UNIVERSITY OF EXETER

Biomechanical, muscle activation and clinical characteristics of chronic exertional compartment syndrome

Submitted by Andrew Roberts to the University of Exeter as a thesis for the degree of Doctor of Philosophy in Sport and Health Sciences in June 2017.

I certify that all material in this thesis which is not my own work has been identified and that no material has previously been submitted and approved for the award of a degree by this or any other University.

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Abstract

Chronic exertional compartment syndrome (CECS) is a common problem within both military and athletic populations that can be difficult to diagnose. Furthermore, it is unclear what causes the development of CECS, particularly in the military population, as personnel undertake a variety of activities that can cause pain with CECS such as fast walking, marching and running. Chronic exertional compartment syndrome has been hypothesised to develop due to excessive muscle activity, foot pronation and abnormal biomechanics predominantly at the ankle. Treatment of CECS through running re-education to correct these abnormalities has been reported to improve symptoms. However no primary research has been carried out to investigate the biomechanical, muscle activation and clinical characteristics of military patients with CECS. The purpose of this thesis was to provide an original contribution to the knowledge through the exploration of these characteristics; and the development of insights into the development of CECS, with implications for prevention and treatment.

Study one investigated the clinical characteristics of 93 service personnel with CECS. Plantar pressure variables, related to foot type and anterior compartment muscle activity, and ankle joint mobility were compared during walking between 70 cases and 70 controls in study two. Study three compared three-dimensional whole body kinematics, kinetics and lower limb muscle activity during walking and marching between 20 cases and 20 controls. Study four compared kinematics and lower limb muscle activity during running in a separate case-control cohort (n=40). Differences in electromyography (EMG) intensity during the gait cycle were compared in the frequency and time domain using wavelet analysis. All studies investigated subject anthropometry.

Cases typically presented with bilateral, 'tight' or 'burning' pain in the anterior and lateral compartments of the lower leg that occurred within 10 minutes of exercise. This pain stopped all cases from exercising during marching and/or running. As such subsequent studies investigated the biomechanics of both ambulatory and running gaits.

Cases in all case-control studies were 2-10 cm shorter; and were typically overweight resulting in a higher body mass index (BMI) than controls. There was strong evidence from study 3 that cases had greater relative stride lengths

than controls during marching gait. This was achieved through an increase in ankle plantarflexion during late stance and a concomitant increase in the gastrocnemius medialis contraction intensity within the medium-high frequency wavelets. Given the differences in height observed, this may reflect ingrained alterations in gait resulting from military training; whereby all personnel are required to move at an even cadence and speed. These differences in stride length were also observed in walking and running gaits although to a lesser extent.

There was no evidence from the EMG data that cases had greater tibialis anterior activation than controls during any activity tested, at any point in the gait cycle or in any frequency band. In agreement, there was also no evidence of differences between groups in plantar pressure derived measures of foot type, which modulate TA activity. Toe extensor - related plantar pressure variables also did not differ between groups. In summary, contrary to earlier theories, increased muscle activity of the anterior compartment musculature does not appear to be associated with CECS.

The kinematic differences observed during running only partially matched the clinical observations previously described in the literature. Cases displayed less anterior trunk lean and less anterior pelvic tilt throughout the whole gait cycle and a more upright shank inclination angle during late swing (peak mean difference 3.5°, 4.1° and 7.3° respectively). However, no consistent differences were found at the ankle joint suggesting that running is unlikely to be the cause of CECS in the military; and that the reported success of biomechanical interventions may be due to reasons other than modifying pathological aspects of gait.

In summary, the data presented in the thesis suggest that CECS is more likely to develop in subjects of shorter stature and that this is associated with marching at a constant speed and cadence. Biomechanical interventions for CECS, such as a change in foot strike or the use of foot orthotics, are unlikely to be efficacious for the military as personnel will continue to be required to march at prescribed speeds to satisfy occupational requirements. Preventative strategies that allow marching with a natural gait and/or at slower speeds may help reduce the incidence of CECS. The lack of association with foot type or

muscle activity suggests that foot orthoses would not be a useful prevention strategy or treatment option for this condition.

Acknowledgements

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I am also thankful to the Academic Department of Military Rehabilitation and the Defence Medical Rehabilitation Centre for their cooperation and support. In particular I am grateful for the valuable discussions and support from Maj David Roscoe and Dr David Hulse.

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List of Abbreviations

Abbreviation	Meaning
AIS	Anterior intermuscular septum
ANCOVA	Analysis of Covariance
ANL	Ankle Lateral Malleolus
ANM	Ankle Medial Malleolus
ASI	Anterior Superior Iliac Spine
AT	Adventure training
ATC	Air Training Corps
BF	Barefoot
BMI	Body mass index
CECS	Chronic exertional compartment syndrome
CI	Confidence interval
COF	Centre of force
CON	Control
COP	Centre of pressure
CSA	Cross-sectional area
DEXA	Dual energy x-ray absorptiometry
DGAMS	Director General Army Medical Services
DMRC	Defence Medical Rehabilitation Centre
DP	Deep posterior compartment
EDL	Extensor digitorum longus
EEC	European Economic Community
EHL	Extensor hallucis longus
EILP	Exercise-induced leg pain

EMG	Electromyography
FAD	Femur Anterior Distal
FAP	Femur Anterior Proximal
FDL	Femur Distal Lateral
FHL	Flexor Hallucis Longus
FLD	Femur Lateral Distal
HEE	Heel
HELP	Headley Exertional Leg Pain
HJC	Hip Joint Centre
HL	Lateral heel zone
HM	Medial heel zone
HS	Heel strike
IFFC	Initial forefoot contact
IM	Interosseous membrane
IMCP	Intramuscular compartment pressure
INRIA	French Institute for Research in Computer Science and Automation
IP	interface pressure
ISB	International Society for Biomechanics
ITC	Infantry Training Centre
KJC	Knee joint centre
KNL	Knee Lateral Femoral
KNM	Knee Medial Femoral
LASI	Left Anterior Superior Iliac Spine
LG	Lateral Gastrocnemius
LHS	Left Heel Strike

LIS	lateral intermuscular septum
LPSI	Left Posterior Superior Iliac Spine
LTO	Left Toe Off
MA	Massachusetts
MD	Maryland
MG	Medial Gastrocnemius
MOD	Ministry of Defence
MODREC	Ministry of Defence Research & Ethics Committee
MPARL	Military Performance Analysis and Research Laboratory
MRI	Magnetic Resonance Image
NATO	North Atlantic Treaty Organisation
NHS	National Health Service
PA	peroneal artery
PAS	Patella Apex Superior
PB	Peroneus Brevis
PFA	Personal Fitness Assessment
PL	Peroneus Longus
POP	Popliteus
PROJ	Projected
PSI	Posterior Superior Iliac Spine
PT	Physical Training
PV	peroneal vein
RASI	Right Anterior Superior Iliac Spine
RBAC	Right Back

RHS	Right Heel Strike
RLEG	Right leg
RMAS	Royal Military Academy Sandhurst
RPSI	Right Posterior Superior Iliac Spine
RTA	Road Traffic Accident
RTO	Right Toe Off
SD	Standard deviation
SE	Standard error
SENIAM	Surface electromyography for non-invasive assessment of muscles
SP	Superficial posterior compartment
SPSS	Statistical Package for the Social Sciences
STRN	Sternal Notch
TA	Tibialis anterior
TAD	Tibia Anterior Distal
TAP	Tibia Anterior Proximal
TO	Toe off
TP	Tibialis posterior
UK	United Kingdom
US	United States/Ultrasound
USA	United States of America
WI	Wisconsin
WRT	Walk to run transition
XYPH	Xyphoid Process

Communications and awards

Communications

1. International Congress on Soldiers Physical Performance 2014 (Boston, USA). Patients with chronic exertional compartment syndrome walk and march differently to asymptomatic controls. Symposium with poster presentation.

2. XXV Congress of the International Society of Biomechanics 2015 (Glasgow, UK). Insights into the biomechanical mechanisms for the development of chronic exertional compartment syndrome. Oral presentation.

3. International Sports Science and Sports Medicine Conference 2016 (Newcastle, UK). Biomechanical differences between cases with chronic exertional compartment syndrome and asymptomatic controls during running. Poster presentation.

4. International Sports Science and Sports Medicine Conference 2016 (Newcastle, UK). Biomechanical differences between cases with chronic exertional compartment syndrome and asymptomatic controls. Oral presentation.

5. 17th International Symposium - Biomechanics of Human Movement 2016 (Jyvaskyla, Finland). Biomechanical differences between cases with chronic exertional compartment syndrome and asymptomatic controls during walking and marching. Poster presentation.

6. 17th International Symposium - Biomechanics of Human Movement 2016 (Jyvaskyla, Finland). Biomechanical differences between cases with chronic exertional compartment syndrome and asymptomatic controls during running. Poster presentation.

7. British Association of Sport and Exercise Science: Biomechanics Interest Group 2017 (Portsmouth, UK). Plantar pressure in chronic exertional compartment syndrome: a case-control study. Poster presentation.

8. European Society of Biomechanics 2017 (Seville, Spain). Plantar pressure in chronic exertional compartment syndrome: a case-control study. Poster presentation.

9. European Society of Sports Science 2017 (Essen, Germany). Muscle activity in chronic exertional compartment syndrome: a case-control study. Oral presentation.

Awards

1. Directorate of Defence Rehabilitation Research Prize 2016

1. Introduction

1.1. Overuse injuries

Musculoskeletal injuries are a common problem in both military and civilian life and can have a great effect on absence from work. Recent data of overall injury rates resulting from exercise within the UK is lacking. The only large-scale national study within England and Wales reported that 8% of all responders reported incidences of exercise related injury (Nicholl, Coleman, & Williams, 1995). This represented 18% of those that undertook vigorous exercise. In comparison, the first national health survey in Germany described an annual sports injury rate of 3.1% with approximately 62% of sports injuries resulting in time taken off work (Schneider, Seither, Tonges, & Schmitt, 2006). While the current incidence of exercise-related injury is not known in the UK; the increase in physical activity levels over the last 15 years (Craig and Mindell, 2012) could be expected to result in a proportionate rise in the number of injuries.

Injuries within military populations have been studied in more detail than the general population. Approximately 30% of military recruits have been reported to experience an overuse injury during training and these account for over 80% of all lower extremity injuries (Cowan et al., 1996; Schwellnus, Jordaan, & Noakes, 1990). Training populations generally experience a rapid change in physical activity, under standardised conditions, that is likely to contribute to the high incidence of injury. These populations can therefore provide excellent models for examining the risk factors for injury. As such, much of the data on these types of injuries within the military comes from training populations. However, injuries continue to occur following the end of training. For example, the incidence of injury in light infantry soldiers has been reported to be 95 injuries per 100 soldiers per year with 50% attributed to physical training and 30% of these linked to running (Smith & Cashman, 2002). It is likely that the higher figures reported in the latter study are due to differences in the period of exposure (14 months vs 9-12 weeks). The physical requirements of military training and certain military trades therefore result in a significant incidence of exercise-related injury.

Exercise-induced leg pain (EILP) encompasses a number of different diagnoses. Patients with EILP may present with pain in the shin, calf, ankle or

foot that is brought on or exacerbated by exercise. Calf and shin problems related to exercise account for c. 13% of military training injuries (DGAMS, 2013). Pain is usually induced by repetitive loading of the lower limb causing a variety of pathologies (Beck, 1998). The term EILP therefore encompasses all injuries such as medial tibial stress syndrome, chronic exertional compartment syndrome (CECS), tibial and fibular stress fracture, popliteal arterial entrapment syndrome, periostitis, muscle herniation, nerve entrapment, and intermittent claudication (Willems et al., 2006).

Differential diagnosis of EILP is an important determinant of treatment which can range from rest, to conservative management or surgery. Classifying EILP into one of the different pathologies is typically carried out either by clinical diagnosis, or investigations that may include medical imaging, nerve conduction studies, or intramuscular compartment pressure (IMCP) testing. However, differential diagnosis of EILP can be challenging (Gaeta et al., 2008).

The perceived cause of lower limb overuse injuries is typically from endurance running (in shoes or boots) or from drill and marching (Figure 1) (DGAMS, 2013). This is also reflected in the literature. However, the differing effects of marching and running on injury rates are not clear. Rudzki (1997) reported no significant differences in the overall injury rates in Australian recruits when exposed to either a marching or a running regimen. However, there were significantly more lower-limb injuries and twice the number of restricted days in the run group. Conversely, Popovich (2000) reported a higher rate of injuries in companies that spent relatively more time marching than running. What is clear is that both these activities can lead to a significant number of injuries within the military.

Most studies have generally identified risk factors and associations for overuse injuries as a whole including the role of gender, body weight and physical fitness (Billings, 2004). Much less work has been carried out on the biomechanical variables that may relate to individual conditions. Undertaking studies to isolate the risk factors for individual conditions can be problematic. The biggest hurdle in prospective studies is the large sample size required. Willems *et al.* (2006) were the first to carry out a full prospective study using 3D gait kinematics and plantar pressure to identify risk factors for EILP.

The study by Willems et al. (2006) provides useful information on risk factors for the EILP group as a whole although it was not clear whether the biomechanical variables identified would predict the development of each distinct cause of EILP. They reported that subjects of the injured group had significant differences in kinematics at the ankle but not at the knee. A number of plantar pressure variables were also implicated.
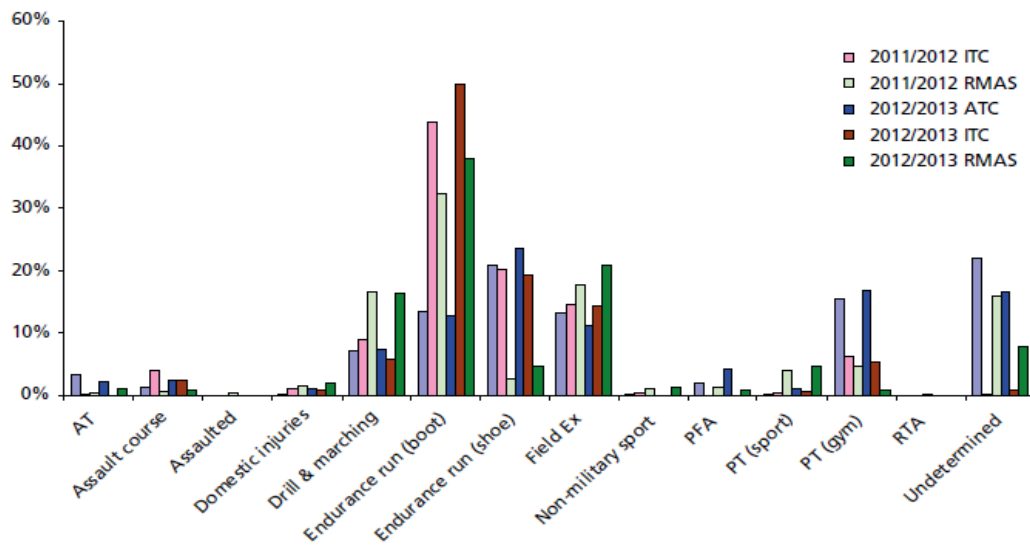
Figure 1 Percentage of injuries by each type of perceived cause (DGAMS, 2013). ITC=Infantry Training Centre, RMAS=Royal Military Academy Sandhurst, ATC=Air Training Corps, AT=Adventure training, PFA=Personal Fitness Assessment, PT=Physical Training, RTA=Road Traffic Accident

1.2. Chronic Exertional Compartment Syndrome in the military

Chronic exertional compartment syndrome was first described in 1956 (Mavor). It is a condition typically affecting the anterior compartment of the lower leg that causes pain during exercise. The presentation of CECS as EILP has proved to be a difficult condition to diagnose and treat within the military. Treatment within the military population may be harder than within the majority of the civilian world due to the persistent physical demands and small allowance for activity modification.

At the point of conception of this series of studies, the Defence Medical Rehabilitation Centre (DMRC) was carrying out invasive diagnostic tests using IMCP measurement for CECS on c.100 patients per year (Franklyn-Miller, Roberts, Hulse, & Foster, 2014). Prior to 2007, IMCP was measured during an exercise protocol consisting of supine dorsi- and plantar-flexion of the ankle (Dharm-Datta et al., 2013). A test was deemed positive based on the Puranen (1981) criteria (mean IMCP >50 mmHg during exercise) and the reproduction of symptoms. However, clinical experience with this protocol suggested that it was hard to reproduce symptoms; furthermore it did not relate well to the activities normally associated with symptom reproduction (Dharm-Datta et al., 2013).

Based on evidence regarding activities associated with symptom reproduction, the diagnostic protocol was therefore changed to a more dynamic situation with IMCP measured during a loaded march. However the technical issues that are associated with the fluid-filled catheter system (Styf, 1995), especially with dynamic testing, resulted in a number of tests being interrupted due to the need to flush the catheter. Using this technique, clinicians reported that the rate of positive diagnosis was higher than expected. The combination of these two issues meant that the clinicians involved in these tests no longer had full confidence in the results. To compound these issues, there was also a perception that the typical surgery recommended for patients with CECS diagnosed in this way was not providing the desired results.

The high incidence of CECS in the military combined with an uncertainty over diagnosis and the efficacy of treatment meant there was a clear requirement within the Defence Medical Services to investigate CECS in more detail and as such was stated as one of the Surgeon General's research priorities. A systematic review was therefore carried out to investigate the validity of the

diagnostic criteria for CECS (Roberts & Franklyn-Miller, 2012); and a retrospective study of the outcomes of surgery from patients diagnosed at DMRC (Roberts, Krishnasamy, Quayle, & Houghton, 2014). These studies identified poor validity of the criteria used to diagnosis CECS and poor outcomes following surgery respectively.

Following these two preliminary studies (Roberts & Franklyn-Miller, 2012; Roberts et al., 2014) and clinical observations of altered biomechanics a new treatment package was developed by the clinical team involving the 're-education' of both running and marching gait. This alternative treatment was set up at DMRC and based on recently published theories of biomechanical overload syndrome for patients presenting with anterior compartment EILP (Franklyn-Miller, Roberts et al., 2014). The programme focussed on encouraging a change in running gait from a heel-strike pattern to a forefoot pattern to try to reduce the activation of the muscles in the anterior compartment. This was in line with the forefoot running treatment packages described for CECS in the literature (Section 2.2.6.2). The DMRC programme also included adjustment of military-specific gait (marching) that has been reported as provoking greater levels of pain than running in the study population (Verleisdonk, Schmitz, & van der Werken, 2004). However quantitative evidence for any biomechanical differences at this stage was absent.

The theory behind biomechanical overload syndrome precluded IMCP from the underlying pathology of these patients and moved the focus away from reducing IMCP to reducing muscle activation. However our research group have since provided evidence that IMCP is elevated in patients, even before movement begins, refuting this hypothesis (Roscoe, Roberts, & Hulse, 2015). Nevertheless, the interaction of muscle activity with the pathology of CECS is likely to play an important role in determining the onset of pain. The exact role of biomechanical factors in the development of this condition is unclear and requires further investigation. The questions arising from the two early studies (Roberts & Franklyn-Miller, 2012; Roberts et al., 2014) and the subsequent changes to the clinical diagnosis and treatment of CECS at DMRC lead to the development of this research program.

1.3. Cost to the military

Injuries to service personnel are associated with a significant cost to the military. All injuries lead to a cost in terms of training days lost, loss of medically fit personnel and the cost of providing rehabilitation. This last point is unique to the military as medical care for private sector workers is typically provided for by the National Health Service (NHS) or under personal insurance. While military personnel are entitled to access NHS facilities, the Defence Medical Services provides extensive health care provision for military personnel including comprehensive care pathways for the diagnosis and rehabilitation of musculoskeletal injuries. The primary role of the Defence Medical Services is to ensure that service personnel are medically fit and ready to go where they are required in the UK and throughout the world. That is, personnel must be 'fit for task'.

Overuse injuries of the lower limb pose a particular problem as they often require prolonged treatment before return to normal duties. This can leave personnel unfit for task for major periods of time leading to significant costs to the military. This is likely to have a significant impact in theatre, where almost 40% of personnel on operations present with a musculoskeletal non-battle injury (DGAMS, 2013). The loss of foot function associated with CECS (Rowdon, Richardson, Hoffmann, Zaffer, & Barill, 2001) may represent an additional risk of tripping for deployed troops suffering from CECS. A large proportion of deployed troops are therefore required to have days off duty or to operate with only light duties to have treatment and aid recovery.

