2016) and Rathleff et al. concluded that reduced hip strength might be a result of PFP rather than the cause (Rathleff, Rathleff, Crossley, & Barton, 2014).

Several studies revealed that a reduced muscle flexibility of the quadriceps (Dixit et al., 2007; Song et al., 2011; Waryasz & McDermott, 2008; Witvrouw et al., 2000) and the hamstrings muscle (Kwon et al., 2014; Song et al., 2011; Waryasz & McDermott, 2008; Witvrouw et al., 2000) seem to be associated with the development of PFP.

Recent studies have found that excessive pronation is an intrinsic factor for PFP (Boling, 2008; Boling, et al., 2009; Kwon et al., 2014) and limited evidence showed that dynamic foot function during walking and running is a risk factor for PFP (Dowling, Murley, Munteanu, Smith, Neal, Griffiths, Collins,2014).Whereas Witvrouw et al. (2000) detected no significant difference between the foot alignment and PFP. Thus, experts agreed that static foot alignment measures are not identified as risk factors for the development of PFP (Cheung & Ng, 2007; Powers et al., 2012).

Hormonal factors, such as oestrogen, progesterone and relaxin are believed to affect the female neuromuscular and musculoskeletal systems and thus, female gender is believed to be a risk factor for the development of PFP (Cowan & Crossley, 2009), which has been proven by several studies (Boling, 2008; Boling, et al., 2009; Lankhorst et al., 2012).

2.3.2. Extrinsic risk factors

Extrinsic risk factors of PFP are factors outside the human body, such as sports activities, environmental conditions, e.g. walking surface and the equipment used, such as. footwear o knee braces (Witvrouw et al., 2000). In contrast to the intrinsic factors which remain understudied, extrinsic factors have been well investigated (Witvrouw et al., 2000).

Studies showed that individuals with PFP had increased pain and more rear-foot pronation in normal cushioned shoes, than in shoes which controlled their foot movement and avoided an excessive foot pronation (Cheung & Ng, 2007; Dicharry & Depenbrock, 2016). However, the direct and exclusively association between a single extrinsic factor, such as footwear and PFP

is challenging to investigate and thus it remains unclear whether footwear might be a risk factor for the development of PFP.

One study investigated the effect of a dynamic patellofemoral brace, that aimed to correct the position of the patella and to stimulate the vastus medialis obliquus (VMO) muscle to prevent the development of PFP (Van Tiggelen, Witvrouw, Roget, Cambier, Danneels, & Verdonk, 2004). This brace was effective, which might indicate that wearing a dynamic patellofemoral brace might decrease the risk to develop PFP (Van Tiggelen, et al., 2004).

This chapter showed that many risk factors seem to be related to PFP. In addition, risk factors are often closely linked to each other; for example reduced gluteal strength can lead to increased hip adductor and hip internal rotation angles, which leads to a dynamic knee valgus and can result in PFP. However, most studies investigated one specific risk factor in isolation rather than comparing several risk factors. Linking these aforementioned risk factors seems to be crucial to gain a full understanding of the impact of risk factors in the development of PFP.

2.4. Prognosis of patellofemoral pain

Several follow-up studies have investigated the long-term outcome of patients with PFP.

Milgrom, Finestone, A., Shlamkovitch, N., Giladi, M., & Radin (1996) determined in a prospective study the natural history of PFP was caused by overactivity. A population of 390 elite Israeli infantry recruits with PFP were included. After 6 years 50% of these participants with PFP were still symptomatic, however, only 8% reported that the severity of the pain hindered them to from their physical activity.

Nimon, Murray, Sandow, & Goodfellow (1998) investigated the progress of girls with idiopathic PFP and showed that one in four patients still suffered from significant symptoms 20 years after the first pain presentation.

Price, Jones, & Allum (2000) reviewed the cases of 46 patients with PFP with chronic traumatic PFP after 4 years and 8 months. 78% of these patients received physiotherapy, but only 12% of these patients with PFP found the treatment significantly effective. After 4 years

and 8 months only 4% of all patients with PFP were pain free. Of the 96% of patients who still suffered from PFP only 20% felt that they are still improving.

Stathopulu & Baildam (2003) contacted patients with PFP 4-18 years after their initial presentation at a hospital. Their results revealed that 91% of patients who replied still suffered from knee pain. 45% of the respondents stated that the pain affected their daily life and more than a third of the respondents required medication. They concluded that even when all non-respondents were pain-free at the time of the follow-up, the total group of patients who are still having pain would be 42%, which could be regarded as high. Furthermore, among the patients being investigated 50% of men and 31% of women reported daily knee pain. All the respondents were active young people and three-quarters of them exercised regularly although they suffered from PFP.

Collins et al. (2013) carried out an observational study to determine the predictors for an unfavourable recovery and analysed the data of 179 individuals with PFP from Australia and 131 individuals with PFP from the Netherlands. 40% of these individuals reported an unfavourable recovery 12 months after a physiotherapeutic intervention (exercises and foot orthoses). An unfavourable recovery was defined as "moderate improvements" to "worse than ever". They also revealed that men had overall a poorer prognosis and poorer function than females after 12 months. Furthermore, they found that patients suffered from PFP for at least 6 months before they visited their health professional, which might affect poorer long-term results.

Lankhorst, van Middelkoop, Crossley, Bierma-Zeinstra, Oei, Vicenzino, & Collins (2015) performed a 5-8 years follow up with the same cohort of the study of Collins et al. (2013). 60 patients replied to the questionnaires after 5-8 years and 57.6% of them reported an unfavourable recovery. Furthermore, they investigated whether the patients had signs of osteoarthritis, using a MRI scan and showed that the majority did not demonstrate signs of knee osteoarthritis.

These results show that PFP is not a self limiting and suggests that PFP should be seen as a condition that has the strong potential to become chronic. These findings also suggest that there is a need to improve treatment outcomes and to critically reflect the current treatment recommendations.

2.5. The pathophysiology of patellofemoral pain

The patellofemoral joint is the compartment of the knee joint, which has remained understudied for a long time (Guillen-Garcia, Concejero-Lopez, Rodriguez-Vasquez, Guillen-Vicente, Vicente, & Fernandez-Jaén, 2014). In addition, it is an often misunderstood region of the knee and a very complex joint (LaParade, Rasmussen, & LaParade, 2014).

The patella is the largest sesamoid bone and is embedded in the tendon of the quadriceps muscle (LaParade et al., 2014; Thomee et al., 1999). The patella articulates with the trochlea, which consists of the lateral and medial facets of the epicondyles of the femur (Fulkerson, 2004; LaParade et al., 2014). The main function of the patella is thereby to improve the quadriceps efficacy by increasing the lever arm for the quadriceps muscle and forming a pulley-rope arrangement (Aglietti, Paolo, & Menchetti, 1999; Fulkerson, 2004; McLester & St. Pierre, 2008; Özkaya & Nordin, 1999; Thomee et al., 1999). In addition, the patella diverges the forces coming from the four heads of the quadriceps muscle and serves as a central structure in the knee extensor mechanism (Aglietti et al., 1999; Fulkerson, 2004). An increased muscle tension of the quadriceps thereby always results in an increased compressive force on the patellofemoral joint (Fulkerson, 2004; Özkaya & Nordin, 1999).

The movement of the patella relative to the trochlea of the femur is called "patellar tracking" and is mainly dynamically controlled. The dynamic stabilisation of the patellofemoral joint is executed by the quadriceps muscle (especially vastus medialis, vastus lateralis and vastus intermedius) and the hamstrings muscles (Abrahamson, Hyland, Hicks, & Koukoullis, 2010; Crossley, Stefanik, Selfe, Collins, Davis, Powers, McConnell, Vicenzino, Bazett-Jones, Esculier, Morrissey, & Callaghan, 2016; Fulkerson, 2004; Swanik, Lephart, Giannantonio, & Fu, 1997; Thomee et al., 1999).

Apart from the dynamic control, the patellar tracking is also influenced by passive structures which provide a passive stabilisation of the patellofemoral joint. These passive structures are the trochlea of the femur, the shape of the patella and the peripatellar retinaculum (Fulkerson, 2004; Thomee et al., 1999).

The pathophysiology of PFP is presumed to be multifactorial (Powers et al., 2012; Song et al., 2011; Thomee et al., 1999). In particular, patellofemoral malalignment and maltracking are believed to play an important role in PFP (Lankhorst et al., 2013; Lopis & Padron, 2007; Pal, Besier, Beaupre, Fredericson, Delp, & Gold, 2013; Powers et al., 2012; Thomee et al.,

1999). Evidence suggests that the shape of the patella and the trochlea of the femur, as well as the patella alignment are associated with PFP and maltracking of the patellofemoral joint (Crossley et al., 2016a; Crossley, Stefanik, et al., 2016; Thomee et al., 1999; Witvrouw, Crossley, Davis, McConnell, & Powers, 2014). Furthermore, poor biomechanical factors are expected to increase the likelihood of patellar maltracking and thereby PFP (Collado & Fredericson, 2010; Crossley, Stefanik, et al., 2016). Poor biomechanical factors are mostly the result of dynamic malalignment, due to muscular dysfunctional factors, such as poor neuromuscular control, weakness, muscle fatigue, or atrophy (Earl, et al., 2005; Powers et al., 2012; Rathleff, Baird, Olesen, Roos, Rasmussen, & Rathleff, 2013; Witvrouw, et al., 2014). Thus, the pathophysiological factors can be divided into three categories:

- Structural factors that contribute to a malalignment of the lower limb
- Abnormal biomechanical factors that contribute to a malalignment of the lower limb
- Muscular dysfunctional factors that contribute to a malalignment of the lower limb

2.5.1. Structural factors

Studies have shown that patella displacement and patella tilting were associated with PFP (Hunter, Zhang, Niu, Felson, Kwoh, Newman, Kritchevsky, Harris, Carbone, & Nevitt, 2007; Luyckx et al., 2009; Pal et al., 2013; Pal et al., 2012; Ward & Powers, 2004; Ward, Terk, & Powers, 2007). It also has been shown that the lateral patellofemoral compartment is more affected than the medial compartment, mainly caused by an increased patella tilt and a lateral subluxation (Hunter et al., 2007; Powers et al., 2017).

Furthermore, studies showed that a patella alta was more prevalent in patients with PFP (Pal et al., 2013; Stefanik et al., 2010; Stefanik, Zumwalt, Segal, Lynch, & Powers, 2013; Powers et al, 2017). Studies investigating the contact force showed that a patella alta was associated with the highest contact force and contact pressure (Luyckx et al., 2009; Ward & Powers, 2004; Ward et al., 2007). Moreover, the patella alta is associated with a lateral patellar displacement and a greater lateral patellar tilt (Stefanik et al., 2013; Ward et al., 2007).

A shallow trochlear grove seems to be another factor which leads to an increased lateral patella tilt and is more prevalent in patients with PFP (Harbaugh, Wilson, & Sheehan, 2010; Powers, 2000).

Structural abnormalities of the patellofemoral joint, such as reduced thickness of the cartilage, cartilage defects, patellar bone marrow lesions and high signal intensity of the Hoffa fat pad seem to be associated with the development of PFP (Van der Heijden, Oei, Bron, van Tiel, van Veldhoven, Klein, Verhaar, Krestin, Bierma-Zeinstra, van Middelkoop, 2016). However, these findings were not consistent across the groups (Powers et al., 2017).

2.5.2. Abnormal biomechanical factors

Previous research has demonstrated that altered knee joint kinematics and kinetics are present in individuals with PFP. The abnormal joint biomechanics often result in a dynamic malalignment, which is defined as a poor alignment of the patella during a movement resulting from a neuromuscular control deficit of the trunk and the lower extremity (Earl, 2002; Earl, et al., 2005)

Dynamic knee valgus during dynamic activities has been described as one of the most important factors in individuals with PFP (Levinger & Gilleard, 2007; Nakagawa, Maciel, & Serrao, 2015; Nakagawa et al., 2012; Nakagawa et al., 2013; Powers, 2003; Willson et al., 2008; Willson & Davis, 2008). The dynamic knee valgus is described as the combination of femoral adduction, femoral internal rotation, tibial abduction and external knee rotation (Levinger & Gilleard, 2007; Powers, 2003). Furthermore, compared with individuals without PFP individuals with PFP have an increased knee abduction angle, an increased internal knee abductor moment (Myer et al., 2010; Nakagawa et al., 2013, Powers et al., 2017) and a decreased knee extensor moment (Bley et al., 2014; Claudon, Poussel, Billon-Grumillier, Beyaert, & Paysant, 2012; Lucareli, Amir, Bley, Nayra, Jeniffer, et al., 2014; Salsich, Brechter, & Powers, 2001).

Several studies have revealed an increased Q-angle in individuals with PFP, which is believed to relate with excessive anterior pelvic tilt, increased femoral anteversion, increased knee valgus, excessive external tibial rotation and foot and patellar position (Almeida, de Moura Campos Carvalho de Silva, Franca, Magalhaes, Burke, & Marques, 2016; Emami, Ghahramani, Abdinejad, & Namazi, 2007; Herrington & Nester, 2004; Kaya & Doral, 2012). However, studies investigating the reliability and validity of the Q-angle in individuals with PFP showed a considerable disagreement and concluded that the use of the Q-angle in

individuals with PFP is not recommended (Aliberti, Costa, João, Pássaro, Arnone, & Sacco, 2012; de Oliveira Silva, Briani, Pazzinatto, Goncalves, Ferrari, Aragao, & de Azevedo, 2015; Smith, Hunt, & Donell, 2008).

Furthermore, it could be shown that an increased hamstrings loading lead to an increase of the total contact force and an increase of the average patellar flexion, lateral tilt and lateral shift (Elias, Kirkpatrick, Saranathan, Mani, Smith, & Tanaka, 2011).

Studies analysing the foot posture in individuals with PFP showed that they had a larger contact area in the medial region of the foot and possessed a more pronated foot posture (Aliberti, Costa, Passaro, Arnone, & Sacco, 2010; Barton, Bonanno, Levinger, & Menz, 2010; Barton, Levinger, Crossley, Webster, & Menz, 2011; Bley, Correa, Dos Reis, Rabelo, Marchetti, Lucareli, 2014). PFP seems to be also associated with an increased foot mobility (Barton, et al., 2010), a greater rearfoot eversion (Barton, et al., 2010; Barton, Levinger, Crossley, et al., 2011; Barton, Menz, Levinger, Webster, & Crossley, 2011; De Oliveira Silva, & Azevedo, 2016) and a delayed peak rearfoot eversion (Levinger, Menz, Morrow, Bartlett, Feller, & Bergman, 2013).

Thus, the pathophysiology of PFP is manifold. Factors that affect the alignment of the patella, the knee, the hip joint and the trunk affect the patellofemoral joint and can provoke and aggravate PFP. Thus, structural factors, as well as abnormal biomechanical factors contribute to the development of PFP. The next chapter will discuss the contribution of muscular dysfunctional factors to PFP.

2.5.3. Muscular dysfunctional factors

Poor biomechanical factors in individuals with PFP mostly result from muscular dysfunctional factors, such as poor neuromuscular control, weakness, or muscle fatigue (Earl, et al., 2005; Powers et al., 2012; C. R. Rathleff et al., 2013; Witvrouw, et al., 2014). Muscle function describes a comprehensive functioning of a muscle, which implies force-generating capacity, muscle balance, neuromuscular control and muscle mass (Herzog, 2000b; Lieber, 2010). Muscular dysfunction describes the alteration of these functions. These dysfunctional factors are interconnected to each other and likely to contribute to pain. For example poor neuromuscular activation, which describes the inability to adjust to sensory information

might result in an abnormal muscle strength, power, or muscle activation pattern leading to increased joint loads (Herzog, 2000b; Hewett et al., 2007). Thus, muscular dysfunctional factors in individuals with PFP are mostly a combination of several factors and only very rarely exist in isolation. The interconnection of muscular dysfunctional factors means that researching these in PFP becomes more complicated. To date, only case studies have described the combination of muscular dysfunction factors in individuals with PFP and outlined muscular weakness in combination with neuromuscular control deficits of lower limb muscles in individuals with PFP (Mascal, Landel, & Powers, 2003; Willy & Davis, 2013). Numerous systematic and literature reviews have been published that analysed muscular dysfunctional factors in individuals with PFP. However, these systematic reviews focussed on specific muscular dysfunctional factors in isolation, such as quadriceps or gluteal weakness, quadriceps atrophy, gluteal or quadriceps muscle activation (Barton, Lack, Malliaras, & Morrissey, 2013; Giles, Webster, McClelland, & Cook, 2013; Lankhorst et al., 2013; Rathleff et al., 2014; Van Cant et al., 2014; Waryasz & McDermott, 2008). This allows a detailed and specific analysis of the individual muscular dysfunctional factor. However, a systematic review that investigates muscular dysfunction in individuals with PFP holistically is still lacking.

Thus, it has been decided to carry out a systematic review on muscular dysfunctional factors of PFP. This will enable the:

(1) Identification of the existing muscular dysfunctional factors in patients with PFP.

(2) Synthesis of the evidence of the identified muscular dysfunctional factors.

2.6. Literature review and meta-analysis methods

The primary search was conducted in PubMed (MEDLINE), Cochrane library, CINAHL, SPORTDiscus and Web of Science (WoS) up to March 2015. The primary search was carried out until March 2015 to ensure that the ethical applications for the main studies were based on the reviewed literature. Therefore the search for studies was completed by March 2015 and the reviewing procedure by August 2015. The Physiotherapy Evidence Database (PedRO) was searched to confirm that all relevant systematic reviews and clinical trials were included in this review. Randomized controlled trials, experimental studies without

randomization, prospective and cohort studies, written in English were included, regardless of the year of publication. References of studies as well as literature and systematic reviews were screened for relevant citations. Search keywords comprised of synonyms of patellofemoral pain, muscle strength, muscular inhibition, atrophy and flexibility (full details of terms used appear in Appendix Methods 2.1). The trials must include 1) a group of adults suffering from PFP, who have not received any operative treatment or arthroscopy and 2) a healthy control group. Owing to the lack of consistent terminology for PFP, the PFP inclusion criteria were: aged 18-50 years old; no other disease, knee pathology or knee surgery and a given patellofemoral/ anterior knee pain criteria. Cadaveric and animal studies as well as reviews, case studies and studies that lacked numerical data were excluded. Trials that analysed individuals with chondromalacia patella were excluded. Data from studies comparing the non-injured limb with the injured limb were excluded as it has been shown that muscular deficits in individuals with unilateral PFP were present bilaterally (Esther Suter, 1998; Magalhaes et al., 2010).

2.6.1. Literature quality assessment

The review process was performed in two-stages. The first reviewer (HG) screened titles and abstracts of all identified citations and searched the reference lists of the retrieved articles to identify potential studies. Titles and abstracts were evaluated for potential inclusion and were excluded if one or more exclusion criteria were met.

During the second stage, all of the admitted articles were read by two reviewers (HG and RJ) and assessed by applying the modified 'Quality Index', developed by Downs and Black (Downs & Black, 1998). The two reviewers applied each scale on the detected articles, whereby any discrepancies were resolved during a consensus meeting in consultation with a third reviewer (LH). The checklist of Downs and Black was chosen as it has been shown to be reliable and can be applied to studies with different study designs. Furthermore, the checklist provided subscales enabling a more accurate assessment of the studies. However, this checklist was designed for assessing interventional studies and thus did not fully match the purpose of evaluating observational studies. To bring this discrepancy into balance the checklist had been adapted and questions concerning the dropout of the individuals, the follow-up length, the compliance with the intervention, the individuals and therapist blinding and the randomisation procedure were excluded. As a result the maximal score for each study

became 13 points on the adapted checklist of Downs and Black. In addition, specific checklists were developed to include questions on the abstract and the specific method (the checklists appear in Methods 2.2).

One reviewer (HG) extracted the relevant data on study design (authors, year of publication), study population (sample size, participant demographics, population sources, pain intensity and duration, gender, age, definition of PFP) and the outcomes (means and SD of all relevant results). The second reviewer RJ checked the data accuracy of the spreadsheet.

2.6.2. Statistical analysis and presentation of the results

The standardised mean differences (SMD) and the matching 95% CI were calculated (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration) (Appendix Table 2.10- 2.30). The level of statistical heterogeneity which was established by X^2 and l^2 statistics, described a significant homogeneity of the comparisons with $p>0.05$. The indicated heterogeneity/ homogeneity are presented together with levels of evidence in the result section. To ensure representativity and an appropriate weighting of the studies within the meta-analysis, only specific data were included for the meta-analysis. The inclusion criteria for the meta-analysis are listed in Appendix Methods 2.3.

Due to the differences in study designs and characteristics, a random-effects model of the generic inverse variance method was used. This model gives more weight to studies with less variance in the pooled analysis. In addition, if the meta-analysis showed significant heterogeneous results ($p\leq 0.05$) a regression-analysis was executed to analyse whether the study characteristics could explain the observed heterogeneity (the complete regression-analysis can be found in Appendix Table 2.28-2.32).

Due to the heterogeneity of the studies the results of atrophy, inhibition, fatigue and the break phenomenon were analysed descriptively.

The individual or pooled SMD were categorised as small ($\leq$ 0.59), medium (0.6-1.19) or large ($\geq$1.2), as these criteria have been used in previous systematic reviews on PFP and have been shown to be valid (Barton et al., 2013; Lack, Barton, Vicenzino, & Morrissey, 2014; Rathleff et al., 2014).

High quality (HQ) studies were defined as studies with an overall score of > 85%, moderate quality (MQ) was defined with an obtained overall score of 70-85% and low quality (LQ) studies were defined as studies which scored overall >70%.

Levels of evidence were defined based on the guidelines of van Tulder, M., Furlan, A., Bombardier, C., & Bouter, (2003):

Strong evidence: pooled results derived from three or more studies, including a minimum of two high quality studies, which are statistical homogenous ($p>0.05$), might be associated with statistically significant or non-significant pooled result.

Moderate evidence: statistically significant pooled results derived from multiple studies, including at least one high quality study which are statistical heterogenous ($p<0.05$), or from multiple low quality studies which are statistical homogenous ($p>0.05$).

Low evidence: Limited evidence: results from multiple LQ studies which are statistically heterogeneous ($p<0.05$); or from one HQ study.

Very limited evidence: results from one LQ study.

Conflicting evidence: pooled results from multiple studies regardless of quality are inconsistent and heterogenous, ($p<0.05$, i.e., inconsistent).

This systematic review aimed to identify and to synthesise the evidence of muscular dysfunctional factors. Therefore the calculated standardised mean differences (SMD), the matching 95% CI and the overall heterogeneity were presented in summary tables instead of being presented in individual forest plots. These summary tables enable a direct overview of the amount of published studies on the specific muscle dysfunctional factor. The forest plots that are summarised in Table 2.1 to 2.6 can be found in Appendix Table 2.10 to 2.30.

2.6.3 Results of the literature review

The initial search identified 3388 records. After removing study duplicates and studies that did not pertain to the research question, the search yielded a total of 168 papers. In total 105 studies were excluded because of the lack of a control group, lacking numerical data, a quality criteria below 50%, unclear participants characteristics, excluded study designs, other knee pathologies or the inaccessibility of the study (Figure 2.1). In total 26 studies on muscle weakness, 25 studies on EMG, 6 studies on muscle flexibility, 4 studies on atrophy, 6 studies on fatigue and endurance, one study on the break phenomenon and 2 studies on muscle inhibition were included. Four studies investigated muscle strength and EMG (Kaya, Callaghan, Ozkan, Ozdag, Atay, Yuksel, & Doral, 2010; Nakagawa et al., 2015; Nakagawa,

Moriya, Maciel, & Serrao, 2012; Ott, Cosby, Grindstaff, & Hart, 2011), one study investigated muscle strength and flexibility (Piva, Goodnite, & Childs, 2005), two studies investigated muscle strength and fatigue (Dierks et al., 2008; McMoreland, O'Sullivan, Sainsbury, Clifford, & McCreesh, 2011), one study investigated muscle flexibility and EMG (Earl, et al., 2005), one study investigated muscle strength and muscle atrophy (Callaghan & Oldham, 2004b) and one study investigated muscle strength and inhibition (Thomee, Grimby, Svantesson, & Osterberg, 1996) in individuals with PFP. Thus, in total 62 studies with a sample size of 1391 individuals with PFP and 1617 healthy controls were included for final review (Aminaka, Pietrosimone, Armstrong, Meszaros, & Gribble, 2011; Anderson & Herrington, 2003; Bazett-Jones, Cobb, Huddleston, O'Connor, Armstrong, & Earl-Boehm, 2013; Bley et al., 2014; Bolgla, Malone, Umberger, & Uhl, 2011; Boling, Padua, Blackburn, Petschauer, & Hirth, 2006; Boling, Padua, & Creighton, 2009; Briani, de Oliveira Silva, et al., 2015; Callaghan, McCarthy, & Oldham, 2001; Callaghan & Oldham, 2004b; Cavazzuti et al., 2010; Cichanowski, Schmitt, Johnson, & Niemuth, 2007; Coqueiro, Bevilaqua-Grossi, Berzin, Soares, Candolo, & Monteiro-Pedro, 2005; de Moura Campos Carvalho, Magalhaes, Bryk, & Fukuda, 2014; Dierks et al., 2008; Duvigneaud, Bernard, Stevens, Witvrouw, & Van Tiggelen, 2008; Dvir et al., 1990; Earl, et al., 2005; Esculier, Roy, & Bouyer, 2015; Felicio, Baffa, Liporacci, Saad, De Oliveira, & Bevilaqua-Grossi, 2011; Ferber, Kendall, & Farr, 2011; Ferrari, Kuriki, Silva, Alves, & Micolis de Azevedo, 2014; Giles, Webster, McClelland, & Cook, 2015; Hudson, 2006; Ireland, Willson, Ballantyne, & Davis, 2003; Jan, Lin, Lin, Lin, Cheng, & Lin, 2009; Karst & Willett, 1995; Kaya, et al., 2010; Liebensteiner, Szubski, Raschner, Krismer, Burtscher, Platzer, Deibl, & Dirnberger, 2008; Magalhaes, Fukuda, Sacramento, Forgas, Cohen, & Abdalla, 2010; McMoreland et al., 2011; Moradi, Akbari, Ansari, Emrani, & Mohammadi, 2014; Mostamand, Bader, & Hudson, 2011; Nakagawa et al., 2015; Nakagawa et al., 2012; Nakagawa, Muniz, Baldon, Maciel, Amorim, & Serrao, 2011; Negahban, Etemadi, Naghibi, Emrani, Shaterzadeh Yazdi, Salehi, & Moradi Bousari, 2013; O'Sullivan, Herbert, Sainsbury, McCreesh, & Clifford, 2012; Ohjeoung, Mijung, & Wanhee, 2014; Oliveira, Saad, Felício, & Grossi, 2014; Ott et al., 2011; Owings & Grabiner, 2002; Pattyn, Verdonk, Steyaert, Vanden Bossche, Van den Broecke, Thijs, & Witvrouw, 2011; Peeler, 2007; Piva et al., 2005; Powers, Landel, & Perry, 1996; Powers, Perry, Hsu, & Hislop, 1997; C. R. Rathleff et al., 2013; Robinson & Nee, 2007; Saad, Felicio, Masullo, Liporaci, & Bevilaqua-Grossi, 2011; Song, Huang, Chen, Lin, & Chang, 2015; Souza & Powers, 2009a; Suter, Herzog, De Souza, & Bray, 1998; Thijs, Pattyn, Van

Tiggelen, Rombaut, & Witvrouw, 2011; Thomee et al., 1996; Van Tiggelen, Witvrouw, Coorevits, Croisier, & Roget, 2004; Werner, 1995; White, 2009; Willson et al., 2008; Willson, Kernozek, Arndt, Reznichek, & Scott Straker, 2011; Witvrouw et al., 2000). Details of the searched results are shown in the flowchart Figure 2.1 and further information about the participant's characteristics are listed in Appendix: Table 2.1-2.8.

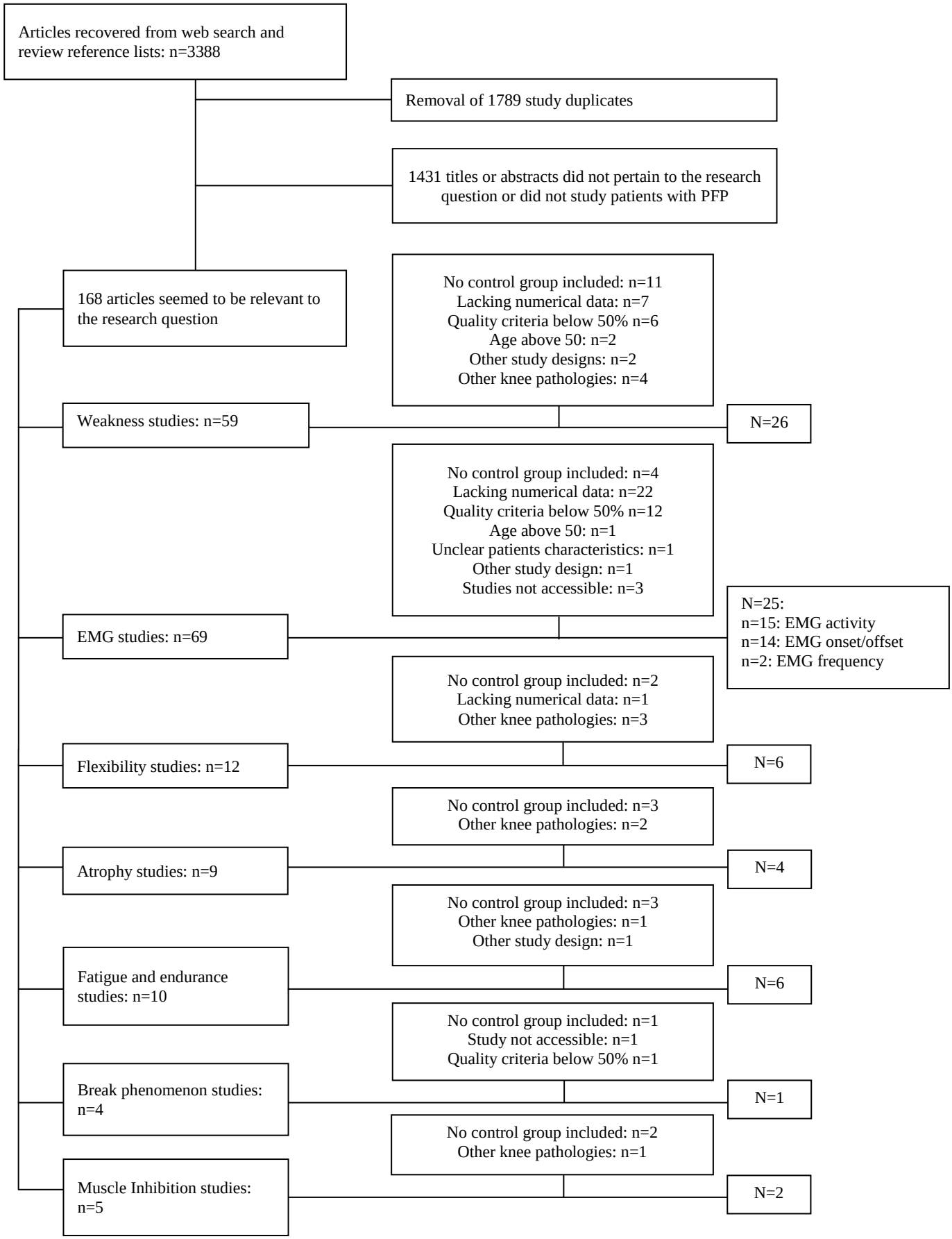


Figure 2.1: Selection process for studies included in this review

2.6.3.1. Muscle weakness

The most common definition of weakness defines muscle weakness as the inability of a muscle or muscle group to produce force at a given speed (Berryman Reese, 2012; Kostek, Hubal, & Pescatello, 2011; McBride, 2016). Muscle weakness is caused by numerous factors, such a loss in the cross-sectional area of individual fibres, and an overall reduction of fibres, (Kostek et al., 2011; Faulkner, Larkin, Clafin & Brooks, 2007). A reduced excitability in the coricospinal pathways, inhibited agonist motor neurons, reduced motor unit firing rates and a reduced motor neuron conduction velocity also result in muscle weakness (Clark & Fielding, 2012). In addition, muscle weakness is believed to be associated to a decrease in the number of cross-bridges per unit area and the averaged force developed per cross-bridge of the fast type 2 fibres (Brooks & Faulkner, 1994; Faulkner et al., 2007). Muscle weakness is also interconnected with other muscular dysfunctional factors, such as atrophy, arthrogenous muscle inhibiton or neuromuscular control deficits. If a muscle is weak over a prolonged period the muscle can also become atrophied. Furthermore, poor neuromuscular activation and arthrogenous muscle inhibition can result in reduced muscle strength and power (Herzog, 2000b; Hewett et al., 2007). Knee injuries can lead to an increased muscle inhibition, an impaired neuromuscular activation or a reduced muscle mass after immobilisation and thereby result in muscle weakness (Karatzaferi & Chase, 2013; Yoshida, Mizner, & Snyder-Mackler, 2013). Studies showed that quadriceps weakness is a common problem after knee injuries and the weakness of the vastus medialis has been frequently addressed in knee injury studies (Callaghan, Parkes, Hutchinson, & Felson, 2014; Felício, Dias, Silva, Oliveira, & Bevilaqua-Grossi, 2011; Glass, Torner, Frey Law, Torner, Frey Law, Wang, Yang, Nevitt, Segal, Wang, Yang, Nevitt, Felson, Lewis, Segal, 2013; Halabchi et al., 2013; Konishi, Fukubayashi, & Takeshita, 2002; Krishnan & Theuerkauf, 2015; Lin et al., 2010; Petterson, Barrance, Buchanan, Binder-Macleod, & Snyder-Mackler, 2008; Saleh, Lee, Gandhi, Ingersoll, Mahomed, Sheibani-Rad, Novicoff, & Mihalko, 2010; Sawatsky, Bourne, Horisberger, Jinha, & Herzog, 2012; Stevens, Mizner, & Snyder-Mackler, 2003). A weak vastus medialis is assumed to be associated with an increased lateral pull of the patella in the femoral grove resulting in a dynamic malalignment of the patellofemoral joint (Cowan, Bennell, Crossley, et al., 2002; Sakai, Luo, Rand, & An, 2000; Sawatsky et al., 2012). In addition, studies on PFP found that an impaired neuromuscular control of the hip muscles could result in an increased hip adduction and internal rotation angle which could cause an

increase in lateral patellofemoral joint (PFJ) stress (Barton et al., 2013; Weiss & Whatman, 2015). This excessive hip motion is believed to be caused by a weak gluteus medius and gluteus maximus muscle (Barton et al., 2013).

For the final meta-analysis in this study twenty-six studies (4HQ, 13 mQ, 9LQ studies) with a sample size of 625 individuals with PFP and 645 healthy controls were included for the final meta-analysis (Appendix: Table 2.1, 2.4 & 2.7) (Boling, Padua, & Creighton, 2009; Callaghan & Oldham, 2004b; Cichanowski et al., 2007; de Moura Campos Carvalho et al., 2014; Dierks et al., 2008; Duvigneaud et al., 2008; Dvir et al., 1990; Ferber et al., 2011; Ireland et al., 2003; Kaya, et al., 2010; Magalhaes et al., 2010; McMoreland et al., 2011; Moradi et al., 2014; Nakagawa et al., 2012; Oliveira et al., 2014; Ott et al., 2011; Piva et al., 2005; Powers et al., 1997; C. R. Rathleff et al., 2013; Robinson & Nee, 2007; Souza & Powers, 2009a; Thijs et al., 2011; Thomee et al., 1996; Van Tiggelen, Witvrouw, Coorevits, et al., 2004; Werner, 1995). Strong evidence indicates that individuals with PFP have weaker hip abductor muscles (3HQ, 8 mQ & 4LQ studies, SMD: -0.68, 95% CI: -0.96 to -0.40, l^2= 63%, p= 0.0005) (Boling, Padua, & Creighton, 2009; Cichanowski et al., 2007; Dierks et al., 2008; Ferber et al., 2011; Ireland et al., 2003; Magalhaes et al., 2010; McMoreland et al., 2011; Moradi et al., 2014; Nakagawa et al., 2015; Nakagawa et al., 2012; Oliveira et al., 2014; Piva et al., 2005; C. R. Rathleff et al., 2013; Robinson & Nee, 2007; Souza & Powers, 2009a; Thijs et al., 2011) and a weaker hip external rotator strength compared with healthy controls (3HQ, 8 mQ & 3LQ studies, SMD: -0.54, 95% CI: -0.81 to -0.26, l^2= 60%, p< 0.002) (Boling, Padua, & Creighton, 2009; Cichanowski et al., 2007; Dierks et al., 2008; Ireland et al., 2003; Magalhaes et al., 2010; McMoreland et al., 2011; Moradi et al., 2014; Nakagawa et al., 2012; Oliveira et al., 2014; Piva et al., 2005; C. R. Rathleff et al., 2013; Robinson & Nee, 2007; Souza & Powers, 2009a; Thijs et al., 2011) (Table 2.1, Appendix: Table 2.11, 2.13).

Moderate evidence indicates that individuals with PFP have reduced knee extensor strength (1HQ, 4 mQ and 6LQ studies, SMD: -0.91, 95% CI: -1.25 to -0.58, l^2= 68%, p= 0.0006) (Callaghan & Oldham, 2004b; Duvigneaud et al., 2008; Dvir et al., 1990; Kaya, et al., 2010; Oliveira et al., 2014; Ott et al., 2011; Powers et al., 1997; C. R. Rathleff et al., 2013; Thomee et al., 1996; Van Tiggelen, Witvrouw, Coorevits, et al., 2004; Werner, 1995), a reduced hip extensor strength (1HQ, 4 mQ& 3LQ studies SMD: -0.48, 95% CI: -0.91 to -0.04, l^2= 70%, p=0.002) (Boling, Padua, & Creighton, 2009; Cichanowski et al., 2007; Magalhaes et al.,

2010; Moradi et al., 2014; Oliveira et al., 2014; Robinson & Nee, 2007; Souza & Powers, 2009a; Thijs et al., 2011), a reduced hip internal rotation strength (1HQ, 4 mQ& 2LQ studies, SMD: -0.51, 95% CI: -0.9 to -0.12, l^2= 59%, p=0.02) and a weaker hip adductor strength in individuals with PFP (1HQ, 3 mQ& 2LQ studies, SMD: -0.51, 95% CI: -1 to -0.02, l^2= 71%, p= 0.004) (Cichanowski et al., 2007; Magalhaes et al., 2010; Moradi et al., 2014; Oliveira et al., 2014; C. R. Rathleff et al., 2013; Thijs et al., 2011) (Table 2.1, Appendix: Table 2.11, 2.13).

Low evidence indicates that individuals with PFP have a reduced hip flexor strength (3 mQ& 2LQ studies, SMD: -0.52, 95% CI: -1.16 to -0.13, l^2= 80%, p= 0.004) (Cichanowski et al., 2007; Magalhaes et al., 2010; Moradi et al., 2014; Oliveira et al., 2014; Thijs et al., 2011) (Table 2.1), a reduced trunk strength (1HQ study, extension: SMD: -0.68, 95% CI: -1.2 to -0.16, side bridging: SMD: -0.68, 95% CI: -1.2 to -0.16, a trunk flexion with rotation: SMD: -1.66, 95% CI: -2.25 to -1.06) (Nakagawa et al., 2015) and pelvis drop deficits (1HQ, SMD: --0.01, 95% CI: -0.64 to 0.63) (Souza & Powers, 2009a) (Table 2.1, Appendix Table 2.12, 2.13).

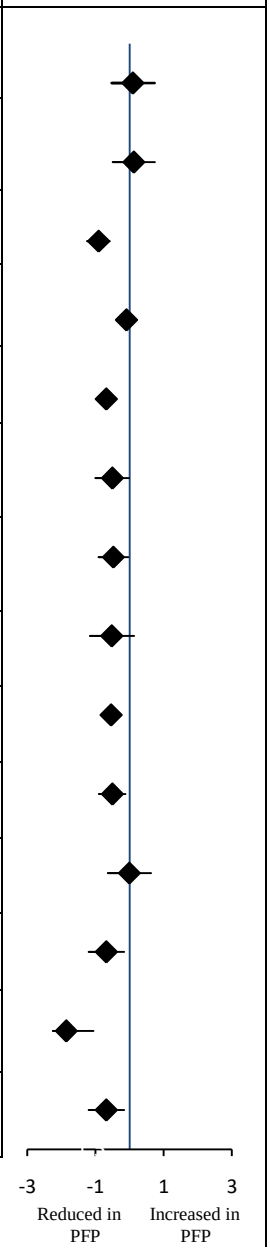
Inconclusive evidence exists about the reduced strength in knee flexors in individuals with PFP (1HQ, 1 mQ and 3LQ studies, SMD: -0.09, 95%CI: -0.33 to 0.14, l^2= 0%, p= 0.86) (Duvigneaud et al., 2008; Oliveira et al., 2014; C. R. Rathleff et al., 2013; Van Tiggelen, Witvrouw, Coorevits, et al., 2004; Werner, 1995) as well as the ankle strength (1 mQ study, ankle dorsiflexion: SMD: 0.1, 95% CI: -0.52 to 0.73, ankle inversion: SMD: 0.11, 95% CI: -0.5 to 0.74) (de Moura Campos Carvalho et al., 2014) (Appendix Table 2.10, 2.11).

This meta-analysis shows that much research has been carried out on the strength of hip and knee muscles. In contrast, the strength of the trunk and ankle muscles in individuals with PFP has only been addressed in single studies and requires further investigation.

The heterogeneity in studies assessing strength was moderate to substantial. The regression-analysis revealed a significant association with the same test position for knee extension (p=0.04), hip abduction (p=0.001) and hip internal rotation (p=0.0005) strength (Appendix: Table 2.31, 2.32 & 2.33). Furthermore, the normalisation method was associated with hip adduction (p=0.003) strength (Appendix: Table 2.30). However, these factors were not consistently associated with strength results throughout the studies (Appendix: Table 2.31, 2.32 & 2.33).

Table 2.1: The comparison of ankle, knee, hip, trunk and pelvis strength between individuals with PFP and healthy controls

Strength	No of studies	Sample size		Std Mean difference IV, Random 95%CI	Heterogeneity	Std Mean difference IV, Random 95%CI
		PFP	Healthy			
Ankle dorsiflexion	1	20	20	-0.1 [-0.52; 0.73]	-	
Ankle inversion	1	20	20	0.12 [-0.5; 0.74]	-	
Knee extension	11	287	283	-0.91 [-1.25; 0.58]	Tau^2=0.21. Chi^2= 31.13, df=10 (p=0.0006), I^2= 68%	
Knee flexion	6	124	168	-0.09 [-0.33; 0.14]	Tau^2=0.00. Chi^2= 1.29, df=4 (p=0.86), I^2=0%	
Hip abduction	15	296	352	-0.68 [-0.96; -0.4]	Tau^2=0.19. Chi^2= 38.31, df=14 (p=0.0005), I^2= 63%	
Hip adduction	6	115	176	-0.51 [-1; -0.02]	Tau^2=0.25. Chi^2= 17.38, df=5 (p=0.004), I^2=71%	
Hip extension	8	144	205	-0.48 [-0.91; -0.04]	Tau^2=0.26. Chi^2= 23.26, df=7 (p=0.002), I^2= 70%	
Hip flexion	5	95	156	-0.52 [-1.16; 0.13]	Tau^2=0.42. Chi^2= 20.36, df=4 (p=0.004), I^2= 80%	
Hip external rotation	14	281	342	-0.54 [-0.81; -0.26]	Tau^2=0.17. Chi^2= 32.87, df=13 (p=0.002), I^2= 60%	
Hip internal rotation	7	127	188	-0.51 [-0.9; -0.12]	Tau^2=0.16. Chi^2= 14.71, df=6 (p=0.02), I^2= 59%	
Pelvis drop	1	19	19	-0.01 [-0.64; 0.63]	-	
Trunk extension	1	30	30	-0.68 [-1.2; -0.16]	-	
Trunk flexion with rotation	1	30	30	-1.66 [-2.25; -1.06]	-	
Side bridging	1	30	30	-0.68 [-1.2; -0.16]	-	



2.6.3.2. Muscle atrophy

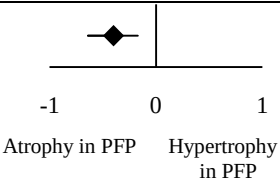
Muscle atrophy describes a decrease in the muscle volume due to a decreased size of muscle cells, often accompanied with a fatty infiltration (Boutin & Pathria, 2013). The decrease in cell size occurs when when functional demand is decreased. It is also characterised by a decreased motor fibre size and motor fibre number, protein/ DNA ratios and a shift in contractile properties towards the slow-twitch fibres (Häkkinen, 2002). Immobilisation and

disuse due to pain leads to a quickly activated reduced muscle protein synthesis and an increase in protein degradation that leads to muscle atrophy (Gibson, 2007; Brocca, McPhee, Longa, Canepari, Seynnes, De Vito, Pellegrino, Narici, & Bottinelli, 2017). Muscle atrophy is a physiological consequence of aging, but it can also be caused by a prolonged period of disuse and unloading of the muscle (Fanzani, Conraads, Penna, & Martinet, 2012; Häkkinen, 2002). Furthermore, it can result from many muscle abnormalities, such as muscle weakness, impaired muscle activation or a reduced neuromuscular control (Boutin & Pathria, 2013). Resistance exercise and heavy strength training have shown to lead to increased cross sectional areas, a greater fast to slow-twitch fibre ratio, increased muscle thickness and increased pennation angles and thereby and resulted in increased muscle strength and power (Suchomel, Comfort, & Stone, 2018). Thus, atrophy and muscular weakness can be prevented by maintaining functional demand on muscles and can be treated by heavy strength and exercise training.

Quadriceps atrophy is commonly seen in patients with lower limb injuries (Callaghan & Oldham, 2004b; Chen, Haas, & Powers, 2008; Giles et al., 2013, 2015; Guler, Mahirogullari, Isyar, Piskin, Yalcin, Mutlu, & Sahin, 2016; Meier, Mizner, Marcus, Dibble, Peters, & Lastayo, 2008; Otzel, Chow, & Tillman, 2015; Pattyn et al., 2011; Thomas, Wojtys, Brandon, & Palmieri-Smith, 2016). In particular, myofibre shrinking was a mechanism which accounted for quadriceps atrophy (Young, Hughes, Round, & Edwards, 1982)..

In the final meta-analysis four MQ studies were included with a total sample size of 192 individuals with PFP and 129 healthy controls (Callaghan & Oldham, 2004b; Giles et al., 2015; Jan et al., 2009; Pattyn et al., 2011) (Appendix: Table 2.3, 2.6 & 2.9). Moderate evidence (4 mQ studies) with a small pooled effect size indicates reduced muscle mass of the quadriceps in individuals with PFP compared with healthy controls (SMD: -0. 4, 95% CI: -0.64 to -0.172, l^2= 0%, p=0.44) (Table 2.2, Appendix Table 2.14).

Table 2.2: The comparison of muscle atrophy in individuals with and without PFP

Atrophy	No of studies	Sample size		Std Mean difference IV, Random 95%CI	Heterogeneity	Std Mean difference IV, Random 95%CI
		PFP	healthy			
Quadriceps atrophy	4	192	129	-0.4 [-0.64; -0.17]	Tau^2=0, Chi^2= 2.72, df=3 (p=0.44), l^2= 0%	

2.6.2.3. Muscle inhibition

Arthrogenic muscle inhibition (AMI) describes an ongoing reflex response, resulting in a neural inhibition which causes the inability to completely contract a muscle voluntarily, despite no structural damage to the muscle or the innervating nerve (Bolgla & Keskula, 2000; Hart, Pietrosimone, Hertel, & Ingersoll, 2010; Hopkins & Ingersoll, 2000; Rice & McNair, 2010). Authors described that this reflex inhibition is modulated by the pre- and postsynaptic mechanism and elicited by abnormal afferents from a damaged joint (Callaghan et al., 2014; Drover et al., 2004). The damaged joint causes a decreased motor drive to muscles and thus a limited potential of the muscle to generate force (Callaghan et al., 2014).

Other authors described AMI as a neurological decline in muscle activation (Palmieri-Smith et al., 2013) or the failure to activate all motor units of a muscle during a maximal voluntary contraction (Drover et al., 2004; Hurley & Newham, 1993; Suter, Herzog, De Souza, et al., 1998). The inhibition occurs because either a reduced number of motor units are recruited or because motor units are recruited at submaximal frequencies (Drover et al., 2004).

Arthrogenic muscle inhibition (AMI) has been reported to be a limiting factor in a wide range of knee joint pathologies, such as knee osteoarthritis and rheumatoid arthritis (Hart et al., 2010; Rice & McNair, 2010).

For the final analysis two studies with the sample size of 30 individuals with PFP and 37 healthy controls were included (Suter et al., 1998; Thomee et al., 1996). Further information about the studies is listed in Appendix Table 2.3, 2.6 & 2.9. Since only two studies were included no pooling of the data was undertaken and the results of the two studies will be presented descriptively. Suter et al. (1998) investigated quadriceps muscle inhibition by calculating the difference of the interpolated twitch torque during a maximum isometric voluntary contraction (MVIC) and the resting twitch torque (RTT). They found significant higher muscle inhibition (MI) and lower extensor moments in individuals with PFP compared with healthy controls. By grouping the subjects according to their pain ratings they identified that individuals with moderate pain had higher MI and lower knee extensor moments compared with control subjects and individuals with low PFP (Suter et al., 1998).

Thomeé et al. (1996) analysed quadriceps inhibition by a single-twitch superimposed electrical stimulation and calculated the additional percentage of generated torque. They

showed that an additional 18% (range 6.7-25%) of knee extensor torque was generated with the single-twitch superimposed electrical stimulation in individuals with PFP, compared with 4.9% in healthy controls (range: 0-12%). These results revealed that individuals with PFP were unable to maximally activate their quadriceps muscle voluntarily, which might be caused by reflex inhibition (Thomee et al., 1996).

2.6.3.4. Poor neuromuscular control

Neuromuscular control or dynamic stability are defined as the ability to produce a controlled movement during a coordinated muscle activity in response to motion or loading in order to maintain functional stability (Madhavan, 2007; Potach & Grindstaff, 2016). Neuromuscular control is also described as a response to sensory, proprioceptive information, which causes a conscious and unconscious efferent control of posture, balance, stability and the sense of position (Potach & Grindstaff, 2016). This neuromuscular control is needed in situations such as running on uneven surface, which require an adjustment to the ground to prevent falls, joint overloading and injuries (Potach & Grindstaff, 2016).

Neuromuscular control involves two mechanisms to interpret information and to coordinate the efferent response; the feed-forward and the feedback process. The feed-forward neuromuscular control plans the movement based on information from past experiences and is a mechanism for preparatory muscle activity. The feedback neuromuscular control is in contrast a reactive control pattern, which is processed through the reflex pathways and is associated with reactive muscle activity (Abrahamson et al., 2010; Swanik et al., 1997). Thereby, the knee is dynamically stabilised through a preparatory/ feed-forward and reflexive/ feedback neuromuscular control system (Iturri, 2003).

Conversely a poor neuromuscular control describes the inability to adjust to sensory information and thus causes an abnormal muscle strength, power, or muscle activation pattern which lead to increased joint loads (Hewett et al., 2007). Studies have shown that neuromuscular control is impaired after lower limb injuries, such as PFP or an anterior cruciate ligament rupture (Aminaka & Gribble, 2008; Aminaka et al., 2011; Bolgla, Malone, Umberger, & Uhl, 2010; Bolgla et al., 2011; Dos Anjos Rabelo, Lima, Dos Reis, Bley, Yi, Fukuda, Pena Costa, & Garcia Lucareli, 2014; Earl, 2002; Kuenze et al., 2015; Lindley,

2015; Potach & Grindstaff, 2016; Rosenthal, Moore, Stoneman, & DeBerardino, 2009). The lack of neuromuscular control can be caused by various reasons. Firstly, the injury might lead to an insufficient somatosensory awareness to coordinate the muscle activity and thereby maintain the dynamic stability (Swanik et al., 1997). Secondly a knee injury might lead to a reduction of joint motion and position sense which affects the feed-forward and feedback mechanism and diminishes the dynamic stability (Swanik et al., 1997).

Each muscle consists of motor units, which are formed by a motorneuron, its axon, the neuromuscular junction and the muscle fibres innervated by that motorneuron (Rhoades & Tanner, 2003). These motor units are classified into low- and high-threshold motor units (Figure 2.2). The high-threshold motor units have a larger α-motorneuron cell and innervate fast-twitch muscle fibres, which are high-force but fatigable muscle fibres (McCorry, 2008; Rhoades & Tanner, 2003). The low-threshold motor units conduct action potentials slower and innervate slow-twitch muscle fibres, which are low-force but fatigue-resistant (Lieber, 2010; Rhoades & Tanner, 2003).

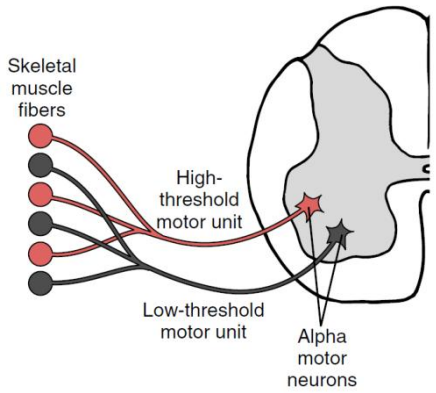


Figure 2.2: Motor unit structure (Rhoades & Tanner, 2003)

Muscles are activated by nerve signals, which originate from the central nervous system leaving the spinal cord via α-motorneurons which terminate at the neuromuscular junction on muscle fibres (Herzog, 2000b; Rhoades & Tanner, 2003). These nerve signals are called Motor Unit Action Potentials (MUAPs) which propagate down to a motorneuron, along the axon and terminate at the neuromuscular junction, where they cause a postsynaptic depolarisation which generates an electromagnetic field (Basmajian & De Luca, 1985).

This electrical activity of the skeletal muscles can be captured qualitatively by measuring the electromyographic (EMG) signal (Multon, 2013). Each action potential produces an electrical signal. If an EMG-electrode is located in the area of the postsynaptic depolarisation the MUAPs of all active motor units it can be recorded in voltage (Figure 2.3) (Basmajian & De Luca, 1985; Herzog, 2000a).

The repetitive sequence of MUAPs is called Motor Unit Action Potential trains (MUAPTs) and produce a waveform (Figure 2.3) (Burden, 2008). The produced electromyography represents the summation of all MUAPTs within the detected volume of the electrodes (Burden, 2008) (Figure 2.3). The more active MUAPs per muscle fibre are present the larger the EMG signal will be (Herzog, 2000a).

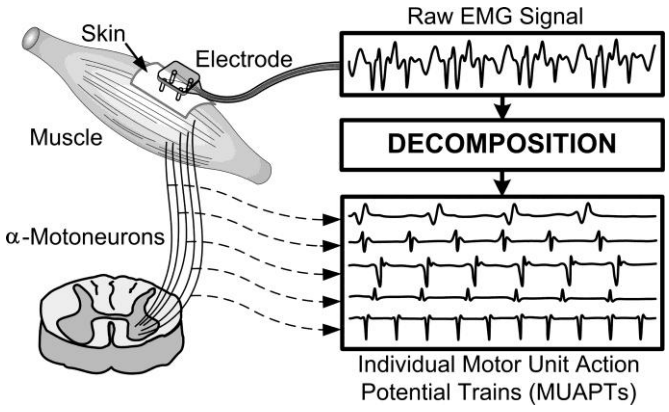


Figure 2.3: Outline of the decomposition of the surface EMG signal (De Luca & Adam, 1999)

A controlled muscle activation will result in force production. The magnitude of the force production depends on the size of the activated motor units, the number of activated motor units and the frequency of the motor unit recruitment (Herzog, 2000b). During a muscle contraction the slow motor units are recruited first and with increasing force the muscle generates more muscle force by: (1) recruiting more motor units (2) higher frequency firing rate of the recruited motor units (3) and an increased amount of tension developed by each muscle fibre (Herzog, 2000a; McCorry, 2008).

Neuromuscular control has been associated with decreased joint stability, reduced muscle weakness, disuse muscle atrophy, deficits in proprioception, balance and altered

neuromuscular activation and has been assessed in different ways, such as analysing balance or performance during functional tasks (e.g. single leg squat and hop down test) (Meininger, 2014). These measurements enable the investigation of functional movement alterations; however, they do not allow insights into the muscle activation.

Since sEMG captures the electromyographic signal of the motor units, it enables the direct link to the muscles (Multon, 2013). The generation of an electrical is closely associated with the generation of force by a muscle. However it is not possible to measure muscle force directly using EMG and the understanding of the relationship between internal forces and movement, as well as movement control is one of the major methodological challenges for biomechanics (Kuriki, Azevedo, Takahashi, Mello, & Filho, 2012). During voluntary contractions, muscle force is modulated by the central nervous system, which controls the number and type of fibres activated, the recruitment frequency of MUAPs and the synchronization of the activated motor units (MUs) (Kuriki, et al., 2012). In addition, muscle strength is influenced by force-length relationship, force-velocity relationship, as well as force-sharing among synergistic muscles. Although sEMG cannot enable direct insights into muscle force, it reflects the recruitment and firing characteristics of MUAPs and thus enables insights into neuromuscular control strategies. Therefore, to analyse neuromuscular control sEMG can be used and measured in mainly in three ways:

- The analysis of the intensity of the MUAPs, by analysing the **EMG amplitude** (De Luca, 1997; Fee & Miller, 2012).
- The analysis of the **EMG onset/ offset**, thus the presence or absence of the muscle activity during a specific movement, such as the stance phase in gait (De Luca, 1997; Fee & Miller, 2012).
- The analysis of the neural drive by analysing the **EMG frequency**, which investigates the frequency of the motor unit recruitment and the firing rate of the recruited motor units (Herzog, 2000b).

In the final meta-analysis of this study in total 25 studies that analysed the EMG signal in individuals with and without PFP were included (Aminaka et al., 2011; Bley et al., 2014; Bolgla et al., 2011; Boling et al., 2006; Briani, de Oliveira Silva, et al., 2015; Cavazzuti et al., 2010; Coqueiro et al., 2005; Earl, et al., 2005; Esculier et al., 2015; Felicio et al., 2011; Ferrari et al., 2014; Karst & Willett, 1995; Kaya et al., 2010; Liebensteiner et al., 2008;

Mostamand et al., 2011; Nakagawa et al., 2015; Nakagawa et al., 2012; Nakagawa, Muniz, et al., 2011; O'Sullivan et al., 2012; Ott et al., 2011; Owings & Grabiner, 2002; Powers et al., 1996; Saad et al., 2011; Song et al., 2014; Willson et al., 2011). Thus, in total 63 studies with a sample size of 1449 individuals with PFP and 1645 healthy controls were included for final review (Appendix Table 2.2, 2.5. & 2.8).

2.6.3.4.1. EMG amplitude analysis

In total fifteen papers (5LQ, 8 mQ and 2HQ studies) that analysed amplitude differences were included in the final meta-analysis, with a total of 295 individuals with PFP and 281 healthy controls (Bley et al., 2014; Coqueiro et al., 2005; Esculier et al., 2015; Felicio et al., 2011; Liebensteiner et al., 2008; Mostamand et al., 2011; Nakagawa et al., 2015; Nakagawa et al., 2012; Nakagawa, Muniz, et al., 2011; O'Sullivan et al., 2012; Ott et al., 2011; Powers et al., 1996; Saad et al., 2011; Song et al., 2014; Willson et al., 2011).

Low evidence shows a reduced iliocostalis activity (1HQ study, SMD: -0.63, 95% CI: -1.15 to -0.11) (Nakagawa et al., 2015) and a reduced vastus lateralis longus (VLL) (2LQ studies, SMD: -0.51, 95% CI: -1 to -0.03, l^2= 0%, p=0.54) (Felicio et al., 2011; Saad et al., 2011) in individuals with PFP compared with healthy controls (Appendix Table 2.18 & Table 2.19).

Very low evidence indicates a reduced semitendinosus activity in individuals with PFP (1LQ study, semitendinosus: SMD: -0.76, 95% CI: -1.42 to -0.1) (Liebensteiner et al., 2008) (Table 2.3, Appendix Table 2.16).

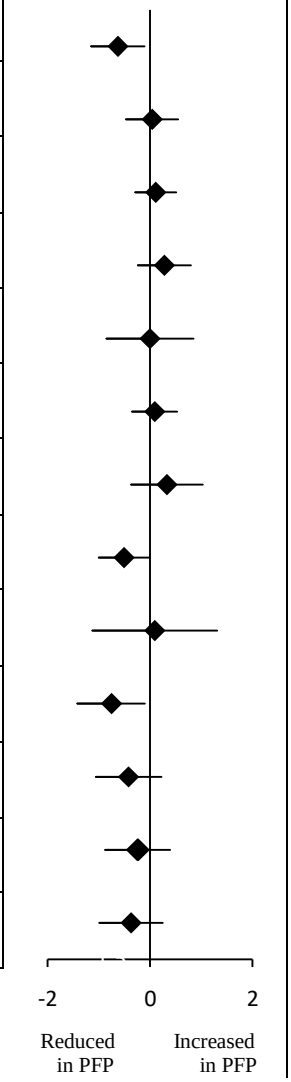
The majority of results revealed no differences in muscular activity between individuals with and without PFP (Table 2.3, Appendix Table 2.15 to 2.19) (1HQ study: obliquus externus: SMD: 0.04. 95% CI: -0.47 to 0.55 (Nakagawa et al., 2015); 1HQ, 6 mQ& 2LQ studies: gluteus medius (GMed): SMD: 0.28, 95% CI: -0.24 to 0.8, l^2=81%, p< 0.00001 (Bley et al., 2014; Esculier et al., 2015; Nakagawa et al., 2012; Nakagawa, Muniz, et al., 2011; O'Sullivan et al., 2012; Ott et al., 2011; Saad et al., 2011; Song et al., 2014; Willson et al., 2011); 1HQ& 4 mQ studies: gluteus maximus (GMax): SMD: 0.11, 95% CI: -0.29 to 0.51, l^2=52%, p= 0.08 (Bley et al., 2014; Esculier et al., 2015; Nakagawa et al., 2012; Song et al., 2014; Willson et al., 2011); 1 mQ study: rectus femoris: SMD: 0, 95% CI: -0.85 to 0.85 (Song et al., 2014), 3 mQ& 5LQ studies: vastus medialis (VM): SMD: 0.09, 95% CI: -0.35 to 0.53, l^2= 69%,

p=0.002 (Coqueiro et al., 2005; Esculier et al., 2015; Felicio et al., 2011; Liebensteiner et al., 2008; Mostamand et al., 2011; Ott et al., 2011; Powers et al., 1996; Saad et al., 2011); 4 mQ& 5LQ studies: Vastus lateralis (VL): SMD: 0.33, 95% CI: -0.37 to 1.03, l^2= 89%, p<0.00001 (Bley et al., 2014; Coqueiro et al., 2005; Esculier et al., 2015; Felicio et al., 2011; Liebensteiner et al., 2008; Mostamand et al., 2011; Ott et al., 2011; Powers et al., 1996; Saad et al., 2011); 1 mQ& 1LQ study: biceps femoris: SMD: 0.09, 95% CI: -1.13 to 1.31, l^2=86%, p=0.008 (Bley et al., 2014; Liebensteiner et al., 2008); 1LQ study: gastrocnemius: SMD: -0.42, 95% CI: -1.06 to 0.22 (Liebensteiner et al., 2008); peroneus longus: SMD: -0.24, 95% CI: -0.88 to 0.39 (Liebensteiner et al., 2008); 1 mQ study: soleus: SMD: -0.37, 95% CI: -0.99 to 0.25 (Esculier et al., 2015) (Table 2.3, Appendix Table 2.15 to 2.19).

The heterogeneity in studies that assessed GMax, VM, VL and biceps femoris activity was substantial. The regression-analysis revealed an association with the two factors. Firstly, the normalisation method was significantly associated with the peak amplitude (GMed: p=0.001, VM: p=0.002, VL: p<0.00001), as well as the rectification method of the sEMG (GMed: p=0.004, VM: p=0.006, VL: p=0.0008) (Appendix: Table 2.34). In addition, a significant difference in SMD could be shown between different tasks in GMed and VL amplitude studies (GMed: p<0.0001, VL: p<0.00001) (Appendix: Table 2.34).

Table 2.3: The comparison of iliocostalis, obliquus externus, gluteus, quadriceps, thigh muscles, lower limb muscles and trunk muscle amplitudes in individuals with and without PFP.

sEMG amplitude	No of studies	Sample size		Std Mean difference, Random 95%CI	Heterogeneity	Std Mean difference, Random 95%CI
		PFP	Healthy			
Iliocostalis	1	30	30	-0.63 [-1.15; -0.11]	-	
Obliquus externus	1	30	30	0.04 [-0.47; 0.55]	-	
Gluteus medius	9	173	165	0.28 [-0.24; 0.8]	Tau^2=0.5. Chi^2= 41.73, df=8 (p<0.00001), I^2= 81%	
Gluteus maximus	5	117	108	0.11 [-0.29; 0.51]	Tau^2=0.11. Chi^2= 8.38, df=4 (p=0.08), I^2= 52%	
Rectus femoris	1	16	8	0 [-0.85; 0.85]	-	
Vastus medialis	8	139	141	0.09 [-0.35, 0.53]	Tau^2=0.28. Chi^2= 22.78, df=7 (p=0.002), I^2= 69%	
Vastus lateralis	9	159	161	0.33 [-0.37; 1.03]	Tau^2=1.02, Chi^2= 69.75, df=8 (p<0.00001), I^2= 89%	
Vastus lateralis longus	2	34	34	-0.51 [-1.00; -0.03]	Tau^2=0. Chi^2= 0.37, df=1 (p=0.54), I^2=0%	
Biceps femoris	2	39	39	0.09 [-1.13; 1.31]	Tau^2=0.66. Chi^2= 7.14, df=1 (p=0.008), I^2= 86%	
Semitendinosus	1	19	19	-0.76 [-1.42; -0.1]	-	
Gastrocnemius	1	19	19	-0.42 [-1.06; 0.22]	-	
Peroneus longus	1	19	19	-0.24 [-0.88; 0.39]	-	
Soleus	1	30	30	-0.37 [-0.99; 0.25]	-	



2.6.3.4.2. EMG onset/ offset analysis

Twelve studies (8 mQ and 4LQ studies) analysed the muscular onset in individuals with PFP and healthy controls (Aminaka et al., 2011; Bolgla et al., 2011; Boling et al., 2006; Cavazzuti et al., 2010; Earl, et al., 2005; Karst & Willett, 1995; Kaya et al., 2010; Mostamand et al., 2011; Nakagawa, Muniz, et al., 2011; Owings & Grabiner, 2002; Powers et al., 1996; Willson et al., 2011). Moderate evidence indicates a delay of the VM in relation to VL activity (3 mQ& 3LQ studies, SMD: -0.62, 95% CI: -1.05 to -0.18, I^2= 54%, p=0.05) (Bolgla

et al., 2011; Boling et al., 2006; Cavazzuti et al., 2010; Kaya et al., 2010; Mostamand et al., 2011; Owings & Grabiner, 2002) (Table 2.4, Appendix Table 2.28).

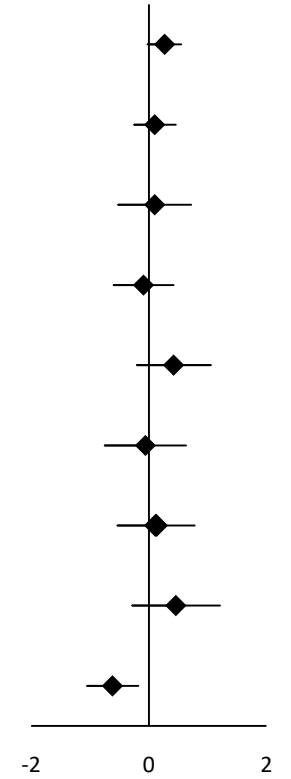
Inconclusive evidence indicates no delay of the quadriceps, the gluteal and the thigh muscles in individuals with PFP compared with healthy controls (4 mQ& 1LQ studies: VM: SMD: 0.27, 95% CI: -0.02 to 0.55, l^2=0%, p= 0.64 (Aminaka et al., 2011; Boling et al., 2006; Earl, et al., 2005; Karst & Willett, 1995; Powers et al., 1996), 3 mQ&1LQ studies: VL: SMD: 0.1, 95% CI: -0.25 to 0.46, l^2=16%, p=0.31 (Boling et al., 2006; Earl, et al., 2005; Karst & Willett, 1995; Powers et al., 1996), 1 mQ study: GMax: SMD: 0.1, 95% CI: -0.52 to 0.72 (Willson et al., 2011), 5 mQ studies: GMed: SMD: -0.09, 95% CI: -0.6 to 0.42, l^2=61%, p= 0.04 (Aminaka et al., 2011; Boling, Bolgla, Mattacola, Uhl, & Hosey, 2006; Earl, et al., 2005; Nakagawa, Muniz, et al., 2011; Willson et al., 2011), 1 mQ study: Adductor longus: SMD: 0.42, 95% CI: -0.2 to 1.05 (Aminaka et al., 2011), 1 mQ study: tensor: SMD: -0.06, 96%CI: -0.75 to 0.63 (Earl, et al., 2005), 1 mQ study: VL/ GMed: SMD: 0.12, 95% CI: -0.53 to 0.78 (Bolgla et al., 2011), 2 mQ studies: VM/ GMed: SMD: 0.46, 95% CI: -0.28 to 1.21, l^2=59%, p=0.12 (Bolgla et al., 2011; Mostamand et al., 2011) (Table 2.4, Appendix 2.20 to 2.22).

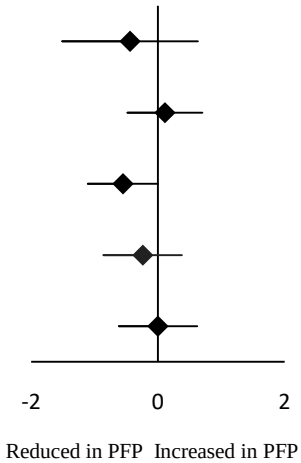
Four studies analysed the onset duration of the VM, VL, GMed, GMax and adductor longus muscle of lower limb muscles, whereby no significant differences could be identified between individuals with PFP and healthy controls (2 mQ studies: VM: SMD: -0.44, 95% CI: -1.51 to 0.63, l^2= 83%, p=0.02 (Aminaka et al., 2011; Powers et al., 1996); 1 mQ study: VL: SMD: 0.11, 95% CI: -0.48 to 0.7 (Powers et al., 1996); 2 mQ studies: GMed: SMD: -0.55, 95% CI: -1.11 to 0, l^2= 35%, p= 0.22 (Aminaka et al., 2011; Willson et al., 2011); 1 mQ: GMax: SMD: -0.24, 95% CI: -0.86 to 0.38 (Willson et al., 2011); 1LQ study: adductor longus: SMD: 0, 95% CI: -0.62 to 0.62 (Aminaka et al., 2011); (Table 2.4, Appendix Table 2.23 to 2.27).

The heterogeneity in studies assessing GMed onset and the onset of VL related to VM was moderate. The regression-analysis showed an association with the different tasks in the onset of the GMed (p=0.04), but not in studies that investigated the onset of VL related to VM (Appendix Table 2.35).

Table 2.4: The comparison of quadriceps, gluteal and thigh muscles onset and the onset duration in individuals with and without PFP

sEMG onset	No of studies	Sample size		Std Mean difference IV, Random 95%CI	Heterogeneity	Std Mean difference IV, Random 95%CI
		PFP	healthy			
Vastus medialis	5	100	93	0.27 [-0.02; 0.55]	Tau^2=0. Chi^2= 2.51, df=4 (p=0.64), I^2= 0%	
Vastus lateralis	4	80	73	0.1 [-0.25; 0.46]	Tau^2=0.02. Chi^2= 3.55, df=3 (p=0.31), I^2= 16%	
Gluteus maximus	1	20	20	0.1 [-0.52; 0.72]	-	
Gluteus medius	5	79	80	-0.09 [-0.6; 0.42]	Tau^2=0.2. Chi^2= 10.15, df=4 (p=0.04), I^2= 61%	
Adductor longus	1	20	20	0.42 [-0.2; 1.05]	-	
Tensor fasciae latae	1	16	16	-0.06 [-0.75, 0.63]	-	
Vastus lateralis-gluteus medius	1	18	18	0.12 [-0.53; 0.78]	-	
Vastus medialis-gluteus medius	2	36	36	0.46 [-0.28; 1.21]	Tau^2=0.17. Chi^2= 2.46, df=1 (p=0.12), I^2=59%	
Vastus lateralis-vastus medialis	6	97	100	-0.62 [-1.05; -0.18]	Tau^2=0.16. Chi^2= 10.88, df=5 (p=0.05), I^2=54%	
sEMG onset duration						
Vastus medialis duration	2	46	39	-0.44 [-1.51; 0.63]	Tau^2=0.49. Chi^2= 5.83, df=1 (p=0.02), I^2=83%	
Vastus lateralis duration	1	26	19	0.11 [-0.48; 0.7]	-	
Gluteus medius duration	2	40	40	-0.55 [-1.11; 0]	Tau^2=0.06. Chi^2= 1.53, df=1 (p=0.22), I^2=35%	
Gluteus maximus duration	1	20	20	-0.24 [-0.86; 0.38]	-	
Adductor longus duration	1	20	20	0 [-0.62: 0.62]	-	





2.6.3.4.3. EMG frequency analysis

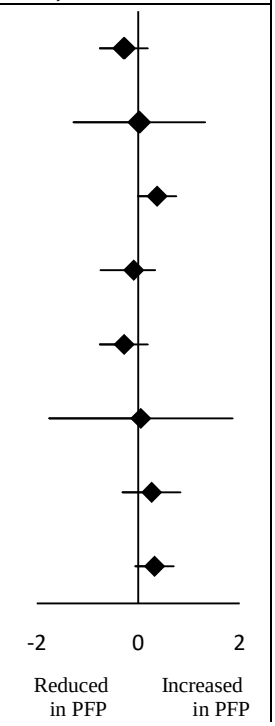
The neural drive of a muscle is a complex neural code of the movement, which implies information about a motor task (Farina & Negro, 2012). The information of the neural drive

can be identified by their frequency bandwidths because altered frequency domain parameters indicate neuromuscular alterations (Briani, de Oliveira Silva, et al., 2015; Farina, Merletti, & Enoka, 2014)

In the final meta-analysis two studies (1 mQ& 1LQ studies) with a total of 53 individuals with PFP and 57 healthy controls investigated the muscular frequency differences between individuals with PFP and healthy participants (Briani, de Oliveira Silva, et al., 2015; Ferrari et al., 2014). Inconclusive evidence indicates no quadriceps frequency differences betweeen individuals with and without PFP (low frequency band: VM: SMD: 0.27, 95% CI: -0.02 to 0.55, I^2=78%, p=0.03, VL: -0.11, 95% CI: -0.65 to 0.43, I^2=37%, p=0.21; medium frequency band: VM: 0.2, 95% CI: -0.02 to 0.41, I^2=91%, p=0.0008, VL: 0.42, 95% CI: -0.2 to 1.05, I^2= 95% p<0.00001; high frequency band: VM: -0.24, 95% CI: -0.86 to 0.38, I^2= 0%, p=0.68, VL: -0.06, 95% CI: -0.75 to 0.63, I^2= 56%, p=0.13, median frequency band: VM: 0.33, 95% CI: -0.09 to 0.75, I^2=0%, p=0.49, VL: 0.32, 95% CI: -0.06 to 0.7, I^2= 0% p=0.69) (Briani, de Oliveira Silva, et al., 2015; Ferrari et al., 2014) (Table 2.5, Appendix Table 2.29).

Table 2.5: The comparison of quadriceps muscles frequency in individuals with and without PFP

sEMG frequency	No of studies	Sample size		Std Mean difference IV, Random 95%CI	Heterogeneity	Std Mean difference IV, Random 95%CI
		PFP	healthy			
Vastus medialis low frequency band	2	53	57	0.27 [-0.02; 0.55]	Tau^2=0.27 Chi^2= 4.53, df=1 (p=0.03), I^2=78%	
Vastus medialis medium frequency band	2	53	57	0.2 [-0.02; 0.41]	Tau^2=0.81. Chi^2= 11.31, df=1 (p=0.0008), I^2=91%	
Vastus medialis high frequency band	2	53	57	-0.24 [-0.86; 0.38]	Tau^2=0. Chi^2= 0.17, df=1 (p=0.68), I^2= 0%	
Vastus medialis median frequency band	2	53	57	0.33 [-0.09; 0.75]	Tau^2=0. Chi^2= 0.49, df=1 (p=0.49), I^2= 0%	
Vastus lateralis low frequency band	2	53	57	-0.11 [-0.65; 0.43]	Tau^2=0.04. Chi^2= 1.59, df=1 (p=0.21), I^2= 37%	
Vastus lateralis medium frequency band	2	53	57	0.42 [-0.2; 1.05]	Tau^2=1.63, Chi^2= 20.71 df=1 (p<0.00001), I^2=95%	
Vastus lateralis high frequency band	2	53	57	-0.06 [-0.75, 0.63]	Tau^2=0.1 Chi^2= 2.27, df=1 (p=0.13), I^2=56%	
Vastus lateralis median frequency band	2	53	57	0.32 [-0.06; 0.70]	Tau^2=0. Chi^2= 0.16, df=1 (p=0.69), I^2= 0%	



2.6.3.4.4. Break phenomenon analysis

The break phenomenon describes a break in torque value during a slow isokinetic eccentric quadriceps open chain activity and is defined as a disturbance in the regularity of the trace if it exceeds more than 10% of the pre-break moment (Anderson & Herrington, 2003). It is believed to be caused by reflex inhibition of the quadriceps muscle, to avoid overstress of the knee joint (Herrington, Williams, & George, 2003). It can be assumed that patients with PFP adopt this strategy to decrease the PFJ load and the experienced pain (Anderson & Herrington, 2003).

In the final meta-analysis only one LQ study (LQ studies) with a total of 20 individuals with PFP and 20 healthy controls was included in this systematic review (Appendix: Table 2.3, 2.6 & 2.9) (Anderson & Herrington, 2003). Anderson & Herrington, 2003 analysed the break phenomenon during an isokinetic measurement and a stair stepping task and showed the presence of the break phenomenon in 60% to 70% of the patients with PFP and in 15% of the control group during both tasks (Anderson & Herrington, 2003).

2.6.3.5. Reduced muscle flexibility

Muscle flexibility refers to the ability of a muscle to yield to a stretch force and the ability to move a muscle through the full range of motion (ROM) (Can, 2012; Wallmann, 2016). Flexibility is classified into static flexibility and dynamic flexibility. Static flexibility relates to the ability of a muscle to be passively moved to the end range of motion and dynamic flexibility refers to the ability of a muscle to be moved as a result of muscle contraction (Can, 2012; Wallmann, 2016).

Reduced muscle flexibility is associated with an increased risk to develop injuries, because only an adequate joint mobility allows a normal kinesiological relationship between the limb segments during a movement (Can, 2012; Williams & Welch, 2015). Immobilisation after a knee injury might be one reason causing a shortness of a muscle (Wallmann, 2016). The shortness is mostly caused by a spasm of the surrounding muscle to protect the affected joint (Alonso, McHugh, Mullaney, & Tyler, 2009; Can, 2012).

In total seven studies (4 mQ and 3LQ studies) with a sample size of 153 individuals with PFP and 426 without PFP analysed muscle flexibility were included (Earl, et al., 2005; Hudson,

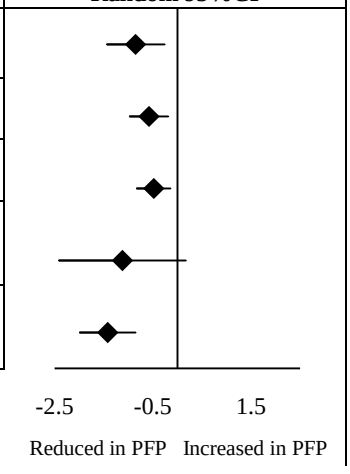
2006; Ohjeoung et al., 2014; Peeler, 2007; Piva et al., 2005; White, 2009; Witvrouw et al., 2000) (Appendix: Table 2.3, 2.6 & 2.9).

Moderate evidence reveals a reduced muscle flexibility of the hamstrings in individuals with PFP compared with healthy controls (hamstrings: 3 mQ& 2LQ studies, SMD: -0.48, 95% CI: -0.83 to -0.14, l^2= 40%, p= 0.15) (Earl, et al., 2005; Ohjeoung et al., 2014; Piva et al., 2005; White, 2009; Witvrouw et al., 2000) (Table 2.6, Appendix Table 2.27).

Low evidence shows that individuals with PFP have a decreased flexibility in ITB and quadriceps compared with healthy controls (ITB: 3 mQ studies, SMD: -0.85, 95%CI: -1.43 to -0.26, l^2= 51%, p=0.13) (Earl, et al., 2005; Hudson, 2006; Piva et al., 2005), (quadriceps: 1 mQ& 2LQ studies, SMD: -0.58, 95% CI: -0.97 to -0.19; l^2= 54%, p= 0.12) (Peeler, 2007; Piva et al., 2005; Witvrouw et al., 2000). Very limited evidence suggests a reduced flexibility of the soleus muscle (1 mQ study, SMD: -1.42, 95% CI: -1.99 to -0.85) (Piva et al., 2005). Inconclusive evidence indicates no difference in flexibility of the gastrocnemius muscle between individuals with PFP and healthy controls (1 mQ& 1LQ studies, SMD: -1.12, 95% CI: -2.41 to 0.17, l^2= 92%, p= 0.0005) (Piva et al., 2005; Witvrouw et al., 2000) (Table 2.6, Appendix Table 2.30).

Table 2.6: The comparison of muscle flexibility in individuals with and without PFP

Flexibility	No of studies	Sample size		Std Mean difference IV, Random 95%CI	Heterogeneity	Std Mean difference IV, Random 95%CI
		PFP	healthy			
Iliotibial band flexibility	3	58	58	-0.85 [-1.43; -0.26]	Tau^2=0.14 Chi^2= 4.12, df=2 (p=0.13), l^2= 51%	
Quadriceps flexibility	3	94	331	-0.58 [-0.97; -0.19]	Tau^2=0.06 Chi^2= 4.31, df=2 (p=0.12), l^2= 54%	
Hamstrings flexibility	5	95	358	-0.48 [-0.83; -0.14]	Tau^2=0.06 Chi^2= 6.72 df=4 (p=0.15), l^2= 40%	
Gastrocnemius flexibility	2	54	288	-1.12 [-2.41; 0.17]	Tau^2=0.8. Chi^2= 12.28, df=1 (p=0.0005), l^2= 92%	
Soleus flexibility	1	30	30	-1.42 [-1.99; -0.85]	-	



2.6.4.6. Muscular fatigue

Muscle fatigue is defined very heterogeneously in the literature (Williams & Ratel, 2009). Two definitions of fatigue are commonly accepted, which are:

1) Fatigue is an inability to maintain and generate a required force after repeated muscle contractions (Jones & Round, 1990; Negahban et al., 2013; Williams & Ratel, 2009).

2) Fatigue is an exercise-induced reduction in the muscular ability to produce power, irrespective of the task completion (Williams & Ratel, 2009).

Fatigue can be caused by various factors, such as an impaired reflex drive, impaired neuromuscular transmission, impaired motor unit action potential (MUAP), impaired excitation, impaired energy supply or a reduced motivation (Williams & Ratel, 2009). Studies revealed that the risk of developing a sport injury increased during the late stage of competitions in which the muscles were more fatigued (Gabbett, 2000; Pinto, Kuhn, Greenfield, & Hawkins, 1999; Reimer & Wikstrom, 2010; Woods, Hawkins, Hulse, & Hodson, 2003). It is believed that muscle fatigue is one of the main mechanisms that causes impaired balance and thereby a dynamic instability of the lower limb (Bayramoglu, Toprak, & Sozay, 2007; Negahban et al., 2013; Reimer & Wikstrom, 2010). Thus, quadriceps fatigue seems to play a particularly important role in knee injuries, such as PFP, knee osteoarthritis and anterior cruciate ligament rupture (Bazett-Jones, Cobb, O'Connor, Huddleston, & Earl-Boehm, 2015; Berger, Regueme, & Forestier, 2010; Bouillard, Jubeau, Nordez, & Hug, 2014; Callaghan et al., 2001; Callaghan, McCarthy, & Oldham, 2009; Chan, Lee, Wong, Wong, & Yeung, 2001; R. T. H. Cheung, 2012; Lessi & Serrao, 2015; Bayramoglu et al., 2007; Negahban et al., 2013; Power, 2008).