The diagnostic test for CECS typically costs c.£500 on consumables alone along with the costs associated with the senior clinicians administering the test. High costs are also associated with subsequent surgery and rehabilitation. For example, intensive rehabilitation has been estimated to cost £500 per day at DMRC (Murrison, 2011) and £1,600 per week in the Royal Marines (House, Reece, & Roiz de Sa, 2013). There are therefore high costs specifically associated with CECS; additional indirect costs are also incurred as described below.

Injuries during training often result in a loss of training time, causing a decline in physical fitness and reduction in the amount of military skills training. Long-lasting injuries will therefore result in recruits being put back in training ('back-

trooped') (Blacker, Wilkinson, Bilzon, & Rayson, 2008). However, if service personnel are unable to return to training or duty following injury (such as CECS) they will often be medically discharged. Musculoskeletal disorders have been reported to account for 52% of medical downgradings and 67% of medical discharges (E. Gibson, Hicks, Butler-Stoney, & Blatchley, 2005; Hawley, 2007). It has also been suggested that there may be voluntary withdrawal, in part due to a consequential disillusionment, following injury (House et al., 2013; Ross & Allsopp, 2002). These scenarios in particular represent a large cost to the military as all investment in the individual is lost. Table 1 describes the typical training costs to the military.

Table 1 Standard Entry Costs , 2010–11 (House of Commons Hansard Debates 15 dec 2011 Volume 537 Column H66W2011)

	Cost per trainee	Cost of whole cohort (n=12,258)
Recruitment	£10k	£123m
Phase One training	£33k- £39k	£402m -£472m
Sum	£43k-£48k	£525m-£594m

Medical discharge due to musculoskeletal injuries is a major burden to the public purse and an unfortunate outcome for those individuals affected. In the Army, 57-62% of medical discharges were due to musculoskeletal injuries between 2008 and 2013 (DGAMS, 2013). Within training, this number appears to be higher with 81-90% of all medical discharges due to injuries to the lower limb (Blacker et al., 2008; DGAMS, 2013). This is disproportionate to the number of referrals with only 55% of injuries related to the lower limb. Injuries involving the lower limb, such as CECS, therefore appear to be more severe and result in higher costs to the military than other musculoskeletal injuries.

1.4. Limitations and constraints at the outset

1.4.1. Choice of marker set

The Military Performance Analysis and Research Laboratory (MPARL) was still under development at the start of this PhD. As part of the developmental process there was a requirement by DMRC for the collection of normal gait data for use as a comparison group within a new clinical gait service. This was also required in a short period of time. In order to prevent duplication of work, the control subjects from these PhD studies were required to be also used as this comparison group. However, the marker set for this comparison group had already been selected by DMRC. As such, only small additions to the marker set could be made for the express purposes of these studies.

1.4.2. Kinematic data use by multiple investigators

As a consequence of the requirement to minimise additional patient attendances and the availability of control subjects, some sessions were used for the simultaneous capture of data for multiple studies by several researchers. In order to avoid the duplication of investigations on several groups for the same purposes, collection of information, allowing multiple work-strands by several investigators to be carried out, required the use of the same kinematic data to inform broader analysis. This included matching plantar pressure, EMG and kinetic findings to global movement patterns as well as the identification of variables to be monitored in future studies and the critical investigation of biomechanical overload syndrome. Advance agreement was made with the University of Exeter, DMRC and other host institutions including MODREC, in order to de-conflict and avoid subsequent suggestion of plagiarism, as this same data would be reported in both instances. Consequently several researchers worked on the capture and processing of kinematic data and the development of the corresponding kinematic model reported in this thesis. This pragmatic solution was also necessitated because, as detailed above, the gait laboratory at DMRC was newly established and no kinematic models were so far in use and all kinematic data was required for normative use.

The key tasks involved in the production of kinematic data were:

a. Surface anatomy for marker placements and repeatability studies
b. Marker set selection including the use of specific markers and clusters

c. Data capture

d. Segment definition and selection (e.g. torsioned vs un-torsioned tibial models)

e. Visual gait event labelling

f. Model labelling

g. Variable selection

h. Data processing (filtering, interpolation and export)

i. Analysis techniques

j. Statistical analysis

k. Data interpretation

l. New hypothesis generation

The author was involved in stages a-j detailed above to varying degrees and data was handled independently from stages k-l.

1.5. Thesis questions

As a result of the high incidence of CECS and associated significant financial cost to the military and personal cost to the patients there were a number of key research questions that were identified:

1. What are the clinical observations that best characterise CECS and which activities may lead to the development of CECS in the military?
2. What plantar pressure variables related to lower limb muscle activity and foot type are associated with CECS?
3. What kinematic, kinetic and muscle activation variables are associated with CECS during walking and marching
4. What kinematic and muscle activation variables are associated with CECS during running?

2. Review of the literature

2.1. Structure and function of the lower leg

2.1.1. Gross anatomy

The lower leg consists of four compartments separated by bone, fascia and septa (Figure 2 & Figure 3). Each compartment contains a combination of muscle, tendon, nerves and a vascular supply. The anterior compartment consists of the extensor muscles (tibialis anterior (TA), extensor hallucis longus, extensor digitorum longus and peroneus tertius), the deep peroneal nerve and the anterior tibial artery and veins (Toomayan, Robertson, & Major, 2005). The lateral compartment consists of the peroneal muscles (peroneus longus and peroneus brevis) and the common peroneal nerve. The superficial posterior compartment consists of the plantarflexor muscles (soleus, gastrocnemius and plantaris (mostly tendon)). The deep posterior compartment has two potentially clinically relevant subcompartments (M. Hislop, Tierney, Murray, O'Brien, & Mahony, 2003; M. Hislop & Tierney, 2004; Kwiatkowski & Detmer, 1997) and consists of the flexor muscles (tibialis posterior, flexor hallucis longus, flexor digitorum longus), popliteus at the proximal end, and neurovascular bundles (peroneal artery and veins, posterior tibial artery and veins and the tibial nerve).

The distribution of these muscles varies according to location (Figure 4). Proportionally the plantarflexors comprise c.72%, while TA comprises c.10% of the total muscle volume of the lower leg (Fukunaga et al., 1992) and c.57% of total dorsiflexor volume (Fukunaga, Roy, Shellock, Hodgson, & Edgerton, 1996).
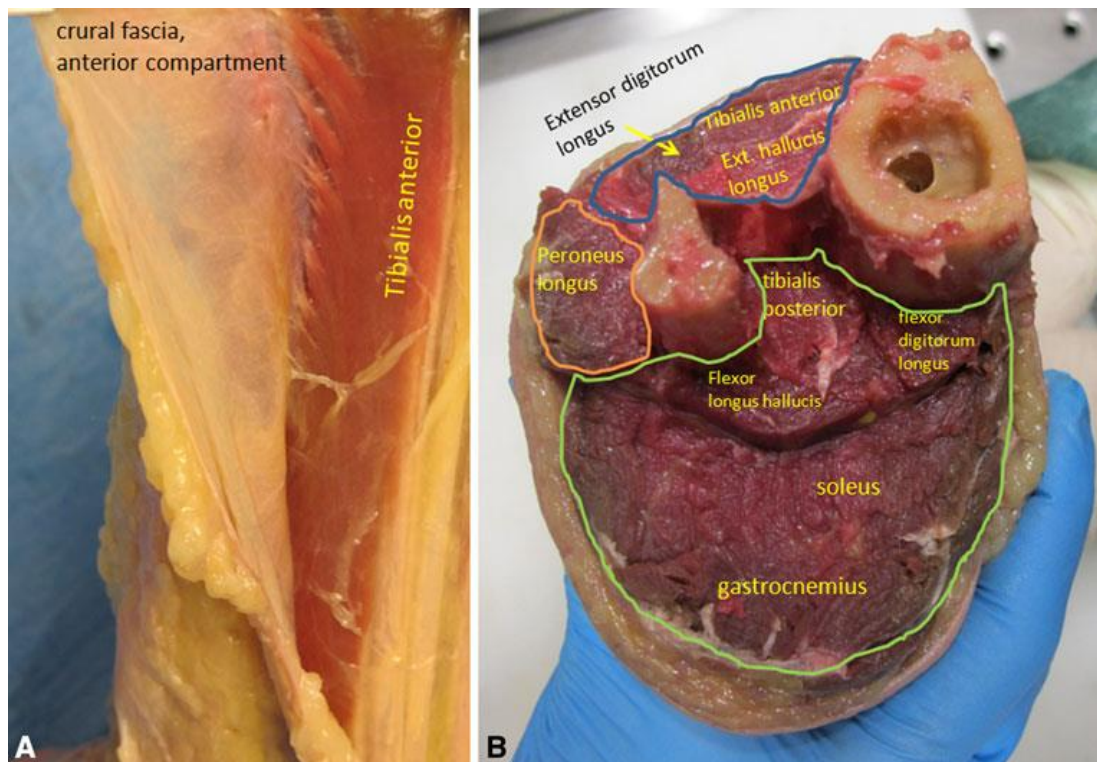
Figure 2 Dissection of the leg. (a) Anterior vision of the leg; the crural fascia is detached from the underlying muscle. (b) transversal section of the leg to show the anterior, posterior and lateral compartments (Stecco et al., 2014).
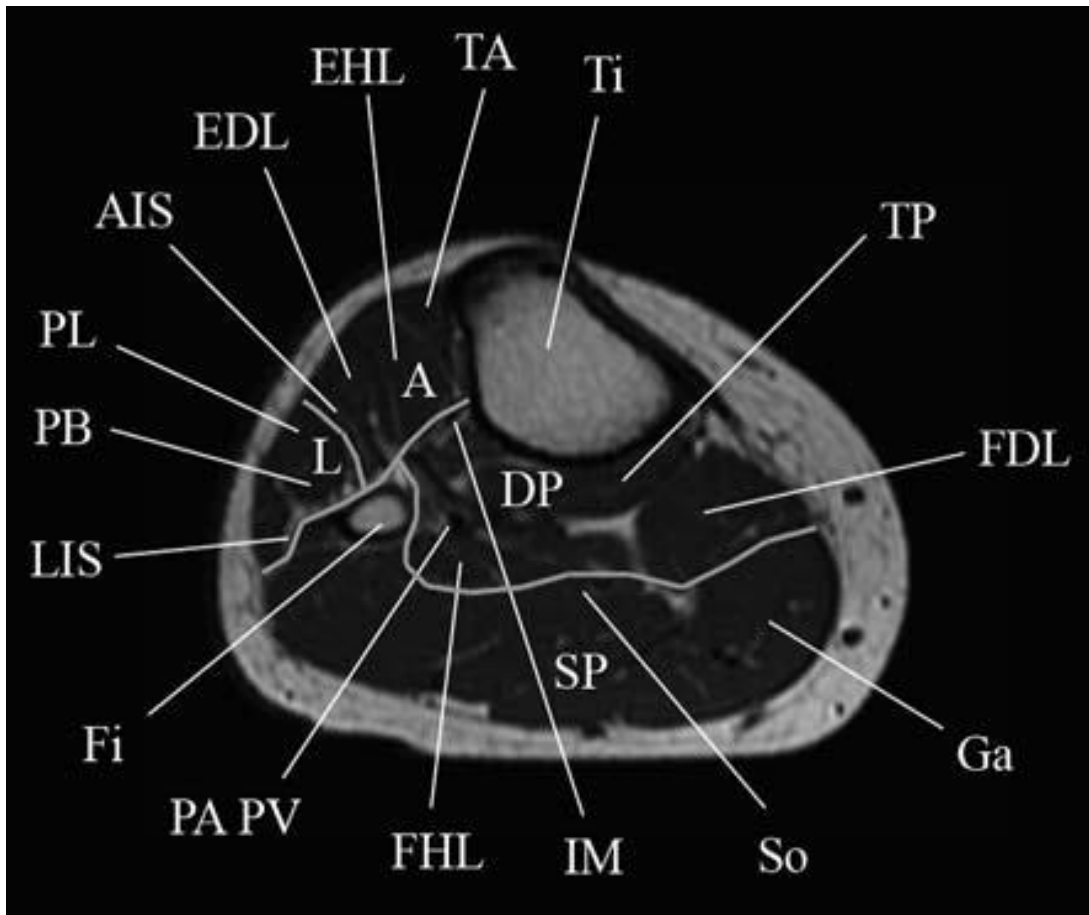
Figure 3 MR image of the mid lower leg demonstrating compartment anatomy. **The anterior compartment (A) contains the m.Tibialis anterior (TA), extensor hallucis longus (EHL), and extensor digitorum longus (EDL). The anterior intermuscular septum (AIS) and lateral intermuscular septum (LIS) are the boundaries of the lateral compartment (L), which contains the peroneus longus (PL) and brevis (PB). The fibula (Fi), tibia (Ti), and interosseous membrane (IM) separate the anterior compartment from the deep posterior compartment (DP), which contains the m.Tibialis posterior (TP), flexor hallucis longus (FHL), and flexor digitorum longus (FDL). The peroneal artery (PA) and vein (PV) are located laterally in this compartment. The superficial posterior compartment (SP) contains the gastrocnemius (Ga) and soleus (So) muscles (Toomayan et al., 2005).**
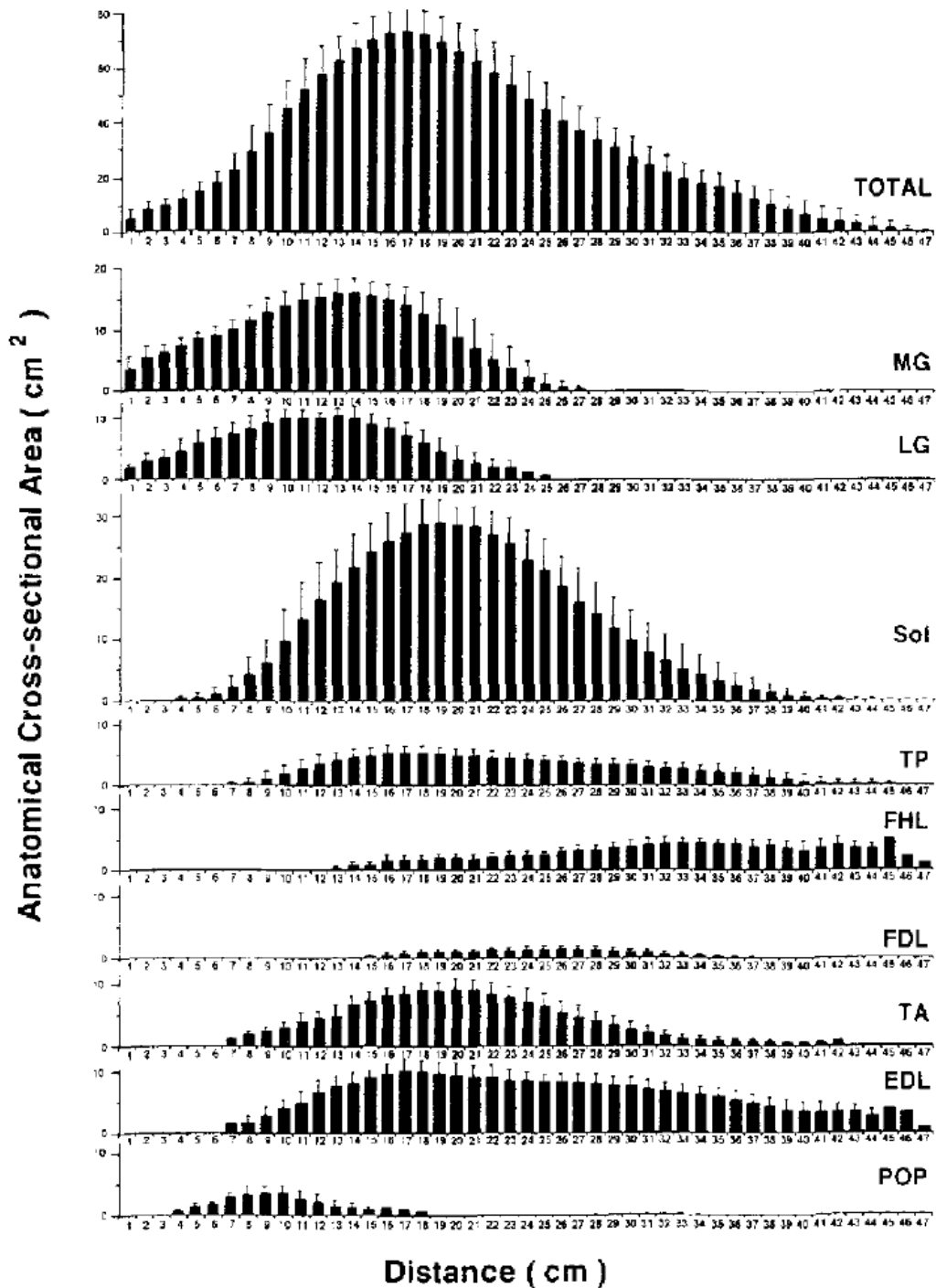
Figure 4 Anatomical cross-sectional areas of all muscles combined (top) and of each muscle at each slice along the length of the leg. MG=Medial Gastrocnemius; LG=Lateral Gastrocnemius; Sol=Soleus; TP=Tibialis posterior; FHL=Flexor hallucis longus; FDL=Flexor digitorum longus; TA=Tibialis anterior; EDL=Extensor digitorum longus (represents all the lateral and anterior compartment muscles except for TA); POP=Popliteus. Each bar represents the mean (SD) for all subjects (n=12). Slice 1 was identified for each subject by the proximal edge of the patella. (Fukunaga et al., 1992)

2.1.2. The crural fascia

Dense connective tissue sheets such as muscle envelopes (e.g. endo-, peri-, and epi-mysium) aponeuroses and joint capsules are often termed fascia (Figure 5). This fascia is often considered as a provider of support for other structures. However recent work has suggested that the fascia may play a bigger role than simply providing support. The fascia also plays an important role in transmitting force from the muscle to the skeleton in addition to the tendon (Huijing & Baan, 2001). Removal of this ability through fasciotomy leads to a reduction in force transmission capability (by 10-16% acutely) and alterations in the force-length curve (Garfin et al., 1981; Huijing & Baan, 2001).

Not only can fascia help with force transmission, there is now evidence that this tissue may also be able to contract in a similar way to smooth muscle (Schleip, Klingler, & Lehmann-Horn, 2005) and therefore actively adjust its stiffness. It is possible that the ability to enhance fascial stiffness could improve fascial proprioception and increase force transmission. The effects of a long term increase in fascial stiffness are unknown, although chronic contractures within the fascia have been documented (Gabbiani & Majno, 1972). Repeated stretching of the fascia has also been shown to lead to an increase in stiffness of the fascia, presumably due to these contractile elements (Yahia, Pigeon, & DesRosiers, 1993). The strength of this force production capacity has been theorised to be in the range capable of causing a compartment syndrome, albeit in the lumbar paraspinal muscles (Huijing & Baan, 2001).

Perhaps due to this new knowledge regarding myofascial force transmission, the anatomy and histology of the deep fascia has only recently become a subject of interest. This has been most intensely studied by Stecco (2009). They reported the mean thickness (±SD) of the posterior crural fascia to be 924 ± 220 µm, formed by three separate layers with a mean thickness (±SD) of 277.6 ± 86.1 µm. This is 2-3 times thicker than reports that sampled the anterior crural fascia (Dahl, Hansen, Stal, Edmundsson, & Magnusson, 2011; Hurschler, Vanderby, Martinez, Vailas, & Turnipseed, 1994; Turnipseed, Hurschler, & Vanderby, 1995). In some areas the layers are connected by isolated bundles of collagen fibres; although usually they are completely independent of each other. It is unclear whether the connections represent a normal or pathological state.
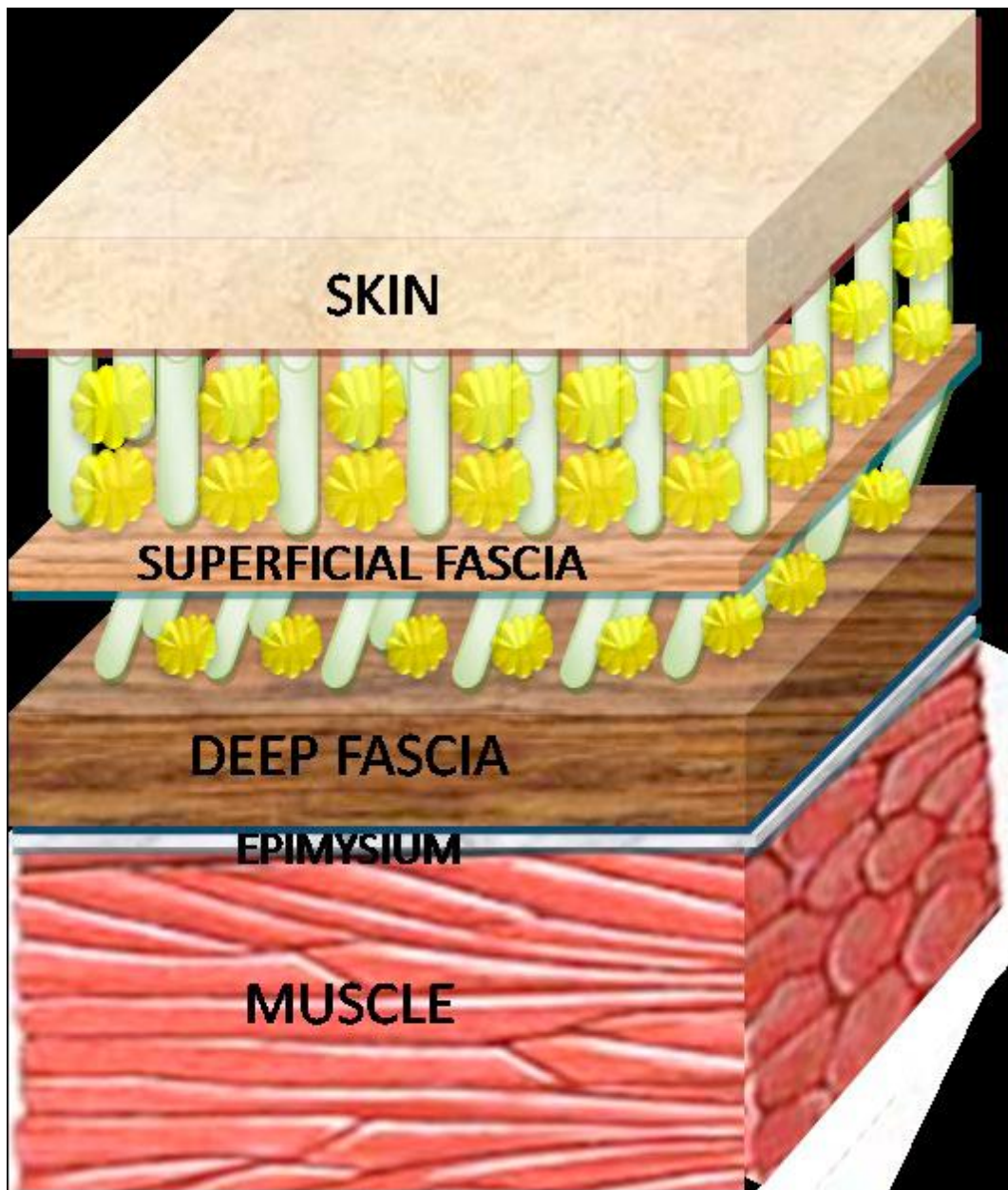
Figure 5 Basic pattern of organisation of subcutaneous tissue and superficial and deep fascia (Stecco et al., 2011).

A model describing how the posterior region of the crural fascia responds to various loadings was then developed using this data (Stecco et al., 2009). Due to the presence and alignment of multiple layers the stress-strain curves vary depending on the direction of loading in relation to the orientation of the fibres (Figure 6). The arrangement of the crural fascia means that it is able to resist the pressure applied by the muscle through the development of tensile stresses acting in the plane of each layer. The crural fascia also contains hyaluronic acid-secreting cells that may provide a smooth gliding surface between the layers (Stecco, Macchi, Porzionato, Duparc, & De Caro, 2011). The Stecco group also hypothesise that in CECS, stiffness may be altered through a loss of

independence of this layer preventing normal adaptation to muscle volume changes (Benetazzo et al., 2011). It is not clear whether this would result in a concomitant change in thickness.
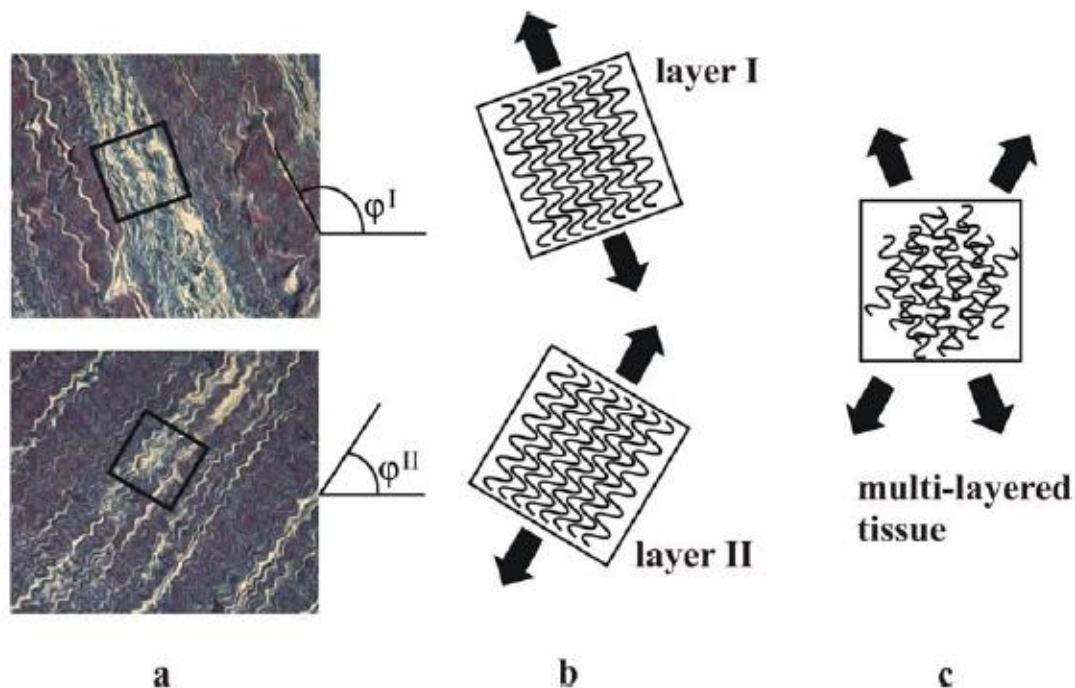
Figure 6 Functional behaviour of a multi-layered tissue : orientation of the collagen fibres in two adjacent layers from histology (a) and consequent schematization of direction of prevalent stiffness/strength of the two layers (b) and whole tissue (Stecco et al., 2009).

More recent data from the same group demonstrated that fascial stiffness was dependent on the location and direction of the force (Stecco, Pavan, Pachera, De Caro, & Natali, 2014). Stiffness in the longitudinal samples was greater than in the transverse samples. This may be a result of and/or to aid force transmission in this direction. The anterior crural fascia was also stiffer than the posterior fascia. This difference was particular pronounced in the longitudinal plane and could help explain why CECS is more prominent in the anterior compartment. The thickness of fascia can differ in other pathologies. Subjects with lower back pain have 25% greater perimuscular connective tissue thickness and ultrasound echogenicity than controls (Langevin et al., 2009). The authors suggest that this may be a result of repeated stresses leading to remodelling over time. Similarly, thickness of the posterior crural fascia is thicker in patients with Achilles tendinopathy and could be diagnostically useful; again the authors suggest this may be due to an increased mechanical loading of the fascia (Stecco et al., 2014).

The fascia is also highly innervated. Nerve fibres, particularly Ruffini and Pacini corpuscles, are mostly located in the middle layer and are closely connected to the collagen fibres suggesting they may be activated each time the fascia is stretched. Stimulation of these structures through excessive stretch has been suggested to be a potential cause of pain in CECS (Balduini, Shenton, O'Connor, & Heppenstall, 1993; Humphries, 1999; Schepsis, Martini, & Corbett, 1993). Numerous vascular vessels have also been documented in the crural fascia (Benetazzo et al., 2011; Stecco et al., 2009).

The anterior, posterior and transverse intermuscular septa are found between the anterior-lateral, lateral-posterior and superficial posterior-deep posterior compartments respectively. An interosseous membrane spans the gap between the tibia and fibula and between the anterior-deep posterior compartments. Canine studies demonstrate that these boundaries are impermeable leading to different pressures in adjacent compartments (Hargens et al., 1978). It is this feature that likely enables CECS to develop.

Tibialis anterior has the longest muscle fibre length (c.7.7 cm) of the lower leg muscles (Fukunaga et al., 1992). By adjusting fibre length to pennation angle, it has been calculated that TA has four times the velocity potential than that of the soleus (but 2.5 times lower power potential). Given the greater velocity potential of the TA, it is possible that its ability to contract rapidly helps to stabilise the ankle joint and control the lowering of the forefoot during early stance. Contraction of the TA at this time point has been proposed to be related to the development of CECS (Tweed & Barnes, 2008).

2.1.3. Morphology and role of tibialis anterior

The course of the tendon, and its insertion points, enable it to invert and extend (dorsiflex) the foot during contraction (Klein, Mattys, & Rooze, 1996). These actions may also allow it to play a role in raising the medial longitudinal arch (Hunt, Smith, & Torode, 2001). Tibialis anterior originates on the upper half of the lateral tibial shaft and interosseous membrane (Wolf & Kim, 1997). The tendon passes under the extensor retinaculum which stabilizes the tendons in the frontal aspect of the ankle and foot ((M. H. Lee et al., 2006); Figure 7). The distal tendon fibres medially rotate from the musculotendinous junction, through a groove on the medial cuneiform and attach to their insertion point (Fennell &

Phillips, 1994). In 96% of subjects (n=156 feet), the tendon inserted onto both the medial cuneiform and first metatarsal bones (Figure 8; Brenner, 2002). The three largest studies suggest that a greater proportion of proximal (deep) tendon fibres than distal (superficial) fibres attach to the foot (Brenner, 2002; Giani, 1909; Musial, 1963).
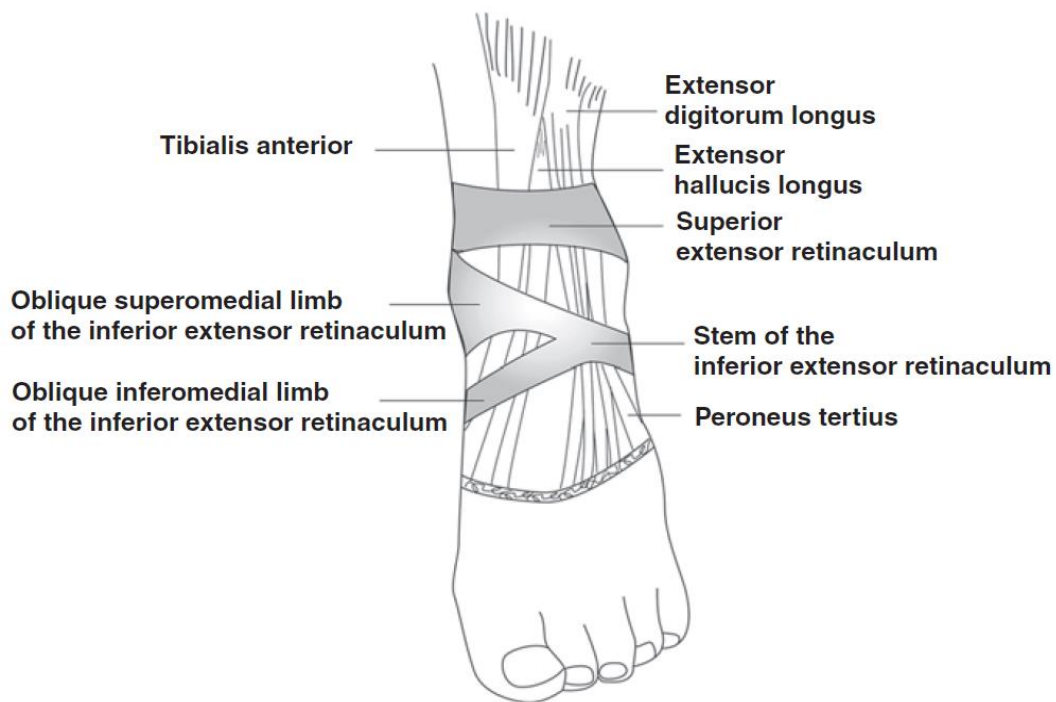
Figure 7 Extensor retinaculum and extensor tendons of the foot and ankle (M. H. Lee et al., 2006)
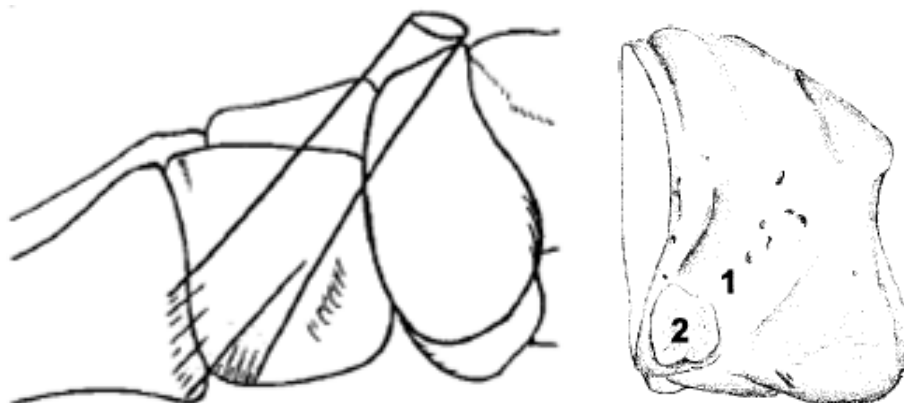
Figure 8 Attachments of the Tibialis anterior tendon to the foot (left) and schematic drawing (right) of the medial cuneiform bone (medial view) showing the groove for the tendon of the TA (1) and an elevated area for insertion (2) (Brenner, 2002).

The muscle is bipennate with a pennation angle of c. 8 degrees (Alexander & Vernon, 1975) and is innervated by the deep peroneal nerve (at the level of L4 and L5 spinous processes) (Lawrence & Botte, 1995; Liguori, Krarup, & Trojaborg, 1992). A cadaver study identified three distinct neuromuscular partitions two of which lie posteriorly (Wolf & Kim, 1997). The superficial fibres originate from the anterior-superior aspect of the tibia, inferolateral to the patella. The deep longitudinal fibres are separated from the superficial fibres by a thin sheet-like aponeurosis that fans out from the insertion tendon but lies deep within the whole muscle. The proximal fibres of all three heads insert into this aponeurosis and the more distal fibres into the tendon. More recent studies using 3D Magnetic Resonance Imaging (MRI) have only reported findings for the superficial and deep partitions (Figure 9) (Lansdown, Ding, Wadington, Hornberger, & Damon, 2007). The authors of these studies estimated that a third partition was only identifiable in c.1% of cases (personal communication). Further work from this group suggests that the superficial compartment is preferentially activated during low-moderate intensity exercise (Damon, Wadington, Lansdown, & Hornberger, 2008).

The muscle consists mainly of slow type I fibres (71%) and 29% fast type fibres (27%:IIA, 0.3% IIX and IIX/IIA, 1.5% I/IIA fibres) (Wahlin Larsson, Kadi, Ulfberg, & Piehl Aulin, 2008). It is not clear whether the fibre type proportions vary in each partition. However fibre type does vary systematically with muscle depth with a greater proportion of type II fibres found superficially and type I fibres in the deeper regions (Henriksson-Larsén, Lexell, & Sjöström, 1983).
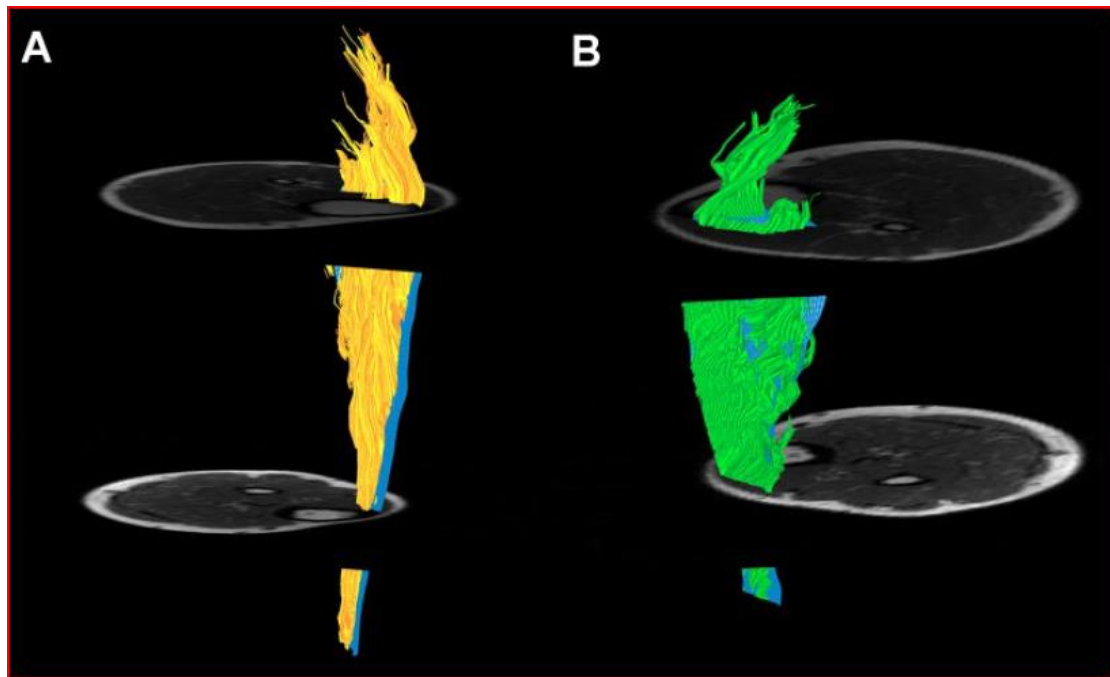
Figure 9 Tibialis anterior neuromuscular compartments. A: fibre tracts of the deep compartment, indicated as gold (and similarly shaded) lines. B: fibre tracts of the superficial compartment, indicated as green (and similarly shaded) lines (Lansdown et al., 2007)**.**

Tibialis anterior is generally accepted to be primarily a dorsiflexor of the foot in addition to its inversion role. In non-weight-bearing it is most active during a dorsiflexion movement when the foot is inverted (Houtz & Walsh, 1959). The most accurate estimates (S. C. Miller, Korff, Waugh, Fath, & Blazevich, 2015) of the dorsiflexion moment arm suggest it is approximately 32 mm – 43 mm long (longer in dorsiflexion); in comparison to its inversion moment arm which is approximately 4 mm long (Klein et al., 1996). The dorsiflexion moment arm also increases by 9 mm – 15 mm during contraction due to the deformation of the extensor retinaculum (Figure 13; Maganaris, Baltzopoulos, & Sargeant, 1999).

2.1.4. Tibialis anterior during contraction and gait

The TA muscle demonstrates peaks in EMG activity pre and post heel strike during walking (van Hedel, Tomatis, & Muller, 2006). During walking, the TA has been reported to become active prior to toe-off and to remain active throughout the swing phase and into the first 10% of the next cycle. The posterior calf muscles (medial gastrocnemius, lateral gastrocnemius, soleus, peroneus longus) are all active at 40% of the cycle when the TA is relatively silent (Cappellini, Ivanenko, Poppele, & Lacquaniti, 2006). During running the

TA muscles increase their activity during the mid-part of the cycle until initial foot contact, whereas the posterior muscles are active instead around the time of foot contact (Gazendam & Hof, 2007). Two studies measuring EMG activity during load carriage found that load had no effect on TA activity (Ghori & Luckwill, 1985; Harman et al., 1992).