In the final meta-analysis in total six studies (3 mQ and 3LQ studies) on fatigue and endurance with a sample size of 96 individuals with and 96 without PFP were included (Bazett-Jones et al., 2013; Callaghan et al., 2001; Dierks et al., 2008; McMoreland et al., 2011; Negahban et al., 2013; Willson et al., 2008). Due to the heterogeneity of outcome measures, no pooling of data from the six included studies was undertaken and the studies are presented descriptively (Appendix: Table 2.3, 2.6 & 2.9).

Two studies (1 mQ, 1LQ) tested fatigue by analysing strength of the hip abductors and external rotators before and after an exhaustive run (Bazett-Jones et al., 2013; Dierks et al., 2008). Bazett Jones et al. (2013) showed that the external hip rotator, hip extensor and hip abductor strength was significantly reduced after the run in individuals with PFP. In contrast, Dierks et al. (2008) detected the only significant difference between both groups in run

duration, whereby the running duration of individuals with PFP was 10 minutes shorter than that in healthy controls.

One LQ study analysed EMG VM: VL fatigue ratio and characteristics after an isometric closed chain quadriceps contraction in individuals with and without PFP. The study could not identify differences between and within the groups, but described a higher variability of VM: VL fatigue ratios in individuals with PFP (Callaghan et al., 2001).

In one MQ study the fatigability of hip muscles in individuals with and without PFP was tested by means of an isokinetic contraction with 30 repetitions. The results demonstrated no significant group difference in endurance for hip abduction and internal rotation and only a moderate correlation between isometric strength and endurance for hip abduction and external rotation (McMoreland et al., 2011).

One LQ study also used an isokinetic strength repetition to fatigue the hip abductors and knee extensors in individuals with and without PFP. Both groups had similar fatigue effects, whereby fatigue significantly influenced stability. Fatigue of the hip abductors led to greater changes in stability compared with quadriceps fatigue (Negahban et al., 2013).

And lastly, one MQ study applied a lower extremity exertion protocol of repetitive single-legged jumps. Individuals with PFP demonstrated a greater pelvis drop than the control group, with a growing difference with exertion. Furthermore, individuals with PFP had an increased hip flexion and hip adduction angle and a decreased hip internal rotation angle throughout the exertion protocol. These group differences were consistent after exertion. Mean strength measurements for the lateral trunk flexion, hip abduction and hip external rotation were significantly lower in individuals with PFP than that in healthy controls, however, these differences were not dependent on exhaustion (Willson et al., 2008).

2.6.5. Discussion

This review provides important findings regarding muscular dysfunction in PFP. The studies that assessed muscle strength revealed a strong evidence for weaker hip abductor and external hip rotator muscles and a moderate evidence for a reduced internal hip rotator, hip extensor, hip adductor and knee extensor strength in individuals with PFP. These findings are in accordance with previous systematic literature reviews, which found reduced hip (Almeida,

de Moura Campos Carvalho de Silva, Franca, Magalhaes, Burke, & Marques, 2015; Lankhorst et al., 2013; Rathleff et al., 2014; Van Cant et al., 2014; Waryasz & McDermott, 2008) and knee muscle strength (Lankhorst et al., 2013; Waryasz & McDermott, 2008). However, a substantial heterogeneity, with I^2 between 59% and 80%, was evident in strength studies, which has also been reported in previous systematic reviews (Almeida et al., 2015; Rathleff et al., 2014). In contrast to previous literature, this study carried out an analysis of factors that potentially relate to the observed heterogeneity, such as gender, test-position, normalisation method and values used (peak or averaged peak). However, neither of these factors influenced the strength results in studies consistently and thus, the present heterogeneity remains unexplained. Furthermore, even factors that revealed a significant association to the heterogeneity, such as the same testing-position during the knee extension strength test ($p=0.04$), still showed a substantial heterogeneity in the subgroups (68% and 72%) (Appendix Table 3.32). This emphasises the complexity of the current assessment of strength and emphasises that further research should strive for a greater homogeneity in strength assessments.

In addition to reduced quadriceps strength, the meta-analysis also revealed that individuals with PFP had reduced quadriceps muscle mass, which is in agreement with previous literature (Giles et al., 2013). However, this result should be interpreted with caution, because despite a significant result only one of the four included studies found a significant difference in quadriceps atrophy between the two groups. Muscle size is strongly correlated to muscle strength (Giles et al., 2013; Lieber, 2010) and thus atrophy is most likely a result of reduced force output, that can be caused by physiological changes or pain induced AMI (Giles et al., 2013). However, it does not allow firm evidence to draw conclusions about the reason for the existence of atrophy nor the conclusion about atrophy being the effect or the cause of PFP. In addition, the number of studies analysing muscular atrophy is still limited and further research is needed to be able to evaluate the extent of atrophy in individuals with PFP.

Although, weakness and atrophy might be caused by pain induced quadriceps arthrogenic muscular inhibition (AMI), only two studies investigated quadriceps AMI in individuals with PFP. These studies demonstrated a significantly higher AMI in individuals with PFP compared to healthy participants. AMI has been commonly observed in individuals with knee injuries and is a protective, reflexive mechanism of the body to alter the neural drive of the joint's surrounding muscles and thereby reducing the joint load (Hart et al., 2010; Rice &

McNair, 2010). Sustained AMI of the quadriceps can lead to persistent quadriceps weakness, which might cause alterations of kinetics and kinematics (Hart et al., 2010; Pietrosimone et al., 2014; Rice & McNair, 2010). Thus, if AMI is left untreated it might prevent recovery and might lead to joint damage (Hart et al., 2010; Palmieri-Smith et al., 2013; Rice & McNair, 2010). Furthermore, AMI can also lead to the loss of the ability to efficiently control the eccentric quadriceps phase (Hart et al., 2010). Such an inability to control the eccentric quadriceps phase can be investigated by analysing the break phenomenon, which describes a break in the quadriceps torque or knee velocity curve during an eccentric quadriceps activity (Anderson & Herrington, 2003) and is believed to be caused by reflex inhibition of the quadriceps muscle, to avoid overstress of the PFJ (Anderson & Herrington, 2003; Herrington et al., 2003) and to decrease the pain experienced at a specific point in range (Anderson & Herrington, 2003). Thus, the break phenomenon might enable crucial insights into the muscle function. Although the majority of studies have investigated the eccentric quadriceps strength (Callaghan & Oldham, 2004b; Duvigneaud et al., 2008; Dvir et al., 1990; Kaya, et al., 2010; Van Tiggelen, Witvrouw, Coorevits, et al., 2004; Werner, 1995), only one study (LQ) analysed the break phenomenon. This study revealed that the break phenomenon was present in individuals with PFP (Anderson & Herrington, 2003). It appears that individuals with PFP are unable to smoothly control the eccentric quadriceps contraction (Anderson & Herrington, 2003; Herrington et al., 2003). However, further research is required to investigate the prevalence of AMI and the associated break phenomenon in individuals with PFP (Anderson & Herrington, 2003). A combined analysis of AMI and the break phenomenon might enable the investigation of their contribution to muscular weakness and neuromuscular control deficits and whether these factors are correlated.

Neuromuscular control deficits are commonly observed due to a relieving posture after an injury (Grimby & Thomee, 2003). Surface EMG can be used as a non-invasive method to supply clinically meaningful information about these neuromuscular control deficits as it provides the direct link to the muscle and information related to disturbed motor control and locomotor gait-related coordination strategies (Farina et al., 2014; Frigo & Crenna, 2009). These neuromuscular control deficits can be analysed by investigating the muscle activation intensity (EMG amplitude), muscle timing (EMG onset/ offset) and the motor unit recruitment (EMG frequency).

EMG amplitude has often been used to provide measures of the intensity of the neural drive and motor unit recruitment strategies (Farina et al., 2014). This systematic review revealed no difference of the EMG amplitude between individuals with and without PFP. These findings are in agreement with a prior systematic review on gluteal muscle activation in individuals with PFP (Barton et al., 2013). However, the included studies demonstrated a great heterogeneity. The analysis of factors that potentially related to the observed heterogeneity showed that two factors were significantly associated with the heterogeneity: (1) the EMG rectification and processing parameters and (2) the normalisation method. However, it should be noted that the heterogeneity within the subgroups was still substantial. To date the maximal voluntary contraction (MVC) normalisation is the most common method used to normalise the EMG signal (Frigo & Crenna, 2009). However, MVC measurements are carried out in different test positions, with different isokinetic and isometric test devices and different test intensities (submaximal and maximal contraction) and the diversity in MVC could be the reason for the differences in the normalised EMG results. Another problem of the MVC normalisation is the fact that it is impossible to ensure that the participant is really performing their maximum force during the MVC test. Furthermore, as several muscles are contributing to a voluntary effort it is difficult to determine the MVC value of a particular muscle correctly (Frigo & Crenna, 2009). Thus, the normalisation of the EMG signal with the MVC method can cause a greater variability within the EMG amplitude studies (Frigo & Crenna, 2009). Even studies that used the same task and the same electrode application showed significant differences (Coqueiro et al., 2005; Mostamand et al., 2011). Two studies described the similar electrode-placement and analysed the amplitude of the VL and the VM during a semi-squat (45° of knee flexion). One study revealed during a bilateral squat significantly higher intensities of VL and VM in the PFP population (Coqueiro et al., 2005), whereas the other study demonstrated significantly reduced intensities during a single leg squat in individuals with PFP (Mostamand et al., 2011). This heterogeneity raises the key question of what portion of variability is truly linked to the differences in motor control and what to the EMG measuring and processing technique. In addition, previous studies have shown that the size of surface action potential is only moderately linked to the motor-unit size and thus the amplitude size depends on factors which are difficult to monitor in experimental conditions (Farina, Holobar, Merletti, & Enoka, 2010). This reveals the impracticality to express the muscle activation in absolute values, as it is currently done with the MVC normalisation.

Another possible reason that no differences between the groups in EMG intensity were detected might be because the tasks were not sufficiently demanding to elicit differences. However, it should be emphasized that if PFP individuals had altered muscle activity within a specific muscle it would be expected to be apparent throughout all tasks even in less demanding tasks.

The analysis of the muscle timing (EMG onset/ offset) suggested a trend towards a delay of VM and VL in individuals with PFP compared with healthy controls, which is in accordance with previous literature (Chester et al., 2008). Previous studies suggested that a delayed onset of the VM in relation to VL causes an abnormal lateral tracking, which results in an increased patellofemoral contact pressure (Bolgla et al., 2010; Fagan & Delahunt, 2008). It has been hypothesized that VM must be activated before VL for an optimal patella-tracking (Cowan et al., 2001). The imbalance is believed to originate from an altered neuromuscular motor control of the VM and VL or from a reduced capability of VM to produce force (Fagan & Delahunt, 2008).

However, the clinical relevance of these significant differences is debatable. Wong (2009) emphasized that the EMG onset does not necessarily show that the muscle tension of the VM is strong enough to mobilize the patella and thus the EMG onset might not represent the mechanical onset of patella motion. Other authors critically scrutinised whether small differences of VM delay are clinically relevant (Chester et al., 2008; Lankhorst et al., 2012). Additionally, studies have reported a considerable heterogeneity between and within studies and remarked that differences in results might be equally due to chance and thus should be viewed with caution (Chester et al., 2008; Hug, 2011; Lankhorst et al., 2012). To date, the methods to determine the onset and offset vary considerably. Most studies defined the onset and offset by using the standard deviation (SD) of the signal above the baseline. But the SD definition for the onset/ offset of the muscles varies between 2SD up to 5SD of the signal above the baseline. Some studies combined the SD with the time of the occurrence by requiring a minimum period of 20 to 25 ms activation. Other studies required for the definition of the onset/ offset an intensity of the signal of at least 200-300 µV to define it as muscle activity or used computer detection algorithms. Another drawback is that onset/ offset detection methods usually do not take inter-cycle variability into account. The inter-cycle variability describes the intra- and inter-individual variability in kinematics during the phases of each task, e.g. stance phase in running. The presence of the inter-cycle variability makes it

difficult to determine the significance of the shift within a subject. That is why a slight shift should not be considered as significant if the inter-cycle variability is high and supports the critical question of the clinical relevance of small differences (Hug, 2011). However, the heterogeneity of the studies that investigated the EMG onset in this meta-analysis of the quadriceps was very low.

The meta-analysis revealed no differences of the frequency bandwidth of the VM and VL in individuals with PFP. It is assumed that EMG frequency domain parameters provide information of the altered muscle activation or muscle inhibition, because these changes are reflected in the properties of the EMG (Farina et al., 2014). However, the studies included in this meta-analysis aimed to investigate the diagnostic accuracy of the EMG parameters associated with PFP and did not focus on the examination of differences between individuals with PFP and healthy controls. Furthermore, although the two studies were conducted by the same research groups, the heterogeneity between the two studies was substantial. Thus, future research is required to analyse the neural drive of lower extremity muscles in individuals with PFP and to investigate the real potential of it.

Electromyography enables a direct link to the muscle performance. However, the EMG signal requires a careful interpretation. Despite the existence of the Standards for Reporting EMG data (Merletti, Wallinga, Hermens, & Freriks, 1999), the SENIAM guidelines (Hermens, Freriks, Merletti, Stegeman, Blok, Rau, Disselhorst-Kling, & Hägg,1999), recommendations provided by the Journal of Electromyography & Kinesiology (Journal of Electromyography & Kinesiology, 1996) and the International Society of Electromyography and Kinesiology (Winter, Rau, Kadefors, Broman, & De Luca, 1980) studies collect, analyse and report differently EMG data. Thus, further research should strive for a harmonisation of the recording techniques in terms of electrode positioning, signal conditioning, signal normalisation and filtering (Frigo & Crenna, 2009; Hug, 2011). In addition, the combination of EMG with kinematic and kinetic measurements might enable a better detection of underlying pathomechanical mechanisms and should receive more attention in future studies (Frigo & Crenna, 2009). The analysis of co-contraction pattern between muscle groups, such as the hamstrings and quadriceps muscle group, would be a useful addition, as this might give important information and should be addressed more in future studies.

The meta-analysis also revealed that individuals with PFP have a reduced flexibility of the hamstrings muscles. Reduced flexibility in the hamstrings might be clinically relevant as it

could elicit more knee flexion during activities and might thereby lead to increased patellofemoral joint reaction forces (Piva et al., 2005). A reduced flexibility of the iliotibialis (ITB) is believed to cause a reduced rotation flexibility of the hip and thereby result in a lateral tracking of the patella, which might lead to higher contact pressure of the patella and thereby increase patellofemoral stress (Hamstra-Wright, Earl-Boehm, Bolgla, Emery, & Ferber, 2016). In addition, reduced flexibility of the hamstrings require a higher quadriceps force to overcome the passive resistance of the hamstrings muscles and can thereby result in an increased patellofemoral joint reaction forces (Piva et al., 2005). Furthermore, a reduction of hamstrings flexibility might increase the hamstrings loading and thereby cause an increase of the total contact force to the lateral facet of the patella (Elias et al., 2011).

This meta-analysis found inconsistent results on differences after fatiguing exercises between individuals with PFP and healthy controls. Low evidence indicates that participants with PFP tend to have weaker hip abductor muscles when running in the exerted state, which was associated with an increased hip adduction angle, which could result in a dynamic knee valgus and might cause an increased lateral patellar tilt and thereby could result in retropatellar stress (Dierks et al., 2008; Willson et al., 2008). Most studies documented the pain levels before and after the fatiguing exercises and reported a pain increase with increased fatigue. This could make it difficult to distinguish if the changes have been triggered by pain or fatigue and requires further research.

2.6.6. Conclusion

This review confirmed the strong to moderate evidence of gluteal and quadriceps weakness in individuals with PFP. However, the review also showed that the existing heterogeneity of the recent studies that assessed lower limb strength remained to be an important and unexplained fact. Further research should strive for a harmonisation of strength assessments. Furthermore, this review showed that, although many studies investigated muscle function of individuals with PFP, some important underlying factors, such as AMI and the break phenomenon remained relatively understudied. These factors might enable an insight into muscular dysfunction and might even lead to an amendment of the current treatment scheme. Thus, future research is needed to investigate AMI and the break phenomenon in individuals with PFP.

This systematic review revealed: (1) no difference of the EMG amplitude between individuals with and without PFP, (2) inconclusive findings of the frequency bandwidth of the VM and VL and (3) a trend towards a delay of VM and VL in individuals with PFP. The different rectification, filtering and normalisation techniques of the EMG signal explained partially the increased heterogeneity between the studies. EMG is a useful tool to investigate muscular dysfunction in individuals with PFP, however, a greater homogeneity in EMG analysis is needed to allow a comparison of the EMG study results and to be able to review the current evidence more appropriately. Furthermore, the combination of EMG with kinematic and kinetic measurements and the analysis of muscular co-contraction patterns might enable a more clinical understanding of contributing muscular dysfunctional factors of PFP.

2.6.7. Methodical considerations and limitations

The literature search was performed in PubMed (MEDLINE), Cochrane library, CINAHL, SPORTDiscus and Web of Science (WoS). Since not all literature databases available were included, there was a risk that relevant literature was missing, this risk was heightened by the exclusion of 24 studies which had not been accessible. Furthermore, only studies with enough numerical data were included, which caused the exclusion of in total 30 articles. This might have biased the results, especially the results of the EMG analysis, with a total of 22 studies excluded.

Since this systematic review aimed to identify the current evidence of muscular dysfunction in PFP it seemed to be essential to include all relevant studies. Consequently the heterogeneity of the included studies increased, especially because some studies recruited exclusively military recruits, students or athletes performing a specific sport. In addition, many studies did not provide information about a clear defined pain location, pain duration, or activities that aggravate the pain. Thus, more homogeneity could have been established by applying stricter inclusion criteria for studies. However, since many studies did not report detailed information about their participants, it would have caused an exclusion of a high number of studies and that would have biased the outcome as the reduced number of studies would have not been representative for the current evidence.

2.7. Treatment of patellofemoral pain

The numerous factors which were linked to PFP resulted in the development of various conservative treatments. Several studies investigated the effects of exercise treatment (Clijsen, Fuchs, & Taeymans, 2014; Heintjes et al., 2003; Honarpishe, Bakhtiary, & Olyaei, 2015; Van der Heijden, Lankhorst, van Linschoten, Bierma-Zeinstra, & van Middelkoop, 2015; Van Linschoten, van Middelkoop, Heintjes, Bierma-Zeinstra, Verhaar, & Koes, 2011), strength training (Chiu, Wong, Yung, & Ng, 2012; Dolak, Silkman, McKeon, Hosey, Lattermann, & Uhl, 2012; Ferber et al., 2015; Fukuda et al., 2012; Ismail, Gamaleldein, & Hassa, 2013; Nakagawa et al., 2008; Willy & Davis, 2011), education (Barton & Crossley, 2016; Barton & Rathleff, 2016), taping (Aminaka & Gribble, 2008; Christou, 2004; Cowan, Bennell, & Hodges, 2002; Crossley et al., 2001; Crossley et al., 2000; Lee Herrington, 2001; Hickey, Hopper, Hall, & Wild, 2016; Mostamand, Bader, & Hudson, 2010; Mostamand, Bader, & Hudson, 2013; Osorio et al., 2013; Salsich, Brechter, Farwell, & Powers, 2002; Song et al., 2014), braces (Denton et al., 2005; Lun, Wiley, Meeuwisse, & Yanagawa, 2005; Petersen, Ellmann, Rembitzki, Scheffler, Herbort, Bruggemann, Best, Zantop, & Liebau, 2016; Petersen, Ellermann, Rembitzki, Scheffler, Herbort, Sprenker, Achtnich, Bruggemann, Best, Hoffmann, Koppenburg, & Liebau, 2014; Powers, Doubleday, & Escudero, 2008; Powers, Ward, et al., 2004a; Powers, Ward, Chen, Chan, & Terk, 2004b; Swart, van Linschoten, Bierma-Zeinstra, & van Middelkoop, 2012), foot orthoses (Barton, Munteanu, et al., 2010; Boldt, Willson, Barrios, & Kernozek, 2013; M. S. Rathleff et al., 2015), manipulation (Crowell & Wofford, 2012; Grindstaff, 2009; Grindstaff, Hertel, Beazell, Magrum, Kerrigan, Fan, & Ingersoll, 2012; Miller, Westrick, Diebal, Marks, & Gerber, 2013) and acupuncture (Bizzini, Childs, Piva, & Delitto, 2003; Crossley et al., 2001).

Although high-quality systematic reviews have been carried out on treatment approaches of individuals with PFP, a paucity of research and a discord between the evidence base and expert clinical reasoning became apparent (Barton et al., 2015). Thus, Barton et al. carried out a high-quality systematic review covering the literature up to September 2013. Moreover they combined the findings with clinical reasoning from 17 international experts, who were required to have at least 5 years clinical experience with PFP as a specialist focus and had to be actively involved in PFP research (Barton et al., 2015). Their opinion was obtained by semi-structured interviews. Based on these findings Barton et al. created a ‘Best Practice Guide to Conservative Management of Patellofemoral Pain’ (Barton et al., 2015).

At the International Patellofemoral Pain Research Retreat in Manchester 2015 a consensus meeting was held to update the evidence base and to generate a consensus-based recommendation. Therefore a systematic review was carried out that summarised the findings between January 2010 and June 2015. Based on the findings of the systematic review and the 'Best Practice Guide to Conservative Management of Patellofemoral Pain' statements were formulated regarding each intervention, which reflected the evidence and the effect on pain, function and overall improvement. A PFP investigators panel was formed by 35 attendees of the International Patellofemoral Research Retreat, including physiotherapists, doctors, podiatrists, biomechanics, epidemiologists and sports therapists. The experts were asked to vote on 24 statements by using a scale from 0 (not appropriate) to 9 (appropriate) (Crossley et al., 2016b). Based on the consensus voting, the following six recommendations were made:

1. To reduce pain in the short, medium and long term and to improve function in the medium and long term, exercise-therapy is recommended.

2. Combining hip and knee exercises is recommended to reduce pain and improve function in the short, medium and long term and this should be favoured over knee exercises alone.

3. To reduce pain in the short and medium term, combined interventions are recommended.

4. To reduce pain in the short term, foot orthoses are recommended.

5. Patellofemoral, knee and lumbar mobilisations are not recommended.

6. Electrophysical agents are not recommended (Crossley et al., 2016b).

These recommendations and the recommendations of Barton et al. (Barton et al., 2015) will be explained more into depth in the following chapter.

2.7.1. Exercise principles

The findings showed that five principles are key factors to ensure a successful treatment:

1) PFP is a multifactorial condition and requires an individually tailored multimodal approach (Barton et al., 2015; Crossley et al., 2016b).

2) Immediate pain relief is a priority to gain the trust of the patients and to improve function (Barton et al., 2015; Crossley et al., 2016b).

3) Active over passive interventions should be emphasised (Barton et al., 2015) and exercises as a stand-alone treatment are recommended Crossley et al., 2016b).

4) Patient education and activity modification is essential for a successful treatment (Barton et al., 2015).

5) Combined interventions are recommended to reduce pain in the short and medium term (Crossley et al., 2016). Furthermore, multimodal interventions, such as the gluteal and quadriceps strengthening and stretching combined with patellofemoral joint mobilisation and taping, resulted in the strongest and most consistent evidence (Barton et al., 2015; Crossley et al., 2016).

The investigators recommended that no more than 3-4 exercises should be prescribed to ensure the compliance of the patient with the treatment. These recommendations were contrary to high dose rehabilitation programmes of more than 4 exercises, which had shown to be more successful than low dose rehabilitation programmes (Barton et al., 2015).

2.7.2. Active interventions

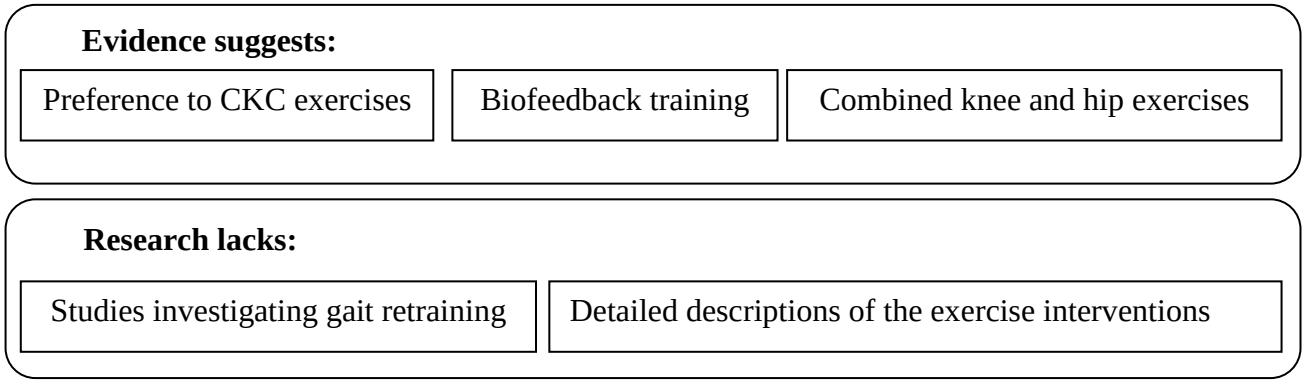


Figure 2.4: Summary of the current recommended active interventions

Active interventions need to include gluteal strengthening exercises to ensure successful rehabilitation (Barton et al., 2015). Whereby knee and hip exercises should be combined to reduce pain and improve function (Crossley et al., 2016). A therapy-regimen tailoring hip-focused combined with knee-focused exercises seem to result in superior outcomes compared with isolated knee-focused exercises (Crossley et al., 2016) (Figure 2.4).

No clarity could be reached if open kinetic or closed kinetic exercises are more effective to train the quadriceps strength. However, it could be concluded that preference should be given to closed kinetic chain (CKC) exercise in order to replicate function (Figure 2.4). Open kinetic chain exercises contrarily can be useful during early stage rehabilitation to strengthen the quadriceps more specifically (Barton et al., 2015).

Current evidence suggests that the vastus medialis shows a delayed activity in relation to the vastus lateralis and thus EMG biofeedback is recommended to address this problem (Barton et al., 2015). If an EMG biofeedback training programme cannot be performed because of the lack of material, instead the biofeedback can be provided by using mirrors, or video recording to facilitate an improvement of hip and knee mechanics (Barton et al., 2015) (Figure 2.4). Furthermore, the active interventions can also incorporate core stability or trunk strengthening exercises (Barton et al., 2015).

Active interventions such as gait retaining were advocated by experts. However, the implementation of these retraining programmes in clinical practice might be challenging, as running retraining is mostly carried out in gait laboratories (Barton et al., 2015).

Although exercise therapy has proven to be successful the current research lacks detailed descriptions of the exercise interventions, which is limiting the translation of research findings into clinical practice (Crossley et al., 2016).

2.7.3. Passive interventions

Evidence suggests:

Patella taping and bracing and foot orthoses if more specifically targeted to individuals	Hamstrings and calf muscles stretching	Trrigger points, electrotherapy, lumbar manipulations cannot be recommended

Research lacks:

Studies investigating braces and straps that focus on the stabilisation of the frontal and transverse plane of the hip, rather than the coronal and sagittal plane of the knee.

Figure 2.5: Summary of the current recommended passive interventions

Studies have shown that patella taping might decrease acute pain and thus can be recommended in early rehabilitation stages (Barton et al., 2015; Logan et al., 2017). Patella braces also showed an immediate pain relief and thus can be recommended in early rehabilitation stages if patella tape cannot be applied due to skin irritation or allergies (Barton et al., 2015) (Figure 2.5).

The evidence on foot orthoses showed conflicting results, which is also caused by the situation that they are heterogenously prescribed for individuals with PFP. Despite the conflicting evidence experts concluded that foot orthoses can be recommended to reduce pain in the early stage of rehabilitation (Crossley et al., 2016) (Figure 2.5). However, the efficacy of foot orthoses might improve if they are more specifically targeted to individuals with a clear foot pronation and thus who are more likely to benefit (Barton et al., 2015).

Passive interventions such as lower limb stretching should not be performed in isolation. However, the involvement of especially hamstrings and calf stretches is recommended to ensure optimised knee and ankle biomechanics (Barton et al., 2015). Experts did not recommend the stretching of the iliotibial band (Barton et al., 2015) (Figure 2.5).

Both guidelines recommended flexible knee braces in acute knee pain conditions (Barton et al., 2015; Crossley et al., 2016). Studies revealed that patellofemoral bracing did not improve patella tracking under dynamic loaded (Powers, Ward, Chan, Chen, & Terk, 2004). It is believed that patellofemoral braces might reduce pain by increasing contact area. A sleeve or stabilising strap might increase the contact of the patella in the femoral tochlea. However, results of knee braces in PFP are still mixed and it is often believed that they might cause weakness in the surrounding muscles (Callaghan, Parkes, & Felson, 2016; Rodriguez-Merchan, 2014; Van der Heijden et al., 2015). Callaghan et al. (2016) tested a flexible knee brace over a period of 6 and 12 weeks in individuals with patellofemoral osteoarthritis and showed that the maximal strength of the quadriceps remained the same, but that the AMI significantly decreased. In addition, the study of Callaghan et al. (2016) revealed that participants with patellofemoral osteoarthritis showed a modest increase in quadriceps strength after 12 weeks. Sinclair et al. (2016) investigated the effect of a knee brace on lower extremity kinematics in participants with PFP. They showed that the knee brace reduced significantly the internal peak knee abduction moment and improved the outcome of pain,

sport function and daily living and quality of life of the knee injury and osteoarthritis Outcome score in individuals with PFP (Sinclair, Selfe, Taylor, Shore, & Richards, 2016). Since flexible knee braces seem to not cause quadriceps weakness and improve lower limb kinetics, they might be a beneficial treatment for participants with PFP to modify lower limb biomechanics. Although it is known that an excessive dynamic knee valgus is prevalent in individuals with PFP, to date braces focus on the stabilisation of the coronal and sagittal plane of the knee joint and do not address the transverse plane of the hip (Figure 2.5).

Other passive interventions, such as trigger points, electrotherapy, lumbar manipulations and ultrasound were not effective and thus are not recommended in the therapy of PFP (Barton et al., 2015; Crossley et al., 2016) (Figure 2.5). However, if muscle and facial tightness is present massage can be additionally performed. Patellofemoral joint mobilisation can be additionally performed, but only if the patellofemoral joint is not hypermobile. Mobilisation of the ankle is considered as an important exercise to avoid an over-pronation and to ensure appropriate shock absorption (Barton et al., 2015; Crossley et al., 2016).

2.8. Discussion and conclusion

Patellofemoral pain is the most frequently diagnosed condition in individuals with knee complaints and especially prevalent in young and physical active adults.

Long term follow up studies revealed that the majority of individuals with PFP experienced an unfavourable recovery, despite initially receiving treatment and education. These results show that PFP is not self-limiting (Lankhorst et al., 2015). Persistent pain can negatively affect daily occupational tasks, physical activity, social participation and general and mental health. Thus, PFP should be framed as a condition that has the potential to become chronic and the treatment should address the chronic aspect as well.

The pathophysiology of PFP is multifactorial and associated with factors which are causing a maltracking of the patellofemoral joint. Biomechanical studies have shown that individuals with PFP demonstrated altered kinematic and kinetic pattern. Although studies emphasise the importance of investigating active structures (muscles and tendons) in combination with a biomechanical analysis, it has not yet been realized in individuals with PFP (Claudon et al., 2012; Dionisio, Marconi, dos Santos, & Almeida, 2011; Kwak et al., 2000; Lucareli, Amir, Bley, Nayra, Garbelotti, et al., 2014; Munkh-Erdene, Masaaki, Nakazawa, Aoyagi, &

Kasuyama, 2011; Powers et al., 1997; Salsich et al., 2001). Many studies have been published on muscular dysfunctional factors and revealed that current research focuses predominantly on muscle strength measurements and the investigation of neuromuscular control deficits by using EMG. In contrast, the investigation of AMI is lacking and to date it remains unclear whether individuals with PFP have weak or inhibited muscles. The advantage of a holistic approach by combining biomechanical analysis with functional muscle measurements has been proven in several studies. However, holistic approaches combing biomechanical analysis with functional muscle measurements have not been applied in individuals with PFP. Thus, it remains unknown which biomechanical alterations are associated with muscular underlying factors of PFP.

Guidelines for treatment programmes of PFP have been recently developed based on systematic reviews on conservative treatments and expert opinions. These guidelines recommend that pain should be reduced in the short, medium and long term. Furthermore, to improve function in the medium and long term, exercise-therapy is recommended. To achieve the reduction in pain and improvement in function it is advised to combine hip and knee exercises. Foot orthoses, knee braces, straps and patellar tape can be applied to reduce pain in the short term. The use of patellofemoral, knee and lumbar mobilisations, as well as electrophysical agents are not recommended.

Despite the well-developed treatment guidelines, the long-term prognosis of PFP is alarming. As it was discussed in chapter 2.4, the prognosis of PFP and the long-term effect of PFP treatments showed that the majority of individuals with PFP still suffered 4-5 years after their initial treatment of PFP. This raises questions over the validity of current treatments and their ability to address and sufficiently alter the pathophysiological factors that might lead to chronic PFP.

Since the guidelines have been published very recently, one explanation why current treatments in individuals with PFP seem to be unable to prevent the chronicity of PFP could be because no treatment has been established based on these guidelines yet. Thus, to date studies that investigate the effect of an intervention based on the current recommendations on muscular dysfunction in individuals with PFP have not been carried out.

2.9. Gaps in literature

This review showed that several knowledge gaps in research on patellofemoral pain currently exist:

1. In 2016 a high-quality guideline on recommended physical interventions for PFP were developed, which included recommendations on exercises, bracing and combined interventions (Crossley et al., 2016). However, to date no study has developed an exercise programme based on these high-quality guideline and investigated the effect of such an exercise programme.
2. Furthermore, the high-quality guideline from 2016 recommended that knee braces and straps could reduce the pain in short term (Crossley et al., 2016). However, to date no brace or strap was able to modify the hip biomechanics to thereby reduce the dynamic knee valgus in individuals with PFP. Thus, further research on the effect of knee braces/ straps that aim to modify hip biomechanics is needed.
3. Although much research has been published on pathophysiological factors in individuals with PFP, yet little is known whether and to what extent acute pain would influence the functional performance, muscular strength and AMI in individuals with PFP.

2.10. Aim of this thesis

This thesis aimed to investigate the effect of treatments on muscular dysfunction in individuals with PFP.

Chapter 3: Therefore a robust holistic test protocol which encompassed the reliable biomechanical measures, patella position and foot posture measures, muscle flexibility, strength and inhibition tests and a reliable measurement tool to investigate muscle activation and co-contraction of the quadriceps and the hamstrings muscles was developed.

Chapter 4: Flexible knee braces are recommended to reduce acute PFP. The Powers^{TM} strap has been invented to decrease the hip internal rotation angle in individuals with PFP. However, the effect of the Powers^{TM} strap has not been investigated. Thus, a study on the effect of the Powers^{TM} strap in individuals with and without PFP was performed. The primary null-hypothesis was as follows:

1. H0: There would be no significant differences in hip and knee internal rotation, flexion and adduction angles and moments when wearing the Powers^{TM} strap.

Null-hypotheses for the secondary outcomes:

1. H0: There would be no significant differences in hip and knee internal rotation, flexion and adduction angles and moments between individuals with and without PFP.
2. H0: There would be no significant difference in co-contraction ratio and the net-activation of the quadriceps and hamstrings muscles between individuals with and without PFP.

Chapter 5: Guidelines for treatment programmes of PFP have been recently published. However, no treatment has been established based on these guidelines yet. Thus, this study aimed to develop a 6-week intervention programme based on the current guidelines and investigated the effect of this 6-week intervention programme on muscular dysfunction and functional performance in PFP.

Therefore the Null-Hypotheses for the primary outcomes were:

1. "Pain and function would not be significantly improved after the 6-week evidence base exercise programme in individuals with PFP."
2. "The 6-week exercise programme would not significantly modify lower limb biomechanics in individuals with PFP."
3. "The 6-week exercise programme would not increase muscle flexibility in individuals with PFP."
4. "Quadriceps strength would not be increased after the 6-week exercise programme."

Secondary outcomes were also investigated whereby the relevant null hypothesis would be that: "There would be no significant differences after a 6-week evidence base exercise programme in individuals with PFP in the following:

- balance
- the break phenomenon
- quadriceps inhibition
- co-contraction ratio and net activation of the quadriceps and hamstrings muscles."

Chapter 6: Pain is believed to be linked to several factors, such as alterations of lower limb biomechanics, muscular coordination, strength and AMI. However, to date in individuals with PFP the isolated effect of pain has not been investigated. This study aimed to investigate this direct link of pain on muscular dysfunction in individuals with PFP.

Therefore, the hypotheses of this study were:

1. H0: There would be no significant differences in knee and hip kinematics and kinetics between pain and no pain in individuals with PFP.
2. H0: There would be no significant differences in AMI and muscular strength between pain and no pain in individuals with PFP.
3. H0: The break phenomenon would be equally present in pain and no pain in individuals with PFP.
4. H0: Participants with PFP would show an equal co-contraction of the quadriceps and hamstrings muscles in a) running, b) step down task and c) single leg squat task.

Chapter 3: Methodology and repeatability

This chapter analysed the reliability of posture and flexibility assessments of the lower limb, measurements to assess strength, arthrogenic muscle inhibition (AMI) of the quadriceps, as well as biomechanical assessments (3D movement analysis, surface EMG of lower limb muscles).

3.1. Introduction

The results of the systematic review demonstrated that a broad range of studies on patellofemoral pain exist but that a more thorough understanding of muscular dysfunction and its effects on functional performance is still lacking. This study aimed to assess the reliability of a test-protocol, which investigated muscle dysfunction in an integrated approach by combing measurements to assess AMI, the break phenomenon, strength of the quadriceps muscle, lower limb flexibility and foot and patella posture assessments, the 3D motion-analysis system and the sEMG analysis during functional tasks in healthy participants. The results of this study will enable the development of a robust and integrated protocol on muscle dysfunction, which will be used to examine how different treatment approaches and pain influence muscle dysfunction in individuals with PFP and healthy controls.

3.2. Experiment procedures

The ethical application HSR 15-22 was obtained from the University of Salford Research and Governance committee on the 21nd May 2015 (Appendix Methods 3.1).

3.2.1. Participants

Four healthy men and five healthy women (age: 26.11± 3.02 years, height: 1.71±0.1 m, mass: 66.96±12.46kg, BMI: 22.73 ±2.74kg/m^2) were tested in two separate sessions within two weeks. Participants were recruited from Salford University staff and student population.

To be included in the study a participant had to meet all of the following criteria: (1) Being healthy and having no previous lower limb injuries, (2) Being able to perform squatting, step

down, running, anterior reach test and the maximal voluntary isometric contraction (MVIC), (3) Age range: 18-45 years old.

Participants were excluded if: (1) They had any history of previous lower limb surgery or patella instability and dislocation (2) They had any history of traumatic, inflammatory or infectious pathology in the lower extremities or any internal derangements. (3) They reported previous or existing knee pain. (4) They could not perform one of the required tests during the measurement.

3.2.2. Procedures

The test was performed in the human performance laboratory in the Mary Seacole building at the University of Salford. If a participant was interested in taking part he/ she received a participant information sheet (Appendix Methods 3.2) and an appointment was booked. Upon arrival at the laboratory, the participant was briefed through the study and the objectives of the investigations and the study equipment was explained. If the participant still agreed to take part in this research study and had no questions, he/ she was asked to sign the informed consent form and a health history questionnaire (Appendix Methods 3.3 and 3.4). The health history questionnaire consisted of 13 questions investigating potential risks associated with the study. If potential risks to the participant were identified, then participation within the study was discussed and the individual was either asked to consult a physician to receive approval for the participation or was advised not to participate in this study.

The individual was then asked to change into their shorts and a comfortable t-shirt. Firstly, the body mass and height of each participant was taken followed by the posture and flexibility assessment.

The following flow-chart gives and overview over the measurement procdure for this study (Figure 3.1).

3.2.3. Main outcome measures

The following outcome measures were investigated:

1. 6-item foot posture index

2. Patella medial/ lateral displacement in cm, patella tilting on grading scale: -2 to 2
3. Hamstrings and quadriceps flexibility in degrees
4. Ankle range of motion in degrees and cm
5. Quadriceps inhibition in % (of the Central Activation Ratio)
6. Isometric quadriceps and hamstrings strength in Nm and normalised to body mass (kg)
7. Eccentric and concentric quadriceps strength in Nm and normalised to body mass (kg)
8. Ant reach test distance in cm and reach distance normalised to leg length
9. Peaks of hip and knee flexion, adduction and internal-rotation angles and moments during functional tasks
10. sEMG waveform and the peak of the sEMG signal during each task.

3.2.4. Flowchart of the testing procedure

The following flowchart (Figure 3.1) describes the originally planned measurement procedure and the amendments undertaken to address the challenges that occurred during the measurement procedure.

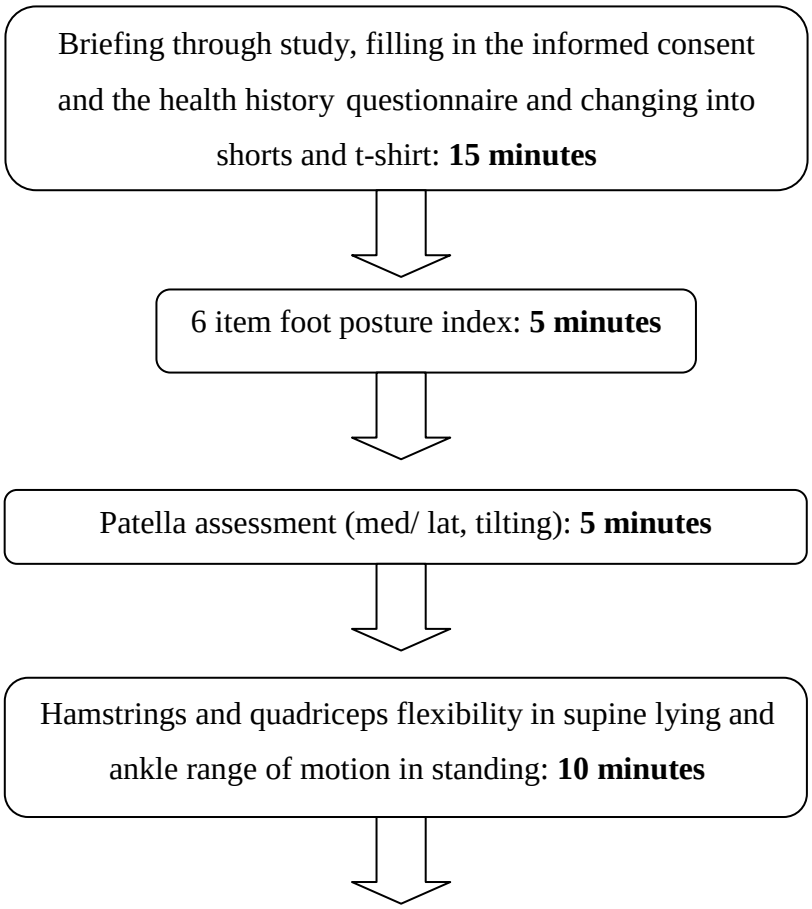


Figure 3.1: Flow chart of the test procedure (part 1)

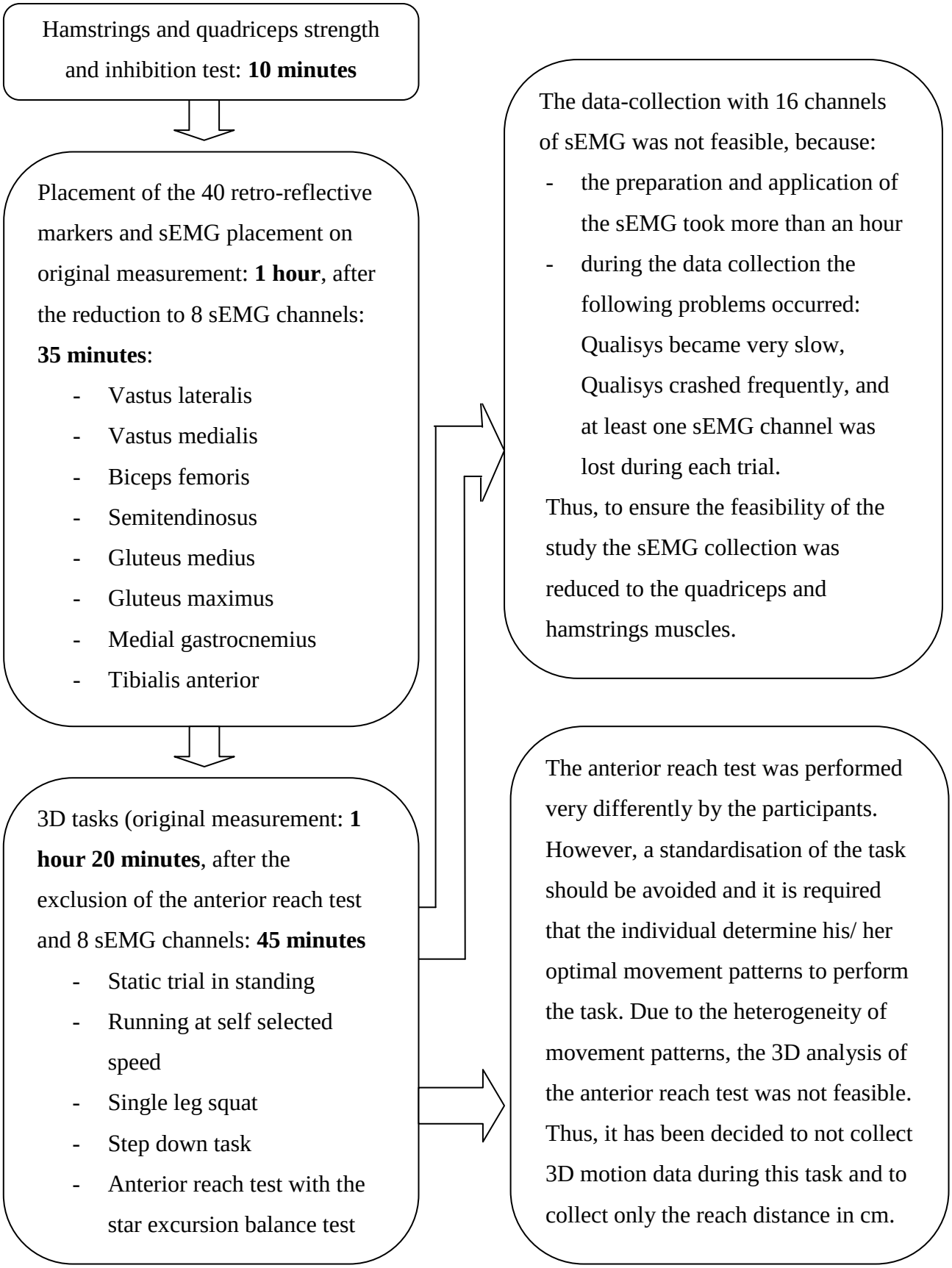


Figure 3.1: Flow chart of the test procedure (part 2)

3.3. Methodology of the static and dynamic measurements

The static and dynamic measurements involved posture, muscle flexibility, strength, quadriceps AMI and the quadriceps break phenomenon assessments.

3.3.1. Posture and flexibility

The examination of the foot posture was performed by using the 6-item foot posture index (FPI-6) (Figure 3.2), which was a novel method of rating foot posture in standing using a simple 6-item scale (Jarvis, Nester, Jones, Williams, & Bowden, 2012). The 6-item foot posture index has been chosen as it is quick and simple to perform and showed excellent intra-rater reliability and good validity as a clinical instrument (Keenan, Redmond, Horton, Conaghan, & Tennant, 2007; Redmond, Crosbie, & Ouvrier, 2006). Furthermore, a moderate correlation between the FPI and the dynamic foot function could be identified in participants with and without PFP (Barton, Levinger, Crossley, et al., 2011). Since participants with PFP showed a more pronated foot posture resulting in an earlier timing of the peak rearfoot eversion during walking, it seemed to be essential that the foot posture was assessed (Barton, Levinger, Crossley, et al., 2011; Barton, Levinger, Webster, & Menz, 2011).

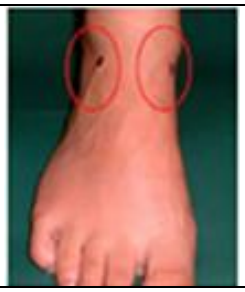
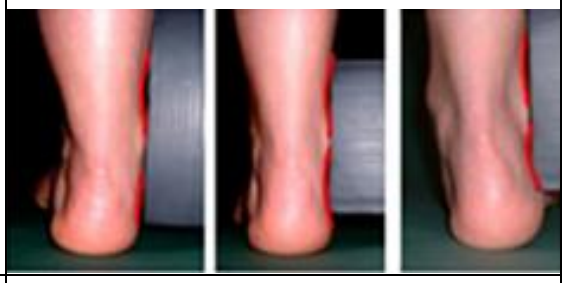
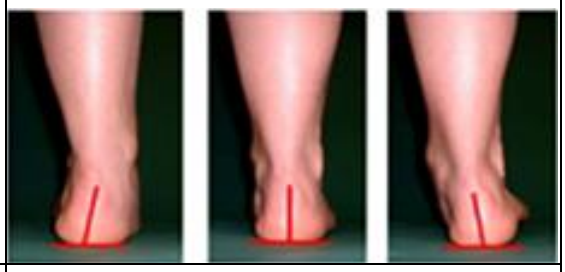
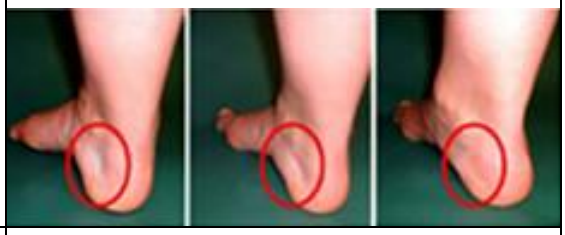
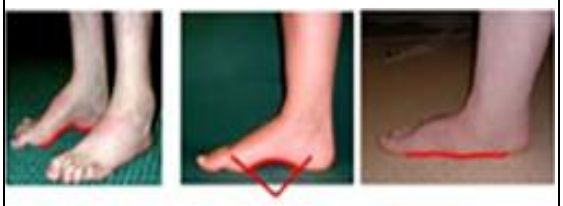
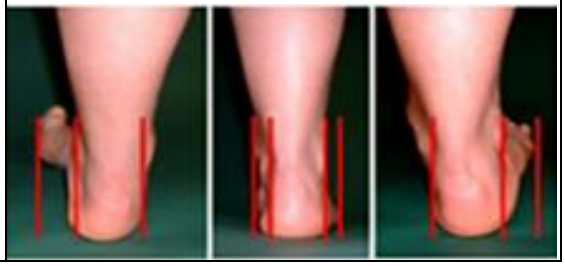
-2	-1	0	1	2	
Talar head palpable on lateral side/ but not on medial side	Talar head palpable on lateral side/ slightly on medial side	Talar head palpable on both sides	Talar head palpable on medial side/ slightly on lateral side	Talar head palpable on medial side/ but not on lateral side	
-2	-1	0	1	2	Supinated (-2) neutral (0) pronated (+2)
Curve below the malleolus either straight or convex	Curve below malleolus concave but flatter/ than the curve above the malleolus	Both infra and supra malleolar curves roughly equal	Curve below malleolus more concave than the curve above malleolus	Curve below malleolus markedly more concave than above	
-2	-1	0	1	2	Supinated (-2) neutral (0) pronated (+2)
More than estimated 5° inverted (varus)	Between vertical and estimated 5° inverted (varus)	Vertical	Between vertical and estimated 5° everted (valgus)	More than estimated 5° everted (valgus)	
-2	-1	0	1	2	Supinated (-2) neutral (0) pronated (+2)
Area of TNJ markedly concave	Area of TNJ slightly, but definitely concave	Area of TNJ flat	Area of TNJ bulging slightly	Area of TNJ bulging markedly	
-2	-1	0	1	2	Supinated (-2) neutral (0) pronated (+2)
Arch high and acutely angeled towards post. end	Arch moderately high and slightly acute posteriorly	Arch height normal and concentric curve	Arch lowered with some flattening in central portion	Arch making ground contact	
-2	-1	0	1	2	Supinated (-2) neutral (0) pronated (+2)
No lateral toes visible, medial toes clearly visible	Medial toes clearly more visible than lateral	Medial and lateral toes equally visible	Lateral toes clearly more visible than medial	No medial toes visible. Lateral toes clearly visible	

Figure 3.2: The 6-item foot posture index (Redmond, 2005)

Patellofemoral malalignment has been shown to be associated with patellofemoral pain progression (Hunter et al., 2007; Lin, Lin, Cheng, Lin, & Jan, 2008; Pal et al., 2013; Pal et al., 2012; Pal et al., 2011), thus patella alignment was assessed. The patella alignment (lateral-medial displacement and lateral-medial tilt) was assessed in supine lying. For assessing the lateral-medial displacement, the method described by McConnell was used (1986), which had been shown to be reliable (Herrington, 2002; McConnell, 1986; McEwan, Herrington, & Thom, 2007). Therefore, the knees were positioned with a pillow in 20° knee flexion, to ensure that the patella was placed in the trochlea groove. A soft tape was gently applied over the knee, starting medially and laterally on the femoral epicondyles. Then, the medial and lateral epicondyles of the femur were palpated and marked with a small line on the previously applied tape. Afterwards, the mid-point on the patella was marked with a pen. The distance from the medial epicondyle to the mid-point of the patella, as well as the lateral epicondyle to the mid-point of the patella were measured and noted in cm (Figure 3.3). Afterwards the lateral distance was subtracted from the medial distance and noted in cm.

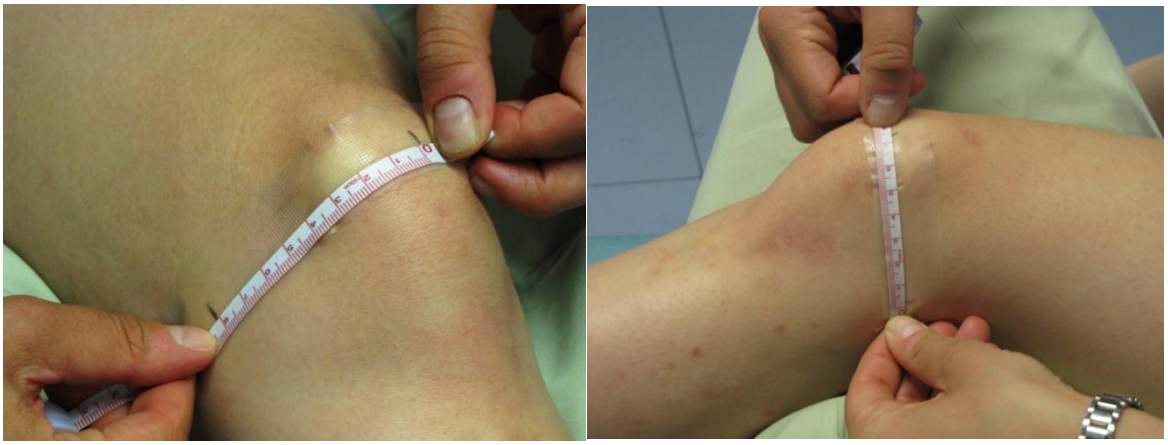


Figure 3.3: Measurement of the lateral-medial patella displacement: left picture medial measurement, right picture lateral measurement

To measure the lateral-medial tilt the method described by Fitzgerald & McClure (1995) was used. Therefore the thumb and the index finger were placed on the medial and lateral boarder of the patella. Both digits should be of equal height (Figure 3.4). If the digit palpating the medial boarder is more anterior than the finger on the lateral boarder, then the patella is laterally tilted. The patella is medially tilted if the finger on the lateral boarder is more anterior than the finger on the medial boarder (Fitzgerald & McClure, 1995). The tilting was ranked on a scale from -2 (= highly medially tilted) to +2 (highly laterally tilted).

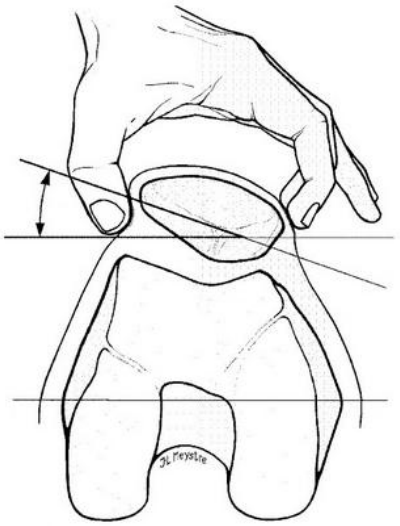


Figure 3.4: Measurement of the medial/ lateral tilt of the patella (Biedert, 2004)

To investigate the anterior/ posterior tilt of the patella, the technique described by Fitzgerald & McClure (1995) was utilised. The anterior tilt was determined by palpating the inferior pole of the patella. If the anterior pole was easily palpable, it was noted as no significant anterior tilt. If the anterior tilt was prevalent a downward pressure was applied on the superior pole of the patella, so that the inferior pole became more superficial enough to palpate (Figure 3.5). The tilting was ranked on a scale from -2 (= highly anteriorly tilted) to +2 (highly posteriorly tilted).

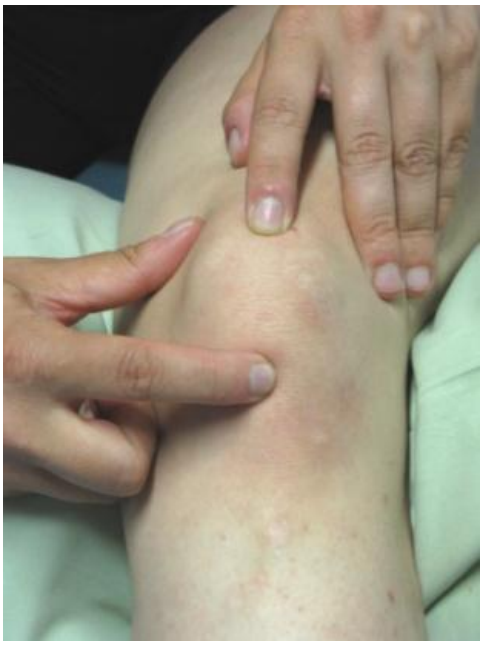


Figure 3.5: Measurement of the anterior/ posterior tilt of the patella

All flexibility measurements were assessed with active tests for feasibility reasons: Firstly, to measure range of motion (ROM) in a reliable way is more challenging with a passive measurement than with an active measurement, because the force exerted by the investigator to push the limb into the end-range position can vary and thereby result in goniometric discrepancies (Gajdosik & Bohannon, 1987). Secondly, a second investigator is needed to carry out passive ROM tests in a standardised manner (Cejudo, Sainz de Baranda, Ayala, & Santonja, 2015; Gabbe, Bennell, Wajswelner, & Finch, 2004). Thus, all ROM tests were carried out with an active ROM test. However, active ROM represents the "initial length" of the hamstrings, whereas the passive ROM represents more the maximal length of the muscle stretch (Gajdosik, Rieck, Sullivan, & Wightman, 1993). Literature revealed that a reduced quadriceps and hamstrings flexibility, as well as a reduced ankle ROM were associated with PFP and should be addressed in current treatments (Barton et al., 2015; Crossley et al., 2016b; Macrum, Bell, Boling, Lewek, & Padua, 2012; Piva, 2005; Piva et al., 2009). Thus, the flexibility of the ankle ROM, the hamstrings and the quadriceps were assessed in this study.

The hamstrings flexibility was measured by using the active knee extension test, which has been shown to be reliable (Gabbe et al., 2004; Gajdosik et al., 1993; Hamid, Ali, & Yusof, 2013; Neto, Jacobsohn, Carita, & Oliveira, 2014). The participants laid down supine, with the arms across the chest. The hip and knee of the dominant leg were actively held in 90° flexion, while the opposite leg fully extended. The participants actively straightened the knee of the dominant leg until the point when the other thigh began to move from the vertical position. The popliteal angle at this point was measured with a goniometer by the assessor (Figure 3.6).

Figure 3.6: Measurement of the hamstrings flexibility

For assessing the flexibility of the quadriceps, the modified Thomas test was utilised, which has been shown to be reliable (Cejudo et al., 2015; Gabbe et al., 2004). Therefore, the participants laid down supine at the edge of the examination couch. The participants were asked to pull the non-dominant leg towards the chest and to hold it. The other knee was extended in a neutral hip position. The participant flexed then slowly the knee of the dominant leg until he/ she was able to maintain a neutral hip position. The assessor measured the knee angle in this position with a goniometer (Figure 3.7).

Figure 3.7: Measurement of quadriceps flexibility

The ankle ROM was measured by using a weight-bearing lunge, which has been shown to be reliable, have a low measurement error and can be obtained from a novice rater (Konor, Morton, Eckerson, & Grindstaff, 2012). The participants were asked to stand facing a wall, with about 10 cm between the feet and the wall. Throughout the test the heel stayed in contact with the ground and the knee was always in line with the second toe. The participants bent the front knee and thereby lunged forward until their knee touched the wall without lifting the heel from the ground. The assessor recorded the distance of the great toe from the wall and the ankle range of motion by using a goniometer (Figure 3.8).

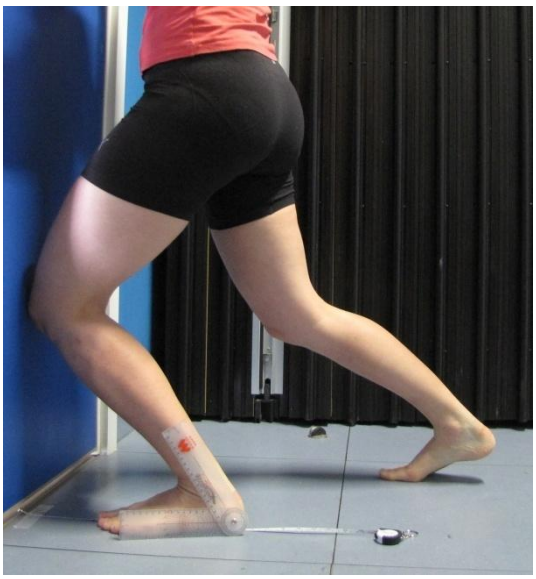


Figure 3.8: Measurement of ankle flexibility

3.3.2. Assessment of arthrogenic muscle inhibition (AMI)

The neurophysiology that causes AMI is quite complex. AMI is characterised by a reduction in the Motor-Neuron (MN) pool recruitment. This MN-pool recruitment can mainly be assessed in two ways:

1. the product of neuromuscular recruitment of the MN pool and
2. the voluntary force output of that MN pool

Both methods have advantages as well as disadvantages (Hopkins & Ingersoll, 2000).

3.3.2.1. Assessment of the neuromuscular recruitment of the MN pool

One possibility to investigate the measure of the MN-pool recruitment is by using the Hoffmann-reflex (H-reflex), which is a low-voltage stimulation of the femoral nerve, resulting in a monosynaptic excitation of alpha-MN in the anterior horn of the spinal cord, (Bolgla & Keskula, 2000; Hopkins & Ingersoll, 2000) or by investigating the V-wave, which is an electrophysiological variant of the H-reflex and recorded during a MVIC (Aagaard, Simonsen, Andersen, Magnusson, & Dyhre-Poulsen, 2002). The V-wave can be used to reflect the level of efferent neural drive from spinal alpha-MNs during a maximum voluntary contraction (MVC). The main difference to the H-reflex is the involvement of the motor cortex (Aagaard et al., 2002). Previous studies have shown that the V-wave response has been reliable in the gastrocnemius medialis, the soleus and the flexor carpi radialis, when it was normalised to the corresponding M-wave (El Bouse, Gabriel, & Tokuno, 2013; Solstad, Fimland, Helgerud, Iversen, & Hoff, 2011; Stutzig & Siebert, 2015). The electric stimulation of the peripheral nerve causes direct activation of the efferent fibers, sending action potentials immediately from the point of stimulation to the neuromuscular junction. This efferent arc produces a response in the EMG known as the muscle response (M-wave). However, so far the reliability of the V-wave in the quadriceps has not been investigated.

Previously in literature it has been described that the H-reflex and V-wave represent the stimulated portion of the MN. This means that a decreased H-reflex indicated an inhibitory action from the knee joint afferents on the quadriceps motor neurons (Bolgla & Keskula, 2000; Hopkins & Ingersoll, 2000). However, the assumption that the H-reflex faithfully represents the MN excitability is inaccurate, as oligosynaptic inputs, Ib and recurrent and presynaptic inhibitory pathways are likely to contribute to the H-reflex as well (Knikou, 2008; Palmieri et al., 2004; Pierrot-Deseilligny & Mazevet, 2000). Moreover presynaptic inhibition differs with age and training type and might be influenced by anatomical or genetic differences (Aagaard et al., 2002; Palmieri et al., 2004). However, altered H-reflexes do not automatically indicate unphysiological changes and inhibition. Endurance athletes showed elevated H-reflexes compared to power and sprint athletes. Whereby ballet dancers had reduced H-reflexes in comparison to physical educational students (Aagaard et al., 2002). Furthermore, the excitability state of cells and their sub-threshold excitability level varies across and within subjects. Thus, the use of the H-reflex in individuals with patellofemoral pain (PFP) should be critically examined as it has been shown to be reliable in healthy controls (Briani, Souto Faria, et al., 2015; Hopkins, Ingersoll, Cordova, & Edwards, 2000), but unreliable in individuals with

PFP (Briani, Souto Faria, Ferraz Pazzinatto, de Oliveira Silva, Ferrari, Magalhaes, & de Azevedo, 2015).

3.3.2.2. Voluntary force output of a motorneuron (MN)

In contrast to the H-reflex and the V-wave, the measurement of force output is easy to execute with only small technical effort and is straightforward to interpret (Hopkins & Ingersoll, 2000). A simple assessment of muscular inhibition is the calculation of the difference in baseline MVC and post-operative/ post-injury MVC, whereby the reduction in torque can be expressed as the percentage of inhibition (Henriksen, Rosager, Aaboe, Graven-Nielsen, & Bliddal, 2011; Hopkins & Ingersoll, 2000; Young, 1993). But this measurement also has drawbacks, which are:

- that a required MVC post-operative/ injured might be not executable, because the participant experiences pain or is too anxious to deliver a MVC.
- that to date, baseline data has been only rarely collected (Hopkins & Ingersoll, 2000).

To overcome these problems other techniques can be used, such as the burst superimposition technique (SIB) or the interpolation twitch technique (ITT) (Hopkins & Ingersoll, 2000). Both techniques are the most commonly used methods in quadriceps AMI. They analyse AMI by calculating the central activation ratio (CAR) by using electrical stimulation to investigate the difference between voluntary activation (during MVC) and involuntary activation (during MVC and electrical stimulation) (Hart et al., 2010; Rice & McNair, 2010).

During the SIB technique a train of submaximal stimuli is delivered via electrodes directly over the quadriceps muscle (Chmielewski, Stackhouse, Axe, & Snyder-Mackler, 2004; Knarr, Higginson, & Binder-Macleod, 2012; Park & Hopkins, 2011; Roberts, Kuenze, Saliba, & Hart, 2012).Whereas during the ITT the femoral nerve is stimulated (Paillard, Noe, Passelergue, & Dupui, 2005; Rutherford, Jones, & Newham, 1986; Suter, Herzog, & Bray, 1998; Suter, Herzog, De Souza, et al., 1998). However, other authors defined the difference between the SIB and ITT by the stimuli, whereby during the ITT one or multiple electrical stimuli are applied and during the SIB a train of stimuli (Callaghan et al., 2014; Rice & McNair, 2010). The SIB technique enables the calculation of the CAR by dividing torque measurements of the MVC by the sum of torque during MVC and the applied superimposed electrical stimuli (Chmielewski et al., 2004; Knarr et al., 2012; Park & Hopkins, 2011; Roberts et al., 2012). Thus, a CAR of 1.0

indicated the full activation of the whole quadriceps and the MN pool and has been described in healthy participants as ranging between 0.93 to 0.99 (Park & Hopkins, 2011). The twitch interpolation technique involves the comparison of the magnitude of an electrically induced muscle twitch in rest to the torque magnitude evoked when the superimposed stimulus is added to a MVC (Figure 3.9) (Chmielewski et al., 2004; Drover et al., 2004; Folland & Williams, 2007). In addition, there is one other commonly used equation to assess muscle activation, which is termed interpolated twitch torque. For this technique an additional electrical twitch is evoked at rest. The percentage voluntary activation is quantified by expressing the stimulus evoked torque during MVC as a percentage of the stimulus-evoked torque at rest (Callaghan et al., 2014; Krishnan & Williams, 2011; Shield & Zhou, 2004).

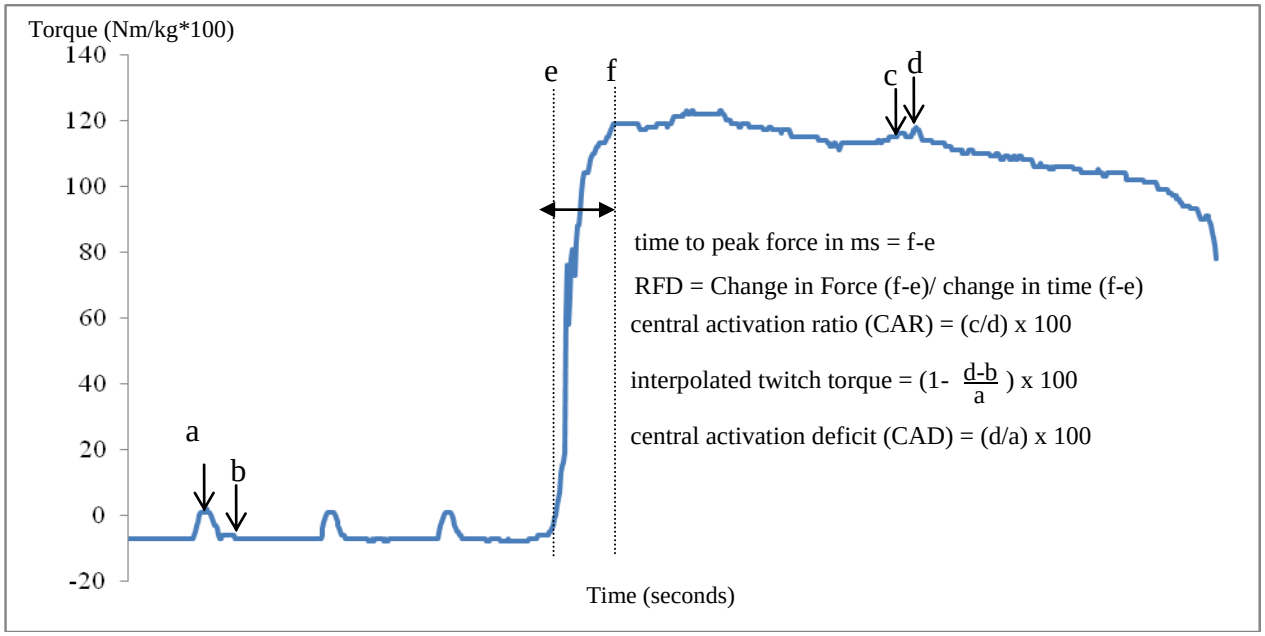


Figure 3.9: Representation of techniques used to estimate voluntary quadriceps activation. a= stimulus evoked torque at rest, b= torque at rest, c= voluntary torque, d= peak torque evoked due to the superimposition of the electrical impulse, e= onset of MVIC, f= peak force

Behm et al (2001) showed that the interpolated-twitch technique was the most valid measure of muscle inactivation when a tetanic stimulation was applied (Behm, Power, & Drinkwater, 2001). However, interpolated twitch torque ratios are likely to overestimate muscle activation (Behm et al., 2001; Kendall, Black, Elder, Gorgey, & Dudley, 2006; Stackhouse, Dean, Lee, & Binder-MacLeod, 2000). Stackhouse et al. (2000) reported that the central activation ratio

(CAR) is curvilinear related to maximal voluntary effort and thus the use of a linear relationship resulted in a markedly overestimated CAR (Stackhouse et al., 2000).

Although these measurements are straightforward, they also have some disadvantages. Even if the tetanic stimulation showed to be the most valid measure of AMI, the tetanic stimulation is often too painful to be executed (Behm et al., 2001). In addition, all these techniques require the ability to effectively isolate knee extensors during a MVC. Thus, an appropriate participant position and fixation to eliminate compensatory muscular patterns is of vital importance (Hart et al., 2010). However, even if the participant position and fixation is optimal, the MVC measurement relies on the ability of the participants to voluntary activate their muscle, which depends on the sex, the training level and other factors, such injuries or pain (Hopkins & Ingersoll, 2000; Paillard et al., 2005). The optimal electrical stimulation settings are crucial, as well as an optimal skin-to-muscle transmission of pulse trains (Dousset & Jammes, 2003; Hart et al., 2010; Shield & Zhou, 2004).

Thus, the SIB as well as the ITT are the most commonly applied techniques for assessing AMI after knee injuries and pain, but reliability results on these techniques are still lacking.

However, if an optimal electrical stimulation setting as well as an accurate participant positioning and fixation was selected, the twitch interpolation torque was shown to be reliable and allowed the examination of the extent to which muscular and neural adaptations influence performance (Callaghan et al., 2014; Norregaard, Lykkegaard, Bulow, & Danneskiold-Samsoe, 1997; Shield & Zhou, 2004). Thus, for this study the assessment using the voluntary force output of a motorneuron (MN) and the interpolated twitch torque technique have been chosen.

3.3.3. Strength and arthrogenic muscle inhibition

The muscular inhibition of the quadriceps was assessed during a maximal isometric contraction (MVIC) of the quadriceps with the interpolated twitch technique. Therefore, the participants were seated in an isokinetic dynamometer and positioned in 90° hip flexion and 60° knee flexion (Kin-Com, Figure 3.10). This position had been chosen as previous studies showed that peak torques and flexor-to-extensor torque ratios were only symmetrical at 60° knee flexion (Krishnan & Williams, 2014). The Kin-Com shin pad was attached 1 cm proximal to the malleoli of the ankle to the dominant shank in line with previous recommendations (Brown & Weir, 2001). The length of the lower lever arm, to which the resistance pad was attached, was

measured in cm and the results were entered into the Kin-Com menu. Each participant was secured to the test chair with a chest and pelvic belt and the dominant thigh was fixated to the seat with another strap. The Kin-Com shin pad was attached 1 cm proximal to the malleoli of the ankle to the dominant shank, according to previous recommendations (Brown & Weir, 2001). The participants were advised to keep their arms across their chest and to hold on to the chest belts for stability during the test. Two electrodes (proximal: 50×130 mm, distal: 7.5×100 mm) (Axelgaard, Fallbrook, Ca, USA) were placed on the quadriceps muscle at one-third and two-thirds from the distance between the anterior superior iliac spine and the upper border of the patella (Figure 3.10).

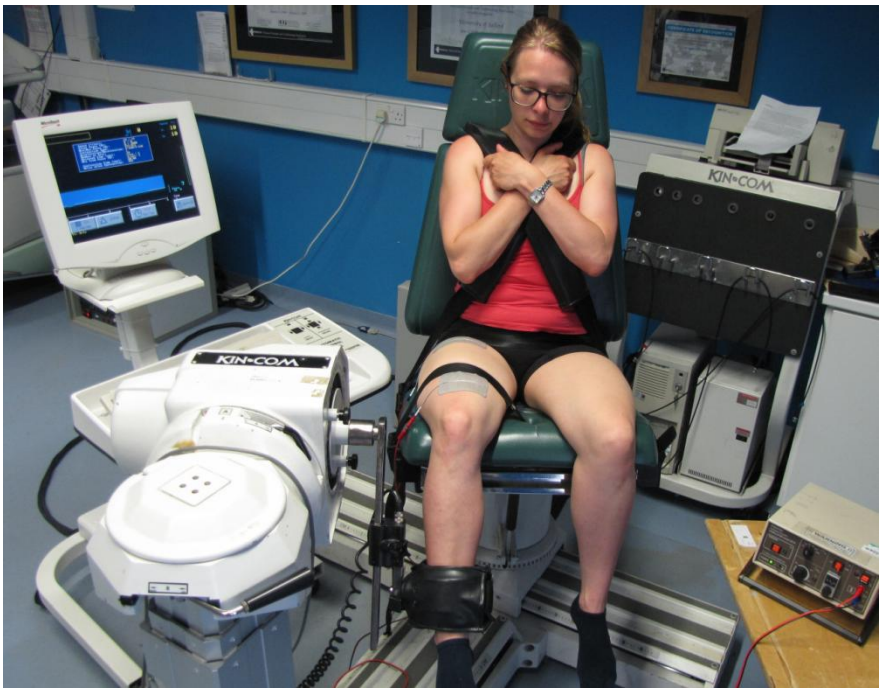


Figure 3.10: Kin-Com dynamometer (left side) and the digitimer (right side)

Prior to the test a warm-up session of 4 submaximal isometric quadriceps contractions was performed to habituate the participants to the test equipment and to ensure that the participants were warmed up. The familiarisation and warm up session was performed in accordance with previous recommendations (Brown & Weir, 2001). The AMI measurements were taken using a Digitimer High Voltage Stimulator (DS7AH Digitimer Ltd, Hertfordshire, England), using a single twitch with a pulse duration of 200 ms. The participants were acclimated to the stimulus through a series of 5 slowly increasing stimulus amplitude (at 40 mA, 60 mA, 80 mA, 100 mA,

125 mA). After the acclimatisation to the electrical twitches the participant delivered two more submaximal warming up contractions.

The test began with applying two resting twitches (RTT) of 125 mA before the MVIC attempt. Directly after these two resting twitches the participant was verbally encouraged with the instruction: "push as much as possible" to ensure their attempt to a maximal voluntary effort. Each participant was verbally encouraged throughout the 5 seconds of maximal attempt. The isometric muscle test was performed using the ‘‘make test’’ method of muscle test. The muscle contraction was held for 3 to 5seconds. During the MVIC attempt two single pulses of 200µs duration, 200Volt and 125 mA were triggered three times (beginning, mid and end of the contraction) manually by the investigator when the MVIC force had plateaued on the monitor (ITT). Thus, electrical twitches were evoked at rest and added during a MVIC. AMI was quantified by calculating the difference between the stimulus-evoked torque during MVIC to the stimulus-evoked torque at rest and expressed in %: activation deficit (AD) at 100% MVIC from the ratio: AD = (ITT/RTT) x 100 (Figure 3.9) (Chmielewski et al., 2004; Drover et al., 2004; Folland & Williams, 2007). The smaller the deficit, the less the inhibition, whereby an inhibition of 0% means that the subject was able to fully recruit the muscle without showing any signs of inhibition.

In addition, the peak of the voluntary MVIC was recorded to assess the maximum strength. Participants were asked to perform 3 maximal contractions of their knee extensor muscles while additional electrical stimulation was applied. In accordance to strength guidelines, the participant performed each maximal contraction for 5 seconds, with resting times of 30 seconds in between each maximal contraction (Brown & Weir, 2001).

After the isometric MVIC test the participants had a break of five minutes before they performed the isokinetic knee extensor strength measurement in sitting. The quadriceps muscle was measured concentrically and eccentrically, each maximal force measurement was performed 3 times with a break of 1 minute between the tests. Each participant was therefore secured to the test chair with a chest and pelvic belt again. Prior to the test, all participants received a warm-up session of six submaximal repetitions of concentric and eccentric quadriceps activation. After completion of the warm-up trials, each participant was tested at the angular velocity of 60°/second through the full available range of motion (ROM) from 90° knee flexion to maximal knee extension. The interaction of velocity and force has been well established and it could be shown that the higher the velocity the lower the force production

becomes (Brown & Weir, 2001). Thus, it is recommended to choose a low velocity for the tests to enable the production of high forces. However, it has been shown that during 30°/second the compressive force is equal to 12 times body mass (Nisell & Ekholm, 1985; Nisell & Ericson, 1992). Thus, to decrease the patella forces 60°/second has been chosen, also because it could be shown that this would be a good velocity to investigate the break phenomenon (Herrington et al., 2003). To test participants with PFP with a velocity of 60°/second is in accordance with the majority of the studies (Duffey et al., 2000; Duvigneaud et al., 2008; Dvir et al., 1990; Kaya et al., 2010; Ott et al., 2011). In addition, strength at 60°/second has been shown to be a predictor for functional quadriceps tasks (Yapici, Findikoglu, & Dundar, 2016).

The break phenomenon was investigated during the eccentric quadriceps task, whereby a "break phenomenon" was defined as a trace dip which exceeded more than 10% (Figure 3.11) (Anderson & Herrington, 2003; Dvir & Halperin, 1992).

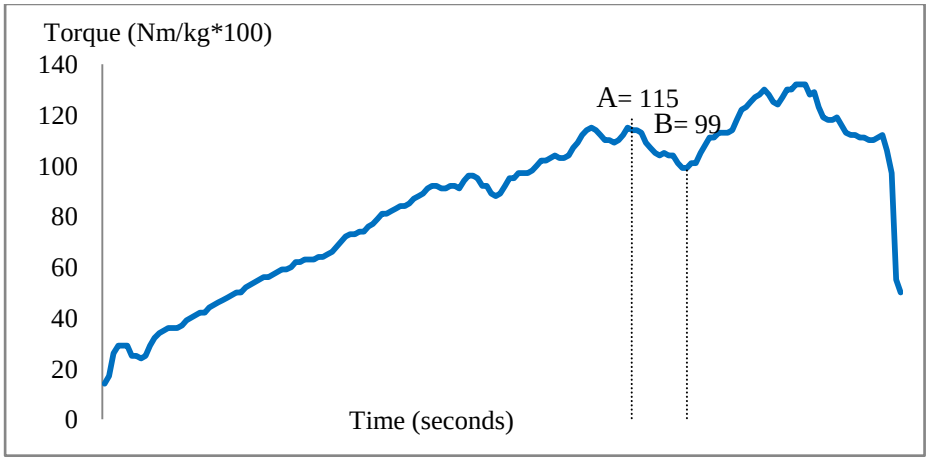


Figure 3.11: Break phenomenon of 14%. A= pre-break maximum, B= within break maximum

3.3.4. Analysis of the strength measurements, AMI and the break phenomenon

The strength data of each participant was exported from the Kin-Com to ascii-files and loaded into Excel. The peak torque was determined for each file. AMI, the time to peak force and the rate to force development (RFD) were calculated from the individual maximal isometric force development record.

AMI was quantified with the following equation: AMI = [(d-c)/(b-a)]*100 (Figure 3.9). An inhibition of 0% means that the subject was able to fully recruit the muscle without showing

any signs of inhibition) (Chmielewski et al., 2004; Drover et al., 2004; Folland & Williams, 2007).

The onset of muscle contraction was defined for the calculation of the time to peak force and RFD as the instant when the knee extensor torque exceeded the baseline by 2% at the start of the MVC (Andersen, Andersen, Zebis, & Aagaard, 2010). The time to peak force expresses the time it takes to develop maximal force and was calculated by the following equation: time to peak force in seconds= f-e (Figure 3.9) (Zatsiorsky & Kraemer, 2006). The rate to force development (RFD) refers to the rate of change in force over time and can be used as a measure of explosiveness. In this study the RFD was defined as the maximal slope of the force time curve. Therefore the average RFD was determined as the time to peak force relative to the onset of force and calculated in the following way: RFD= Change in Force (f-e)/ change in time (f-e) (Figure 3.9) (Andersen, et al. 2010; Zatsiorsky & Kraemer, 2006).

The break phenomenon was investigated during the eccentric quadriceps task. A break was defined as a trace dip which exceeded more than 10% of the pre-break moment (Figure 3.11).

3.4. Methodology of the functional measurements

The functional investigation involved 3-dimensional gait analysis combined with a surface electromyography analysis of the quadriceps and hamstrings muscles.

3.4.1. Three dimensional (3D) motion data, force data and EMG data capture:

The three dimensional motion (3D) capture system (QTM Oqus300, Qualisys AB, Sweden) enables the conversion of the image of a movement into quantified data by transmitting the data directly to the computer, rather than providing the usual video image (Perry & Burnfield, 2010). Positional markers are recorded by at least two cameras and redefined with their new 3D location in the global coordinate system (LAB system), which enables the storage of positional information that can be used to analyse the kinematics (Perry & Burnfield, 2010). Powerful infrared light reflects from the retro-reflective markers and produces a bright spot in each image. These spots are then reconstructed and generate a 3D position in the LAB system, a series of such position spots then forms the trajectories of the markers (Kirtley, 2006).

To generate 3D trajectories, the software firstly looks for a time when at least two cameras record the same marker. This image of the marker is then processed. The camera operation software will look for the same marker in the next time frame. If a marker is found it will be jointed to the former marker to form a trajectory. To ensure a smooth trajectory of each marker, QTM© software uses a 3D tracking function of a buffer of 4-10 frames to predict the next location of the trajectory's marker (2011). The maximal frame gap, which specifies the number of frames allowing the joining of two trajectories, had been set in this study to 10 frames (42 ms). Although this is a precise system, this algorithm might still cause problems such as the (1) prediction error or the (2) maximum residual.

1) Prediction error: To predict the next marker a mathematically deviation (Figure 3.12) is included to enable the next marker to be detected and to resolve the changes of unpredictability during a real movement. However, the greater the deviation, the higher the chance for a cross-over swapping between two trajectories. If the prediction error value is set too high, the likelihood increase that jumpy motions within single trajectories are seen. If this parameter is set too small, division of trajectories can occur, which might result in many more trajectories than markers. Thus, QTM recommends a prediction error value of 30 mm (QTM, 2011), which had been applied in this study.

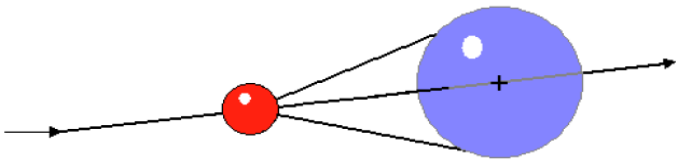


Figure 3.12: Prediction error (red ball: marker, arrow: prediction, red ball: deviation) (QTM©) (QTM, 2011)

2) Maximum residual: The maximum residual function has been implemented together with the prediction error to ensure the continuation of the trajectory and sets the limit to the distance from the final location of the 3D point. If the value is too large, it can slow down the calculation and can cause a merger of 3D points, if it is too small it can cause ghost markers and results in more trajectories than markers (QTM, 2011). The default value of the maximum residual is 10 mm, however, due to the good visibility it has been set in this study to 5 mm.

For the collection of 3D kinematic and kinetic data, 12 infrared cameras (Pro-Reflex MCU, Qualisys AB, Sweden) with a sampling rate of 250Hz were positioned around the gait track and

adjusted. The cameras were centered around three force platforms (BP600900, AMTI, USA), which had a sampling rate of 1500Hz embedded into the floor.

To allow the conversion of the given 2-dimensional (2D) image of the cameras into a 3-dimensional (3D) workspace, a spatial calibration is needed. To complete the calibration procedure, the position of an L-shaped frame with mounted markers, which are positioned at known locations and distances to each other was recorded. This reference L-shaped metal frame (equipped with 4 markers along the frame) was placed on the corner of the third force platform and aligned with the two sides of the force plate. The calibration process was performed by moving a T-wand, equipped with two markers at the end, randomly around the test space for 45 seconds. During the calibration, the position of each marker relative to the origin of the global coordinate system (LAB System) was collected by cameras and recorded in the computer. The L-shaped frame stayed in position on the platform during the calibration. (David A. Winter, 2005). The T-shaped wand had a length of 750.7 mm and was moved during the calibration in as many orientations as possible to ensure that the volume between the lower floor level and the top level were covered completely.

The resulting calibration values indicate the difference between the factory-measured distance between the two static markers on the L-frame and the calculated distance based on the actual marker coordinates of the wand in the lab coordinate system. It was aimed that the errors were as low as possible, because the higher the residuals are, the more inaccurate the calibration and the more likely a higher error will be involved in the results of the measurements. Therefore the result of a calibration was accepted only when the standard deviation of the wand length was below 1 mm (Figure 3.13). Although only the overall result was used to accept or reject the calibration, the results of each camera were examined to ensure that the average residual of each camera was below 1.3 mm (Figure 3.13).

The calibration established the global coordinate system so that the output of the data could be saved as a file of *x, y,* z coordinates of each marker at each sample point of time. Whereby *x* is the forward/ backward, *z* the vertical and y the left/ right (medial/ lateral) axis. After the calibration, the accuracy of tracking markers was typically ±0.1% of the captured volume (Kirtley, 2006).

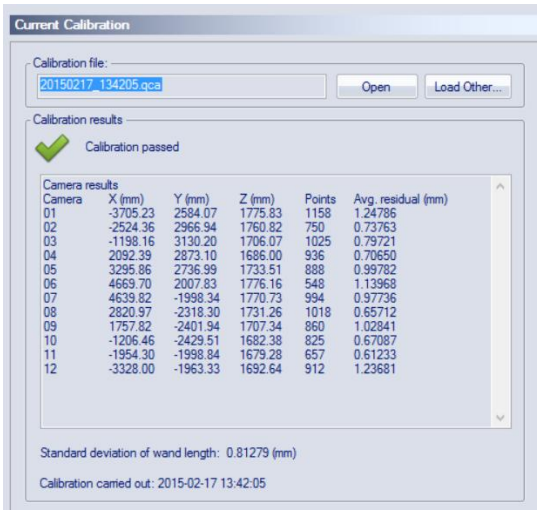
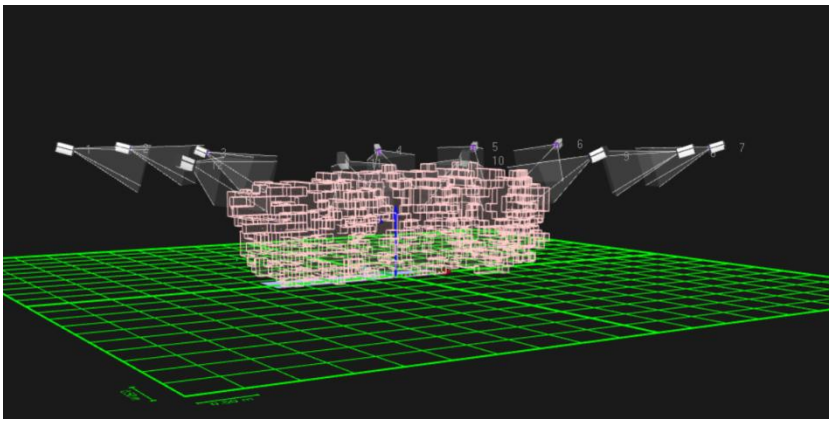


Figure 3.13: The calibration results

To ensure that the measured area was well covered, the calibrated volume was additionally visually checked (Figure 3.14).

A



B

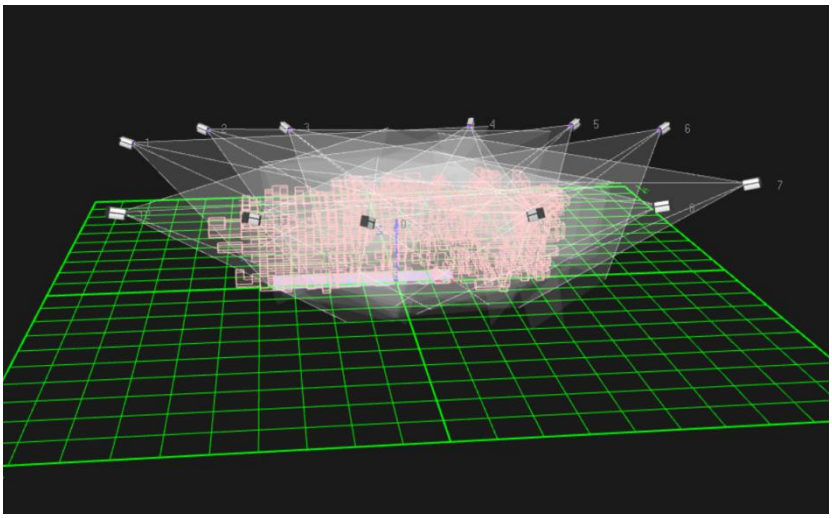


Figure 3.14: A shows calibration volume and B shows the calibrated volume in relation to the camera cone length.

3.4.1.1. Retro-reflective marker set up

For the 3D movement analysis 40 retroflective markers, with a diameter of 14.5 mm, were placed on the lower limb of the participants. The markers were attached, with double sided hypoallergic tape, on the surface of body segments that are aligned with particular bony landmarks (Schneck & Bronzino, 2003). To process 3D-coordinates of each marker trajectory at least three markers of reference points had to be identified of each body segment, as they enable the calculation of a body-fixed coordinate system for each cluster (Schneck & Bronzino, 2003). Cappozzo, Catani, Leardini, Benedetti, & Croce, (1996) investigated the number of markers needed to define one segment and showed that the number of 4 represented the most advisable solution. Thus, all segments (pelvis, thigh, shank and foot) have been tracked with 4 markers.

The calculation of the body-fixed coordinate system is based for practical reasons on a bone-frame and thus should meet requirements which are rigidly associated with the anatomy of the bone. As the markers are placed on the skin and not directly on the bone, the position of the marker is estimated and associated with the underlying bone. This causes instrumental errors due to the position error in the reconstructed coordinate system relative to the global frame and skin artefacts caused by the movement of the skin relative to the bone (Cappozzo, Catani, Croce, & Leardini, 1995). To overcome these challenges Cappozzo, Catani, Croce, & Leardini, (1995) developed a calibration procedure which involved anatomical landmarks (markers on anatomical bony landmarks) in combination with anatomical frames (segment mounted markers). This calibrated anatomical system technique (CAST) model enables that during dynamic trials only the segment mounted markers are used to decrease the skin artefacts of anatomical landmarks. Therefore, a calibration trial with anatomical landmarks and frames is needed. After the calibration, the majority of the anatomical landmarks will be taken off during the dynamic trials to reduce the data amount and obstruction to the participant.

The CAST model was introduced to standardise and define the references and to bring the internal anatomical landmarks in accordance to the external technical markers (Salah & Gevers, 2011). Cappozzo et al. (1996) investigated the position artefacts of the markers and revealed that the displacement with respect to the underlying bone during the movements amounted up to 40 mm. They also showed that skin movement artefacts can cause maximal errors in the estimation of bone orientation (Cappozzo, Catani, Leardini, Benedetti, & Croce, 1996). As the marker placements on anatomical landmarks, such as greater trochanter, lateral epicondyle of

the femur, head of the fibula and lateral malleolus undergo significant displacements in relation to the underlying bone, it has been concluded that these markers are not suitable for tracking the movement of the bone. Skin markers which were located on the lateral portion of the thigh and shank caused smaller artefacts and are thus more suitable (Cappozzo et al., 1996). Thus, the calibrated anatomical system technique (CAST) has been proven to be reliable and reduce skin artefacts (Cappozzo et al., 1995; Pinzone, Baker, Preece, & Jones, 2015). Manal, McClay, Stanhope, Richards, & Galinat (2010) investigated differences between various marker sets and revealed good results of markers mounted to a moulded overwrapped Orthoplast shell. Thus, for this study, the shank and thigh markers were mounted on rigid plates and were attached to the segments with an overwrapped technique.

In this study a 6 degrees of freedom modelling method was used, which provides six variables for each segment to describe its position and orientation. It provides information about the origin of *x,y,z* and the rotation about the principal axes. Thereby it describes the segment translation along the three axes (vertical, medial/lateral and anterior/posterior) and the rotation is described about each axis of the segment (sagittal, frontal and transversal). It has been shown to be valid and repeatable and thus has been applied in this study (Collins, Ghoussayni, Ewins, & Kent, 2009; Schmitz et al., 2016; Żuk & Pezowicz, 2015).

3.4.1.2. The marker placement

The researcher attached in total 40 retro-reflective markers to the skin of the lower limb on both legs (Figure 3.15). All markers were put on the subjects through palpating the anatomical landmarks by the same researcher.

To define the pelvis segment the markers were positioned on the anatomical landmarks of the anterior-superior and posterior-superior iliac spine. Additionally, markers were placed on the landmark of the greater trochanter. On each side one marker was placed on the iliac crest vertically aligned with the greater trochanter marker (Figure 3.15).

The cluster, each of which had 4 markers mounted on a moulded Orthoblast shell, was placed laterally on each segment of thighs and shanks. They were attached to the skin by using double-sided tape and elastic bandages to avoid sliding on the skin surface. The position of the corners of each cluster were marked with a pen, to ensure that the clusters did not move during the

trials. If they moved the data would be scrapped and the experiment would be started again with new marker placement.

Markers were placed on the femoral epicondylus medialis and lateralis on each leg. Therefore, the assessor palpated the epicondylus from inferiorly and placed the marker slightly above the knee joint onto the epicondylus. One marker was placed on the malleolus medius and one on the malleolus lateralis. The lateral marker was aligned vertically with the medial marker to ensure that the markers defining the knee axis were aligned with the landmark that defined true knee axis of the knee joint (Figure 3.15). To ensure that the markers were placed on the true knee axis, the participant was asked to squat and the marker placement was visually checked.

Lastly, four foot markers were permanently attached to the test shoes, which were provided in several different sizes. This permanent attachment of markers to the shoes enabled a consistent marker placement for the feet. On each shoe one marker was placed on the heel (calcaneus), one marker on the proximal head of the 1st and 5th metatarsal bone and one marker was placed distally on the metatarsal head of the 2nd toe (Figure 3.15).

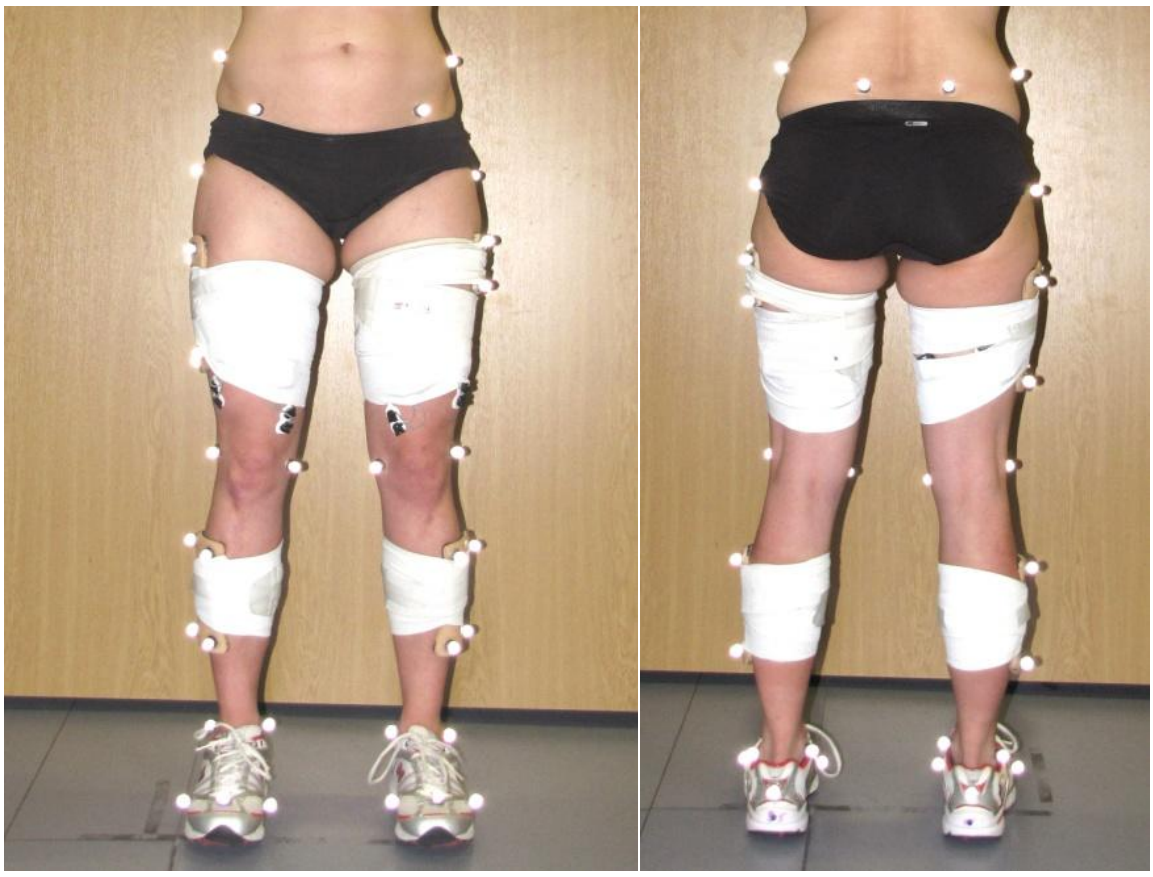


Figure 3.15: Marker and electromyographic electrodes placement (four muscles on each leg were measured)

3.4.1.3. Surface electromyography (sEMG)

Although the sEMG might enable a great insight into the muscle, the sEMG signal always contains unavoidable noise and might lead to an erroneous interpretation of the signal (De Luca, Gilmore, Kuznetsov, & Roy, 2010). The amount of noise depends on the signal influencing factors such as the fat-tissue thickness between the skin and the muscle, the action potential shapes and the muscle types (Clancy, Morin, & Merletti, 2002; De Luca et al., 2010). Thus, to increase the fidelity of the sEMG signal attention should be paid in particular to the sampling rate, the skin preparation, the position of the electrodes as well as the signal analysis (filtering, rectification and smoothing).

The sEMG data was collected by using the Noraxon Telemyo DTS system which is a surface EMG system that can collect up to 16 channels of single differential surface data. The sampling rate was 1500Hz. Based on the Nyquist Theorem, the selection of an adequate sampling frequency should be at least twice as high as the frequency component being measured (Millette, 2013). As the content of sEMG signals can be up to 500Hz (Clancy et al., 2002; Winter, 2009), the sEMG signal should be sampled at a minimum of 1000Hz to avoid aliasing of the signals (Burden, 2008; Ives & Wigglesworth, 2003).

A key factor when using sEMG is the electrode placement and the skin preparation (Farina, Cescon, & Merletti, 2002; Farina et al., 2014; Wong & Ng, 2006). To ensure a high fidelity of the sEMG signal, the skin preparation and placement was performed in strict accordance to the SENIAM guidelines (Hermens et al., 1999). Therefore, the skin was shaved if the electrode placement spot was covered with hair. The shaved area was then rubbed with a hypoallergenic abrasive gel and then wiped with alcohol. As action potentials from motor neurons propagate along the muscle fibre, the self-adhesive electrodes were placed on the skin in the direction of the muscle fibres (Hermens et al., 1999; Nishihara & Isho, 2012).

The sEMG electrodes were placed to collect the signals of the vastus medialis (VM) and lateralis (VL), biceps femoris and semitendinosus. To avoid additional artefacts, the electrodes, sEMG boxes and the cable were covered and fixated with bandages. The VM and VL electrodes were not covered with bandages because they were closely located to the knee and the bandages in this area might influence the knee motion. As the electrodes and boxes were occasionally covered with bandages, the question arose whether the bandages and the box placement might affect the sEMG signal. Thus, a pilot study on this was completed (chapter 3.4.5.1).

Supine position:

The participants were asked to lie on the examination couch with the knees resting on a pillow with 20° knee flexion.

Vastus medialis (VM):

The electrode was placed at 80% on the line between the anterior spina iliaca superior and the joint space in front of the anterior border of the medial ligament. The participants were then asked to extend their knee to confirm the placement by visually controlling the muscle bulge (Figure 3.16)

Vastus lateralis (VL):

The electrode was placed at 2/3 on the line between the anterior spina iliaca superior and the lateral side of the patella. The participants were then asked to extend their knee to confirm the placement by visually controlling the muscle bulge of the vastus lateralis (Figure 3.16).

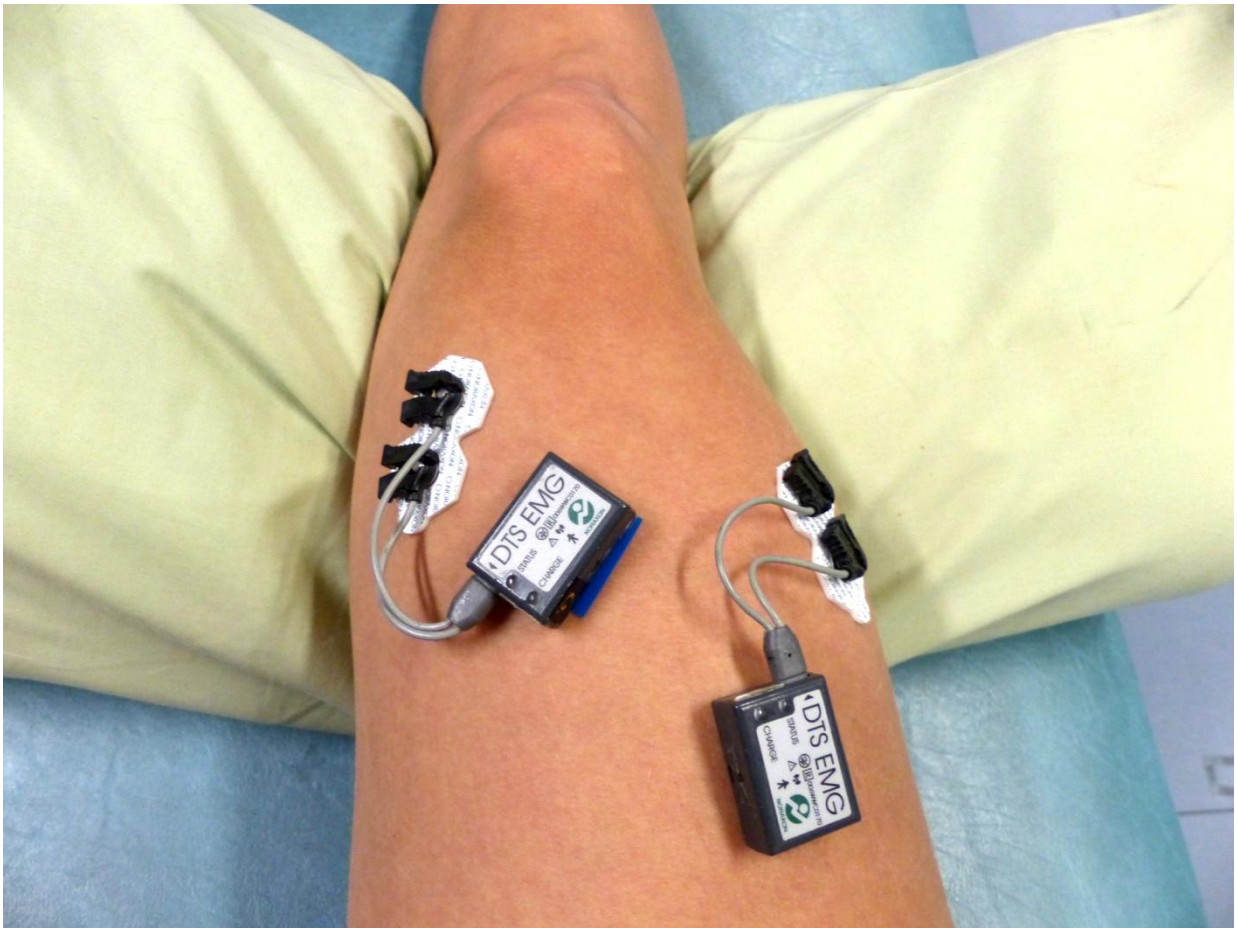


Figure 3.16: Photos of the sEMG application: vastus medials and vastus lateralis

Prone position:

The participants were asked to lie prone on the examination couch.

Biceps femoris:
The electrode was placed at 50% on the line between the ischial tuberosity and the lateral epicondyle of the tibia. The participants were then asked to bend their knee against the resistance applied by the examiner. The electrode position was then controlled by palpating the muscular contraction of the biceps femoris (Figure 3.17).

Semitendinosus:
The electrode was placed at 50% on the line between the ischial tuberosity and the medial epycondyle of the tibia and controlled by palpating the muscle activation during knee flexion contraction with resistance (Hermens et al., 1999) (Figure 3.17).

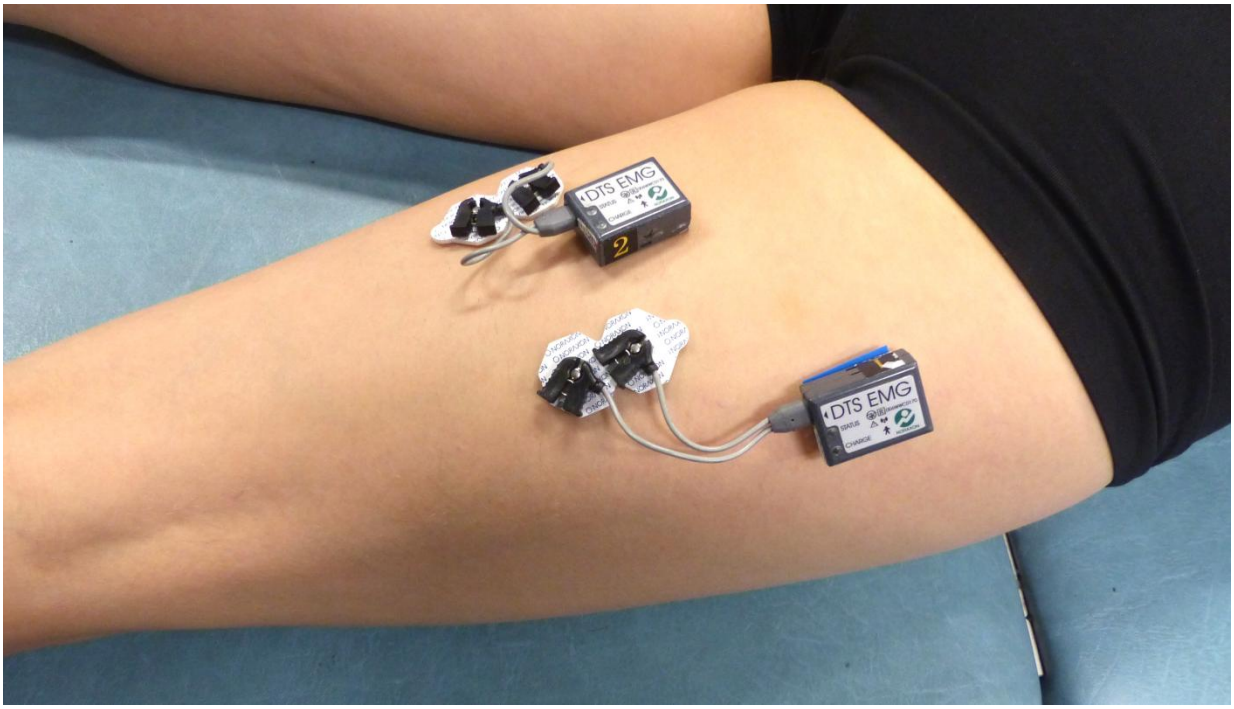


Figure 3.17: Photos of the sEMG application: semitendinosus and biceps femoris

After all markers and EMG electrodes were attached, the test was ready to start. Each trial was firstly explained and demonstrated to the participant. Then each participant had three practice trials to habituate to the task.

The first task was a static trial. The participant was asked to stand on the ground next to the third platform. When the trial started the participant was asked to step onto the third platform and then to stand still for 8 seconds with the arms across the chest. After ensuring that all of the markers were captured during the static trial, the following markers were removed for the dynamic trials: iliac crest, greater trochanter, epicondylus lateralis and medialis, malleolus lateralis and medialis. Thus, each segment (pelvis, thigh, shank, foot) was defined with a total of four markers during the dynamic trials.

3.4.1.4. Running

The participant was asked to run on a 15 m walkway at a self-selected speed and to walk back slowly to ensure a sufficient recovery time and to limit fatigue. The self-selected speed has been chosen as it has been previously shown to increase gait symmetry (Chung & Giuliani, 1997). The participant was asked to practice these running trials 3 times as a period of habituation. During this habituation phase, the assessor adjusted the start position for the participant so that he/ she would hit one platform with the dominant leg without an overlap of the foot between the force platform and ground floor. Running speed was controlled and reported by using Brower timing lights (Draper, UT) to ensure that each trial was within ±5% of the original self-selected speed. The set of Brower timing lights (Draper, UT) were set at hip height for all participants. Each participant was asked to perform five successful running trials at a self-selected speed for the dominant and non-dominant leg. A successful trial required an occurrence of the stance phase on the force plate (AMTI), without an overlap of the foot between force plate and ground floor, within the field of the view of the high-speed motion analysis camera system. Unsuccessful trials were ones whereby less than three markers per segment were visible, speed changes were seen during the trials, or a partial/double contact with the force platforms occured.

3.4.1.5. Step down task

The participant was then asked to perform five times a unipedal step-down test. The participant stood on a 15.8 cm high step and was holding his/her arms folded across his/her chest. Throughout the whole test the participant stood on his/her dominant leg. Each participant was then asked to lower the non-dominant leg down from the step as far as possible and return the leg back to the starting position. If the investigator observed compensatory movement strategies, such as lateral flexion of the trunk or trunk rotation, the participant was verbally cued. If the participant attempted to push off the ground to propel themselves upward while returning to level with the platform, they were warned and instructed to step down less deep to ensure that they could maintain their balance. The participant was instructed to perform that task until five successful trials were recorded. A trial was successful when the participants performed that task without losing the balance during the trial.

3.4.1.6. Single leg squat

For the performance of a single leg squat task, the participant was asked to maintain a single-leg stance on the dominant leg and to fold his/her arms across his/her chest. Then he/ she was asked to squat down as far as possible in a slow, controlled manner, while maintaining his/her balance, at a rate of approximately 1 squat per 2 seconds. The single leg squat was performed until five successful trials were recorded. A trial was successful when the participants performed that task without shifting any weight to the non-dominant leg and without losing balance during the trial.

3.4.1.7. Star excursion balance test

The star excursion balance test (SEBT) is an assessment to investigate dynamic postural control (Hertel, Miller, & Denegar, 2010; Kinzey & Armstrong, 1998). The SEBT is a closed-kinetic chain exercise which mimics the single leg squat exercise and thereby requires adequate stance leg strength, proprioception, neuromuscular control and adequate range of motion at the hip, knee and ankle joints (Olmsted, Carcia, Hertel, & Shultz, 2002; Robinson & Gribble, 2008).

The participant stood on the platform of the star excursion balance test (SEBT) and was asked to maintain a single-leg stance on the dominant leg whilst reaching the opposite leg forwards to

move the reach indicator as far forward as possible along the arm of the SEBT with the most distal part of his/her foot. The participant was instructed to maintain the weight on the dominant leg and was not allowed to touch down the free leg to keep balance or to put the foot on top of the reach indicator to gain support. Furthermore, the participant was instructed to keep the arms folded across the chest throughout the task. This was attempted until five successful trials were recorded. A trial was successful when the participant performed that task without shifting any weight to the non-dominant leg and without losing balance during the trial. The reach direction was evaluated by moving the counter with the foot, where the distance was identified on the arm of the SEBT. Whilst eight directions can be assessed, the reaching direction was reduced to the anterior direction as this produces a high level of quadriceps muscle activation which commonly is observed clinically as a deficiency in individuals with PFP (Earl & Hertel, 2001; Gribble, Hertel, & Plisky, 2012)

3.4.2. Kinetic and kinematic data processing

After the 3D, force and sEMG recordings were recorded with Qualisys 2.11 Track Manager (QTM^{TM}), the markers were labelled and inspected for any marker irregularities or inconsistencies and exported to C3D files. The files were then loaded onto Visual3D v5 Professional (C-motion, inc., USA).

In Visual3D, a six degrees of freedom model was adopted for each segment. Therefore the height and weight of each participant was entered to enable the calculation of moments and forces. For each segment: Pelvis, right thigh, right shank, right foot, left thigh, left shank and the left foot the proximal and distal joint and radius were defined. By setting the proximal and distal joints and radius, the position and orientation of each segment was created in Visual3D (Figure 3.18).

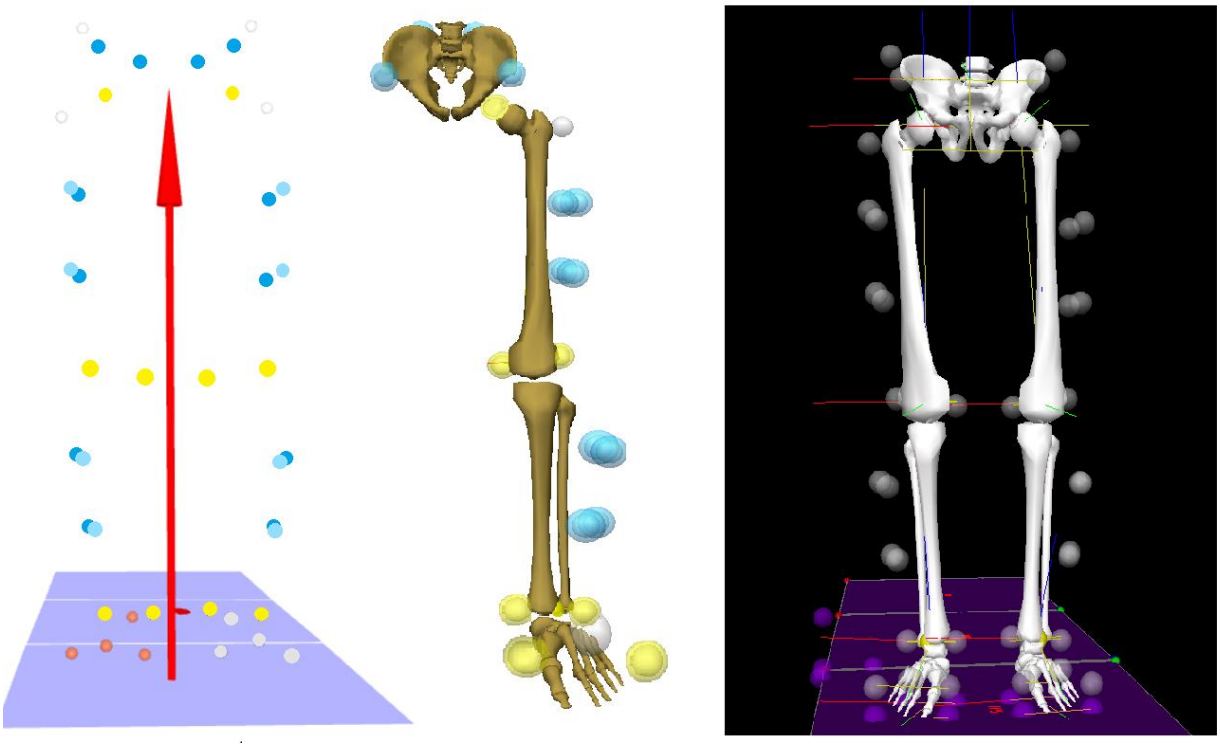


Figure 3.18: QTM™ (left) and Visual3D segment models (middle) and Visual3D full bone model (right)

For the pelvis segment the CODA model was used. For this pelvis coda model, the anatomical locations of the Anterior Superior Iliac Spine (ASIS) and the Posterior Superior Iliac Spine (PSIS) on both sides were utilised. The x-y plane of the segment coordinate system is defined as the plane passing through the right and left ASIS markers and the mid-point of the right and left PSIS markers and the z-axis is perpendicular to the (x-y) plane (Figure 3.19).

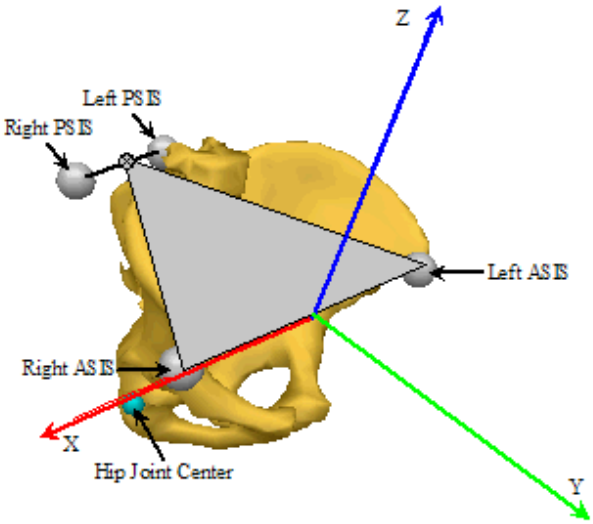


Figure 3.19: Pelvis coda model by Charnwood Dynamics

Based on the coda pelvis segment the centre of the hip joint was calculated in the following way:

- the coordinates of the right hip joint centre: 0.36*ASIS_Distance, -0.19*ASIS_Distance, -0.3*ASIS_Distance (ASIS_Distance is the distance between the ASIS of both sides)
- the coordinates of the left hip joint centre: -0.36*ASIS_Distance, -0.19*ASIS_Distance, -0.3*ASIS_Distance

This estimation is based on the established prediction method of Bell et al. (Bell, Brand, & Pedersen, 1989; Bell, Pedersen, & Brand, 1990), which has been recommended for the use in motion analysis as a non-invasive technique with relatively small and un-biased errors (Leardini et al., 1999).

The thigh segment was created using the hip joint centre as the proximal marker and the medial and lateral femoral epicondylus as distal landmarks. The thigh cluster was used as tracking targets.

The proximal landmarks of the shank segment were the medial and lateral femoral epicondylus and the distal landmarks were the medial and lateral malleolus. The four markers on the shank clusters were the tracking targets.

The proximal markers for the foot segment were the medial and lateral malleolus and the distal landmarks were the 1st and 5th toe. Since the ankle joint and the toe targets were not parallel to the floor, an offset was caused in the ankle angle which resulted an increased plantarflexion. To remove this offset, a left and right virtual foot were built to create a clinical relevant ankle joint angle. Therefore the neutral ankle angle was defined as a flat foot with a vertical shank segment, regardless of the actual foot posture during the static trial. Three landmarks were created which represented the lab and removed the offset. Then four further landmarks representing the projection of the malleolus medialis and lateralis, the 5th and the 1st toe were used to build the neutral virtual foot and to calculate the ankle kinematics.

Automatic gait events were created with Visual3D for the running trials, whereby right/ left heel strike (RHS/ LHS) and right/ left toe off (RTO/ LTO) were created for kinematic based categories and right/ left on (RON/ LON) and right/ left off (ROFF/ LOFF) for kinetic based categories. RON/ LON and ROFF/ LOFF events were only created when stance phase was

completed on a force platform (Figure 3.20). The single leg squat and step down task started when the dominant leg was in 10-15° knee flexion and ended when the dominant leg reached 10-15° knee flexion (Figure 3.20).

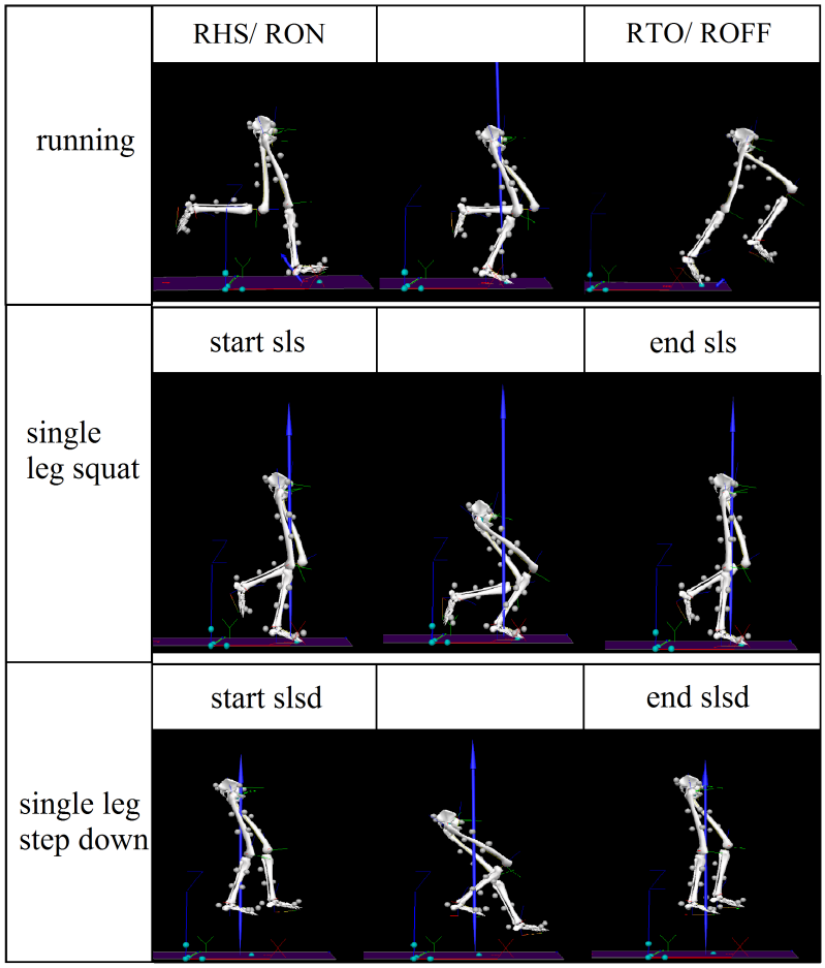


Figure 3.20: Events during running, the single leg squat and the step down task (Visual 3D).

A Butterworth Bidirectional Filter for low-pass filtering with a cut-off frequency of 12Hz was used to filter the markers raw data. Then the marker coordinate data was interpolated for all tasks, to fill the gaps for any markers which had absent data for maximally 10 frames (Besier, Fredericson, Gold, Beaupre, & Delp, 2009; Mok, Kristianslund, & Krosshaug, 2015) (Figure 3.21).

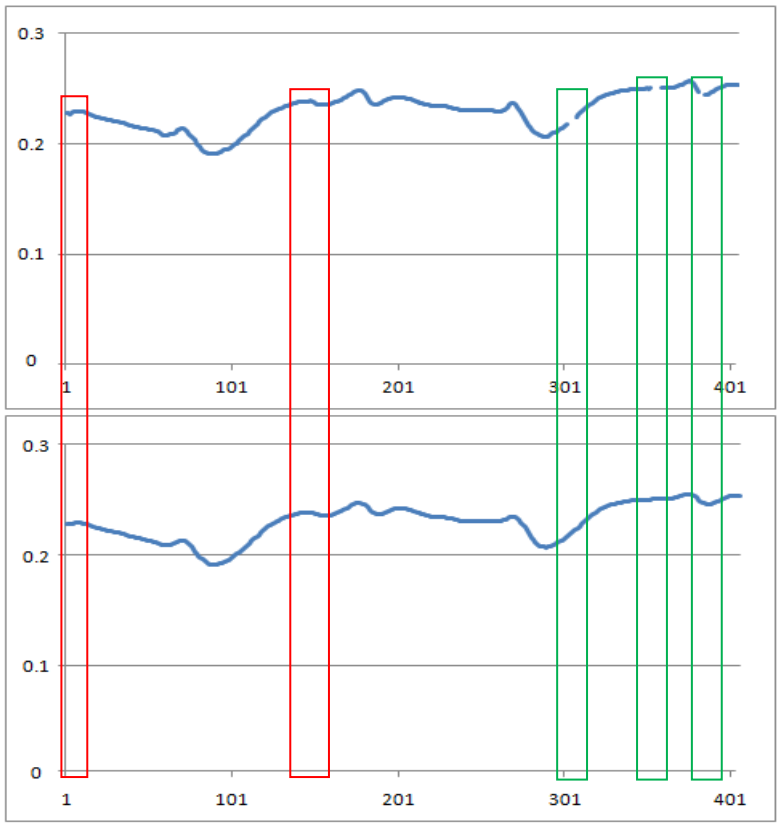


Figure 3.21: Sagittal right anterior superior iliac spine marker during running without (graph above) and with a 12Hz low-pass filter and an interpolation of a maximum of 10 frames(graph below). The red framed areas show the effect of the 12Hz low-pass filter on the force data. The green framed areas show missing data (graph above), which was interpolated successfully with a maximum of 10 frames (graph below).

To delete unwanted electrical interference noise, kinematic and kinetic data were filtered with a Butterworth Bidirectional Filter with a cut-off frequency of 12Hz. Kristanslund et al (2012) revealed a significant effect on joint moments when different cut-off frequencies had been chosen for movement and force data. Thus, to avoid impact artefacts, they strongly recommended that kinetic and kinematic data should be processed with the same filter (Kristianslund, Krosshaug, & van den Bogert, 2012). To make the data comparable to findings from previous studies a filter of 12Hz has been chosen as this was the most frequently applied filter (Alenezi, Herrington, Jones, & Jones, 2014; Almonroeder, Benson, & O'Connor, 2015; Bazett-Jones et al., 2013; Liew, Morris, Robinson, & Netto, 2016).

The three dimensional inverse dynamics were used to calculate the external hip and knee joint moments. The joint moments were normalised to body mass to ensure that the observed differences are related to the physical characteristics and task rather than the body mass (Andriacchi, Natarajan, & Hurwitz, 2005). The joint moments were presented as external

moments referenced to the proximal segment. The external moments are the gravitational forces that act on the joint. Thus, an external knee flexion load describes the tendency to flex the knee (Hewett et al., 2005). In contrary, the internal moments are generated by muscle contractions and bone-on-bone forces by tension in the soft tissue and are the reaction to maintain a joint equilibrium to the external moments acting on the body (Levine, Richards, & Whittle, 2012).

3.4.3. Electromyographic analysis

The data collection was synchronised with the motion capture system. To reduce the influence of variability in sEMG signals during functional tasks, a maximum number of recordings per participant and per velocity condition were included and a minimum of 5 trials per measurement was required.

The surface electromyography (sEMG) signal is inevitably affected by noise and artefacts. At the high-frequency end of the sEMG signal, the bandpass filter cut-off should be set where the noise exceeds the sEMG signal (De Luca et al., 2010). This high frequency cut-off is set in most studies at 500Hz (Aminaka et al., 2011; Boling et al., 2006; Cavazzuti et al., 2010; Coqueiro et al., 2005; Earl, et al., 2005; Ferrari et al., 2014; Nakagawa et al., 2015; Nakagawa et al., 2012; Ott et al., 2011; Owings & Grabiner, 2002; Saad et al., 2011; Tang et al., 2001). Furthermore, guidelines recommended the use of a high frequency cut-off of 500Hz (Hermens et al., 1999; Merletti et al., 1999). Based on these findings, a high-frequency cut-off of 500Hz was chosen. To define a filter for the low-frequency end is more challenging, as the low-frequency noises overlap with the signals of the sEMG. Low frequency noises are mostly baseline noises, such as skin-electrical noise and the movement artefact noise. To date, different recommendations for a low end of a bandpass filter have been reported, such as the recommendation for 5Hz by the Standards for Reporting EMG data (Merletti et al., 1999), 10Hz by the Journal of Electromyography & Kinesiology (Kinesiology, 1996), 20Hz by the International Society of Electromyography and Kinesiology (Winter et al., 1980) and 10-20Hz by the SENIAM guidelines (Hermens et al., 1999). DeLuca et al. (2010) investigated the effect on the sEMG data with low-frequency cut-offs of 10, 20, 30 and 40Hz and showed that the rate of artefact where the greatest between 1 and 10Hz and showed that 30 and 40Hz filter caused a signal loss of the sEMG signal of 7 to 13%. The 20Hz filter showed to retrain the desired sEMG content and remove the low frequency noise, thus they recommended for natural and

common movements a corner frequency of 20Hz (De Luca et al., 2010), which was chosen and applied in this study as well (Figure 3.22).

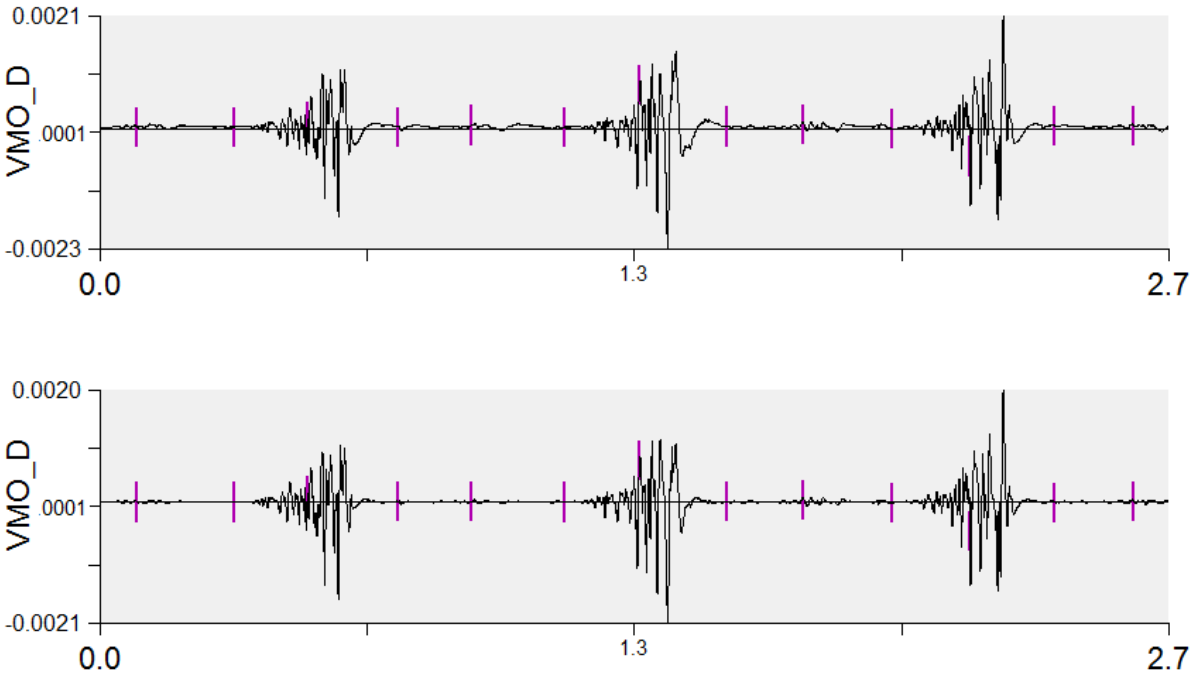


Figure 3.22: Vastus medialis sEMG signal of the dominant leg during running: raw data (graph above) and after the band-pass filter of 20-500Hz (graph below).

After band-pass filtering, the sEMG signal is assumed to be noise-free and uncorrelated (Clancy, Negro, & Farina, 2016). Since averaging the EMG signal would result in zero, the signal has to be rectified. The rectification can be carried out with two different techniques: the half and the full rectification. The half rectification removes the negative values, whereas the full rectification takes the absolute values or the square of each sample (Clancy et al., 2016; Gerdle, Karlsson, Day, & Djupsjöbacka, 1999) (Figure 3.23).

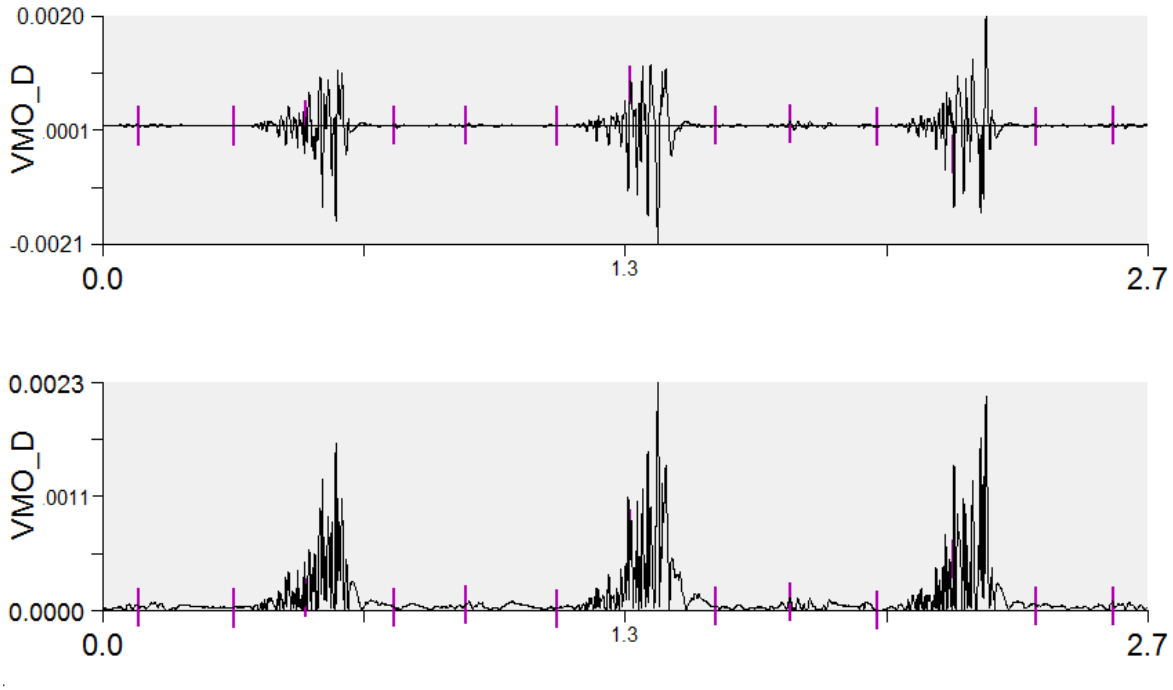


Figure 3.23: Vastus medialis sEMG signal of the dominant leg during running: band-pass filtered sEMG signal (20-500Hz) (graph above) and the full rectified signal (graph below).

After a full-rectification of the sEMG signal, a digital smoothing algorithm had to be applied to diminish the random fluctuations and to outline the trend of the signal development (Clancy et al., 2016; Gerdle et al., 1999; Konrad, 2005). This smoothing process can be accomplished by using a linear low-pass filter or a moving average (Clancy et al., 2016). The alternative for smoothing the signal without a previous rectification is to compute the root mean square (rms), where the squared values of the original EMG signal at each moment of time are calculated and thus do not require a previous rectification (Kamen, 2014) (Figure 3.24). The moving average is calculated by averaging a certain amount of data using a gliding window technique (Figure 3.25). In literature, the moving average is often called average rectified value (ARV), because it describes the process of averaging the rectified signal (Burden, 2008; Gerdle et al., 1999; Konrad, 2005). Alternatively the signal can be smoothed with a linear envelope which is computed with a low-pass filter, which is a type of moving average indicator of the EMG magnitude (Figure 3.24). Although all smoothing methods are recognised as appropriate, the rms is considered to provide the most insight of the EMG signal, as it averages the electrical power and thereby measures the power of the EMG signal (Burden, 2008; Gerdle et al., 1999; Konrad, 2005). In addition, the rms produces a waveform which is easily analysable (Delsys,

2016). Thus, the rms has been recommended to smooth the sEMG signal and was used for the sEMG analysis in this thesis (Burden, 2008; Gerdle et al., 1999; Konrad, 2005).

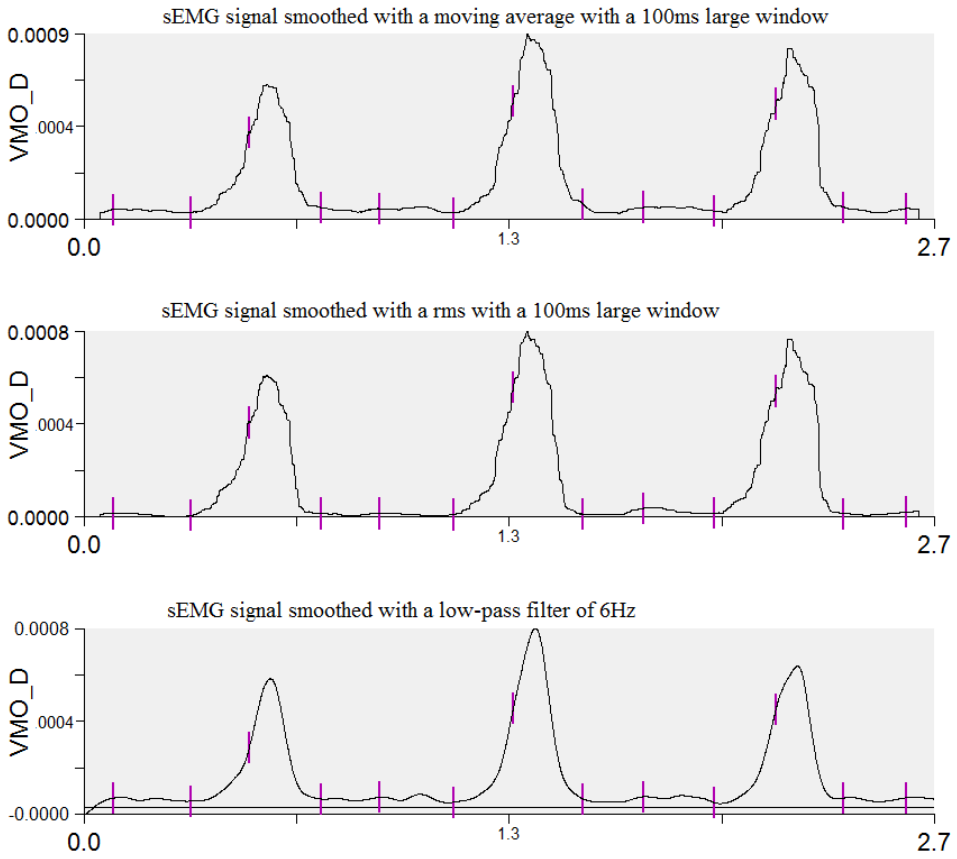


Figure 3.24: Vastus medialis sEMG signal of the dominant leg during running: smoothed with a moving average of 100 ms (first graph), smoothed with a rms of 100 ms (graph in the middle), smoothed with a low-pass filter of 6Hz (graph below).

The envelope filtering and smoothing of the sEMG signal has a significant influence on the within and between subjects variability, but also on the variations which occur in the signal (Burden, 2010; Burden, Lewis, & Willcox, 2014). However, the smoothing of the sEMG signal is essential to increase the reliability and validity of the findings (Konrad, 2005). One study recommended that a linear envelope cut-off should be at least 9Hz during a gait task (Burden et al., 2014). Although it is known that an inadequate envelope filtering can result in sEMG data loss, the envelope EMG frequency still ranges in studies from 3.8Hz up to 12.8Hz during gait (Frigo & Crenna, 2009). So far there is no recommendation for the choice of the size of the envelope filter or sEMG signal smoothing during single leg squat, step down or the running

task. Thus, the current literature was reviewed to investigate which envelope filter in these tasks have been applied so far. Eight identified studies analysed sEMG amplitude data in participants with patellofemoral pain (PFP) during stair stepping (Bolgla et al., 2011; Crossley, Cowan, Bennell, & McConnell, 2004; Earl, et al., 2005; Kim & Chang Ho, 2012; McClinton, Donatell, Weir, & Heiderscheit, 2007; Nakagawa, Muniz, et al., 2011; O'Sullivan et al., 2012; Powers, 1996), four during squatting (Boling et al., 2006; Cavazzuti et al., 2010; Nakagawa et al., 2012; Tang et al., 2001) and two during running (Esculier et al., 2015; Willson et al., 2011). The stair stepping task had been smoothed with a rms or moving average with window sizes of 10 ms (Earl, et al., 2005; Powers et al., 1996), 50 ms (Kim & Chang Ho, 2012), 55 ms (Bolgla et al., 2011) and 150 ms (O'Sullivan & Popelas, 2005) and had been smoothed with a low-pass filtered of 4Hz (K. M. Crossley et al., 2004), 6Hz (McClinton et al., 2007; Tang et al., 2001), 10Hz (Cavazzuti et al., 2010) and 15Hz (Nakagawa, Muniz, et al., 2011). The envelope filtering during the squat task had been carried out with rms windows of 20 ms (Boling et al., 2006) and 75 ms (Nakagawa et al., 2012) and a low-pass filter of 6Hz (Tang et al., 2001) and 10Hz (Cavazzuti et al., 2010). The running task had been rectified and smoothed with a low-pass filter of 6Hz (Willson et al., 2011) and 20Hz (Esculier et al., 2015). These results show the current heterogeneity of envelope filtering and sEMG smoothing in studies which investigate the sEMG amplitude in participants with PFP. This heterogeneity is also caused by the variety of analysed muscles and the different purposes of the sEMG analysis, such as the investigation of neuromuscular control, peak amplitude or cocontraction. To investigate which sEMG smoothing might be the most appropriate for this study, a pilot study on different rms window sizes had been carried out, which can be found in chapter 3.4.4.2.

The magnitude of the EMG signal can be influenced by many anatomical and physiological factors, such as cross-talk, joint angles, velocity, or muscle length (De Luca, 1997). To eliminate these influences, the EMG signal has to be normalised, which is carried out by dividing the EMG signal by a reference contraction value (Burden, 2010; De Luca, 1997). Additionally, the normalisation method allows that the EMG data is presented as a percentage of the reference contraction and thereby allows comparisons between individuals or different muscles (French, Huang, Cummiskey, Meldrum, & Malone, 2015). The Journal of Electromyography and Kinesiology and the SENIAM guidelines recommend the normalisation by using a MVC as the reference contraction (Kinesiology, 1996; Merletti, 1999), which expresses the task EMG as a percentage of the maximal activation capacity of the muscle (Burden, 2010). Alternatively to the MVC normalisation, dynamic normalisation methods exist

such as the mean or peak normalisation. The dynamic normalisation method express the task EMG as a percentage of the mean or peak of the same EMG signal (Burden, 2010; Burden, Trew, & Baltzopoulos, 2003). The dynamic normalisation has also been individually adapted to the study design by expressing the running task EMG by 70% of a peak sprint (Albertus-Kajee, Tucker, Derman, Lamberts, & Lambert, 2011) or by expressing a squat EMG by 60%, 70% and 80% of the mean squat (Balshaw & Hunter, 2012). Although to date, the MVC normalisation method is the most commonly applied normalisation method, no consensus has been reached about which method is the most appropriate normalisation method. Several studies investigated different normalisation methods and showed a higher intra-subject variability and reduced sensitivity of the MVC normalisation method compared with dynamic normalisation methods (Albertus-Kajee et al., 2011; Balshaw & Hunter, 2012; Burden & Bartlett, 1999; Burden et al., 2003; Chapman, Vicenzino, Blanch, Knox, & Hodges, 2010; French et al., 2015). Two other studies found that, in contrary, the MVC normalisation method demonstrated a high repeatability (Bolgla & Uhl, 2007) and high sensitivity (Benoit, Lamontagne, Cerulli, & Liti, 2003). Burden (2010) carried out a literature review on normalisation methods and revealed that the mean and peak normalisation techniques reduced the inter-subject variability more than any other normalisation technique (Burden, 2010). In addition, during the quadriceps MVIC testing in this reliability study the muscles were also stimulated to investigate quadriceps AMI. The application of the electrodes for the stimulation was not possible without overlapping with the quadriceps sEMG electrodes and boxes. However, it is not known whether the stimulation might damage the Noraxon equipment. Thus, to ensure that the Noraxon equipment remained intact, it has been decided to not collect MVIC values with the sEMG for this study. The disadvantage of using the mean normalisation technique is that it does not enable the investigation of the co-contraction ratio of the quadriceps and the hamstring muscle group, because the magnitude would be reflected in the denominator (i.e. the peak or mean EMG) (Burden, 2010). However, since this study aimed to investigate the reliability of the sEMG data, the mean normalisation did not cause any disadvantages and was used in this study.

3.4.3. Pilot studies to investigate sEMG analysis

As previously described the sEMG boxes and electrodes were partly covered with bandages to fixate them appropriately. As it was unclear whether the bandages above the boxes and the electrodes affect the sEMG signal, a pilot study was carried out. Furthermore, it is important

that the sEMG smoothing results in a waveform that represents the EMG signal and eliminates the random fluctuations of the sEMG signal. Thus, the second pilot study investigated the optimal window width for the sEMG during the stance phase of running and during the step down task.

3.4.4.1 Pilot study on sEMG application

The sEMG boxes and electrodes were partly covered with bandages to fixate them appropriately. As it was unclear whether the bandages above the boxes and the electrodes affect the sEMG signal following pilot study was carried out.

Methodology

One male participant (age: 28 years, 1.75 m height, 74kg weight) was tested. Before electrode placement, the skin was shaved, cleaned with an abrasive gel and alcohol to reduce the electrical impedance. The electrode was then placed on the medial gastrocnemius according to the SENIAM guidelines (Hermens et al., 1999). Furthermore, retro-reflective markers were attached to the skin of the lower limb on the tested leg and the pelvis, so that the start and end of the tip-toe standing task could be defined.

The participant was asked to slowly perform a tip toe stand and then to return back to standing. This task was performed five times for each of the following conditions:

- A: no bandages on the box and the electrode
- B: two tight bandages on the box
- C: two tight bandages on the electrode
- D: two tight bandages on the box and the electrode

The sEMG signal was filtered with a fourth order zero-lag Butterworth filter of 20-500Hz, smoothed with a rms of 300 ms and mean-normalised.

The statistical analysis was performed using SPSS (v. 20, IBM corporation, USA) and Excel 2013 (Microsoft, Office Ultimate 2013, USA). The graphs were plotted by using Matlab (R2016b, Math Works, USA). The difference of the averaged peak activity during the tip toe standing task during the four different conditions was analysed by using the Friedman test

(p=0.05) and the Wilcoxon test as a post-hoc analysis (p=0.017). The mean and one standard deviation (SD) of the normalised sEMG signal of the gastrocnemius muscle were plotted for each of the four conditions.

Results

The averaged peak activity during the tip toe standing task during the four different conditions was not significantly different (p=0.443), which were confirmed with the results of the post hoc analysis (Table 3.1). The averaged peak results during the tip toe standing were highest when the bandages were applied on the electrodes and the boxes and lowest when the electrodes were applied without bandages (Table 3.2). In addition, the graphs showed the highest variability when no bandages were applied and the lowest variability with bandages on the box and the electrodes (Figure 3.25).

Table 3.1: comparison of the peak sEMG signal of the Gastrocnemius muscle during the tip toe stand

Test condition		**P value: (Wilcoxon, sig 2-tailed)**
A. no bandage	B. bandage on electrode C. bandage on box D. bandage on box & electrode	0.327 0.327 0.249
B. bandage on electrode	C. bandage on box D. bandage on box & electrode	0.889 0.345
C. bandage on box	D. bandage on box & electrode	0.753

* *indicate significant differences between the four conditions.*

Table 3.2: Averaged peak sEMG signal (% norm) of the Gastrocnemius muscle during the tip-toe stand.

	Averaged peak value (% norm) of the sEMG activity			
	No bandage	Bandage on electrode	Bandage on box	Bandage on both
Mean (SD)	1.67 ±0.03	1.72 ±0.9	1.75 ±0.17	1.79 ±0.16

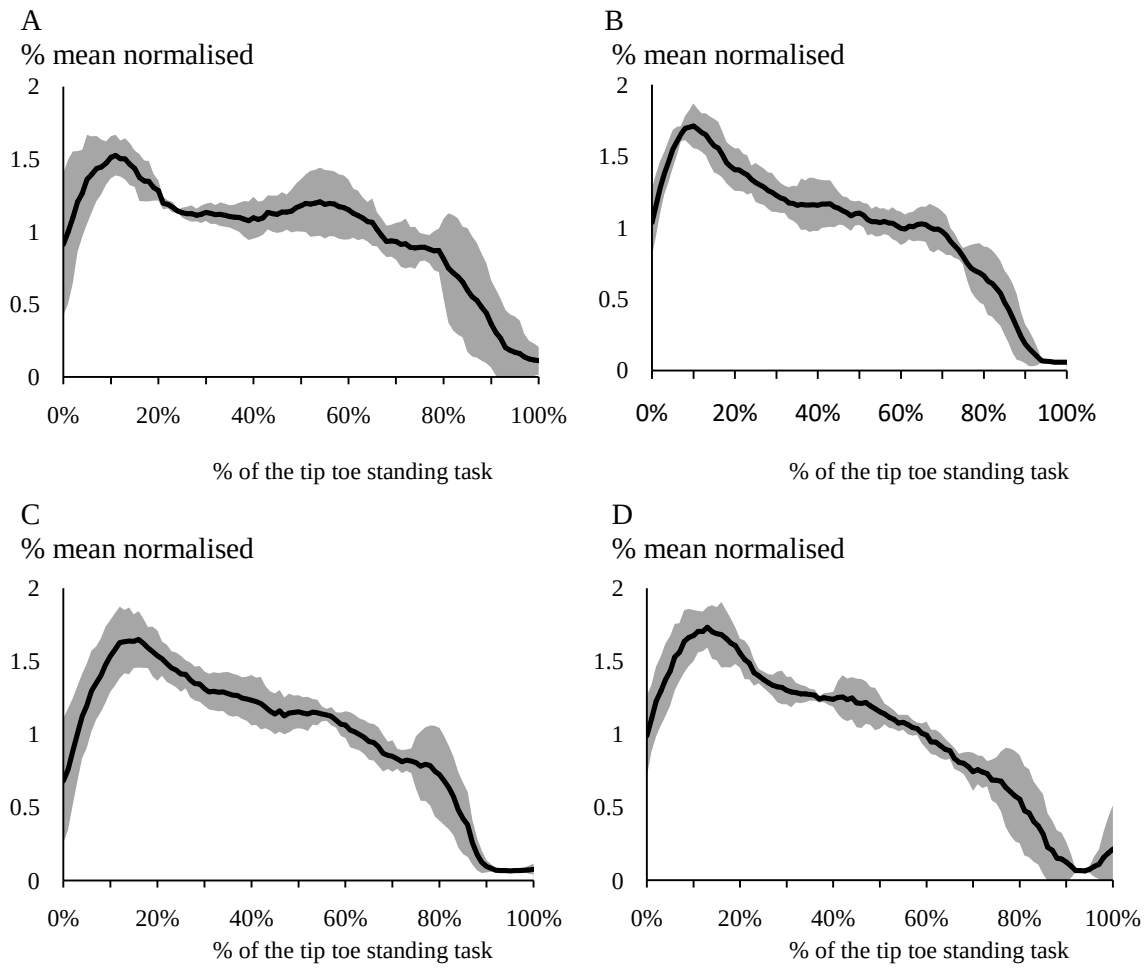


Figure 3.25: Gastrocnemius activity averaged during tip toe standing task: A= without bandage, B=Bandage on electrode, C= Bandage on Box, D= Bandage on both

Discussion and conclusion

The results showed that the differences between the conditions were not significant and thus, the electrodes and boxes could be either fixated with or without bandages. However, the results also showed that the signal was less variable when the boxes and electrodes were secured with bandages. Thus, if the bandages did not limit the comfort and movement of the participant, the electrodes as well as the boxes should be fixated with bandages to receive a clear and less variable EMG signal.

3.4.4.2. Pilot study on sEMG smoothing

As this thesis aimed to investigate the cocontraction of the quadriceps muscle (vastus medialis, vastus lateralis) and the hamstring muscles (biceps femoris and semitendinosus), it is important that the sEMG smoothing results in a waveform of the sEMG, which represents the EMG signal and eliminates the random fluctuations of the sEMG signal. Smaller window widths, such as 10-50 ms, allow the detection of rapid activity alterations, whereby larger widths, such as 100-500 ms decrease the variability of the amplitude and can be applied in slow or static activities (Burden, 2008; Konrad, 2005). Thus, different window widths of 25 ms up to 500 ms were applied for the stance phase of running and the step down task. The aim of this pilot study was to investigate the optimal window width for the sEMG during the stance phase of running and during the step down task.

Methodology

5 healthy participants, three female and two male individuals (age: 24.6 ±2.9 years, height: 1.72 ±0.1 m, mass: 64.18 ±7.66kg, BMI: 21.6 ±0.52kg/m^2) were tested twice, with a 7-day gap between the two test sessions. Electrodes were applied on the vastus medialis, vastus lateralis, biceps femoris and semitendinosus as described in chapter 3.4.1.3. Each participant was asked to perform the step down task until 5 successful trials were recorded and then he/ she was asked to run 5 times along a 15 m walkway at his/her own selected speed. The sEMG signal of the VM, VL, biceps and semitendinosus were sampled with a frequency of 1500Hz. The sEMG data was filtered using a fourth order zero-lag Butterworth filter of 20-500Hz. The sEMG data was smoothed during the stance phase of running by using a rms with window widths of 25, 50, 75 and 100 ms and was mean normalised. The sEMG data during the step down task was smoothed by applying a rms with 25, 50, 75, 100, 150, 300 and 500 ms window widths and was mean normalised. The step down task was investigated with larger window widths as it is a slower activity, then running.

The statistical analysis was performed using SPSS (v. 20, IBM corporation, USA) and Excel 2013 (Microsoft, Office Ultimate 2013, USA). The graphs were plotted by using Matlab (R2010a, Math Works, USA).

The difference of the averaged peak activity during the stance phase in running and the step down task with different window sizes were analysed using the Friedman test and the Wilcoxon

test as a post-hoc analysis. The percentage of alteration of the signal caused by an increased window size was expressed in %. Therefore the peak value of the signal smoothed with a window size of 25 ms was set as equal to 100% of the EMG signal. The percentage of the cut-off of the EMG signal peak caused by a smaller window was calculated by the following equation:

% = 100- [(100/ peak of 25 ms window)* peak of 50/ 75/ 100/ 150/ 300/ 400/ 500 ms window]

The mean and one standard deviation (SD) of the normalised sEMG signal of the VM and the biceps muscle were plotted for the first and the second test and the different window sizes for each task. The graphs were plotted to visually examine the effect of the smoothing of the signal with different window sizes.

The reliability of the sEMG signal between-session with different window sizes were assessed by using the intra-class correlation coefficients (ICC) and the correlation of multiple coefficient (CMC). The average of the peak values of the sEMG curves during the stance phase of running and the step down task were used to investigate the between-session reliability by using the ICC, model 3.5. The model 3 indicated the use of the two-way-mixed model of ICC, whereas the second number represents the number of the averaged measurement (Denegar, 1993; Portney, 2009; Weir, 2005).

The CMC is a measure of similarity of waveforms (Røislien, Skare, Opheim, & Rennie, 2012). The CMC analysis was carried out by comparing the five curves of each subject and each task of the first test session to the five curves of the same participant to the second test session (intersession CMC). In addition, the sEMG data of the five trials running and the five trials of the step down task were averaged for each subject for the first and the second test. The averaged EMG curves of the five subjects of the first test session were then compared with the second test session for the stance phase and the step down task by using the CMC (inter-subject CMC).

ICC and CMC values below 0.5 represent poor, between 0.5 and 0.75 moderate and above 0.75 good reliability (Kadaba, Ramakrishnan, Wootten, Gainey, Gorton, & Cochran, 1989; Portney, 2009).

Results

The post-hoc analysis showed no significant differences between the different window sizes (Table 3.3 & Table 3.4).

Table 3.3: Comparison of the peak sEMG signal of the Quadriceps (VM, VL) and Hamstrings (biceps, semitendinosus) muscles during the stance phase in running

Rms window width		P value: (Wilcoxon, sig 2-tailed)							
		Biceps		Semitendinosus		VL		VM	
		Test 1	Test 2	Test 1	Test 2	Test 1	Test 2	Test 1	Test 2
25 ms	50 ms	0.04	0.04	0.04	0.04	0.04	0.04	0.07	0.07
	75 ms	0.04	0.04	0.04	0.08	0.04	0.04	0.04	0.04
	100 ms	0.04	0.35	0.04	0.04	0.04	0.04	0.04	0.04
50 ms	75 ms	0.04	0.04	0.23	0.23	0.04	0.04	0.04	0.14
	100 ms	0.04	0.04	0.23	0.04	0.04	0.04	0.04	0.08
75 ms	100 ms	0.04	0.89	0.23	0.04	0.04	0.04	0.07	0.04

* Significant (p< 0.0125)

Table 3.4: Comparison of the peak sEMG signal of the Quadriceps (VM, VL) and Hamstrings (biceps, semitendinosus) muscles during the step down task

Rms window width		P value: (Wilcoxon, sig 2-tailed)							
		Biceps		Semitendinosus		VL		VM	
		Test 1	Test 2	Test 1	Test 2	Test 1	Test 2	Test 1	Test 2
25 ms	50 ms	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
	75 ms	0.08	0.04	0.04	0.04	0.04	0.04	0.04	0.04
	100 ms	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
	150 ms	0.04	0.04	0.04	0.14	0.04	0.04	0.04	0.08
	300 ms	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
	400 ms	0.04	0.04	0.08	0.04	0.04	0.04	0.04	0.04
	500 ms	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
50 ms	75 ms	0.22	0.04	0.04	0.08	0.08	0.04	0.69	0.08
	100 ms	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
	150 ms	0.04	0.04	0.04	0.89	0.04	0.04	0.08	0.50
	300 ms	0.04	0.04	0.04	0.22	0.04	0.04	0.08	0.08
	400 ms	0.04	0.04	0.14	0.14	0.04	0.04	0.04	0.08
	500 ms	0.04	0.04	0.08	0.08	0.04	0.04	0.04	0.04
75 ms	100 ms	0.69	0.22	0.08	0.35	0.50	0.50	0.08	0.69
	150 ms	0.22	0.89	0.08	0.50	0.35	0.89	0.08	0.22
	300 ms	0.04	0.22	0.04	0.69	0.08	0.69	0.04	0.22
	400 ms	0.04	0.14	0.35	0.35	0.04	0.04	0.04	0.04
	500 ms	0.04	0.04	0.22	0.22	0.04	0.04	0.04	0.04
100 ms	150 ms	0.04	0.04	0.14	0.69	0.04	0.08	0.50	0.69
	300 ms	0.04	0.04	0.04	0.69	0.04	0.04	0.22	0.35
	400 ms	0.04	0.04	0.50	0.50	0.04	0.04	0.08	0.08
	500 ms	0.04	0.04	0.50	0.35	0.04	0.04	0.08	0.04
150 ms	300 ms	0.04	0.04	0.04	0.04	0.04	0.08	0.04	0.04
	400 ms	0.04	0.04	0.50	0.04	0.04	0.04	0.04	0.04
	500 ms	0.04	0.04	0.50	0.04	0.04	0.04	0.04	0.04
300 ms	400 ms	0.04	0.04	0.50	0.04	0.04	0.04	0.04	0.08
	500 ms	0.04	0.04	0.50	0.04	0.04	0.04	0.04	0.04
400 ms	500 ms	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04

* Significant (p< 0.007)

The percentage of peak cut-off showed that the peak value was on average 19.6% reduced with a window size of 50 ms, 26.5% with a window size of 75 ms and 32.1% with a window size of 100 ms during the stance phase (Table 3.5). During the step down task the 50 ms window size reduced the peak value on average 15.6%. Window sizes of 75 ms, 100 ms and 150 ms window sizes reduced the peak value on average, between 25.6% and 28.1%. Window sizes of 300 ms up to 500 ms reduced the peak value between 35.3% and 40.8% (Table 3.6).

Table 3.5: Averaged peak sEMG (% norm) and percentage of the cut-off of the peak sEMG (%) signal of the Quadriceps (VM, VL) and Hamstrings (biceps, semitendinosus) muscles during the stance phase in running.

Rms window width	**Averaged peak value (% norm) of the sEMG activity**								
	biceps		**semitendinosus**		**VL**		**VM**		**mean of all muscles**
	Test 1	Test 2	Test 1	Test 2	Test 1	Test 2	Test 1	Test 2	
25 ms	2.45	2.8	2.51	2.67	3.21	3.21	2.87	2.76	2.81
50 ms	1.91	2.13	1.98	2.24	2.54	2.37	2.4	2.33	2.24
75 ms	1.68	1.9	1.89	2.11	2.27	2.16	2.14	2.17	2.04
100 ms	1.55	1.92	1.82	1.87	2.05	1.93	1.93	1.94	1.88
Rms window width	**% cut-off of the averaged peak value of the sEMG activity**								
	biceps		**semitendinosus**		**VL**		**VM**		**mean of all muscles**
	Test 1	Test 2	Test 1	Test 2	Test 1	Test 2	Test 1	Test 2	
50 ms	23.24	21.72	21.11	15.38	20.45	24.42	16.12	14.7	19.64
75 ms	31.12	31.24	24.09	19.41	28.88	31.32	25.01	20.88	26.49
100 ms	29.33	36.25	26.65	28.37	35.8	38.48	32.66	29.37	32.11

Table 3.6: Averaged peak sEMG (% norm) and percentage of the cut-off of the peak sEMG (%) signal of the quadriceps (VM, VL) and hamstrings (biceps, semitendinosus) muscles during the step down task.

Rms window width	**Averaged peak value (% norm) of the sEMG activity**								
	biceps		**semitendinosus**		**VL**		**VM**		**mean of all muscles**
	Test 1	Test 2	Test 1	Test 2	Test 1	Test 2	Test 1	Test 2	
25 ms	3.98	2.90	2.90	2.79	3.05	2.76	3.24	2.71	3.04
50 ms	3.27	2.48	2.48	2.28	2.56	2.47	2.67	2.30	2.56
75 ms	2.54	1.95	1.95	2.06	2.24	2.03	2.63	1.99	2.17
100 ms	2.62	2.11	2.11	1.99	2.22	2.16	2.32	2.05	2.19
150 ms	2.30	1.97	1.97	2.22	2.12	2.06	2.31	2.19	2.14
300 ms	1.93	1.73	1.73	2.00	1.91	1.86	2.09	1.86	1.88
400 ms	1.80	1.65	1.65	1.89	1.83	1.73	2.00	1.78	1.79
500 ms	1.73	1.58	1.58	1.82	1.77	1.66	1.93	1.59	1.71
Rms window width	**% cut-off of the averaged peak value of the sEMG activity**								
	biceps		**semitendinosus**		**VL**		**VM**		**mean of**
	Test 1	Test 2	Test 1	Test 2	Test 1	Test 2	Test 1	Test 2	**all muscles**
50 ms	17.64	14.45	17.84	23.24	15.59	10.32	17.36	15.15	16.45
75 ms	29.11	33.21	24.01	31.12	25.94	26.78	18.41	26.07	26.83
100 ms	32.10	27.27	31.25	29.33	26.90	21.52	28.22	23.93	27.56
150 ms	39.92	31.91	33.23	23.24	30.34	25.49	27.41	18.62	28.77
300 ms	47.84	40.44	39.80	31.12	37.13	32.55	34.00	30.84	36.72
400 ms	50.73	42.88	34.05	29.33	39.60	37.51	36.95	33.88	38.12
500 ms	52.54	45.47	35.87	29.33	41.73	39.99	39.13	40.99	40.63

The ICC for the peak values during the stance phase revealed a poor reliability for all window sizes (Table 4.5). The CMC results showed good reliability for all muscles during stance phase in running when the data was smoothed with a 50 ms, 75 ms and 100 ms window (Table 3.7).

The ICC for the peak values during the step down task showed moderate to good reliability when the sEMG signal was smoothed with a window size greater than 300 ms. The CMC results showed a moderate to good reliability for all window sizes greater than 50 ms. The CMC results were overall good when the data was smoothed with a window size of 75 ms and a window size greater than 300 ms, with exception of the semitendinosus (Table 3.8).

Table 3.7: Between sessions reliability of the sEMG signal, smoothed with different window sizes of 25, 50, 75 and 100 ms: ICC, intersession CMC and intersubject CMC), during the stance phase in running.

Window size	ICC				CMC intersession				CMC intersubject			
	Biceps	Semiten*.	VL	VM	Biceps	Semiten.*	VL	VM	Biceps	Semiten.*	VL	VM
25 ms	0.37	0.24	0.41	0.44	0.68	0.77	0.91	0.92	0.73	0.7	0.91	0.95
50 ms	0.62	0	0	0	0.73	0.82	0.94	0.96	0.78	0.77	0.95	0.97
75 ms	0.62	0	0	0	0.77	0.83	0.97	0.96	0.81	0.83	0.96	0.98
100 ms	0	0	0	0.23	0.8	0.84	0.96	0.97	0.83	0.87	0.96	0.98

*Semiten.= semitendinosus

Table 3.8: Between sessions reliability of the sEMG signal, smoothed with different window sizes of 25, 50, 75, 100, 150, 300, 400 and 500 ms: ICC, intersession CMC and intersubject CMC), during the step down task.