Recent studies analysing the variability in TA activation suggest that the muscle can also demonstrate different phases of activation within the same activity (Di Nardo, Mengarelli, Maranesi, Burattini, & Fioretti, 2014). To the author's knowledge, the only study to specifically report the duration of TA activation during the gait cycle described activation lasting for 21% ± 6 while walking in a normal sports shoe (Li & Hong, 2007). This contrasts with the visual representation (Figure 10) by Di Nardo (2014) that would suggest much longer durations. It is possible that the determination of TA duration may be particularly susceptible to differences in thresholds because of ongoing low level activity. This low-level activity may also make it more susceptible to fatigue overload. In fact, the TA has been described as contracting for more than 85% of the gait cycle at greater than 20% of its maximal contraction during running (Reber, Perry, & Pink, 1993). This may explain why the TA fatigues quicker than the gastrocnemius during running (Mizrahi, Verbitsky, & Isakov, 2000). Alternative methods of analysis, for example those examining EMG frequency and intensity, may therefore be preferable during gait. The long duration of low-level activity has also been suggested to make it more susceptible to fatigue overload (Reber et al., 1993).

The stretch responses of the TA (and soleus) are largest during the stance phase of walking (L. O. Christensen, Andersen, Sinkjaer, & Nielsen, 2001). This reflex is also present during simulated inversion stress suggesting a role in the response to deviations from level ground (Ebig, Lephart, Burdett, Miller, & Pincivero, 1997). During the swing phase a stretch reflex is also present but has a longer latency (L. O. Christensen, Morita, Petersen, & Nielsen, 1999). Its function is assumed to be part of the 'stumbling corrective reactions' aiding with the avoidance of obstacles while the foot is in the air (Duysens, Trippel, Horstmann, & Dietz, 1990). Loss of function of the TA due to CECS could foreseeably lead to greater trips; within a military context this could be particularly dangerous while on operations.

The TA reflex is also regulated in response to stimulation of cutaneous foot afferents through a trans-cortical pathway (Nielsen, Petersen, & Fedirchuk, 1997; Zuur, Christensen, Sinkjaer, Grey, & Nielsen, 2009). The TA EMG signal is facilitated following stimulation of the medial plantar nerve (as occurs during the stance phase of normal gait). Inhibition occurs when the superficial peroneal or sural nerves that innervate the dorsum of the foot are stimulated (as may occur when the foot meets an obstacle).

Activity of the TA can also modulate other muscles. For example, common peroneal nerve stimulation that activates the TA also results in inhibition of the soleus during walking; similarly the TA is inhibited following tibial nerve stimulation (Petersen, Morita, & Nielsen, 1999). Positive feedback carried by the TA afferents has been proposed to facilitate contraction of the quadriceps muscle just after heel strike (Marchand-Pauvert & Nielsen, 2002). In summary, activity of the TA is modulated and modulates in response to external stimuli without central command.
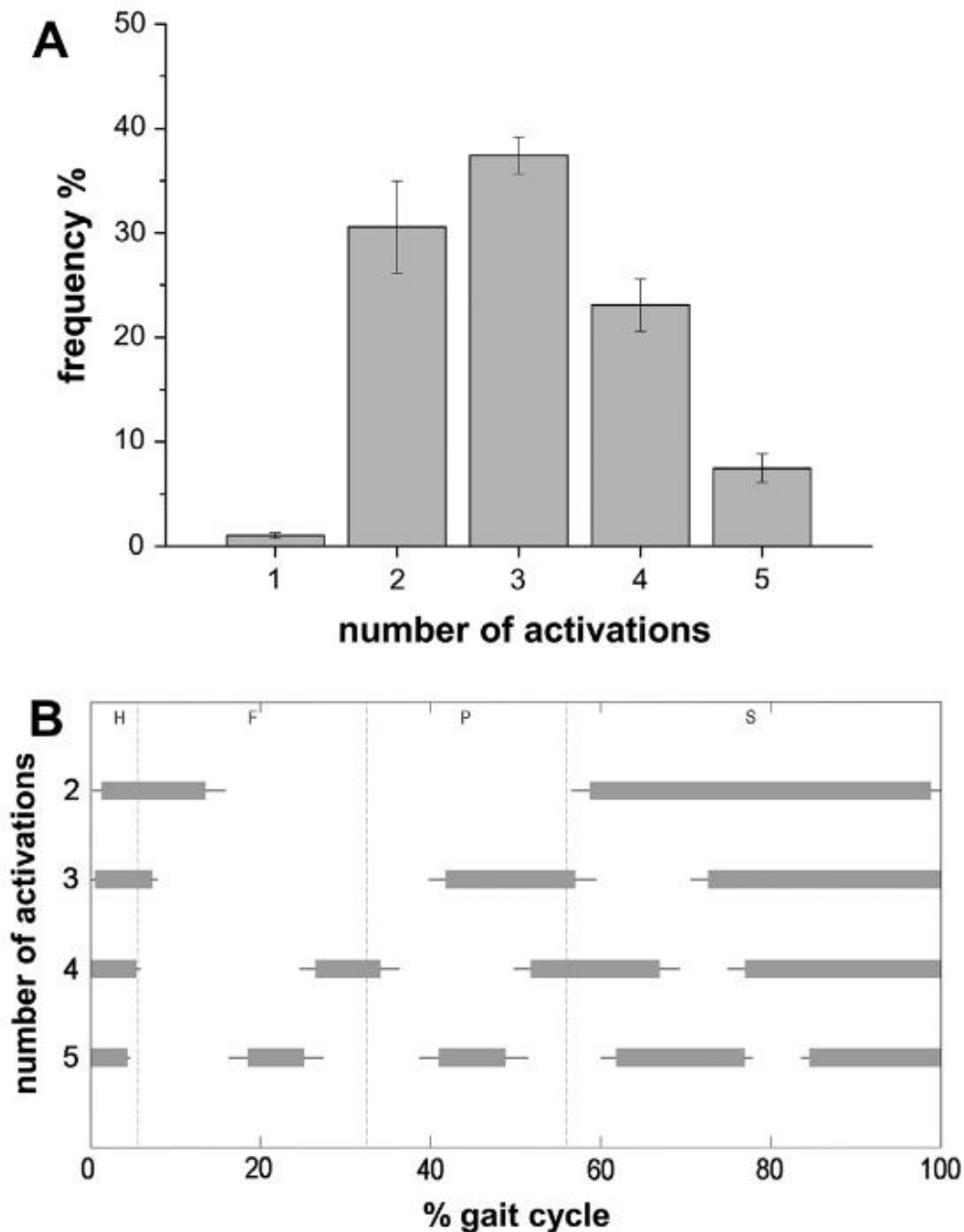
Figure 10 Variability in Tibialis anterior EMG: Mean (+SE) percentage frequency of each of the five different modalities of activation patterns (panel A) and mean (+SE) activation intervals vs. percentage of gait cycle for the modalities with 2, 3, 4 and 5 activations, respectively (panel B), detected during the walk. The heel contact, flat foot contact, push off and swing phases are delimited by dashed vertical lines (Di Nardo et al., 2014).

As described in Section 2.1.3, the TA is comprised of three separate neuromuscular partitions. The reasons for this are unclear as force transmission through a common tendon (and attached fascia) is generally assumed to result in the same mechanical action; although this assumption is now being questioned. For example, differential activation of the lateral gastrocnemius

neuromuscular partitions can lead to the production of different resultant joint torques (Carrasco, Lawrence, & English, 1999).

During dynamic dorsiflexion exercise, greater superficial TA muscle activity is detected using MRI than the deep neuromuscular partition (Akima, Ito, Yoshikawa, & Fukunaga, 2000). Data during isometric contractions also suggests that the magnitude of this difference is related to exercise intensity (Damon et al., 2008). This may be explained by varying muscle fibre type distributions in each partition (Dum & Kennedy, 1980). These results therefore suggest that the TA partitions can also be preferentially recruited. However, the exact function of the partitions during gait is therefore not well understood.

In summary, the TA functions to generate inversion and dorsiflexion moments during gait. This aids in the prevention of 'foot slap' during heel strike and in toe clearance during swing. It also reacts to the environment via stretch and sensory innervation to enable the body to cope with uneven surfaces and obstacles. The role that the TA partitions play in this however is not well understood.

2.1.4.1. Effect of foot type, footwear, orthoses and surfaces

Several studies have suggested that foot type, footwear and foot orthoses can have an effect on muscle activity (Murley, Landorf, Menz, & Bird, 2009). The first observation that an individual's foot type affects TA muscle activity was made in 1968 (Gray & Basmajian). Increased peak EMG amplitude has been demonstrated during the contact phase in flat arched subjects in comparison to those with a normal arch (Murley, Menz, & Landorf, 2009). Similarly, subjects with musculoskeletal symptoms attributed to their 'planus' or 'pronated' static foot posture have greater activity at heel contact than controls (Hunt & Smith, 2004). Cornwall (1994) found that 'early pronators' displayed a shorter time to the minimum EMG amplitude. However, during running foot type was not observed to correlate with integrated EMG, onset or co-activation (Williams, Davis, Scholz, Hamill, & Buchanan, 2004).

The use of footwear and the type of footwear may also have an effect on TA activation. Increasing heel height has been observed to decrease EMG amplitude (K. H. Lee, Shieh, Matteliano, & Smiehorowski, 1990) and lead to a shorter duration of activation during walking (Li & Hong, 2007). Conversely,

three other studies did not find evidence of an effect of heel height (Joseph, 1968; C. Lee, Jeong, & Freivalds, 2001; Stefanyshyn, Nigg, Fisher, & Liu, 2000).

The shoe sole characteristics do not appear to affect muscle activity during walking. Three different types of nursing shoe with different sole, midsole, upper and innersole characteristics had no effect on mean normalised EMG amplitude (Chiu & Wang, 2007). Similarly, three different types of 'clean room' boots with different shock-absorbing and elastic properties had no effect (Lin, Wang, & Drury, 2007). However, Wakeling (2002) observed that running in a shoe with either a soft or hard midsole significantly alters EMG intensity pre- heel strike. Unfortunately, they did not specify which of the four muscles tested these changes related to.

On the other hand, the use of unstable shoes has been associated with increased EMG amplitude in comparison to barefoot walking (Forestier & Toschi, 2005) and altered root mean square EMG amplitude within defined intervals of stance and swing phase in comparison to walking in a running shoe (Romkes, Rudmann, & Brunner, 2006). Nigg (2006) however found no difference in total EMG amplitude using wavelet analysis when comparing an unstable shoe to the subjects' own shoe.

During shod running, greater EMG intensity has been observed before heel strike in comparison to after heel strike; this difference is further increased when barefoot (von Tscharner, Goepfert, & Nigg, 2003). However, an earlier study did not find any differences between barefoot running, using an athletic shoe with a rigid heel counter or with the heel counter removed (Jorgensen, 1990). The study compared normalised EMG amplitude, time to peak amplitude and the number of turns of the EMG signal. This agrees with the study by Komi (1987) who did not find any differences in the mean or integrated EMG when running barefoot or in five different shoes. The wavelet analysis technique utilised by von Tscharner (2003) may therefore be able to better identify differences in the EMG signal than conventional analyses.

The use of foot orthoses has also been observed to affect TA activity (Tomaro & Burdett, 1993). Orthotics designed to place feet in the neutral subtalar joint position increased the duration of TA activity during stance phase without an effect on average EMG activity. The function of the TA to actively aid balance

can also be inferred by the observation of greater activity during walking in subjects with chronic ankle instability (Louwerens, van Linge, de Klerk, Mulder, & Snijders, 1995). This balance function may also explain the increased EMG amplitude observed during running with a medial wedged midsole when compared to a neutral midsole (O'Connor, Price, & Hamill, 2006).

Muscle activity of the TA also changes with non-level walking. Patla (1986) observed that the normalised average EMG increased linearly with increases in incline (R=0.986 swing phase, R=0.83 stance phase). In comparison to changes in plantarflexor and knee extensor/flexor activity this was particularly pronounced in the swing phase. Sheehan (2014) also demonstrated greater TA muscle activity during the swing phase with uphill walking (Figure 11) but not in the stance phase. These observations both suggest a greater response in the swing phase to slopes. This conclusion is also represented by Lay (2007) who did not find any significant differences in stance phase muscle activity between uphill and level walking; although there were significant increases with downhill walking. They also did not report any differences in burst duration. Conversely, Franz (2013) suggests that there is a significantly shorter period of activation when walking uphill in comparison to level or downhill walking. These findings may have been due to the sampling of an older adult group (mean age 72).
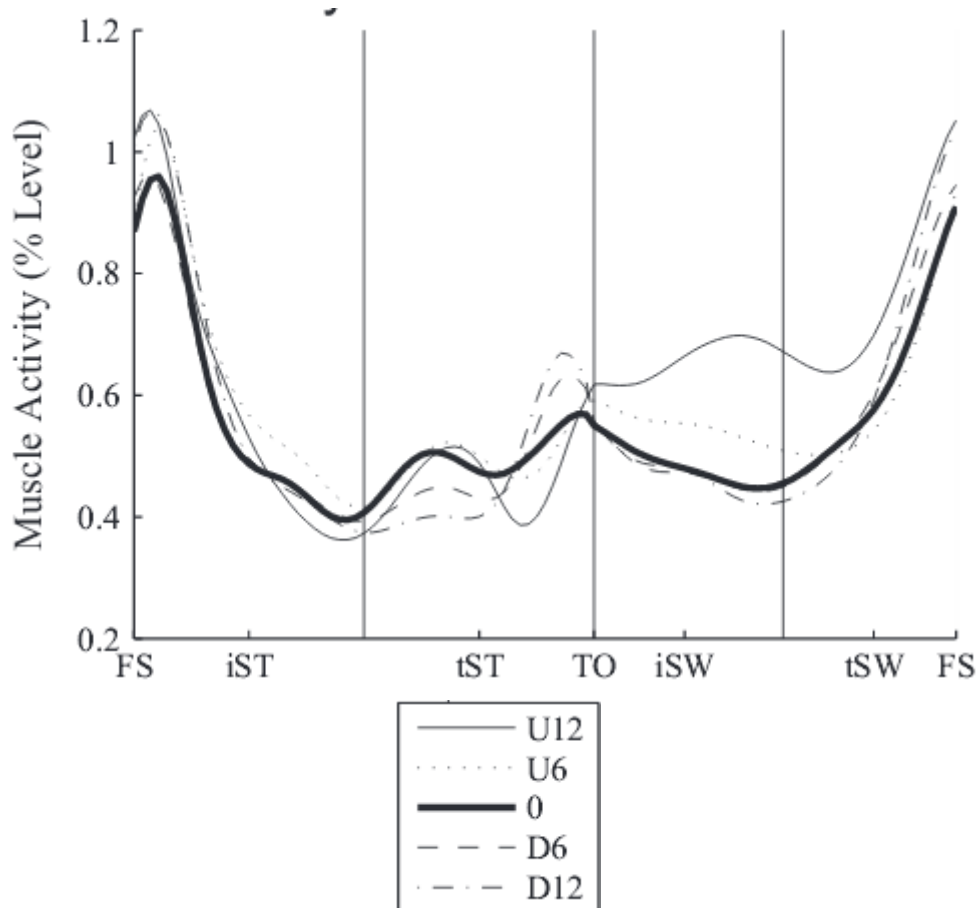
Figure 11 Muscle activity curves averaged across 20 participants. The values have been normalized to the maximum during level walking and stance and swing phases have been time normalized. (U:Uphill D:Downhill 0/6/12: angle in degrees) (Sheehan & Gottschall, 2014)

Sheehan (2014) also report that muscle activity is inversely proportional to height, shank length and leg length when walking on slopes. In the initial stance phase there was a significant correlation with shank length and leg length when walking downhill (12 degrees) and with just shank length when walking uphill (12 degrees). No significant differences were found for level walking or on shallower uphill or downhill slopes (6 degrees). In the initial swing phase there were significant correlations when walking uphill (12 degrees). The strongest correlation was with shank length (R^2=0.46;Figure 12) in comparison to leg length (R^2=0.24) and height (R^2=0.23).
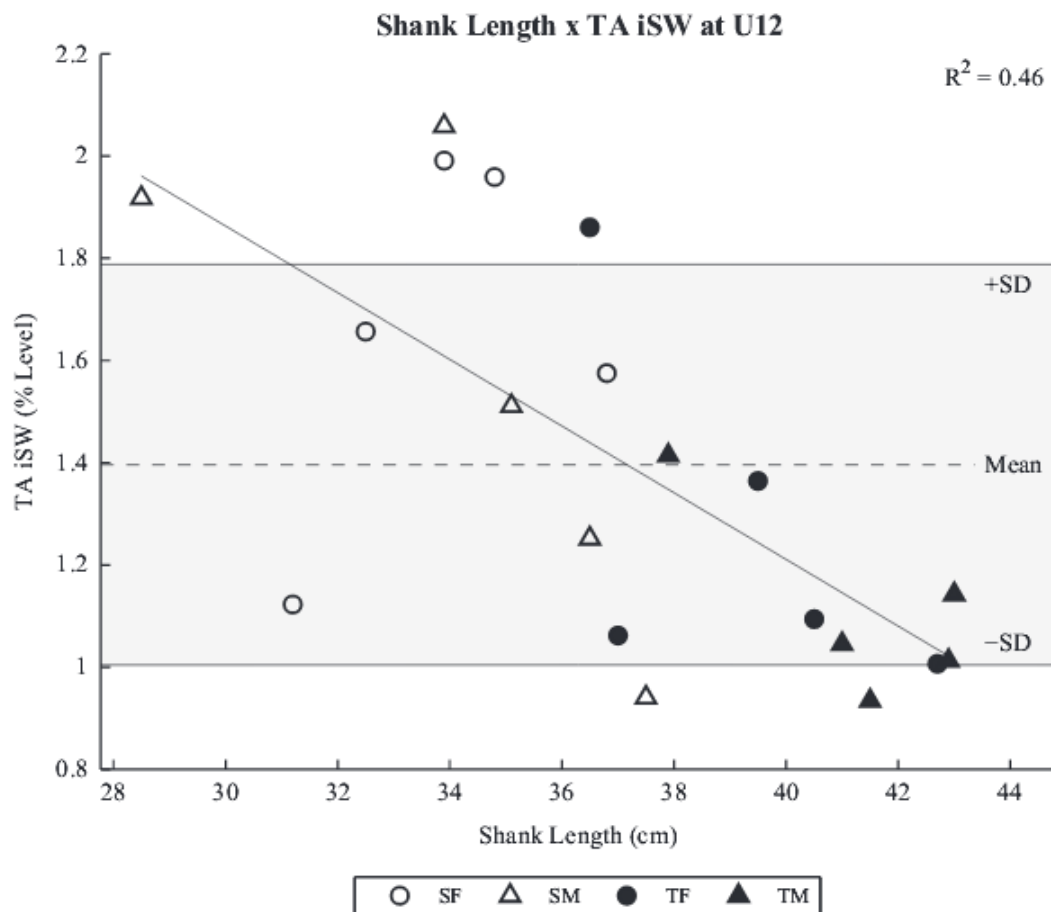
Figure 12 Correlation between shank length and normalized tibialis anterior initial swing phase muscle activity during uphill walking at 12 degrees. The mean is denoted by the dashed line with ± SD shaded around it. The individual values are separated by their initial collection groups of male and female (Δ and x, respectively) and short and tall (open and filled, respectively).

2.1.4.2. Contraction properties

In vivo imaging demonstrates that during walking gait the TA acts isometrically (the fascicles are at constant length) during the loading response and pre-swing phase (Campbell, Graham, Stuckey, & Chleboun, 2003). As the ankle plantarflexes during these stages, this finding means that other components of the musculotendinous complex must be lengthening. They also demonstrate that the muscle shortens (concentric contraction) nearly 10% during initial swing while the ankle dorsiflexes. Similar findings were also reported by (Chleboun, Busic, Graham, & Stuckey, 2007). Cadaver studies suggest that this may also be the case for the extrinsic toe flexors (Hofmann, Okita, & Sharkey, 2013).