Window size	ICC				CMC intersession				CMC intersubject			
	Biceps	Semiten*.	VL	VM	Biceps	Semiten.*	VL	VM	Biceps	Semiten.*	VL	VM
25 ms	0.87	0	0.22	0.81	0.51	0.44	0.69	0.75	0.68	0.52	0.81	0.76
50 ms	0.83	0.37	0.52	0.73	0.58	0.50	0.77	0.82	0.73	0.55	0.84	0.77
75 ms	0.37	0.32	0.61	0.78	0.56	0.69	0.82	0.86	0.76	0.65	0.82	0.87
100 ms	0.89	0.33	0.57	0.85	0.64	0.54	0.83	0.87	0.75	0.56	0.85	0.8
150 ms	0.92	0.16	0.50	0.97	0.66	0.55	0.85	0.88	0.75	0.55	0.87	0.87
300 ms	0.95	0.55	0.53	0.82	0.74	0.72	0.89	0.91	0.77	0.55	0.88	0.86
400 ms	0.92	0.81	0.63	0.79	0.71	0.61	0.88	0.91	0.78	0.56	0.89	0.87
500 ms	0.85	0.62	0.64	0.82	0.74	0.76	0.90	0.93	0.79	0.57	0.89	0.88

*Semiten.= semitendinosus

The plotted curves of the VM and biceps during the stance phase showed that the variability of the curves was reduced with larger window sizes. The VM and biceps curves showed that the activation peaks were highest in the window size of 25 ms. The activation peak of the VM plateaued from 15- 20% stance phase. The plateau became longer with greater window sizes: 50 ms, 75 ms: 10-35% and 100 ms: 10-45%. Furthermore, the second test (red line and red shaded area) showed also that two peaks occurred during the beginning stance phase in the VM muscle (Figure 3.26). These two peaks disappeared in the smoothing with a 100 ms window size (Figure 3.26).

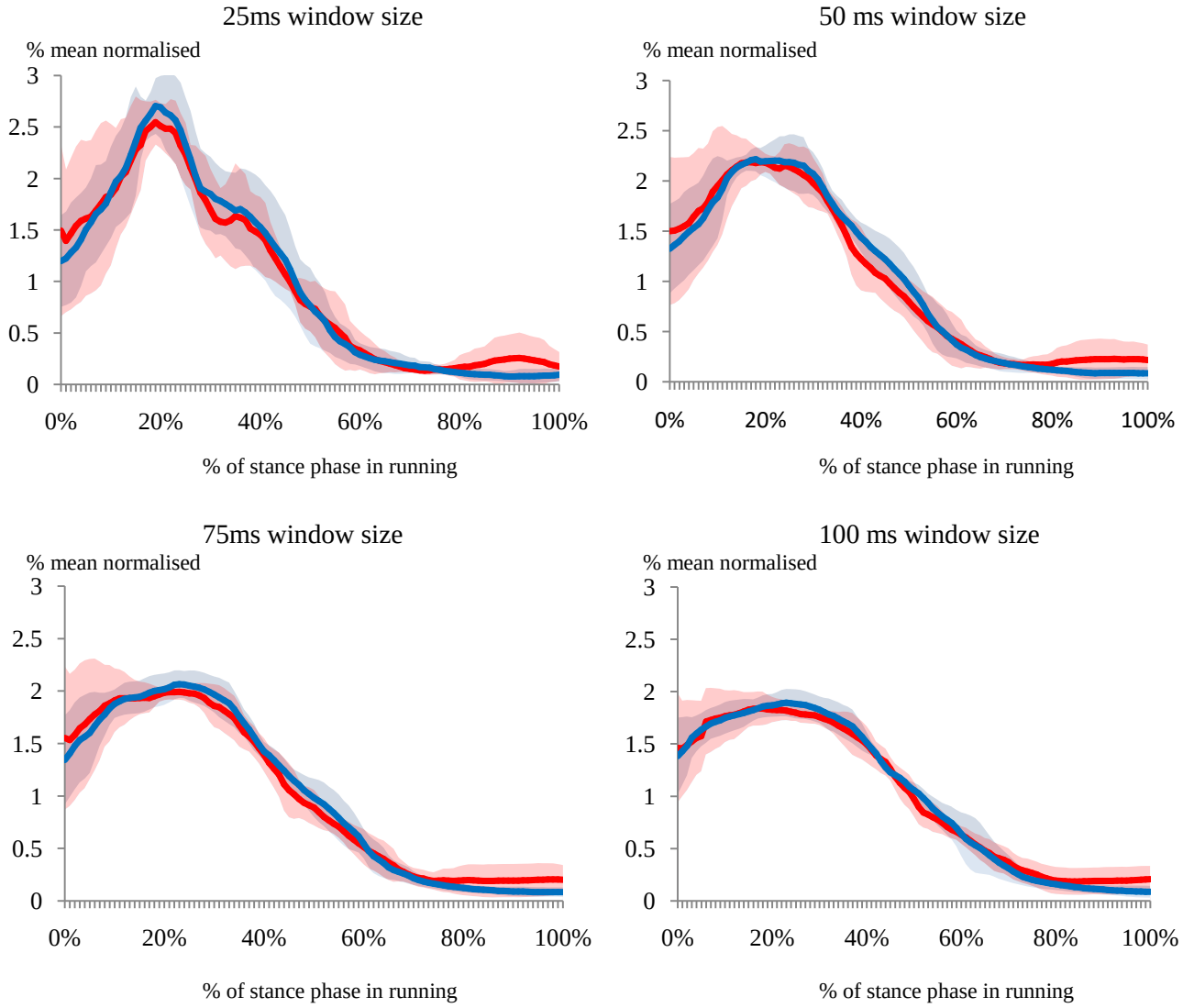


Figure 3.26: VM smoothing with a 25 ms, 50 ms, 75 ms and 100 ms window size for the stance phase in running (first test (blue line) and the second test (red line). The shaded area represents ±1SD.

The first test of the biceps showed that two peaks occurred during the biceps activity during the stance phase. The first peak appeared during 20-35% of the stance phase and the second peak during 40 and 60% of the stance phase. These two peaks disappeared when the data was smoothed with a 100 ms window size (Figure 3.27).

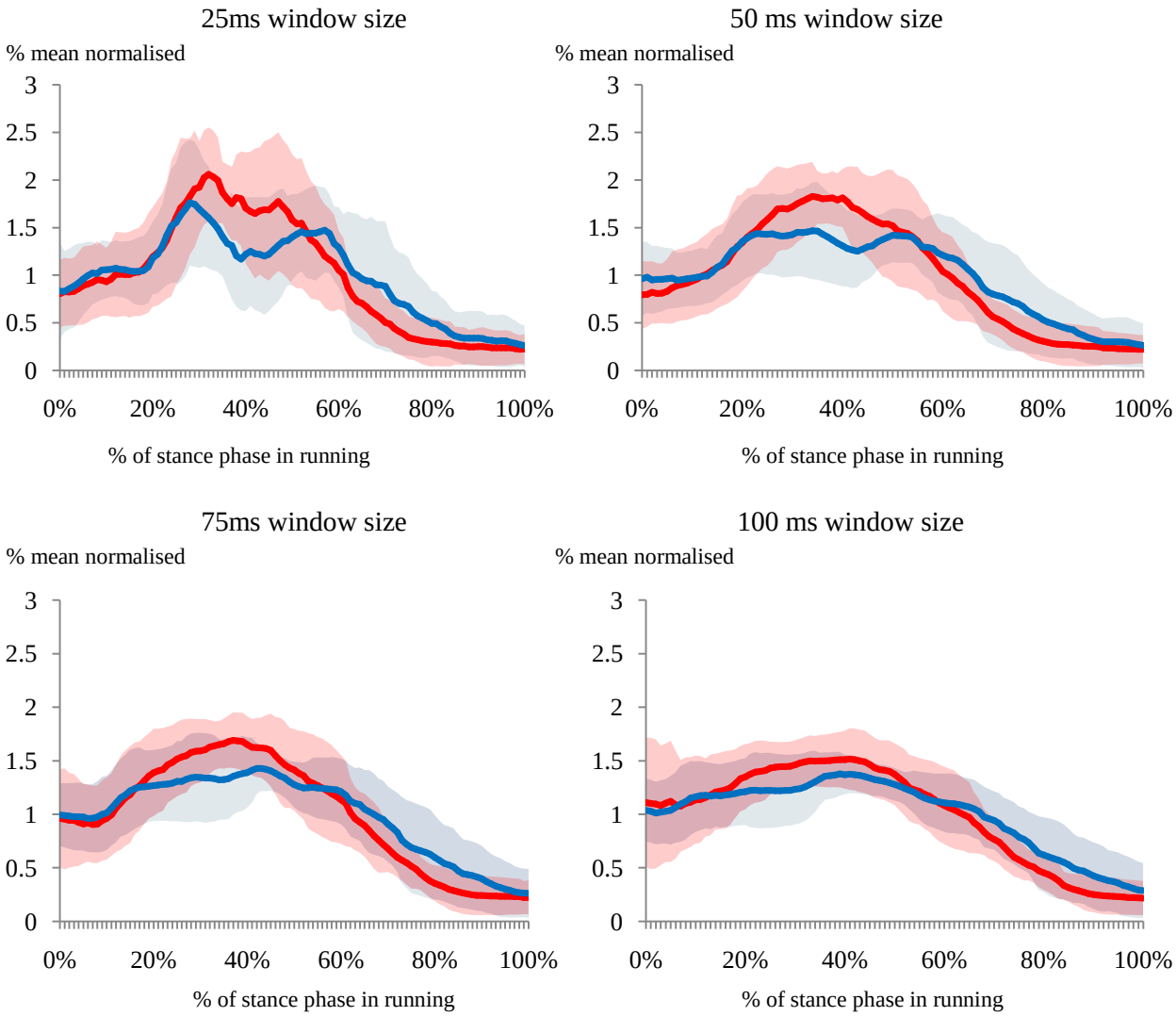


Figure 3.27: Biceps smoothing with a 25 ms, 50 ms, 75 ms and 100 ms window size for the stance phase in running (first test (blue line) and the second test (red line). The shaded area represents ±1SD.

The step down test was more variable than the stance phase and thus the curves were dominated by spikes when they were smoothed with window sizes smaller than 300 ms. The smoothing with window sizes between 300 ms and 500 ms seem to not influence the peak nor the shape of the curve much in both muscles (Figure 3.28, 3.29).

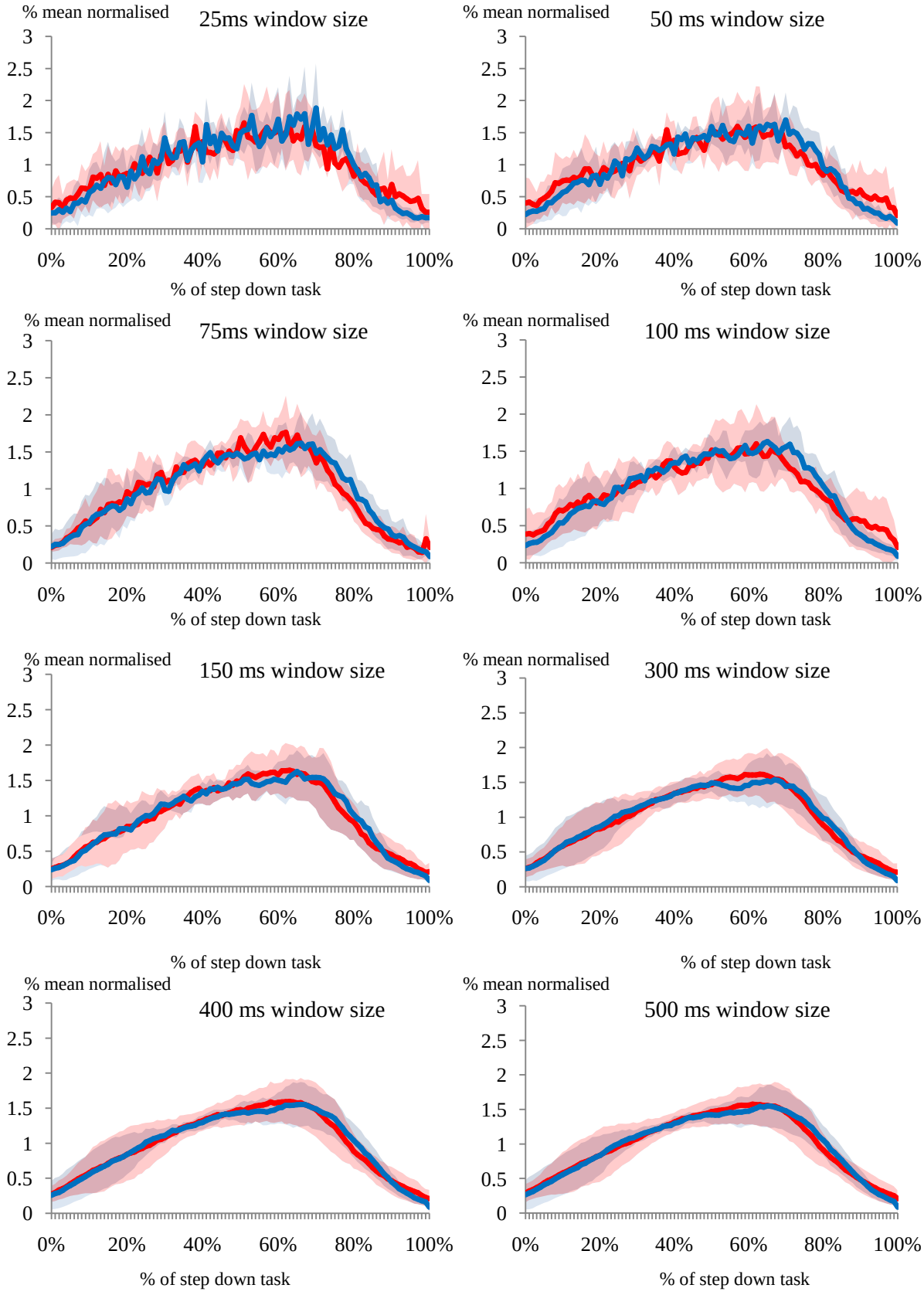


Figure 3.28: VM smoothing with a 25 ms, 50 ms, 75 ms, 100 ms, 150 ms, 300 ms, 400 ms and 500 m window size for the step down task. The shaded area represents ±1SD.

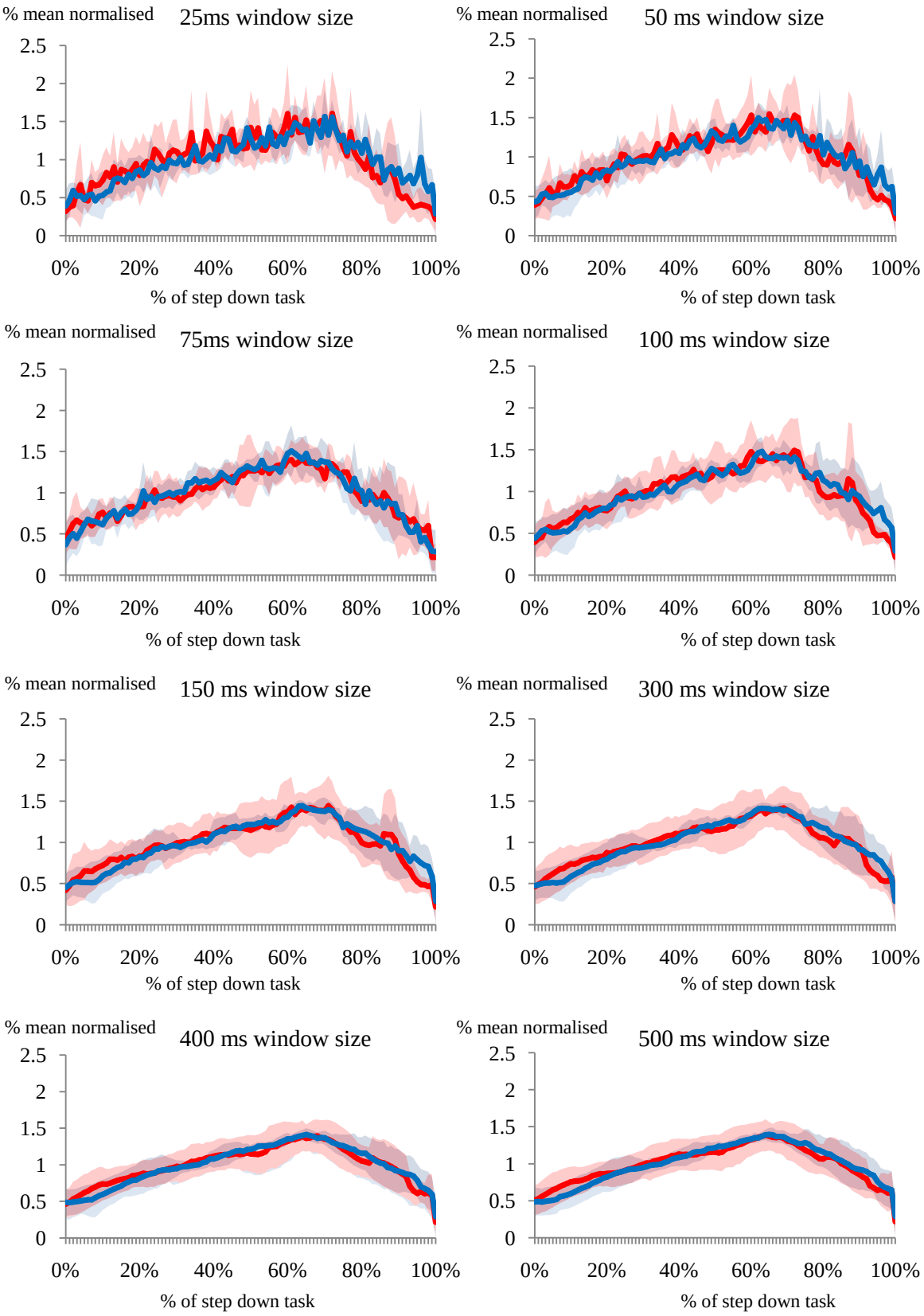


Figure 3.29: Biceps smoothing with a 25 ms, 50 ms, 75 ms, 100 ms, 150 ms, 300 ms, 400 ms and 500 m window size for the step down task. The shaded area represents ±1SD.

Discussion and conclusion

The smoothing of the sEMG signal with different window sizes demonstrated a significant difference in the averaged peak values and the % of cut-off showed that the greater the window size, the smaller the averaged peak of the signal became. Window sizes greater than 100 ms resulted in a decline of the peak by 27-38%. The ICCs showed poor reliability during the stance phase with all window sizes and moderate to good reliability during the step down task when the signal was smoothed with window sizes above 300 ms. During the stance phase the CMCs revealed good repeatability for window size greater than 75 ms and during the step down task the CMCs revealed good repeatability for window size greater than 300 ms.

The plotted curves illustrated that too small window sizes resulted in spiky curves and had a greater variability, whereby too large window sizes smoothed the curves in such a way that the individuality of the curves, such as two occurring peaks, disappeared. Furthermore, the graphs also showed that the stance phase in running was less variable than the slower step down task. Based on these results, the stance phase in running will be smoothed with a rms and a window size of 75 ms. The slower tasks "step down task" and "single leg squat" will be smoothed with a rms and a window size of 300 ms. These window sizes will allow curves to be smoothed, without losing the individuality of each curve. In addition, this pilot study showed the strong influence of smoothing on the peak value of each curve and revealed a low repeatability for the peak of the signal during stance phase. Thus, the peak values of each curve will not be investigated. However, the reduced peaks will not affect the data in this study, because to be able to analyse cocontraction, the aim is to receive curves which represent the sEMG activity without losing important signal information. In addition, it could be shown that the peaks of the sEMG curves were equally reduced throughout the muscles with different window sizes and thus the relation between quadriceps and hamstrings muscles will not be affected by the window size.

3.5. Statistical analysis

The statistical analysis was performed using SPSS (v. 20) and Excel 2013. The graphs were plotted by using Matlab (R2010a).

The peaks of the five trials of the flexibility, anterior reach and strength tests, as well as the angles and moments of the hip and knee flexion, adduction and rotation and the sEMG signal

were averaged for the first and second test and used to assess the within-day reliability by using the ICC. Furthermore, these averaged peaks were used to investigate if significant differences between the first and second test were present (Wilcoxon).

The means of the five trials of the patella assessments, the running speed, the knee and hip angles and moments and the sEMG signals were averaged and used to investigate the within-day reliability (ICC) and if significant differences between the first and second test occurred (Wilcoxon).

Non-parametric tests had been chosen because the sample size of 9 participants was too small to represent a normal distribution.

The reliability of the averaged means and peaks for the numeric outcome were assessed by using the intra-class correlation coefficients (ICC), model 3.5, for the ordinal data (patella position and foot posture) the weighted Kappa was used. The CMC was utilised to compare the five sEMG curves and the hip and knee kinetic and kinematic curves of each subject and each task of the first and second test (intra-subject CMC). In addition, the averaged sEMG curves of the participants were compared between the first and second test for each muscle and each task to investigate the intersubject CMC. The CMCs examine if the sEMG waveforms are similar between the first and the second session.

Although the ICC and CMCs provide a lot of information about the reliability, they do not indicate the amount of disagreement between measurements. The standard error of the measurement (SEM) indicated the standard deviation of the measurement errors and reflects the reliability of the measure (Portney, 2009). A low SEM in combination with a high ICC, Kappa and CMC indicated good reliability of a measure. The SEM was calculated by using the formula: $SD\sqrt{(1 - ICC)}$ (Harvill, 1991; Portney, 2009). The SEM was expressed in the units of each particular measure (Carter & Lubinsky, 2016; Portney, 2009).

The patella displacement was categorised as a central patella position when the distance was -0.5 to 0.5 cm. If the distance was greater than 0.5 cm, the patella position was categorised as lateral and below -0.5 cm as medial displaced position.

The results of the 6-item foot posture index were categorised as a normal foot posture when the overall score was between -2 to 2. If the participant had a score below -2, the foot posture was classified as supinated and below -6 as a much supinated foot posture. If the participant had an

overall score above 2 the foot posture was classified as pronated and above 6 as a much pronated foot.

3.6. Results

Significant differences were found in the anterior reach test (p=0.03) and the concentric quadriceps strength (p=0.02, normalised strength: p=0.02). The knee adduction angle during the step down task (p=0.004) and the knee rotation angle during running (p=0.005) were significant different between the two different days. Furthermore, the knee flexor impulse during the single leg squat task (p=0.01) and running (p=0.03) was different between the test days.

The between-sessions ICC values showed a moderate to excellent reliability for the flexibility assessments (hamstrings and quadriceps flexibility and ankle range of motion) (ICC: 0.61-0.93) (Table 5.9).

The assessment of the patella to investigate lateral/ medial patella displacement was reliable (ICC: 0.6), whereas the assessment of the medial/ lateral tilt and anterior/ posterior tilt of the patella were unreliable (Kappa: 0-0.21). The 6-item foot posture index showed to be reliable measurement outcome (Kappa: 0.73) (Table 3.9, Table 3.10).

Although the anterior reach distance was significantly different between the days (first test mean: 68.6 cm, second test mean: 73.41 cm), the test seem to be reliable (ICC: 0.66, 0.75) (Table 5.9).

The strength tests of the quadriceps and hamstrings were very reliable (ICC: 0.76-0.94). Although, the concentric quadriceps strength was significantly different between the first and the second meeting, it still revealed a high repeatability. The ratio of force development and the time to peak strength measurement during the isometric quadriceps strength test were very reliable (ICC: 0.78-0.83), as well as the quadriceps inhibition measurement (ICC: 0.83) (Table 3.9).

*Table 3.9: Between sessions mean, SD, p-value, ICC and SEM (*indicated the results were significantly different)*

	mean, SD		P value: (Wilcoxon, sig 2-tailed)	ICC (95% CI)	SEM
	Test 1	Test 2			
hamstrings flexibility in degrees	28.89 ±10.54	27.78 ±11.76	0.59	0.86 (0.49-0.97)	4.17
quadriceps flexibility in degrees	110 ±7.07	106.88 ±7.04	0.4	0.61 (0-0.84)	4.40
ankle range of motion in cm	11. ±3.74	11.33 ±2.96	0.36	0.93 (0.74-0.99)	0.89
ankle range of motion in degrees	54.44 ±10.44	52.78 ±7.12	0.32	0.84 (0.45-0.96)	3.50
anterior reach test in cm	68.64 ±8.32	73.41 ±6.39	0.04*	0.66 (0.5-0.91)	4.29
anterior reach test (distance in cm/ leg length)	75.8 ±10.3	81.1 ±8.67	0.03*	0.75 (0.23-0.94)	4.75
patella lateral-medial displacement in cm	0.39 ±0.45	0.25 ±0.4	0.91	0.6 (0-0.92)	0.28
isometric quadriceps strength in Nm	166.67 ±42.08	175.63 ±47.58	0.59	0.94 (0.77-0.98)	10.99
isometric quadriceps strength (Nm/ kg)	1.91 ±0.56	1.81 ±0.58	0.77	0.94 (0.79-0.99)	0.14
AMI in %	9.92 ±10.52	13.38 ±13.7	0.18	0.83 (0.46-0.96)	4.99
time to peak in s	0.67 ±0.17	0.65 ±0.21	0.68	0.78 (0.27-0.93)	0.09
rate to force development in s/Nm	258.36 ±87.02	243.36 ±81.33	0.39	0.84 (0.48-0.96)	33.66
isometric hamstrings strength in Nm	88.89 ±27.73	84.33 ±43.87	0.59	0.9 (0.58-0.98)	9.52
isometric hamstrings strength (Nm/kg)	1.31±0.26	1.24±0.56	0.77	0.81 (0.3-0.96)	0.13
eccentric quadriceps strength in Nm	128 ±37.28	145.78 ±42.09	0.1	0.87 (0.49-0.97)	12.64
eccentric quadriceps strength (Nm/kg)	1.93 ±0.36	2.12± 0.46	0.21	0.76 (0.18-0.95)	0.20
concentric quadriceps strength in Nm	91.63 ±37.5	120.56 ±49.35	0.01*	0.94 (0.73-0.99)	10.64
concentric quadriceps strength (Nm/kg)	1.36 ±0.44	1.74 ±0.58	0.02*	0.87 (0.48-0.97)	0.18
self-selected speed in m/s	3.66 ±0.54	3.66 ±0.33	0.86	0.76 (0.24-0.94)	0.21
self-selected speed [(m/s)/ leg length*100]	4.05 ±0.61	4.03 ±0.52	0.95	0.82 (0.38-0.96)	0.24

Table 3.10: Between sessions median, 25th and 75th interquartile range, p-value and Kappa.

	median (interquartile range)		P value: (Wilcoxon, sig 2-tailed)	Kappa
	Test 1	Test 2		
6-item foot posture	5 (3 to 5)	4 (1.5 to 5)	0.34	0.73
medial/ lateral patella tilt	0 (0 to 1)	0 (0 to 1)	0.48	0.21
anterior/ posterior patella tilt	0 (0 to 1)	0 (0 to 1)	0.16	0

The between-session reliability of the posture and flexibility assessments were also investigated when the results were categorised. Therefore the hamstrings flexibility was classified as normal when the participants had a knee flexion between 20 and 40°. Hamstrings stiffness was described when they had a knee flexion greater than 40° and an increased hamstrings flexibility with a knee flexion less than 20°. The quadriceps stiffness was defined as such when the participants had a knee flexion during the test which was less than 90° and an increased quadriceps flexibility with a knee flexion greater than 115°.

The between sessions reliability of the categorised flexibility and posture data showed that the tests were also reliable when they were categorised (Table 3.11).

Table 3.11: Between sessions median, 25th and 75th interquartile range, p-value and Kappa.

	median (interquartile range)		P value: (Wilcoxon, sig 2-tailed)	Kappa
	Test 1	Test 2		
Quadriceps flexibility in °	1 (1-2)	1 (1-2)	0.89	0.98
Hamstrings flexibility in °	1 (0-2)	1 (0-2)	0.99	0.55
Ankle range of motion in °	1 (1-2)	1 (1-2)	0.32	0.77
patella medial/ lateral displacement in cm	1 (1-2)	1 (1-2)	0.16	0.5
6-item foot posture index	1 (1-2)	1 (1-2)	0.32	0.73

Throughout all tasks, the knee and hip angles and moments showed a moderate to good reliability (ICC: 0.51- 0.97). The CMC results during the single leg squat and step down task were high for the knee flexion and hip adduction (CMC: 0.67-0.93), low for the hip and knee rotation, as well as the knee valgus (CMC: 0.1-0.54) (Table 3.12, Table 3.13). The intersession CMC results for the knee and hip angles and moments during running were all moderate to very good (CMC: 0.48-0.97) (Table 3.14). The intersubject CMC results were good for knee flexion, rotation and hip adduction angle and moments (CMC: 0.65-0.97) and lower for the knee valgus angles and moment and hip internal rotation angle (CMC: 0.18-0. 59).

The knee adductor angular impulse was not reliable (ICC: 0-0.35). The knee flexor impulse was highly reliable during the single leg squat and step down task (ICC: 0.78, 0.82), but unreliable during the stance phase in running (ICC: 0.27) (Table 3.12-3.14).

*Table 3.12: Between sessions mean, SD, p-value, ICC, SEM and CMCs for the single leg squat task. Hip and knee flexion, adduction and internal rotation are reported in positive values (*indicated the results were significantly different).*

	mean, SD		P value: (Wilcoxon, sig 2-tailed)	ICC (95% CI)	SEM	CMC intra-subject	CMC inter-subject
	Test 1	Test 2					
Ankle flexion angle	34.25 ±5.99	33.83 ±4.53	0.67	0.86 (0.43-0.97)	1.97	0.88	0.69
Ankle flexion moment	0.96 ±0.17	30.88 ±0.38	0.67	0.53 (0-0.86)	0.19	0.45	0.32
Knee flexion angle	78.09 ±4.98	77.59 ±4.27	0.44	0.75 (0.2-0.95)	3.20	0.93	0.84
Knee abduction angle	4.79 ±5.4	5.14 ±2.96	0.86	0.58 (0-0.91)	2.73	0.39	0.2
Knee int. rotation angle	1.39 ±3.91	0.86 ±4.67	0.67	0.51 (0-0.86)	2.93	0.37	0.76
Knee flexion moment	1.59 ±0.22	1.65 ±0.25	0.37	0.77 (0.27-0.94)	0.11	0.86	0.67
Knee adduction moment	0.35 ±0.17	0.31 ±0.13	0.44	0.77 (0.27-0.94)	0.07	0.78	0.1
Knee int. rotation moment	0.4 ±0.09	0.41 ±0.1	0.68	0.71 (0.16-0.93)	0.05	0.31	0.51
Hip flexion angle	72.41 ±12.69	73.4 ±12.43	0.48	0.91 (0.61-0.98)	3.78	0.86	0.74
Hip adduction angle	16.42 ±6.12	17.4 ±6.17	0.11	0.97 (0.85-0.99)	1.04	0.72	0.67
Hip int. rotation angle	4.86 ±6.72	0.41 ±4.23	0.05*	0.51 (0-0.86)	4.14	0.31	0.1
Hip flexion moment	0.85 ±0.64	0.87 ±0.59	0.78	0.93 (0.70-0.99)	0.16	0.72	0.67
Hip adduction moment	0.97 ±0.21	0.96 ±0.13	0.77	0.8 (0.34-0.95)	0.08	0.46	0.51
Hip int. rotation moment	-0.23 ±0.07	-0.19 ±0.9	0.11	0.6 (0-0.89)	0.52	0.49	0.55
KAAI (%Bw*height*s)	0.82 ±0.78	0.54 ±0.53	0.31	0 (0-0.64)	0.66		
Knee flexor angular impulse (%Bw*height*s)	4.9 ±1.67	3.82 ±1.21	0.01*	0.82 (0.39-0.96)	0.64		

*Table 3.13: Between sessions mean, SD, p-value, ICC, SEM and CMCs for the step down task. Hip and knee flexion, adduction and internal rotation are reported in positive values (*indicated the results were significantly different).*

	mean, SD		P value: (Wilcoxon, sig 2-tailed)	ICC (95% CI)	SEM	CMC intra-subject	CMC inter-subject
	Test 1	Test 2					
Ankle flexion angle	36.12 ±5.39	7 35.11 ±4.06	0.24	0.85 (0.43-0.97)	1.81	0.90	0.79
Ankle flexion moment	1.30 ±0.28	3 1.27 ±0.21	0.92	0.52 (0-0.88)	0.17	0.66	0.53
Knee flexion angle	78.76 ±2.94	80.11 ±2.79	0.26	0.53 (0-0.89)	1.96	0.93	0.88
Knee abduction angle	6.99 ±5.22	3.59 ±4.8	0.04*	0.64 (0.01-0.91)	3.10	0.42	0.43
Knee int. rotation angle	2.24 ±4.74	5.59 ±5.84	0.14	0.51 (0-0.86)	3.81	0.39	0.35
Knee flexion moment	1.55 ±0.3	1.57 ±0.23	0.95	0.74 (0.2-0.93)	0.13	0.90	0.89
Knee adduction moment	0.43 ±0.19	0.37 ±0.12	0.44	0.51 (0-0.86)	0.11	0.86	0.2
Knee int. rotation moment	0.4 ±0.12	0.41 ±0.07	0.37	0.51 (0-0.86)	0.06	0.29	0.8
Hip flexion angle	62.71 ±11.83	62.14 ±5.88	0.78	0.74 (0.14-0.94)	4.52	0.9	0.74
Hip adduction angle	17.89 ±4.3	18.8 ±5.74	0.68	0.61 (0-0.91)	3.09	0.77	0.74
Hip int. rotation angle	7.16 ±7.74	3.25 ±5.21	0.14	0.59 (0-0.88)	4.30	0.56	0.2
Hip flexion moment	1.11 ±0.47	0.99 ±0.32	0.74	0.51 (0-0.92)	0.28	0.79	0.77
Hip adduction moment	1.1 ±0.23	1.1 ±0.22	0.95	0.64 (0.02-0.91)	0.13	0.50	0.45
Hip int. rotation moment	-0.19 ±0.09	-0.16 ±0.08	0.44	0.67 (0.69-0.92)	0.05	0.54	0.5
KAAI (%Bw*height*s)	0.8 ±0.77	0.86 ±0.63	0.86	0.32 (0-0.79)	0.56		
Knee flexor angular impulse (%Bw*height*s)	3.56 ±0.88	3.29 ±1.03	0.14	0.78 (0.29-0.95)	0.44		

Table 3.14: Between sessions mean, SD, p-value, ICC, SEM and CMCs for the stance phase in running. Hip and knee flexion, adduction and internal rotation are reported in positive values.

	mean, SD		P value: (Wilcoxon, sig 2-tailed)	ICC (95% CI)	SEM	CMC intra-subject	CMC inter-subject
	Test 1	Test 2					
Ankle flexion angle	25.03 ±4.16	7 26.14 ±3.97	0.40	0.63 (0-0.91)	2.47	0.96	0.84
Ankle flexion moment	2.49 ±0.89	3 1.83 ±1.10	0.21	0.52 (0-0.88)	0.67	0.45	0.95
Knee flexion angle	45.89 ±4.59	44.21 ±3.44	0.21	0.7 (0.13-0.92)	2.21	0.75	0.85
Knee abduction angle	2.33 ±3.28	1.99 ±3.04	0.59	0.75 (0.22-0.94)	1.54	0.64	0.41
Knee int. rotation angle	3.04 ±4.93	5.9 ±6.85	0.05*	0.75 (0.23-0.94)	2.99	0.82	0.65
Knee flexion moment	2.6 ±0.22	2.5 ±0.41	0.37	0.5 (0-0.86)	0.23	0.97	0.94
Knee adduction moment	0.54 ±0.39	0.63 ±0.47	0.26	0.87 (0.53-0.97)	0.15	0.89	0.59
Knee int. rotation moment	0.4 ±0.18	0.39 ±0.2	0.77	0.88 (0.56-0.97)	0.06	0.48	0.81
Hip flexion angle	45.65 ±8.12	47.19 ±7.20	0.40	0.77 (0.22-0.95)	3.67	0.89	0.65
Hip adduction angle	11.59 ±5.93	11.47 ±5.2	0.44	0.89 (0.61-0.98)	1.79	0.84	0.72
Hip int. rotation angle	6.28 ±6.55	6.48 ±6.71	0.95	0.59 (0-0.91)	4.12	0.86	0.18
Hip flexion moment	1.84 ±0.68	2.04 ±0.53	0.21	0.79 (0.27-0.96)	0.28	0.84	0.75
Hip adduction moment	1.84 ±0.34	1.67 ±0.38	0.17	0.7 (0.12-0.92)	0.20	0.68	0.93
Hip int. rotation moment	0.07 ±0.06	0.09 ±0.07	0.77	0.74 (0.2-0.93)	0.03	0.97	0.77
KAAI (%Bw*height*s)	0.06 ±0.06	0.04 ±0.03	0.68	0.35 (0-0.81)	0.04		
Knee flexor angular impulse (%Bw*height*s)	0.25 ±0.08	0.19 ±0.05	0.03*	0.27 (0-0.77)	0.06		

Table 3.15: Between sessions mean, SD, p-value, ICC, SEM and CMCs for the single leg squat, step down task and the stance phase in running. Quadriceps and hamstrings sEMG activity is reported in % of the peak EMG activity.

sEMG activity in % of peak EMG activity	mean, SD		P value: (Wilcoxon, sig 2-tailed)	ICC (95% CI)	SEM	CMC intra-subject	CMC inter-subject
	Test 1	Test 2					
single leg squat							
Vastus medialis	1.52 ±0.21	1.6 ±0.21	0.44	0.5 (0-0.86)	0.15	0.88	0.86
Vastus lateralis	1.5 ±0.21	1.62 ±0.24	0.21	0.47 (0-0.85)	0.17	0.89	0.87
semitendinosus	1.52 ±0.16	1.53 ±0.12	0.95	0.53 (0-0.87)	0.10	0.71	0.67
biceps femoris	1.55 ±0.16	1.63 ±0.23	0.77	0.05 (0-0.67)	0.19	0.65	0.76
step down task							
Vastus medialis	1.67 ±0.2	1.68 ±0.3	0.77	0.57 (0-0.88)	0.16	0.88	0.88
Vastus lateralis	1.65 ±0.23	1.64 ±0.24	0.95	0	0.23	0.88	0.90
semitendinosus	1.44 ±0.18	1.56 ±0.24	0.09	0.11 (0-0.92)	0.20	0.69	0.53
biceps femoris	1.49 ±0.1	1.52 ±0.15	0.59	0.1 (0-0.69)	0.12	0.73	0.82
running stance phase V1							
Vastus medialis	2.09 ±0.13	2.08 ±0.18	0.77	0.44 (0-0.84)	0.12	0.97	0.97
Vastus lateralis	2.21 ±1.04	2.15 ±0.19	0.31	0	0.15	0.97	0.97
semitendinosus	1.69 ±0.22	1.81 ±0.29	0.21	0.53 (0-0.87)	0.18	0.82	0.81
biceps femoris	1.64 ±0.1	1.63 ±0.17	0.77	0.38 (0-0.82)	0.11	0.82	0.82

The peak values of the sEMG were low to moderate (ICC: 0-0.57). However, the waveform of the sEMG signal during each task was moderate to highly reliable (CMC: 0.53-0.97) (Table 3.15).

3.7. Discussion

The aim of this chapter was to investigate the between-session reliability of the AMI, the break phenomenon, strength of the quadriceps muscle, lower limb flexibility and foot and patella posture assessments, the 3D motion-analysis system and the sEMG analysis system during functional tasks.

The high repeatability of the hamstrings flexibility measurement by using the active knee extension (AKE) test is in line with repeatability results in previous studies (Gabbe et al., 2004; Gajdosik & Lusin, 1983; Gajdosik et al., 1993; Hamid et al., 2013; Neto et al., 2014). The reliability of the modified Thomas test to assess the quadriceps flexibility was only moderate, which has been reported in previous studies as well (Peeler & Anderson, 2008).

The current study revealed a high reliability of the ankle ROM measurement, which was in line with previous studies (Calatayud et al., 2015; Konor et al., 2012). Konor et al. (2012) emphasised the advantage of the weight bearing lunge because it showed to be reliable even when it was assessed by novice raters.

The posture assessment of the patella showed that only the assessment of the medial/ lateral patella displacement was reliable which has been confirmed in previous studies (Herrington, 2002). However, the patella tilt assessments were unreliable which has also been reported in previous research (Fitzgerald & McClure, 1995).

The assessment of the foot posture investigated using the 6-item foot posture index was reliable, which is in accordance with previous studies (McLaughlin, Vaughan, Shanahan, Martin, & Linger, 2016; Terada, Wittwer, & Gribble, 2014).

The strength tests showed that the quadriceps and hamstrings strength tests were reliable. These results were in accordance with previous literature showing that the quadriceps strength test was reliable (Pincivero, Lephart, & Karunakara, 1997; Sole, Milosavljevic, Sullivan, Nicholson, & Hamrén, 2007; Wollin, Purdam, & Drew, 2016). Although the reliability of the

normalised quadriceps strength (Nm/ kg) was lower than the raw strength data, it still showed good reliable results.

The knee and hip angles and moments were moderate to good reliable throughout all tasks. However, the CMC results were low for the hip and knee rotation, as well as the knee valgus during the single leg squat and step down task. Røislien et al. (2012) described that kinematic curves with a larger range of motion (ROM) appeared more similar, which was reflected in a higher CMC result. This might be an explanation for the decreased CMC results, because the rotation and adduction angles and moments are relatively small during these tasks (Røislien et al., 2012). Thus, Røislien et al. (2012) concluded that the CMC results should be interpreted with caution. During the stance phase in running, the ICCs and CMCs were from ‘moderate' to 'good' for the repeatability of the hip and knee angles and moments. The CMC results during the stance phase in running were from ‘moderate’ to ‘good’ and thereby in line with previous reliability findings during running (Alenezi, Herrington, Jones, & Jones, 2016). The reliability of the single leg squat ranged from ‘moderate’ to ‘good’, which was in accordance to the previous findings (Alenezi et al., 2014). Although the knee flexor impulse was reliable during the step down and single leg squat task, it was not reliable during the stance phase in running. The knee adductor impulse was unreliable through all tasks.

The intersession CMC results for the knee and hip angles and moments during running were all moderate to very good (CMC: 0.48-0.97) (Table 5.14). The inter-subject CMC results were good for knee flexion, rotation and hip adduction angle and moments (CMC: 0.65-0.97) and lower for the knee valgus angles and moment and hip internal rotation angle (CMC: 0.18-0.59). Although only one assessor applied the markers, a variability between sessions became apparent. To reduce this variability within the study, the CAST marker-based protocol (Cappozzo et al., 1995) was used, which attempts to reduce skin-movement artefacts by attaching markers to the centre of segments rather than single markers close to the joints, as in the Helen Hayes model (Collins et al., 2009). However, it could still be shown that the single leg squat as well as the step down task were less reliable than the stance phase in running. The lower reliability might be caused by different velocities during these tasks. Thus, to reduce the variability and improve the reliability, in the test protocol for the further studies the velocity will be verbally cued to provide the desired movement speed. Therefore the patient will be instructed to squat down/ lower the leg down during two seconds which will be verbally cued by the instructor saying: "One, two" and instructed to come back into the starting position

within a period of two seconds which will be again verbally cued with "one, two". In addition, the participant will be instructed to maintain an upright posture and to hold the non-stance foot in line with the anle of the stance leg.

The peak values of the sEMG were low to moderate (ICC: 0-0.57). However, the waveform of the sEMG signal during each task was moderate to highly reliable (CMC: 0.53-0.97) (Table 5.15). Not many studies investigated the reliability of sEMG during the single leg squat task, step down and running task and thus the comparison to previous literature remains challenging. However, these results indicate that the analysis of the peak values of the sEMG signal would be inappropriate as they seem to not be reliable. Whereas the waveform of the sEMG signal showed moderate to high reliability and thus can be used for further investigations.

This study also provided the SEM reference values for all tests. The SEM calculation depends on the standard deviation of the measurement, which allows the clinician to be 68% confident that the true value lies within ±1 SEM of an observed value or 95% confident that the true value lies within ±2 SEMs (Portney, 2009). The SEM values for hamstrings and quadriceps flexibility ranged in previous studies from 2° to 7° and thus are in accordance with the findings in this study that showed for both measurements a SEM value of 4° (Cejudo et al., 2015; Clapis, Davis, & Davis, 2008; Gabbe et al., 2004; Neto et al., 2014; Peeler & Anderson, 2008; Reurink, Goudswaard, Oomen, Moen, Tol, Verhaar, & Weir, 2013). The ankle range of motion SEM values in this study were 3.5° and 0.89 cm, which is in accordance with the reliability findings in previous studies, which ranged from 2° to 4° and 0.6 cm (Cejudo et al., 2015; Konor et al., 2012). The SEM values in the star excursion balance test were 4.29 cm and normalised to the leg length 4.75 cm, which is greater than reported in previous literature where the SEM ranged from 2.01 cm to 3.43 cm (Hertel et al., 2010; Hyong & Kim, 2014; Kinzey & Armstrong, 1998; Munro, Herrington, & Carolan, 2012; Plisky et al., 2009). The SEM for the lateral/ medial patella displacement was only investigated by McEwan et al. (2007), who reported a smaller SEM of 0.1 mm, in comparison to 0.28 mm in this study. The SEM values for the quadriceps isometric strength ranged from 10.64 to 12.64 Nm and from 0.14 to 0.20 Nm/kg when it was normalised to the body mass, which is in accordance to previous literature of ranging SEM values from 6.48 Nm to 12.24 Nm (De Araujo Ribeiro Alvares et al., 2015; De Carvalho Froufe Andrade, Caserotti, de Carvalho, de Azevedo Abade, & da Eira Sampaio, 2013; Sole et al., 2007). Only one study investigated the reliability of quadriceps inhibition assessments (Norte, Frye, & Hart, 2015). They reported a ranging AMI from 2.97 to 4.53%,

which is in agreement to the SEM in this study of 4.99%. Previous literature that investigated the reliability of 3D kinetics and kinematics showed very comparable results regarding the mean, SD and SEM (Alenezi et al., 2014; Alenezi, Herrington, Jones, & Jones, 2016; Ferber, McClay Davis, Williams, & Laughton, 2002). Those studies have been carried out with a larger sample size and concluded that all kinematic and kinetic variables showed good to excellent consistency (Alenezi et al., 2014, 2016; Ferber et al., 2002). Thus, the reliability findings of this study were in line with previous research and confirmed that the lower limb kinematics and kinetics were repeatable.

Due to the different normalisation techniques of the sEMG signal, it was difficult to compare the mean, SD and SEM with previous reported results. However, the SEM was reported as approximately 10% of the mean of the sEMG signal (Bolgla et al., 2010; Pazzinatto et al., 2015). Thus, these findings are in accordance with the result in this study.

3.8. Limitations to the study

Although the reliability study was planned as a pilot study to develop the test protocol, the sample size of 9 participants was low. Previously, it has been reported that 10-12 participants are sufficient for a pilot study (Johanson & Brooks, 2010). However, it has been recommended to increase the sample size to ensure a representativeness (Johanson & Brooks, 2010).

It should be addressed that the assessor's ability of markers placement might affected the results. However, this effect should be small because the assessor had 3 years of clinical experience as a physiotherapist and was specialised in manual therapy. Furthermore, the assessor participated in the clinical gait analysis course at the University of Salford, in which marker placement was discussed and practised.

Subjects were instructed to squat down, step down as far as possible and return to a single-legged standing position without losing his/her balance. Thus, the squat and step down depth were not sufficiently controlled for each participant, which reflects normal practice, but challenges the comparability. Since the repeatability for these two tasks was lower it has been decided to standardise the task velocity by providing a verbal cue to the participant.

To standardise the running task, the participants wore standard trainers. However, this does fail to represent typical shoe-surface interactions in real environment.

3.9. Conclusion

Based on these results, it could be proven that the following outcome measures were reliable:

1. Hamstrings and quadriceps flexibility in degrees
2. Ankle range of motion in degrees and cm
3. Anterior reach test distance in cm and reach distance normalised to leg length
4. Patella medial/lateral displacement in cm,
5. 6-item foot posture index
6. Isometric quadriceps strength in Nm and normalised to body mass
7. Eccentric and concentric quadriceps and hamstrings strength in Nm and normalised to body mass
8. Quadriceps inhibition in %
9. Peaks of hip-flexion, adduction and internal-rotation angles and moments.
10. Peaks of knee-flexion, adduction and internal-rotation angles and moments.
11. sEMG waveform
12. Knee angular velocity

Whereas, these outcome measures revealed to be poor in reliability:

1. patella tilting on grading scale: -2 to 2
2. the peak of the sEMG signal during each task
3. Knee adductor angular impulse (KAAI) and the knee flexor impulse.

Thus, only the reliable outcome measures will be carried forward as part of the test protocol.

Chapter 4: Influence of the Powers™ strap on lower limb kinetics and kinematics in individuals with and without PFP

The first intervention assessed was the Powers™ strap. This chapter will present the results of how the the Powers™ strap influenced pain and lower limb biomechanics in individuals with and without PFP. This allowed the analysis of the mechanistic and the clinical aspects of the Powers™ strap.

4.1. Introduction

Abnormal biomechanics, especially the dynamic knee valgus, which is a combination of femoral adduction, femoral internal rotation, external knee rotation, tibial abduction and ankle eversion are known to be associated with PFP (Nakagawa et al., 2015; Nakagawa et al., 2012; Powers, 2003; Willson & Davis, 2008). Studies that have investigated the biomechanics of individuals with PFP reported an increased hip internal rotation and hip adduction angle compared with individuals without PFP (Araújo, de Souza Guerino Macedo, Ferreira, Shigaki, & da Silva, 2016; Bley et al., 2014; Graci & Salsich, 2015; Lucareli, Amir, Bley, Nayra, Garbelotti, et al., 2014; Lucareli, Amir, Bley, Nayra, Jeniffer, et al., 2014; McKenzie, Galea, Wessel, & Pierrynowski, 2010; Nakagawa et al., 2015; Nakagawa et al., 2012; Nakagawa et al., 2013; Noehren, Pohl, et al., 2012; Souza & Powers, 2009b). Furthermore, it was shown that an increased hip adduction and internal rotation angle is associated with higher levels of pain and reduced function in individuals with PFP (Graci & Salsich, 2015; Nakagawa et al., 2013; Souza, 2008; Souza, Draper, Fredericson, & Powers, 2010).

Studies that have investigated the influence of knee braces and straps on lower limb biomechanics in individuals with PFP have demonstrated heterogeneous findings. Several studies reported that knee braces modified the frontal and transverse planes of the knee joint (McCall et al., 2014; Richards et al, 2015.; Theoret & Lamontagne, 2006), whereas other studies could not identify any significant changes (Denton et al., 2005; Devita et al., 1992; Powers, Ward, et al., 2004a). However, current research is focused on knee braces that aim to stabilise the knee joint locally, so directly influencing the joint (Bolgla & Boling, 2011; Smith, Drew, Meek, & Clark, 2015; Swart et al., 2012; Yeung & Yeung, 2001; Selfe, Selfe, Richards, Thewlis, & Kilmurray, 2008; Selfe, Thewlis, Hill, Whitaker, Sutton, & Richards, 2011). Since hip internal rotation appears to be associated with PFP, a brace or strap that aims to reduce the

excessive hip internal rotation and thereby potentially reduce the dynamic knee valgus might be a potential treatment for running related injuries, such as PFP. Only one study has investigated the influence of such a knee strap in patients with PFP during an unilateral squat and a step landing task (Herrington, 2013). They found that the strap significantly reduced pain during these functional tasks and in addition significantly reduced knee valgus (Herrington, 2013). The authors measured the two-dimensional (2D) frontal-plane projection angle of the knee-valgus alignment by using a digital video camera. However, this 2D measurement did not allow the investigation of whether the strap modified the transverse plane of the hip and the knee, nor whether the strap modified lower limb kinetics.

The quadriceps avoidance strategy is a mechanism that minimises the demand of knee extensor muscles and is commonly observed in individuals with knee injuries such as patellofemoral pain (Clark et al., 2016; Salsich et al., 2001; Torry et al., 2000). The quadriceps and hamstring muscle groups provide dynamic frontal-plane stability of the knee joint (Palmieri-Smith et al., 2009). Decreased hamstrings/ quadriceps activation ratio is associated with an increased risk of lower limb injuries (Hewett et al., 2006; Hewett et al., 2008; Myer et al., 2005). Previous studies showed that straps and patellar tapes were able to influence and modify quadriceps activation (Cowan et al., 2002; Gilleard et al., 1998; Herrington, 2001; Kaya, et al., 2010; Keet et al., 2007; Ng & Cheng, 2002; Ng & Wong, 2009; Ryan & Rowe, 2006; Warden et al., 2008; Werner, Knutsson, & Eriksson, 1993). Thus, this study also aimed to investigate whether the Powers^{TM} strap influences and modifies the co-contraction of the quadriceps and the hamstrings muscles as well.

Therefore, this study aimed to investigate whether a strap designed to increase hip external rotation was able to modify hip kinematics and kinetics and whether these alterations would also modify knee kinematics and kinetics and the co-contraction of the quadriceps and the hamstrings muscles during sports activities in individuals with and without PFP.

1. H0: There would be no significant differences in hip internal rotation angle and moment when wearing the Powers^{TM} strap in individuals with and without PFP.
2. H0: There would be no significant differences in hip flexion and adduction and knee flexion, adduction and internal rotation angles and moments when wearing the Powers^{TM} strap in individuals with and without PFP.
3. H0: The Powers^{TM} strap would not significantly decrease pain in individuals with PFP.

4. H0: There would be no significant difference in co-contraction ratio and the net-activation of the quadriceps and hamstrings muscles when wearing the Powers^{TM} strap in individuals with and without PFP.

4.2. Methodology

Ethical approval was obtained in compliance with the Declaration of Helsinki Committee for Proprietary Medicinal Products "Note for Guidance on Good Clinical Research Practice". Therefore, the ethical approval HSR 15-142 was obtained from the University of Salford Research and Governance Committee and the trial was registered with clinicaltrials.gov (NCT02914574; Appendix Methods 4.1).

Advertisements placed at fitness centres, gyms, climbing centres and sports clubs in Manchester and Salford were used to recruit participants with PFP and without PFP.

The Powers^{TM} strap is a knee strap that has been developed by researchers in the US and aimed to stabilise the patellofemoral joint through external rotation of the femur. The Powers^{TM} strap is still a prototype and not yet available for commercial sale. Thus, the principal researcher contacted the inventor of the strap, Prof. Powers and informed him about the planned study. Prof. Powers provided a prototype of the strap for the study.

4.2.1. Participants

To be included in the study a healthy participant PFP had to meet all of the following criteria: (1) performing sports activities for at least 2 hours a week, (2) no previous significant lower limb injuries, (3) aged: 18-45 years.

Participants without PFP were excluded if: (1) they had any history of previous lower limb surgery or patella instability and dislocation, (2) they had lower limb deformities or any history of traumatic, inflammatory or infectious pathology in the lower extremities or any internal derangements, (3) they reported previous or existing knee pain, (4) they could not perform running, squatting and the step down task during the measurement.

The eligibility criteria for individuals with PFP were: 1) aged 18-45 years; 2) antero- or retro-patellar pain with at least two of these activities: ascending or descending stairs or ramps,

squatting, kneeling, prolonged sitting, hopping/ jumping, isometric quadriceps contraction or running 3) duration of current PFP symptoms >1 month.

The exclusion criteria for individuals with PFP were: (1) any history of previous lower limb surgery or patella instability and dislocation, (2) lower limb deformities or any history of traumatic, inflammatory or infectious pathology in the lower extremities or any internal derangements, (3) not able to perform running, squatting and/ or the step down task during the measurement.

The principal investigator assessed suitability for the trial using the aforementioned inclusion and exclusion criteria. Participants were asked to fill in an online survey and had afterwards a telephone interview with the principal investigator prior to the study starting. Once the inclusion criteria were met, the participant received via email an invitation letter and an information sheet about the study. If the participant agreed to participate, he/ she arranged a date for the gait laboratory measurement with the principal investigator. Following this an email with a confirmation of his/her booking with a route description, important information, such as which clothing to wear at the test, contact details of the principal investigator, as well as an informed consent form was sent one week prior to the test. Upon arrival at the laboratory, the participants were briefed through the study and the objectives of the investigations and the study equipment were explained to all participants. Each participant was asked to sign the informed consent form and a health history questionnaire (Appendix Methods 4.2). The health history questionnaire for all participants consisted of 13 questions investigating potential risks associated with the study. If potential risks were identified, study participation was discussed and the individual was either asked to consult a physician to receive an approval for the participation or was advised not to participate. The health history questionnaire for individuals with PFP included additionally 4 questions that were related to PFP. The individual was then asked to change into his/her shorts and a comfortable t-shirt and was fitted with standard running shoes (New Balance, UK), to control the interface of the shoe and the surface. Before the test, the mass and height of each participant were measured.

A clinical assessment was carried out for individuals with PFP, which involved the Clarke's test and a palpation test to investigate the pain region. The participant with PFP was then asked to run 15 m, to perform a single leg squat and step down task and to show the pain location during these tests and to rate his/her pain intensity using the numeric pain rating scale (NPRS).

The NPRS is a unidimensional measure of pain intensity and is the numeric version of the visual analogue scale (VAS) scale. The 11-point numeric scale ranges from "0", representing "no pain", to "10", representing the “worst pain imaginable” and has been shown to be valid, reliable and sensitive (Williamson & Hoggart, 2005).

4.2.2. Procedure

Three-dimensional movement data was collected with ten Qualisys OQUS7 cameras (Qualisys AB, Sweden) at a sampling rate of 250Hz. The ground reaction forces were collected with three force plates (BP600900, Advanced Mechanical Technology, Inc.USA) at a sampling rate of 1500Hz, which were embedded into the floor and synchronised with the Qualisys system. Forty retro-reflective markers with a diameter of 14 mm were attached, with double sided hypoallergic tape and bandages, to the lower limb of the participants (Figure 4.1). The calibrated anatomical system technique (CAST) model, which included anatomical landmarks (markers on anatomical bony landmarks) and anatomical frames (segment mounted marker clusters), was used (Cappozzo et al., 1995).

The retro-reflective markers were placed as explained in chapter 3.4.1.2. In this study, a smaller thigh cluster was a used, to ensure that the Powers^{TM} strap could be applied below the thigh cluster and thereby did not affect the cluster placement. The ankle and knee joint centres were calculated as midpoints between the medial and lateral malleoli and femoral epicondyles respectively. The hip joint centre was calculated using the regression model of Bell, et al. 1990. For the electrode placement of the EMG, the skin was shaved, abraded and cleaned with isopropyl alcohol and the electrodes were placed as described in chapter 3.4.1.3 (Figure 4.1).

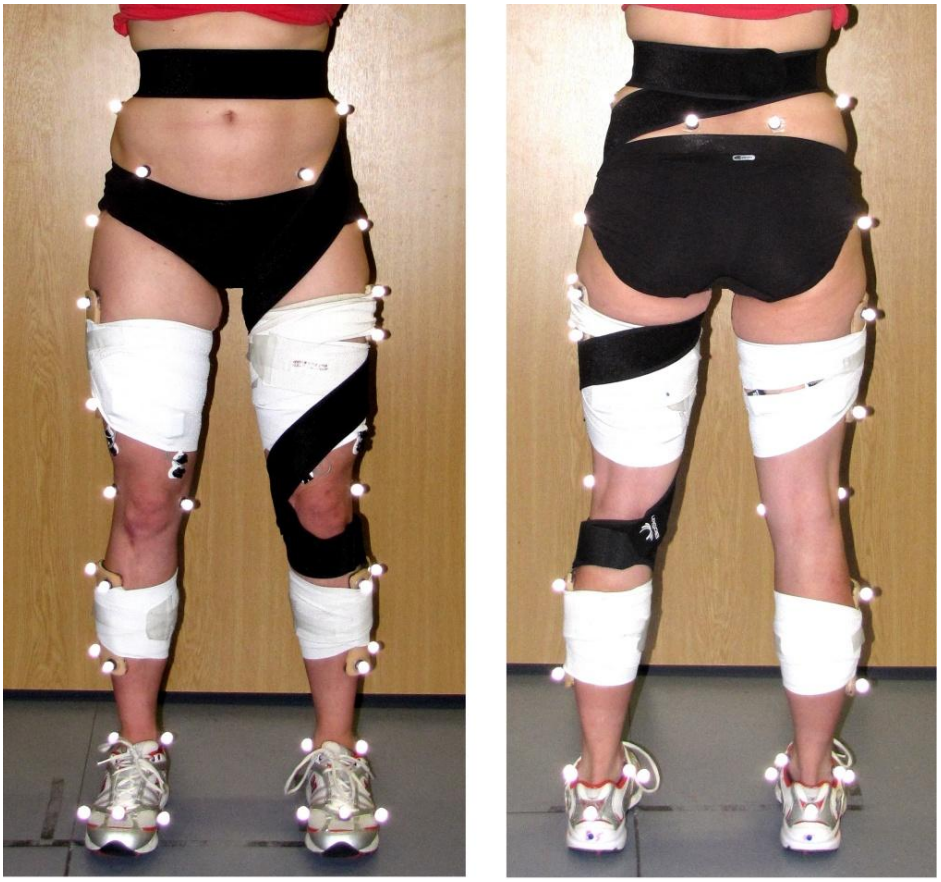


Figure 4.1.: The application of the markers and the Powers™ strap

A static reference trial was collected without the applied Powers™ strap but was used for both conditions with and without the Powers™ strap because the marker clusters remained in the same place during both conditions (Figure 4.1.).

Each subject was then asked to run on a 15 m walkway at his/her own selected speed, to perform a single leg squat and step down tasks during two conditions: without and with the Powers™ strap. The Powers™ strap was only applied on the preferred limb in individuals without PFP, whereby the limb preference was established by asking participants which limb they would prefer to kick a ball. In individuals with PFP the Powers™ strap was applied on the more painful limb. To investigate whether the application of the 3D markers and bandages modified the pain, the participants with PFP were asked to rate his/her pain intensity (using the NPRS) after performing the tasks without and with the Powers™ strap.

Running speed was controlled and reported by using Brower timing lights (Draper, UT) to ensure that each trial was within ±10% of the original self-selected speed. Each task was

performed until five successful trials were collected. Unsuccessful trials were ones whereby less than three markers per segment were visible, speed changes were seen during the trials, or a partial/double contact with the force platforms occured.

The participants received a voucher of £10 as compensation for his/her time participation in this study. This voucher was exchangeable for goods in shops in Manchester and Salford.

4.2.3. Data processing

The kinematic and kinetic outcomes were calculated by utilising a 6 degrees of freedom model in Visual3D (Version 5, C-motion Inc, USA). Motion and force plate data were filtered with a 4th order Butterworth filter with cut-off frequencies of 12Hz. The Cardan sequence used in the kinematics calculation with Visual3D was the ordered sequence of rotations (x, y, z), with: x = flexion/extension, y = abduction/adduction, z = longitudinal rotation (R. B. Davis, Ounpuu, Tyburski, & Gage, 1991).

The joint kinetic data was calculated using a three-dimensional inverse dynamics algorithm. The joint moments were normalised to body mass and presented as external moments referenced to the proximal segment. The kinematic and kinetic data were normalised to 100% of the single leg squat, step down task and the stance phase, whereby the stance phase was sub-grouped in early-stance (0-24% of stance phase), mid-stance (25-62%) and late-stance phase (63%-100%) (Perry & Burnfield, 2010). The peaks of the hip and knee flexion, adduction and internal rotation angles and the moments were calculated for the single leg squat, step down task and the early, mid and late stance phase. Furthermore, the average knee angular velocity was calculated for the eccentric phase during the single leg squat and step down task.

The sEMG data was band-pass filtered at 20-500Hz and rectified by using a root mean square over a 75 ms window for running and a 300 ms window for the single leg squat and step down task. Co-contraction ratios (CCR) were calculated using the following formula:

If agonist mean EMG > antagonistic mean EMG:

CCR= 1- antagonistic mean EMG/agonist mean EMG

If agonist mean EMG < antagonistic mean EMG:

CCR= agonist mean EMG/ antagonistic mean EMG -1

(Heiden, Lloyd, & Ackland, 2009)

4.3. Statistical analysis

The statistical analysis was performed using IBM SPSS (v. 20) and Microsoft Excel 2013. The normality was assessed by applying the Shapiro-Wilk test and by the investigation of the normal q-q plots. For the data that was normally distributed paired t-tests were performed at the 95% confidence interval to investigate whether the Powers^{TM} strap significantly influenced the lower limb biomechanics. If the data was not normal distributed and for ordinal data (pain scale) the Wilcoxon rank test was used with a significance level set at $p<0.05$.

To investigate whether there were significant differences in hip and knee biomechanics between individuals with and without PFP a two-tailed t-test was used when the data was normal distributed and a Mann Whitney test was used when the data was not normal distributed.

The peak of the hip flexion, hip adduction, hip internal rotation, knee flexion, knee adduction and knee internal rotation angles and moments, the co-contraction ratio, net activation of the quadriceps and hamstrings activation, as well as the averaged knee angular velocity were compared between the conditions: individuals with and without PFP and both with and without the Powers^{TM} strap.

The standard error mean (SEM) is the estimated standard deviation of the sample mean and was calculated using the following formula: SEM = SD/$\sqrt{\text{sample size}}$. The effect size for each significant variable was calculated using the Cohen d to give an indication of the magnitude of the effect of the intervention (>0.8 large effect, 0.5 moderate effect, <0.3 small effect) (Cohen, 1988).

4.3.1. Power calculation:

A post hoc power calculation on individuals with PFP with G-Power (Version 3.1.9.2) (n=24, one tailed t-test) was performed for all three tasks on hip internal rotation angle, by using a two-tailed t-test for two dependent means. The effect size (ES) was calculated by using the following equation (McCrum-Gardner, 2010):

$$ES = \frac{\text{(Mean of the hip IR angle with the brace)-(Mean of the hip IR angle without the brace)}}{\text{Standard deviation}}$$

The calculated effect size for the stance phase in running was d= 0.54 (medium) and thus a power of 85% was reached. The calculated effect size for the single leg squat task was ES= 0.31 and thus only a power of 45% was achieved. For the step down task an effect size of ES=0.17 was calculated and thus a power of 20% was reached.

4.4. Results

A total of 22 individuals without PFP (11 males and 11 females, age: 27.45 ±4.43 years, height: 1.73 ± 0.06 m, mass: 66.77 ±9.24kg) and 24 individuals with PFP (12 males and 12 females, age: 29.55 ±6.44 years, height: 1.74 ± 0.09 m, mass: 70.08 ±8.78kg) participated in the study. The groups were age and BMI matched (age: p= 0.213, BMI: p= 0.308). The speed was not significantly different between these two conditions (Individuals without PFP: p= 0.08, individuals with PFP p=0.06).

Participants without PFP had an average running speed of 3.44 m/s (±0.33 m/s) without the Powers^{TM} strap and 3.34 m/s (±0.26 m/s) and with the Powers^{TM} strap. The running speed of participants with PFP was on average without the Powers^{TM} strap 3.46 m/s (±0.15 m/s) and with the Powers^{TM} strap 3.38 m/s (±0.17 m/s). The speed was not significantly different between these two conditions (Individuals without PFP: p= 0.08, individuals with PFP p=0.06).

Pain was significantly reduced with the Powers^{TM} strap during the functional tasks (p=0.0001) (without the marker and bandage application: 4.04±1.91; with the Powers^{TM} strap application: 1.93±2.13, effect size: 1.04). Whereas the marker and bandage application did not modify the pain significantly (p=0.48, with the marker and bandage application: 3.76±2.07).

Hip internal rotation angle was significantly reduced in both groups throughout the entire stance phase when the participants were running with the Powers™ strap (early stance phase (ESP): in individuals without PFP: 3.2°, with PFP: 6°, mid-stance phase (MSP): in individuals without PFP: 3.4°, with PFP: 3.5°, late-stance phase (LSP): in individuals without PFP: 4.9°, with PFP: 4.3°) (Table 4.1, Figure 4.2, 4.3). However, the effect size for the early stance phase was moderate for early and small for the mid and late stance phase. Furthermore, knee internal rotation angle was significantly decreased with small effect sizes during the entire stance phase in running in individuals with PFP and during the early and mid-stance phase in individuals without PFP (ESP: in individuals without PFP: 1.6°, with PFP: 1.5°, MSP: in individuals without PFP: 2°, with PFP: 2.7°, LSP: in individuals with PFP: 2.8°, Table 4.1, Figure 4.4, 4.5). In individuals with and without PFP the hip rotation moment was modified during the early stance phase with the applied Powers™ strap with a moderate effect size (in individuals with PFP: ESP: 0.07 Nm/kg, in individuals without PFP: MSP: 0.1 Nm/kg). However, the kinetic changes were not visible in the averaged curves of the hip rotation moments curves (Figure 4.6 to Figure 4.7). Lastly, the knee adduction moment was significantly increased in individuals with PFP during the early and mid-stance phase (ESP: 0.09 Nm/kg, MSP: 0.09 Nm/kg, Table 4.2., Figure 4.9), however only with small effect sizes. But the changes in hip and knee rotation angles were also apparent during the mean kinematic curves. The averaged hip rotation moment showed no clear differences with and without the Powers strap. The averaged knee adduction curve showed a significant increase during the stance phase in running.

*Table 4.1: The lower extremity kinematics during the stance phase in running (*indicated the results were significantly different.)*

The kinematic variables (º) during stance phase			Individuals without PFP					Individuals with PFP				
			Mean	SD	Std. Error Mean	P value: (T-test, sig 2-tailed)	Effect size	Mean	SD	Std. Error Mean	P value: (T-test, sig 2-tailed)	Effect size
Early stance phase	Hip flexion angle	without strap	36.7	7.4	1.6	0.071	0.18	36.3	5.3	1.1	0.535	0.11
		with strap	35.4	7.0	1.5			35.9	5.1	1.0		
	Hip adduction angle	without strap	8.3	3.7	0.8	0.842	0.03	7.0	4.6	0.9	0.716	0.06
		with strap	8.2	3.7	0.8			7.3	5.1	1.0		
	Hip internal rotation angle	without strap	4.3	7.0	1.5	0.011*	0.42	3.2	8.3	1.7	0.0001*	0.79
		with strap	1.1	8.3	1.8			-3.2	8.0	1.6		
	Knee flexion angle	without strap	29.6	4.8	1.0	0.626	0.08	31.8	4.2	0.9	0.847	0.02
		with strap	29.2	4.7	1.0			31.7	4.1	0.8		
	Knee adduction angle	without strap	2.6	3.6	0.8	0.238	0.13	2.3	4.1	0.8	0.058	0.24
		with strap	2.1	4.0	0.9			1.2	4.9	1.0		
	Knee internal rotation angle	without strap	-1.4	5.1	1.1	0.025*	0.29	-3.2	5.3	1.1	0.037*	0.27
		with strap	-3.0	6.0	1.3			-4.7	5.7	1.2		
Mid-stance phase	Hip flexion angle	without strap	37.4	8.5	1.8	0.116	0.18	34.5	5.7	1.2	0.498	0.11
		with strap	36.0	7.3	1.5			35.1	5.1	1.0		
	Hip adduction angle	without strap	11.4	3.9	0.8	0.374	0.12	9.7	5.3	1.1	0.567	0.10
		with strap	10.9	4.5	1.0			9.1	6.8	1.4		
	Hip internal rotation angle	without strap	4.2	6.6	1.4	0.001*	0.51	-1.0	8.8	1.8	0.0002*	0.40
		with strap	0.8	6.8	1.5			-4.5	8.7	1.8		
	Knee flexion angle	without strap	42.0	4.9	1.0	0.361	0.09	43.4	6.3	1.3	0.422	0.16
		with strap	41.6	4.5	1.0			42.5	4.4	0.9		
	Knee adduction angle	without strap	3.6	3.2	0.7	0.307	0.11	0.5	5.0	1.0	0.651	0.04
		with strap	3.2	3.9	0.8			0.7	5.2	1.1		
	Knee internal rotation angle	without strap	3.9	6.5	1.4	0.0001*	0.29	1.9	5.7	1.2	0.0002*	0.47
		with strap	1.9	7.2	1.5			-0.8	5.9	1.2		
Late-stance phase	Hip flexion angle	without strap	5.1	5.2	1.1	0.895	0.03	20.4	5.5	1.1	0.330	0.13
		with strap	5.3	6.8	1.5			21.1	5.1	1.0		
	Hip adduction angle	without strap	-0.3	3.0	0.7	0.371	0.15	7.2	4.6	0.9	0.274	0.14
		with strap	-0.8	3.6	0.8			6.5	5.2	1.1		
	Hip internal rotation angle	without strap	3.8	6.9	1.5	0.0001*	0.69	-0.2	9.8	2.0	0.0001*	0.43
		with strap	-1.1	7.3	1.6			-4.5	10.2	2.1		
	Knee flexion angle	without strap	23.0	4.4	0.9	0.321	0.21	41.5	4.5	0.9	0.501	0.09
		with strap	24.1	5.8	1.3			41.1	4.1	0.8		
	Knee adduction angle	without strap	2.0	2.6	0.6	0.034*	0.32	1.0	4.3	0.9	0.495	0.05
		with strap	1.1	3.0	0.7			0.8	4.3	0.9		
	Knee internal rotation angle	without strap	-7.4	7.1	1.6	0.985	0	1.1	5.8	1.2	0.002*	0.45
		with strap	-7.4	7.9	1.7			-1.7	6.7	1.4		

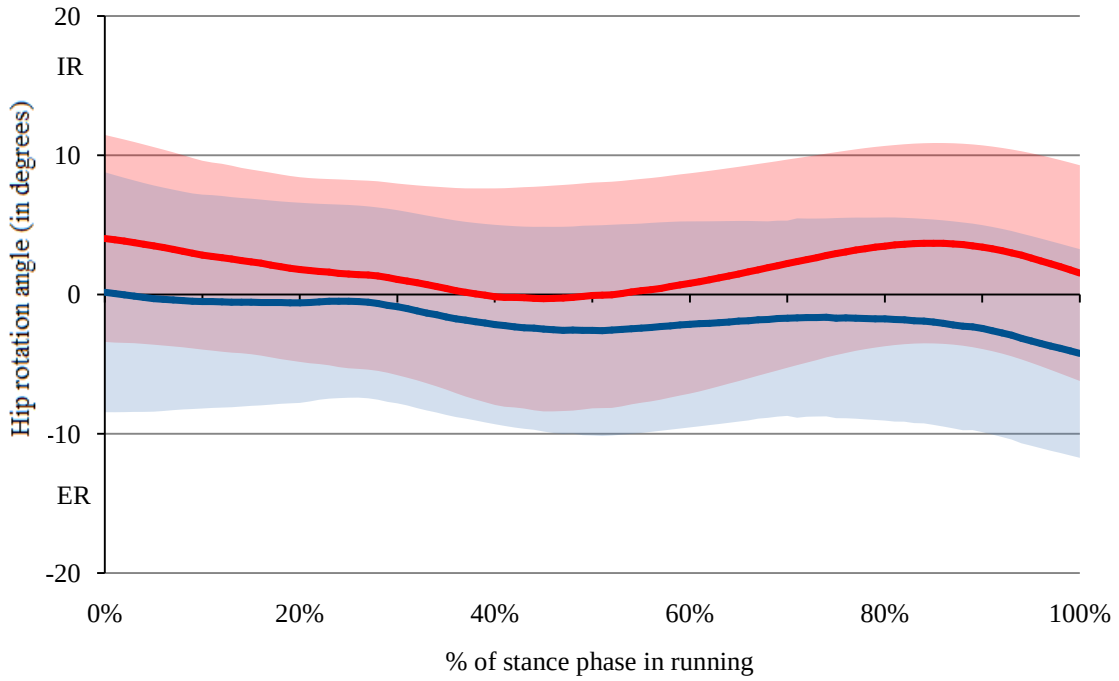


Figure 4.2: The transverse plane hip angle during the stance phase of running under 2 conditions: without (red) and with the Powers™ strap (blue) in individuals without PFP. The shaded areas represent ±1SD for each condition, internal rotation as the positive angle.

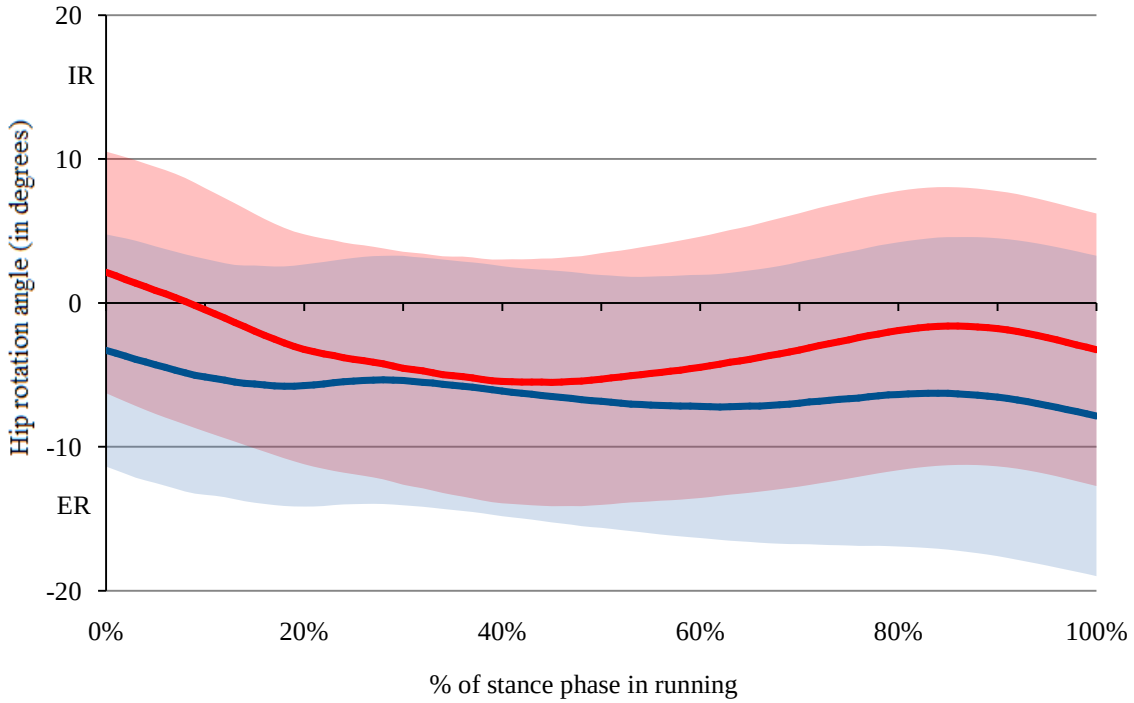


Figure 4.3: The transverse plane hip angle during the stance phase of running under 2 conditions: without (red) and with the Powers™ strap (blue) in individuals with PFP. The shaded areas represent ±1SD for each condition, internal rotation as the positive angle.

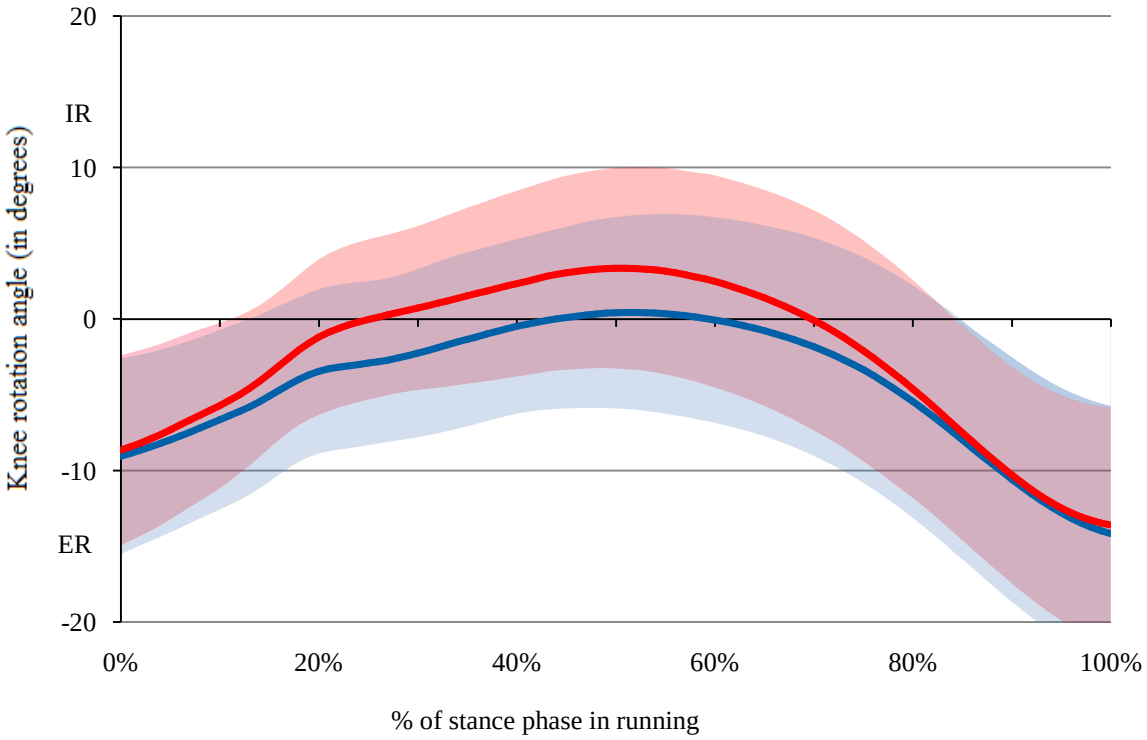


Figure 4.4: The transverse plane knee angle during the stance phase of running under 2 conditions: without (red) and with the Powers™ strap (blue) in individuals without PFP. The shaded areas represent ±1SD for each condition, internal rotation as the positive angle.

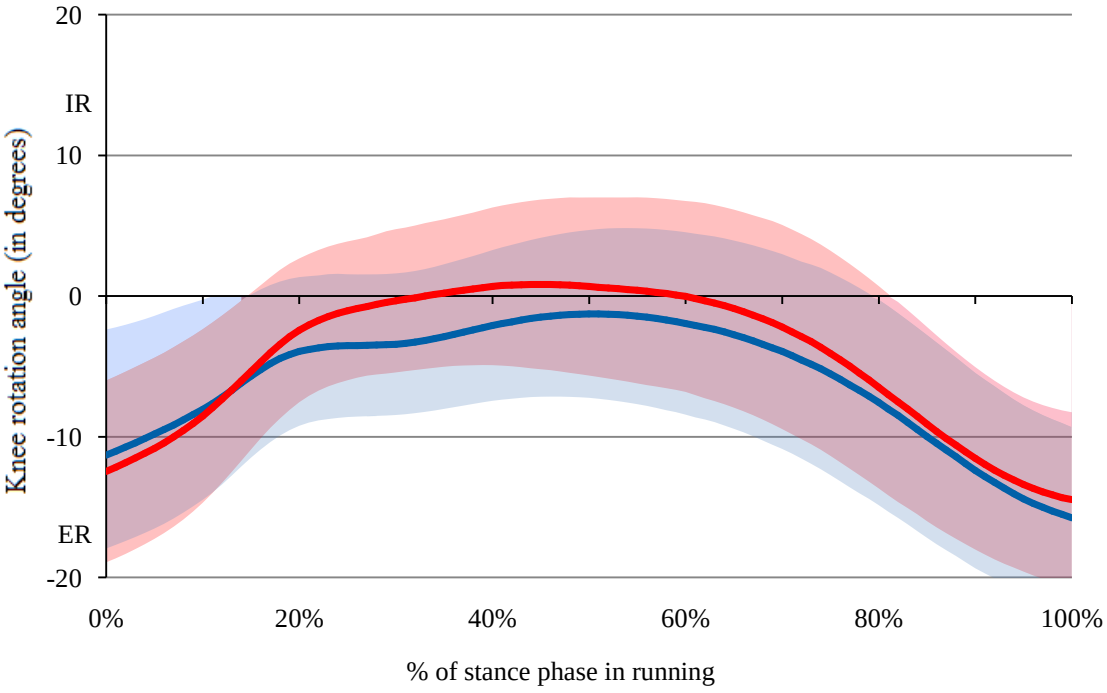


Figure 4.5: The transverse plane knee angle during the stance phase of running under 2 conditions: without (red) and with the Powers™ strap (blue) in individuals with PFP. The shaded areas represent ±1SD for each condition, internal rotation as the positive angle.

*Table 4.2: The lower extremity kinetics during stance phase in running (*indicated the results were significantly different.)*

The kinetic variables (º) during stance phase			Individuals without PFP					Individuals with PFP				
			Mean	SD	Std. Error Mean	P value: (T-test, sig 2-tailed)	Effect size	Mean	SD	Std. Error Mean	P value: (T-test, sig 2-tailed)	Effect size
Early stance phase	Hip flexion moment	without strap	1.75	0.58	0.12	0.469	0.17	2.01	0.44	0.09	0.852	0.02
		with strap	1.66	0.45	0.10			2.00	0.51	0.10		
	Hip adduction moment	without strap	1.47	0.31	0.07	0.135	0.49	1.12	0.33	0.07	0.059	0.35
		with strap	1.30	0.38	0.08			1.26	0.45	0.09		
	Hip internal rotation moment	without strap	0.03	0.23	0.05	0.556	0.11	0.05	0.10	0.02	0.0001*	0.77
		with strap	0.05	0.13	0.03			0.12	0.08	0.02		
	Knee flexion moment	without strap	1.38	0.39	0.08	0.774	0.05	1.32	0.49	0.10	0.177	0.20
		with strap	1.36	0.44	0.09			1.43	0.58	0.12		
	Knee adduction moment	without strap	0.61	0.23	0.05	0.607	0.08	0.44	0.28	0.06	0.037*	0.29
		with strap	0.59	0.25	0.05			0.53	0.33	0.07		
	Knee internal rotation moment	without strap	0.26	0.11	0.02	0.889	0	0.20	0.11	0.02	0.18	0.40
		with strap	0.26	0.09	0.02			0.25	0.14	0.03		
Mid-stance phase	Hip flexion moment	without strap	1.33	0.61	0.14	0.211	0.20	0.90	0.64	0.13	0.919	0.04
		with strap	1.21	0.58	0.12			0.92	0.49	0.10		
	Hip adduction moment	without strap	2.00	0.24	0.05	0.240	0.38	1.82	0.45	0.09	0.719	0.04
		with strap	1.81	0.66	0.14			1.84	0.52	0.11		
	Hip internal rotation moment	without strap	-0.01	0.06	0.01	0.744	0.09	-0.24	0.20	0.04	0.198	0.27
		with strap	0.00	0.15	0.03			-0.29	0.17	0.04		
	Knee flexion moment	without strap	2.57	0.45	0.10	0.480	0.14	2.41	0.99	0.20	0.561	0.11
		with strap	2.50	0.54	0.12			2.52	0.99	0.20		
	Knee adduction moment	without strap	0.85	0.32	0.07	0.290	0.23	0.46	0.32	0.07	0.009*	0.32
		with strap	0.75	0.42	0.09			0.57	0.37	0.08		
	Knee internal rotation moment	without strap	0.46	0.13	0.03	0.418	0.16	0.41	0.15	0.03	0.278	0.18
		with strap	0.44	0.12	0.03			0.44	0.17	0.03		
Late-stance phase	Hip flexion moment	without strap	-0.07	0.35	0.08	0.38	0.16	0.00	0.26	0.05	0.486	0.07
		with strap	-0.12	0.28	0.06			-0.02	0.28	0.06		
	Hip adduction moment	without strap	0.24	0.14	0.03	0.772	0.07	1.37	0.44	0.09	0.586	0.06
		with strap	0.23	0.14	0.03			1.40	0.50	0.10		
	Hip internal rotation moment	without strap	0.01	0.03	0.01	0.157	0.24	0.01	0.04	0.01	0.202	0.48
		with strap	0.02	0.05	0.01			0.05	0.11	0.02		
	Knee flexion moment	without strap	-0.01	0.14	0.03	0.063	0.33	1.67	0.66	0.14	0.478	0.13
		with strap	0.04	0.16	0.04			1.78	0.95	0.20		
	Knee adduction moment	without strap	0.09	0.11	0.02	0.822	0	0.31	0.23	0.05	0.063	0.29
		with strap	0.09	0.12	0.03			0.38	0.26	0.05		
	Knee internal rotation moment	without strap	0.02	0.04	0.01	0.180	0	0.23	0.11	0.02	0.204	0.17
		with strap	0.02	0.03	0.01			0.25	0.12	0.02		

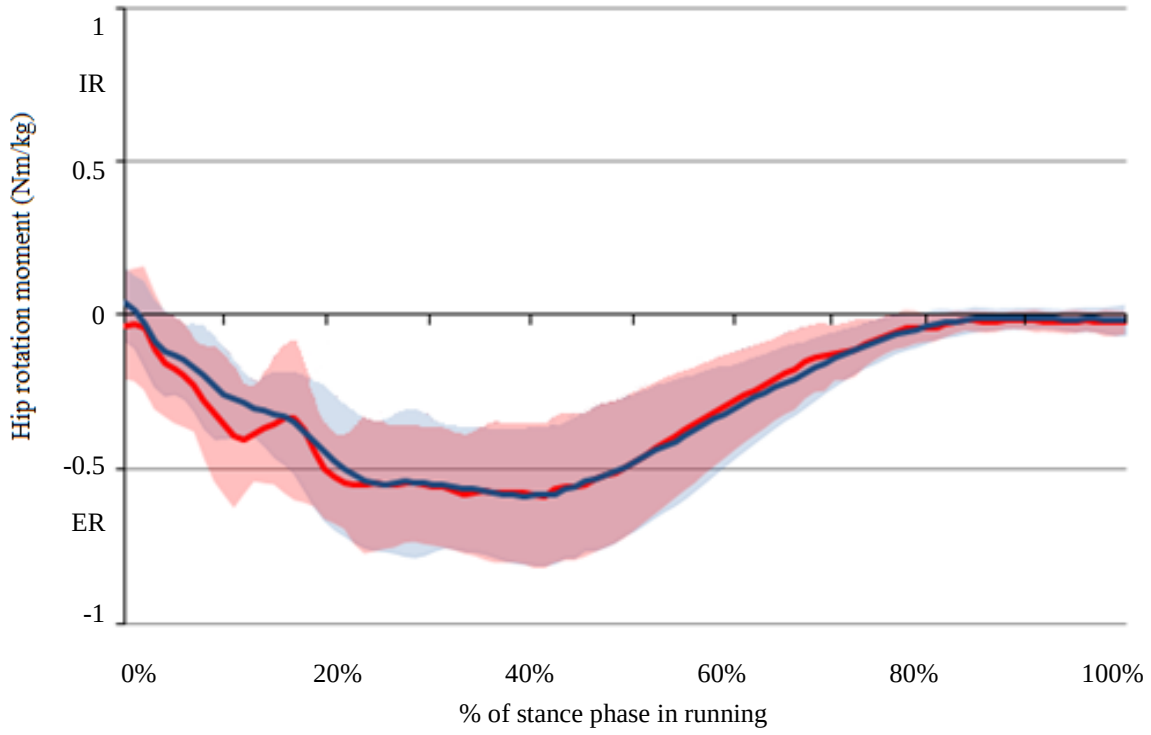


Figure 4.6: The transverse plane hip moment during the stance phase of running under 2 conditions: without (red) and with the Powers™ strap (blue) in individuals without PFP. The shaded areas represent ±1SD for each condition, internal rotation as the positive angle.

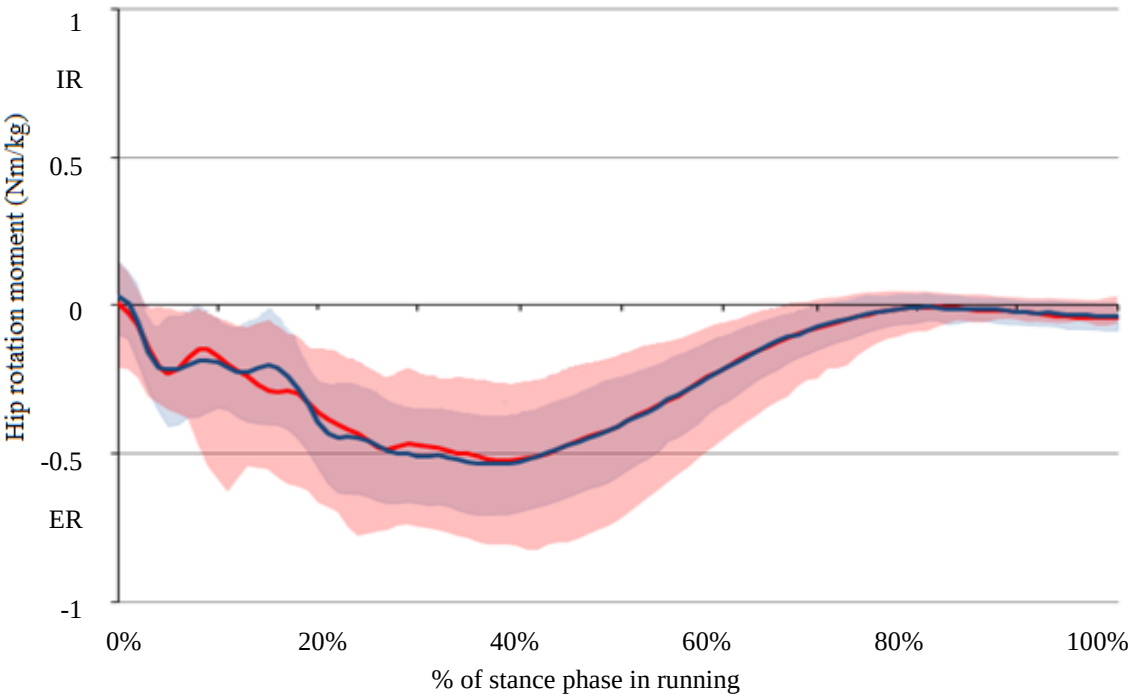


Figure 4.7: The transverse plane hip moment during the stance phase of running under 2 conditions: without (red) and with the Powers™ strap (blue) in individuals with PFP. The shaded areas represent ±1SD for each condition, internal rotation as the positive angle.

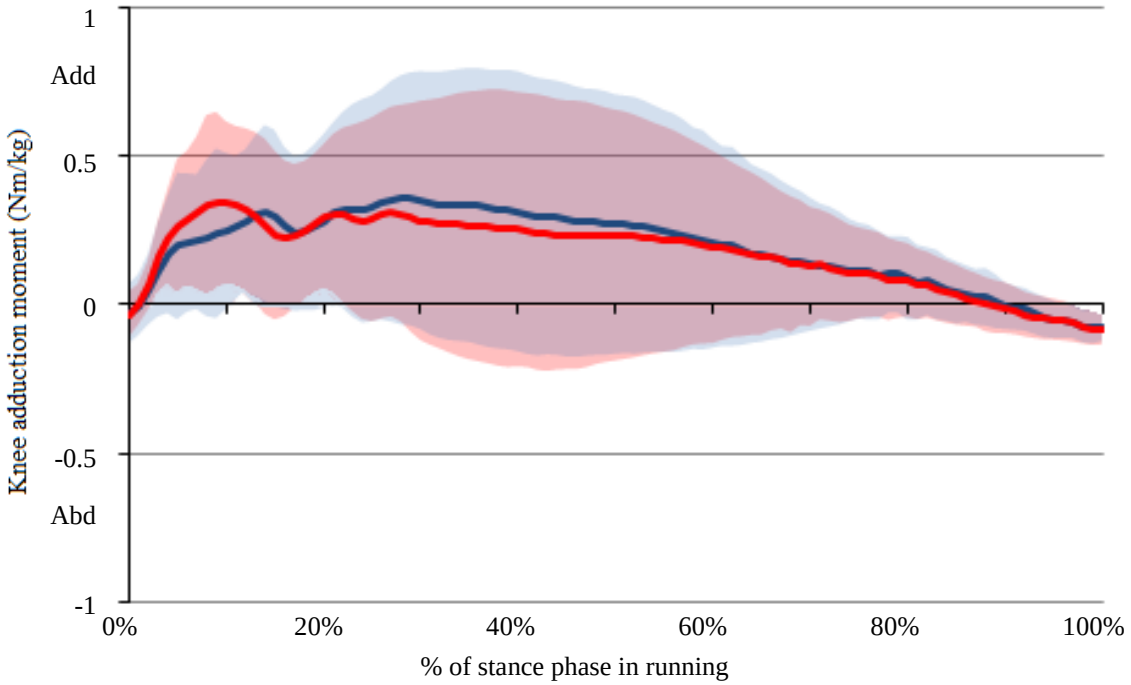


Figure 4.8: The frontal plane knee moment during the stance phase of running under 2 conditions: without (red) and with the Powers™ strap (blue) in individuals with PFP. The shaded areas represent ±1SD for each condition, internal rotation as the positive angle

Individuals without PFP reduced their squatting depth with the Powers strap and flexed the hip on average 5.5° and the knee 3.5° less with the Powers strap (Table 4.3). A reduction in hip and knee flexion angles and moments might affect the hip and knee rotation and abduction angles as well. The hip internal rotation angle significantly decreased by 2° during the single leg squat in individuals without PFP and by 2.4° in individuals with PFP (Table 4.3, Figure 4.7). Furthermore, the knee external rotation angle increased by 1.7° in healthy controls and 1.9° in individuals with PFP (Table 4.3, Figure 4.10). In individuals with PFP also the hip adduction angle decreased by 1.1° (Table 4.3). However, these changes were not apparent in the averaged curve of the hip adduction angle in individuals with PFP (Figure 4.11). However, the kinematic changes during the single leg squat and step down task showed only small effect sizes. The external knee adduction moment was significantly increased in both groups with a moderate effect size for individuals with PFP (in individuals without PFP: 0.4 Nm/kg and in individuals with PFP: 0.6 Nm/kg, Table 4.4, Figure 4.15). This increase was visible during the averaged knee adduction curves (Figure 4.8) However, in individuals without PFP also the hip and knee flexor moments were significantly reduced (hip flexor moment: 0.11 Nm/kg, knee flexor moment: 0.05 Nm/kg), as well as the knee internal rotation moment (0.02 Nm/kg, Table 4.4). But all of these changes had only small effect sizes.

During the step down task the hip adduction and knee internal rotation angle were significantly reduced in both groups when participants performed the task with the Powers strap. The hip adduction angle was 1.7° reduced in individuals without PFP and 1.8° in individuals with PFP (Table 4.3, Figure 4.12). The knee internal rotation angle was 2° decreased in individuals without PFP and knee external rotation angle was 2.2° increased in individuals with PFP (Figure 4.13). But these changes in Individuals with PFP also showed a significant increase of the knee adduction angle of 0.8° (Figure 4.14). Individuals without PFP showed a significant reduced hip internal rotation angle of 2.9° (Table 4.3). However, lower limb kinetic and kinematic changes during the step down task had only small effect sizes (Table 4.4.).

*Table 4.3: The lower extremity kinematics during the single leg squat task and the step down task (*indicated the results were significantly different.)*

The kinematic variables (º) during stance phase			Individuals without PFP					Individuals with PFP				
			Mean	SD	Std. Error Mean	P value: (T-test, sig 2-tailed)	Effect size	Mean	SD	Std. Error Mean	P value: (T-test, sig 2-tailed)	Effect size
Single leg squat	Hip flexion angle	without strap	64.0	16.7	3.7	0.002*	0.29	73.4	18.2	3.7	0.378	0.07
		with strap	59.5	14.5	3.2			72.2	18.3	3.7		
	Hip adduction angle	without strap	12.0	4.7	1.1	0.623	0.10	13.6	7.6	1.6	0.015*	0.12
		with strap	11.5	5.4	1.2			12.7	7.0	1.4		
	Hip internal rotation angle	without strap	5.7	7.6	1.7	0.0001*	0.26	0.6	8.1	1.7	0.0001*	0.31
		with strap	3.7	7.9	1.8			-1.8	7.6	1.6		
	Knee flexion angle	with strap	78.2	11.5	2.6	0.034*	0.22	80.8	10.7	2.2	0.876	0.02
		without strap	75.7	10.9	2.4			81.0	11.4	2.3		
	Knee adduction angle	with strap	7.2	5.0	1.1	0.156	0.17	4.3	4.9	1.0	0.172	0.1
		without strap	8.1	5.4	1.2			4.8	5.5	1.1		
	Knee internal rotation angle	with strap	1.1	5.5	1.2	0.002	0.29	-1.4	5.6	1.1	0.017*	0.34
		without strap	-0.6	6.2	1.4			-3.3	5.6	1.1		
	Knee angular velocity (°/seconds)	without strap	-35.9	9.9	2.2	0.389	0.13	-35.3	13.6	2.8	0.791	0.52
		with strap	-34.7	9.1	2.0			-36.0	13.4	2.7		
Step down task	Hip flexion angle	without strap	57.0	13.3	3.0	0.297	0.08	71.8	16.1	3.3	0.306	0.08
		with strap	55.9	14.2	3.2			70.5	16.3	3.3		
	Hip adduction angle	without strap	13.4	5.7	1.3	0.029*	0.30	15.5	6.6	1.4	0.013*	0.26
		with strap	11.7	5.6	1.3			13.7	7.1	1.5		
	Hip internal rotation angle	without strap	5.4	6.8	1.5	0.0001*	0.41	0.6	7.9	1.6	0.286	0.17
		without strap	2.5	7.2	1.6			-0.8	8.6	1.8		
	Knee flexion angle	with strap	81.6	14.4	3.2	0.264	0.07	88.6	12.9	2.6	0.281	0.24
		without strap	80.6	14.6	3.3			84.4	21.1	4.3		
	Knee adduction angle	with strap	7.4	5.0	1.12	0.139	0.15	4.4	4.9	1.0	0.043*	0.15
		without strap	8.2	5.5	1.22			5.2	5.6	1.1		
	Knee internal rotation angle	with strap	2.2	5.7	1.26	0.002*	0.33	-0.8	5.8	1.2	0.044*	0.31
		without strap	0.2	6.4	1.44			-3.0	8.3	1.7		
	Knee angular velocity (°/seconds)	with strap	-32.5	11.4	2.54	0.534	0.05	-35.3	12.5	2.5	0.864	0.12
		without strap	-33.1	11.0	2.46			-33.7	14.8	3.0		

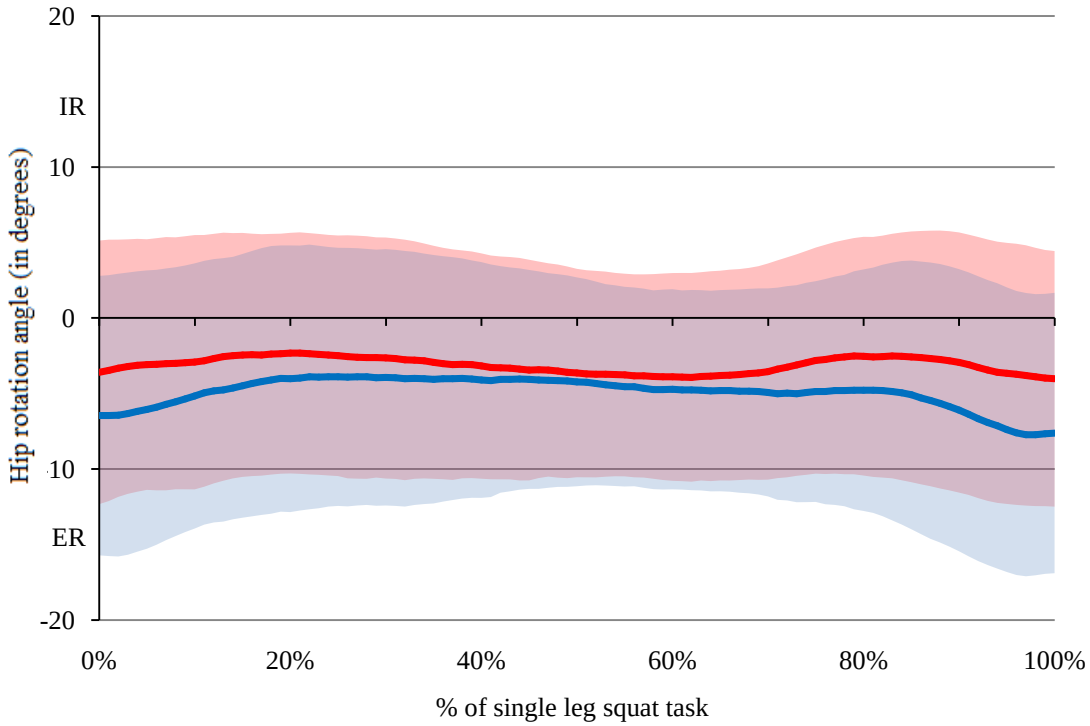


Figure 4.9: The transversal plane hip angle during the single leg squat under 2 conditions: without (red) and with the Powers™ strap (blue) in individuals with PFP. The shaded areas represent ±1SD for each condition, internal rotation as the positive angle.

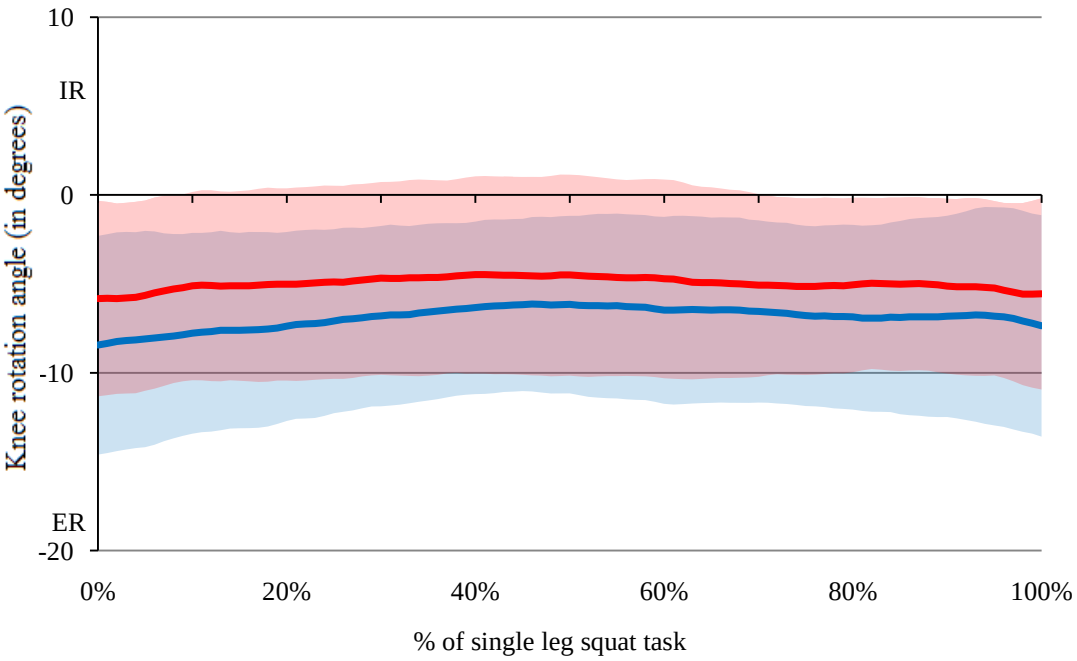


Figure 4.10: The transversal plane knee angle during the single leg squat under 2 conditions: without (red) and with the Powers™ strap (blue) in individuals with PFP. The shaded areas represent ±1SD for each condition, internal rotation as the positive angle.

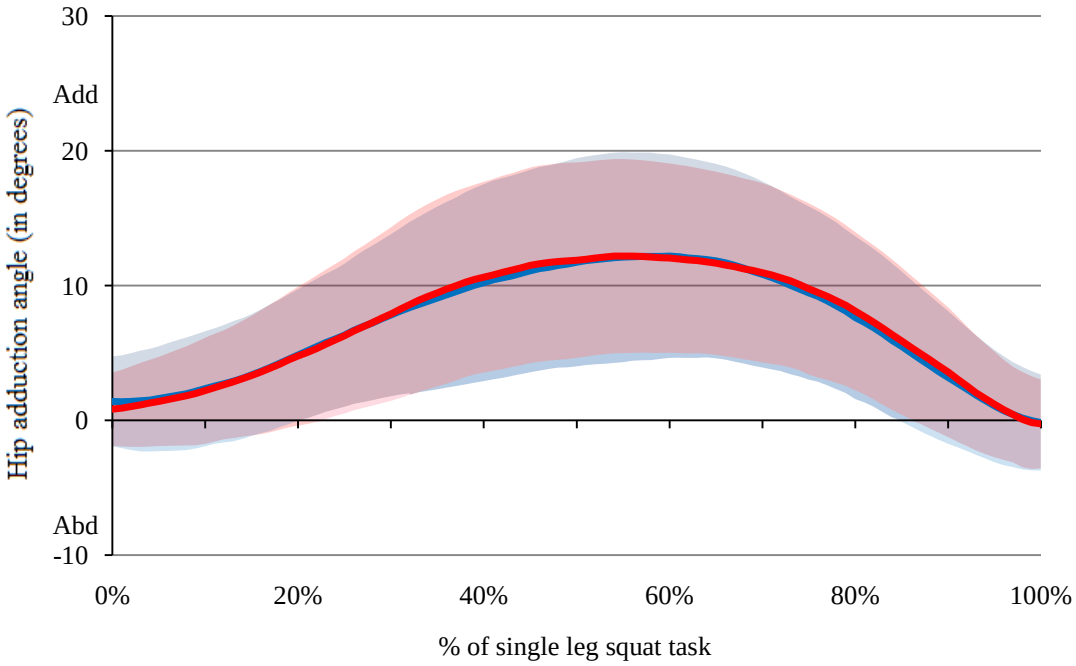


Figure 4.11: The frontal plane hip angle during the single leg squat under 2 conditions: without (red) and with the Powers™ strap (blue) in individuals with PFP. The shaded areas represent ±1SD for each condition, internal rotation as the positive angle.

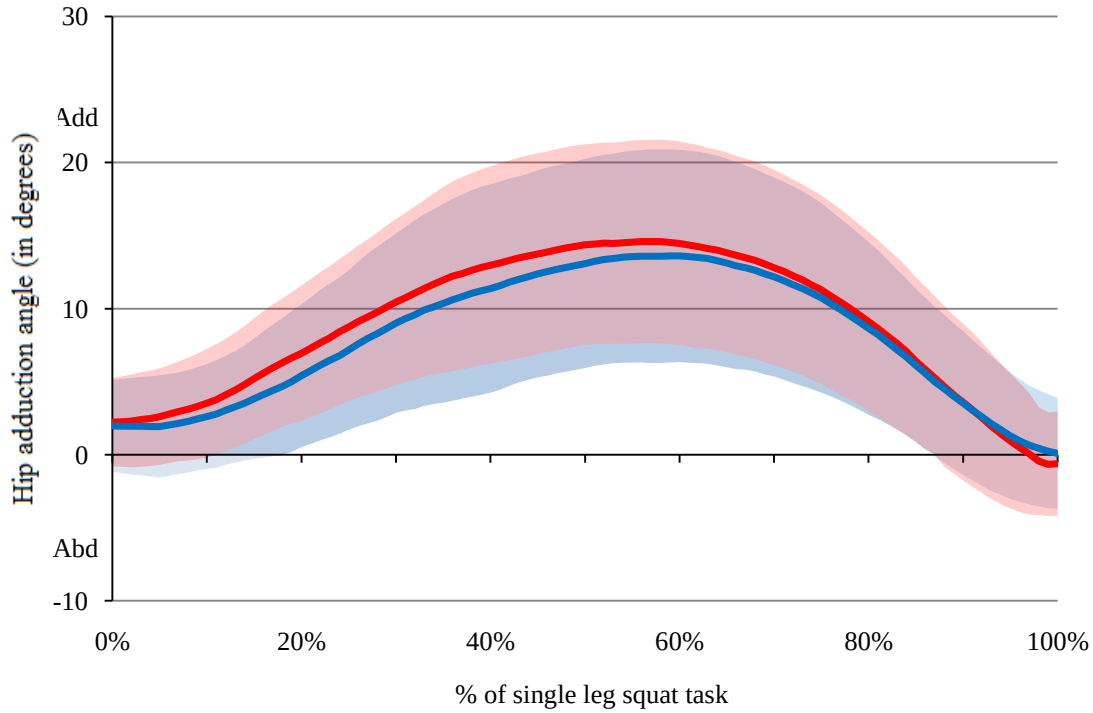


Figure 4.12: The frontal plane hip angle during the step down task under 2 conditions: without (red) and with the Powers™ strap (blue) in individuals with PFP. The shaded areas represent ±1SD for each condition, internal rotation as the positive angle.

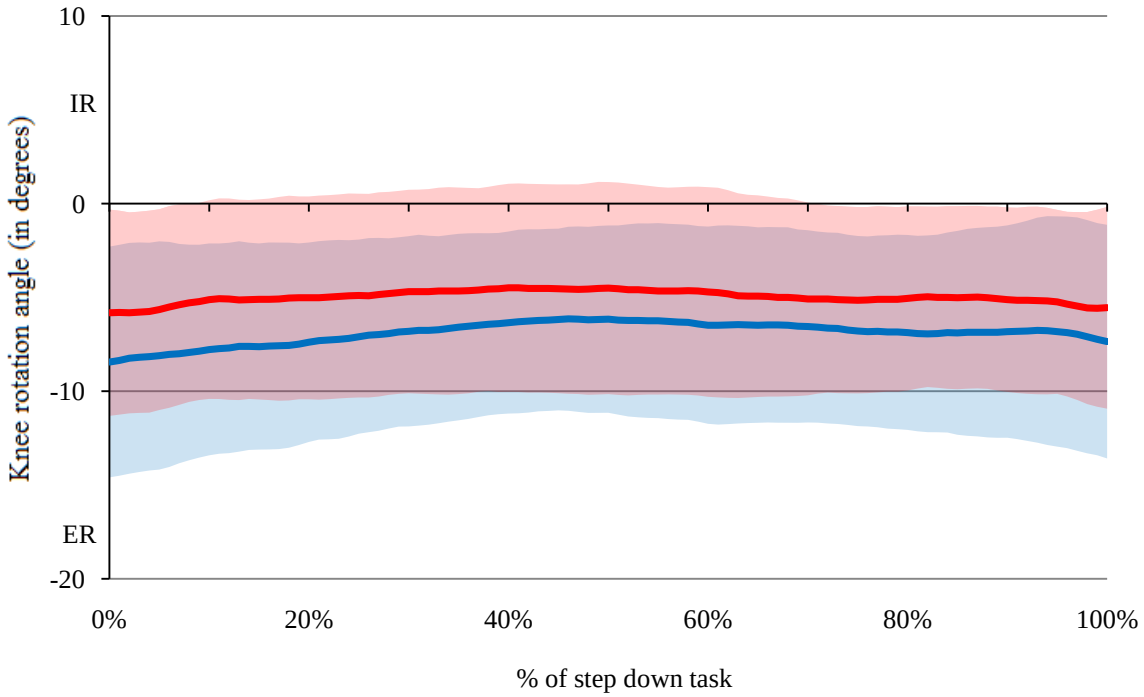


Figure 4.13: The transversal plane knee angle during the step down task under 2 conditions: without (red) and with the Powers™ strap (blue) in individuals with PFP. The shaded areas represent ±1SD for each condition, internal rotation as the positive angle.

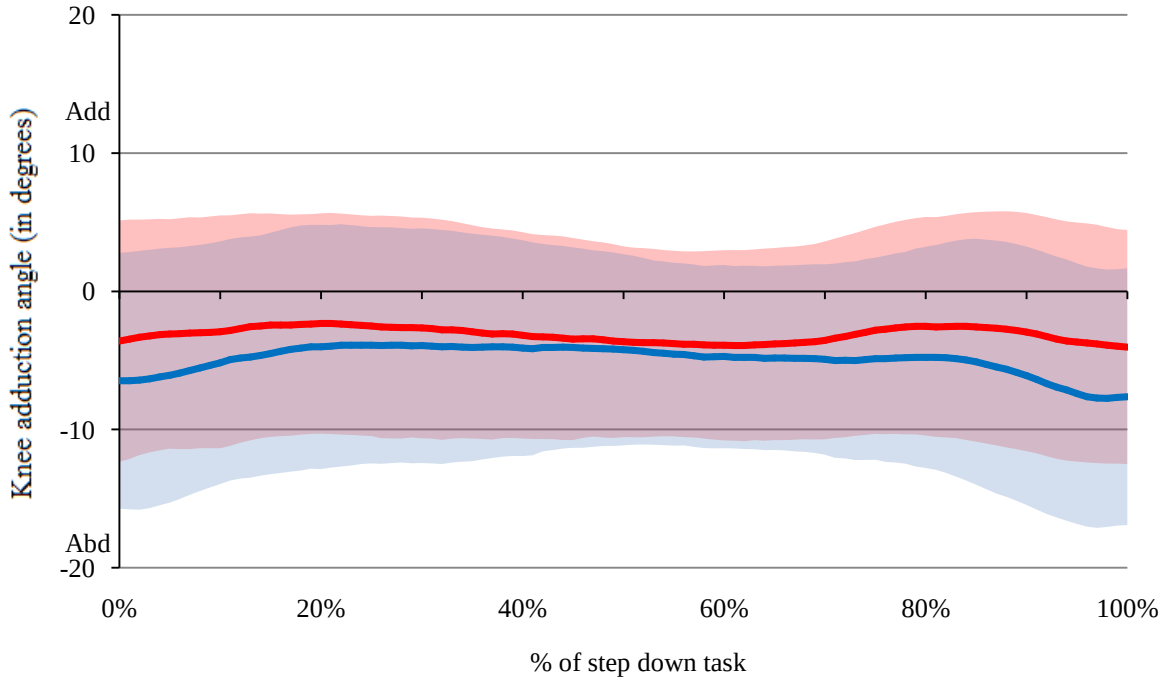


Figure 4.14: The frontal plane knee angle during the step down task under 2 conditions: without (red) and with the Powers™ strap (blue) in individuals with PFP. The shaded areas represent ±1SD for each condition, internal rotation as the positive angle.

*Table 4.4: The lower extremity kinetics during the single leg squat task and the step down task (*indicated the results were significantly different.)*

The kinetic variables (º) during stance phase			Individuals without PFP					Individuals with PFP				
			Mean	SD	Std. Error Mean	P value: (T-test, sig 2-tailed)	Effect size	Mean	SD	Std. Error Mean	P value: (T-test, sig 2-tailed)	Effect size
Single leg squat	Hip flexion moment	without strap	1.02	0.57	0.13	0.006*	0.20	1.25	0.58	0.12	0.935	0
		with strap	0.91	0.52	0.12			1.25	0.67	0.14		
	Hip adduction moment	without strap	1.00	0.13	0.03	0.653	0.08	0.92	0.20	0.04	0.821	0
		with strap	0.99	0.13	0.03			0.92	0.19	0.04		
	Hip internal rotation moment	without strap	-0.15	0.08	0.02	0.075	0.27	-0.14	0.08	0.02	0.302	0.13
		with strap	-0.13	0.07	0.02			-0.13	0.08	0.02		
	Knee flexion moment	with strap	1.73	0.29	0.06	0.008*	0.17	1.70	0.28	0.06	0.689	0.03
		without strap	1.68	0.30	0.07			1.71	0.30	0.06		
	Knee adduction moment	with strap	0.38	0.14	0.03	0.020*	0.26	0.30	0.10	0.02	0.009*	0.57
		without strap	0.42	0.17	0.04			0.36	0.11	0.02		
	Knee internal rotation moment	with strap	0.43	0.10	0.02	0.022*	0.21	0.37	0.09	0.12	0.109	0.21
		without strap	0.41	0.09	0.02			0.39	0.10	0.14		
Step down task	Hip flexion moment	without strap	1.00	0.56	0.13	0.263	0.10	1.50	0.70	0.14	0.158	0.17
		with strap	1.06	0.63	0.14			1.38	0.70	0.14		
	Hip adduction moment	without strap	1.10	0.17	0.04	0.521	0.06	1.06	0.19	0.04	0.103	0.29
		with strap	1.09	0.14	0.03			0.99	0.28	0.06		
	Hip internal rotation moment	without strap	-0.08	0.11	0.02	0.887	0.08	-0.10	0.06	0.01	0.133	0.14
		without strap	-0.07	0.09	0.02			-0.09	0.08	0.02		
	Knee flexion moment	with strap	1.77	0.30	0.07	0.160	0.14	1.71	0.28	0.06	0.265	0.20
		without strap	1.73	0.27	0.06			1.64	0.42	0.09		
	Knee adduction moment	with strap	0.43	0.14	0.03	0.533	0.13	0.35	0.13	0.03	0.217	0.29
		without strap	0.45	0.16	0.04			0.39	0.15	0.03		
	Knee internal rotation moment	with strap	0.42	0.11	0.02	0.522	0.22	0.38	0.09	0.02	0.952	0.10
		without strap	0.44	0.07	0.02			0.37	0.11	0.02		

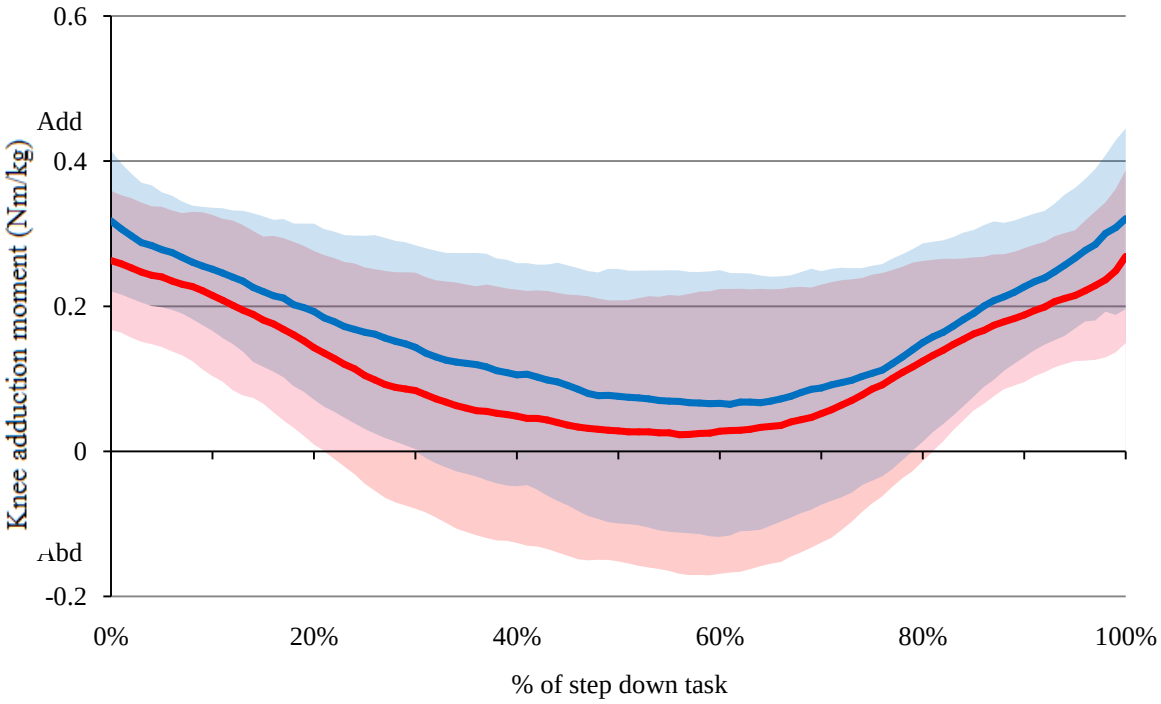


Figure 4.15: The frontal plane knee moment during the step down task under 2 conditions: without (red) and with the Powers™ strap (blue) in individuals with PFP. The shaded areas represent ±1SD for each condition, internal rotation as the positive angle.

The Powers™ strap did not result in significant changes in co-contraction ratio and the net activation of the knee extensors and knee flexors in individuals with PFP during the functional tasks. In individuals without PFP, the knee flexor net activation decreased during the single leg squat (p=0.0001), step down task (p=0.048) and the early stance phase (p=0.0001) of running (Table 4.5). However, these changes only had very small effect sizes (< 0.048) and thus need to be critically questioned.

*Table 4.5: Differences in lower sEMG activity with and without the Powers™ strap (*indicated the results were significantly different.)*

			Individuals without PFP					Individuals with PFP				
			Mean	SD	Std. Error Mean	P value: (T-test, sig 2-tailed)	Effect size	Mean	SD	Std. Error Mean	P value: (T-test, sig 2-tailed)	Effect size
Single leg squat	Co-contraction ratio (knee ext: knee flx.)	without strap	0.70	0.17	0.04	0.618	0.06	0.67	0.18	0.04	0.879	0
		with strap	0.69	0.17	0.04			0.67	0.19	0.04		
	Net activation knee extensors in %	without strap	82.35	38.13	8.75	0.04*	0.43	104.7	31.53	6.58	0.062	0.24
		with strap	68.27	26.61	6.10			97.74	26.87	5.60		
	Net activation knee flexors in %	without strap	24.23	11.72	2.69	0.001*	0.34	32.11	13.89	2.90	0.137	0.15
		with strap	20.44	10.58	2.43			29.98	14.68	3.06		
Step down task	Co-contraction ratio (knee ext: knee flx.)	without strap	0.63	0.19	0.04	0.966	0	0.62	0.20	0.04	0.876	0.05
		with strap	0.63	0.18	0.04			0.61	0.21	0.05		
	Net activation knee extensors in %	without strap	72.84	28.49	6.72	0.064	0.18	99.97	29.31	6.25	0.292	0.12
		with strap	67.80	28.04	6.61			96.38	30.17	6.43		
	Net activation knee flexors in %	without strap	27.52	13.60	3.21	0.048*	0.13	35.79	15.77	3.36	0.313	0.10
		with strap	25.84	12.18	2.87			34.21	16.38	3.49		
Early stance phase	Co-contraction ratio (knee ext: knee flx.)	without strap	0.59	0.22	0.05	0.201	0.10	0.66	0.21	0.04	0.738	0.05
		with strap	0.61	0.20	0.04			0.67	0.22	0.05		
	Net activation knee extensors in %	without strap	118.00	69.60	14.51	0.212	0.15	142.84	60.97	12.71	0.879	0.02
		with strap	107.15	77.28	16.11			144.02	83.20	17.35		
	Net activation knee flexors in %	without strap	45.04	31.73	6.62	0.0001*	0.29	43.44	29.41	6.13	0.094	0.09
		with strap	36.78	24.48	5.10			40.82	31.75	6.62		
Mid stance phase	Co-contraction ratio (knee ext: knee flx.)	without strap	0.31	0.34	0.07	0.274	0.05	0.38	0.29	0.06	0.605	0.14
		with strap	0.29	0.40	0.08			0.31	0.67	0.14		
	Net activation knee extensors in %	without strap	67.93	43.50	9.07	0.447	0.10	90.64	40.44	8.43	0.362	0.05
		with strap	65.35	50.53	10.54			88.44	48.37	10.09		
	Net activation knee flexors in %	without strap	41.96	26.52	5.53	0.121	0.15	50.15	23.88	4.98	0.101	0.01
		with strap	38.33	22.45	4.68			50.43	38.17	7.96		
Late stance phase	Co-contraction ratio (knee ext: knee flx.)	without strap	-0.39	0.57	0.12	0.976	0.09	-0.40	0.72	0.15	0.543	0.33
		with strap	-0.34	0.52	0.11			-0.15	0.81	0.17		
	Net activation knee extensors in %	without strap	8.66	6.89	1.44	0.465	0.29	11.45	12.07	2.52	0.412	0.10
		with strap	14.45	27.42	5.72			13.55	25.93	5.41		
	Net activation knee flexors in %	without strap	15.44	15.11	3.15	0.346	0.15	16.80	9.82	2.05	0.171	0.26
		with strap	13.47	10.03	2.09			14.32	9.15	1.91		

4.5. Discussion

To the authors knowledge this is the first study that has investigated hip and knee kinematics and kinetics, as well as the quadriceps and hamstrings activation during functional tasks with and without a strap that is designed to reduce hip internal rotation and thereby modify lower limb alignment. This study revealed that the hip rotation angle and moment were significantly modified with the Powers™ strap and thus, the first null-hypothesis was rejected. The second null-hypothesis stating that there would be no kinetic or kinematic changes of the knee and hip joint was rejected, because it could be shown that the Powers™ strap significantly modified the knee internal rotation angle and the knee adduction moment. The third hypothesis stating that

there would be no significant differences in co-contraction ratio and hamstrings and quadriceps activation was accepted, because no differences could be identified with and without the Powers™ strap.

This study showed that the Powers™ strap significantly reduced pain and the hip internal rotation angle during running and eccentric quadriceps tasks in individuals with and without PFP. Pain decreased by 1.9 on the NRPS, which has been rated as a small to moderate change in pain (Abbott & Schmitt, 2014). Thus, although the pain rating was relatively small before the strap application (NPRS: 4.04), the pain still decreased by almost 2 on the NPRS to 1.93 with the strap application. The reduced hip internal rotation angle is important, because altered patellofemoral joint kinetics are often a result of excessive hip internal rotation in individuals with PFP (Almonroeder & Benson, 2017; Baldon et al., 2009; Bolgla et al., 2008; Mirzaie, Kajbafvala, Rahimi, Manshadi, & Kalantari, 2016; Neal, Barton, Gallie, O'Halloran, & Morrissey, 2016; Song et al., 2014; Souza, 2008). Studies revealed that controlled femur rotation can restore normal patellofemoral joint kinetics (Powers, 2010; Souza et al., 2010). Furthermore, increased femoral internal rotation leads to increased shear stress of the patella and increased patellofemoral contact pressure (Besier, Gold, Delp, Fredericson, & Beaupre, 2008; Lee, Morris, & Csintalan, 2003). The Powers™ strap significantly reduced hip internal rotation angle throughout the stance phase. Furthermore, the strap also modified the knee external rotation angle towards a neutral transverse alignment in both groups. However, the changes were lower than the modifications of the hip internal rotation. The Powers™ strap also resulted in an increased knee adduction moment during the early and mid-stance phase in running in individuals with PFP. Thus, the assumption that a transverse correction of the hip might decrease the dynamic knee valgus could be confirmed in running and the single leg squat task. The dynamic knee valgus creates a lateral force vector on the patella, thereby increasing patellofemoral joint stress, particularly on the lateral face of the patella (Almeida et al., 2016) and is associated with an increased risk of PFP (Myer et al., 2015). In addition, the hip IR moment was significantly increased during the early stance phase, which is in accordance to the significantly increased hip external rotation angle. However, the increase of the hip internal rotation moment might also be related to an increase of the gluteal muscle activity or to an earlier and longer activation of the gluteal muscles, especially of the gluteus medius and gluteus maximus muscle. A reduced and delayed activity of the gluteal muscles has been described in individuals with PFP in previous literature (Barton et al., 2013; Hollman, Galardi, Lin, Voth, &

Whitmarsh, 2014; Nakagawa, Muniz, et al., 2011; Souza & Powers, 2008, 2009a, 2009b; Willson et al., 2011). This tendency might have been triggered from the strap that brought the hip passively into this position and thereby facilitated the gluteal activation. Thus, future research should investigate the activity of the gluteal muscles with and without the strap. The increased knee adduction moment and the decreased hip IR angle during the early and mid stance phase are important clinical findings, because the patellofemoral joint stress reaches a peak during the early and mid-stance phase (Wirtz, Willson, Kernozek, & Hong, 2012) and most injuries, such as patellofemoral pain occur as a result of the high impact forces at the time of the initial contact (Novacheck, 1998). Furthermore, the early stance phase is a crucial phase in which the quadriceps absorbs the shock at impact (Novacheck, 1998; Pink, 2010). Previous research reported that the hip abductor, hip extensor, knee extensor and knee flexor muscles exhibited a burst of activity during the early and mid-stance phase to stabilise the knee and hip joint motion and were only slightly active in the late-stance phase (McClay, Lake, & Cavanagh, 1990; Novacheck, 1998; Pink, 2010). In addition, the late-stance phase as the push off and transition phase to the swing phase is believed to be irrelevant in the development of PFP (McClay et al., 1990; Novacheck, 1998).

The results during the single leg squat and step down task were more heterogeneous. Individuals without PFP performed the squat to less depth with the Powers^{TM} strap, which caused a reduction in hip and knee flexion angles and moment and would affect the hip and knee rotation and abduction angles significantly as well. Since individuals without PFP performed the single leg squat differently with the Powers^{TM} strap, it could not be analysed whether the Powers^{TM} strap reduced the hip internal rotation or whether the reduction was caused by a reduced hip and knee flexion. In contrast, individuals with PFP did not change the depth of the squat and showed a significant decrease of hip and knee internal rotation angle and hip adduction angle, as well as a significant increased knee adduction moment with the Powers^{TM} strap. These kinetic and kinematic changes indicate that the Powers^{TM} strap did not only successfully reduced pain but also reduced effectively the dynamic knee valgus in individuals with PFP.

During the step down task, individuals with and without PFP showed a decrease of the hip adduction angle, and knee internal rotation and an increase of the knee adduction with the Powers^{TM} strap. In both groups were no kinetic changes observed during the step down task. Thus, although it seems that the Powers^{TM} strap was able to decrease the dynamic knee valgus

in individuals with PFP during both eccentric tasks, it did not influence the dynamic knee valgus kinetically during the step down task. Since both tasks are closely related to each other, the kinetic influence of the Powers™ strap remains uncertain during eccentric quadriceps activities. However, the tendency of a decrease of hip internal rotational, hip adduction angle and an increase of knee adduction moment became apparent and shows a promising approach to reduce effectively the dynamic knee valgus in individuals with PFP.

In individuals without PFP, hamstrings activation was significantly decreased during the single leg squat and the step down task, as well as the early stance phase in running with the applied Powers™ strap. However, the reduction of hamstrings activation ranged from 1.7% up to 8% and thus it is questionable if these differences are clinically meaningful. It seems that the tactile stimulus that was applied by the Powers™ strap was not sufficient to alter neuromuscular performance of hamstrings and quadriceps function. One explanation might be that the participants did not exhibit neuromuscular dysfunctions that could be modified or that the localisation of the strap did not stimulate the population of recruited motor units.

Thus, the first and second hypothesis suggesting no change of the hip and knee angles and moments were rejected. The Powers™ strap significantly reduced pain in individuals with PFP and thus, the third hypothesis suggesting no changes in pain with the Powers™ strap was rejected. Although biomechanical changes could be achieved, the Powers strap did not modify significantly the quadriceps and hamstrings activation in individuals with PFP. Thus, the fourth hypothesis suggesting no difference in co-contraction ratio and the net-activation of the quadriceps and hamstrings muscles with the Powers™ strap was accepted.

Previous literature reported that tibial external rotation increases patellofemoral contact pressures (Lee et al., 2003; Powers, 2003). The knee internal rotation significantly decreased with the Powers™ strap throughout the tasks, which would be a harmful effect of the strap. However, increased patellofemoral contact pressures have been reported in an excessive external rotation of at least 15° external rotation (Csintalan, Schulz, Woo, McMahon, & Lee, 2002; Lee et al., 2003). The data was subsequently checked to determine if participants showed an excessive external rotation of >15° and revealed that none of the participants in this study showed an excessive external rotation. The knee rotation ranged from 1.9° internal rotation to maximal 4.5° external rotation and thus no increase of patellofemoral contact pressure can be expected due to an increased external rotation with the Powers™ strap. However, the effect of

the Powers™ strap on knee rotation should be investigated in individuals with PFP that show an increase in tibial external rotation.

To date, only limited research on knee braces, straps and patellar taping is available with heterogeneous findings (Theoret & Lamontagne, 2006; Van Tiggelen, et al., 2004; Wilson, Weltman, Martin, & Weltman, 1998; Yeung, Yeung, & Gillespie, 2011). Studies that investigated the influence of knee braces, straps and patellar taping in individuals with patellofemoral pain, concluded that bracing or taping seem to improve acute pain, however, it does not seem to help function and stability (Bolgla & Boling, 2011; Collins, Bisset, Crossley, & Vicenzino, 2012; Swart et al., 2012; Theoret & Lamontagne, 2006; Van Tiggelen, et al., 2004; Wilson et al., 1998; Yeung et al., 2011). Thus, the evidence supporting the use of patellar taping, knee straps and braces to modify lower limb biomechanics in individuals with PFP is still lacking (Barton et al., 2015; Richards et al., 2015; Smith et al., 2015). One reason for this deficit is that current research shows a great heterogeneity in the types and use of knee orthoses and taping techniques (N. J. Collins et al., 2012), as well as vast hetereogeneity in the patient population (Lack et al., 2014). But despite the great heterogeneity of braces and taping techniques, to date literature is focused on knee braces, straps and sleeves that aim to provide a local stabilisation of the knee and the patella (Barton et al., 2015; Richards et al., 2015; Smith et al., 2015).

The design of the Powers™ strap is fundamentally different and aims to facilitate an external rotation of the thigh and not a local stabilisation of the knee. The strap focuses on the decrease of an excessive internal rotation of the hip, which is an important risk factor for patellofemoral pain (Boling et al., 2009; Powers et al., 2012). An increased femoral internal rotation has been commonly observed in individuals with PFP and is linked to an increased lateral patellar tilt, peak patella shear stress and can result in excessive lateral patellar displacement and tilt (Besier et al., 2008; Lee et al., 2003; Powers, 2003; Souza, 2008; Souza et al., 2010; Souza & Powers, 2009a). Furthermore, an increased femoral internal rotation causes a rapid decrease of patellofemoral contact area (Besier et al., 2008). To the authors' knowledge, this was the first study that investigated with 3D gait analysis the influence of a knee strap that aimed to reduce of the hip internal rotation during running and eccentric quadriceps tasks. This study showed that the Powers™ strap has the potential to decrease hip internal rotation during running and squatting. Besides the influence of the Powers™ strap on lower limb biomechanics it also reduced the acute pain significantly. The Powers™ strap has been tested in individuals with

and without PFP and reduced hip internal rotation in both groups. This is important from a mechanistic perspective as even in individuals who do not have pain, hip internal rotation can be reduced with the strap and gives confidence that this change was not influenced by pain changes. The reduction of the hip internal rotation angles were ranging from 2.2° to 6° and although these changes were partially quite small, they seemed to result in clinically significant changes, with a significant decrease in pain.

Thus, this strap might be a promising treatment approach to treat patients with patellofemoral pain in acute pain and during sports activities, and might enable the decrease of patellofemoral contact pressure and shear stress. However, the individuals in this study did not show an excessive hip internal rotation angle and thus, the effect of the Powers^{TM} strap should be further investigated in individuals with PFP that show an excessive hip internal rotation.

4.6. Limitations to the study

There were some limitations in regards to the findings of the study. It is important to note that the participants were fitted with standard training shoes to control the shoe-surface interface and to minimise the influence of footwear. However, the standard training shoes might have limited the comfort during running and thereby might have influenced the running performance.

Furthermore, the single leg squat and the step down task showed only small effect sizes and only a maximal power of 43% was achieved. Thus, a greater sample size is needed to establish significant findings during the single leg squat and step down task. However, a post-hoc power calculation was carried out for the hip internal rotation during stance phase, which revealed a power of 85% and thus it could be concluded that enough power was reached to present significant results during running.

This study investigated the effect of the Powers^{TM} strap within the same session and did not analyse the effect of the Powers^{TM} strap over time. Thus, further research is required that analyses the effect of the Powers^{TM} strap over a longer period of time to examine whether the strap might result in long-term modifications of the lower limb biomechanics and pain reduction.

And lastly, the range of motion of the hip and knee of the individuals with and without PFP were in the normal range of motion and individuals with PFP did not show an excessive hip adduction or a hip internal rotation (Alenezi et al., 2016; Novacheck, 1998). Thus, further research is required to investigate the effect of the Powers^{TM} strap in individuals with PFP that show an excessive hip internal rotation angle.

4.7. Conclusion

In conclusion, this study has demonstrated that the Powers^{TM} strap altered the transverse plane rotations of the hip and knee and might be a therapy to prevent excessive internal rotation in individuals with patellofemoral pain. Future research should investigate the influence of the Powers^{TM} strap on the lower limb kinematics and kinetics during eccentric quadriceps activities, such as squatting and the step down task in a larger sample of individuals with patellofemoral pain to achieve enough power.

Chapter 5: How does a 6-week exercise intervention influence pain, functional performance, balance, quadriceps strength and inhibition in individuals with patellofemoral pain?

The second intervention assessed was the influence of a 6-week exercise intervention programme, which was investigated in individuals with PFP. This chapter will present the findings from the study focussing on the lower limb kinematics and kinetics, quadriceps strength, quadriceps inhibition, lower limb flexibility, patella and foot posture and clinical outcomes.

5.1. Introduction:

Long term follow up studies have shown that the majority of individuals with PFP develop chronic knee pain despite receiving treatment (chapter 2.4). This underlines that the condition of PFP is not self-limiting and requires a comprehensive rehabilitation programme (Lankhorst et al., 2015). The guidelines for such comprehensive rehabilitation programmes have been developed by international investigators during a consensus meeting at the International Patellofemoral Pain Research Retreat in Manchester 2015 (Crossley et al., 2016b). These guidelines recommend the reduction of pain in the short, medium and long term and the improvement of function in the medium and long term through exercise-therapy (Crossley et al., 2016b). Therefore, the combination of hip and knee exercises is recommended to reduce pain and improve function and should be favoured over knee exercises alone (Crossley et al., 2016b). The guidelines support the use of active over passive exercises and recommend exercise programmes. However, since the guidelines are very recent, no study has developed and investigated the effect of an exercise programme, which is based on the current guidelines on PFP and functional performance.

Thus, this study aimed to develop an exercise programme based on the current guidelines and to investigate whether and how such an exercise programme influences pain, function, functional performance, strength, muscle flexibility, balance and AMI in individuals with PFP.

Therefore Null-Hypotheses for the primary outcomes were:

1. "Pain and function would not be significantly improved after the 6-week evidence based exercise programme in individuals with PFP."

2. "The 6-week exercise programme would not significantly modify lower limb biomechanics in individuals with PFP."
3. "The 6-week exercise programme would not increase muscle flexibility in individuals with PFP."
4. "Quadriceps strength would not be increased after the 6-week exercise programme."

The Null-Hypothesis for the secondary outcomes was: "There would be no significant differences after a 6-week evidence based exercise programme in individuals with PFP in:

- balance
- the break phenomenon
- quadriceps inhibition
- co-contraction ratio and net activation of the quadriceps and hamstrings muscles."

5.2. Methodology

The ethical application HSR 15-142 was obtained from the University of Salford Research and Governance committee on the 11th January 2016. The HRA approval was received on the 12th August 2016, with the REC reference: 16/NW/0497 (Appendix Methods 6.1). Informed consent was obtained from each study participant.

5.2.1. Development of a 6-week exercise programme:

A six-week exercise programme was developed based on the current recommendations, and consisted of four strength exercises and two stretching exercises. Since the current guidelines recommend an exercise programme as a stand-alone treatment (Crossley et al., 2016b), it has been decided to develop a 6-week exercise programme that patients could follow on his/her own at home.

An exercise booklet was created, which described the correct execution of the exercise programme. To ensure that participants were able to understand the exercises without a therapist, each exercise was additionally video recorded and all videos were uploaded on a password-protected website (vimeo). The website address, as well as the password were provided in the exercise booklet.

The introduction in the exercise booklet gave information about the PFP exercise training programme and the handling of the booklet. The brochure then introduced a short selection of warm up and cooling down exercises, such as leg swing, low resistance cycling or slow walking in place.

The main exercise programme consisted of four exercises, which aimed to strengthen the gluteus medius, maximus and the muscle. Experts recommended that not more than 3-4 exercises should be prescribed to ensure the compliance of the patient with the treatment (Crossley et al., 2016b). The exercise programme included the combination of hip and knee strength focused exercises which has been shown to reflect the strongest current evidence and clinical practice (Barton et al., 2015; Crossley et al., 2016b).

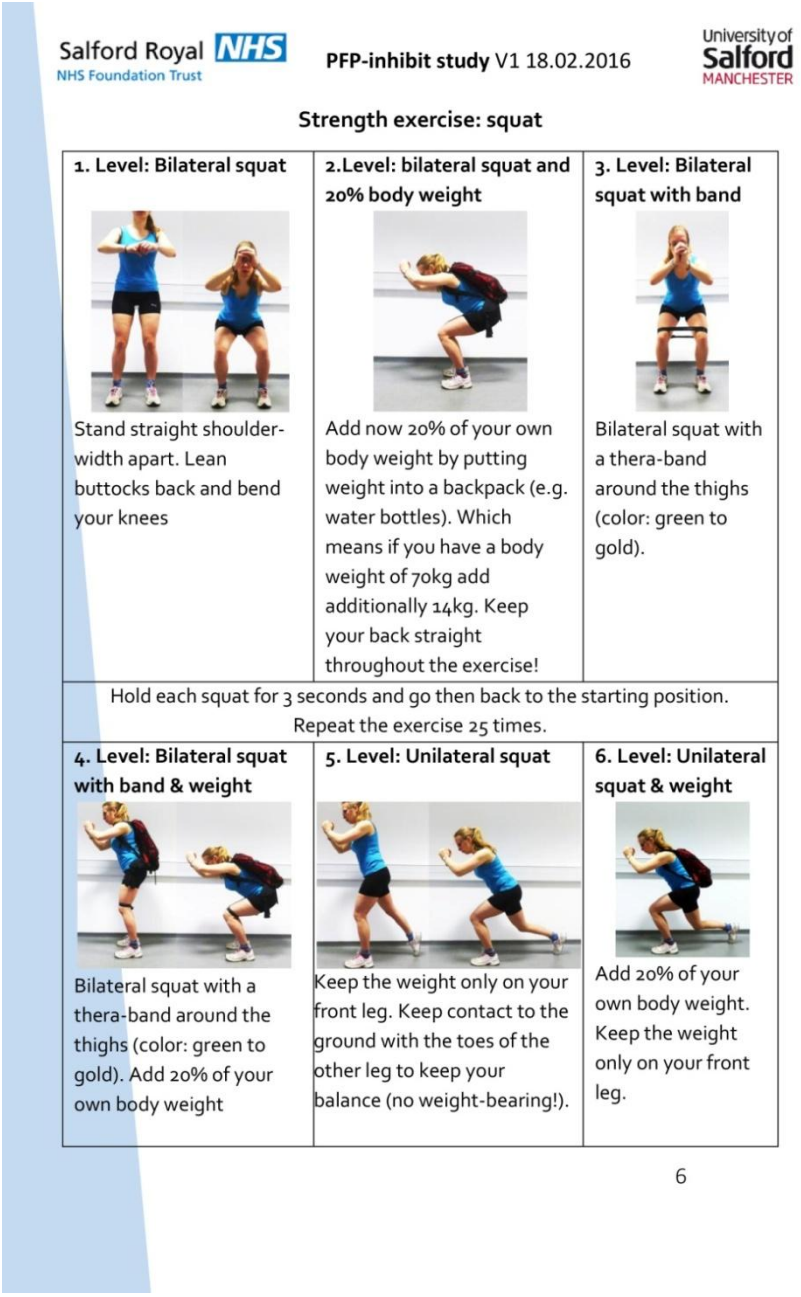
In addition to the four strength exercises, two exercises that aimed to stretch the hamstrings muscles and to increase the ankle dorsiflexion range of motion were included. Reduced ankle dorsiflexion range of motion has shown to increase dynamic knee valgus during functional tasks (Rabin & Kozol, 2010). Thus, mobilisations to address dorsiflexion restrictions to limit compensatory pronation, optimise shock absorption and internal tibial rotation was recommended (Barton et al., 2015). Reduced hamstring flexibility was associated with an increased knee extensor moment during gait (Williams & Welch, 2015). To ensure optimised knee and ankle biomechanics, the integration of a hamstrings stretch exercise has been recommended by other investigators (Barton et al., 2015).

The exercise programme was organised as a circuit training strategy, with three sets and a total circuit time of maximal 30 minutes.

The current PFP treatment guidelines emphasised that there was a need to individualise the treatments to each patient, as not all patients will require the same treatment (Barton et al., 2015; Crossley et al., 2016b). To meet these needs, each exercise included a progressive loading in six steps. The participants were instructed to progress individually for each exercise. They were allowed to enter a higher progression stage, if they did not experience any pain and if they felt only light or no exertion. If patients experienced pain during an exercise, they were instructed to either progress to the next lower level of the exercise or to contact the Principal Investigator of the study.

Studies have shown that the combination of open and closed kinetic chain strength exercises seem to be the most effective method to strengthen the quadriceps (Herrington & Al-Sherhi,

2007; Witvrouw, Danneels, Van Tiggelen, Willems, & Cambier, 2004). The first exercise was the squatting exercise, which has shown to strengthen and activate successfully the quadriceps and gluteal muscles with a relative low hamstrings co-activation (Begalle, Distefano, Blackburn, & Padua, 2012; Claiborne, Armstrong, Gandhi, & Pincivero, 2006; Lee et al., 2016; Reiman, Bolgla, & Loudon, 2012; Shields et al., 2005; Willson, Ireland, & Davis, 2006; Willy & Davis, 2011). Furthermore, patellofemoral joint contact forces during the squat exercise are relatively low when knee flexion is limited to 90° knee flexion and thus the squat is a safe exercise for individuals with PFP (Powers, Ho, Chen, Souza, & Farrokhi, 2014; Wood, Metcalfe, Dodge, & Templeton-Ward, 2016). If the participant experienced pain, he/ she were instructed to lean their trunk more forward or/ and place their feet wider (Escamilla, Fleisig, Zheng, Lander, Barrentine, Andrews, Bergemann, & Moorman, 2001; Kulas, Hortobagyi, & DeVita, 2012). The exercise progressed from a bilateral squat (stage 1) to an unilateral squat combined with 20% body mass (stage 6) (Figure 5.1).



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Strength exercise: squat

1. Level: Bilateral squat	**2.Level: bilateral squat and 20% body weight**	**3. Level: Bilateral squat with band**
Stand straight shoulder-width apart. Lean buttocks back and bend your knees	Add now 20% of your own body weight by putting weight into a backpack (e.g. water bottles). Which means if you have a body weight of 70kg add additionally 14kg. Keep your back straight throughout the exercise!	Bilateral squat with a thera-band around the thighs (color: green to gold).
Hold each squat for 3 seconds and go then back to the starting position. Repeat the exercise 25 times.		
4. Level: Bilateral squat with band & weight	**5. Level: Unilateral squat**	**6. Level: Unilateral squat & weight**
Bilateral squat with a thera-band around the thighs (color: green to gold). Add 20% of your own body weight	Keep the weight only on your front leg. Keep contact to the ground with the toes of the other leg to keep your balance (no weight-bearing!).	Add 20% of your own body weight. Keep the weight only on your front leg.

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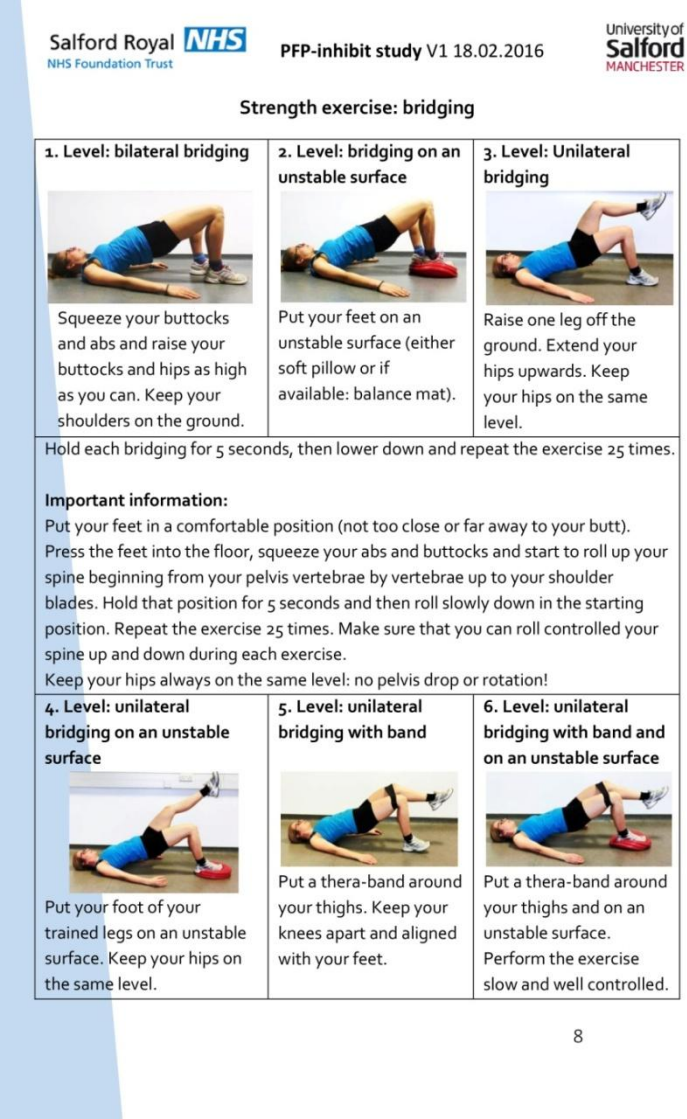
Figure 5.1: Strength exercise: squat

Poor hip stability is associated with PFP and increased knee loads and needs addressing in the management of PFP (Barton et al., 2015; Barton et al., 2013; Esculier et al., 2015; Ramskov, Barton, Nielsen, & Rasmussen, 2015; Rathleff et al., 2014). The bridging exercise has been shown to be a successful method to strengthen the gluteus medius muscle (Choi, Cynn, Yi, Kwon, Yoon, Choi, & Lee, 2015; Reiman et al., 2012). In addition, the bridging exercise has also proven to target the gluteus maximus activity (Reiman et al., 2012). Unilateral bridging resulted in increased gluteus maximus activity as the gluteus maximus has to control the hip

and the pelvis movement in multiple planes (Reiman et al., 2012). The addition of the theraband and the unstable surface generated more gluteus medius activity (Choi et al., 2015; Reiman et al., 2012). Thus, the second exercise in the programme was the bridging exercise, which progressed from a bilateral bridging (stage 1) to an unilateral bridging with a thera-band around the knees, which progressed to the use of an unstable surface (stage 6) (Figure 5.2).



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Strength exercise: bridging

1. Level: bilateral bridging	**2. Level: bridging on an unstable surface**	**3. Level: Unilateral bridging**
Squeeze your buttocks and abs and raise your buttocks and hips as high as you can. Keep your shoulders on the ground.	Put your feet on an unstable surface (either soft pillow or if available: balance mat).	Raise one leg off the ground. Extend your hips upwards. Keep your hips on the same level.

Hold each bridging for 5 seconds, then lower down and repeat the exercise 25 times.

Important information:
Put your feet in a comfortable position (not too close or far away to your butt). Press the feet into the floor, squeeze your abs and buttocks and start to roll up your spine beginning from your pelvis vertebrae by vertebrae up to your shoulder blades. Hold that position for 5 seconds and then roll slowly down in the starting position. Repeat the exercise 25 times. Make sure that you can roll controlled your spine up and down during each exercise.
Keep your hips always on the same level: no pelvis drop or rotation!

4. Level: unilateral bridging on an unstable surface	**5. Level: unilateral bridging with band**	**6. Level: unilateral bridging with band and on an unstable surface**
Put your foot of your trained legs on an unstable surface. Keep your hips on the same level.	Put a thera-band around your thighs. Keep your knees apart and aligned with your feet.	Put a thera-band around your thighs and on an unstable surface. Perform the exercise slow and well controlled.

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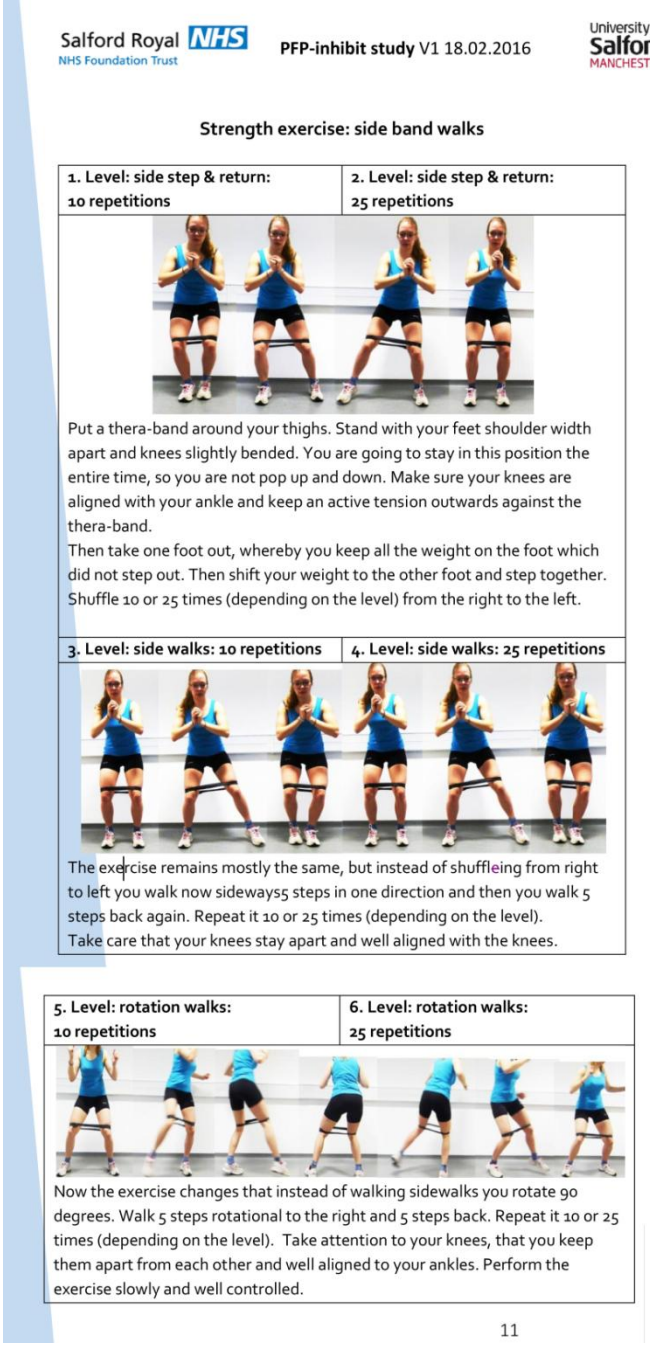
Figure 5.2: Strength exercise: bridging

The third strengthening exercise were the side band (stage 1) and rotational walks (stage 6). This exercise acts as an active alignment control exercise, which have shown to be successful in female basketball players (Kato, Urabe, & Kawamura, 2008). Besides the active modification of the lower limb alignment, the side band and rotational walks produce consistently high levels of gluteus medius and maximus activity and thus are believed to

successfully strengthen the gluteus medius muscle (Boren, Conrey, Le Coguic, Paprocki, Voight, & Robinson, 2011; De Marche Baldon, Serrao, Silva, & Piva, 2014; Distefano, Blackburn, Marshall, & Padua, 2009) (Figure 5.3).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Strength exercise: side band walks

1. Level: side step & return: 10 repetitions	**2. Level: side step & return: 25 repetitions**

Put a thera-band around your thighs. Stand with your feet shoulder width apart and knees slightly bended. You are going to stay in this position the entire time, so you are not pop up and down. Make sure your knees are aligned with your ankle and keep an active tension outwards against the thera-band.
Then take one foot out, whereby you keep all the weight on the foot which did not step out. Then shift your weight to the other foot and step together. Shuffle 10 or 25 times (depending on the level) from the right to the left.

3. Level: side walks: 10 repetitions	**4. Level: side walks: 25 repetitions**

The exercise remains mostly the same, but instead of shuffleing from right to left you walk now sideways5 steps in one direction and then you walk 5 steps back again. Repeat it 10 or 25 times (depending on the level).
Take care that your knees stay apart and well aligned with the knees.

5. Level: rotation walks: 10 repetitions	**6. Level: rotation walks: 25 repetitions**

Now the exercise changes that instead of walking sidewalks you rotate 90 degrees. Walk 5 steps rotational to the right and 5 steps back. Repeat it 10 or 25 times (depending on the level). Take attention to your knees, that you keep them apart from each other and well aligned to your ankles. Perform the exercise slowly and well controlled.

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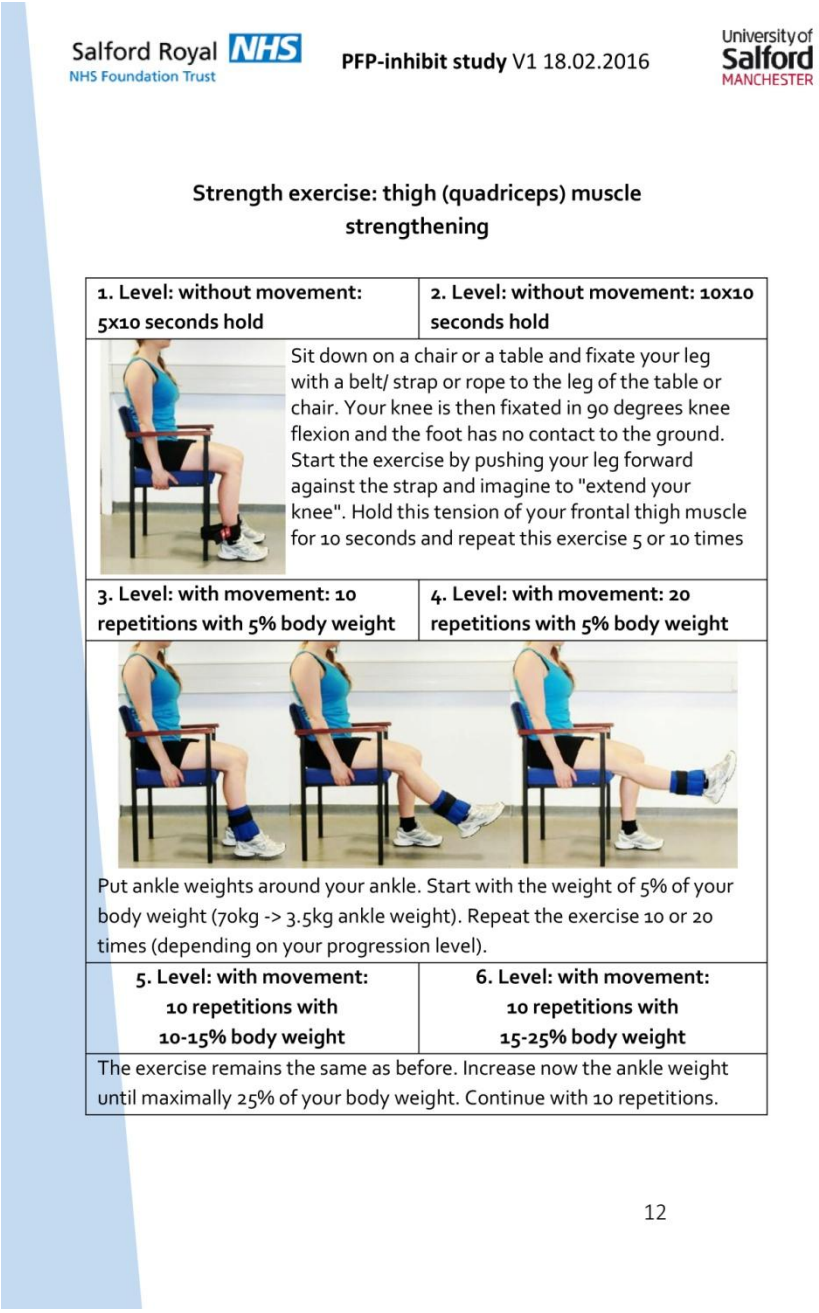
Figure 5.3: Strength exercise: side bend and rotational walks

The fourth strengthening exercise was an open kinetic chain exercise to strengthen the quadriceps. Stage 1 of this exercise was an isometric knee extension exercise and the exercise

progressed to stage 6: knee extension exercise with a resistance of 15-25% of the own body mass (Figure 5.4).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Strength exercise: thigh (quadriceps) muscle strengthening

1. Level: without movement: 5x10 seconds hold	**2. Level: without movement: 10x10 seconds hold**
Sit down on a chair or a table and fixate your leg with a belt/ strap or rope to the leg of the table or chair. Your knee is then fixated in 90 degrees knee flexion and the foot has no contact to the ground. Start the exercise by pushing your leg forward against the strap and imagine to "extend your knee". Hold this tension of your frontal thigh muscle for 10 seconds and repeat this exercise 5 or 10 times	
3. Level: with movement: 10 repetitions with 5% body weight	**4. Level: with movement: 20 repetitions with 5% body weight**
Put ankle weights around your ankle. Start with the weight of 5% of your body weight (70kg -> 3.5kg ankle weight). Repeat the exercise 10 or 20 times (depending on your progression level).	
5. Level: with movement: 10 repetitions with 10-15% body weight	**6. Level: with movement: 10 repetitions with 15-25% body weight**
The exercise remains the same as before. Increase now the ankle weight until maximally 25% of your body weight. Continue with 10 repetitions.	

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Figure 5.4: Strength exercise: quadriceps strengthening in open kinetic chain

The exercise booklet involved an exercise schedule. The participants were asked to note on a daily basis his/her level of progression and the number of repetitions for each exercise. In addition, the exercise schedule involved a box in which participants were asked to note when an unexpected event happened, such as pain or swelling. They were asked to bring the booklet back after the 6-week exercise treatment, so that the individual progression could be examined.

Ankle weights and thera-bands were given to the participants and were returned to the Principal Investigator after the 6-week exercise treatment.

5.2.2. Participants recruitment

The participants were recruited by physiotherapists of the Salford Royal Hospital (Salford Royal NHS Foundation Trust, SRFT). The study and especially the recruitment process has been introduced within three different meetings to the physiotherapists and the leading orthopaedic consultant. Regular meetings with the recruiting physiotherapists were scheduled to ensure that questions and concerns could be raised and discussed. Therefore, the Principal Investigator visited the Physiotherapy department to explain the study and provided the required information and material. The physiotherapists and the Principal Investigator agreed on a procedure of how patients should be screened and how the study should be introduced to the patients, if they met the inclusion criteria. Beside the clinical examination, a standardised, feasible and quick screening was essential to ensure that all patients met the study inclusion criteria (chapter 4.2.1.). Therefore nine questions that checked the inclusion and exclusion criteria were integrated in the computer system as additional questions, that each patient with PFP was asked by his/ her physiotherapist. If the patient met the inclusion criteria the physiotherapist explained the study to the patient and asked for his/her interest in participation, whereby each patient was informed that his/her decision would not affect any treatment plans. If the patients were unwilling to participate they were thanked for considering taking part. If the patient was willing to participate the inclusion/ exclusion-criteria and the patients' details were forwarded either online or via mail to the Principal Investigator. Furthermore, these patients received the study information pack consisting of an invitation letter, the patient information sheet and the informed consent form.

After receiving the patient information from the physiotherapist, the Principal Investigator called the patient, explained the study more into detail and replied to questions that arouse. If the patient decided at this point to not take part, they were thanked for considering and advised to follow a treatment programme at the Salford Royal hospital (Figure 5.5). If participants decided to take part, a date for the gait laboratory measurement was arranged and the patient received an email that confirmed their measurement date and provided a route description, car park information, contact details of the Principal Investigator and gave information about which clothing should be worn during the test.

In addition to the recruitment from the SFRT patients were also recruited via advertisements at fitness centres, gyms, climbing centres and sports clubs in Manchester and Salford, as described in chapter 4.2.