During maximal isometric contraction (dorsiflexion) the TA has been reported to be capable of producing forces of up to 336N (Houtman, Heerschap, Zwarts, &

Stegeman, 2001). At the end of fatiguing dorsiflexion exercise the toe extensors also activate. Clinical observations of 'persistent toe extension at mid-stance' have previously been described in patients with CECS (Franklyn-Miller, Roberts et al., 2014). The activation of the toe extensors only with fatigue suggests that these observations may not be a cause of CECS but a response to either too much load or a loss of TA function. Further information on these 'forgotten' muscles contributing to IMCP in the anterior compartment is required.

During fatiguing exercise phosphocreatine levels (corresponding to pH levels) decrease to a greater extent on the medial side than the lateral side of the TA (Houtman et al., 2001). The production of protons is dependent on the energy source (anaerobic glycolysis produces more protons) and therefore also the fibre type distribution (Type II are better at anaerobic glycolysis). However the authors suggest that the pH heterogeneity seen in the TA may be due to differences in blood supply and subsequent removal of protons. They postulate that this would be caused by greater compliance on the lateral side (fascia) in comparison to the medial side (tibia) causing increased IMCP medially and therefore reduced blood flow.

Under maximum isometric load various properties of the tendon have been measured in vivo potentially reflecting the maximum properties during gait (Maganaris & Paul, 1999). Tendon force, displacement, stiffness and Young's modulus were observed to be 530 N, 4.1 mm, 161 $N.mm^{-1}$ and 1.2 $kN.mm^{-2}$ respectively under stress and strain of 25 MPa and 2.5% respectively. The same group later demonstrated that the tendon lengthens to a smaller extent than its central aponeurosis in response to load (Maganaris, 2000).
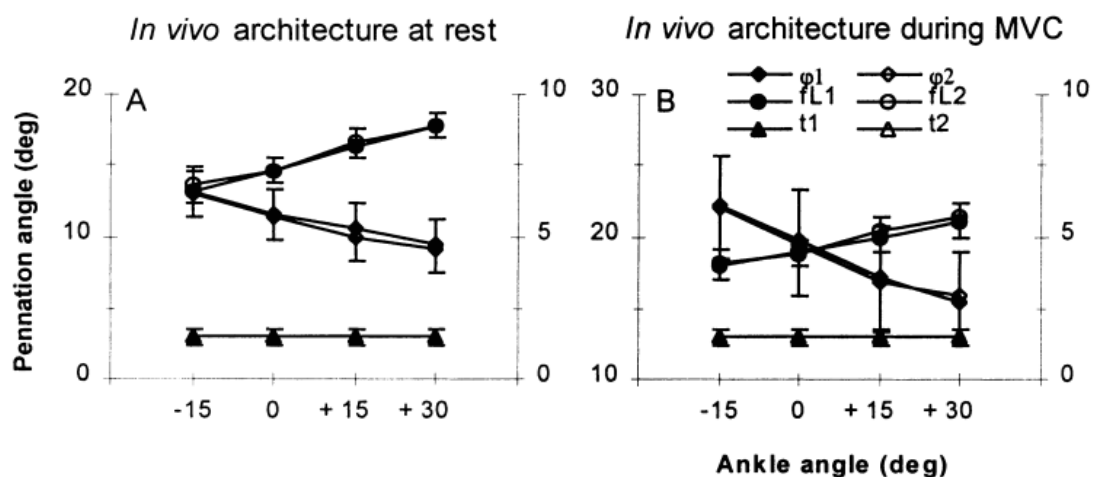
Figure 13 In vivo and modelled architecture of the superficial (1) and deep (2) unipennate parts of TA . u: pennation angle, fL: fibre length, t: muscle thickness between aponeuroses. Notice the consistency in architecture between the two unipennate parts at a given ankle angle and state of contraction. Values are means ± SD (n = 6) (Maganaris et al., 1999)**.**

2.1.4.3. Role in walk to run transition

Humans naturally change from walking to running around 2 m/s (A. Hreljac, Imamura, Escamilla, & Edwards, 2007). This is close to the 1.8 m/s march required during the 2-3 hour combat fitness test that also requires the carriage of loads ranging from 15-25 kg (Ministry of Defence, 2015a; Ministry of Defence, 2015b). The muscles of the ankle have been identified as key determinants of this change (Malcolm, Segers, Van Caekenberghe, & De Clercq, 2009) and the transition has been suggested to transfer work from the dorsiflexor muscles that perform close to maximum capacity during fast walking, to the larger proximal muscles (A. Hreljac, 1995). In fact it has been noted that when walking at the preferred transition speed or faster subjects feel discomfort or fatigue in the anterior compartment (Bartlett & Kram, 2008). This likely explains why 90% of competitive race walkers complain of anterior compartment pain during walking (Sanzen, Forsberg, & Westlin, 1986). During the military fitness tests only 'small shakeout runs of no more than 200 m are permitted to help reduce lower limb discomfort' suggesting that the speed and gait requirements are not compatible (Ministry of Defence, 2015b, p.21). This also helps explain the reduction in the rating of perceived exertion following transition at the preferred speed (A. Hreljac, 1993).

The transition speed is also dependent on leg length, a relationship that persists both within and across species. Humans and most quadrupeds transition to running (or trotting) at the same Froude number, as defined in Equation 1, of c.0.5 (Alexander, 1984). In humans, Hreljac (1995) examined a number of correlations with preferred transition speed and reported coefficients of 0.73-0.89 with Froude number, and 0.35-0.76 with leg length. The increased TA muscle activity described earlier with incline (Patla, 1986) may also explain the reported reduction in the preferred transition speed to just 1.8 m/s on 15% inclines (A. Hreljac, 1995).

Equation 1 Froude number where V=walking speed (m/s), g=acceleration due to gravity (9.81 m/s^2) and L=leg length (m)

$$\frac{V^2}{gL}$$

2.1.5. The role of other lower limb muscles

All of the muscles of the anterior compartment have a dorsiflexor moment arm. They provide differing roles in the non-sagittal planes although exhibit similar activation patterns (Bogey, Perry, & Gitter, 2005; Hunt et al., 2001; Jungers, Meldrum, & Stern, 1993). The differing roles of all of the other lower limb muscles are reviewed briefly below and representative EMG profiles presented in Figure 15.

2.1.5.1. Extensor digitorum longus and extensor hallucis longus

The extensor hallucis longus and extensor digitorum longus activate in a similar pattern to TA and have similar dorsiflexion moment arms (Bogey et al., 2005; Hunt et al., 2001). However their specific role is to extend the interphalangeal joint of the lesser toes and the hallux. They slow down both ankle and toe plantarflexion during the initial stance phase of walking; and act concentrically to help provide toe dorsiflexion at toe off. Along with TA, extensor digitorum longus may play a role in raising the medial longitudinal arch (Hunt et al., 2001). In the frontal plane both extensors can act as an evertor (and abductor) of the foot (Riegger, 1988); extensor hallucis longus can also act as an invertor (and

adductor) depending on the orientation of the subtalar joint axis. During walking extensor hallucis longus activity is greatest when there is a low lateral force at heel strike thus decelerating the rapid eversion, dorsiflexion and abduction movements (Matsusaka, 1986).

2.1.5.2. Triceps surae

In the sagittal plane the triceps surae (soleus and gastrocnemius) act as plantarflexors through a common insertion into the Achilles tendon (Stewart, Postans, Schwartz, Rozumalski, & Roberts, 2007). The muscle force and muscle impulse generated during running by soleus has been estimated to be over three to four times larger than the combined force of the gastrocnemius heads (R. H. Miller, Gillette, Derrick, & Caldwell, 2009). Both the triceps surae muscles contribute to vertical support of the whole body (Francis, Lenz, Lenhart, & Thelen, 2013). The gastrocnemius also generates knee flexion moments as it is biarticular; whereas only a plantarflexion moment can be generated by the uniarticular soleus muscle. This may explain their different roles in gait with gastrocnemius activity contributing to forward propulsion whereas soleus induces braking of forward velocity (Francis et al., 2013).

Two recent studies using functional electrical stimulation suggest that during gait the gastrocnemius has a dorsiflexion role (Lenhart, Francis, Lenz, & Thelen, 2014; Stewart et al., 2007). The ability of gastrocnemius to induce dorsiflexion in relation to posture was described as early as 1989 (Zajac & Gordon, 1989). Dorsiflexion occurs when the knee flexor moment, produced by gastrocnemius activity, induces ankle dorsiflexion of greater magnitude than the plantarflexion motion induced by the plantarflexion moment produced at the ankle.

The inversion/eversion moment arm of the triceps surae changes depending on the position of the ankle (Klein et al., 1996; R. Wang & Gutierrez-Farewik, 2011). In a subtalar inverted position the triceps surae have an eversion moment arm, and in an everted position an inversion moment arm. As such, activation could be expected to always return the ankle back towards a neutral position. However in an everted position, the acceleration caused by the plantarflexor moment may also cause an eversion acceleration (through inertial

coupling) that could be enough to overcome the inversion moment applied through the Achilles tendon.

As with TA there is some variation in the muscle activation during walking (Di Nardo, Ghetti, & Fioretti, 2013). When represented together the majority of gastrocnemius activity is concentrated during mid-stance (Figure 14). During running, the gastrocnemius is active from late swing stage to mid-stance (Mann, Moran, & Dougherty, 1986). Gastrocnemius and soleus demonstrate very similar activation profiles during both walking and running (Gazendam & Hof, 2007).
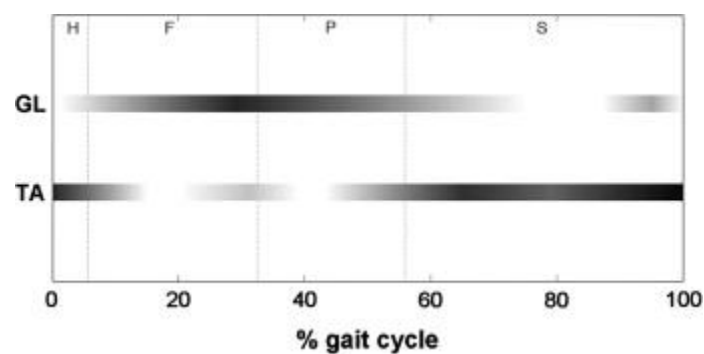
Figure 14 Muscle activation onset and offset instants for gastrocnemius lateralis and tibialis anterior, as percentage of gait cycle, considering, for each muscle, the four main modalities of activation all together. Horizontal bars are grey-level coded, according to the number of subjects where a certain condition is observed; black: condition observed for all subjects in every modality of activation, white: condition never met. The phases of Heel contact (H), Flat foot contact (F), Push off (P), Swing (S) are shown superimposed, delimited by dashed vertical lines (Di Nardo et al., 2013).

2.1.5.3. Peroneus longus and peroneus brevis

Peroneus longus and peroneus brevis are principally evertors that are active at the same time (Hunt et al., 2001; Riegger, 1988). Bursts of activity have been reported during the beginning of stance phase and from mid-late stance phase during walking (Bogey et al., 2005; Hunt et al., 2001). During late stance they also act as plantarflexors of the foot (Riegger, 1988). The peroneus longus is estimated to be able to generate more than twice the force of peroneus brevis (Silver, de la Garza, & Rang, 1985). They function similarly during running (Mann et al., 1986).

2.1.5.4. Peroneus (fibularis) tertius

Of the primates, Peroneus tertius (aka fibularis tertius) occurs most frequently in man and therefore has been linked to the evolution of bipedalism (Joshi, Joshi, & Athavale, 2006). It can range in size from being larger than the extensor digitorum longus to being absent in c.10% of individuals. Its course follows the extensor digitorum longus tendon before attaching to the fifth and fourth metatarsals resulting in a dorsiflexion and eversion moment arm. The only published EMG data suggests that it acts as an antagonist to the inversion actions of TA and extensor digitorum longus during the swing phase of walking and running (Jungers et al., 1993). Thus peroneus tertius brings the foot into a more plantigrade position prior to initial foot contact while aiding ankle dorsiflexion.

2.1.5.5. Tibialis posterior

Tibialis posterior is a plantarflexor and has the largest inversion moment arm (Perry & Davids, 1992) acting on the subtalar joint (Klein et al., 1996) and similar strength to TA (Silver et al., 1985). Surprisingly subjects with dysfunction of this muscle do not demonstrate altered ankle inversion (Rattanaprasert, Smith, Sullivan, & Gilleard, 1999). This may be due to compensatory activity of supporting muscles. It also has a major role in supporting the medial longitudinal arch (Kaye & Jahss, 1991). During walking, two bursts of EMG activity are present; one during the initial contact phase and then again during mid-stance (Bogey et al., 2005; Murley, Menz et al., 2009). During running there is a similar peak during mid-stance that co-activates with peroneus brevis (Reber et al., 1993).

2.1.5.6. Flexor digitorum longus and flexor hallucis longus

The toe flexors demonstrate similar activation profiles to tibialis posterior (Bogey et al., 2005). They play a primary role in flexing the interphalangeal joint of the lesser toes and the hallux, and a secondary role in ankle plantarflexion (Riegger, 1988). Flexor hallucis longus is estimated to be twice as strong as flexor digitorum longus (Silver et al., 1985). They also react to the medial-lateral force at initial contact by increasing activity (Matsusaka, 1986).

This knowledge of the function of all the lower limb muscles is important as it facilitates interpretation of EMG when used; and also provides insight into potential contributors to joint kinematics and the calculated joint moments.
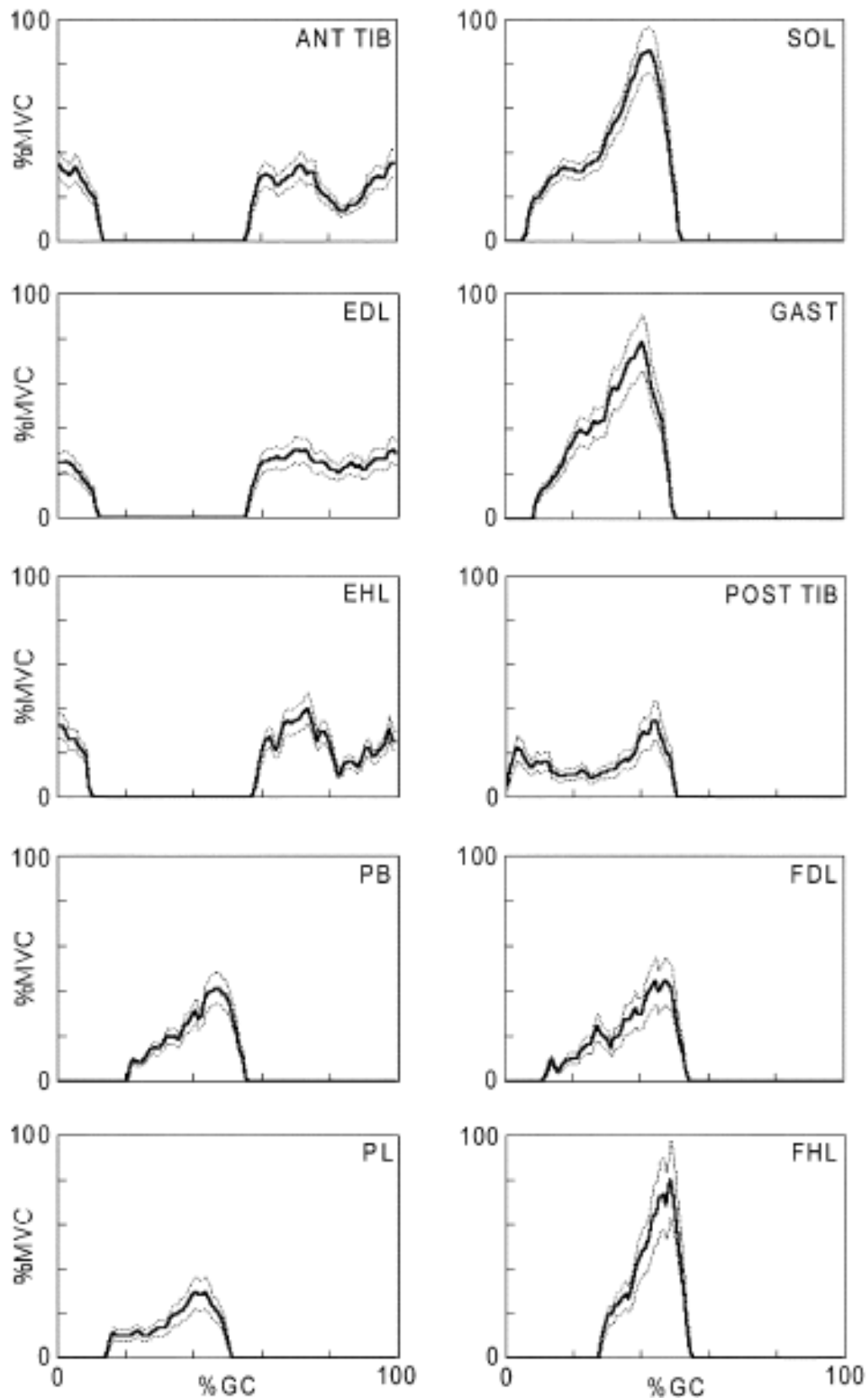
Figure 15 EMG profiles for ankle muscles. Percent gait cycle is represented on the y-axis; mean (1 SD) percent maximum voluntary contraction on the x-axis (Bogey et al., 2005).

2.2. Chronic Exertional Compartment Syndrome

2.2.1. Epidemiology

Chronic exertional compartment syndrome has been described in numerous compartments of the body. The anterior compartment of the lower leg is affected most often (Reneman, 1975). Although this is not exclusive with the deep posterior compartment of the lower leg, the erector spinae, tensor fasciae lata, the extensor compartment of the forearm, the adductor compartment of the foot, and the first dorsal interosseous muscle of the hand all reported with CECS type symptoms and elevated IMCP in the literature (Brown, Wheeler, Boyd, Barnes, & Allen, 2011; Padhiar, Allen, & King, 2009; Rydholm, Brun, Ekelund, & Rydholm, 1983; Rydholm, Werner, & Ohlin, 1983; Styf, 1987; Styf, Forssblad, & Lundborg, 1987). These small compartments are typically associated with endurance/impact exercise. The quadriceps femoris muscle is the only large compartment reported and is seen mainly in those undergoing resistance training (Orava et al., 1998), although the atypical presentation suggests that this may not truly represent the CECS pathology.

Symptoms of CECS generally only occur during sporting activities although a small percentage develop symptoms with daily living alone (Davis et al., 2013). Anterior compartment CECS is primarily seen in the military (Almdahl & Samdal, 1989), runners (Detmer, Sharpe, Sufit, & Girdley, 1985), skaters (Garcia-Mata, Hidalgo-Ovejero, & Martinez-Grande, 2001), cross-country skiers (Lawson, Reid, & Wiley, 1992) and race walkers (Sanzen et al., 1986). Forearm CECS has been reported in motocross racers (Gielen et al., 2009), kayakers (Piasecki, Meyer, & Bach, 2008), rowers (Harrison, Thomas, Aster, Wilkes, & Hayton, 2013; O'heireamhoin, Baker, & Neligan, 2011), and has also been related to work (Pritchard, Williams, & Heath, 2005) or secondary to weight-training (Jawed, Jawad, Padhiar, & Perry, 2001).

The incidence of CECS within both the general population and specific populations is not well reported. This has been suggested to be due to CECS being a self-limiting condition resulting in potential cases giving up their activity rather than seeking treatment (Barnes, 1997). This bias may further be compounded by some medical practitioners recommending that "if it hurts don't do it". An early study by Qvarfordt (1983) reported that 14% of an unselected sample of patients with lower leg pain had anterior CECS. Within those who only had exercise-induced anterior leg pain an incidence of 27% has been

reported (Styf, 1988). As described in Chapter 1.2, the UK military sees a large number of patients with this problem each year. However, actual figures for incidence are not yet available and may suffer from some of the same problems as described above.

In up to 98% of cases the condition is bilateral (Reneman, 1975). Anthropometrically, no difference in height or body mass has been observed between civilian CECS patients and controls (Rorabeck, Bourne, Fowler, Finlay, & Nott, 1988; Varelas, Wessel, Clement, Doyle, & Wiley, 1993). Although the only military study that has reported anthropometrics suggested that patients have a larger BMI and body mass than controls (Birtles et al., 2002).