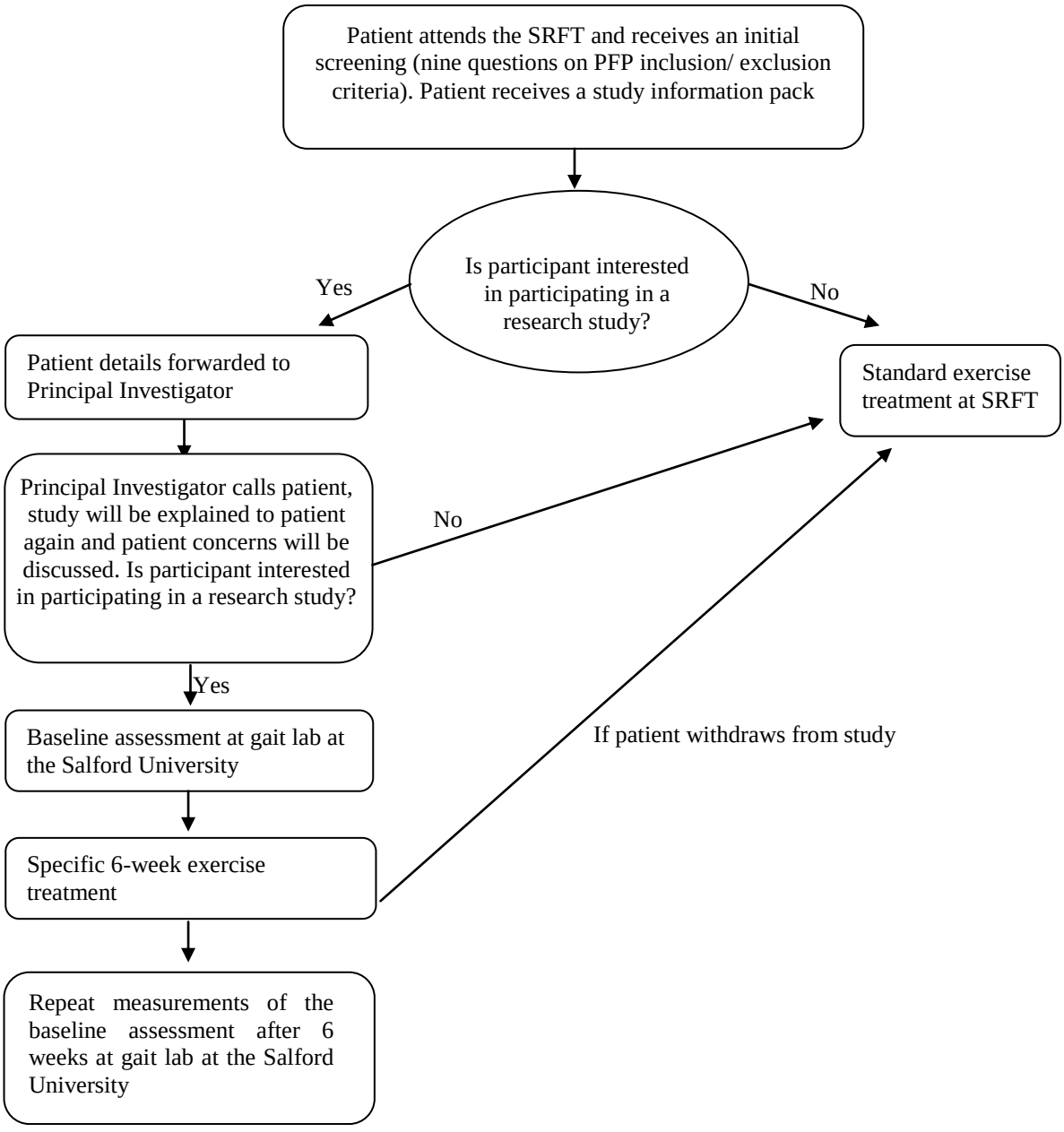

Figure 5.5: Recruitment process for this study

5.2.3. Procedure

Upon arrival at the laboratory, the participants were briefed through the study and the objectives of the investigations and the study equipment was explained to them. They were

asked to sign the informed consent form and a health history questionnaire, which consisted of 13 questions. If potential risks were identified the individual was either asked to consult a physician to receive an approval for the participation or was advised not to participate in this study. Furthermore, they were asked to fill in the Knee injury and osteoarthritis outcome score (KOOS), the anterior knee pain scale KUJALA score and the Tampa scale for kinesiophobia. The KOOS consists of 5 subscales; Pain, Other Symptoms, Function in daily living (ADL), Function in sport and recreation (Sport/Rec) and Knee related quality of life (QOL). Each question is ranked on a score from 0 to 4. A normalized score (100 indicated no symptoms and 0 indicated extreme symptoms) wass calculated for the overall score and each subscale. The Kujala score is a 13-item scale, which contains questions related to symptoms at rest as well as during functional tasks. Each item includes a specific response, which is assigned to a point value to allow an easy scoring. A result of the maximum score of 100 represents the presence of no pain and 0 the maximum presence of pain. The Tampa Scale of Kinesiophobia is a 17-item instrument assessing pain-related fear of movement. All questions are ranked on a 4 point Likert scale (from 1= strongly disagree, to 4= strongly agree). The total score was calculated, ranging from 17=no fear to 68=strong fear avoidance beliefs.

The individual was then asked to wear shorts and a comfortable t-shirt and standard running shoes (New Balance, UK). Before the test, the mass and height of each participant was measured. The foot posture was assessed by using the 6-item foot posture index. The ankle ROM was measured by using a weight-bearing lunge (chapter 3.3. 1). The hamstrings flexibility was measured by using the active knee extension test and the quadriceps flexibility was assessed by using the modified Thomas test. Furthermore, the dynamic balance was measured by using the reaching forward test on the balance board of the star excursion balance test and the reach distance was normalised to the leg length (chapter 3.3.1).

Each individual performed three isometric and isokinetic knee extensor strength tests. The peak isometric, eccentric and concentric torque were measured with an isokinetic dynamometer (Kin-Com, Chattanooga, USA). The muscular inhibition, averaged rate to force development (RFD) and peak force of the quadriceps was assessed during the maximal isometric contraction of the quadriceps with the interpolated twitch technique, using a Digitimer High Voltage Stimulator (DS7AH Digitimer Ltd, Hertfordshire, England) (chapter 3.3.3). The participants were seated in an isokinetic dynamometer and positioned in 90° hip flexion and 60° knee flexion. The isokinetic knee extensor measurements were tested at the angular velocity of 60°/second (chapter 3.3.3).

For the electrode placement of the EMG, the skin was shaved, abraded and cleaned with isopropyl alcohol and the sEMG electrodes were applied on the vastus medialis, vastus lateralis, semitendinosus and the biceps femoris, in accordance with the SENIAM guidelines (chapter 3.4.1.3). The surface EMG data was collected with the Noraxon Telemyo system and sampled at 1500Hz. The sEMG data was synchronised to the kinematic and kinetic data.

Three-dimensional movement data was collected with ten Qualisys OQUS7 cameras (Qualisys AB, Sweden) at a sampling rate of 250Hz. Therefore, forty retroflective markers were placed as described in the previous chapters 3.4.1.2. Force data was collected with three force plates (BP600900, Advanced Mechanical Technology, Inc.USA), at a sampling rate of 1500Hz, which were synchronised with the Qualisys system. The calibrated anatomical system technique (CAST) was used to calculate lower limb biomechanics.

After the static trial, each subject was asked to run on a 15 m walkway at his/her own selected speed, to perform the single leg squat and step down task. The running speed was controlled and reported (Brower timing lights, Draper, UT), to ensure that each trial was within ±10% of the original self-selected speed. Each task was performed until five successful trials were collected. Unsuccessful trials were ones whereby less than three markers per segment were visible, speed changes were seen during the trials, or a partial/double contact with the force platforms.

After finishing all the tasks, the exercise programme was introduced to the patients, whereby each exercise was explained and shown to the patients. The booklet and especially the exercise schedule were explained to the patient and he/she was instructed how to document the exercises for the upcoming 6 weeks. They received the information that they should contact the researcher if they struggle with an exercise or if they develop pain. Furthermore, each participant was offered that a skype call could be arranged, in which the Principal Investigator could show the correct exercise execution again, could follow up the treatment progress and where questions and concerns could be addressed.

After finishing the six week exercise programme a second measurement was arranged, at which the strength and inhibition, flexibility, the dynamic balance assessment and the functional performance of each participant was reassessed. Furthermore, the patient was asked to fill in the KOOS, the Tampa scale and the KUJALA score. Each participant received on each occasion as a compensation a voucher of £15, which was exchangeable for goods in shops in Manchester and Salford.

5.2.4. Data processing

The kinematic and kinetic outcomes were calculated by utilising a 6 degrees of freedom model in Visual3D (Version 5, C-motion Inc, USA). Motion and force plate data was filtered with a 4th order Butterworth filter with cut-off frequencies of 12Hz and the joint moments were normalised to body mass. The kinematic and kinetic data was normalised to 100% of the single leg squat, step down task and the stance phase. The stance phase was sub-grouped into early (0-24% of stance phase), mid (25-62%) and late-stance phase (63%-100%) (Perry & Burnfield, 2010). The peaks of the hip and knee flexion, adduction and internal rotation angles and the moments were calculated for the single leg squat, step down task and the early, mid and late-stance phase. Furthermore, the average knee angular velocity was calculated for the eccentric phase during the single leg squat and step down task.

The sEMG data was band-pass filtered at 20-500Hz and rectified by using a root mean square over a 75 ms window for the running task and 300 ms for the single leg squat and step down task. Co-contraction ratios were (CCR) calculated by using the formula of Heiden et al. (Heiden et al., 2009).

The strength data of each participant was loaded into Excel. The peak torque, AMI, time to peak, the break phenomenon and the rate to force development (RFD) were determined and calculated by using Excel (chapter 3.3.4).

5.3. Statistical analysis

The statistical analysis was performed using SPSS (v. 20) and Excel 2013. Normality was assessed by applying the Shapiro-Wilk test and by the investigation of the normal q-q plots. For the data that was normally distributed, paired sample t-tests were performed at the 95% confidence interval to investigate whether the 6 week exercise programme significantly influenced the lower limb biomechanics. Data that was not normal distributed, as well as ordinal data (pain scale) was tested by using the Wilcoxon rank test with a significance level set at $p<0.05$.

To investigate whether the 6-week intervention treatment resulted in significant differences in hip and knee biomechanics in individuals with PFP a paired two-tailed t-test was used, if the data was normal distributed and a Wilcoxon test, if the data was not normal distributed.

The following values were compared before and after the 6-week exercise intervention:

Primary outcomes:

- the final score of the KOOS, Tampa scale of kinesiophobia and the KUJALA score
- pain rated on the numeric pain rating scale
- peak of the hip flexion, hip adduction, hip internal rotation, knee flexion, knee adduction and knee internal rotation angles and moments
- peak isometric, eccentric and concentric knee extensor torque
- RTF development and time to peak of the knee extensor muscle
- quadriceps AMI in %
- the peak score in degrees of the quadriceps and hamstrings flexibility, as well as the ankle range of motion
- the peak score in cm of the ankle range of motion

Secondary outcomes:

- the co-contraction ratio, net activation of the quadriceps and hamstrings activation
- averaged knee angular velocity during the eccentric quadriceps tasks (single leg squat and step down task)
- the peak score in cm of the star excursion balance test

5.4. Results

Twenty-five participants with PFP were measured and started the 6-week intervention programme. However, after a drop-out of in total 9 participants, only 16 participants with PFP (9 males and 7 females, age: 30.75± 6.34 years, height: 1.73± 0.08 m, mass: 69.04± 9.07kg) completed the 6-week intervention programme and were reassessed (Figure 5.6).

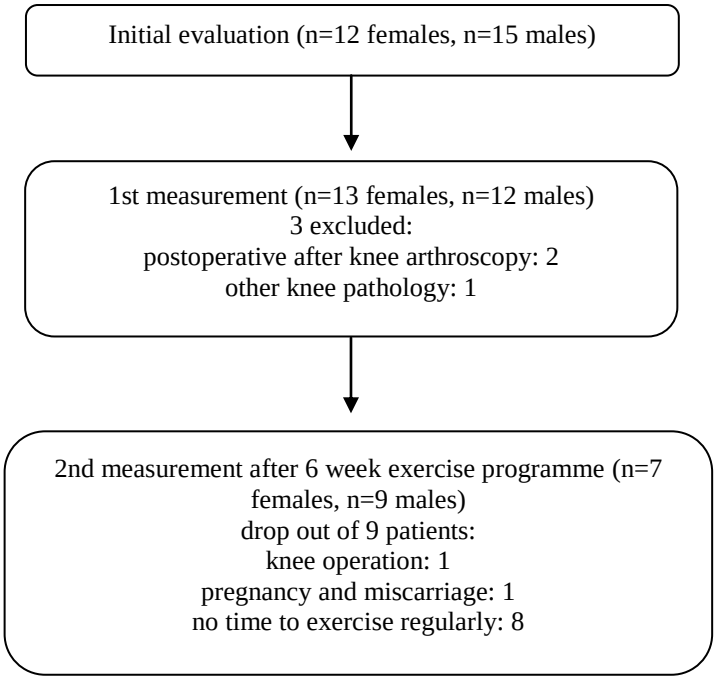

Figure 5.6: Study flow diagram

The foot posture index was on average 4.0± 0.63. However, three individuals with PFP had a foot posture index above 6. The participants running speed before and after the exercise treatment was not significantly different (p= 0.717, before the treatment: 3.42 m/s ±0.12 m/s, after the treatment: 3.43 m/s ±0.12 m/s).

Function was assessed by using the KUJALA and the KOOS and improved significantly in patients with PFP after the 6-week intervention programme. The KUJALA score is a 100-point patient-reported outcome that measures 13 domains of knee function. A low score suggests knee dysfunction and a higher score indicated no disability (Bolgla, Earl-Boehm, Emery, Hamstra-Wright, & Ferber, 2016). The KUJALA improved by 10.06 points (p=0.003) and the KOOS by 16.25 points (p=0.0001) (Table 5.1). Both improvements had large effect sizes. To investigate how patients improved with a lower KUJALA score, all patients that a KUJALA score lower than 70 were compared separately before and after the treatment. These patients improved by 21.33 points with a large effect size of 2.87 (KUJALA score before the treatment: 68.33, after the treatment: 89.67).

Furthermore, function was assessed by using the KOOS. The KOOS is a knee-specific instrument, which assessed the patients' opinion about their knee associated disability and

consisted of 42 items in 5 separately scored subscales (Roos & Lohmander, 2003). Patients with PFP improved after the exercise programme by 16.26 points, which represents an improvement of 22.1%. The KOOS is structured into five separately scored subscales: Pain, other symptoms, function in daily living (ADL), function in sports and recreation (Sport/ Rec), and knee-related Quality of Life (QOL). The changes in all 5 subscales were significant and presented a meaningful difference (KOOS-working-group, 2012). The subscales of pain, symptoms and ADL improved on average between 8 to 13 points and thus resulted in an improvement of 10.2 to 16.5%. The subscales of Sport/ Rec and QOL increased by 23.4 and 25.7 points and thereby improved on average by 40% (Table 5.1). The changes in all subscales of the KOOS had large effect sizes, ranging from 071 to 1.79.

The Tampa scale of kinesiophobia, is an instrument that has been developed to measure the fear of movement related to pain (Hapidou, O'Brien, Pierrynowski, de Las Heras, Patel, & Patla, 2012; Neblett, Hartzell, Mayer, Bradford, & Gatchel, 2016). In this study, patients showed a reduced kinesiophobia of 3.44 points ($p=0.021$) after the treatment with a moderate effect size (Table 5.1). However, the overall Tampa score was mild to moderate in the recruited group (Neblett et al., 2016). To investigate how patients improved with a mild, moderate and severe kinesiophobia, patients with a mild kinesiophobia ($\leq$ 32 points), moderate kinesiophobia (33-42 points) and severe kinesiophobia ($\geq$ 43 points) were compared separately within their groups. It could be shown that patients with a mild kinesiophobia improved by 1.83 points, with a moderate kinesiophobia by 4.11 points and one patient with a severe kinesiophobia improved by 12 points (Table 5.1). The changes of the subgroups showed large effect sizes.

The patients recorded on the numeric pain rating scale their pain level before the study on average 0.88. After the study no patient reported any pain anymore (NPRS: 0) (Table 5.1). Since the baseline pain was very low, the pain change was not significantly different after the exercise-programme ($p=0.068$). However, despite no significant difference the change in pain the effect size for the change in pain was large. Furthermore, the pain-subscale of the KOOS significantly improved from 79.7 points before the intervention to 92.88 points after the 6-week exercise treatment with a large effect size ($p=0.001$) (Table 5.1).

The lower limb biomechanics during the stance phase in running did not significantly change after the exercise intervention (Table 5.2 & 5.3). In contrast, the lower limb biomechanics during the single leg squat and the step down task were modified after the 6-week exercise programme (Table 5.4 & 5.5). The patients squatted deeper after the 6-week intervention

programme and flexed his/her hips 10.0° (p=0.004) and his/her knees 8.4° more (p=0.023) (Table 5.4, Figure 5.7& 5.8). The changes in knee and hip flexion angle showed moderate effect sizes. Furthermore, the hip flexor and knee internal rotation moment increased significantly with moderate effect sizes (p=0.003, p=0.008) (Table 5.5, Figure 5.10 & 5.11). Also the step down task was performed with a significantly increased knee flexion angle after the exercise programme, with only a small effect size (5.6°, p=0.011) (Table 5.4, Figure 5.9). The changes during the step down task did not result in modified lower limb kinetics (Table 5.5).

The quadriceps strength was not significantly different after the 6-week exercise programme (isometric: p=0.570, concentric: p=0.064, eccentric: p=0.594). However, the concentric strength showed the tendency to increase with a moderate effect size. When the groups were divided into females and males the tendency of an increase in isometric strength could be observed with moderate to large effect sizes. However, the eccentric quadriceps strength showed the tendency to decrease with small effect sizes (Table 5.1). The rate to force development and time to peak were not significantly modified (p-value: RTF development: 0.394, time to peak: 0.112). The break phenomenon was present in 4 out of 16 participants before the treatment and in only 3 after the treatment. However, the change was not significant (p=1.0). Although the quadriceps AMI was not significantly changed (p-value: 0.096), the inhibition decreased by 5.3% after the 6-week exercise programme with a large effect size (Table 5.1).

The flexibility of the hamstrings muscles increased significantly after the exercise treatment with a large effect size (decreased knee flexion of 6.1°, p=0.014) (Table5.1). The flexibility of the quadriceps muscle increased. Although, the change was not significant (p=0.087), the effect size was moderate. The range of motion (ROM) of the dorsi-flexion increased significantly by 1.16 cm (p=0.024). However, the ROM measured in degrees was not significantly increased (p=0.058, increase by 2.8°) and the effect sizes were small to moderate (Table 5.1).

The net-activation of the knee extensors increased significantly during the early stance phase in running after the 6-week exercise programme with a moderate effect size (p=0.019).

The averaged knee angular velocity during the eccentric quadriceps tasks was not significantly different after the 6-week exercise treatment (p-value: single leg squat: 0.211, step down task: 0.82).

And lastly, the balance was measured by using the star excursion balance test (SEBT) and the reach distance was normalised to the leg length of each participant. The SEBT showed an increased reach distance of 4.46 cm after the 6-week exercise intervention with a large effect size (p=0.008) (Table 5.1).

*Table 5.1: The lower extremity kinetics during the single leg squat task and the step down task (*indicated the results were significantly different.)*

		Before the exercise treatment			After the exercise treatment			P value: (T-test, sig 2-tailed)	Effect size
		Mean	SD	Std. Error Mean	Mean	SD	Std. Error Mean		
Strength (Nm/kg)0.28	Quadriceps isometric torque	2.92	0.65	0.16	2.91	0.57	0.15	0.570	0.02
	Quadriceps concentric torque	1.78	0.59	0.15	2.08	0.39	0.10	0.064	0.60
	Quadriceps eccentric torque	3.36	1.29	0.33	3.05	0.74	0.19	0.594	0.29
Strength (Nm/kg) Females	Quadriceps isometric torque	2.62	0.56	0.21	2.6	0.45	0.17	1.000	0.04
	Quadriceps concentric torque	1.46	0.52	0.2	1.85	0.21	0.08	0.063	0.98
	Quadriceps eccentric torque	2.78	0.56	0.21	2.6	0.49	0.18	6.12	0.34
Strength (Nm/kg) Males	Quadriceps isometric torque	3.15	0.64	0.21	3.18	0.54	0.19	0.484	0.05
	Quadriceps concentric torque	2.05	0.52	0.19	2.27	0.41	0.14	0.237	0.47
	Quadriceps eccentric torque	3.87	1.56	0.55	3.44	0.73	0.26	0.735	0.35
Time to peak (ms)		0.74	0.40	0.10	0.82	0.24	0.06	0.112	0.24
Rate to force development (torque/ms)		283.06	141.10	36.43	247.81	112.54	29.06	0.394	0.28
Quadriceps AMI in %		13.04	10.84	2.80	7.72	5.66	1.46	0.096	0.62
Pain	numeric pain rating scale	0.88	0.46	1.82	0	0	0	0.068	2.71
	KOOS pain	79.70	11.19	2.80	92.88	8.42	2.11	0.001*	1.33
Tampa scale: all results		32.63	6.34	1.59	29.19	7.70	1.93	0.021*	0.46
Tampa: mild kinesiophobia (≤ 32 points)		25.5	2.07	0.85	23.67	1.51	0.61	0.176	1.01
Tampa: moderate kinesiophobia (33-42 points)		36.11	2.20	0.73	40.22	1.39	7.13	0.593	2.23
Tampa: severe kinesiophobia (≥43 points)		44	-	-	32	-	-	-	
Balance in cm/leg length		90.21	5.62	1.45	94.67	6.94	1.79	0.008*	0.71
Function	KUJALA scale	81.69	9.23	2.31	91.75	7.23	1.81	0.003*	1.21
	KUJALA scale (≤ 70 points)	68.33	0.58	0.33	89.67	10.50	6.06	0.11	2.87
	KOOS sum	73.50	10.54	2.63	89.76	8.89	2.22	0.0001*	1.67
	KOOS symptoms	79.62	13.11	3.28	87.72	9.40	2.35	0.059	0.71
	KOOS ADL	87.08	12.91	3.23	96.34	6.46	1.61	0.016*	0.91
	KOOS Sport/ Rec	65.31	16.88	4.22	91.00	11.25	2.81	0.0001*	1.79
	KOOS QOL	57.42	17.26	4.32	80.86	18.88	4.72	0.004*	1.30
Flexibility	Ankle ROM in cm	12.60	3.03	0.78	13.73	3.46	0.89	0.024*	0.35
	Ankle ROM in degrees	50.3	5.0	1.3	47.5	6.3	1.6	0.058	0.49
	Quadriceps flexibility in degrees	106.0	16.9	4.4	113.3	13.2	3.4	0.089	0.48
	Hamstrings flexibility in degrees	154.4	8.4	2.2	160.3	8.1	2.0	0.015*	0.72

*Table 5.2: The lower extremity kinematics during the stance phase in running (*indicated the results were significantly different.)*

The kinematic variables (º) during stance phase		Before the exercise treatment			After the exercise treatment			P value: (T-test, sig 2-tailed)	Effect size
		Mean	SD	Std. Error Mean	Mean	SD	Std. Error Mean		
Early stance phase	Hip flexion angle	35.1	6.5	1.7	34.2	5.9	1.5	0.427	0.15
	Hip adduction angle	5.9	5.0	1.3	6.4	3.8	1.0	0.609	0.11
	Hip internal rotation angle	4.5	7.2	1.9	3.4	7.0	1.8	0.910	0.15
	Knee flexion angle	32.1	3.5	0.9	30.8	2.9	0.8	0.173	0.40
	Knee adduction angle	3.6	3.7	1.0	3.0	3.3	0.9	0.691	0.17
	Knee internal rotation angle	-4.5	4.8	1.3	-4.4	6.2	1.6	0.955	0.02
Mid-stance phase	Hip flexion angle	35.1	6.8	1.8	33.6	6.2	1.6	0.233	0.23
	Hip adduction angle	8.6	5.2	1.3	9.9	5.4	1.4	0.570	0.25
	Hip internal rotation angle	0.7	8.6	2.2	-0.8	8.1	2.1	0.570	0.18
	Knee flexion angle	45.3	4.4	1.1	43.2	5.7	1.5	0.125	0.41
	Knee adduction angle	2.9	3.6	0.9	2.0	3.2	0.8	0.609	0.26
	Knee internal rotation angle	0.9	4.8	1.2	2.3	5.9	1.5	0.256	0.26
Late-stance phase	Hip flexion angle	20.8	6.4	1.7	19.4	5.6	1.4	0.233	0.23
	Hip adduction angle	5.7	4.7	1.2	6.2	4.7	1.2	0.394	0.11
	Hip internal rotation angle	1.7	8.4	2.2	-0.2	7.9	2.0	0.233	0.23
	Knee flexion angle	42.0	4.7	1.2	40.8	4.5	1.2	0.334	0.26
	Knee adduction angle	2.2	3.4	0.9	1.6	2.5	0.6	0.609	0.20
	Knee internal rotation angle	0.3	3.9	1.1	0.8	6.2	1.6	0.433	0.10

*Table 5.3: The lower extremity kinetics during stance phase in running (*indicated the results were significantly different.*

The kinematic variables (º) during stance phase		Before the exercise treatment			After the exercise treatment			P value: (T-test, sig 2-tailed)	Effect size
		Mean	SD	Std. Error Mean	Mean	SD	Std. Error Mean		
Early stance phase	Hip flexion moment	1.92	0.43	0.11	1.85	0.47	0.12	0.776	0.16
	Hip adduction moment	1.23	0.36	0.09	1.28	0.35	0.09	0.460	0.14
	Hip internal rotation moment	0.06	0.09	0.02	0.09	0.15	0.04	0.532	0.24
	Knee flexion moment	1.52	0.31	0.08	1.40	0.18	0.05	0.125	0.47
	Knee adduction moment	0.58	0.27	0.07	0.54	0.25	0.06	0.334	0.16
	Knee internal rotation moment	0.25	0.11	0.03	0.24	0.07	0.02	0.496	0.11
Mid-stance phase	Hip flexion moment	0.74	0.52	0.13	0.82	0.35	0.09	0.820	0.18
	Hip adduction moment	1.87	0.39	0.10	1.92	0.34	0.09	0.691	0.14
	Hip internal rotation moment	-0.27	0.21	0.05	-0.25	0.18	0.05	0.281	0.10
	Knee flexion moment	2.64	0.63	0.16	2.80	0.49	0.13	0.460	0.28
	Knee adduction moment	0.54	0.25	0.06	0.57	0.25	0.07	0.865	0.12
	Knee internal rotation moment	0.44	0.13	0.03	0.45	0.13	0.03	0.776	0.08
Late-stance phase	Hip flexion moment	-0.08	0.24	0.06	-0.12	0.22	0.06	0.570	0.17
	Hip adduction moment	1.37	0.45	0.12	1.41	0.31	0.08	0.570	0.10
	Hip internal rotation moment	0.02	0.03	0.01	0.03	0.04	0.01	0.532	0.28
	Knee flexion moment	1.80	0.49	0.13	1.98	0.34	0.09	0.233	0.43
	Knee adduction moment	0.36	0.19	0.05	0.38	0.22	0.06	0.532	0.10
	Knee internal rotation moment	0.24	0.11	0.03	0.27	0.11	0.03	0.460	0.27

*Table 5.4: The lower extremity kinematics during the single leg squat task and the step down task (*indicated the results were significantly different.)*

The kinematic variables (º) during the single leg squat and step down task		Before the exercise treatment			After the exercise treatment			P value: (T-test, sig 2-tailed)	Effect size
		Mean	SD	Std. Error Mean	Mean	SD	Std. Error Mean		
Single leg squat	Hip flexion angle	72.2	19.6	5.1	82.5	15.8	4.1	0.004*	0.58
	Hip adduction angle	15.1	7.1	1.8	15.4	6.0	1.5	1.000	0.05
	Hip internal rotation angle	4.0	6.9	1.8	1.0	7.4	1.9	0.100	0.42
	Knee flexion angle	81.8	9.9	2.5	88.4	11.4	2.9	0.023*	0.62
	Knee adduction angle	6.3	4.6	1.2	5.6	3.7	1.0	0.609	0.17
	Knee internal rotation angle	-2.1	5.4	1.4	-0.3	5.4	1.4	0.496	0.33
	Knee angular velocity (°/sec.)	-35.9	9.9	2.2	-35.3	13.6	2.8	0.211	0.05
Step down task	Hip flexion angle	70.4	20.6	5.3	77.4	16.8	4.3	0.061	0.37
	Hip adduction angle	15.6	7.3	1.9	17.0	5.3	1.4	0.088	0.22
	Hip internal rotation angle	4.1	6.0	1.5	1.2	6.9	1.8	0.191	0.45
	Knee flexion angle	89.8	13.9	3.6	95.4	11.4	2.9	0.011*	0.44
	Knee adduction angle	6.9	4.2	1.1	5.7	3.7	0.9	0.532	0.30
	Knee internal rotation angle	-0.5	5.4	1.4	1.3	5.6	1.4	0.233	0.33
	Knee angular velocity (°/sec.)	-35.8	14.1	3.7	-35.7	10.6	2.7	0.820	0.01

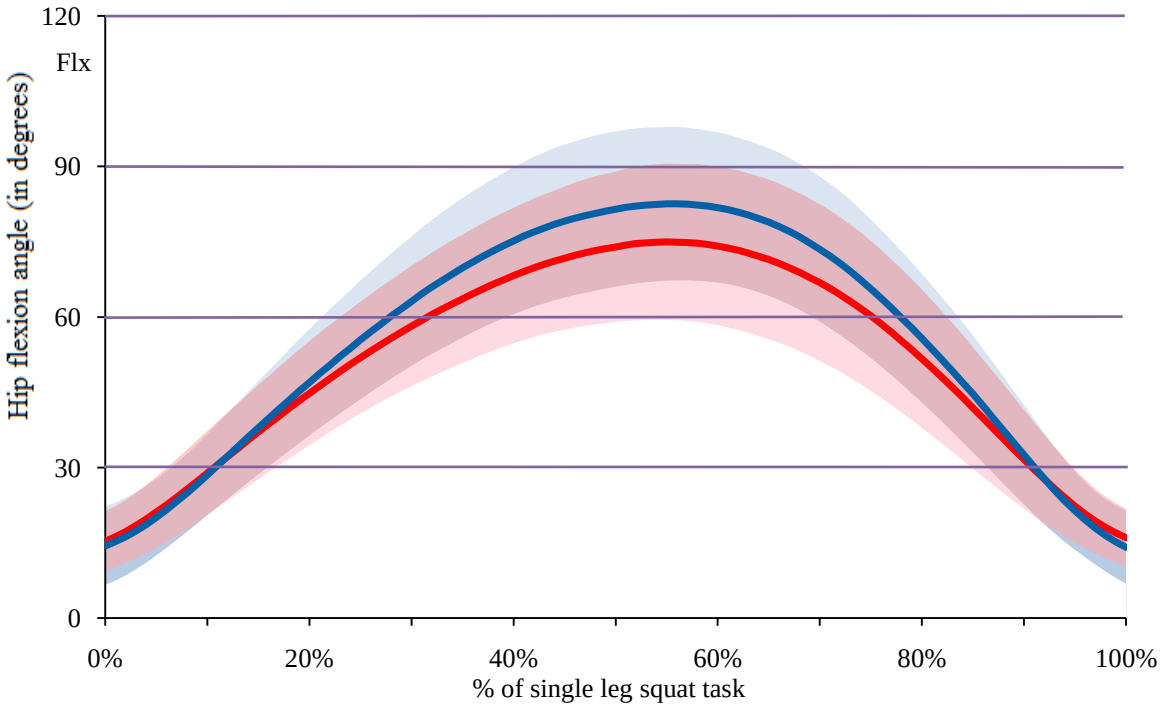

Figure 5.7: The sagittal plane hip angle during the single leg squat task under 2 conditions: before (red) and after (blue) the 6-week exercise treatment. The shaded areas represent ±1SD for each condition, internal rotation as the positive angle.

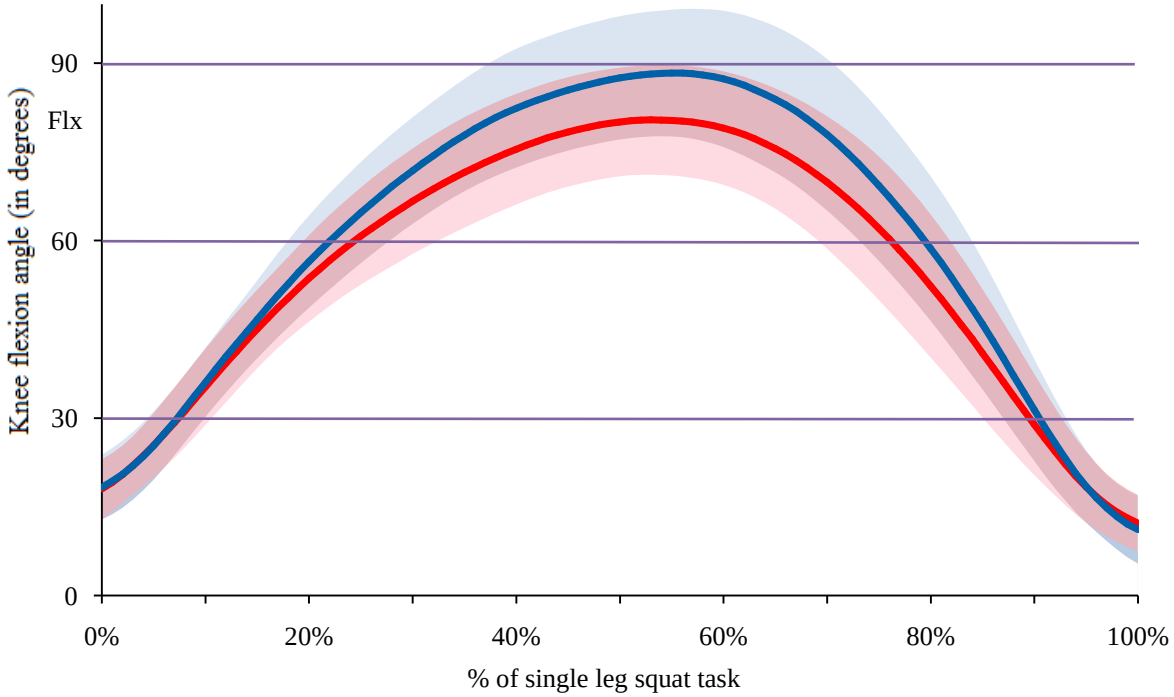

Figure 5.8: The sagittal plane knee angle during the single leg squat task under 2 conditions: before (red) and after (blue) the 6-week exercise treatment. The shaded areas represent ±1SD for each condition, internal rotation as the positive angle.

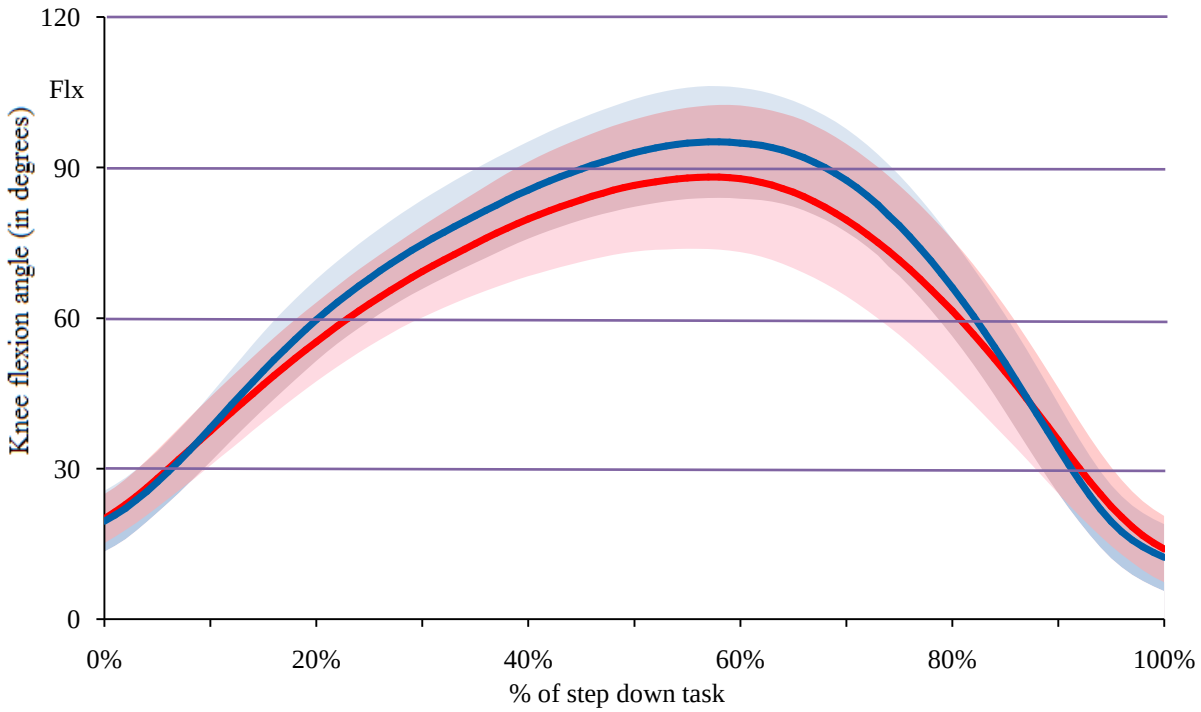

Figure 5.9: The sagittal plane knee angle during the step down task under 2 conditions: before (red) and after (blue) the 6-week exercise treatment. The shaded areas represent ±1SD for each condition, internal rotation as the positive angle.

*Table 5.5: The lower extremity kinetics during the single leg squat task and the step down task (*indicated the results were significantly different.)*

The kinetic variables (Nm/kg) during the single leg squat and step down task		Before the exercise treatment			After the exercise treatment			P value: (T-test, sig 2-tailed)	Effect size
		Mean	SD	Std. Error Mean	Mean	SD	Std. Error Mean		
Single leg squat	Hip flexion moment	1.07	0.64	0.16	1.37	0.56	0.01	0.003*	0.50
	Hip adduction moment	0.95	0.29	0.07	0.95	0.16	0.16	0.156	0
	Hip internal rotation moment	-0.13	0.06	0.02	-0.11	0.08	0.36	0.363	0.28
	Knee flexion moment	1.82	0.44	0.11	1.82	0.23	0.19	0.191	0
	Knee adduction moment	0.35	0.11	0.03	0.37	0.13	0.11	0.112	0.17
	Knee internal rotation moment	0.39	0.09	0.02	0.43	0.08	0.01	0.008*	0.47
	Hip flexion moment	1.31	0.80	0.21	1.46	0.70	0.36	0.363	0.20
Step down task	Hip adduction moment	1.12	0.31	0.08	1.05	0.35	0.14	0.140	0.21
	Hip internal rotation moment	-0.08	0.07	0.02	-0.06	0.08	0.11	0.112	0.27
	Knee flexion moment	1.82	0.36	0.09	1.61	0.50	0.46	0.460	0.48
	Knee adduction moment	0.43	0.17	0.04	0.34	0.13	0.53	0.532	0.59
	Knee internal rotation moment	0.41	0.09	0.02	0.41	0.14	0.21	0.211	0
	Hip flexion moment	1.07	0.64	0.16	1.37	0.56	0.01	0.003*	0.50
	Hip adduction moment	0.95	0.29	0.07	0.95	0.16	0.16	0.156	0

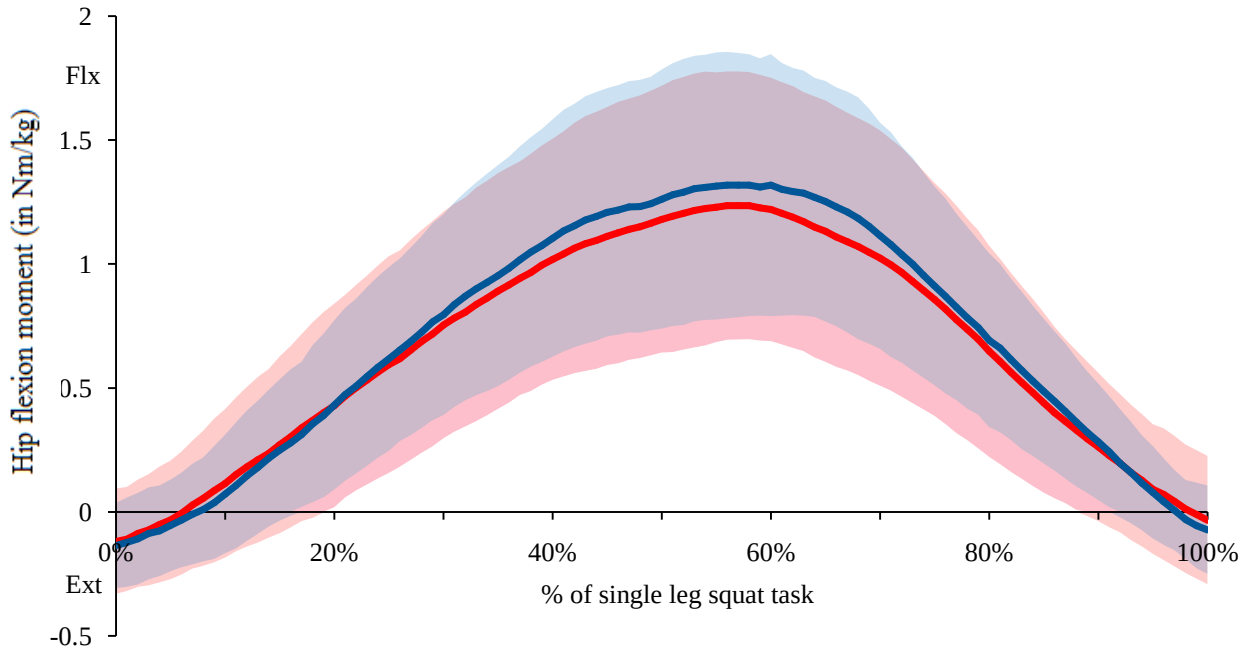

Figure 5.10: The sagittal plane hip moment during the single leg squat under 2 conditions: before (red) and after (blue) the 6-week exercise treatment. The shaded areas represent ±1SD for each condition, internal rotation as the positive angle.

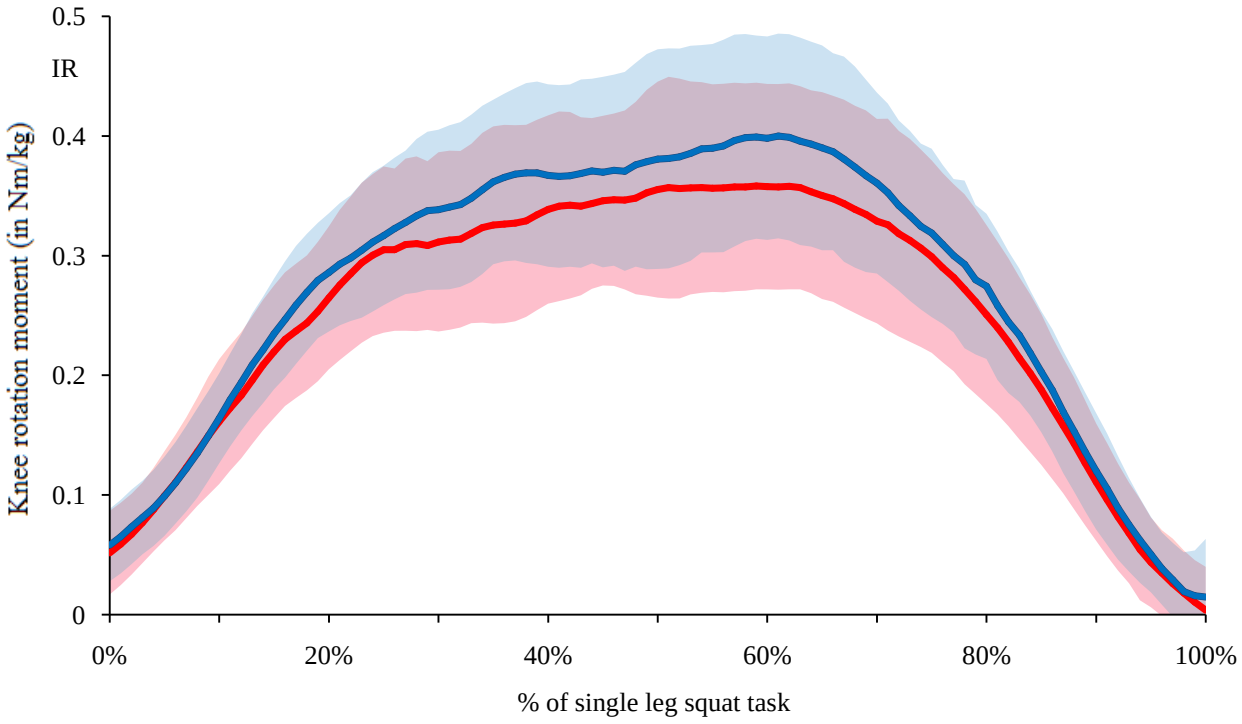

Figure 5.11: The transverse plane knee moment during the single leg squat under 2 conditions: before (red) and after (blue) the 6-week exercise treatment. The shaded areas represent ±1SD for each condition, internal rotation as the positive angle.

*Table 5.6: Co-contraction ratio, net activation of the knee flexors and knee extensors during the stance phase in running, the single leg squat task and the step down task with and without acute pain (*indicated the results were significantly different.)*

		Before the exercise treatment			After the exercise treatment			P value: (T-test, sig 2-tailed)	Effect size
		Mean	SD	Std. Error Mean	Mean	SD	Std. Error Mean		
Early stance phase	Co-contraction ratio	0.53	0.62	0.17	0.71	0.08	0.02	0.814	0.41
	Net activation knee extensors in %	**137.22**	**54.00**	**14.98**	**166.57**	**75.80**	**20.26**	**0.019***	**0.45**
	Net activation knee flexors in %	40.31	37.31	10.35	47.14	23.70	6.33	0.084	0.22
Mid-stance phase	Co-contraction ratio	0.30	0.33	0.09	0.30	0.30	0.08	0.272	0
	Net activation knee extensors in %	75.01	35.78	9.92	89.56	46.56	12.44	0.060	0.35
	Net activation knee flexors in %	48.35	27.76	7.70	52.88	20.72	5.54	0.272	0.18
Late-stance phase	Co-contraction ratio	-0.24	0.15	0.56	-0.44	0.09	0.34	0.084	1.62
	Net activation knee extensors in %	9.00	2.08	7.50	7.54	1.21	4.51	0.695	0.86
	Net activation knee flexors in %	15.75	3.04	10.96	18.75	3.41	12.77	0.239	0.93
Single leg squat	Co-contraction ratio	0.68	0.21	0.06	0.68	0.16	0.04	0.272	0
	Net activation knee extensors in %	104.69	36.86	10.22	109.10	42.37	11.32	0.638	0.11
	Net activation knee flexors in %	31.06	14.66	4.07	32.70	13.38	3.58	0.638	0.12
Step down task	Co-contraction ratio	0.62	0.24	0.07	0.63	0.19	0.05	0.433	0.05
	Net activation knee extensors in %	102.75	35.11	9.38	103.91	41.53	11.10	0.311	0.03
	Net activation knee flexors in %	36.36	17.78	4.93	35.01	15.43	4.13	0.875	0.08

5.5. Discussion and conclusion

This study showed that individuals with PFP improved in function and showed reduced pain after the 6-week exercise treatment. Thus, the first null-hypothesis was rejected. The second hypothesis suggesting that the 6-week exercise programme would not modify the lower limb biomechanics was rejected for the single leg squat and step down task and accepted for the stance phase in running. The third hypothesis suggesting that the exercise programme would not increase muscle flexibility was rejected and the fourth hypothesis suggesting that the treatment would result in increased quadriceps strength was accepted.

Individuals with PFP showed a significantly improved function after the 6-week exercise programme. Function in this study was assessed using the KUJALA score and the KOOS. In this study, patients with PFP showed an improved KUJALA score of 10.06 points after the exercise programme. It has been previously reported that a clinically meaningful difference in the KUJALA score should be 14 points and thus it is not clear whether the change is clinically meaningful (Watson et al., 2005). That the patients improved only by 10 points in this study might also be caused by the relatively high KUJALA score before the exercise treatment. Thus, to investigate how patients with more pain and less function improved, patients with a KUJALA score below 70 were analysed separately and it could be shown that they improved by 21.33points.

Function had been additionally assessed with the KOOS, a knee-specific instrument (Roos & Lohmander, 2003). Patients with PFP improved after the exercise programme by 16.26 points, which represents an improvement of 22.1%. The meaningful difference of the KOOS is reflected by a change of the score between 8- 10 points improvement (Roos & Lohmander, 2003). Thus, the result of this study shows a clinically meaningful improvement of function. The KOOS is structured into five separately scored subscales: Pain, other symptoms, function in daily living (ADL), function in sports and recreation (Sport/ Rec) and knee-related Quality of Life (QOL). The changes in all 5 subscales were significant and presented a meaningful difference (KOOS-working-group, 2012). The subscales of pain, symptoms and ADL improved on average between 8 to 13 points and thus resulted in an improvement of 10.2 to 16.5%. The subscales of Sport/ Rec and QOL increased by 23.4 and 25.7 points and thereby improved on average by 40%. Thus, the exercise programme seemed to have especially a positive impact on function in sports and quality of life in the patients with PFP.

The Tampa scale showed a significant reduction of kinesiophobia by 3.44 points after the exercise treatment (p=0.021). However, the overall Tampa score was mild to moderate in the recruited group (Neblett et al., 2016). Thus, the subgroups mild, moderate and severe kinesiophobia were investigated independently. These results showed that the greater the kinesiophobia before the exercise programme, the more patients improved in kinesiophobia after the exercise programme. However, the sample size of this study was too small to draw conclusions from this analysis, but it revealed the potential of the exercise treatment to improve kinesiophobia in patients with a moderate and severe kinesiophobia. Previous studies reported that a change of 5.5 points should be reported to define a clinical meaningful difference for the Tampa Scale of Kinesiophobia (Monticone, Ambrosini, Rocca, Foti, & Ferrante, 2016). The groups with mild and moderate kinesiophobia showed no change of 5.5 points and thus despite the tendency of an improved kinesiophobia, it should be critically questioned whether these differences are clinical meaningful.

Pain was assessed with the numerical pain rating scale and did not improve significantly. However, the patients had very low pain scores to begin (0.88± 0.46 on the numeric pain rating scale (NPRS) and thus only little room for improvement (p=0.068). Although, pain did not significantly improve no patient reported pain after the 6-week intervention treatment (0 ± 0 on the NPRS). Furthermore, the pain assessed with the KUJALA and the KOOS subscale improved significantly (KUJALA: p=0.003 and KOOS pain subscale: p=0.001). The large improvements in function and pain are strong clinical indicators of the effectiveness of the 6-week exercise programme in individuals with PFP. Thus, the first null-hypothesis suggesting that the exercise programme would not result in decreased pain and improved function was rejected.

The biomechanical outcomes were more heterogeneous than the findings on function and pain. During the stance phase in running no changes of the lower limb kinematics and kinetics could be observed after the 6-week exercise treatment. However, the single leg squat as well as the step down task were significantly modified. The patients with PFP were able to squat deeper (10° increased hip and 8.4° increased knee flexion) and to reach lower during the step down task (5.6° increased knee flexion). In addition, the internal hip flexor moment significantly increased which might indicate an increased activity of the hip stabilising gluteal muscles, resulting from the gluteal muscle strengthening. However, an increased hip flexor moment might also be linked to an increased trunk flexion, which moved the line of gravity closer to the knee and away from the hip thereby decreasing the knee flexor moment and increasing the hip

flexor moment (Salem, Salinas, & Harding, 2003). This might explain why the knee flexor moment was not significantly increased despite the significantly increased knee flexion angle. In addition, the hip flexion angle was increased which supports the assumption of an increased trunk flexion. However, the biomechanical model that was used did not describe the trunk movement and thus this assumption cannot be proven. Another explanation for an unchanged knee flexor moment might be a compensatory mechanism of the hip flexor moment. One study described this compensatory strategy in individuals with PFP during stair descending (Salsich et al., 2001). Here the elevated hip flexor moment maintains a consistent support and thereby compensates for the less active knee extensors muscle (Salsich et al., 2001). The sEMG analysis showed no increased quadriceps net activation after the 6-week exercise, which either might confirm the presumption of a compensatory strategy or might confirm the hypothesis of an increased trunk flexion.

In addition, the knee internal rotation moment was significantly increased. Such an increase of the knee external rotation has been associated with an increased trunk flexion, as well as an increased supination (Frank et al., 2013; Williams, Zambardino, & Banning, 2008). Not much literature in individuals with PFP has been published on the rotational moments of the knee. However, an increased knee external rotation angle has been associated with an increased dynamic knee valgus and the development of PFP and ACL ruptures (Schwane et al., 2015; Shimokochi & Shultz, 2008). Thus, an increased knee internal rotation moment might also indicate a shift towards a decreased dynamic knee valgus in PFP.

Although the patients flexed their hips on average 7° and their knees 5.6° more during the step down task after the 6-week exercise treatment, no changes in the hip or knee kinetics could be observed. However, the hip flexion moment showed the tendency to be increased and the knee flexion moment showed a tendency for a decrease, which suggests a similar movement modification as described during the single leg squat. However, based on the results of the reliability study of Alenezi et al. (2014) and the results in chapter 3.7 the MDDs for hip and knee flexion angle are reported to range from 4.1 to 5.4 degrees. Thus, it should be critically questioned if these changes between 5.6 and 7° are clinically significant. In addition, no changes could be identified during the stance phase in running. Thus, the second hypothesis suggesting that the 6-week exercise programme would not modify the lower limb biomechanics was accepted (Tables 5.1 to 5.5).

Flexibility of the ankle ROM, the quadriceps and the hamstrings muscles were assessed before and after the exercise programme. The exercise programme included flexibility exercises to increase the ankle dorsi-flexion ROM and the hamstrings flexibility. It could be shown that ankle ROM, as well as hamstrings flexibility significantly increased. However, the ankle ROM should be interpreted with caution. The minimal detectable difference (MDD) of the distance-to-wall has been reported ranging from 1.1 to 2.2 cm (Calatayud, Martin, Gargallo, Garcia-Redondo, Colado, & Marin, 2015; Konor et al., 2012). Thus, the observed distance-to-wall of 1.13 cm might not describe a clinically meaningful change. The change in the degrees of dorsi-flexion ROM, assessed with the goniometer, was 2.81° ($p=0.058$). The MDD of the dorsi-flexion angle ranged between 3.7 to 7.7° (Konor et al., 2012). Thus the dorsi-flexion angle seemed to not only be statistically not significant, but also not clinically meaningful. Although it is not clear whether the change in ankle dorsi-flexion ROM represents a clinically meaningful result, it indicated the tendency of an improvement in dorsi-flexion ROM. The flexibility of the hamstrings improved by 5.7° ($p=0.015$). However, the MDD has been reported between 8.3° and 15°, thus it is questionable if a difference of 6° is clinically meaningful. The quadriceps flexibility did not improve ($p=0.089$). This was expected since the exercise programme did not include exercises to increase the quadriceps ROM. However, future research is needed to further investigate the effect of the exercise programme on muscle flexibility and ankle ROM. In summary, although the clinically meaningfulness should be critically discussed, the flexibility of the ankle dorsi-flexion as well as the hamstrings muscle was increased Thus, the third hypothesis suggesting that the exercise programme would not increase muscle flexibility was rejected.

The exercise programme consisted of four strengthening exercises, whereby three of the four exercises focussed on quadriceps strengthening. To analyse if the quadriceps strength improved the isometric, concentric and eccentric quadriceps torque were measured before and after the intervention. In addition, the time to peak and the rate to force development (RFD) were calculated. None of the strength values of the quadriceps was significantly modified after the exercise treatment and thus, the fourth hypothesis suggesting that the treatment would result in an increased quadriceps strength was accepted.

However, some of the findings in this study are surprising, such as that no improvement of the quadriceps strength were achieved, despite an evidence-based strengthening programme. Secondly, it was surprising that no kinematic or kinetic changes of the sagittal and transverse

plane of the hip and the sagittal plane of the knee after the intervention programme were detected. Thus, these findings will be discussed in the following paragraph in more detail.

To date, guidelines on exercise trainings for individuals with PFP are still lacking. However, the exercise treatment in this study has been developed based on the current guidelines and previous exercise treatments. Previous studies that focussed on gluteal and quadriceps strengthening in individuals with PFP performed the exercises with 10-15 repetitions in 3 sets at 60-70% 1 repetition maximum (1RM), which has been applied in this study as well (Bisi-Balogun & Torlak, 2016; Ramazzina, Pogliacomi, Bertuletti, & Costantino, 2016; Rathleff et al., 2016; Santos, Oliveira, Ocarino, Holt, & Fonseca, 2015). The decreased loads and the higher amount of repetitions compared to a traditional hypertrophy/ strength training are chosen to reduce the flare up of symptoms. However, such a strength endurance programme has shown to increase muscle endurance and muscle power, but only increased slightly muscle strength (American College of Sports Medicine, 2011). That previous exercise trainings in individuals with PFP were still successful in increasing significantly muscle strength might be related to the training status and quadriceps strength of the recruited individuals. The isometric quadriceps strength of the individuals with PFP in this study was on average before the treatment 2.92± 0.65 Nm/kg. Compared to individuals with PFP in previous studies, the individuals with PFP in this study produced two to three times higher isometric quadriceps torque (Callaghan & Oldham, 2004b; Duffey et al., 2000; Duvigneaud et al., 2008; Dvir et al., 1990; Kaya et al., 2010; Oliveira et al., 2014; Ott et al., 2011; Powers et al., 1997; C. R. Rathleff et al., 2013; Thomee et al., 1996; Van Tiggelen, Witvrouw, Coorevits, et al., 2004; Werner, 1995). Thus, the individuals with PFP in this study appeared to be very strong and the strength endurance training was very likely not demanding enough to improve quadriceps strength. It seems that individuals with PFP require strength training and not a strength endurance training to enhance their quadriceps performance. To ensure that an increased loading does not flare up the PFP, modifications of a traditional strength training should be investigated. One study investigated the application of a blood flow restriction (BFR) training in individuals with PFP (Giles, Webster, McClelland, & Cook, 2017). The BFR training uses the application of a pneumatic cuff proximal to the target muscle during strengthening exercises to restrict arterial blood flow and venous return, causing a greater rate of muscle fatigue than normal conditions. Thereby it aims to induce muscle hypertrophy and increase strength more than the same programme without BFR (Giles et al, 2017). This study showed that a low load with BFR reduced PFP and had larger improvements in quadriceps strength, compared to a

standardies quadriceps strengthening group (Giles et al., 2017). This study showed that strong individuals with PFP were not able to improve quadriceps strength with a low-load and high repetition strength endurance training. Thus, the currently recommended exercise programmes are not in line with current strength training guidelines (American College of Sports Medicine, 2011). Furthermore, they are not appropriate in terms of increasing strength in individuals with PFP, which emphasises the need for a reconsideration of the current available exercise guidelines in strong individuals with PFP. Furthermore, it also shows the need of further studies that investigate forms of modified hypertrophy trainings in individuals with PFP.

To investigate whether the strength is related to the sex, the groups were divided into male and female. Females produced before the treatment maximal isometric quadriceps forces of: 2.62± 0.56 Nm/kg and men of: 3.15± 0.64 Nm/kg. Thus, although females were weaker than males, overall in this study the individuals with PFP produced two to three times higher isometric quadriceps torque values than previously observed in individuals with PFP (Callaghan & Oldham, 2004b; Duffey et al., 2000; Duvigneaud et al., 2008; Dvir et al., 1990; Kaya et al., 2010; Oliveira et al., 2014; Ott et al., 2011; Powers et al., 1997; C. R. Rathleff et al., 2013; Thomee et al., 1996; Van Tiggelen, Witvrouw, Coorevits, et al., 2004; Werner, 1995). Thus, the recruited individuals appeared to be a very strong patient group and it might be difficult to compare this patient group results to previously published findings. The diversity of patients with PFP emerged during the International Patellofemoral Research Retreat (Davis & Powers, 2010). Selfe et al. (2013) addressed this challenge and developed a framework of subgroups of individuals with PFP. They defined three main subgroups: 1. "Weak and tighter", 2. "Weak and pronated", 3. "strong" individuals with PFP (Selfe, Callaghan, Witvrouw, Richards, Dey, Sutton, Dixon, Martin, Stokes, Janssen, Ritchie, & Turner et al., 2013; Selfe, Janssen, Callaghan, Witvrouw, Sutton, Richards, Stokes, Martin, Dixon, Hogarth, Baltzopoulos, Ritchie, Arden, & Dey, 2016). The ‘strong’ subgroup showed the highest mean quadriceps and hip abductor strength, a flexible rectus femoris, lower BMI scores, higher levels of activity, reduced pain and improved levels of function.The ‘weak and tighter’ subgroup was characterised by a weak mean quadriceps and hip abductor strength, a reduced flexibility of the rectus femoris and the gastrocnemius and increased BMI levels. Furthermore, they showed a trend towards low physical activity and a longer duration of PFP. The ‘weak and pronated foot’ subgroup showed an increased foot pronation and patellar mobility. Furthermore, they were significantly younger at time of first assessment and had the shortest duration since the onset of their PFP (Selfe et al., 2016). The strength results of the quadriceps showed that the recruited individuals with PFP in

this study could be categorised as "strong". Selfe et al. also observed that the "strong" patients showed a trend towards less pain, higher function and better quality of life (Selfe et al., 2016). These findings could be supported by this study, because the patients showed very low pain scores in the beginning (NPRS: 0.88) and a higher KUJALA score than in previous studies on individuals with PFP (Callaghan & Oldham, 2004a; Collins, Crossley, Darnell, & Vicenzino, 2010; Kettunen, Harilainen, Sandelin, Schlenzka, Hietaniemi, Seitsalo, Malmivaara, & Kujala, 2012; Lantz, Emerson-Kavchak, Mischke, & Courtney, 2016; Petersen et al., 2016; Van Linschoten et al., 2009). However, the scores of the KOOS were similar to previous studies on individuals with PFP (Esculier, Roy, & Bouyer, 2013; Lankhorst et al., 2015; Petersen et al., 2016; C. R. Rathleff et al., 2013; Sinclair et al., 2016). That the patients were strong and did not show signs of quadriceps weakness might also be an explanation why they did not show an excessive dynamic knee valgus pattern. Excessive dynamic knee valgus pattern have been commonly observed in previous studies in individuals with PFP. The hip and knee adduction and internal rotation angles in this study were comparable to the range of motion described in studies on healthy individuals (Alenezi et al., 2014, 2016; Novacheck, 1998). In previous studies on individuals with PFP, it could be shown that individuals with PFP exhibited a greater hip adduction and internal rotation as well as tibial abduction and knee rotation (Myer et al., 2015; Nakagawa et al., 2012; Neal et al., 2016; Noehren, Pohl, et al., 2012). Thus, it seems that the recruited study group also showed a different biomechanical movement than previously described in individuals with PFP. These individuals with PFP seem to not show lower limb abnormalities, which explains why no kinematic or kinetic changes of the sagittal and transverse plane of the hip and the sagittal plane of the knee after the intervention programme were found.

The secondary outcomes in this study showed that the anterior reach distance during the SEBT was significantly increased by 4.46 cm ($p=0.008$). Previous studies reported a MDD of 6.9 cm (Munro & Herrington, 2010), 9 cm (Hyong & Kim, 2014; Plisky et al., 2009) and thus the clinically meaningfulness of the difference in this balance test could be questioned. However, the improvement in balance in this study showed a large effect size and this might be one explanation for the significant improvement in function and pain. One explanation for the increased anterior reach distance might be the increased range of ankle dorsiflexion motion after the 6 week exercise treatment. However, the effect sizes of the increased ankle ROM were only small and thus it should be critically questioned whether this might have influenced the forward reaching distance enough. Another explanation might be that the strength endurance

exercises (squatting, side walks, rotational walks, and the open kinetic chain quadriceps exercise) may have resulted in an improved neuromuscular knee control, which has been observed in previous studies (Rathleff et al., 2016; Ferber et al, 2011; Earl and Hoch, 2011). Previous studies also observed improved function and pain without alterations in biomechanics and linked the improvements to an increase in strength and neuromuscular control (Ferber et al., 2011; Bolgla et al., 2008). Furthermore, the quadriceps inhibition reduced from 13.04% before to 7.72% after the treatment. Although this change was not significant ($p=0.096$) it showed the tendency of a reduced quadriceps inhibition of 5.32% with a large effect size. The reduced quadriceps inhibition might be one explanation why individuals with PFP improved significantly in function and pain without observed improvements in strength or loer limb biomechanics. Furthermore, in chapter 6 it could be shown that an increase in pain caused also no alterations of lower limb biomechanics or strength but resulted in an increased quadriceps AMI by 6%. Thus, it seems that quadriceps AMI might be a key factor in individuals with PFP. However, to date studies investigating quadriceps AMI in individuals with PFP are rare and more research that investigates the relationship of AMI and PFP is needed.

However, further research should be performed with a greater sample size. In addition, it could be shown that the break phenomenon was present in 4 out of 16 participants before the treatment and only 3 after the treatment. The break phenomenon has been previously described as a compensatory mechanism of individuals with PFP that were intolerant to eccentric quadriceps contractions, avoided loading and increased the knee angular velocity during eccentric quadriceps activities (such as stair descending) (Anderson & Herrington, 2003). However, the patients with PFP in this study showed a good tolerance to quadriceps loading during eccentric activities and were able to deliver high quadriceps torques. Thus, it seems that the break phenomenon is not common in individuals with PFP that have a high tolerance to quadriceps loading. However, further research is required to prove these findings.

Thus, the hypothesis of the secondary outcomes was accepted for the break phenomenon, AMI, the co-contraction ratio and the net activation of the knee flexors and rejected for balance and the net-activation of the knee extensor muscles.

5.6. Limitations to the study

One great limitation of this study is the high-drop-out rate of the individuals with PFP that caused an underpowered sample size. However, in total 24 participants were included in this study and a drop-out ratio of 5-10% (a total of 2 participants) was expected. Thus, the high drop-out rate of 33.3% indicated that the exercise programme should be amended to increase compliance with the exercise programme. In future one solution could be a follow-up meeting after 3 weeks between the Principal Investigator and the patients, either by a personal treatment session or via a skype call. During this meeting the exercise programme could be discussed and the programme could be amended. Furthermore, this might also ensure that motivational support could be given to encourage a successful treatment participation. However, it was not possible to reliably document compliance with the programme. Besides compliance, other factors might have contributed to unsuccessful results, such as that patients did not increase the intensity enough or progressed adequately, individual differences in exercise response, or psychological factors.

The sample size was too small to allow an investigation of subgroups of the data. Consequently, although some results, such as the results of the Tampa Scale of Kinesiophobia or the KOOS, were further investigated by sub-classifying the groups, the sample size was too small to receive reliable results. Thus, more individuals are needed to allow an investigation into depth after of the data and to allow subgroup-classification.

Another limitation is that the individuals with PFP in this study represented a sample of very active and strong individuals with PFP. However, there is limited literature on this group of individuals with PFP and thus the results could not be compared with previous findings.

Lastly, participants were fitted with standard training shoes to control the shoe-surface interface, which might negatively influenced the comfort during running and thereby might have influenced the movement performances. Future studies should be conducted in their own training shoes.

5.7. Conclusion

The condition of PFP is not self-limiting and requires a comprehensive rehabilitation programme. Based on the current evidence and guidelines an exercise programme was developed and investigated. To date, this was the first study that investigated the influence of

an evidence-based exercise programme on pain, function, the functional performance, strength, muscle flexibility, balance and AMI in individuals with PFP.

The individuals with PFP showed a significantly improved in function and pain and were able to perform the single leg squat as well as the step down task lower. Despite the strength training the quadriceps strength did not increase, however, it emerged that the recruited individuals with PFP were stronger than in previous literature reported. The quadriceps AMI decreased by 5.3%, although this change was not significant, it did show a tendency of an improved quadriceps AMI. However, the sample size was small and thus future research is required with enough power to verify the findings of this study.

Chapter 6: How does acute pain influence functional performance, quadriceps strength and inhibition in individuals with patellofemoral pain

The previous intervention studies showed that despite relatively small or no biomechanical changes of the lower limb, the pain decreased significantly. This raised the question whether and how pain might be linked to alterations of the lower limb biomechanics, strength, and inhibition in individuals with PFP. Thus, this chapter investigated the direct influence of pain in 21 individuals with PFP on the lower limb kinematics and kinetics, quadriceps strength and inhibition, as well as quadriceps-hamstrings cocontraction.

6.1. Introduction:

Both intervention studies in individuals with PFP (chapter 4 and 5) demonstrated that pain significantly decreased, although only small or no biomechanical changes of the lower limb were achieved. These significant changes in pain raised the question of whether and how pain might be linked to lower limb biomechanics, strength, inhibition and lower limb co-contraction in individuals with PFP.

Bazett et al. (2011) described that pain "is more than a symptom and might play a role in the aetiology or progression of PFP" (Bazett-Jones, 2011). This description has been confirmed by long-term studies that showed that individuals with longer baseline pain and worse pain were more likely to develop an unfavourable outcome and a more progressive pathology (Collins et al., 2013; Rathleff et al., 2015; Wyndow et al., 2016).

Previous studies reported the link of pain in individuals with PFP and described a link to quadriceps strength deficits, gluteal strength deficits, knee stability, irregularities in the quadriceps torque curve, AMI and functional performance (Dvir & Halperin, 1992; Dvir et al., 1991; Guney et al., 2015; Hart et al., 2015; Khayambashi et al., 2012; Long-Rossi & Salsich, 2010; Nakagawa et al., 2013; Noehren, Sanchez, et al., 2012; Riddle & Stratford, 2011; Silva et al., 2015; Yilmaz et al., 2015). But all of these studies either correlated the pain intensity to specific factors or based their findings on the comparison of the pain intensity before and after a treatment. To date, no study investigated the direct influence of pain by comparing the individual's performance without pain to the individual's performance in acute pain. The only studies that investigated the influence of acute knee pain on muscular coordination, lower limb biomechanics and quadriceps AMI, were studies that analysed the effect of an artificial induced

knee pain (Henriksen, Alkjaer, Simonsen, & Bliddal, 2009; Henriksen, Alkjær, Lund, Simonsen, Graven-Nielsen, Danneskiold-Samsøe, & Bliddal, 2011; Park et al., 2016; Rice, Graven-Nielsen, Lewis, McNair, & Dalbeth, 2015; Seeley, Park, King, & Hopkins, 2013). Furthermore, one conference abstract examined the influence of fatigue and pain on kinematic changes in individuals with PFP (Bazett-Jones et al., 2015). The authors identified no changes of the lower limb kinematics following exhaustion but significant changes due to pain. However, they concluded that further research is needed to understand the relationship of pain and lower limb biomechanics (Bazett-Jones et al., 2015).

Thus, it seems that pain is linked to several factors, such as alterations of lower limb biomechanics, muscular coordination, quadriceps strength and AMI. However, to date in individuals with PFP the isolated effect of pain on these factors has not been investigated. Therefore, this study aimed to investigate the effect of acute pain on quadriceps strength and AMI, the break phenomenon, quadriceps and hamstrings co-contraction and hip and knee biomechanics in individuals with PFP.

Therefore the hypotheses of this study were:

1. H0: There would be no significant differences in knee and hip kinematics and kinetics between acute pain and no pain in individuals with PFP.
2. H0: There would be no significant differences in quadriceps AMI and strength between acute pain and no pain in individuals with PFP.
3. H0: The break phenomenon would be equally present in acute pain and no pain in individuals with PFP.
4. H0: Participants with PFP would show an equal co-contraction of the quadriceps and hamstrings muscles in acute pain and no pain in a) running, the b) step down task and the c) single leg squat task.

6.2. Methodology

The ethical application HSR 15-143 was obtained from the University of Salford Research and Governance committee on the 1st February 2016. Informed consent was obtained from each participant (Appendix B4).

Advertisements at fitness centres, gyms, climbing centres and sports clubs in Manchester and Salford were used to recruit participants with PFP.

To be included in the study a participant with PFP had to meet all of the following criteria:

1) aged 18-45 years; 2) antero- or retro-patellar pain with at least two of these activities: ascending or descending stairs or ramps, squatting, kneeling, prolonged sitting, hopping/ jumping, isometric quadriceps contraction or running 3) duration of current PFP symptoms >1 month;

The exclusion criteria were: (1) any history of previous lower limb surgery or patella instability and dislocation, (2) lower limb deformities or any history of traumatic, inflammatory or infectious pathology in the lower extremities or any internal derangements, (3) not able to perform running, squatting and the step down task during the measurement.

Suitability for the trial was first assessed by the principal investigator. Therefore the participants were asked to fill in an online survey and the responses were checked against the inclusion and exclusion criteria. If responses were unclear the participants had a telephone conversation with the principal investigator prior to the study begin. Once the inclusion criteria were met, the participant received via email an invitation letter and an information sheet about the study, as well as the informed consent form. If the participant was willed to participate, an appointment with the principal investigator at the gait laboratory measurement was arranged. Upon the arrival a clinical assessment was carried out, which involved the Clarke's test and a palpation test to investigate the pain region. The participant was asked to run 15 m, to perform a single leg squat and step down task and to show the pain location during these test and to rate his/her pain intensity using the numeric pain rating scale (NPRS).

If the participant was still suitable, he/ she was briefed through the study and he/ she was asked to sign the informed consent form and a health history questionnaire, consisting of 13 questions investigating potential risks associated with the study. Furthermore, the participant was asked to fill in the KOOS questionnaire, the KUJALA score, and the Tampa scale for kinesiophobia.

The participant changed into his/her shorts and a comfortable t-shirt and was fitted with standard running shoes (New Balance, UK). Then, the mass and height of each participant were measured.

6.2.2. Procedure

Three-dimensional motion data were collected with ten Qualisys OQUS7 cameras (Qualisys AB, Sweden) at a sampling rate of 250Hz. Three force plates (BP600900, Advanced Mechanical Technology, Inc. USA) collected force data at a sampling rate of 1500Hz. Sixteen retroflective markers were attached, with double sided hypoallergic tape to anatomical landmarks of the lower limb of the participants (Figure 6.1). Twenty-four segmental mounted markers were applied with double sided tape and bandages to the shank, thigh and feet, as described in chapter 3.4.1.2.

For the electrode placement of the EMG, the skin was shaved, abraded and cleaned with isopropyl alcohol, in accordance with the SENIAM guidelines (Figure 6.1.). The surface EMG electrodes (Noraxon Dual Electrodes, 2 cm spacing) were placed on the vastus medialis, vastus lateralis, biceps femoris and semitendinosus muscle, as described in chapter 3.4.1.3. The surface EMG data was collected through the Noraxon Telemyo system and sampled at 1500Hz. The sEMG data was synchronised to the kinematic and kinetic data.

All participants were measured at one occasion without acute pain or only very light pain and at the second occasion while the participant experienced acute PFP. The participants were asked on both occasions to rate their pain intensity using the numeric pain rating scale (NPRS) after performing the tasks. To investigate whether the application of the 3D markers and bandages modified the pain, the participant was asked to rank his/her pain intensity with and without the applied bandages and markers. Each subject was asked at both occasions to perform a static trial, to run on a 15 m walkway at his/her own selected speed, to perform a single leg squat and step down task. The running speed was controlled and reported (Brower timing lights, Draper, UT). Each task was performed until five successful trials were collected. Unsuccessful trials were ones whereby less than three markers per segment were visible, speed changes were seen during the trials, or a partial/double contact with the force platforms.

Each individual performed at both occasions three times an isometric and isokinetic knee extensor strength test. The peak isometric, eccentric and concentric torque were measured with an isokinetic dynamometer (Kin-Com, Chatanooga, USA). The isokinetic knee extensor measurements were tested at the angular velocity of 60 degrees/second (chapter 3.3.3). The muscular inhibition of the quadriceps was assessed, during a maximal isometric contraction of the quadriceps with the interpolated twitch technique, using a Digitimer High Voltage Stimulator (DS7AH Digitimer Ltd, Hertfordshire, England) (chapter 3.3.3).

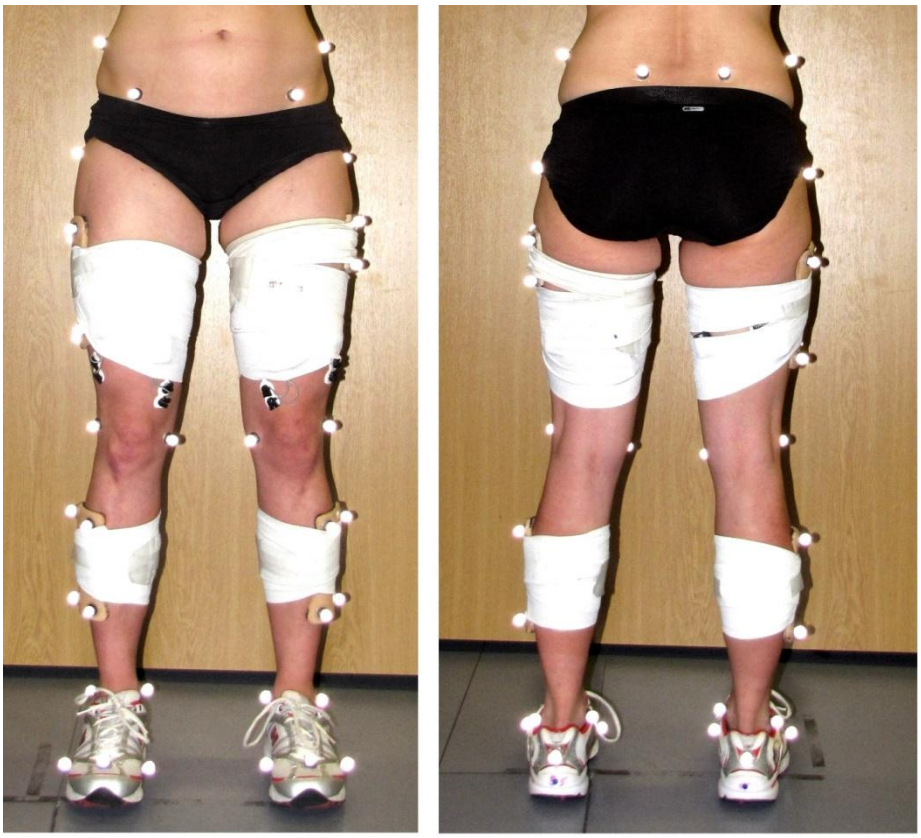

Figure 6.1.: The application of the markers and the sEMG electrodes

The participant received as a compensation for his/her participation in this study a voucher of £10 on each occasion. This voucher was exchangeable for goods in shops in Manchester and Salford.

6.2.3. Data processing

The kinematic and kinetic outcomes were calculated by utilising a 6 degrees of freedom model in Visual3D (Version 5, C-motion Inc, USA). Motion and force plate data were filtered with a 4th order Butterworth filter with cut-off frequencies of 12Hz. The joint moments were calculated using three dimensional inverse dynamics and normalised to body mass. The kinematic and kinetic data were normalised to 100% of the single leg squat, step down task and the stance phase, whereby the stance phase was sub-grouped in early (0-24% of stance phase), mid (25-62%) and late-stance phase (63%-100%) (Perry & Burnfield, 2010). The peaks of the hip and knee flexion, adduction and internal rotation angles and the moments were calculated

for the single leg squat, step down task and the early, mid and late-stance phase. Furthermore, the average knee angular velocity was calculated for the eccentric phase during the single leg squat and step down task.

The sEMG data was band-pass filtered at 20-500Hz and rectified by using a root mean square over a 75 ms window for the running task and 300 ms for the single leg squat and step down task. Co-contraction ratios were (CCR) calculated by using the formula of Heiden et al. (Heiden et al., 2009):

If agonist mean EMG > antagonistic mean EMG:

CCR= 1- antagonistic mean EMG/ agonist mean EMG

If agonist mean EMG < antagonistic mean EMG:

CCR= agonist mean EMG/ antagonistic mean EMG -1(Heiden et al., 2009)

The strength data of each participant was exported from the Kin-Com to asc-files and loaded into Excel. The peak torque was determined for each file. AMI, the time to peak and rate to force development (RFD) were determined during the isometric contraction. The break phenomenon was investigated during the eccentric quadriceps task, whereby a break was defined as a trace dip which exceeded more than 10% of the pre-break moment.

6.3. Statistical analysis

The statistical analysis was performed using SPSS (v. 20) and Excel 2013. The normality was assessed by applying the Shapiro-Wilk test and by the investigation of the normal q-q plots. For the data that was normal distributed paired sample t-tests were performed at the 95% confidence interval, to investigate whether acute pain significantly influenced the lower limb biomechanics. If the data was not normally distributed and for ordinal data (pain scale) the Wilcoxon rank test was used with a significance level set at $p<0.05$.

The peak of the hip flexion, hip adduction, hip internal rotation, knee flexion, knee adduction and knee internal rotation angles and moments, as well as the averaged knee angular velocity were compared between the two conditions: with and without acute pain.

The quadriceps isometric, concentric, and eccentric strength torque, quadriceps AMI and the break phenomenon were compared between with and without acute pain.

The co-contraction ratios during early, mid and late-stance phase, as well as the single leg squat and step down task were compared between with and without acute pain.

6.4. Results

Twenty-one individuals with PFP (11 males and 10 females, age: 29.76 ±6.36 years, height: 1.74 ± 0.09 m, mass: 70.12 ±8.56kg) participated in the study.

Pain was significantly increased when participants performed the tasks with acute pain (with and without pain: p=0.0001) (without acute pain: without the marker and bandage application: 1.29±1.95; with the marker and bandage application: 1.17±1.95, in acute pain: without the marker and bandage application: 3.88±1.92; with the marker and bandage application: 3.86±1.96). The marker and bandage application did not modify the pain significantly (without pain: p=0.598, with acute pain: p=0.864). A clinically significant change in pain has been described as 1.74, thus the pain increase by 3.0 represents a clinical meaningful increase in pain (Farrar, Young, LaMoreaux, Werth, & Poole, 2001).

The running speed without and with pain was not significantly different (p=0.608) (without pain: 3.32±0.71 m/s, with pain: 3.4 ±0.15 m/s).

The lower limb biomechanics during the single leg squat and step down task did not change with or without acute pain (Table 6.1& 6.2). The lower limb kinematics during the entire stance phase in running, as well as the lower limb kinetics during the early stance remained unchanged with or without experiencing acute pain (Table 6.3). During the mid and late-stance phase in running the external knee flexor moment was significantly decreased when the individuals run in acute pain (p=0.017) (Table 6.4, Figure 6.3). In addition, it could be shown that the variability during running was greater in acute than without acute pain (Figure 6.3).

The net activation of the knee extensors and flexors decreased significantly during the single leg squat (quadriceps: 22.02% reduction, p=0.025, hamstrings: 9.98% reduction, p=0.010) and the step down task (quadriceps: 19.62% reduction, p=0.028, hamstrings: 11.26% reduction, p=0.016) in acute pain (Table 6.5). During the early and mid-stance phase the net activation of the knee flexors was significantly reduced in acute pain (early stance phase: 11.04% reduction,

p=0.0019, mid-stance phase: 16.92% reduction, p= 0.010). Furthermore, during the early stance phase in acute pain the ratio significantly changed towards an increased knee flexor activation in relation to the knee extensor activity (p=0.019). Although the ratio of knee flexor-knee extensor activation changed only significantly during the early stance phase, the results showed a trend towards an increase in knee flexor activity and a decrease in knee extensor activity during all tasks and stance phases in acute pain (Table 6.5).

The peak isometric, concentric and eccentric torque did not change with or without acute pain. Neither the time to peak and the rate to force development were significantly altered by acute pain. The occurrence of the break phenomenon was without acute pain: n=5 and n=7 with acute pain and thus was not significantly changed (p=0.48) (Table 6.6). However, the AMI increased significantly in acute pain (5.56% increase, p=0.024) (Table 6.6).