2.2.2. History and physical examination

Knowledge of the clinical characteristics of CECS is important for clinicians to help support diagnosis. Patients with CECS experience a gradual increase in pain in the affected compartment with exercise (Roscoe et al., 2015). Symptoms typically get worse over time (Howard, Mohtadi, & Wiley, 2000). Pedowitz (1990) reported that CECS patients use a number of terms to describe this pain. Ache was the most commonly used term, followed by dull, pressure, fullness and sharp. Only a few patients described a cramp-like pain. In contrast, Turnipseed (2002) and Orlin (2013) report that between 80-100% of patients experienced both daytime and night time cramps. The exertional pain is usually fully relieved following cessation of exercise within 20 minutes (Edwards & Myerson, 1996). The features of CECS reported in the aforementioned studies provide a disjointed description of some of the clinical characteristics. They also lack the identification of activities that may be associated with the development of CECS in the military population. Formal investigation of the clinical characteristics is therefore required.

Passive stretching of the muscles may elicit symptoms (Gill, Halstead, & Matava, 2010; Tucker, 2010); although this may only be associated with recent exercise (Diebal, Gregory, Alitz, & Gerber, 2012). There is generally no history of trauma, although previous soft tissue trauma has been reported in a few cases (D. Edmundsson, Toolanen, & Sojka, 2007; Tubb & Vermillion, 2001). When symptoms are present, active dorsiflexion of the ankle is difficult (Qvarfordt, Christenson, Eklof, Ohlin et al., 1983).

Muscle herniations (Figure 16) are more prevalent in those with CECS (36%) compared to symptomatic controls (8%) without elevated IMCP (Verleisdonk et al., 2004). A similar incidence is obtained when comparing to asymptomatic controls (Fronek et al., 1987). In other studies, muscle herniation has been reported to be present in between 19% and 60% of CECS patients (Fronek et al., 1987; Garcia-Mata et al., 2001; Martens, Backaert, Vermaut, & Mulier, 1984; Pedowitz et al., 1990; Qvarfordt, Christenson, Eklof, Ohlin et al., 1983; Reneman, 1975; Schepsis et al., 1993). The development of hernias in these patients is typically attributed to the high IMCP and are more prominent after exercise (Qvarfordt, Christenson, Eklof, Ohlin et al., 1983). However if the reason for high IMCP is a stiffer fascia this could be expected to be more resistant to herniation.

Patients with CECS may have a mild impairment in vibratory sensation in the deep peroneal distribution (Rowdon et al., 2001). No other differences in pre-exercise neuromuscular examinations have been found. Despite this, reduced skin sensation in this distribution using cotton swab and pin prick has been used as part of a diagnostic protocol that excludes IMCP testing (Orlin et al., 2013). It has been reported in the literature that, as symptoms progress, parasthesia and numbness in the deep peroneal distribution, and foot drop or loss of ankle control occur; although the prevalence and magnitude of these issues is not well documented (Edwards & Myerson, 1996; Gill et al., 2010; Rowdon et al., 2001). The loss of nerve functions in compartment syndrome is attributed to ischemia rather than the direct effect of pressure (Mubarak, Hargens, Garfin, Akeson, & Evans, 1979). It is unclear however, on the type and number of neuromuscular symptoms that patients may report in the clinic.

Figure 16 Tibialis anterior muscle herniation(Rho et al., 2008)

2.2.3. Diagnosis and pathology

2.2.3.1. Intramuscular compartment pressure

The gold standard diagnosis technique for CECS is generally accepted as IMCP measurement. This originates from the diagnosis of acute compartment syndrome, which is often the direct result of tissue trauma leading to fluid extravasation and a rise in IMCP leading to tissue hypoxia and subsequent necrosis. The first record of its use in CECS is in 1962 by French and Price. Since then various IMCP parameters and diagnostic criteria have been proposed to determine whether CECS is the cause of a patients' symptoms.

Perhaps the most widely used criteria are those set by Pedowitz *et al.* (1990). However this study was severely limited as a valid comparison group was not used: the reference test and the index test were not independent (they were in fact the same test). Groups of symptomatic individuals that failed to meet pre-set IMCP cut-off points (that were changed during the study) were compared with those with IMCP above the cut-off point. As such the groups were already pre-selected to have differences in IMCP. Other studies that have proposed alternative criteria are similarly limited; with the most prominent limitation being the lack of inclusion of healthy controls for comparison.

A systematic review of anterior compartment IMCP before, during and after exercise in healthy subjects was therefore carried out for comparison with the

diagnostic criteria commonly in use for CECS (Roberts & Franklyn-Miller, 2012). The diagnostic criteria, considered at the time to be the gold standard, overlapped the range found in normal healthy subjects, with the exception of relaxation pressure. Multiple studies reported mean IMCP's above the diagnostic threshold despite the use of asymptomatic subjects. The IMCP was also shown to vary, at all time-points, due to several additional factors not associated with the condition. Taken together, these data had major implications on the ability to use these published criteria for diagnosis and questioned the underlying pathophysiology.

A further systematic review on the diagnosis of CECS using IMCP measurement was also published in the same year by an independent group (Aweid et al., 2012). Both reviews highlighted the limitations of previous studies and found the evidence for the currently used criteria to be weak. In light of these reviews, the clinical team at DMRC reverted to using clinical examination alone which has been suggested to provide an accurate diagnosis for referral for surgery (Ali, Mohammed, Mencia, Maharaj, & Hoford, 2013; Orlin et al., 2013; van den Brand, Nelson, Verleisdonk, & van der Werken, 2005). Since then, our research group has improved on the limitations of previous studies by undertaking a case-control study to provide the best evidence to date on the role of IMCP in the diagnosis and pathology in CECS (Roscoe et al., 2015). It was demonstrated that anterior compartment IMCP is elevated immediately upon standing at rest in subjects with CECS (Roscoe et al., 2015). In patients with symptoms consistent with CECS, the diagnostic utility of IMCP measurement is improved when measured continuously during exercise resulting in a likelihood ratio of 12.5. This suggests that IMCP measurement at this time point is diagnostically conclusive.

2.2.3.2. Blood flow

The cause of pain in CECS patients is not well understood, however the predominant theory is one of ischemia during exercise. The increase in IMCP is usually believed to lead to a reduction in blood flow before causing pain. The direct cause of pain has been suggested to be through the production of kinins following exercise with restricted blood flow (Balduini et al., 1993). Increased IMCP, through external compression, will result in compression of the deep veins (Figure 17) of the leg before the superficial veins (Uhl, Benigni, Cornu-

Thenard, Fournier, & Blin, 2014). The increase in IMCP that occurs with normal muscle contraction is even high enough to result in arterial occlusion (Radegran, 1997). The measurement of changes in blood flow with exercise should in theory provide a better diagnosis of CECS than IMCP. This is especially true if the level of IMCP required to reduce blood flow varies on an individual basis.
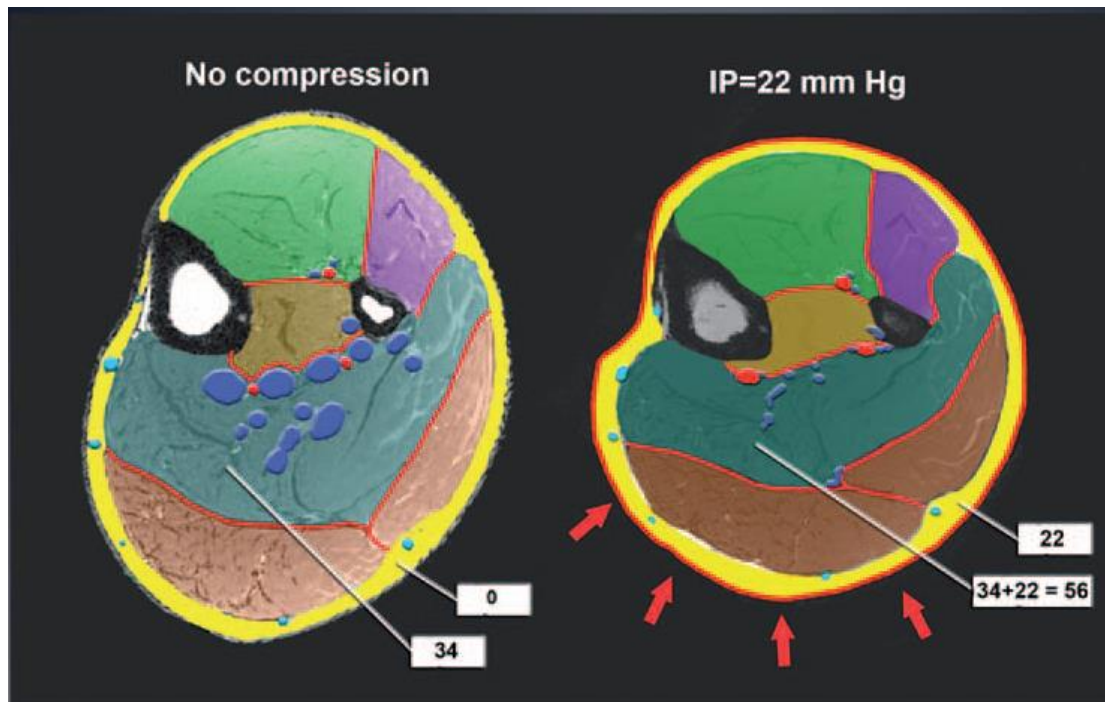
Figure 17 External compression of the lower leg resulting in compression of the deep veins. IP=interface pressure, other numbers represent pressure (mmHg) in various locations.

As expected, due to the relatively low pressures reported at rest, there is no evidence of tibial artery occlusion in patients pre- or post-exercise (Turnipseed et al., 1995). Systolic pressure of the hallux and resting ankle-brachial indexes are normal; as is the presence of the peripheral pulses (Qvarfordt, Christenson, Eklof, Ohlin et al., 1983; Rowdon et al., 2001). The investigations by Turnipseed (1995) also suggested that venous return at rest is generally normal. They observed normal functioning of the proximal deep venous system (popliteal vein to common femoral vein); and the presence of anterior tibial venous flow. Tibial venous flow following mechanical calf compression or treadmill exercise was also enhanced in all patients (and controls). They did observe an absence of spontaneous and phasic venous flow signals in all CECS patients that was only

absent in 70% of age-matched controls. However the significance of this finding is unclear.

Muscle blood flow has been measured in CECS patients using nuclear techniques in several studies and using blood oxygen level-dependent and arterial spin MRI in a single study (Oturai, Lorenzen, Norregaard, & Simonsen, 2006). However there does not seem to be a consensus on whether blood flow is reduced in these patients. The majority of reports have suggested reduced blood flow (French & Price, 1962; Hayes, Bower, & Pitstock, 1995; Kennelly & Blumberg, 1968; Styf, Korner, & Suurkula, 1987; Takebayashi et al., 1997). In contrast, the three most recent studies have not found any correlation between increased IMCP and muscle hypoperfusion (Andreisek et al., 2009; Oturai et al., 2006; Trease et al., 2001). Similar findings were also reported by Balduini (1993). Perhaps importantly, Trease (2001) also demonstrated that blood flow was dependent on the exercise type; this may explain some of the differences between studies.

2.2.3.3. Muscle oxygenation

The cause of the pain in CECS is often attributed to a shortage of oxygen within the muscles (due to high IMCP reducing blood flow). Muscle oxygenation can be measured directly using an invasive pO_2 electrode or indirectly using near-infrared spectroscopy (Evers, Odemis, & Gerngross, 1997; van den Brand, Verleisdonk, & van der Werken, 2004). The use of blood oxygen level dependent contrast imaging used in functional magnetic resonance imaging has also been used in CECS patients (Oturai et al., 2006).

The first report of muscle oxygenation in CECS patients comes from an abstract in 1993 by Royle. They tested pO_2 and IMCP simultaneously at rest before exercise, standing, walking, running and at rest post-exercise in patients suspected of CECS. They concluded that the IMCP has a linear relationship with pO_2 at all activity levels (r=0.56-0.84). From this they suggest that the pain from CECS is ischemic in origin. A later study using the same technology demonstrated similar results; significantly this was also associated with the level of pain experienced after exercise (Evers et al., 1997).

More recently, near-infrared spectroscopy has been used as a non-invasive measurement of muscle oxygenation and has shown potential in diagnosing

acute compartment syndromes (Giannotti et al., 2000). Its usefulness for CECS is yet to be fully determined. This modality has been shown to be able to detect de-oxygenation caused by increased IMCP in a CECS model (Breit, Gross, Watenpaugh, Chance, & Hargens, 1997). Mohler (1997) and van den Brand (2004) both demonstrated that CECS patients have greater relative de-oxygenation during exercise than asymptomatic controls (Figure 18). However two more recent studies comparing anterior CECS patients to patients with other sources of anterior pain found no difference in the same parameter (Rennerfelt, Zhang, Karlsson, & Styf, 2016; Zhang, Rennerfelt, & Styf, 2012).

Three studies and a case report suggest that CECS patients take longer after exercise for their muscles to re-oxygenate, suggesting continued reductions in blood flow (Breit et al., 1997; Mohler et al., 1997; Ota, Senda, Hashizume, & Inoue, 1999; Zhang et al., 2012). This is in line with the current diagnostic focus on post-exercise IMCP (see Chapter 2.2.3.1). However, this phenomenon was not found by van den Brand (van den Brand et al., 2004).

In summary, the majority of data suggest that CECS patients have reduced oxygenation during exercise that is associated with high IMCP and consequently slower re-oxygenation. The reasons for this reduction are likely to be due to reduced blood flow as previously discussed; although muscle blood flow has not been measured concurrently with muscle oxygenation.
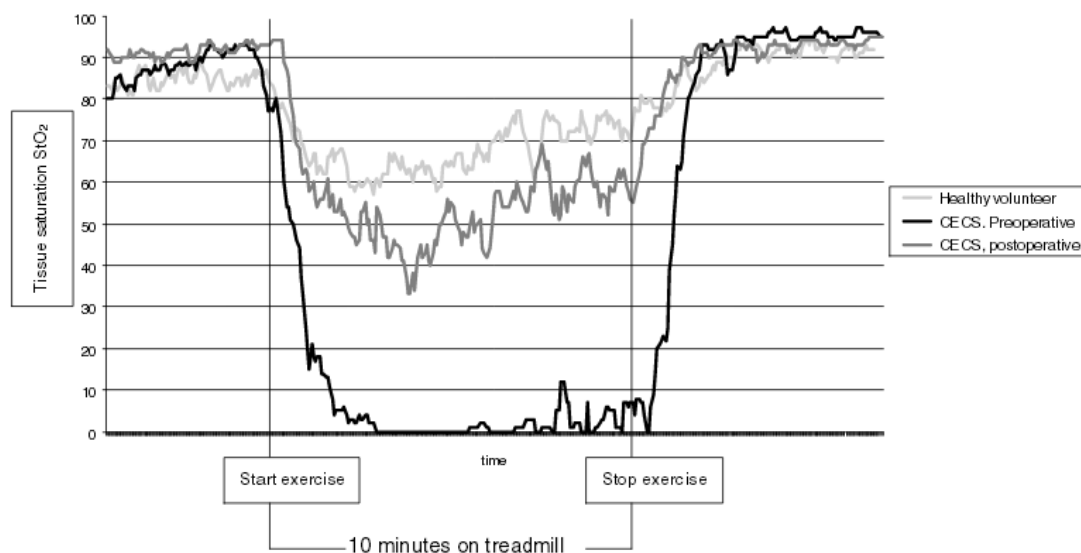
Figure 18 Typical oxygenation in CECS patients and healthy volunteers (van den Brand et al., 2004)

2.2.3.4. Muscle properties

Various properties of the muscles have been described that differ between patients and controls providing more information on the pathophysiology of CECS, however they do not seem to be sensitive enough for diagnosis.

Patients with CECS were found to have better dorsiflexor endurance than controls (Varelas et al., 1993). The same trend was shown in another study although this was not significant (Andreisek et al., 2009). This improved endurance may be at the expense of muscle strength with two studies demonstrating reductions in dorsiflexor strength relative to body mass and relative to muscle CSA (Birtles et al., 2002; Varelas et al., 1993). Further evidence for a preference for endurance over strength comes from their fibre type distribution. Patients with CECS were found to have increased type II fibres in comparison to controls (Wallensten & Karlsson, 1984). Although caution must be made with interpreting these results as the controls in this study were weightlifters. Perhaps also due to this unusual selection of controls, a medial tibial stress syndrome group also demonstrated these same differences. One possibility is that the increased endurance represents greater muscle activity during every day and athletic activities; however it is not clear if some 'at risk' athletes have greater muscle activity for running or marching; or if this simply represents a higher training load.

The TA has been reported to be the same thickness as controls before exercise (Birtles et al., 2002; Birtles et al., 2003; Rajasekaran, Beavis, Aly, & Leswick, 2013). However Rajasakeran (2013) demonstrated an increased thickness up to 5 minutes after exercise. The studies by Birtles *et al.* (2002; 2003) did not demonstrate any significant differences after exercise although the differences tended towards greater thickness in CECS patients. Of interest, the CECS group in the Birtles (Birtles et al., 2003) study experienced much greater delayed onset muscle soreness following the eccentric exercise protocol. In contrast, a small study found that the increase in cross-sectional area after exercise was 44% less in patients (n=3) than controls (n=5) (Theodosopoulos, Raymer, Allman, Luke, & Marsh, 2004). Interpreting these studies is difficult as changes in muscle geometry with exercise will be affected by fluid content, compartment compliance, and exercise volume/intensity; all of which have been proposed to be affected in CECS patients.

2.2.3.5. Fascia properties

A number of properties of the surrounding fascia have also been described that differ between patients and controls. Again these findings can provide insight into the pathophysiology of CECS, but due to the inability to test the fascia *in vivo* and the lack of sensitivity these are not suitable for diagnosis. Perhaps the most pertinent question regarding this syndrome is whether the increase in IMCP is due to a reduction in compliance or stiffness of the fascia. A few studies have tried to answer this question along with measures of fascial thickness and structure that may influence compliance. These studies have been described fully in Chapter 2.2.5.1 on compartmental compliance.

2.2.4. Biomechanical factors

Biomechanical factors have been considered to play a role in the development of CECS for a long time (Bates, 1985; Slimmon, Bennell, Brukner, Crossley, & Bell, 2002). Changes in biomechanical demands (from traditional to in-line skates) have been noted in skaters to result in the rapid development of CECS (Garcia-Mata et al., 2001). However, very little primary research has been carried out to investigate these factors. A review by Tweed (2008) suggested that CECS may develop as a result of excessive eccentric contraction. However the review did not consider that the muscle may not act eccentrically at any time during gait. Real-time ultrasound of the tendon demonstrate that, during walking at least, the TA contracts isometrically with lengthening of the tendon during plantarflexion (Campbell et al., 2003; Chleboun et al., 2007).

Reference to biomechanics in the CECS literature appears to be gathering momentum. Conservative treatment through forefoot running has only recently been suggested to be a viable option for CECS. This is discussed in more detail in Chapter 2.2.6.2. Importantly, to date, there have been no studies examining the biomechanical differences between patients and controls in order to better define the pathophysiology and accurately inform such treatments.

The only study that has attempted to detect differences in movement strategies was carried out on cross-country skiers (Federolf & Bakker, 2012). They identified inconsistent muscle activation properties between patients (n=5) and controls (n=4). They found increased EMG intensity of TA, peroneus longus and gastrocnemius lateralis in patients. The groups also demonstrated differences in

the EMG spectrum, suggesting patients may activate predominantly type I (slow twitch) muscle fibres, while controls may activate both type I and type IIb/x (fast-twitch) muscle fibres. This latter finding may be due to the greater proportion of type I fibres found in controls (Wallensten & Karlsson, 1984). Differences were also observed in timing of muscle activation. Clearly the small sample size and specific biomechanical demands of skiing prevent generalisation of the results to our military population. Nevertheless, these results suggest that detectable differences in biomechanics may exist in this patient population. Further investigations of muscle activity during military specific activities are now required.