*Table 6.1.: The lower extremity kinematics during the single leg squat task and the step down task with and without acute pain (*indicated the results were significantly different.)*

The kinematic variables (º) during the single leg squat and step down task		Without pain			With acute pain			P value: (T-test, sig 2-tailed)	Effect size
		Mean	SD	Std. Error Mean	Mean	SD	Std. Error Mean		
Single leg squat	Hip flexion angle	75.7	15.6	3.4	76.9	16.4	3.6	0.656	0.08
	Hip adduction angle	14.5	7	1.5	13.6	7.6	1.7	0.335	0.08
	Hip internal rotation angle	1.9	7.5	1.6	0.7	7.8	1.7	0.256	0.16
	Knee flexion angle	81.1	9.3	2	81.9	10.7	2.3	0.656	0.08
	Knee adduction angle	5.3	4.7	1	4.2	4.5	1	0.179	0.24
	Knee internal rotation angle	-2.5	6.3	1.4	-1.5	5.9	1.3	0.232	0.16
	Knee angular velocity (°/sec.)	-38.9	11.7	2.5	-35.6	14.6	3.2	0.263	0.25
Step down task	Hip flexion angle	71.8	18.2	4	74.5	15	3.3	0.168	0.16
	Hip adduction angle	16.4	6.7	1.5	15.7	6.7	1.5	0.459	0.10
	Hip internal rotation angle	2.2	6.8	1.5	0.6	7.6	1.7	0.141	0.22
	Knee flexion angle	89.4	14	3.1	90.3	13	2.8	0.553	0.07
	Knee adduction angle	5.4	4.4	1	4.5	4.6	1	0.134	0.2
	Knee internal rotation angle	-1.1	6.5	1.4	-1.1	6.1	1.3	0.950	0
	Knee angular velocity (°/sec.)	-38.2	14	3.1	-35.6	13.1	2.9	0.289	0.19

*Table 6.2.: The lower extremity kinetics during the single leg squat task and the step down task with and without acute pain (*indicated the results were significantly different.)*

The kinetic variables (Nm/kg) during the single leg squat and step down task		Without pain			With acute pain			P value: (T-test, sig 2-tailed)	Effect size
		Mean	SD	Std. Error Mean	Mean	SD	Std. Error Mean		
Single leg squat	Hip flexion moment	1.29	0.55	0.12	1.34	0.55	0.12	0.495	0.09
	Hip adduction moment	0.95	0.28	0.06	0.91	0.2	0.04	0.473	0.16
	Hip internal rotation moment	-0.14	0.05	0.01	-0.15	0.07	0.02	0.501	0.16
	Knee flexion moment	1.74	0.41	0.09	1.67	0.28	0.06	0.313	0.20
	Knee adduction moment	0.33	0.12	0.03	0.3	0.11	0.02	0.351	0.26
	Knee internal rotation moment	0.4	0.09	0.02	0.37	0.09	0.02	0.291	0.33
Step down task	Hip flexion moment	1.49	0.72	0.16	1.58	0.69	0.15	0.167	0.13
	Hip adduction moment	1.13	0.27	0.06	1.06	0.2	0.04	0.140	0.29
	Hip internal rotation moment	-0.1	0.07	0.02	-0.12	0.06	0.01	0.137	0.31
	Knee flexion moment	1.74	0.35	0.08	1.69	0.29	0.06	0.353	0.16
	Knee adduction moment	0.39	0.18	0.04	0.35	0.14	0.03	0.342	0.25
	Knee internal rotation moment	0.4	0.09	0.02	0.37	0.09	0.02	0.224	0.33

*Table 6.3.: The lower extremity kinematics during the stance phase in running with and without acute pain (*indicated the results were significantly different.)*

The kinematic variables (º) during stance phase		Without pain			With acute pain			P value: (T-test, sig 2-tailed)	Effect size
		Mean	SD	Std. Error Mean	Mean	SD	Std. Error Mean		
Early stance phase	Hip flexion angle	36.5	5.9	1.3	36.8	5.5	1.2	0.738	0.05
	Hip adduction angle	7.1	4.6	1	6.7	4.8	1.1	0.848	0.09
	Hip internal rotation angle	2.9	7.9	1.7	3.4	7.4	1.6	0.829	0.07
	Knee flexion angle	30.6	3.9	0.9	31.6	4	0.9	0.964	0.25
	Knee adduction angle	2.2	3.4	0.7	2.5	3.9	0.8	0.829	0.08
	Knee internal rotation angle	-4.8	5.9	1.3	-3.9	5.2	1.1	0.171	0.18
Mid-stance phase	Hip flexion angle	34.6	6.5	1.4	34.9	5.9	1.3	0.964	0.05
	Hip adduction angle	11.5	4.8	1	10.1	5.3	1.2	0.486	0.28
	Hip internal rotation angle	-0.1	7.5	1.6	-0.9	8.7	1.9	0.829	0.10
	Knee flexion angle	43.3	5	1.1	44.6	5	1.1	0.246	0.26
	Knee adduction angle	1.7	3.3	0.7	0.9	4.8	1	0.171	0.19
	Knee internal rotation angle	1	6.3	1.4	1.2	5.5	1.2	0.713	0.03
Late-stance phase	Hip flexion angle	21.1	5.7	1.2	21	5.2	1.1	0.964	0.18
	Hip adduction angle	7.2	5	1.1	7	4.9	1.1	0.762	0.04
	Hip internal rotation angle	1.1	7.4	1.6	0.2	9.2	2	0.486	0.11
	Knee flexion angle	40.9	4	0.9	41.7	4.6	1	0.216	0.19
	Knee adduction angle	1.2	2.7	0.6	1.1	3.8	0.8	0.829	0.03
	Knee internal rotation angle	0	7.1	1.5	0.6	5.4	1.2	0.510	0.10

*Table 6.4.: The lower extremity kinetics during stance phase in running with and without acute pain, (*indicated the results were significantly different.)*

The kinetic variables (Nm/kg) during stance phase		Without pain			With acute pain			P value: (T-test, sig 2-tailed)	Effect size
		Mean	SD	Std. Error Mean	Mean	SD	Std. Error Mean		
Early stance phase	Hip flexion moment	2.03	0.42	0.09	1.99	0.4	0.09	0.876	0.10
	Hip adduction moment	1.24	0.45	0.1	1.08	0.33	0.07	0.130	0.41
	Hip internal rotation moment	0.05	0.12	0.03	0.06	0.09	0.02	0.511	0.09
	Knee flexion moment	1.42	0.48	0.11	1.38	0.33	0.07	0.395	0.10
	Knee adduction moment	0.52	0.28	0.06	0.45	0.26	0.06	0.511	0.26
	Knee internal rotation moment	0.22	0.1	0.02	0.2	0.11	0.02	0.374	0.19
Mid-stance phase	Hip flexion moment	0.94	0.59	0.13	0.87	0.42	0.09	0.395	0.14
	Hip adduction moment	1.95	0.42	0.09	1.82	0.47	0.1	0.491	0.29
	Hip internal rotation moment	-0.26	0.17	0.04	-0.26	0.17	0.04	0.511	0
	Knee flexion moment	2.89	0.72	0.16	2.48	0.77	0.17	0.017*	0.55
	Knee adduction moment	0.55	0.29	0.06	0.5	0.3	0.07	0.374	0.17
	Knee internal rotation moment	0.44	0.14	0.03	0.41	0.15	0.03	0.281	0.21
Late-stance phase	Hip flexion moment	-0.03	0.28	0.06	0.02	0.26	0.06	0.395	0.19
	Hip adduction moment	1.43	0.42	0.09	1.37	0.46	0.1	0.503	0.14
	Hip internal rotation moment	0.02	0.03	0.01	0.02	0.04	0.01	0.491	0
	Knee flexion moment	1.96	0.51	0.11	1.68	0.51	0.11	0.017*	0.55
	Knee adduction moment	0.36	0.21	0.05	0.33	0.21	0.05	0.511	0.14
	Knee internal rotation moment	0.25	0.11	0.02	0.23	0.11	0.02	0.253	0.19

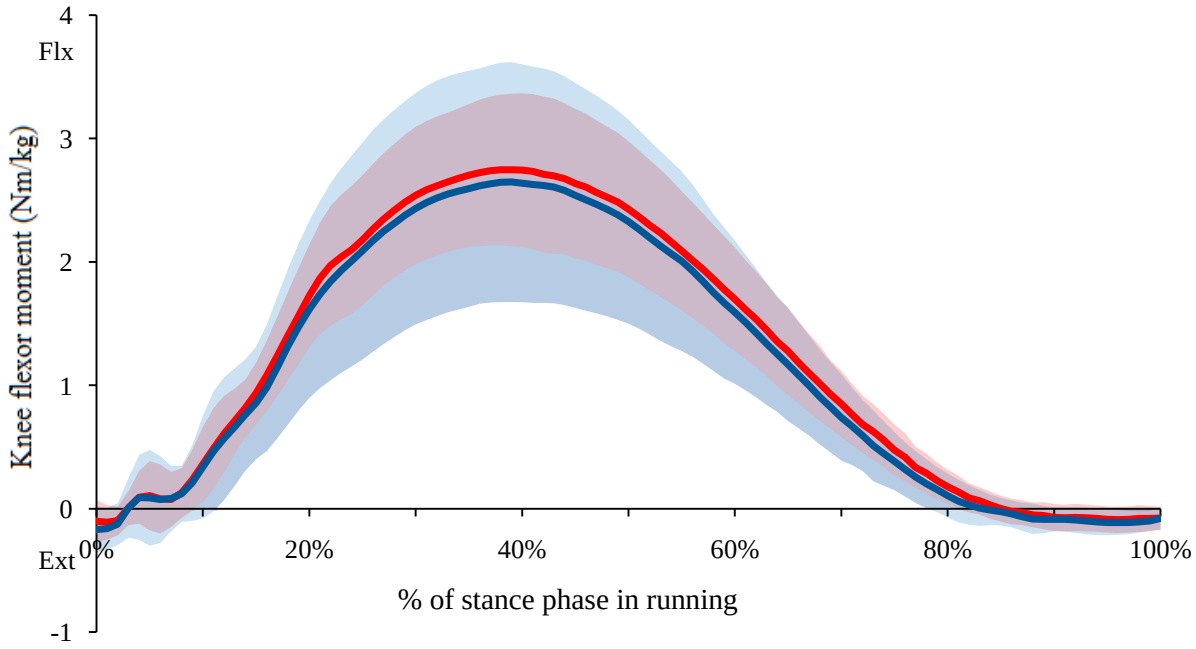

Figure 6.2: The sagittal plane knee moment during the stance phase in running without acute pain (red) and with acute pain (blue). The shaded areas represent ±1SD for each condition, internal rotation as the positive angle.

*Table 6.5.: Co-contraction ratio, net activation of the knee flexors and knee extensors during the stance phase in running, the single leg squat task and the step down task with and without acute pain, (*indicated the results were significantly different.)*

		Without pain			With acute pain			P value: (T-test, sig 2-tailed)	Effect size
		Mean	SD	Std. Error Mean	Mean	SD	Std. Error Mean		
Single leg squat	Co-contraction ratio (knee ext: knee flx.)	0.6	0.28	0.07	0.65	0.19	0.05	0.141	0.20
	Net activation knee extensors in %	74.97	36.65	8.64	52.95	35.32	8.32	0.025*	0.61
	Net activation knee flexors in %	28.81	16.93	3.99	18.83	14.78	3.48	0.010*	0.63
Step down task	Co-contraction ratio (knee ext: knee flx.)	0.58	0.29	0.07	0.63	0.23	0.05	0.396	0.19
	Net activation knee extensors in %	72.43	30.6	7.21	52.81	36.72	8.66	0.028*	0.58
	Net activation knee flexors in %	30.55	20.7	4.88	19.29	14.74	3.47	0.016*	0.63
Early stance phase	Co-contraction ratio (knee ext: knee flx.)	0.66	0.15	0.04	0.72	0.13	0.03	0028*	0.43
	Net activation knee extensors in %	134.49	67	15.79	102.29	59.11	13.93	0.068	0.51
	Net activation knee flexors in %	38.26	17.91	4.22	26.86	17.99	4.24	0.019*	0.64
Mid-stance phase	Co-contraction ratio (knee ext: knee flx.)	0.32	0.24	0.06	0.41	0.25	0.06	0.117	0.37
	Net activation knee extensors in %	81.74	41.9	9.88	63.16	35.75	8.43	0.093	0.48
	Net activation knee flexors in %	50.21	21.43	5.05	33.29	19.61	4.62	0.010*	0.82
Late-stance phase	Co-contraction ratio (knee ext: knee flx.)	-0.44	0.47	0.11	-0.33	0.44	0.1	0.113	0.24
	Net activation knee extensors in %	6.76	5.67	1.34	8.9	16.29	3.84	0.554	0.18
	Net activation knee flexors in %	20.03	15.55	3.67	14.05	10.98	2.59	0.149	0.44

*Table 6.6.: Strength, AMI, time to peak, rate to force development and the break phenomenon with and without acute pain. (*indicated the results were significantly different.)*

	Without pain			With acute pain			P value: (T-test, sig 2-tailed)	Effect size
	Mean	SD	Std. Error Mean	Mean	SD	Std. Error Mean		
Isometric quadriceps strength (Nm/kg*100)	2.86	0.76	0.17	2.90	1.26	0.27	0.859	0.04
Eccentric quadriceps strength (Nm/kg*100)	3.14	1.40	0.30	2.74	0.69	0.15	0.067	0.36
Concentric quadriceps strength (Nm/kg*100)	1.74	0.71	0.15	1.88	0.57	0.12	0.433	0.22
AMI in %	10.58	9.33	2.04	16.14	12.71	2.77	0.024*	0.50
Time to peak (ms)	0.62	0.21	0.05	0.73	0.36	0.08	0.455	0.37
Rate to force development (torque/ms)	281.53	120.62	26.32	248.24	136.14	29.71	0.079	0.26

6.5. Discussion

To the authors' knowledge, this is the first study that has investigated the direct influence of acute pain on hip and knee kinematics and kinetics, quadriceps and hamstrings activation and quadriceps strength and AMI. This study showed that despite pain, hip and knee kinematics were not significantly changed. Thus, the first hypothesis suggesting no significant differences in knee and hip kinematics and kinetics between acute pain and no pain in individuals with PFP was accepted. The second null-hypothesis was partially accepted, because no differences in strength could be shown. However, AMI significantly increased in

acute pain. Since no differences in the occurrence of the break phenomenon, nor in the co-contraction of the thigh muscles were identified the third and fourth null-hypotheses were accepted.

However, the external knee flexor moment was significantly decreased in acute pain during the early and mid-stance phase in running. This is in accordance with previous studies which demonstrated that artificially induced knee pain resulted in a decreased knee flexor moment (Henriksen et al., 2007; Seeley et al., 2013). Furthermore, a decreased knee flexor moment has been also shown in individuals with PFP (Besier et al., 2009; Bley et al., 2014; Claudon et al., 2012; Dos Reis et al., 2015; Salsich et al., 2001). It is believed that a decreased knee flexor moment might be caused by the quadriceps avoidance strategy and is believed to be a compensatory strategy to decrease joint loading (Henriksen et al., 2007;Salsich et al., 2001). Although this assumption could be supported by the findings of a significantly increased quadriceps inhibition, it could not be supported by the co-contraction results, which showed a significantly decreased hamstrings activity. Furthermore, the co-contraction ratio was shifted towards an increased knee extensor activation in relation to the knee flexor activity during the early stance phase. However, throughout the stance phase the knee extensors activity appeared to be reduced. Although the quadriceps and the hamstrings activity decreased the ratio still shifted towards an increased knee extensor activation. The same tendency of a shifted co-contraction ratio towards a greater quadriceps muscle activity in relation to hamstrings activity became apparent during the single leg squat and step down task. Besier et al. (2009) found an increased hamstrings and quadriceps activity in individuals with PFP, compared to healthy individuals and concluded that the experienced pain might be a result of increased joint contact forces due to a greater co-contraction of the hamstrings and quadriceps muscles (Besier et al., 2009). Another study reported that quadriceps weakness resulted in an increased hamstrings loading which lead to an increase of the total contact force and an increase of the average patellar flexion, lateral tilt and lateral shift (Elias et al., 2011). This could not be confirmed, because the individuals with PFP in this study showed a shift towards more quadriceps activity in acute pain. However, a balanced co-contraction of the quadriceps and hamstrings activation leads to increased knee joint stabilisation in the frontal plane, due to increased joint compression (Palmieri-Smith et al., 2009). Thus, the overall reduced co-contraction of the quadriceps and hamstrings might result in knee instability during the loading response and thus also might be responsible for the

development of pain and the greater reduction and variability of the knee flexor moment (Besier, Lloyd, & Ackland, 2003; Henriksen et al., 2007; Henriksen et al., 2009). The reduced activation of the quadriceps and hamstrings activity has also been described in individuals with artificial induced pain (Henriksen et al., 2007; Henriksen et al., 2009). The reduced quadriceps muscle activation during the single leg squat and step down task could also be a compensatory strategy to reduce patellofemoral joint reaction forces during painful activities (Nadeau, Hebert, Arsenault, & Lepage 1997). In the present study, pain caused an overall decrease of the activity of the hamstrings and quadriceps muscles during the single leg squat and step down task, as well as the stance phase in running, where the quadriceps muscles controls eccentrically the knee flexion and the hamstrings contribute to knee stability. Especially during the eccentric quadriceps tasks (the single leg squat and step down task) the quadriceps activation decreased, which demonstrates that pain might result in a quadriceps avoidance strategy and is capable of modulating the movement pattern significantly. Previous literature described that the quadriceps avoidance strategy might be linked to quadriceps inhibition (Henriksen et al., 2007; Henriksen et al., 2009; Sterling, Jull, & Wright, 2001). This link could be proven in this study, because it could be shown that the quadriceps AMI significantly increased in acute pain. Several previous studies suggested that the voluntary antagonist neural drive can be increased, overcoming any inhibitory contractions (Graven-Nielsen, Lund, Arendt-Nielsen, Danneskiold-Samsoe, & Bliddal, 2002; Lund, Donga, Widmer, & Stohler, 1991; Sterling et al., 2001). However, this study showed that the nociceptive input caused a decrease of the antagonistic muscles and thus indicates that not only the quadriceps, but also the hamstrings muscles might be inhibited due to pain (Henriksen et al., 2011). The results of this study suggest that pain suppressed the motor output globally, however, despite the significant altered muscle activity of the quadriceps and the hamstrings muscle, no biomechanical changes during the step down and single leg squat task occurred. Although, the quadriceps AMI indicated that central neural control mechanisms are involved in the altered movement pattern, in contrast to previous studies, the pain did not result in a reduced maximal voluntary quadriceps contraction and also did not result in a more hamstrings dominant, but rather a more quadriceps dominant pattern (Graven-Nielsen et al., 2002; Henriksen et al., 2007; Henriksen et al., 2009), The hamstring muscles work antagonistically to the quadriceps muscle. Reduced hamstring activity reduces the antagonist hamstring moment that the quadriceps must overcome to enable the loading

phase in running with reduced net extensor moment and EMG activity. This study revealed a reduced knee flexor moment during the stance phase in running, which might be caused by an overall reduced quadriceps activity resulting in a decreased knee flexor moment.

AMI is present in a wide range of knee joint pathologies, such as knee osteoarthritis, rheumatoid arthritis, anterior knee pain, patella contusion, anterior cruciate ligament rupture, meniscal damage and after knee arthroplasty (Hart et al., 2010; Rice & McNair, 2010). AMI is believed to be caused by altered afferent input originating from mechanoreceptors and nociceptors which reflexively reduce the efferent quadriceps alpha MN output (Hart et al., 2010; Rice & McNair, 2010). The protective, reflexive and unconscious mechanism to reduce the neural drive to the surrounding musculature is described as a reflexive "shut-down" mechanism and is an initially protective mechanism (Hart et al., 2010). Studies which investigated the corticospinal excitability of the vastus medialis (VM) and vastus lateralis (VL) showed that the corticospinal excitability was significantly increased during experimental knee pain (On, Uludag, Taskiran, & Ertekin, 2004; Rice et al., 2015; Rice, McNair, Lewis, & Dalbeth, 2014). Rice et al. (2015) described that the inhibitory response occurs partially due to spinal reflex inhibition of the quadriceps alpha-motor-neuron (MN). In contrast, a recent study found no association between AMI and measures of corticospinal or intracortical excitability (Kittelson, Thomas, Kluger, & Stevens-Lapsley, 2014). These findings indicate that although pain is involved in the neural mechanisms of quadriceps activation, corticospinal or intracortical pathways are not directly involved within the primary motor cortex in the mechanisms of CAD (Kittelson et al., 2014). Studies which investigated the association of pain to AMI found that it was significantly associated to knee pain (Callaghan et al., 2014; Drover et al., 2004; Graven-Nielsen et al., 2002; Hart et al., 2010; Hopkins & Ingersoll, 2000; Palmieri-Smith et al., 2013) and that already the increase of 1 on the VAS scale caused an increase in AMI of 1.6% (Callaghan et al., 2014). These findings are in accordance with the results of this study, where the pain increase of 1 on the NPRS caused an increase of 2.1% AMI. Thus, AMI seems to play an important role in the injury cycle of knee pain. Another indicator for AMI is the break phenomenon, which is believed to be caused by reflex inhibition of the quadriceps muscle, to avoid overstress of the knee joint (Herrington et al., 2003). However, although the break phenomenon occurred more often in acute pain, this study did not find a significant increase in the occurrence of the break phenomenon in acute pain.

As previously explained the participants with PFP did not show decreased quadriceps strength, despite the significant increase of quadriceps inhibition. These results are in contrast to results of studies that showed a decreased quadriceps strength in the presence of quadriceps inhibition (Henriksen et al., 2011; Park, Chinn, Squires, & Hopkins, 2012). These results are difficult to interpret, however, in comparison to strength results of individuals with PFP in previous studies the participants with PFP in this study were very strong. Selfe et al. (2016) carried out a study to explore whether subgrouping of non-specific individuals with PFP is possible. They concluded that three subgroups of patients with PFP exist; a "strong subgroup" with high quadriceps and hip abductor strength scores, a "weak and tight subgroup" with weak quadriceps and hip abductor muscles and low muscle flexibility and a "weak and pronated foot subgroup" with weak quadriceps and hip abductor muscles, greater patellar mobility and an increased foot pronation (Selfe et al., 2016). The strong subgroup had quadriceps strength scores of 1.65 ±0.53 Nm/kg in comparison with the weak groups that had quadriceps strength values of 0.84 ±0.32 Nm/kg and 0.82 ±0.32 Nm/kg. The group of individuals with PFP who participated in this study were highly active and had an isometric quadriceps strength score of: 2.86±0.76 Nm/kg without acute pain and with acute pain of 2.90±1.26 Nm/kg. These results show that the participants with PFP who participated in this study were stronger than previously reported in literature. Even literature that described quadriceps strengthening in athletes with PFP showed smaller quadriceps strength results than the results of this study, which makes an interpretation of the findings challenging (Ramazzina, Pogliacomi, Bertuletti, & Costantino, 2016; Yildiz et al., 2003). Furthermore, research on strong individuals with PFP remains understudied (Selfe et al., 2016). However, one explanation for these results might be that the good training status of the participants with PFP enabled them to deliver maximal contractions even if they experience pain.

Thus, it could be shown that pain did not alter lower limb kinematics, but resulted in a decreased knee flexor moment. Although the AMI was significantly increased, the quadriceps strength torque remained unchanged. Lastly, this study showed that acute pain caused a decreased quadriceps and hamstrings activity.

6.6. Limitations to the study

One great limitation of this study was that the activities that caused pain were not monitored and standardised. The participants were asked to come to the first appointment whilst not experiencing pain and to the second appointment after performing exercises that caused them acute pain. To ensure that they were not fatigued they were asked to not perform the painful activity at least 5 hours before coming to the appointment and were advised to rest before arriving at the gait laboratory. Thereby the participant performed his/her functional activities that caused them pain. However, this procedure did not allow us to monitor and standardise the painful activities.

It is important to note that the participants were fitted for this study with standard training shoes to control the shoe-surface interface and to minimise the influence of footwear. The standard training shoes might have negatively influenced the comfort during running and thereby might have influenced the movement performances.

6.7. Conclusion

Pain in individuals with PFP is more than a symptom and is believed to play a role in the aetiology of PFP. To the authors knowledge this was the first study investigating the effect of knee pain on lower limb biomechanics, AMI and strength. It could be shown that pain significantly decreased the knee flexor moment, caused a significant decrease of muscular activity of the quadriceps and hamstrings muscles and resulted in a significant increase of AMI of the quadriceps. Furthermore, this was the first holistic investigation of acute pain in individuals with PFP, combining the assessment of AMI, the break phenomenon, muscular strength and coordination, with a biomechanical analysis.

Chapter 7: Discussion

This last chapter aims to summarise and to discuss the findings of this thesis and to contextualise the findings to contemporary research.

This study started with a thorough literature review and a meta-analysis, with which the definition, the prevalence, the risk factors, the prognosis, the pathophysiology and different treatments of PFP were identified and addressed in detail. Following the literature review, the research gaps were identified and the focus of this study was determined. Then a reliability study was performed to develop a robust and reliable test protocol for the investigation of lower limb kinematics and kinetics, quadriceps strength, quadriceps inhibition, lower limb flexibility, patella and foot posture and clinical outcomes. To ensure that the sEMG data was collected and analysed in a reliable way, two pilot studies were carried out. As the focus of the main study was to investigate the effect of several chosen treatments such as Power strap and a 6-week exercise programme. The developed reliable test protocol was firstly applied in the study which investigated the influence of the Powers^{TM} strap on pain and lower limb biomechanics in individuals with and without PFP. Then the effect of a 6-week exercise programme on lower limb kinematics and kinetics, quadriceps strength, quadriceps inhibition, lower limb flexibility, patella and foot posture and clinical outcomes in individuals with PFP was studied. The last chapter explored the effect of acute PFP pain on functional performance, the quadriceps strength and quadriceps inhibition in individuals with PFP.

This is to the author's knowledge the first study that investigated the influence of a the Powers^{TM} strap as a passive intervention and the evidence based 6 week exercise programme as an active treatment on muscular dysfunction in individuals with PFP. This was also the first study that investigated the direct influence of pain on muscle dysfunction in individuals with PFP.

7.1. Hypotheses $H0_1$-$H0_4$: Influence of the Powers^{TM} strap on lower limb kinetics and kinematics in individuals with and without PFP

The first objective of the thesis was to investigate the influence of the Powers^{TM} strap as a novel passive intervention in individuals with PFP. This study revealed that the Powers^{TM} strap was able to modify lower limb biomechanics during functional tasks in individuals with and without PFP and reduced pain in individuals with PFP. To date, no study investigated

whether a strap or brace reduced the hip internal rotation angle and thus, these results cannot be compared with previously published studies. However, in comparison with studies that investigated the hip internal rotation in individuals with PFP it became apparent that the individuals in this study did not show an excessive hip internal rotation and hip adduction during running and performed the tasks comparable to the healthy individuals (Table 7.1).

The kinematics during the single leg squat and step down task are more diverse and are linked to hip and knee flexion. The knee and hip flexion angle appear to be greater in this study compared with previous literature (Table 7.2. and 7.3.), which indicates that the participants in this study squatted deeper and flexed their knee more during the step down task. However, many studies did not report the hip and knee flexion angle and thus it is difficult to compare the kinematic data to previously reported data (Table 7.2. and Table 7.3.).

However, to date no study investigated the influence of a knee strap or brace on hip internal rotation and adduction. Thus, the findings of the hip internal rotation cannot be compared with any previous data.

Table 7.1.: Comparison of the hip and knee kinematics (in degrees) during the stance phase in running in the literature (IR: Internal rotation, Add: Adduction)

Author	Subject population	Hip IR	Hip Add	Knee IR	Knee Add
Noehren et al., 2011	10 subjects	11.0± 4.1	22.0± 1.5		
Souza & Powers, 2009a	21 females	11.8± 6.9			
Souza & Powers, 2009b	19 females	8.2± 6.6			
Noehren et al., 2012	30 females	9.7± 3.9	16.7±3.2	-1.1± 4.9	4.1± 4.1
Willy at al., 2012	18 males, 18 females	6.0± 3.8	11.9± 3.0		2.7± 3.2
Esculier et al., 2015	21 subjects	7.9±5.5	12±3.4		
Dierks et al., 2008	5 males, 15 females	5.1± 6.8	8.7± 5.2		1.6± 5.1
Bazett-Jones et al., 2013	10 males, 9 females	3.03± 4.2	13.2± 3.3	1.52± 4.1	0.24± 2.1
Willson et al., 2011	20 females	2.94± 4.43	13.67± 4.41		
This study (stance phase)	*12 males, 12 females*	*2.0± 7.9*	*8.0± 4.8*	*-0.1± 5.6*	*1.3± 4.5*

Table 7.2.: The comparison of the hip and knee kinematics (in degrees) during single leg squat in the literature

Author	Subject population	Hip Flx	Hip IR	Hip Add	Knee Flx	Knee IR	Knee Add
Song et al., 2014	16 females	27.7± 6.0	27.1±15.6	23.5±11.3			
Willy et al., 2012	18 males, 18 females		5.7± 5.1	6.2± 3.7			2.74± 4.3
Nakagawa et al., 2012	20 males, 20 females		12.7± 6.1	14.8± 7.8			9.2± 5.0
De Marche Baldon et al., 2014	31 females	46.9± 9.3 52.5± 14.6		17.1± 4.3 23.5± 6.2			-11.0± 7.2 -12.3± 5.2
Noehren et al., 2011	10 subjects		11.0± 4.1	22.0± 1.5			
Salsich et al., 2012	20 females		1.1± 5.8	14.3± 5.9	70.0± 7.5	2.7± 5.7	0.3± 6.9
This study	*12 males, 12 females*	*73.4± 18.2*	*0.6± 8.1*	*13.6± 7.6*	*80.8± 10.7*	*-1.4± 5.6*	*4.3± 4.9*

Table 7.3.: The comparison of the hip and knee kinematics (in degrees) during the step down task in the literature

Author	Subject population	Hip Flx	Hip IR	Hip Add	Knee Flx	Knee IR	Knee Add
Cheung et al., 2012	22 males		9.98±3.14				
Willy et al., 2012	10 females		7.0± 5.7	7.8± 2.7			
Grenholm et al., 2009	17 females			7.3± 4.3	54.2± 4.2		
McKenzie et al., 2010	10 females	52.3± 9.4	-11.7± 5.0	-2.8± 5.0	86.6± 7.4		
This study	*12 males, 12 females*	*71.8± 16.1*	*0.6± 7.9*	*15.5± 6.6*	*88.6± 12.9*	*-0.8± 5.8*	*4.4± 4.9*

Previous studies described the reduction of pain after the application of a brace, and thus, the application of the knee brace or patellar tape in individuals with PFP has been recommended (Barton et al., 2015; Crossley, van Middelkoop, et al., 2016). However, to date no brace achieved a significant reduction of the hip internal rotation angle (Aminaka & Gribble, 2005; Barton et al., 2015; Bolgla & Boling, 2011;Crossley et al., 2001; Swart et al., 2012; Warden et al., 2008). The Powers^{TM} strap showed the ability to significantly modify the lower limb biomechanics in individuals with PFP, which gives confidence that the Powers^{TM} strap has a mechanical influence on the hip internal rotation angle. Thus, the Powers^{TM} strap seems to not only be able to reduce pain significantly, but also to modify lower limb biomechanics. However, the individuals with PFP in this study did not show an excessive hip IR or

adduction angle. Thus, future research is required, to investigate the influence of the Powers^{TM} strap to examine the effect of the strap in individuals with PFP that show an excessive hip internal rotation angle and dynamic knee valgus.

Previous research on the effect of patellar taping on quadriceps activation showed contradictory results (Christou, 2004; Cowan, Bennell, & Hodges, 2002; Herrington, 2001; Macgregor et al., 2005; Ng & Cheng, 2002; Salsich et al., 2002; Song et al., 2014). Some studies reported an increased quadriceps activity and earlier VM onset (Christou, 2004; Cowan, Bennell, & Hodges, 2002; Herrington, 2001; Macgregor et al., 2005), other studies reported a decreased quadriceps activity (Ng & Cheng, 2002; Song et al., 2014) and other studies reported no changes in quadriceps activity (Salsich et al., 2002; Song et al., 2014). This study is in agreement with studies that reported a decreased quadriceps activity. However, the heterogeneity in findings emphasises the importance of further research to understand whether and how bracing and taping can affect the quadriceps activity.

7.2. Hypotheses $H0_5$-$H0_9$: Influence of a 6 week exercise treatment on pain, functional performance, balance, muscular strength and inhibition in individuals with patellofemoral pain

This study was to the author's knowledge the first study that developed an exercise programme based on the current recommendations and evaluated its effect in individuals with PFP. Pain as well as function significantly improved after the 6-week exercise programme. Especially the function during sport and recreational activities as well as quality of life improved on average by over 40%. Previous studies that investigated exercise programmes in individuals with PFP, that consisted of quadriceps and/ or gluteal exercises also reported improvements of function and pain (Alba-Martin et al., 2015; Bily, Trimmel, Modlin, Kaider, & Kern, 2008; Clark et al., 2000; Clijsen et al., 2014; Collins et al., 2008; Earl & Hoch, 2011; Harrison EL, 1999; Hazneci, Yildiz, Sekir, Aydin, & Kalyon, 2005; Khayambashi, Fallah, Movahedi, Bagwell, & Powers, 2014; Khayambashi et al., 2012; Lack, Barton, Sohan, Crossley, & Morrissey, 2015; Loudon, 2004; Petersen et al., 2016; Santos, Oliveira, Ocarino, Holt, & Fonseca, 2015; Syme, Rowe, Martin, & Daly, 2009; Thomson, Krouwel, Kuisma, & Hebron, 2016; Van Linschoten et al., 2009; Witvrouw et al., 2004; Yilmaz, Baltaci, Tunay, & Atay, 2011; Yip & Ng, 2006).

However, the participants in this study had lower pain and had a higher KUJALA score than individuals with PFP in previous studies (Table 7.4). Selfe et al. (2016) reported that the "strong" subgroup showed a trend towards less pain, higher function and better quality of life. Based on these results the trend of less pain and a higher function in this group of individuals with PFP could be confirmed.

Table 7.4: The comparison of the pain and function of the individuals with PFP in the literature

Author	Subject population	Pain (VAS or NPRS)	KUJALA
Harrison & McQuarrie, 1999	113 subjects	4.6±2.51	
Bolgla et al., 2016	61 males, 124 females	4.8± 1.7	76.5± 9.2
Syme et al., 2009	110 subjects	4.8± 3.0	
Loudon, 2004	22 males, 7 females	4.3± 2.6	66.9±8.1
Hazneci et al., 2005	24 males	4.6± 0.9	
Earl & Hoch, 2011	19 females	4.0± 1.8	70.4± 11.2
Van Linschoten et al., 2009	131 subjects	4.1± 2.3	65± 14.1
Clark et al., 2000	49 subjects	7.8± 40	
Bily et al., 2008	14 males, 24 females	5.5	78
Khayambashi et al., 2014	18 males, 18 females	7.3± 1.8	
Khayambashi et al., 2012	28 females	7.2± 1.8	
Witvrouw et al., 2004	60 subjects	3.5±2.2	~70
Callaghan & Oldham, 2004a	33 males, 47 females	3	70± 13.6
Collins et al., 2010	179 subjects	3.6± 1.7	71.5± 9.8
Kettunen et al., 2012	56 subjects	3.8± 2.6	71.5± 12.4
Sinclair et al., 2016	11 males, 9 females		
Lankhorst et al., 2015	100 subjects	6.1± 1.9	68.8± 12.4
C. R. Rathleff et al., 2013	40 subjects	5.5	
This study (early stance)	*12 males, 12 females*	*0.8±0.5*	*81.7±9.2*

*Table 7.5: The comparison quadriceps of the strength before and after an exercise treatment in the literature (Nm/kg*100)*

Author	Subject population		Isometric	eccentric	concentric
Yip & Ng, 2006	16 females, 10 males	Pre intervention			1.01± 0.77
		Post intervention			1.1± 0.74
Witvrouw et al., 2004 (data estimated based on graphs)	60 subjects	Pre intervention			~2.25
		Post intervention			~2.35 (3 months) ~2.60 (5years)
Rathleff et al., 2016	47 females	Pre intervention	2.17		
		Post intervention	2.54		
Bily et al., 2008	14 males, 24 females	Pre intervention			1.77±0.61
		Post intervention			1.74±0.55
This study	*9 males, 7 females*	Pre intervention	2.92± 0.65	3.36± 1.29	1.78±0.59
		Post intervention	2.91±0.57	3.05± 0.74	2.08± 039

However, studies that analysed "strong" individuals with PFP are still lacking and further research of this subgroup is required to confirm the findings of this study.

In this study, individuals with PFP did not gain quadriceps strength after the exercise treatment that contained quadriceps strengthening. These results are in contrast to previous findings (Rathleff et al., 2016; Witvrouw et al., 2004; Yip & Ng, 2006) (Table 7.5). Only Bily et al. (2008) reported no significant changes after the exercise treatment. However, the individuals with PFP in previous studies showed a considerable weakness of the quadriceps muscle and thus should not be compared to strong individuals with PFP. Since function and pain improved significantly in individuals with PFP despite no changes in strength it seems that quadriceps weakness cannot be associated with pain and function in strong individuals with PFP. However, further research on a larger sample size of strong individuals with PFP is required to confirm these results.

Most of the previous studies investigated the effect of an exercise programme that was supervised by physiotherapists in a clinical setting (Baldon, Serrao, Scattone Silva, & Piva, 2014; Boling et al., 2006; Clark et al., 2000; Collins et al., 2008; Coppack, Etherington, & Wills, 2011; Dolak et al., 2011; Earl & Hoch, 2011; Fukuda et al., 2012; Fukuda et al., 2010; Harrison EL, 1999; Hazneci et al., 2005; Ismail et al., 2013; Khayambashi et al., 2014;

Khayambashi et al., 2012; Lee, Lee, & Lee, 2014; Loudon, 2004; McMullen, Roncarati, & Koval, 1990; Moyano et al., 2013; Nakagawa et al., 2008; Syme et al., 2009; Van Linschoten et al., 2009; Witvrouw et al., 2004; Yilmaz et al., 2011; Yip & Ng, 2006) and only the minority of studies investigated the effect of home-based exercises pain (Bily et al., 2008; Harrison, 1999; L. Herrington & Al-Sherhi, 2007; Tyler, Nicholas, Mullaney, & McHugh, 2006). Thus, not many studies investigated the effect of a home-based exercise programme. In addition, only the study of Herrington et al. (2007) contained an individualised progression (Herrington & Al-Sherhi, 2007). However, the study of Herrington et al. (2007) investigated only the effect of quadriceps exercises (Herrington & Al-Sherhi, 2007). Thus, this study was the first study that investigated the effects of a home-based exercise programme that was based on the current guidelines and consisted of quadriceps, as well as gluteal strengthening exercises and flexibility exercises for the hamstrings and ankle dorsi-flexion ROM.

Although no biomechanical changes were identified during the stance phase in running, the participants with PFP flexed their knees and hips more during the single leg squat and the step down task. However, studies investigating the influence of exercises on lower limb biomechanics are still lacking. Baldon et al. (2014) analysed the effect of exercises on the squatting performance and reported that an exercise treatment in these individuals with PFP resulted in an increased demand of the gluteal muscles and thereby a decreased demand of the quadriceps during the single leg squat (Baldon, Serrao, Scattone Silva, & Piva, 2014). They also found that individuals with PFP demonstrated a greater forward trunk lean during the single-leg squat and thereby decreased the knee-flexion moment and increased the hip-flexion-moment (Baldon et al., 2014), which is in accordance with the findings of this study. Witvrouw et al. (2004) investigated the maximal knee flexion during a squat task and found that individuals with PFP who were pain free five years after the intervention were able to bend their knees 10° more during the squat (Witvrouw et al., 2004). The increase of knee flexion is very similar to the findings of this study, however this study lack long-term results. Earl et al. (2011) investigated the lower limb biomechanics during running and found a significant decreased external knee abduction moment (Earl & Hoch, 2011). They viewed this change as positive, however, since no kinematic changes were observed it remained unclear what contributed to the increased knee abduction moment (Earl & Hoch, 2011). To date, most studies investigate the effect of exercises on function, pain and muscular strength, but not on the effect on functional performance. Thus, more attention in studies should be

given to the effect of exercises on the functional performance, by investigating lower limb biomechanics, in individuals with PFP.

7.3. Hypotheses $H0_{10}$-$H0_{13}$: Influence of acute pain on functional performance, quadriceps strength and inhibition in individuals with patellofemoral pain

The passive as well as the active intervention study showed that despite relatively small or no biomechanical changes of the lower limb, the pain was significantly decreased and function improved. These observations raised the question whether and how pain might be linked to alterations of the lower limb biomechanics, strength and inhibition in individuals with PFP. Although previous studies analysed pain in healthy individuals and individuals with PFP no study investigated the direct influence of pain by comparing the individuals' performance without pain with the individual's performance in acute pain. Thus, this study aimed to investigate the effect of pain in individuals with PFP by combining the assessment of AMI, the break phenomenon, muscular strength and coordination, with a biomechanical analysis.

Previous studies analysing artificially induced knee pain also found a decreased knee flexor moment (Henriksen et al., 2007; Seeley et al., 2013). However, none of the studies reported lower limb kinematics, thus it is difficult to compare the data, because it is not clear if in these studies pain resulted in altered kinetics without altered kinematics. Bazett Jones et al. (2015) investigated whether pain influenced lower limb biomechanics in individuals with PFP and they reported a significant decrease of the hip internal rotation angle during acute pain. Although a slight decrease of the hip internal rotation was apparent in this study as well, the differences were not significant. These findings emphasise that an increase in pain does not always result in altered lower limb biomechanics.

Previous literature described a link of the quadriceps avoidance strategy to quadriceps AMI (Henriksen et al., 2007; Henriksen et al., 2009; Sterling et al., 2001). This study could confirm this link, because this study showed an overall decrease of the knee flexor and extensor muscles activity, increased quadriceps inhibition and a co-contraction shift towards the knee extensor activation. Although the shift was towards an increased quadriceps activation, the overall reduction in muscle activation might indicate an inhibition of the knee flexors as well as knee extensor muscles, which was previously described by Henriksen et al. (2011). Also other studies described that a reduced quadriceps muscle activation might be a

compensatory strategy to reduce patellofemoral joint reaction forces during painful activities (Henriksen et al., 2007; Henriksen et al., 2009; Nadeau et al., 1997).

The findings of this study are in accordance to previous studies that revealed that increased knee pain caused a significant increase of AMI (Callaghan et al., 2014; Drover et al., 2004; Graven-Nielsen et al., 2002; Hart et al., 2010; Hopkins & Ingersoll, 2000; Palmieri-Smith et al., 2013). AMI has been described as a reflexive and unconscious mechanism to reduce the neural drive to the surrounding musculature to protect the muscles from further damage by a decrease in muscle activity (Hart et al., 2010). Only three other studies investigated AMI in individuals with PFP. Drover et al. (2004) investigated AMI in 9 individuals with PFP and showed that they had 18.3% AMI (Drover et al., 2004). Suter et al. (1998) reported AMI in 42 individuals with PFP and showed an inhibition of 30-40%. Furthermore, they also reported that the AMI was higher in individuals with higher pain levels (Suter, Herzog, Souza, et al., 1998). Thomee (1996) reported in 5 individuals with PFP an AMI of 17.8% (Thomee et al., 1996). The results of this study are comparable to the results of Drover et al. and Thomee et al. However, the study of Drover and Thomee had very small sample sizes, which did not enable an appropriate representativeness. This highlights the current lack of studies investigating AMI in individuals with PFP.

7.4. Implications for clinical practice

Numerous factors are linked to the development of PFP. To address these numerous factors a multimodal conservative treatment is required. The current recommendation of a multimodal intervention include:

- active over passive exercises are recommended to reduce pain in the medium and long term and to improve function in the medium and long term
- knee braces, taping and straps to reduce acute pain
- combined interventions are recommended to reduce pain in the short and medium term

In this study, these recommendations have been transferred into two studies. The first study investigated the effect of a specific knee strap (the Powers^{TM} strap) in individuals with and without PFP. And the second study investigated the effect of an exercise programme based on the current guidelines in individuals with PFP.

The first study showed that the strap significantly decreased pain in individuals with PFP and increased the hip internal rotation angle in both groups. In the clinical context, these findings of this study have crucial value, as they indicate that the strap was able to reduce immediately pain during a number of functional lower limb-loading tasks (running, single leg squat and step down task). The reduction of pain is a crucial feature in early patient management to gain trust, but also to facilitate active engagement (Barton et al., 2015). If the patient is able to participate in lower limb-loading tasks without pain, it allows a further progression of the patient down a loading continuum, increasing their envelope of function to safely build up their activity levels (Barton & Rathleff, 2016; Herrington, 2013).

But also the findings of a significantly decreased hip internal rotation angle are of clinical importance. An increased femoral internal rotation has been commonly observed in individuals with PFP and leads to increased lateral patellar tilt, patellar shear stress and patellofemoral contact pressure (Besier et al., 2008; Lee et al., 2003; Powers, 2003; Souza, 2008; Souza et al., 2010; Souza & Powers, 2009a). The Powers^{TM} strap has been tested in individuals with and without PFP and the decrease of hip internal rotation could be proven in both groups. This is important from a mechanistic perspective as even in individuals who do not have pain, internal rotation can be reduced with the strap and gives confidence that this change was not influenced by pain changes. Although, the reduction of the hip internal rotation were quite small, they resulted in clinically significant changes, with a significant decrease in pain. Thus, this strap has not only the potential to decrease pain but also to control and modify femoral rotation and thus might be able to restore normal patellofemoral joint kinetics. In addition, the effect sizes for the hip internal rotation angle during the stance phase in running were moderate. Thus, it could be concluded that enough participants were recruited to present significant results. The results suggest that individuals with PFP might benefit from the Powers^{TM} strap to reduce pain in the short term. In addition, the results of this study indicate that especially individuals with PFP and an increased hip internal rotation might benefit from the Powers^{TM} strap to reduce pain in the short term and lower limb alignment in the short term.

PFP is one of the most challenging pathologies, because of its multifactor nature and the challenge to address the various factors that contribute to PFP (Bolgla et al., 2016). The second study addressed in a 6-week exercise programme function, pain, lower limb biomechanics, flexibility, muscle activation and muscle flexibility and showed that function and pain improved in individuals with PFP. The participants were also able to squat lower

and flex their knees more during the single leg squat task after the exercise programme. The flexibility of the hamstring muscles increased and the ankle range of motion showed the tendency of an increased ankle dorsi-flexion ROM. In addition, the results suggest the trend of a decreased quadriceps inhibition after the exercise treatment. However, no improvements of quadriceps strength, nor a change of co-contraction ratio and hamstrings and quadriceps activation could be identified.

The significant improvements of pain and function were reflected in the self-reported recovery and suggest the potential of the 6-week exercise programme to improve pain and function in the short and medium term. Also the improvements in flexibility and lower limb biomechanics indicate the benefit for individuals with PFP to perform the 6-week exercise programme. Based on these findings, the 6-week exercise programme can be recommended for individuals with PFP to improve pain and function, modify lower limb biomechanics, increase hamstrings flexibility. Potentially the exercise programme is also able to decrease quadriceps inhibition and improve ankle-dorsi-flexion ROM. However, the findings of this study are not strong enough to recommend the 6-week exercise programme for individuals with PFP to improve quadriceps inhibition and ankle-dorsi-flexion ROM.

No changes in quadriceps strength were identifiable, which critically questions whether the exercise programme is able to improve quadriceps strength in individuals with PFP. Although quadriceps strengthening is recommended as a treatment approach, several previous studies reported as well that the individuals with PFP did not or only slightly improve the quadriceps strength after an exercise programme (Bily et al., 2008; Witvrouw et al., 2004; Yip & Ng, 2006). The only study that reported a significant improvement of quadriceps strength tested a 3 months exercise programme (Rathleff et al., 2016). The length of the programme might be an important influential factor. Although not much literature has been published on the muscular changes over time during a strength training, one study reported that muscle strength increased after 2 months training by 7.9% and by 8.9% after three months (Kubo, Ikebukuro, Yata, Tsunoda, & Kanehisa, 2010). However, they reported that cross-sectional areas did not change until 2 months strength training (Kubo et al., 2010). The exercise programme in this study was 6 weeks long and thus might be too short to capture changes in quadriceps muscle strength. In addition, no studies have been published on "strong" individuals with PFP (Selfe et al., 2016). It might be that strong individuals with PFP adapt slower to a strength training programme, or that they do not increase quadriceps strength.

Thus, further research is required. However, based on the results in this study, the exercise programme cannot be recommended to increase quadriceps strength in individuals with PFP.

The third study investigated the effect of acute pain on lower limb biomechanics, quadriceps strength and inhibition in individuals with PFP. This study showed that despite the increase of pain the lower limb biomechanics and quadriceps strength remained unchanged. On the contrary, the quadriceps inhibition significantly increased in acute pain. Furthermore, the study showed a reduction of the quadriceps and hamstrings muscle activation during all tasks, which is has also been described in individuals with artificial induced pain (Henriksen et al., 2007; Henriksen et al., 2009). Especially the quadriceps muscle activation during the single leg squat and step down task was reduced which might be a compensatory strategy to reduce patellofemoral joint reaction forces during painful activities (Nadeau et al., 1997). These findings demonstrate that pain is capable of modulating the muscle activation pattern significantly and is linked to quadriceps inhibition. However, this study also showed that pain does not necessarily result in abnormalities of lower limb biomechanics or muscle weakness. These results are important because to date studies on PFP focus on muscle strength and lower limb alignment. Despite the extensive research on PFP, studies on quadriceps inhibition in these individuals have not been carried out. However, the results of this study emphasise the importance on future research on quadriceps inhibition.

7.5. Future studies

The majority of studies investigated the influence of coronal and sagittal stabilising knee straps and braces on PFP. The study on the Powers^{TM} strap was to the author's knowledge the first study that examined the lower limb biomechanics with a strap that aims to stabilise the patellofemoral joint through an external rotation of the femur.

This study proved the positive effect of the strap on pain, as well as lower limb biomechanics. However, the recruited group of participants with PFP appeared to be strong and had neither an excessive hip internal rotation angle nor a dynamic knee valgus. Thus, the study could not conclude whether and how the Powers^{TM} strap is able to align the lower limb if the participant has an excessive hip internal rotation or dynamic knee valgus. Thus, it is recommended that the Powers^{TM} strap should be analysed in future studies in "weak" and "weak and tight" groups of individuals with PFP (Selfe et al., 2016) and thereby especially in groups that are likely to show an excessive hip internal rotation or dynamic knee valgus.

In addition, the strap was only investigated short-term for the tasks and no medium or long term results were achieved. Further research should investigate the effect of the Powers^{TM} strap over a longer period of time. Therefore, the effect of the strap on individuals with PFP when they wear the strap over a longer period of time and regularly during sport and daily life activities should be fully investigated.

And lastly the study did not reach enough power during eccentric quadriceps activities, therefore more individuals should be recruited to reach enough power for the analysis.

The second study investigated the effect of a 6-week exercise treatment on pain, function, lower limb biomechanics, strength, muscle flexibility, balance and AMI in individuals with PFP. The study showed an improvement of pain, function, muscle flexibility and a debatable influence on muscle activation, quadriceps AMI and lower limb kinetics. However, the drop-out rate was very high (33%) in this study and only 16 participants with PFP completed successfully the study. Thus, more individuals should be recruited to investigate the effect with a larger sample size. One previous study showed good results in a home-based programme that was combined with a video-conference (e.g. via skype) (Bennell, Nelligan, Dobson, Rini, Keefe, Kasza, French, Bryant, Dalwood, Abbott, & Hinman, 2017). This might be an opportunity as well to reduce the drop-out rate and motivate the participants to continue with the exercises.

In addition, the recruited participants in this study appeared to be a "strong" patients group and showed no differences in quadriceps strength after the treatment (Selfe et al., 2016). This might have been caused because current treatment programmes recommend decreased loads and a higher amount of repetitions compared to a traditional hypertrophy/ strength training to reduce the flare up of symptoms. However, this study showed that strong individuals with PFP were not able to improve quadriceps strength with a low-load and high repetition strength endurance training. Thus, the currently recommended exercise programmes are not appropriate in terms of increasing strength in strong individuals with PFP, and further studies should investigate forms of modified hypertrophy trainings in individuals with PFP that are able to increase strength without flaring up the symptoms.

Furthermore, the results on "strong" individuals with PFP show that the underlying mechanisms in these individuals still remain understudied and need further investigation. Thus, a larger sample size of "strong" individuals with PFP should be compared with weak" and "weak and tight" individuals with PFP before and after the exercise treatment. These

findings might enable insights in underlying mechanisms in these three groups and how they can be influenced by an exercise treatment that is based on the current guidelines.

The third study investigated whether and how acute pain influenced lower limb biomechanics, quadriceps activation, strength and inhibition in individuals with PFP. This study demonstrated that the quadriceps inhibition increased and quadriceps and hamstrings muscle activation decreased in acute pain. Thus, although a significant inhibition was apparent the quadriceps strength was not significantly influenced.

The participants in this study were as in the previous two studies also "strong" individuals with PFP. These individuals might be able to compensate the pain without showing a decrease in quadriceps strength. Thus, the influence of acute pain should be investigated in "weak" and "weak and tight" groups of individuals with PFP. These findings will enable the insight whether pain influences lower limb biomechanics, quadriceps activation, strength and inhibition differently in these three groups and how the "weak" and "weak and tight" individuals with PFP compensate the acute pain compared with "strong" individuals with PFP.

7.6. Conclusions

The aim of this thesis was to provide a multifaceted investigation of the effect of current recommended treatment approaches on muscular and biomechanical factors in individuals with PFP.

The literature review showed that, although many studies investigated muscle function of individuals with PFP, important underlying factors, such as AMI and the break phenomenon remain relatively understudied. In addition, the review showed that although studies emphasise the importance of investigating active structures (muscles and tendons) in combination with a biomechanical analysis, it has not yet been realized in individuals with PFP to explore the effect of active and passive treatments in a holistic way.

The methodology and repeatability study enabled the development of a holistic measurement protocol, which was applied in the further studies.

The intervention studies revealed that the Powers^{TM} strap as a passive intervention is able to reduce pain short term and moreover is able to decrease the hip internal rotation angle and

decrease the dynamic knee valgus during eccentric quadriceps tasks. The 6-week exercise treatment proved to be effective in modifying lower limb biomechanics, decreasing pain and improving function. However, strong individuals with PFP did not improve quadriceps strength with a low-load and high repetition strength endurance training.

Lastly this thesis examined the effect of acute pain in individuals with PFP and showed that pain caused a significant increase in quadriceps inhibition and a reduced muscle activation of the knee flexor and knee extensor muscles.

However, future research should focus on:

- the medium and long term effects of the Powers^{TM} strap and the 6-week exercise treatment,
- the effects of an exercise treatment in "strong" individuals with PFP compared with "weak" and "weak and tight" individuals with PFP,

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Appendices

Appendix Chapter 2:

Methods 2.1 Literature search keywords

Methods 2.2 Quality checklists

Methods 2.3 Inclusion criteria for the meta-analysis

Table 2.1-2.3. Characteristics of included studies: study demographics

Table 2.4-2.6 Characteristics of included studies: Downs and Black quality checklist

Table 2.7-2.9 Characteristics of included studies: additional quality checklist

Table 2.10-2.30 Meta-Analysis: forest plots of all studies

Table 2.31-2.35 Regression-analysis of Factors potentially related to heterogeneity

Appendix Chapter 3:

Methods 3.1: HSCR 15-22 approval letter

Methods 3.2: Participant information sheet

Methods 3.3: Informed Consent form

Methods 3.4: Health history questionnaire

Appendix Chapter 4:

Methods 4.1.: HSCR 15-22 approval letter

Methods: 4.2 History questionnaire for individuals with PFP

Appendix Chapter 5:

Methods 5.1.: HSCR 15-22 approval letter

Appendix Chapter 6:

Methods 6.1.: HSCR 15-22 approval letter

Methods 2.1 Literature Search Keywords

1. PFPS
2. PFP
3. AKP
4. AKPS
5. Patellar pain
6. Knee pain
7. Anterior knee pain
8. Patellofemoral pain
9. OR 1 2 3 4 5 6 7 8 9
10. Muscle strength
11. Strength
12. Weak*
13. Weakness
14. Vast*
15. Vastus
16. Glut*
17. Gluteus
18. Force
19. Muscle force
20. Power
21. Muscle power
22. Imbalance
23. Dysbalance
24. Isometric
25. Isokinetic
26. Concentric
27. Eccentric
28. EMG
29. Electromyography
30. Electromyographic
31. Onset
32. Amplitude
33. frequency
34. OR 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33
35. 9 AND 35
36. Inhibition
37. AMI
38. Central activation ratio
39. CAR
40. Central fatigue
41. OR 36 37 38 39 40
42. 9 AND 41
43. Flexibility
44. Hamstrings
45. Quadriceps
46. Iliotibial band
47. ITB

48. Quad*
49. OR 43 44 45 46 47 48
50. 9 AND 49
51. Atrophy
52. Muscle mass
53. OR 51 52
54. 9 AND 53

The syntax was altered appropriately when using other databases, but the search keywords remained identical in
all searches.

Methods 2.2 Quality checklists

Downs checklist:

11. *Is the hypothesis/aim/objective of the study clearly described?*
12. *Are the main outcomes to be measured clearly described in the Introduction or Methods section?* If the main outcomes are first mentioned in the Results section, the question should be answered no.
13. *Are the characteristics of the patients included in the study clearly described*? In cohort studies and trials, inclusion and/or exclusion criteria should be given. In case-control studies, a case-definition and the source for controls should be given.
14. *Are the interventions of interest clearly described?* Treatments and placebo (where relevant) that are to be compared should be clearly described.
15. *Are the distributions of principal confounders in each group of subjects to be compared clearly described?* A list of principal confounders is provided
16. *Are the main findings of the study clearly described?* Simple outcome data (including denominators and numerators) should be reported for all major findings so that the reader can check the major analyses and conclusions. (This question does not cover statistical tests which are considered below).
17. *Does the study provide estimates of the random variability in the data for the main outcomes?* In non normally distributed data the inter-quartile range of results should be reported. In normally distributed data the standard error, standard deviation or confidence intervals should be reported. If the distribution of the data is not described, it must be assumed that the estimates used were appropriate and the question should be answered yes.
18. *Have all important adverse events that may be a consequence of the intervention been reported?* This should be answered yes if the study demonstrates that there was a comprehensive attempt to measure adverse events. (A list of possible adverse events is provided).
19. *Have the characteristics of patients lost to follow-up been described?* This should be answered yes where there were no losses to follow-up or where losses to follow-up were so small that findings would be unaffected by their inclusion. This should be answered no where a study does not report the number of patients lost to follow-up.
20. *Have actual probability values been reported (e.g. 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?*

	Yes	No	comments
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			

External validity

All the following criteria attempt to address the representativeness of the findings of the study and whether they may be generalised to the population from which the study subjects were derived.

21. Were the subjects asked to participate in the study representative of the entire population from which they were recruited? The study must identify the source population for patients and describe how the patients were selected. Patients would be representative if they comprised the entire source population, an unselected sample of consecutive patients, or a random sample. Random sampling is only feasible where a list of all members of the relevant population exists. Where a study does not report the proportion of the source population from which the patients are derived, the question should be answered as unable to determine.

	yes	no	UTD[1]	comments
11				

[1] Unable to determine

	yes	no	UTD	comments
12				
13				

22. *Were those subjects who were prepared to participate representative of the entire population from which they were recruited?* The proportion of those asked who agreed should be stated. Validation that the sample was representative would include demonstrating that the distribution of the main confounding factors was the same in the study sample and the source population.
23. *Were the staff, places and facilities where the patients were treated, representative of the treatment the majority of patients receive?* For the question to be answered yes the study should demonstrate that the intervention was representative of that in use in the source population. The question should be answered no if, for example, the intervention was undertaken in a specialist centre unrepresentative of the hospitals most of the source population would attend.

Internal validity - bias

	yes	no	UTD	comments
14				
15				
16				
17				
18				
19				
20				

24. *Was an attempt made to blind study subjects to the intervention they have received?* For studies where the patients would have no way of knowing which intervention they received, this should be answered yes
25. *Was an attempt made to blind those measuring the main outcomes of the intervention?*
26. *If any of the results of the study were based on "data dredging", was this made clear?* Any analyses that had not been planned at the outset of the study should be clearly indicated. If no retrospective unplanned subgroup analyses were reported, then answer yes.
27. *In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls?* Where follow-up was the same for all study patients the answer should yes. If different lengths of follow-up were adjusted for by, for example, survival analysis the answer should be yes. Studies where differences in follow-up are ignored should be answered no.
28. *Were the statistical tests used to assess the main outcomes appropriate?* The statistical techniques used must be appropriate to the data. For example nonparametric methods should be used for small sample sizes. Where little statistical analysis has been undertaken but where there is no evidence of bias, the question should be answered yes. If the distribution of the data (normal or not) is not described it must be assumed that the estimates used were appropriate and the question should be answered yes.
29. *Was compliance with the intervention/s reliable?* Where there was non compliance with the allocated treatment or where there was contamination of one group, the question should be answered no. For studies where the effect of any misclassification was likely to bias any association to the null, the question should be answered yes.
30. *Were the main outcome measures used accurate (valid and reliable)?* For studies where the outcome measures are clearly described, the question should be answered yes. For studies which refer to other work or that demonstrates the outcome measures are accurate, the question should be answered as yes.

Internal validity - confounding (selection bias)

31. *Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?* For example, patients for all comparison groups should be selected from the same hospital. The question should be answered unable to determine for cohort and case-control studies where there is no information concerning the source of patients included in the study.
32. *Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?* For a study which does not specify the time period over which patients were recruited, the question should be answered as no.
33. *Were study subjects randomised to intervention groups?* Studies which state that subjects were randomised should be answered yes except where method of randomisation would not ensure random allocation. For example alternate allocation would score no because it is predictable.
34. *Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?* All non-randomised studies should be answered no. If assignment was concealed from patients but not from staff, it should be answered no.
35. *Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?* This question should be answered no for trials if: the main conclusions of the study were based on analyses of treatment rather than intention to treat; the distribution of known confounders in the different treatment groups was not described; or the distribution of known confounders differed between the treatment groups but was not taken into account in the analyses. In nonrandomised studies if the effect of the main confounders was not investigated or confounding was demonstrated but no adjustment was made in the final analyses the question should be answered as no
36. *Were losses of patients to follow-up taken into account?* If the numbers of patients lost to follow-up are not reported, the question should be answered as unable to determine. If the proportion lost to follow-up was too small to affect the main findings, the question should be answered yes.

	yes	no	UTD	comments
21				
22				
23				
24				
25				
26				

Further checklist: Strength studies

		Yes	no	UTD	comments
Abstract	Is the abstract clear, transparent and sufficiently detailed written?				
Introduction	Is the scientific background and explanation of rationale provided?				

Participant information: (one reviewer)

Sample size, Gender				Mean age (range/ SD)	
PFP (S)		Control		PFP(S)	Control
♀	♂	♀	♂		

PFP criteria: (one reviewer)

Inclusion criteria PFP(S)			Exclusion criteria PFP(S)		
Clearly defined pain location	Duration longer than at least 6 weeks	reproducible pain with: stairs, squatting, kneeling, prolonged sitting, isom. quadr. contraction	Previous surgery	Ligamentous instability	Internal derangement or other causes

One reviewer:	yes	no	Comments/ details
Are questionnaires included?			
Which tasks (squat, running,...)			
How was pain assessed?			If VAS mean & SD:
Are patients having pain during the task/ strength measurement/...?			If yes how much (mean & SD)?

		Yes	**no**	**UTD**	**comments**
Methods	A power calculation was executed?				If yes: value = if not: calculation with GPower
	Is the assessment with sufficient details to allow replication?				
	Reliability and validity is provided or mentioned for each assessment?				
	If walking as a task was included, was the gait cycle model explained?				
Discussion	The study discussed the clinical relevance of the data?				

Isokinetic/ isometric measurements:

		Yes	No	UTD	Comments
Methods	Is the position of how resistance was applied well described to allow replication? (height of resistance, degrees of flexion/ abd., etc)?				
	Does the study provide enough numerical data?				
	Did they ensure an appropriate fixation?				
	Did they test the reliability and validity of their methods?				
	If HHD was used did they fixate it in a standardized manner?				

EMG checklist:

EMG (just one reviewer):

What did they analyze?	On- offset	Amplitude	Frequency
Procedure of normalization			
Which muscles have been assessed?			
Values of measurements:			

EMG measurements:

		Yes	no	UTD	comments
Methods	Did they follow guidelines for the application of the EMG?				
	Is the position of how electrodes were placed well described to allow replication?				
	Is the filtering procedure well described to allow replication?				
	Is the normalization procedure well described to allow replication?				

Methods 2.3 Inclusion criteria for the meta-analysis:

1. If studies provided data from patients-group with different pain-levels, the data of all patients with the different pain levels was averaged.
2. If studies provided data from patient-groups which were subdivided into bilateral and unilateral pain, the data of both groups was averaged.
3. If studies tested the affected and the not affected leg, only the data of the affected leg was included
4. If studies provided data of individual components of a muscles (e.g. quadriceps: vastus medialis, lateralis, rectus femoris) as well as the overall result of the muscle, only the overall result of the quadriceps was included. If the overall result of the muscle was not given, it was calculated by averaging the results of the individual components.
5. If studies included different step heights, only the step height which was closest to the average step height of 19.5 cm (± 3.03SD, range: 15.24 to 25.4 cm) was included.
6. If studies had published raw data and normalised strength data, only the normalised data was included, as normalised data is more representative and was published in all strength studies.
7. If studies published data of the average and the peak strength, only the peak strength results were included, as the majority of studies had published peak strength.
8. If studies published data of the isometric and isokinetic strength, only the data of the isokinetic strength was included, as the isokinetic dynamometers are considered as the gold standard in simultaneous strength and angle measurements for the evaluation of dynamic muscular performance (Kannus, 1994; H. Lund et al., 2005; Pincivero et al., 1997)
9. If studies presented results for the eccentric and concentric phase these results were averaged, as most studies presented the average force of the movement throughout an isokinetic task.
10. If studies provided data from isokinetic measurements at different speeds only the results at 60 degrees/seconds were included, as this speed had been assessed in all isokinetic trials.
11. If studies reported the mean and peak results of the amplitude. Only the mean amplitude results had been included, as the differences between mean and peak amplitude had been

shown to be not significant and the mean amplitude was more representative throughout the studies (Esculier: peak amplitude: SMD: -0.52, 95% CI: -1.15 to 0.1, Willson: peak amplitude: SMD: 0.54, 95% CI: -0.1 to 1.17) (J.-F. Esculier et al., 2015; Willson et al., 2011).

12. To ensure that the results within the meta-analysis were representative and that the heterogeneity between the studies was reduced, a hierarchy of activities was developed. If studies measured the individual during several activities only the data from the activity which was highest in the hierarchy was included. The main two criteria for the hierarchy were:
    a. The more frequently activities were used within the studies the higher the activity was ranked.
    b. The more similar the activities were, the higher they were ranked. Additionally the following criteria were applied: closed kinetic chain over open kinetic chain and eccentric over concentric exercises.

    The highest rank (1) was assigned to "squatting" (single leg squat or double leg squat). The second highest rank (2) was given to closed kinetic chain exercises, which were mostly leg press exercises and thus closely related to squatting. The third rank (3) was assigned to "stair stepping" (whereby in studies data on ascending and descending stairs was averaged to make it comparable to studies which had analysed the "stair stepping" task). The following ranks were 4) eccentric quadriceps exercises; 5) stair descending, 6) stair ascending, 7) ramp descending and 8) ascending, 9) anterior reach test and 10) single leg vertical jump. More information can be found in the table of hierarchy
13. If studies compared the muscle activity ratio during different joint angles of knee flexion, only the knee flexion degree results which were closest to the average of 45° degrees knee flexion were included.
14. If studies had assessed the quadriceps flexibility by using different tests, only the data from the Ely's test was included as it was used in all studies.
15. If studies distinguished the results between female and male participant the data was averaged.

Table 2.1: Characteristics of included studies: strength studies

Paper	sample size PFP			sample size control			low: range	upper: range	age		height (m)		weight (kg)		VAS	AKPS
	♀	♂	♂♀	♀	♂	♂♀			PFP	control	PFP	control	PFP	control	mean	mean
Boling (2009)	13	7	20	13	7	20	18	40	26.8	25.6	171.8	169.5	72.4	70	5.06	68.9
Callaghan (2004)	35	22	57	6	4	10	-	-	-	-	-	-	-	-	-	-
Cichanowski (2007)	13	0	13	13	0	13	-	-	19.3	19.5	177	192	68.6	61.4	-	-
De Moura Campos (2014)	20	0	20	20	0	20	20	40	23	24	162	163	56.8	61.9	6	78.9
Dierks (2008)	15	5	20	15	5	20	18	45	24.1	24.6	171	170	65.75	63.02	4.9	-
Duvigneaud (2008)	26	0	26	36	0	36	18	34	-	-	166.8	167.1	60.2	61.9	-	-
Dvir (1990)	21	34	55	15	15	30	18	42	20.5	19	-	-	-	-	-	-
Ferber (2011)	10	5	15	6	4	10	-	-	35.2	29.9	165	173	69.1	73.1	-	-
Ireland (2003)	15	0	15	15	0	15	12	21	15.7	15.7	-	-	63.1	56.6	5.8	-
Kaya (2010)	0	12	12	0	16	16	15	45	26.08	22.37	173.75	176	72.83	76.62	6.33	-
Magalhaes (2010)	50	0	50	50	0	50	15	40	24.6	24.1	161.8	161.2	59.7	57.9	1.3	-
McMoreland (2011)	12	0	12	12	0	12	19	31	23	21	165.75	164.58	62.75	62.58	-	-
Moradi (2014)	12	0	12	12	0	12	19	23	20.58	20.83	162	162	58.74	58.54	-	-
Nakagawa (2012)	20	20	40	20	20	40	18	35	23.25	22.7	173	169.5	69.05	67	-	-
Nakagawa (2015)	20	10	30	20	10	30	18	35	22.7	22.3	171.3	168.6	65.3	63.3	-	-
Oliveira (2014)	25	0	25	20	0	20	-	-	22.2	23.36	159.3.4	154.62	55.34	57.36	-	-
Ott (2011)	-	-	20	-	-	20	18	45	20.9	22.6	170.69	168.21	70.34	65.5	1.24	
Piva (2005)	17	13	30	17	13	30	20	42	25.8	25.7	169.7	170.9	76.9	68.8	3.9	-
Powers (1997)	19	0	19	19	0	19	14	46	25.4	27.5	165.1	165.3	62.4	59.2	4.4	-
Rathleff (2013)	16	4	20	16	4	20	12	16	14.6	14.8	167	167.4	55.2	56.1	5.5	-
Robinson (2007)	10	0	10	10	0	10	12	35	21	26.6	-	-	63.5	66.5	-	69.7
Souza (2009)	19	0	19	19	0	19	-	45	27	26	169	169	64.7	62.9	-	-
Thijs (2011)	16	0	16	61	0	61	-	-	41.6	37.5	166	167	70.1	68.3	-	-
Thomeé (1996)	11	0	11	20	0	20	17	30	23.5	24.7	165.6	167.3	60.7	61.8	4.2	-
Van Tiggelen (2004)	0	31	31	0	65	65	17	27	-	-	178.4	181.5	70.6	70.2	-	-
Werner (1995)	14	13	27	14	13	27	-	-	28.1	-	-	-	-	-	-	-
mean x (SD)	19.38 (15.02)	7.69 (10.46)	26.81 (19.42)	19.12 (14.5)	7.62 (13.63)	26.48 (16.98)	16.74 (2.62)	35.85 (8.85)	24.62 (6.05)	24.15 (5.2)	168.8 (4.7)	169.19 (7.51)	65.15 (5.87)	64.2 (5.48)	4.42 (1.73)	72.5 (5.56)

Table 2.2: Characteristics of included studies: electromyographic studies

Paper	sample size PFP			sample size control			lower range:	upper: range	age		height (m)		weight (kg)		VAS	AKPS
	♀	♂	♂♀	♀	♂	♂♀			PFP	control	PFP	control	PFP	control	mean	Mean
Aminaka (2011)	13	7	20	13	7	20	-	-	21.45	21.35	169.96	172.21	71.3	69.68	-	-
Bley (2014)	20	0	20	20	0	20	18	35	23.5	23.1	165	162	55.3	55.9	4.9	80.2
Bolgla (2011)	18	0	18	18	0	18	-	-	24.5	23.9	170	170	63.1	62.1	4.4	-
Boling (2006)	9	5	14	9	5	14	18	42	24	23	167.5	171	71.6	72.4	5.32	-
Briani (2015)	31	0	31	28	0	28	-	-	21.9	22.07	165	165	65.72	62.3	-	-
Cavazzuti (2010)	13	2	15	10	10	20	12	50	19	23	-	-	-	-	-	-
Coqueiro (2005)	10	0	10	10	0	10	-	-	23.2	21.8	158	165	50.53	58.38	-	-
Earl (2005)	13	3	16	13	3	16	-	-	21.5	21.1	165.3	165.6	62.1	65	-	-
Esculier (2015)	16	5	21	15	5	20	18	45	34.1	33.2	167.8	169.1	67.4	62.8	2.8	-
Felicio (2011)	19	0	19	20	0	20			23.5	21.5	161.6	160.8	57.9	54.4	-	-
Ferrari (2014)	-	-	22	-	-	29	18	30	20.42	22.65	164	164	57.94	61.79	-	-
Karst (1995)	18	6	24	16	8	24	15	46	28.3	28.8	172	173.6	64.4	66	-	-
Kaya (2010)	0	12	12	0	16	16	15	45	26.08	22.37	173.75	176	72.83	76.62	-	-
Liebensteiner (2008)	11	8	19	11	8	19	-	40	25.2	25.7	174	177	66.1	66.9	-	-
Mostamand (2011)	7	11	18	7	11	18	-	40	27.9	26.4	171	172	71.5	71.6	-	-
Nakagawa (2011)	9	0	9	10	0	10	18	35	23.33	22.7	165.2	163.4	61.39	56	-	73
Nakagawa (2012)	20	20	40	20	20	40	18	35	23.25	22.7	173	169.5	69.05	67	-	-
Nakagawa (2015)	20	10	30	20	10	30	18	35	22.7	22.3	171.3	168.6	65.3	63.3	-	-
O'Sullivan (2012)	12	0	12	12	0	12	18	35	23	21	165.7	164.6	62.8	62.6	0.33	78
Ott (2011)	-	-	20	-	-	20	18	45	20.9	22.6	170.69	168.21	70.34	65.5	1.24	-
Owings (2002)	12	8	20	4	10	14	-	-	31.86	23.89	169.8	175.78	77.12	74.19	-	-
Powers (1996)	26	0	26	19	0	19	14	46	25.6	27.5	165.1	165.3	63.9	59.2	-	-
Saad (2011)	15	0	15	15	0	15	-	-	23.16	23.3	159.66	160.4	58.66	53.47	-	-
Song (2014)	16	0	16	8	0	8	-	-	25.7	28.6	164.1	161.1	55.5	52.1	4.16	77.8
Willson (2011)	20	0	20	20	0	20	18	35	21.3	21.6	168	169	62.9	62.1	-	-
mean x (SD)	15.13 (6.55)	4.22 (5.36)	19.48 (6.92)	13.83 (6.37)	4.91 (5.87)	19.2 (7.05)	16.86 (1.99)	39.94 (5.78)	24.21 (3.45)	23.85 (2.96)	167.39 (4.32)	167.88 (4.94)	64.36 (6.41)	63.39 (6.55)	3.31 (1.91)	77.25 (3.03)

Table 2.3: Characteristics of included studies: flexibility, fatigue/ endurance, inhibition, atrophy and break phenomenon studies

Flexibility	sample size PFP			sample size control			lower range:	upper: range	age		height (m)		weight (kg)		VAS	PSS
	♀	♂	⚥	♀	♂	⚥			PFP	control	PFP	control	PFP	control	mean	Mean
Earl (2005)	13	3	16	13	3	16	-	-	21.5	21.1	165.3	165.6	62.1	65	-	
Hudson (2009)	4	8	12	4	8	12	18	40	32.9	30.6	171.5	173.8	75.3	71	-	-
Ohejoung (2014)	9	5	14	23	19	42	18	25	22.1	21.9	167.4	167.1	62	57.64	-	-
Peeler (2007)	24	16	40	13	30	43	18	45	31	28	169	167	71.2	68.2	-	28
Piva (2005)	17	13	30	17	13	30	20	42	25.8	25.7	169.7	170.9	76.9	68.8	3.9	-
White (2009)	11	6	17	12	13	25	18	35	27	25.2	171	175	77.7	74.3	3.1	-
Witvrouw (2000)	13	11	24	118	140	258	17	21	-	-	179.3	180.16	68.14	69.96	-	-
mean x (SD)	13 (6.3)	8.86 (4.67)	21.86 (10.14)	28.57 (39.84)	32.29 (48.26)	60.86 (87.73)	18.17 (0.98)	34.67 (9.69)	26.72 (4.6)	25.42 (3.6)	170.46 (4.44)	171.37 (5.28)	70.48 (6.64)	67.84 (5.31)	3.5 (0.57)	28
Fatigue/ endurance	sample size PFP			sample size control			lower range:	upper: range	age		height (m)		weight (kg)		VAS	PSS
	♀	♂	⚥	♀	♂	⚥			PFP	control	PFP	control	PFP	control	mean	Mean
Bazett Jones (2013)	9	10	19	9	10	19	18	40	26	24.3	174	174	77.3	70.2	-	-
Callaghan (2001)	-	-	10	-	-	10	-	-	31.3	29.7	-	-	-	-	4	-
Dierks (2008)	15	5	20	15	5	20	18	45	24.1	24.6	171	170	65.75	63.02	4.9	-
Negahban (2013)	12	3	15	12	3	15	19	35	25.8	25.2	164	164	-	-	5.66	-
McMoreland (2011)	12	0	12	12	0	12	19	31	23	21	165.75	164.58	62.75	62.58	-	-
Willson (2008)	20	0	20	20	0	20	18	35	23.3	23.7	166	166	61.5	61.1	-	80.4
mean x (SD)	13.6 (4.16)	6 (3.6)	16 (4.34)	13.6 (4.16)	6 (3.6)	16 (4.34)	18.4 (0.55)	37.2 (5.4)	25.58 (3.07)	24.75 (2.84)	168.15 (4.18)	167.72 (4.22)	66.83 (7.21)	64.23 (4.07)	4.85 (0.83)	80.4
Inhibition	sample size PFP			sample size control			lower range:	upper: range	age		height (m)		weight (kg)		VAS	PSS
	♀	♂	⚥	♀	♂	⚥			PFP	control	PFP	control	PFP	control	mean	Mean
Suter (1998)	6	13	19	5	12	17	-	-	35.6	-	-	-	-	-	-	-
Thomeé (1996)	11	0	11	20	0	20	17	30	23.5	24.7	165.6	167.3	60.7	61.8	4.2	-
mean x (SD)	8.5 (3.54)	6.5 (9.19)	15 (5.66)	12.5 (10.61)	6 (8.49)	18.5 (2.12)	17	30	29.55 (8.56)	24.7	165.6	167.3	60.7	61.8	4.2	-
Atrophy	sample size PFP			sample size control			lower range:	upper: range	age		height (m)		weight (kg)		VAS	PSS
	♀	♂	⚥	♀	♂	⚥			PFP	control	PFP	control	PFP	control	mean	Mean
Callaghan (2004)	35	22	57	6	4	10			34.4	30.6	-	-	-	-	-	-
Giles (2015)	20	15	35	20	15	35	18	40	28.2	28.3	172.5	171.2	72.6	72.6	5.4	-
Jan (2009)	41	13	54	41	13	54		50	40.8	40.8	160.7	160.1	58.4	57.9	-	-
Pattyn (2011)	25	21	46	17	13	30	12	40	25	21.6	173.4	173.1	68.9	66.7	-	-
mean x (SD)	30.25 (9.5)	17.75 (4.43)	48 (9.83)	21 (14.63)	11.25 (4.92)	32.25 (18.08)	15 (4.25)	43.33 (5.77)	32.1 (6.99)	30.33 (7.96)	168.87 (7.09)	168.13 (7.02)	66.63 (7.37)	65.73 (7.4)	5.4	-
Break phenomenon	sample size PFP			sample size control			lower range:	upper: range	age		height (m)		weight (kg)		VAS	PSS
	♀	♂	⚥	♀	♂	⚥			PFP	control	PFP	control	PFP	control	mean	Mean
Anderson (2003)	20	0	20	20	0	20	19	29	166	167	63.7	62.7	29	166	-	-

Table 2.4: Characteristics of included studies: Downs and Black quality checklist for strength studies

Paper	1 clear aim	2 clear outcome measure	3 clear patients characteristics	4 clear explanation of methodology	6 clear findings	7 random variability outcome	10 clear p-values	11 subject representativity	12 population representativity	18 appropriate statistics	20 accurate outcomes	21 appropriate case-control matching	27 power analysis	total of 13
Boling (2009)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	No	Yes	Yes	No	9
Callaghan (2004)	Yes	Yes	No	No	Yes	Yes	Yes	UTD	UTD	Yes	Yes	UTD	Yes	8
Cichanowski (2007)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	No	Yes	Yes	Yes	10
De Moura Campos (2014)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	11
Dierks (2008)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	No	Yes	Yes	Yes	10
Duvigneaud (2008)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	No	11
Dvir (1990)	Yes	Yes	No	Yes	Yes	Yes	Yes	UTD	UTD	No	Yes	Yes	No	9
Ferber (2011)	Yes	Yes	Yes	No	Yes	Yes	Yes	UTD	UTD	Yes	Yes	No	Yes	9
Ireland (2003)	Yes	Yes	No	Yes	Yes	Yes	Yes	UTD	UTD	No	Yes	Yes	Yes	9
Kaya (2010)	Yes	Yes	Yes	No	Yes	Yes	Yes	UTD	UTD	No	Yes	No	Yes	8
Magalhaes (2010)	Yes	Yes	Yes	Yes	Yes	Yes	No	YES	UTD	No	Yes	Yes	No	9
McMoreland (2011)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	No	Yes	UTD	No	8
Moradi (2014)	Yes	Yes	Yes	Yes	Yes	Yes	No	UTD	UTD	No	Yes	Yes	No	8
Nakagawa (2012)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	13
Nakagawa (2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	Yes	Yes	Yes	No	10
Oliveira (2014)	Yes	Yes	Yes	No	Yes	Yes	No	UTD	UTD	UTD	Yes	Yes	No	7
Ott (2011)	Yes	Yes	No	Yes	Yes	Yes	Yes	UTD	UTD	No	Yes	UTD	No	7
Piva (2005)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	Yes	Yes	Yes	Yes	11
Powers (1997)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	Yes	Yes	Yes	No	10
Rathleff (2013)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	13
Robinson (2007)	Yes	Yes	No	Yes	Yes	Yes	Yes	UTD	UTD	Yes	Yes	UTD	No	8
Souza (2009)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	11
Thijs (2011)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	10
Thomeé (1996)	Yes	Yes	Yes	UTD	Yes	Yes	Yes	UTD	UTD	No	Yes	Yes	No	8
Van Tiggelen (2004)	Yes	Yes	No	Yes	Yes	Yes	Yes	UTD	UTD	No	Yes	UTD	No	8
Werner (1995)	Yes	Yes	No	Yes	Yes	Yes	Yes	UTD	UTD	Yes	Yes	UTD	No	8

Table 2.5: Characteristics of included studies: Downs and Black quality checklist for electromyographic studies