Clinical observations of 'persistent toe extension at mid-stance' have previously been described in patients with CECS (Franklyn-Miller, Roberts et al., 2014). Clinicians at DMRC have also noted that some patients use their toe extensors to dorsiflex the ankle instead of TA. However empirical evidence is needed to support these clinical observations.

2.2.5. Potential causes of increased IMCP in CECS

A number of variables are known to have an effect on IMCP. These may be structural or occur dynamically through an effect on either compartment content or compliance. Alternatively muscle activity has a well-established effect on IMCP that acts through the generation of forces orthogonal to the direction of pull along the longitudinal axis of the muscle/tendon during contraction. The evidence behind these three potential mechanisms is explored below.

2.2.5.1. Compartment compliance

The compliance of the fascia surrounding the compartment will by definition have an effect on IMCP. However the only study investigating IMCP and fascial stiffness found no relationship between the two variables in CECS patients (Dahl et al., 2011). The lack of association may be due to the small sample size and large variations in stiffness values between subjects. It is important to note that IMCP in this study was measured at rest, 5 minutes after exercise, that has relatively poor diagnostic accuracy (Roscoe et al., 2015). They did however report a negative correlation between the two in patients with concomitant diabetes and CECS. The reasons for this and the influence of the diabetic state are unknown.

It is not yet clear if there are differences in the structure of the fascia between patients and controls. The most recent study by Dahl (2011) suggests there are no differences in the axial plane stiffness, thickness, peak strain or peak force of the fascia. On the other hand, two research groups have reported differences in fascial structure including greater thickness (Hurschler et al., 1994; Turnipseed et al., 1995). Hurschler (1994) also reported greater axial plane fascial structural stiffness in CECS but no difference in transverse stiffness. Turnipseed (1995) also described testing both axial and transverse specimens, however only a single structural stiffness value is reported. This value of structural stiffness was also reported to be greater in patients with CECS. The axis tested may be of significance as a recent model of the anterior crural fascia suggests that transverse stiffness plays a larger role in modulating IMCP than axial stiffness (Pavan, Pachera, Stecco, & Natali, 2015).

There may also be differences in fascial collagen structure. Hurschler (1994) observed greater irregularity in collagen cross-linking but no differences in collagen content. This is in line with Barbour (2004) who observed greater irregularity in deep posterior CECS patients with longer symptom duration; although cases surprisingly had less irregularity than controls. These differences may be due to various stages of the remodelling process whereby tensile forces, potentially generated by muscle activity, stimulate fibroblasts to remodel collagen. No other histological differences in the amount of fibrocyte activity, chronic inflammatory cell activity, mononuclear cells or ground substance have been observed (Barbour et al., 2004).

The studies described above are limited in a number of ways. Firstly, the selection of a suitable control group in these studies has been variable. Turnipseed (1995) and Dahl (2011) utilised fascia from post-traumatic patients (above knee amputation, acute tibial condyle fractures or acute compartment syndrome) whereas Barbour (2004) used tissue obtained from autopsy cases. All these groups may have had differing exercise histories. On the other hand Hurschler (1994) used the fascia from the lateral compartment of the same patient as a control; though it has been since shown that stiffness of the crural fascia varies according to the sampling location (Stecco et al., 2014). Secondly, the studies are limited by a low number of controls with only six to eleven non-

CECS individuals included in each study. Finally, the effect of testing *ex vivo* is unknown.

There is a high incidence of muscle herniation in patients with CECS (Fronek et al., 1987; Garcia-Mata et al., 2001; Martens et al., 1984; Pedowitz et al., 1990; Qvarfordt, Christenson, Eklof, Ohlin et al., 1983; Reneman, 1975; Schepsis et al., 1993). The development of hernias in these patients is typically attributed to the high IMCP. This hypothesis however doesn't fit perfectly with the theory of a stiffened fascia in CECS patients, as the fascia could be expected to be more resistant to herniation. Despite this, a less compliant fascia appears to be the best current explanation of the increase in IMCP. This concurs with a few surgical reports of abnormal fascia. For example, a second layer or 'pseudofascia' has been reported in a small proportion of patients (Garcia-Mata et al., 2001); and a case report also described an 'aberrant fascial band' in one patient (Soffer, Martin, Stanish, & Michael, 1991).

2.2.5.2. Compartment content

Compartment volume has been shown experimentally to have a direct effect on IMCP (Hargens et al., 1978). A few studies have attempted to measure muscle volume (using thickness as a surrogate) in CECS as described in detail in Chapter 2.2.3.4. These studies have typically reported that the muscle is only thicker than controls after exercise (Birtles et al., 2002; Birtles et al., 2003; Rajasekaran et al., 2013). Identifying the underlying cause of these changes is difficult as changes in muscle geometry with exercise will be affected by exercise volume and intensity, compartment compliance and fluid content; all of which have been suggested to differ in CECS patients.

Structurally, muscle hypertrophy in a non-compliant compartment could be expected to increase IMCP. However, there are a number of reasons that suggest this is not the case. Firstly, in acute compartment syndrome muscle thickness is not related to IMCP (at rest) (S. H. Wang et al., 2014). Secondly, CECS is most commonly seen in endurance sports, although the post-pubertal stage of muscular hypertrophy has been suggested as a potential etiological factor (Garcia-Mata et al., 2001). Forearm CECS has been suggested to be associated with weight lifting; although this has only been in a single case report (Jawed et al., 2001). The exception to this rule appears to be for CECS of the

quadriceps femoris when the majority of patients are power- or weight-lifters (Orava et al., 1998); although it is not clear if this is a true CECS. Thirdly, this hypothesis is refuted by the three studies demonstrating no difference in thickness at rest (Birtles et al., 2002; Birtles et al., 2003; Rajasekaran et al., 2013). Finally, rest is not considered a viable treatment option (Van der Wal, Heesterbeek, Van den Brand, & Verleisdonk, 2014) despite generally leading to muscle atrophy.

A more plausible explanation for increased IMCP in CECS is through an increased fluid content within the compartment. Fluid within the compartment is found either within the vasculature or as interstitial fluid. The interstitial fluid content can fluctuate depending on the hydrostatic and oncotic pressure in the capillary blood and tissue fluid. These are dependent on a number of factors including: capillary pressure; interstitial fluid protein concentration and colloid osmotic pressure; capillary reflection coefficient for plasma proteins; osmotic effects of small molecules; IMCP; compliance of the interstitial space; the amount of glycosaminoglycans; and lymphatic drainage (Aukland & Nicolaysen, 1981). The interstitial volume can also be regulated locally to help prevent edema or dehydration. Fluid is transported between the capillaries and tissue across the capillary membrane as described by Starling (1896).

In addition to the experimental demonstration by Hargens (1978), increases in fluid content have been linked to raised IMCP through creatine supplementation (Potteiger et al., 2002); lymphedema (Qvarfordt, Christenson, Eklof, Jonsson, & Ohlin, 1983); and occlusion of the lymphatic system (presumably also leading to lymphedema) or the venous system (Christenson, Shawa, Hamad, & Al-Hassan, 1985). The finding of a reduction in the capillary density in CECS patients provides some insights into the possible mechanisms for increased fluid content (D. Edmundsson, Toolanen, Thornell, & Stål, 2009). Primarily this evidence suggests that patients do not have the capacity to have an increased fluid content in the small vessels (or alternatively have adapted to reduce this capacity). Fluid content changes in CECS are therefore likely to be due to changes in the interstitial fluid volume.

The orthostatic response results in a shift of 300-800 ml blood from the chest to the lower parts of the body (Asmussen, 1943). The greater blood volume in both the large and smaller blood vessels and augmented fluid filtration into the

interstitial space results in increases in leg volume (Truijen et al., 2012). Our research group recently demonstrated that IMCP before exercise was only elevated in patients upon standing (Roscoe et al., 2015). However the patient group was on average 10 cm shorter than controls that would result in a lower orthostatic response. This therefore suggests that increased fluid content is not the primary cause of elevated IMCP in CECS.

Eccentric contractions lead to greater post-exercise IMCP than concentric contractions (Hargens, Parazynski, Aratow, & Friden, 1989). During and after eccentric contractions, sarcomere structure is disordered, releasing Na^+ and increasing the pH of the interstitial fluid (Yeung, Bourreau, Allen, & Ballard, 2002; Yeung, Ballard, Bourreau, & Allen, 2003). This may in turn explain the increase in fluid content in the compartment and therefore raised IMCP. The development of transverse-tubular vacuoles in eccentrically exercised muscles may also contribute to increased IMCP (Yeung, Balnave, Ballard, Bourreau, & Allen, 2002). However, the TA may not contract eccentrically during gait at all (Campbell et al., 2003; Chleboun et al., 2007). Without *in vivo* measurements it is not clear whether the observations made by Hargens (1989) were truly made with eccentric contractions or isometric contractions with concomitant increases in the joint angle. Certainly pain at rest associated with eccentric contractions (delayed onset muscle soreness) does not appear to be related to IMCP (Newham & Jones, 1985).

Creatine supplementation is prevalent in the athletic population and increases body mass due to either increased total body water and/or increased protein synthesis (Clark, 1997). Fluid content and IMCP pre- and post-exercise in the anterior compartment may also become increased through the use of creatine supplements (Hile et al., 2006; Potteiger et al., 2002). This has also been reported to be accompanied by symptoms associated with CECS during exercise in a few subjects (Schroeder et al., 2001). However creatine supplementation is unlikely to be the main cause of IMCP related compartment pain.

2.2.5.3. Muscle activity within the compartment

The degree of muscle contraction is directly related to the IMCP. This phenomenon was first described by Baskin (Baskin & Paolini, 1967) in association with the changes in volume that occur with muscle contraction. Since then IMCP has been shown to correlate well with torque production during eccentric and concentric contractions of TA (and soleus); demonstrating better correlations than electromyography (EMG) during eccentric torque production (Ballard et al., 1992; Sporrong & Styf, 1999b). However the IMCP: torque ratio is lower during eccentric contraction (Crenshaw, Karlsson, Styf, Backlund, & Friden, 1995; Styf et al., 1995).

When the muscle contracts, force is developed in the direction of the muscle fibres; this force can be considered as having two components: a force transmitted through the tendon, and an orthogonal force transmitted through the muscle (Figure 19). Sporrong (1999a) then applied the law of Laplace to transform this orthogonal force in the muscle into a hydrostatic pressure (Equation 2). Passive effects resulting from muscle length changes can also have an effect on IMCP. Jenkyn (2002) developed a finite element model of IMCP during isometric contraction. The model predicted that IMCP increased non-linearly with muscle length due to the effects of tension in the passive elastic structures. Further evidence supporting this has been demonstrated through testing of IMCP at rest in different joint positions. Passive ankle dorsiflexion has been reported to cause 10-20 mmHg increases in IMCP in supine and sitting (Gershuni et al., 1984; Tsintzas, Ghosh, Maffulli, King, & Padhiar, 2009); while no changes have been observed with knee joint position (Gershuni et al., 1984). The state of contraction and muscle length changes are therefore key contributors to IMCP during exercise.
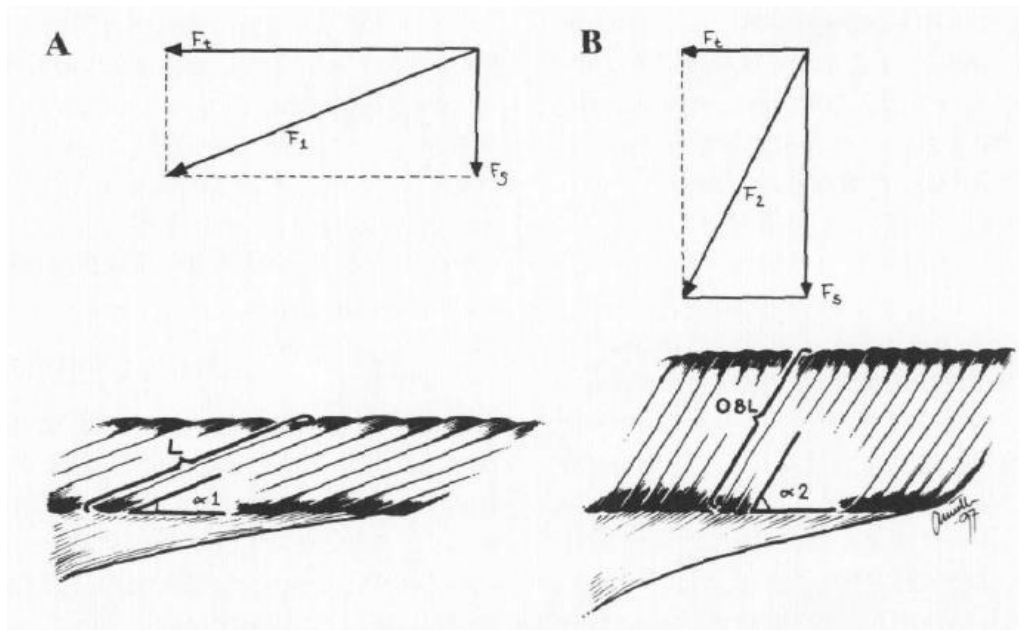
Figure 19 Schematic drawing of a muscle at the beginning (A) and end (B) of a concentric contraction . L= Length of the fibre, $\alpha 1$=pennation angle in the resting muscle, $\alpha 2$=pennation angle during contraction, F_1 and F_2 = force exerted by muscle fibres, F_t =force transmitted to the tendon, F_s=stress force transformed into hydrostatic pressure (Sporrong & Styf, 1999b).

Equation 2 Transformation of muscle force into a hydrostatic pressure (Sporrong & Styf, 1999b).

$$IMCP = \frac{\text{pressure underneath the fascia} + (\text{fibre thickness} \times \text{number of fibres} \times \text{fibre stress})}{\text{radius of the curvature of the fibres}}$$

The elevation of IMCP (Roscoe et al., 2015) during standing (when the muscle is not active) strongly suggests that there is reduced compartment compliance in patients with CECS as discussed in Chapter 2.2.5.2; however CECS by definition results in pain only during exertion. All populations at risk of CECS demonstrate the same needs for repetitive muscle activity of the affected compartment. It is therefore likely that, in order to experience pain from CECS, the muscle activity required must be of sufficient intensity and/or duration to interact with the pathology such that IMCP is raised to a critical level. At this point, blood flow would be impeded to such an extent that the muscles can no longer function normally.

Despite the observations on the positive effects of a biomechanical treatment package described in Chapter 2.2.4 and the knowledge that muscle activity has the largest potential effect on IMCP, very little primary research has been carried out to investigate these factors. Changes in movement technique (for

example reduced dorsiflexion) may be able to reduce IMCP either through a reduction in muscle activation or through the passive effects on muscle length. New treatments have recently been introduced that modify running style in an attempt to reduce the anterior compartment muscle activity of CECS patients. These have typically encouraged changing from a heel strike to a forefoot strike; increasing cadence; reducing step length and increasing forward lean (Helmhout et al., 2015). However there have been no studies comparing the biomechanics of patients to controls. This is a key area that requires investigation.

Forefoot running was first described as a possible treatment for CECS in a case report by Cunningham (2004) that may reduce the anterior compartment muscle activity (Jerosch, Geske, Castro, & Hille, 1989) and therefore pain. This has since been followed up by further case reports and a case series of ten US military patients (Diebal, Gregory, Alitz, & Gerber, 2011; Diebal et al., 2012; A. R. Gibson, 2013).

2.2.6. Treatment Methods, Effects and Outcome

The effects of treatment of CECS both in terms of outcome and variables of interest described above can provide useful information on both treatment efficacy and the pathophysiology of CECS. The mainstay of treatment for CECS is surgical fasciotomy or fasciectomy with few other options. Despite this, patients often experience symptoms for 2-4 years before receiving this intervention (1985; Pasic, Bryant, Willits, & Whitehead, 2015). Part of the problem may be due to delays in diagnosis; that can often take over 2 years (Davis et al., 2013). This in turn could be affected by delays in presentation. However return to activity following surgery can be reasonably quick. For example, cycling and other non-impact activities have been allowed after 1-3 weeks (Slimmon et al., 2002; Turnipseed, 2002); and impact activities including light running have been started between a minimum of 2-6 weeks (Schepsis et al., 1993; Styf & Korner, 1986).

The surgery divides the fascia longitudinally in order to release the tension and reduce IMCP. This has traditionally been carried out with a single long incision (Detmer et al., 1985; Tzortziou, Maffulli, & Padhiar, 2006), although scissor dissection with two or more incisions has also been described (Detmer et al.,

1985; Rorabeck, Bourne, & Fowler, 1983; Wiley, Clement, Doyle, & Taunton, 1987). More recently there have been reports of various arthroscopic methods (Kitajima et al., 2001; Kitajima, Tachibana, Hirota, Nakamichi, & Miura, 2001; Lohrer & Nauck, 2007; Lohrer & Nauck, 2007; Mouhsine, Garofalo, Moretti, Gremion, & Akiki, 2006; Ota et al., 1999; Sebik & Dogan, 2008; Wittstein, Moorman, & Levin, 2010).

2.2.6.1. Clinical outcomes of surgery

The occupational outcomes from surgery in the UK military population were recently documented in a retrospective analysis (Roberts et al., 2014). This suggested that following fasciectomy a large proportion of patients do not return to full fitness. This coincided with the publication of a paper demonstrating similarly poor outcomes within the US military (Waterman, Laughlin, Kilcoyne, Cameron, & Owens, 2013). Understanding the causes of CECS in the military population; identifying potential preventative strategies or alternative conservative treatment options may therefore be required to reduce the burden of this condition.

Civilian outcome studies have generally suggested more positive outcomes (Qvarfordt, Christenson, Eklof, Ohlin et al., 1983; Reneman, 1975; Schepsis et al., 1993); however this is not always the case. For example, poor long-term civilian outcomes, with some patients reporting early improvement followed by later decline, have been reported (Slimmon et al., 2002). This difference was suggested to be due to issues such as response bias caused by the involvement of the surgeon in outcome assessment.

The poor outcomes reported in the aforementioned studies contributed to the heightened interest in a biomechanical treatment package (Franklyn-Miller, Roberts et al., 2014). Poor surgical outcome has also be attributed to overdiagnosis (Roberts & Franklyn-Miller, 2012; Roscoe et al., 2015); delays in presentation, diagnosis and therefore surgery (Slimmon et al., 2002); differences in surgical technique (Detmer et al., 1985); post-operative rehabilitation (Schubert, 2011); and post-operative physical demands (Slimmon et al., 2002). However the effect of each if these potential factors is unclear.

Surgery also comes with the risk of complications. Garfin (1977) suggest that failure to decompress the superficial peroneal nerve when there is the presence

of a fascial defect may account for 'the occasional failure' due to continued irritation of the nerve. There is also a risk of causing superficial peroneal injury, especially when performed blindly (Hutchinson, Bederka, & Kopplin, 2003). Although Packer (2013) found that this was only a risk when a combined anterior and lateral compartment fasciotomy was carried out rather than just the anterior compartment. This may explain the poorer outcomes reported by Schepsis (1999) with the combined operation. Detmer (1985) reported that 22 of 100 patients experienced swelling due to capillary leak. Infection at the epidural site and haemorrhage have also been described in a limited number of patients (Wiley et al., 1987). Scarring following open surgery can also be a cosmetic issue in some patients (Packer et al., 2013). Outside of CECS, fasciotomy has been shown to impair the function of the calf muscle pump function in the long-term (Rosfors, Bygdeman, & Wallensten, 1988). There is no reason to believe that this would not also be the case in surgery for CECS. Alternative more conservative methods of treatment such as a biomechanical intervention are therefore of interest.

2.2.6.2. Conservative treatment

Most reports or studies of outcomes following surgery describe failure of some sort of conservative treatment although it is not generally clear how controlled these interventions were employed (Fronek et al., 1987; Martens et al., 1984; Sebik & Dogan, 2008; Wiley et al., 1987). Only recently a study demonstrated that, with a 'wait and see' approach, symptoms of CECS do not resolve and increased IMCP is still evident after 50 months (Van der Wal et al., 2014). This is important as it suggests that any structural changes, such as increased fascial stiffness, that may cause CECS do not abate with rest. Perhaps the most telling is the statement in a study of 80 patients with CECS: 'All had tried various conservative treatments including rest, reduced training, anti-inflammatory drugs, diuretics, physical therapy, US, stretching, local heat and cold, modification of shoes, different training programs, and orthotic applications; nothing had relieved their pain' (Styf & Korner, 1987, p.139).