Paper	1 clear aim	2 clear outcome measure	3 clear patients characteristics	4 clear explanation of methodology	6 clear findings	7 random variability outcome	10 clear p-values	11 subject representativity	12 population representativity	18 appropriate statistics	20 accurate outcomes	21 appropriate case-control matching	27 power analysis	total of 13
Aminaka (2011)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	Yes	Yes	Yes	No	10
Bley (2014)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	Yes	Yes	Yes	Yes	11
Bolgla (2011)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	No	UTD	Yes	No	8
Boling (2006)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	No	Yes	Yes	No	9
Briani (2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	Yes	Yes	Yes	Yes	11
Cavazzuti (2010)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	No	Yes	No	No	8
Coqueiro (2005)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	No	Yes	Yes	No	9
Earl (2005)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	No	Yes	Yes	Yes	10
Esculier (2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	Yes	Yes	Yes	No	10
Felicio (2011)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	No	Yes	Yes	No	9
Ferrari (2014)	Yes	Yes	No	No	Yes	Yes	No	UTD	UTD	No	Yes	UTD	No	5
Karst (1995)	Yes	Yes	Yes	No	Yes	Yes	Yes	UTD	UTD	No	Yes	Yes	No	8
Kaya (2010)	Yes	Yes	Yes	UTD	Yes	Yes	Yes	UTD	UTD	No	Yes	UTD	Yes	8
Liebensteiner (2008)	Yes	Yes	Yes	No	Yes	Yes	Yes	UTD	UTD	Yes	Yes	Yes	Yes	10
Mostamand (2011)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	No	Yes	Yes	No	9
Nakagawa (2011)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	Yes	Yes	Yes	No	10
Nakagawa (2012)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	13
Nakagawa (2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	Yes	Yes	Yes	No	10
O'Sullivan (2012)	Yes	Yes	Yes	No	Yes	Yes	Yes	UTD	UTD	Yes	Yes	Yes	Yes	10
Ott (2011)	Yes	Yes	No	No	Yes	Yes	Yes	UTD	UTD	Yes	Yes	UTD	No	7
Owings (2002)	Yes	Yes	Yes	No	Yes	Yes	Yes	UTD	UTD	Yes	Yes	No	No	8
Powers (1996)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	Yes	Yes	Yes	No	10
Saad (2011)	Yes	Yes	Yes	No	Yes	Yes	Yes	UTD	UTD	No	Yes	Yes	No	9
Song (2014)	Yes	Yes	Yes	No	Yes	Yes	Yes	UTD	UTD	Yes	Yes	Yes	Yes	10
Willson (2011)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	No	Yes	Yes	Yes	10

Table 2.6: Characteristics of included studies: Downs and Black quality checklist for flexibility, fatigue/ endurance, inhibition, atrophy and break phenomenon studies

Paper	1 clear aim	2 clear outcome measure	3 clear patients characteristics	4 clear explanation of methodology	6 clear findings	7 random variability outcome	10 clear p-values	11 subject representativity	12 population representativity	18 appropriate statistics	20 accurate outcomes	21 appropriate case-control matching	27 power analysis	total of 13
Flexibility studies														
Earl (2005)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	No	Yes	Yes	Yes	10
Hudson (2009)	Yes	Yes	No	Yes	Yes	Yes	Yes	UTD	UTD	Yes	Yes	Yes	Yes	10
Ohejoung (2014)	Yes	Yes	No	No	Yes	Yes	No	UTD	UTD	No	Yes	Yes	No	6
Peeler (2007)	Yes	Yes	Yes	Yes	Yes	Yes	No	UTD	UTD	No	Yes	Yes	No	8
Piva (2005)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	Yes	Yes	Yes	Yes	11
White (2009)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	Yes	Yes	UTD	No	9
Witvrouw (2000)	Yes	Yes	No	No	Yes	Yes	Yes	UTD	UTD	Yes	Yes	UTD	Yes	8
Fatigue and endurance studies														
Bazett Jones (2013)	Yes	Yes	Yes	No	Yes	Yes	Yes	UTD	UTD	Yes	Yes	Yes	No	9
Callaghan (2001)	Yes	Yes	No	Yes	Yes	Yes	Yes	UTD	UTD	Yes	Yes	UTD	UTD	8
Dierks (2008)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	No	Yes	Yes	Yes	10
McMoreland (2011)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	No	Yes	UTD	No	8
Negahban (2013)	Yes	Yes	No	Yes	Yes	Yes	No	UTD	UTD	No	Yes	UTD	No	6
Willson (2008)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	Yes	Yes	UTD	Yes	10
Muscle inhibition studies														
Suter (1998)	Yes	Yes	No	Yes	No	No	No	UTD	UTD	Yes	Yes	UTD	No	5
Thomeé (1996)	Yes	Yes	Yes	UTD	Yes	Yes	Yes	UTD	UTD	No	Yes	Yes	No	8
Muscle atrophy studies														
Callaghan (2004)	Yes	Yes	No	Yes	Yes	Yes	Yes	UTD	UTD	Yes	Yes	UTD	Yes	9
Giles (2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	No	Yes	Yes	No	9
Jan (2009)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	No	Yes	Yes	No	9
Pattyn (2011)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	UTD	UTD	Yes	Yes	Yes	No	10
Break phenomenon studies														
Herrington (2003)	Yes	Yes	No	Yes	Yes	Yes	Yes	UTD	UTD	UTD	UTD	UTD	No	6

Table 2.7: Characteristics of included studies: additional quality checklist for strength studies

Paper	general questionnaire					strength questionnaire				total	Max score	Overall score	High/ Moderate or low quality
	clear abstract	clear introduction	allow replication	Reliability for measures	clinical relevance	clear position	enough numerical data	appropriate fixation	HHD fixated				
Boling (2009)	Yes	Yes	8	Yes	Yes	Yes	Yes	Yes	Not needed	8	21	17	81% MQ
Callaghan (2004)	Yes	Yes	7	Yes	Yes	Yes	Yes	Yes	Not needed	7	22	15	68.2% LQ
Cichanowski (2007)	Yes	Yes	5	No	No	Yes	Yes	No	No	5	22	15	68.2% LQ
De Moura Campos (2014)	Yes	Yes	6	Yes	No	Yes	Yes	No	No	6	22	17	77.3% MQ
Dierks (2008)	Yes	Yes	8	Yes	No	Yes	Yes	Yes	Yes	8	22	18	81.8% MQ
Duvigneaud (2008)	Yes	Yes	6	No	No	Yes	Yes	Yes	Not needed	6	21	17	81% MQ
Dvir (1990)	Yes	Yes	8	Yes	Yes	Yes	Yes	Yes	Not needed	8	21	17	81% MQ
Ferber (2011)	Yes	Yes	5	No	Yes	No	Yes	UTD	UTD	5	22	14	63.6% LQ
Ireland (2003)	Yes	Yes	8	No	Yes	Yes	Yes	Yes	Yes	8	22	17	77.3% MQ
Kaya (2010)	Yes	Yes	4	No	Yes	No	Yes	UTD	Not needed	4	21	12	57.4% LQ
Magalhaes (2010)	Yes	Yes	7	Yes	Yes	Yes	Yes	No	No	7	22	16	72.7% MQ
McMoreland (2011)	Yes	Yes	8	Yes	Yes	Yes	Yes	Yes	Not needed	8	21	16	76.2% MQ
Moradi (2014)	Yes	Yes	8	No	Yes	Yes	Yes	Yes	Yes	8	22	16	72.7% MQ
Nakagawa (2012)	Yes	Yes	8	Yes	Yes	Yes	Yes	Yes	Yes	8	22	21	95.5% HQ
Nakagawa (2015)	Yes	Yes	9	Yes	No	Yes	Yes	Yes	Yes	9	22	19	86.4% HQ
Oliveira (2004)	Yes	Yes	6	Yes	Yes	Yes	Yes	UTD	Not needed	6	21	13	61.9% LQ
Ott (2011)	Yes	Yes	4	No	Yes	No	Yes	UTD	Not needed	4	22	12	54.5% LQ
Piva (2005)	Yes	Yes	6	Yes	No	Yes	Yes	No	No	6	22	17	77.3% MQ
Powers (1997)	Yes	Yes	5	No	Yes	No	Yes	Yes	Not needed	5	21	15	71.4% MQ
Rathleff (2013)	Yes	Yes	9	Yes	Yes	Yes	Yes	Yes	Yes	9	22	22	100% HQ
Robinson (2007)	Yes	Yes	6	Yes	No	Yes	Yes	No	UTD	6	22	14	63.6% LQ
Souza (2009)	Yes	Yes	7	Yes	No	Yes	Yes	Yes	Not needed	7	21	18	85.7% HQ
Thijs (2011)	Yes	Yes	6	Yes	No	Yes	Yes	No	No	6	22	16	72.7% MQ
Thomeé (1996)	Yes	Yes	7	Yes	Yes	Yes	No	Yes	Not needed	7	21	15	71.4% MQ
Van Tiggelen (2004)	Yes	Yes	6	No	No	Yes	Yes	Yes	Not needed	6	21	14	66.7% LQ
Werner (1995)	Yes	Yes	5	Yes	Yes	No	No	UTD	Not needed	5	21	13	61.9% LQ

Table 2.8: Characteristics of included studies: additional quality checklist for electromyographic studies

Paper	general questionnaire					Muscle activity questionnaire				total	Max score	Overall score	High/ Moderate or low quality
	clear abstract	clear introduction	allow replication	Reliability for measures	clinical relevance	Existing guidelines	Electrode placement allow replication	Filtering procedure well described	Normalisation procedure well described				
Aminaka (2011)	Yes	Yes	UTD	No	Yes	No	Yes	Yes	Not needed	5	21	15	71.4% MQ
Bley (2014)	Yes	Yes	UTD	UTD	Yes	No	Yes	Yes	UTD	5	22	16	72.7% MQ
Bolgla (2011)	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Not needed	7	21	15	71.4% MQ
Boling (2006)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Not needed	8	21	17	81% MQ
Briani (2015)	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Not needed	6	21	17	81% MQ
Cavazzuti (2010)	Yes	Yes	Yes	No	Yes	UTD	Yes	Yes	Yes	7	22	15	68.2% LQ
Coqueiro (2005)	Yes	Yes	No	Yes	Yes	No	Yes	No	Yes	6	22	15	68.2% LQ
Earl (2005)	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Not needed	6	21	16	76.2% MQ
Esculier (2015)	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	7	22	17	77.3% MQ
Felicio (2011)	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No	6	22	15	68.2% LQ
Ferrari (2014)	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Not needed	6	21	11	52.4% LQ
Karst (1995)	Yes	Yes	No	Yes	Yes	Yes	UTD	UTD	Not needed	5	21	13	61.9% LQ
Kaya (2010)	Yes	Yes	Yes	No	Yes	No	Yes	No	Not needed	5	21	13	61.9% LQ
Liebensteiner (2008)	Yes	Yes	No	No	No	No	No	No	No	2	22	12	54.5% LQ
Mostamand (2011)	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	7	22	16	72.7% MQ
Nakagawa (2011)	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	7	22	17	77.3% MQ
Nakagawa (2012)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8	22	21	95.5% HQ
Nakagawa (2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9	22	19	86.4% HQ
O'Sullivan (2012)	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	6	22	16	72.7% MQ
Ott (2011)	Yes	Yes	No	No	Yes	Yes	Yes	No	No	5	22	12	54.5% LQ
Owings (2002)	Yes	Yes	No	No	No	Yes	No	No	Yes	4	22	12	54.5% LQ
Powers (1996)	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	6	22	16	72.7% MQ
Saad (2011)	Yes	Yes	No	No	Yes	No	Yes	No	Yes	5	22	14	63.6% LQ
Song (2014)	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No	6	22	16	72.7% MQ
Willson (2011)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8	22	18	81.8% MQ

Table 2.9: Characteristics of included studies: additional quality checklist for flexibility, fatigue/ endurance, inhibition, atrophy and break phenomenon studies

Paper	general questionnaire					total	Overall score	High/ Moderate or low quality
	clear abstract	clear introduction	allow replication	Reliability for measures	clinical relevance			
Flexibility studies								
Earl (2005)	Yes	Yes	Yes	No	Yes	4	14	77.8% MQ
Hudson (2009)	Yes	Yes	Yes	No	Yes	4	14	77.8% MQ
Ohejoung (2014)	Yes	Yes	No	No	Yes	3	9	50% LQ
Peeler (2007)	Yes	Yes	Yes	No	No	3	11	61.1% LQ
Piva (2005)	Yes	Yes	Yes	Yes	No	4	15	83.3% MQ
White (2009)	Yes	Yes	Yes	Yes	No	4	13	72.2% MQ
Witvrouw (2000)	Yes	Yes	UTD	No	UTD	2	10	55.6% LQ
fatigue and endurance studies								
Bazett Jones (2013)	Yes	Yes	No	No	Yes	3	12	66.7% LQ
Callaghan (2001)	Yes	Yes	Yes	Yes	UTD	4	12	66.7% LQ
Dierks (2008)	Yes	Yes	Yes	No	No	3	13	72.2% MQ
McMoreland (2011)	Yes	Yes	Yes	Yes	Yes	5	15	83.3% MQ
Negahban (2013)	Yes	Yes	Yes	No	Yes	4	10	55.6% LQ
Willson (2008)	Yes	Yes	Yes	No	Yes	4	14	77.8% MQ
Muscle inhibition studies								
Suter (1998)	Yes	Yes	Yes	No	Yes	4	9	50% LQ
Thomeé (1996)	Yes	Yes	Yes	Yes	Yes	5	13	72.2% MQ
Muscle atrophy studies								
Callaghan (2004)	Yes	Yes	No	Yes	Yes	4	13	72.2% MQ
Giles (2015)	Yes	Yes	Yes	No	Yes	4	13	72.2% MQ
Jan (2009)	Yes	Yes	Yes	Yes	Yes	5	14	77.8% MQ
Pattyn (2011)	Yes	Yes	Yes	Yes	Yes	5	15	83.3% MQ
Break phenomenon studies								
Herrington (2003)	Yes	Yes	Yes	No	Yes	4	9	50% LQ

Table 2.10: Forest plot of Effect Size for ankle strength

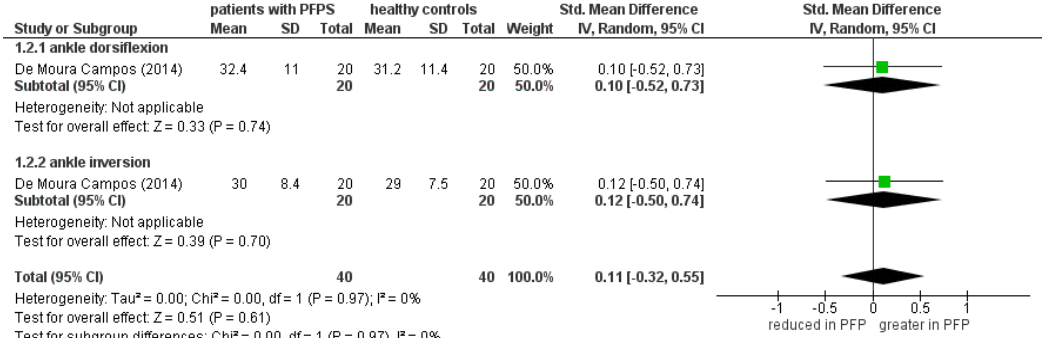

Table 2.11: Forest plot of Effect Size for knee strength

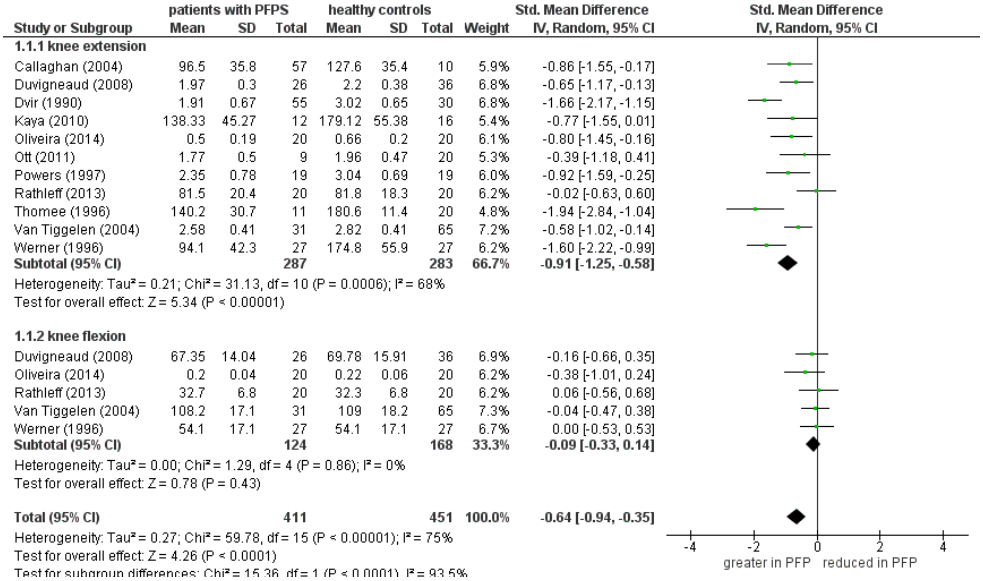

Table 2.12: Forest plot of Effect Size for trunk and pelvis strength

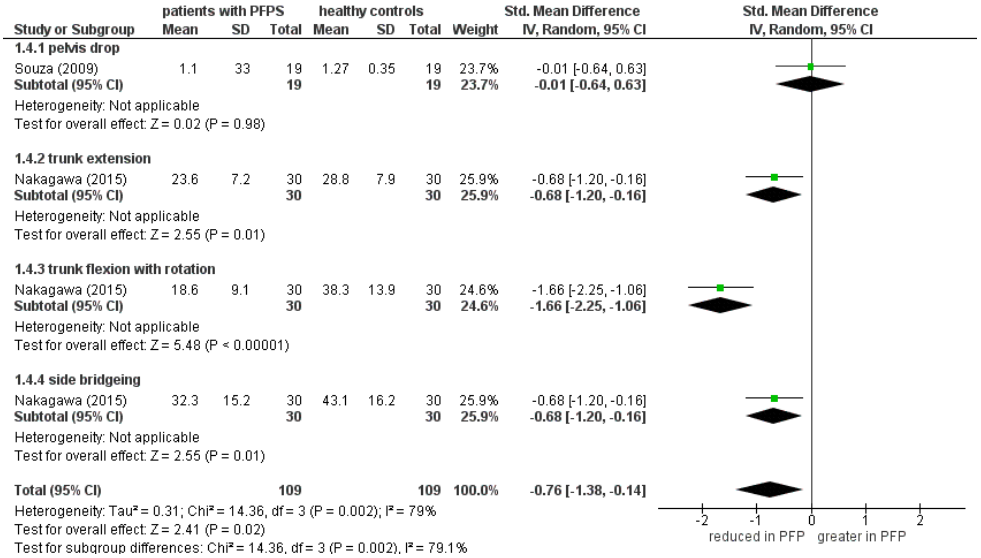

Table 2.13: Forest plot of Effect Size for hip strength

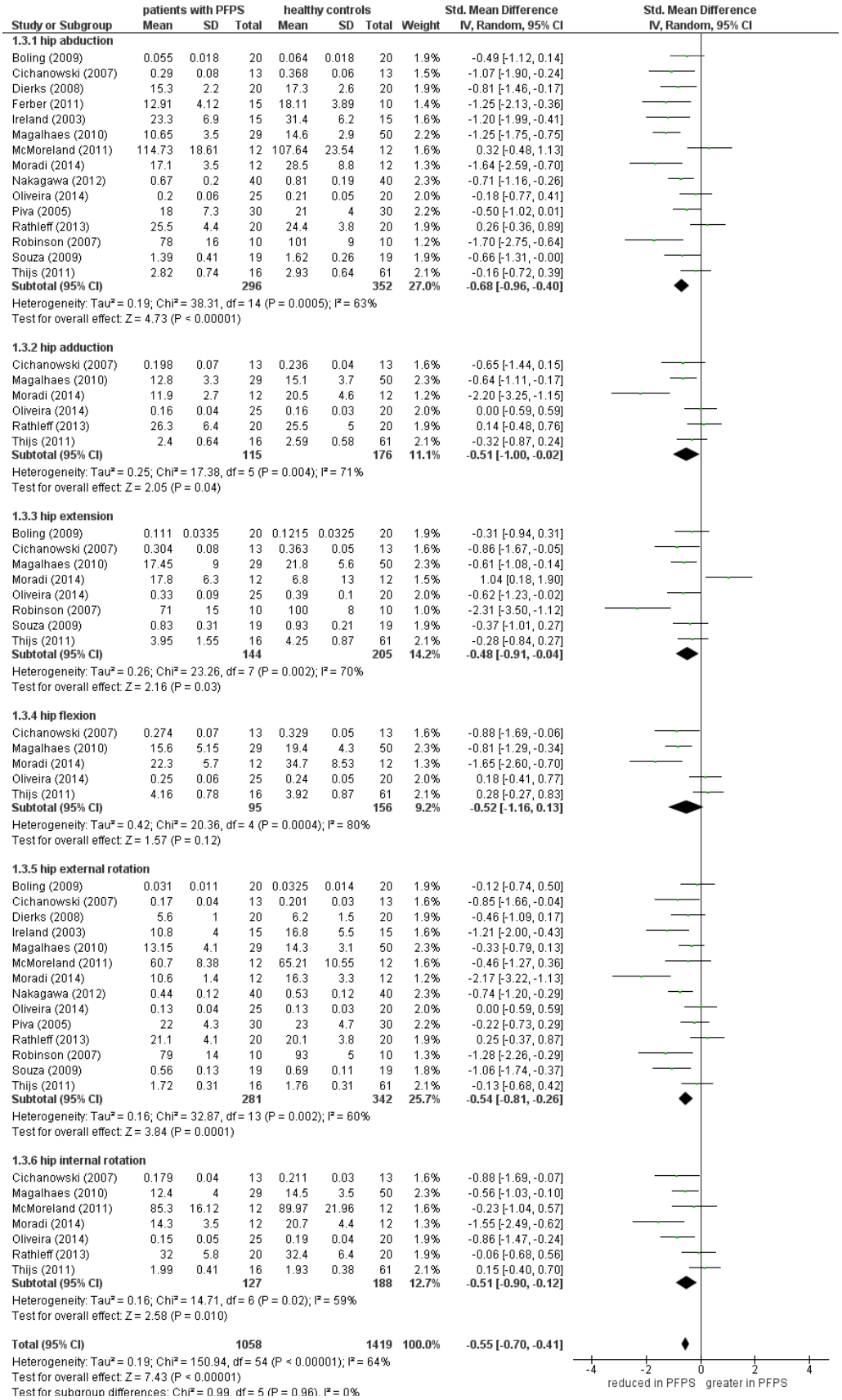

Table 2.14: Forest plot of Effect Size for quadriceps atrophy

Study or Subgroup	PFP Mean	PFP SD	PFP Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.1.1 Quadriceps atrophy								
Pattyn (2011)	11.23	2.59	46	12.11	3.18	30	25.8%	-0.31 [-0.77, 0.16]
Jan (2009)	1.8	1.5	54	3	2.2	54	36.9%	-0.63 [-1.02, -0.25]
Giles (2015)	11.81	1.73	35	12.08	2.03	35	25.1%	-0.14 [-0.61, 0.33]
Callaghan (2004)	18.06	4.6	57	20.08	5.1	10	12.1%	-0.43 [-1.10, 0.25]
Subtotal (95% CI)			**192**			**129**	**100.0%**	**-0.40 [-0.64, -0.17]**
Heterogeneity: Tau² = 0.00; Chi² = 2.72, df = 3 (P = 0.44); I² = 0%								
Test for overall effect: Z = 3.34 (P = 0.0008)								
Total (95% CI)			**192**			**129**	**100.0%**	**-0.40 [-0.64, -0.17]**
Heterogeneity: Tau² = 0.00; Chi² = 2.72, df = 3 (P = 0.44); I² = 0%								
Test for overall effect: Z = 3.34 (P = 0.0008)								
Test for subgroup differences: Not applicable								

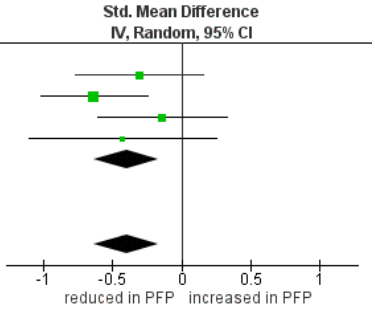

Table 2.15: Forest plot of Effect Size for lower limb muscle amplitude

Study or Subgroup	Patients with PFP Mean	Patients with PFP SD	Patients with PFP Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.3.1 Gastrocnemius amplitude								
Liebensteiner (2008) (CKC: leg press)	109	41	19	130	56	19	32.3%	-0.42 [-1.06, 0.22]
Subtotal (95% CI)			**19**			**19**	**32.3%**	**-0.42 [-1.06, 0.22]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.28 (P = 0.20)								
1.3.2 Peroneus longus amplitude								
Liebensteiner (2008) (CKC: leg press)	114	36	19	124	44	19	32.8%	-0.24 [-0.88, 0.39]
Subtotal (95% CI)			**19**			**19**	**32.8%**	**-0.24 [-0.88, 0.39]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.75 (P = 0.45)								
1.3.3 Soleus amplitude								
Esculier (2015) (running)	453	208	21	524.5	171.3	20	35.0%	-0.37 [-0.99, 0.25]
Subtotal (95% CI)			**21**			**20**	**35.0%**	**-0.37 [-0.99, 0.25]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.16 (P = 0.24)								
Total (95% CI)			**59**			**58**	**100.0%**	**-0.34 [-0.71, 0.02]**
Heterogeneity: Tau² = 0.00; Chi² = 0.15, df = 2 (P = 0.93); I² = 0%								
Test for overall effect: Z = 1.84 (P = 0.07)								
Test for subgroup differences: Chi² = 0.15, df = 2 (P = 0.93), I² = 0%								

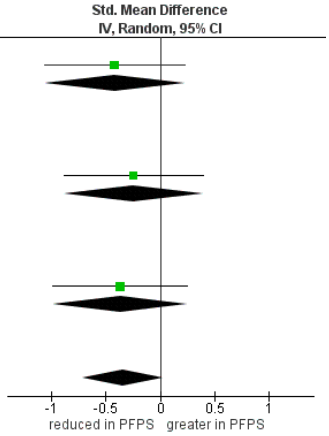

Table 2.16: Forest plot of Effect Size for thigh muscle amplitude

Study or Subgroup	Patients with PFP Mean	Patients with PFP SD	Patients with PFP Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.4.1 Biceps femoris amplitude								
Bley (2014) (single-leg, triple-hop test)	15.9	7.2	20	8.5	12.5	20	33.5%	0.71 [0.07, 1.35]
Liebensteiner (2008) (CKC: leg press)	85	24	19	101	34	19	33.4%	-0.53 [-1.18, 0.12]
Subtotal (95% CI)			**39**			**39**	**66.9%**	**0.09 [-1.13, 1.31]**
Heterogeneity: Tau² = 0.66; Chi² = 7.14, df = 1 (P = 0.008); I² = 86%								
Test for overall effect: Z = 0.15 (P = 0.88)								
1.4.2 Semitendinosus amplitude								
Liebensteiner (2008) (CKC: leg press)	81	22	19	101	29	19	33.1%	-0.76 [-1.42, -0.10]
Subtotal (95% CI)			**19**			**19**	**33.1%**	**-0.76 [-1.42, -0.10]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.26 (P = 0.02)								
Total (95% CI)			**58**			**58**	**100.0%**	**-0.19 [-1.09, 0.71]**
Heterogeneity: Tau² = 0.52; Chi² = 11.52, df = 2 (P = 0.003); I² = 83%								
Test for overall effect: Z = 0.42 (P = 0.68)								
Test for subgroup differences: Chi² = 1.45, df = 1 (P = 0.23), I² = 30.9%								

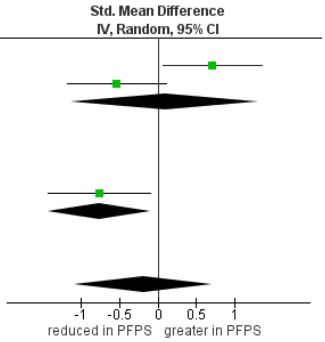

Table 2.17: Forest plot of Effect Size for gluteal muscle amplitude

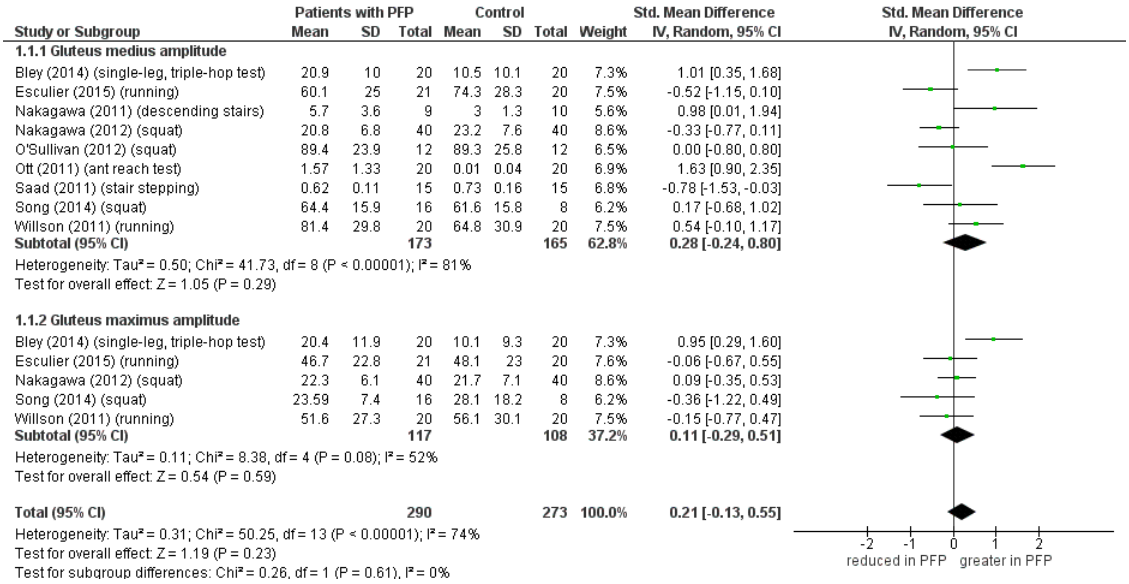

Table 2.18: Forest plot of Effect Size for quadriceps muscle amplitude

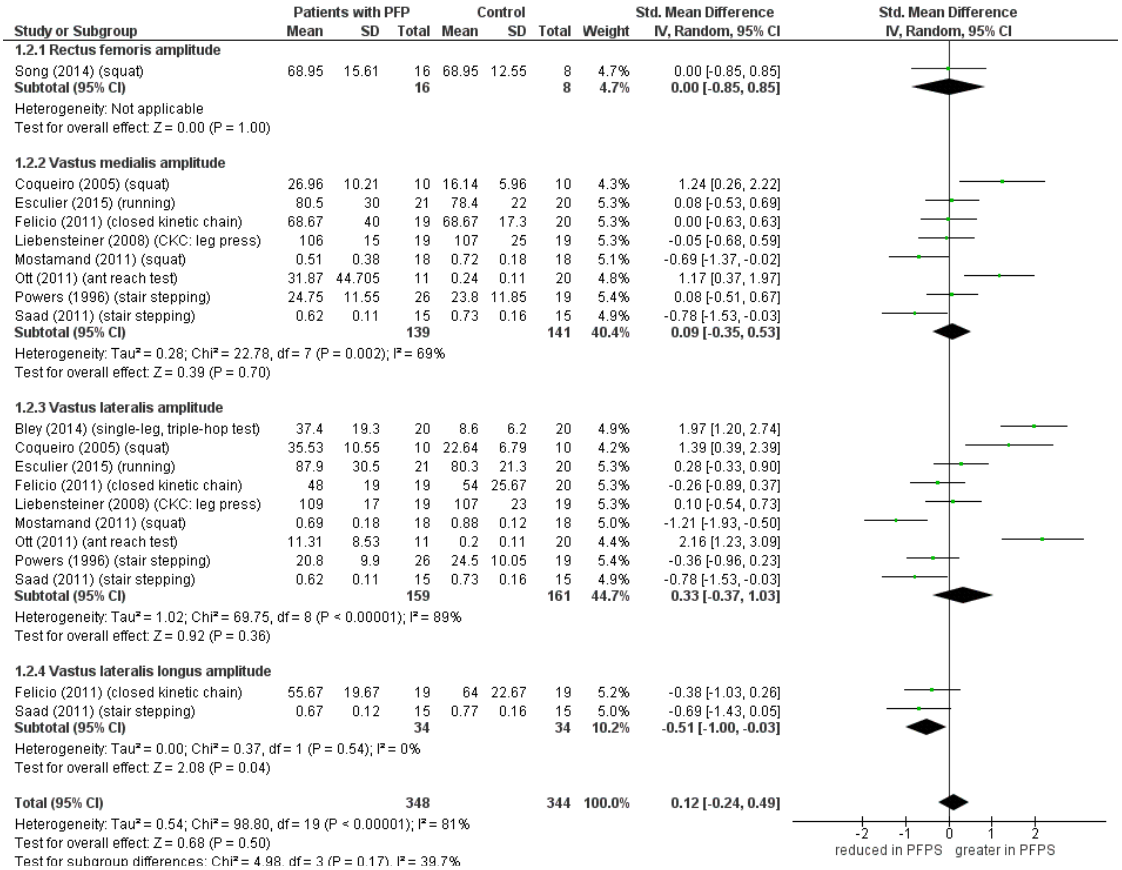

Table 2.19: Forest plot of Effect Size for trunk muscle amplitude

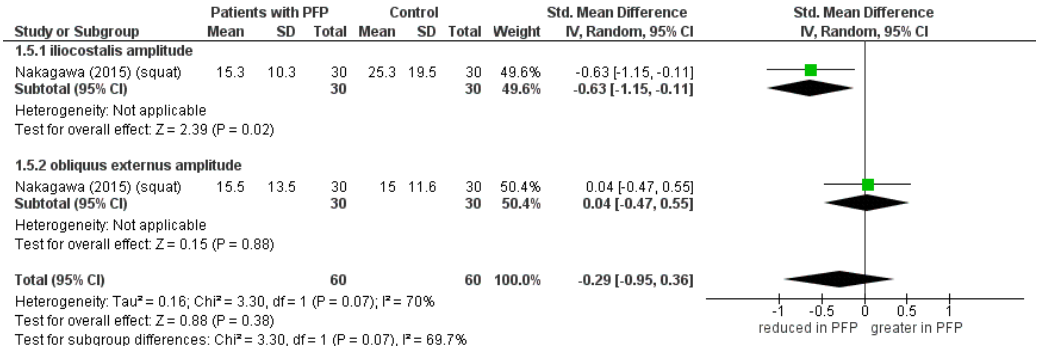

Table 2.20: Forest plot of Effect Size for thigh muscle onset

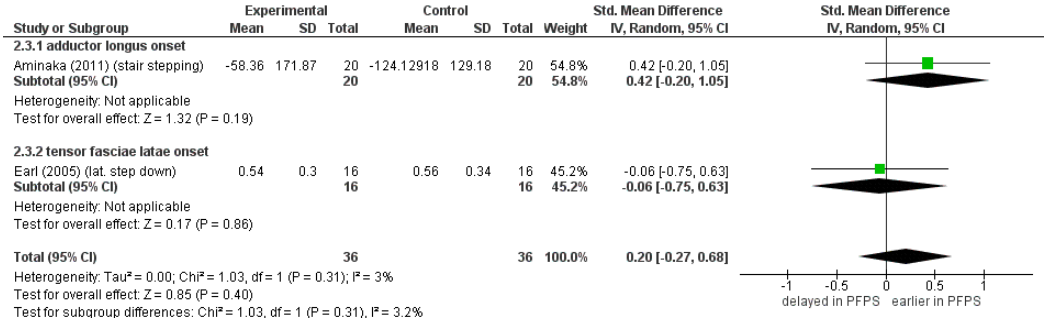

Table 2.21: Forest plot of Effect Size for gluteal muscle onset

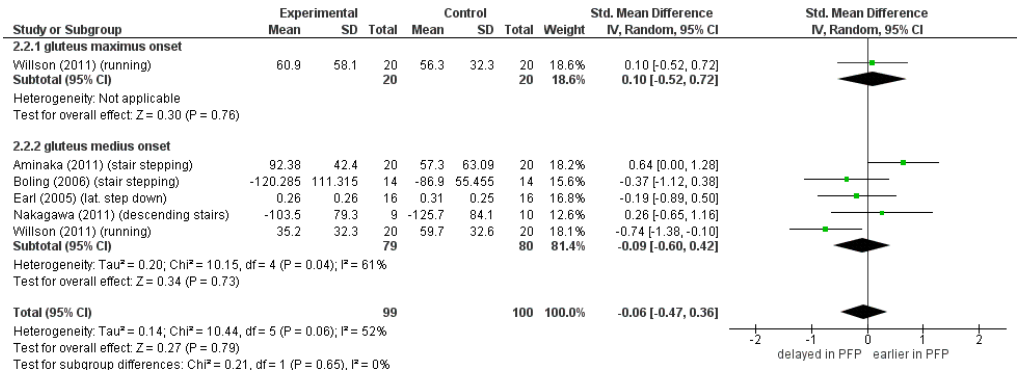

Table 2.22: Forest plot of Effect Size for quadriceps muscle onset

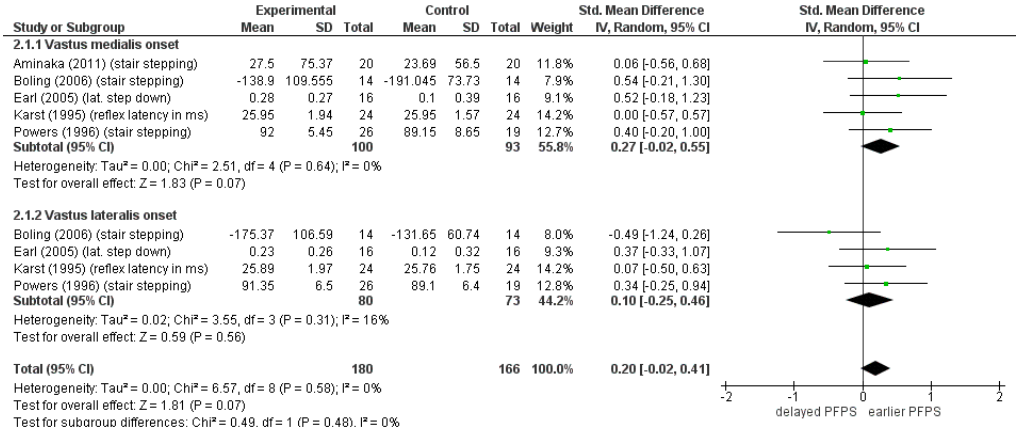

Table 2.23: Forest plot of Effect Size for thigh muscle onset duration

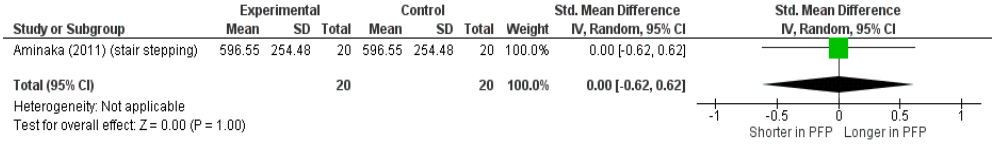

Table 2.24: Forest plot of Effect Size for gluteal muscle onset duration

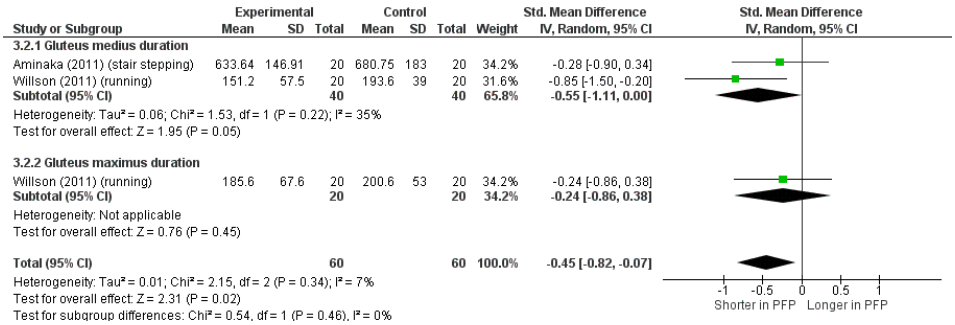

Table 2.25: Forest plot of Effect Size for quadriceps muscle onset duration

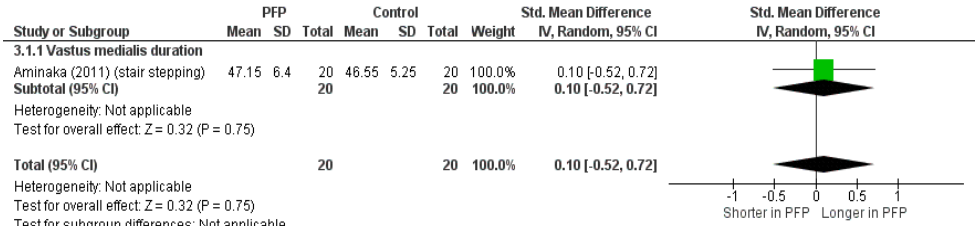

Table 2.26: Forest plot of Effect Size for quadriceps muscle onset duration ratio of VM and GMed

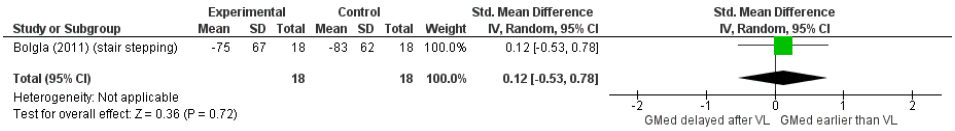

Table 2.27: Forest plot of Effect Size for quadriceps muscle onset duration ratio of VL and GMed

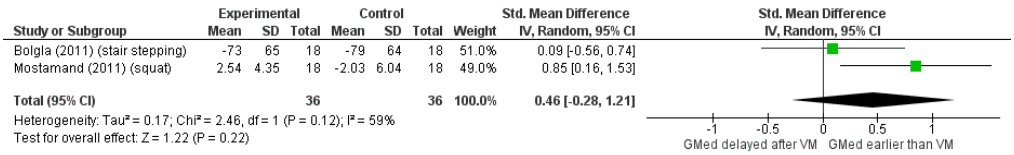

Table 2.28: Forest plot of Effect Size for quadriceps muscle onset duration ratio of VL and VM

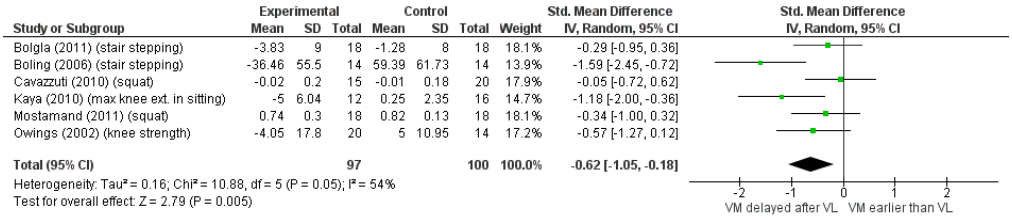

Table 2.29: Forest plot of Effect Size for quadriceps muscle frequency

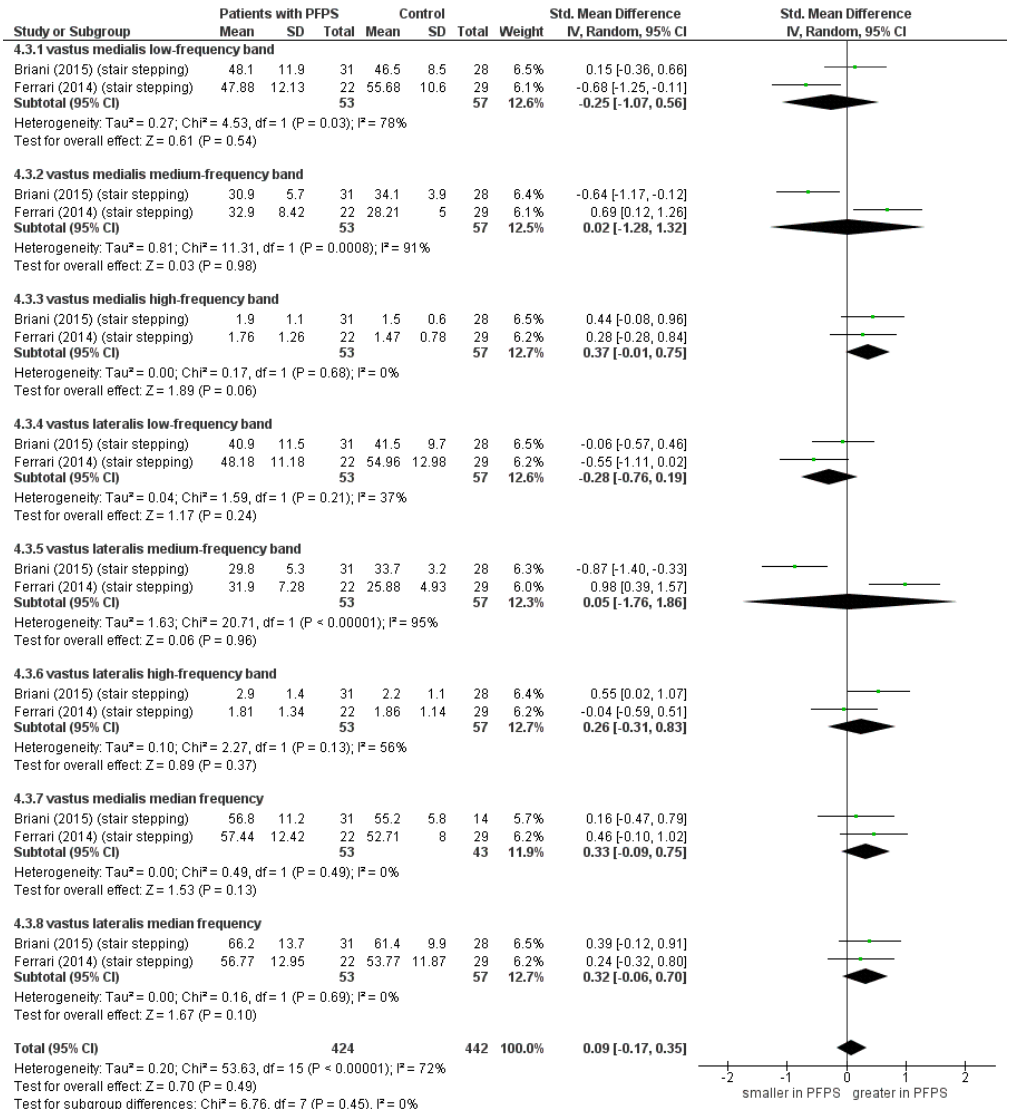

Table 2.30: Forest plot of Effect Size for muscle flexibility

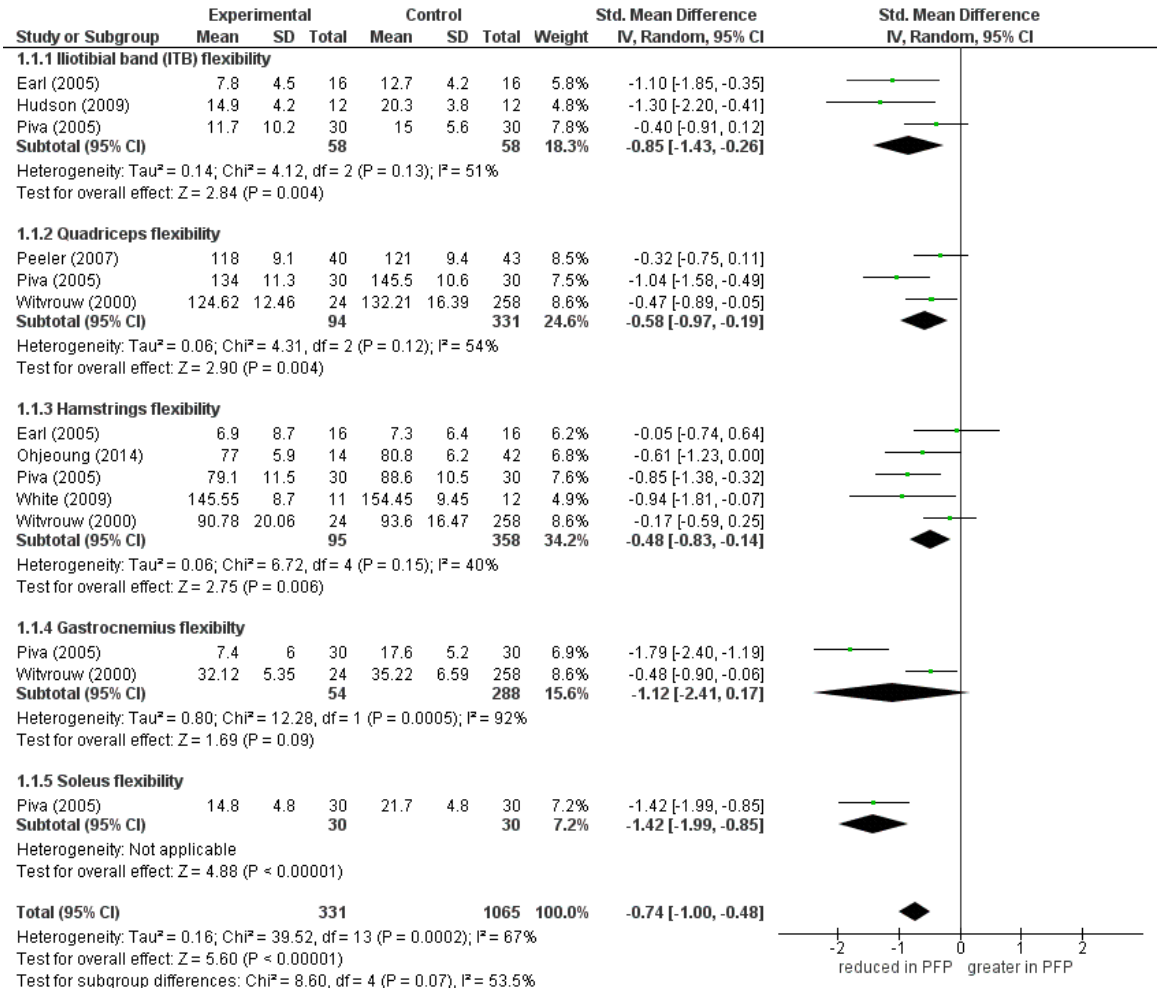

Table 2.31: Regression-analysis of Factors potentially related to heterogeneity in knee strength studies

Strength	**subgroups**	**Test for subgroup differences (p-value)**	**No of studies**	**Knee extension**	
				SMD (95% CI)	**I^2, P value**
Testing position	Squat	**0.04**	2	-1.36 (-2.42; -0.3)	72%, 0.06
	Sitting		6	-1.03 (-1.44; -0.61)	68%, 0.008
	60 degrees knee flx		2	-0.64 (-1.14; -0.14)	0%, 0.42
	90 degrees knee flx		1	-0.02 (-0.63; 0.6)	
Testing[a]	isometric testing	0.54	4	-0.75 (-1.49; 0)	76%, 0.006
	Isokinetic testing		7	-1.01 (-1.37; -0.65)	62%, 0.01
Normalisation method[a]	Nm/body weight	0.60	5	-0.75 (-1.33; -0.16)	78%, 0.001
	Nm		4	-0.95 (-1.48; -0.43)	58%, 0.07
Values used for analysis[a]	averaged peak torque of all trials[b]	**0.0001**	7	-1.02 (-2.21; 0.17)	82%, 0.02
	peak		2	-0.91 (-1.36; -0.46)	75%, <0.0001
gender	Female	0.46	4	-0.99 (-1.46; -0.51)	51%, 0.11
	Male		2	-0.63 (-1.01; -0.25)	0%, 0.68
	both		5	-0.92 (-1.59; -0.25)	82%, 0.00002

[a] Studies were excluded if they not reported the factor

Table 2.32: Regression-analysis of Factors potentially related to heterogeneity in hip flexion and rotator strength studies

Strength	subgroups	Test for subgroup differences (p-value)	No of studies	Hip flexion		Test for subgroup differences (p-value)	No of studies	Hip external rotation		Test for subgroup differences (p-value)	No of studies	Hip internal rotation	
				SMD (95% CI)	I^2, P value			SMD (95% CI)	I^2, P value			SMD (95% CI)	I^2, P value
Testing position	Prone lying					0.5	12	-1.14 (-3.05; 0.77)	**91%. 0.001**	**0.0005**	1	-2.17 (-3.22; -1.13)	
	Sitting						2	-0.47 (-0.73; -0.22)	**49%, 0.03**		6	-0.24 (-0.54; 0.06)	30%, 0.21
Normalisation method[a]	Nm/kg* height	0.15				0.34	2	-0.47 (-1.08; 0.14)	61%, 0.11	0.49			
	Nm/BW		2	-0.26 (-1.39; 0.87)	81%, 0.02		4	-0.41 (-1.01, 0.18)	69%, 0.02		3	-0.2 (-0.75; 0.36)	54%, 0.12
	kg/cm*BW						1	-0.46 (-1.09, 0.17)					
	kg/BW						1	-1.21 (-2; -0.43)					
	Nm/BW*100		1	-1.65 (-2.6; -0.7)			3	-1.17 (-2.04; -0.3)	69%, 0.04		2	-0.87 (-2.16; 0.42)	77%, 0.04
	kg/BW*100		1	-0.81 (-1.29; -0.34)			2	-0.7 (-1.61; 0.21)	66%, 0.09		1	-0.56 (-1.03; -0.1)	
	kg/BMI*100						1	-0.22 (-0.73; 0.29)					
Values used for analysis[a]	averaged peak torque of all trials[b]	0.22	2	-1.13 (-1.92; -0.33)	81%, 0.02	0.41	3	-0.76 (-1.62; 0.09)	83%, 0.003	0.19	2	-1.3 (-2.87; 0.27)	87%, 0.006
	peak		2	-0.26 (-1.39; 0.87)	81%, 0.02		6	-0.37 (-0.76; 0.03)	54%, 0.05		3	-0.2 (-0.75; 0.36)	54%, 0.12
gender	Female					0.1	9	-0.73 (-1.13; -0.33)	66%, 0.003	0.27	6	-0.52 (-1.05; 0.01)	73%, 0.002
	both						5	-0.29 (-0.63; 0.05)	45%, 0.12		1	-0.06 (-0.68; 0.56)	

[a] Studies were excluded if they not reported the factor

Table 2.33: Regression-analysis of Factors potentially related to heterogeneity in hip abductor, adductor and extension strength

Strength	subgroups	Test for subgroup differences (p-value)	Hip abduction		Test for subgroup differences (p-value)	Hip adduction		Test for subgroup differences (p-value)	Hip extension	
			No of studies	SMD (95% CI)	I^2, P value		No of studies	SMD (95% CI)	I^2, P value		No of studies	SMD (95% CI)	I^2, P value
Testing position	Side lying	**0.001**	13	-0.8 (-1.07; -0.53)	53%, 0.01	0.12	2	-0.11 (-0.56; 0.33)	13%, 0.28				
	Supine lying		2	0.02 (-0.39; 0.44)	1%, 0.31		4	-0.77 (-1.48; -0.06)	77%, 0.005				
Normalisation method[a]	Nm/kg* height	0.93	2	-0.64 (-1; -0.27)	0%, 0.58	**0.003**				0.92	1	-0.31 (-0.94; 0.31)	
	Nm/BW		4	-0.7 (-1.19; -0.21)	47%, 0.13		3	-0.24 (-0.65; 0.18)	20%, 0.29		3	-0.43 (-0.81; -0.06)	0%, 0.51
	kg/cm*BW		1	-0.81 (-1.46; -0.17)									
	kg/BW		3	-0.73 (-1.73; 0.27)	87%, 0.0005								
	Nm/BW*100		4	-1.04 (-1.92; -0.16)	80%, 0.002		1	-0.64 (-1.11; -0.17)			3	-0.58 (-2.1; 0.94)	91%, <0.00001
	kg/BW*100						1	-2.2 (-3.25; -1.15)					
	kg/BMI*100		1	-0.5 (-1.02; 0.01)									
Values used for analysis[a]	averaged peak torque of all trials	0.1	4	-1.08 (-1.58; -0.59)	55%, 0.09	0.17	2	-1.35 (-2.87; 0.18)	86%, 0.0008	0.49	2	0.17 (-1.45; 1.79)	91%, 0.001
	peak		6	-0.53 (-0.97; -0.1)	61%, 0.02		3	-0.63 (-1.2; -0.06)	20%, 0.29		3	-0.41 (-0.78; -0.04)	0%, 0.48
gender	Female	0.4	9	-0.79 (-1.22; -0.35)	70%, 0.0007	0.06	5	-0.65 (-1.18; -0.11)	71%, 0.008	0.63	7	-0.51 (-1.01; 0)	74%, 0.0008
	both		6	-0.55 (-0.9; -0.2)	51%, 0.07		1	0.14 (-0.48; 0.76)			1	-0.31 (-0.94; 0.31)	

[a] Studies were excluded if they not reported the factor

Table 2.34: Regression-analysis of Factors potentially related to heterogeneity in muscle amplitude studies

Amplitude	subgroups	Test for subgroup differences (p-value)	No of studies	Gluteus medius		Test for subgroup differences (p-value)	No of studies	Vastus medialis		Test for subgroup differences (p-value)	No of studies	Vastus lateralis	
				SMD (95% CI)	I^2, P value			SMD (95% CI)	I^2, P value			SMD (95% CI)	I^2, P value
Task	Single leg triple hop test	**<0.0001**	1	1.01 (0.35; 1.68)		0.09				**<0.00001**	1	1.97 (1.2; 2.74)	
	Running		2	0.01 (-1.03; 1.04	82%, 0.02		1	0.08 (-0.53; 0.69)			1	0.28 (-0.33; 0.9)	
	Stairs stepping		2	0.07 (-1.65; 1.79)	87%, 0.005		2	-0.32 (-1.16; 0.52)	68%, 0.08		2	-0.53 (-0.99; -0.06)	0%, 0.4
	squat		3	-0.18 (-0.53; 0.17)	0%, 0.52		2	0.24 (-1.65; 2.13)	90%, 0.001		2	0.06 (-2.49; 2.62)	94%, <0.0001
	Anterior reach test		1	1.63 (0.9; 2.35)			1	1.17 (0.37; 1.97)			1	2.16 (1.23; 3.09)	
	CKC						2	-0.02 (-0.47; 0.42)	0%, 0.92		2	-0.08 (-0.53; 0.37)	0%, 0.44
Normalisation method[a]	MVIC	**0.001**	6	0.24 (-0.3; 0.77)	75%, 0.001	**0.002**	6	0.04 (-0.35; 0.43)	52%, 0.07	**<0.00001**	7	0.24 (-0.48; 0.96)	87%, <0.00001
	Mean		2	-0.33 (-1.26; 0.6)	63%, 0.1		1	-0.78 (-1.53; -0.03)			1	-0.78 (-1.53; -0.03)	
	Other method		1	1.63 (0.9; 2.35)			1	1.17 (0.37; 1.97)			1	2.16 (1.23. 3.09)	
Rectification and processing method[a]	Rms	**0.04**	4	0.73 (0; 1.46)	73%, 0.01	**0.006**	4	0.53 (-0.15; 1.2)	70%, 0.02	**0.0008**	5	1.04 (0.03; 2.04)	88%, <0.00001
	"full wave rectification"		1	-0.52 (-1.15; 0.1)			2	0.08 (-0.35; 0.5)	0%, 1		2	-0.05 (-0.68; 0.59)	54%, 0.14
	Bandpass filter		4	0.05 (-0.64; 0.74)	77%, 0.005		2	-0.73 (-1.23; -0.23)	0%, 0.86		2	-1.01 (-1.52; -0.49)	0%, 0.41
Gender	Female	0.45	6	0.1 (-0.42; 0.62)	72%, 0.003	0.96	4	0.08 (-0.59; 0.75)	71%, 0.02	0.94	5	0.36 (-0.64; 1.36)	89%, <0.00001
	Both gender		3	0.68 (-0.73, 2.08)	90%, <0.0001		4	0.1 (-0.58; 0.79)	76%, 0.006		4	0.3 (-0.86; 1.46)	91%, <0.00001

[a] Studies were excluded if they not reported the factor

Table 2.35: Regression-analysis of Factors potentially related to heterogeneity in sEMG onset studies

sEMG onset	subgroups	Test for subgroup differences (p-value)	No of studies	Gluteus medius		Test for subgroup differences (p-value)	No of studies	Vastus medialis-Vastus lateralis	
				SMD (95% CI)	I^2, P value			SMD (95% CI)	I^2, P value
Task	Stairs stepping	**0.04**	4	0.1 (-0.38; 0.57)	41%, 0.17	0.2	2	-0.91 (-2.17; 0.36)	82%, 0.02
	Running		1	-0.74 (-1.38; -0.1)					
	squat						2	-0.2 (-0.67; 0.27)	0%, 0.55
	Strength testing						2	-0.84 (-1.43; -0.25)	18%, 0.27
Onset definition[a]	2SD for 25 ms	0.12	3	0.05 (-0.58; 0.68)	59%, 0.08	0.25			
	3SD for 25 ms		1	0.26 (-0.65; 1.16)			3	-0.69 (-1.44; 0.06)	69%, 0.04
	5SD for 25 ms		1	-0.74 (-1.38; -0.1)					
	Double threshold onset						1	-0.05 (-0.72; 0.62)	
Gender	Female	0.56	2	-0.29 (-1.27; 0.68)	68%, 0.08	0.21	1	-0.29 (-0.95; 0.36)	
	Both gender		3	0.05 (-0.58; 0.68))	59%, 0.08		4	-0.59 (-1.18; 0)	63%, 0.05
	male						1	-1.18 (-2; -0.35)	

[a] Studies were excluded if they not reported the factor

Chapter 3:

Methods 3.1.: HSCR 15-22 approval letter

University of Salford MANCHESTER

Research, Innovation and Academic Engagement Ethical Approval Panel

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AD 101 Allerton Building
University of Salford
M6 6PU

T +44(0)161 295 2280
HSresearch@salford.ac.uk

www.salford.ac.uk/

21 May 2015

Dear Henrike,

RE: ETHICS APPLICATION HSCR 15-22 – Reliability of tests to assess muscle dysfunction related to patellofemoral pain (PFP)

Based on the information you provided, I am pleased to inform you that application HSCR15-22 has been approved.

If there are any changes to the project and/ or its methodology, please inform the Panel as soon as possible by contacting HSresearch@salford.ac.uk

Yours sincerely,

Sue McAndrew
Chair of the Research Ethics Panel

Methods 3.2: Participant information sheet

Appendix 2 research participant information sheet, 20.05.2015 v4

University of Salford MANCHESTER

Information to participate in the research project:

Reliability of tests to assess muscle dysfunction related to patellofemoral pain (PFP)

You are invited to take part in the research study which will provide important information on muscular function and dysfunction that will be used in future studies on patellofemoral pain syndrome.

What is the purpose of the study?

The purpose of the study is to investigate the reliability of a test protocol which investigates muscle strength, inhibition, activity and flexibility in healthy controls. This study will enable the development of a reliable test protocol which can be used in further studies to examine muscular dysfunction in patients with patellofemoral pain syndrome and healthy controls.

Why have I been chosen?

You have been chosen as you are healthy and without any previous lower limb injuries and you are able to do running, and participate in strength tests without aids.

What will I have to do?

You will be asked to wear a loose pair of shorts to expose your lower limb and a short top to visualise the trunk in order to allow the video cameras to record you during the study and to ensure that the very sensitive recordings of the surface electromyographic electrodes are not disturbed by external factors, such as clothes moving above the electrodes.

Your age, height and mass will be asked and noted by the researcher.

The flexibility of two lower limb muscles and your ankle will be measured, as well as the leg length, the kneecap position and the foot posture.

1

Following this, the researcher will attach 40 retro-reflective markers to the skin of your lower limb on both legs and attach surface electromyographic electrodes to four muscles as in figure 1 on your dominant leg. You will then be required to undertake five tests: a static standing assessment, running, running faster, a step down of a stair, a single leg squat and a balance test. These tests will be recorded in a controlled laboratory environment of the University of Salford.

After the testing the markers and the electromygraphic electrodes of the non-dominant leg will be taken off.

You will then be required to perform, in sitting, a strength test for your knee and hip muscles. In the last strength test when you are straightening you knee and moving your hips to the side the test will be combined with an electrical impulse. Therefore an electrode will be placed and an electrical current sent to the muscle in a short impulse. The testing will not involve any exertion that provokes pain. The measurement will be conducted over a single session and will take around 3 hours in duration.

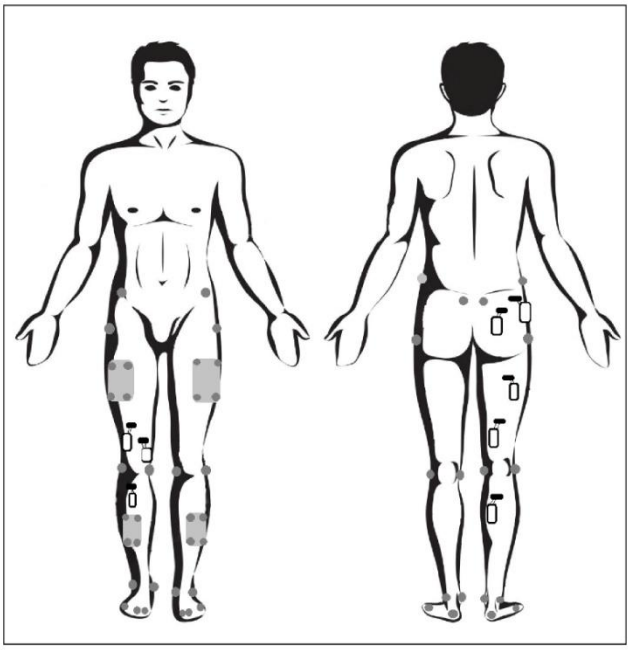


Figure 1: Picture of the 40 retro-reflective markers (grey) and the EMG electrodes in a right dominant person (white: electrodes, black: EMG-boxes and cables)

Your identity will not be revealed: the video recording will only capture the markers which are on your lower limbs. All information obtained from these measurements will remain confidential and anonymous. All data will be directly coded with a study number, so you will remain anonymous to all but the researcher. The data will be stored on the computer of the researcher which is password protected. On completion of the study, the video-recordings will be deleted from the computer system according to the rules of the University of Salford.

What benefits are involved in participating in the study?

You will not personally benefit from undertaking the study in terms of the data that has been collected. However, your participation in the research will benefit both the researchers and future participants in developing a reliable trial protocol. This will help us to further understand muscle dysfunction in healthy participants. However, you will gain information about your data in the tests which may be of use to you.

If I participate in this study, can I also take part in other studies?

As the study is not including a treatment or long-term assessment, taking part should not affect any other studies that you are involved in. However, if you are taking part in other research or would like to do so, please discuss it with the researcher (Henrike Greuel).

Is there an inherent risk involved?

There is an inherent risk with any type of testing. However, this risk is reduced to a minimum by testing in a controlled laboratory environment.

What if something goes wrong?

The university has insurance to cover against harm to you which may occur whilst you are taking part in this study. If you wish to complain, or if you have any concerns about any aspect of the way you have been treated during the study, you can contact the University of Salford. If you decide to take legal action, you may have to pay for this.

What if I want to leave the study earlier?

You are free to withdraw from the study at any time. If you want to withdraw you do not have to inform us of the reason. However, we will use the data that we have recorded unless you inform us you wish us not to do so.

Who will see my details and results?

All personal information will be kept confidential. The final results of the study will be available to you and may be published.

Will I be compensated for participating?

On completion of the study, you will be reimbursed with a voucher for a maximum of £20 for attending both visits.

What will happen to the results of the research study?

A summary of the research findings will be sent to everyone who participates in the study. Important findings will be published in clinical and engineering journals.

Contact information:
Henrike Greuel
Email: H.Greuel@edu.salford.ac.uk
Phone number: 07762218764
Address: School of Health Sciences,
Blatchford Building,
Postgraduate students room: PO30
University of Salford
Frederick Road Campus,
Salford, M6 6PU

If you are unhappy with the study, contact:
Anish Kurien
Email: A.Kurien@edu.salford.ac.uk
Phone number: 01612955276
Address: University of Salford
Allerton building,
AD101,
University of Salford
Frederick Road Campus,
Salford, M6 6P

Thank you very much for taking the time to read this document and many thanks for your participation.

Henrike Greuel

Methods 3.3: Informed Consent form

Appendix 3: Informed consent form, 19.05.2015 v2

Research Participant Consent Form

Title of Project :

Reliability of tests to assess muscle dysfunction related to patellofemoral pain (PFP)

Ethics Ref No. :

1. I confirm that I have read and understood the information sheet for the above study (version 20.05.2015 v4) and what my contribution will be.	Yes	No
2. My involvement in the study and its purpose has been fully explained to me. I have been given the opportunity to ask questions and any questions that I have asked have been answered to my satisfaction.	Yes	No
3. I understood that my participation in this test will include a number of tests which are detailed in the information sheet (version 20.05.2015 v4).	Yes	No
4. I have the right to withdraw from the research at any time without objection from the researcher and I understand that my data may be used unless I request not to do so.	Yes	No
5. I have been informed that I will be compensated for my participation if I complete both testing sessions.	Yes	No
6. I understand how the researcher will use my responses, who will see them and how the data will be stored.	Yes	No
7. I understand that the results of this research may be published but that my name and identity will not be revealed at any time. All information as numbered codes in computer files will be kept confidential on the computer of Henrike Greuel, that is only available for her.	Yes	No

1

Appendix 3: Informed consent form, 19.05.2015 v2

8. I agree to take part in the above study as a volunteer — Yes / No

9. I agree to have my details kept on a contact list and be sent ethically approved information sheets for other studies, related to this project, to see if I would be interested in taking part. — Yes / No

Name of participant ……

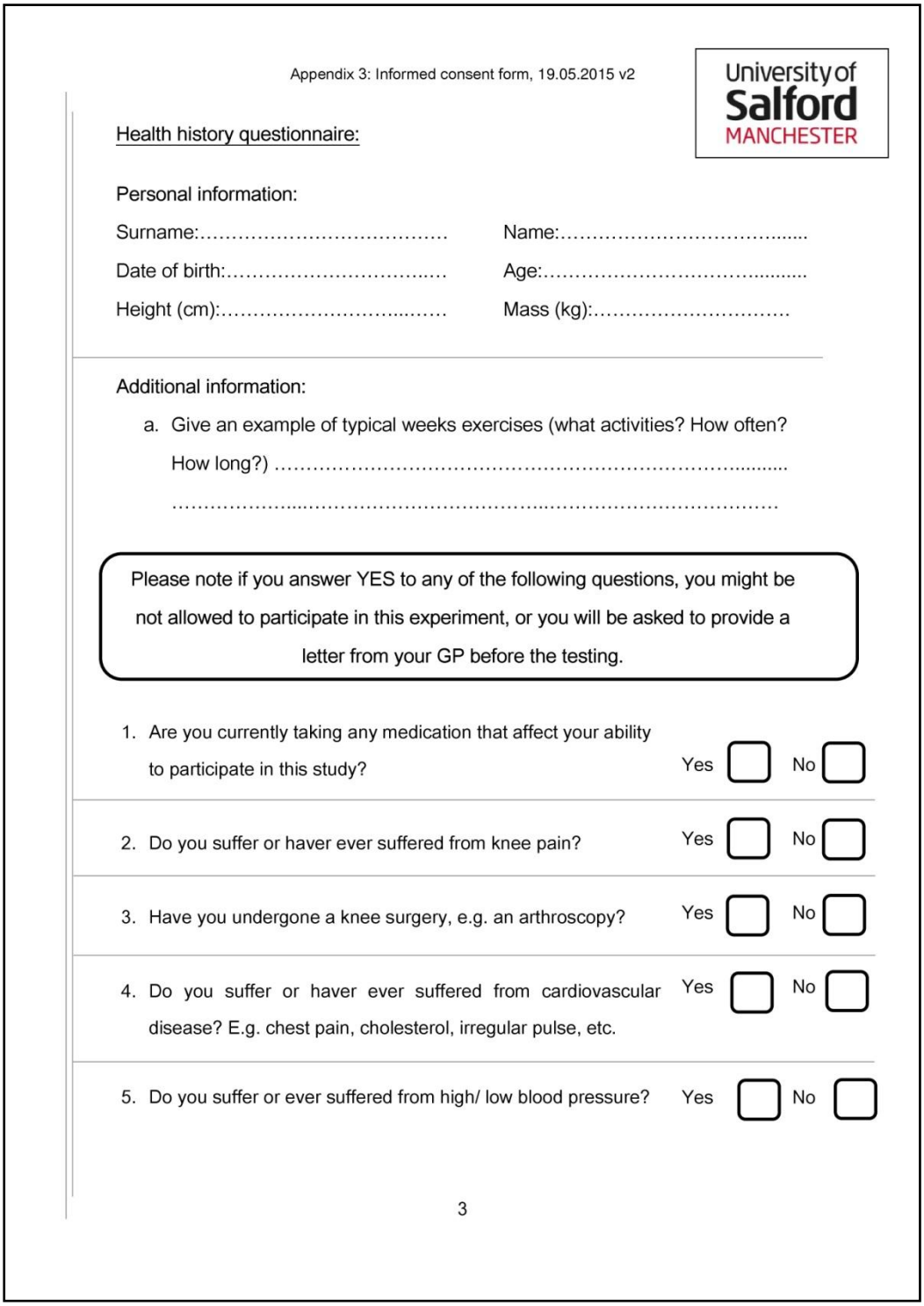
Signature ……..…… Date ……..

Name of researcher taking consent ……

Signature ……... Date ……

2

Methods 3.4: Health history questionnaire



Appendix 3: Informed consent form, 19.05.2015 v2

University of Salford MANCHESTER

Health history questionnaire:

Personal information:

Surname:…… Name:……..

Date of birth:…….. Age:……..

Height (cm):……..…… Mass (kg):……

Additional information:

a. Give an example of typical weeks exercises (what activities? How often? How long?) ……..

……..……..……

Please note if you answer YES to any of the following questions, you might be not allowed to participate in this experiment, or you will be asked to provide a letter from your GP before the testing.

1. Are you currently taking any medication that affect your ability to participate in this study? Yes ☐ No ☐
2. Do you suffer or haver ever suffered from knee pain? Yes ☐ No ☐
3. Have you undergone a knee surgery, e.g. an arthroscopy? Yes ☐ No ☐
4. Do you suffer or haver ever suffered from cardiovascular disease? E.g. chest pain, cholesterol, irregular pulse, etc. Yes ☐ No ☐
5. Do you suffer or ever suffered from high/ low blood pressure? Yes ☐ No ☐

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6. Do you suffer or ever suffered from respiratory disease? E.g. asthma, bronchitis, etc.	Yes ☐	No ☐
7. Do you suffer or ever suffered from diabetes?	Yes ☐	No ☐
8. Do you suffer or ever suffered from epilepsy/ seizures?	Yes ☐	No ☐
9. Have you had a cold or feverish illness within the last two weeks?	Yes ☐	No ☐
10. Do you ever lose balance because of dizziness, or do you ever lose consciousness?	Yes ☐	No ☐
11. Are you currently receiving treatment or medical advice from a GP or physiotherapist?	Yes ☐	No ☐
12. Are there other reasons, not mentioned above, why you should not exercise? E.g. an accident, pregnancy, surgeries, or anything else?	Yes ☐	No ☐

Informed consent:

The full details of the text, as well as the purpose of the test have been explained to me. I certify that I fully understand in what I will be involved and I am aware of the potential benefits and potential risks. I know that I am not obliged to participate in this study and that I am free to stop at any time.

The test results are treated confidentially and the data will be fully anonymized.

I agree that the data being collected can be used within this research project (tick as appropriate): yes ☐ no ☐

Chapter 4:

Methods 4.1.: HSCR 15-22 approval letter

University of Salford MANCHESTER

Research, Innovation and Academic Engagement Ethical Approval Panel

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15 February 2016

Dear Henrike,

RE: ETHICS APPLICATION HSCR 15-142 – Treatment effect on arthrogenic muscular inhibition in patellofemoral pain (the PFP-Inhibit study)

Based on the information you provided, I am pleased to inform you that application HSCR15-142 has been approved.

If there are any changes to the project and/ or its methodology, please inform the Panel as soon as possible by contacting Health-ResearchEthics@salford.ac.uk

Yours sincerely,

Sue McAndrew
Chair of the Research Ethics Panel

Methods: 4.2 History questionnaire for individuals with PFP

University of Salford MANCHESTER

Health history questionnaire:

Personal information:

Surname: …… Name: ……

Date of birth: …… Age: ……

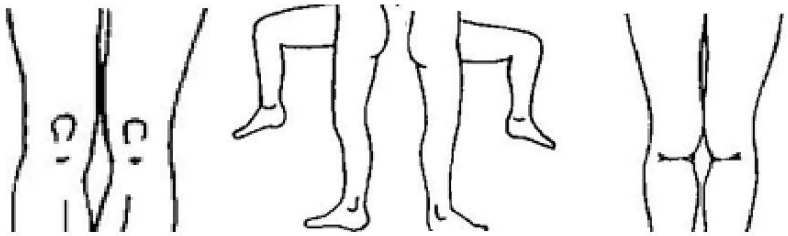
Height (cm): …… Mass (kg): ……

Additional information:

a. Give an example of typical weeks exercises (what activities? How often? How long?) ……

……

Please use the diagram below to indicate the symptoms you have experienced over the last week. Be VERY precise when drawing the location of your pain.



Please provide a short explanation of the above indicated pain:

……

……

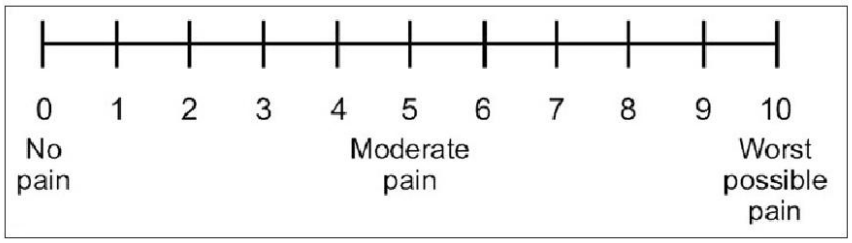
……

……

……

……

Please rate your current pain using the following scale:



Please note if you answer YES to any of the following questions, you might be not allowed to participate in this experiment, or you will be asked to provide a letter from your GP before the testing.

1. Are you currently taking any medication that affect your ability to participate in this study? Yes ☐ No ☐
2. Have you undergone a knee surgery, e.g. an arthroscopy? Yes ☐ No ☐
3. Do you suffer or haver ever suffered from cardiovascular disease? E.g. chest pain, cholesterol, irregular pulse, etc. Yes ☐ No ☐
4. Do you suffer or ever suffered from high/ low blood pressure? Yes ☐ No ☐
5. Do you suffer or ever suffered from respiratory disease? E.g. asthma, bronchitis, etc. Yes ☐ No ☐
6. Do you suffer or ever suffered from diabetes? Yes ☐ No ☐
7. Do you suffer or ever suffered from epilepsy/ seizures? Yes ☐ No ☐

8. Have you had a cold or feverish illness within the last two weeks?	Yes ☐	No ☐
9. Do you ever lose balance because of dizziness, or do you ever lose consciousness?	Yes ☐	No ☐
10. Are you currently receiving treatment or medical advice from a GP or physiotherapist?	Yes ☐	No ☐
11. Are there other reasons, not mentioned above, why you should not exercise? E.g. an accident, pregnancy, surgeries, or anything else?	Yes ☐	No ☐

Informed consent:

The full details of the text, as well as the purpose of the test have been explained to me. I certify that I fully understand in what I will be involved and I am aware of the potential benefits and potential risks. I know that I am not obliged to participate in this study and that I am free to stop at any time.

The test results are treated confidentially and the data will be fully anonymized.

I agree that the data being collected can be used within this research project (tick as appropriate): yes ☐ no ☐

Name of the participant: ……

Signature of the participant: …… Date:……

Name of the principal investigator: ……

Signature of the principal investigator: …… Date:……

Chapter 5:

Methods 5.1.: HSCR 15-22 approval letter

NHS
Health Research Authority

North West - Greater Manchester South Research Ethics Committee
3rd Floor, Barlow House
4 Minshull Street
Manchester
M1 3DZ

Telephone: 0207 104 8002

Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

12 August 2016

Ms Henrike Greuel
PO30 Brian Blatchford Building
Frederick Road
Salford
M66PU

Dear Ms Greuel

Study title:	**The role of arthrogenic muscular inhibition in patellofemoral pain and the response to an exercise programme (the PFP-Inhibit study)**
REC reference:	**16/NW/0497**
Protocol number:	**HSCR 15-142**
IRAS project ID:	**194530**

Thank you for your letter of 03 August 2016, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by Mr Richard Hovey, Mrs Lesley Thornton and Dr Joel Sanderson.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact the REC Manager, Mrs Kieran Hall, nrescommittee.northwest-gmsouth@nhs.net.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start

A Research Ethics Committee established by the Health Research Authority

of the study.

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for NHS permission for research is available in the Integrated Research Application System, www.hra.nhs.uk or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact Catherine Blewett (catherineblewett@nhs.net), the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided within IRAS.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Confirmation of any other Regulatory Approvals (e.g. NIGB) and all correspondence [Ethical approval letter of the Salford University]	1	15 February 2016
Contract/Study Agreement [Evidence of the professional registration]	1	27 October 2014
Copies of advertisement materials for research participants [Facebook and Twitter Text]		17 June 2016
Copies of advertisement materials for research participants [recruitment poster for healthy individuals]	v2	27 July 2016
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Employers liability]	1	17 July 2015
GP/consultant information sheets or letters [information sheet for physios and GP]	1	18 February 2016
Instructions for use of medical device [Exercise booklet]	1	18 February 2016
IRAS Application Form [IRAS_Form_13062016]		13 June 2016
IRAS Checklist XML [Checklist_03082016]		03 August 2016
Letter from sponsor [Employers liability]	1	17 July 2015
Letters of invitation to participant [Study invitation letter]	1	18 February 2016
Non-validated questionnaire [Healthy assessment questionnaire for healthy individuals]	v2	27 July 2016
Non-validated questionnaire [Healthy assessment questionnaire for individuals with PFP]	v2	27 July 2016
Participant consent form [participant consent form]	v2	27 July 2016
Participant information sheet (PIS) [participant information sheet]	v2	27 July 2016
Participant information sheet (PIS) [patient information sheet]	v2	27 July 2016
Research protocol or project proposal [Scientific Research Protocol]	2	27 July 2016
Response to Request for Further Information		03 August 2016
Summary CV for Chief Investigator (CI) [CV of the Chief Investigator]	1	18 May 2016
Summary CV for Chief Investigator (CI) [CV Lee Herringotn]	1	17 June 2016
Summary CV for student [CV of the PI]	1	18 May 2016
Summary CV for supervisor (student research) [CV of the academic supervisor]	1	18 May 2016
Validated questionnaire [Tampa Scale: Kinesiophobia]	1	18 May 2016
Validated questionnaire [KUJALA questionnaire]	1	18 May 2016
Validated questionnaire [KOOS questionnaire]	1	18 May 2016

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

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After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

16/NW/0497	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

On behalf of
Professor Sobhan Vinjamuri
Chair

Email: nrescommittee.northwest-gmsouth@nhs.net

Enclosures: "After ethical review – guidance for researchers"

Copy to: Ms Kay Hack

Dr Richard Jones,
University of Salford

Mr Dayle Roberts,
RM&G Coordinator (Primary Care), Greater Manchester Comprehensive Local Research Network

A Research Ethics Committee established by the Health Research Authority

Chapter 6:

Methods 6.1.: HSCR 15-22 approval letter

University of Salford MANCHESTER

Research, Innovation and Academic Engagement Ethical Approval Panel

Research Centres Support Team
G0.3 Joule House
University of Salford
M5 4WT

T +44(0)161 295 2280

www.salford.ac.uk/

1 February 2016

Dear Henrike,

RE: ETHICS APPLICATION HSCR 15-143 – The patellofemoral pain functional performance study (PFP-FP)

Based on the information you provided, I am pleased to inform you that application HSCR15-143 has been approved.

If there are any changes to the project and/ or its methodology, please inform the Panel as soon as possible by contacting Health-ResearchEthics@salford.ac.uk

Yours sincerely,

Sue McAndrew
Chair of the Research Ethics Panel