Conservative treatment in the form of alterations in the biomechanics of CECS patients has only recently been reported to provide a positive effect as described in Chapter 2.2.5.3. Those studies described all demonstrated a reduction in pain and disability. Diebal (2012) also demonstrated a reduction in

post-exercise IMCP after 6 weeks of training; although the effect on IMCP during exercise is lacking.

In response to the outcome of the systematic review (Roberts & Franklyn-Miller, 2012) that highlighted the strong relationship between IMCP and muscle activation, a gait re-education programme was independently set up at DMRC. This programme focussed on encouraging a change in running gait from a heel-strike pattern to a forefoot pattern to try to reduce the activation of the muscles in the anterior compartment. However, adjustment of military-specific gait (marching) was minimal as it was considered to be less amenable to modification.

A novel treatment using Botox injection has recently been reported to eliminate pain in 94% of patients (n=15/16), while decreasing IMCP after exercise (Isner-Horobeti, Dufour, Blaes, & Lecocq, 2013). The method of action has been suggested to be either through the muscle atrophy, muscle relaxation or analgesia associated with Botox. Perhaps expectedly, this also reduced the strength of the injected muscles, although the authors report that this had no further functional consequences. In line with the gait treatments, this option may simply reduce muscle activity, rather than directly affect the underlying cause. Alternatively, Botox has previously been demonstrated to reduce thickness and pain in the plantar fascia (Huang, Wei, Wang, & Lieu, 2010), and could act in a similar way with the crural fascia.

Prior to these reports, two interventions had shown promising results in a small number of patients. Massage with stretching in seven patients demonstrated significant improvements in the amount of time to the onset of pain (Blackman, Simmons, & Crossley, 1998). However there was no difference in IMCP post-exercise, perhaps suggesting this should only be used as an adjunct to current treatment. A similarly small study of only five men suggested diuretic medication (bendroflumethiazide) can reduce IMCP before and after exercise along with relief of symptoms (L. V. Christensen, 1971). It must be noted that the patients in the latter study were older than the typical patient presenting with CECS. This may explain why, as described earlier, this was later tried by Styf without success (Styf & Korner, 1987).

2.3. Summary

The evidence presented within this literature review demonstrates clear areas of research that require investigation for CECS. The literature describing the clinical characteristics of CECS is disjointed and generally lacks quantitative data on the key characteristics and less acknowledged features such as neuromuscular symptoms. The activities that may be associated with the development of CECS in the military population are also unclear. This information is essential for the development of future biomechanical studies. Formal investigation of the clinical characteristics was therefore undertaken.

The clinical observations of abnormal biomechanics and rationale for the biomechanical treatments largely lack empirical evidence. However the literature demonstrates that muscle activity has the largest potential effect on IMCP. Pathologically a less compliant fascia appears to be the best current explanation of the increase in IMCP; however it is unclear whether altered biomechanics cause this to develop. The poor outcomes reported in military populations, following surgery, suggest that understanding the biomechanical causes of CECS may be required to reduce the burden of this condition. Methods of treatment that avoid the complications associated with surgery such as a biomechanical intervention are also of interest. Given the lack of supporting studies, three case-control studies investigating the biomechanical and muscle activation characteristics were undertaken and are reported as part of this thesis.

Chapter 3 provides detailed descriptions and associated limitations of the common methodology used in the case-control studies. Chapter 4 then describes the study investigating the clinical characteristics of CECS patients. Chapter 5 describes the first case-control study that investigated the foot type related and toe-extensor activity related plantar pressure characteristics. The biomechanics of walking and marching was then investigated in the second case-control study; the comparison of kinematics and kinetics is described in Chapter 6 and muscle activity in Chapter 7. The final study investigated the biomechanics of running and is described in Chapter 8. The main findings are then summarised in Chapter 9 alongside a discussion on the potential insights into the development of CECS; implications for prevention and treatment; and the limitations and direction of future research.

3. Methodology

Chapters 5, 6, 7 and 8 describe the case-control studies investigating the kinematic, kinetic, plantar pressure and muscle activation characteristics of CECS during walking, marching and running. This Chapter describes the general methodology used for these studies. The methodology for the first study differs from the other chapters, and as such is described fully in Chapter 4.

3.1. Equipment

Walking and marching trials took place along an 18 m walkway surrounded by 10 Vicon (Oxford, UK) motion capture cameras (4xT160 (16 megapixel), 4xT40-S (4 megapixel), 2xT10 (1 megapixel)). Two additional T160 cameras were acquired for treadmill data collection due to issues with marker dropout. Four Vicon Bonita 720c (Resolution: 1280 x 720) cameras collected synchronised high definition video data calibrated to force plate and optical data. The maximum frame rate of the T160 and Bonita 720c cameras is 120 Hz. All cameras were therefore set to capture data at this frame rate. Two marker sizes were used: 14 mm diameter markers were placed on the upper body and 9.5mm markers were placed on the lower body. Both markers had the same depth base (2 mm).

Three 0.6 m x 0.6 m AMTI OR-6 force plates were used for testing. The force plates are hidden from the view of participants as they are the same size as the floor tiles and have the same covering. Data was collected at 1200 Hz.

A 2 m x 0.4 m x 0.02 m plantar pressure plate (RSScan International, Olen, Belgium) embedded in the floor that collects data from 16384 sensors (3 sensors per cm^2) was used to collect plantar pressure data. Data was collected at 120 Hz to match the motion capture system.

A Delsys Trigno (Boston, MA, USA) wireless EMG system was used to collect data on muscle activity. The EMG sensors consist of four silver (99.9%) contacts each 5 mm x 1 mm in size and a fixed 10 mm inter-electrode distance. These create two differential EMG inputs with two stabilising references. Data was collected at 1200 Hz. All EMG sensors have an inter-sensor latency less than 500 μs and a fixed group delay of 0.048 ms allowing synchronisation within the software. The analog output channels have an actual gain of 909 V/V that is

used to convert the measured voltage output of an EMG channel to the original amplitude on the skin. The common mode rejection ratio is greater than 80 dB.

The walkway length was considered sufficient for walking and marching as a steady state is typically reached in just five steps (Gormley, Barr, Bell, Ravey, & Mollan, 1993). A Woodway Desmo (Woodway USA, Waukesha, WI) treadmill was used for running allowing a longer period for participants to attain a natural gait. This treadmill aims to minimise the problems associated with belt-type treadmills that exhibit intra-stride speed variations due to belt-slippage (Savelberg, Vortenbosch et al. 1998), through the use of a direct-drive system on a slat-style running surface.

3.2. Testing Protocols

3.2.1. Motion capture

3.2.1.1. Marker locations

Retro-reflective markers were attached to the skin surface with double-sided tape and located as shown in Figure 20 and described in Table 2. As described in Chapter 1.4.1, the choice of marker set was limited by that already selected by DMRC. References to marker names in the Chapters 3.2.1.2-3.2.1.3 omit the L or R prefix that indicates left or right sided markers for simplicity.

Table 2 Description of marker locations N.b. markers not used as part of this PhD program, but were present on the participant, are not described. The L or R prefix that indicates left or right sided markers has been omitted for simplicity on bilateral markers. *Unilateral/central marker

Marker	Description
C7*	7th Cervical Vertebra
T10*	10th Thoracic Vertebra
RBAC*	Right Back
STRN*	Sternal Notch
XYPH*	Xyphoid Process
ASI	Anterior Superior Iliac Spine
PSI	Posterior Superior Iliac Spine
FAP	Femur Anterior Proximal
FAD	Femur Anterior Distal
FLD	Femur Lateral Distal
PAS	Patella Apex Superior
KNL	Knee Lateral Femoral
KNM	Knee Medial Femoral
TAP	Tibia Anterior Proximal
TAD	Tibia Anterior Distal
SK1-4	Shank Cluster
ANL	Ankle Lateral Malleolus
ANM	Ankle Medial Malleolus
1MT	1st Metatarsal Head
5MT	5th Metatarsal Head
HEE	Heel
RLEG*	Right leg
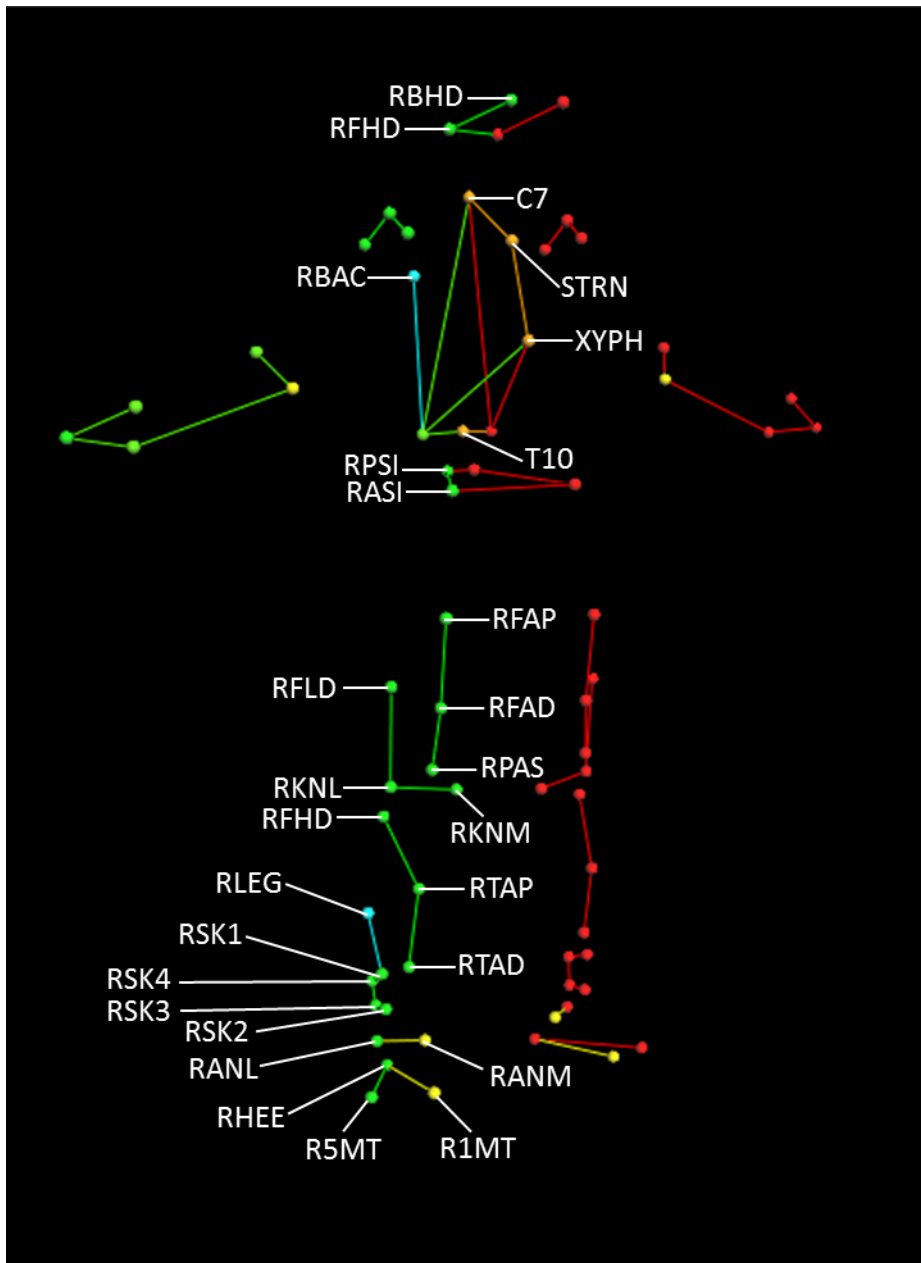
Figure 20 Central and right-sided marker locations and labels. N.b. markers not used as part of this PhD program are not labelled.

3.2.1.2. Segment definitions

Fourteen body segments were defined in Visual 3D™ software (C-Motion, Inc., Rockville, MD, USA) including the feet, shank, thigh, pelvis, trunk, upper arm, forearm and hand. The upper arm, forearm and hand were not analysed as part of this PhD programme – no further information on these segments is therefore provided. A virtual lab (global reference frame) was defined according to ISB recommendations ((Wu & Cavanagh, 1995);Table 3). This enabled the creation of virtual landmarks used in segment definition (e.g. joint centres, virtual markers corrected for marker size) and the calculation of kinematic variables in relation to the lab. An additional foot segment was created for kinetic calculations only as described in Chapter 3.2.1.2.5.

The segment definitions below describe the geometric model used for each segment. Implementation of inverse dynamics also requires the estimation of various other segmental parameters. A number of studies have attempted to provide standard values of relative segmental mass, segment centre of mass, radius of gyration and segment moment of inertial for input into the model. These include measures from direct cadaver segmentation and non-invasive estimates of living humans (for example using MRI, Dual Energy X-Ray Absorptiometry (DEXA), hydrostatic weighing). Nguyen (2014) investigated the effect of the variability in the body segment parameters from 24 of these studies on calculated joint moments using Monte Carlo simulations. Their data suggests that variability in parameters had little effect on joint moments except for a small effect in the swing phase moments of the knee and hip. The measurements reported by Dempster (1955) are perhaps one of the most commonly used for biomechanical models and are implemented by default within Visual 3D™ software (C-Motion, Inc., Rockville, MD, USA). The segments were therefore defined using these parameters and geometrically reflect the dissection positions used by Dempster (1955) if used in kinetic calculations. Slight deviations from these positions were not expected to cause a significant effect on inverse dynamic calculations (Nguyen & Reynolds, 2014).

Table 3 Definition of the lab co-ordinate system

Axis	Definition
X	Positive in the direction of travel
Y	Positive upward and parallel with the field of gravity
Z	Orthogonal to X and Y axes

3.2.1.2.1. The pelvis

The pelvis was defined as per the CODA pelvis ((A. L. Bell, Pedersen, & Brand, 1990);Figure 21) and is very similar in definition to the Helen Hayes pelvis (Davis III, Ounpuu, Tyburski, & Gage, 1991); both are used in many laboratories. While it has since been shown that they are not as reliable for tracking overweight and obese subjects in comparison to a back cluster, both methods generally show high repeatability (Borhani, McGregor, & Bull, 2013). The proximal and distal locations of the pelvis are defined and tracked by the virtual ASI and midPSI landmarks.
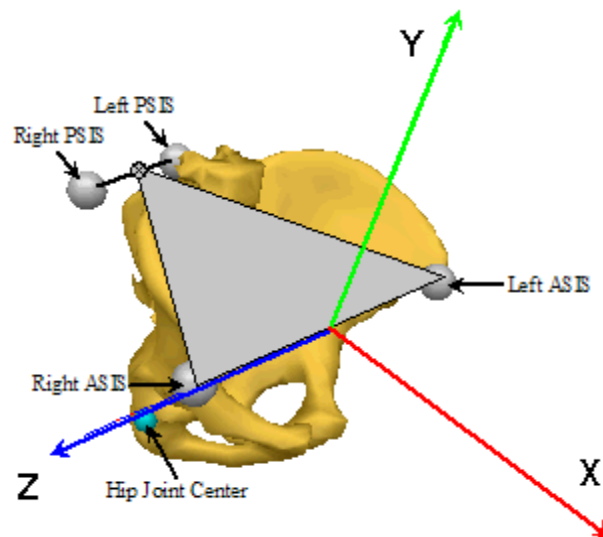
Figure 21 CODA pelvis definition

3.2.1.2.2. The thigh

The proximal and distal locations of the thigh were defined by the hip joint centre landmark and the virtual knee markers respectively in line with the mass definitions (Figure 22; Dempster, 1955). It was tracked by the FAP, FAD, FLD

and PAS markers. As described in Chapter 3.3.2 the FAP and FAD markers may be susceptible to relatively more soft tissue artefact that can affect the accuracy of non-sagittal movements. However it is not clear whether any marker set can fully reflect the non-sagittal movements of the underlying bone. As previously noted, the author was also limited in the choice of marker set (Chapter 1.4.1). This effect would have been mitigated to some extent with the use of the PAS marker as this has been demonstrated to improve the measurement of hip rotation (Wren, Do, Hara, & Rethlefsen, 2008).
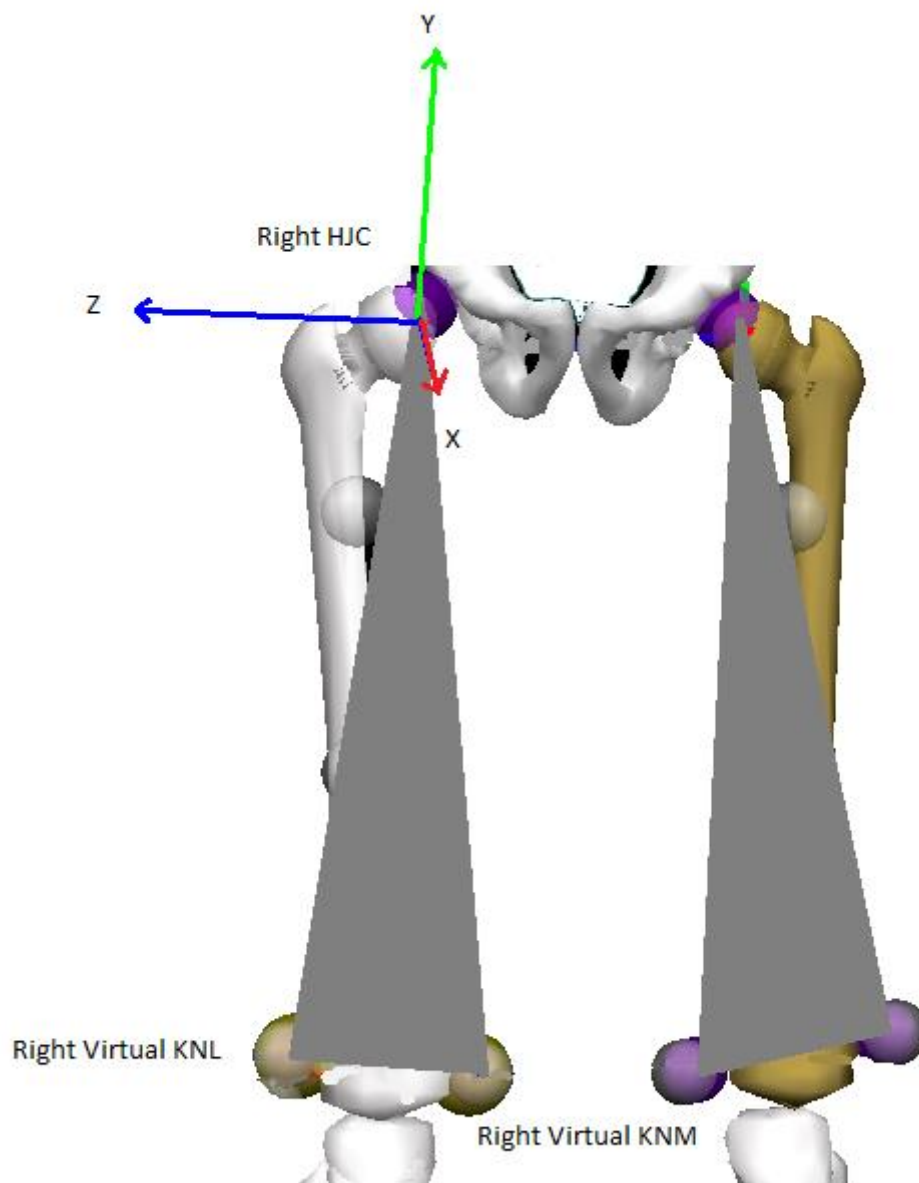
Figure 22 Thigh segment definition. HJC=Hip Joint Center, KNM=Medial Femoral Condyle, KNL=Lateral Femoral Condyle

3.2.1.2.3. The shank

The proximal and distal locations of the shank were defined by the virtual knee markers and the ankle joint centre landmark in line with the mass definitions (Figure 23; Peters, Sangeux, Morris, & Baker, 2009). It was tracked by the four shank cluster markers (SK1-4) recommended by Manal (2000) and the two anterior shank markers (TAP, TAD).
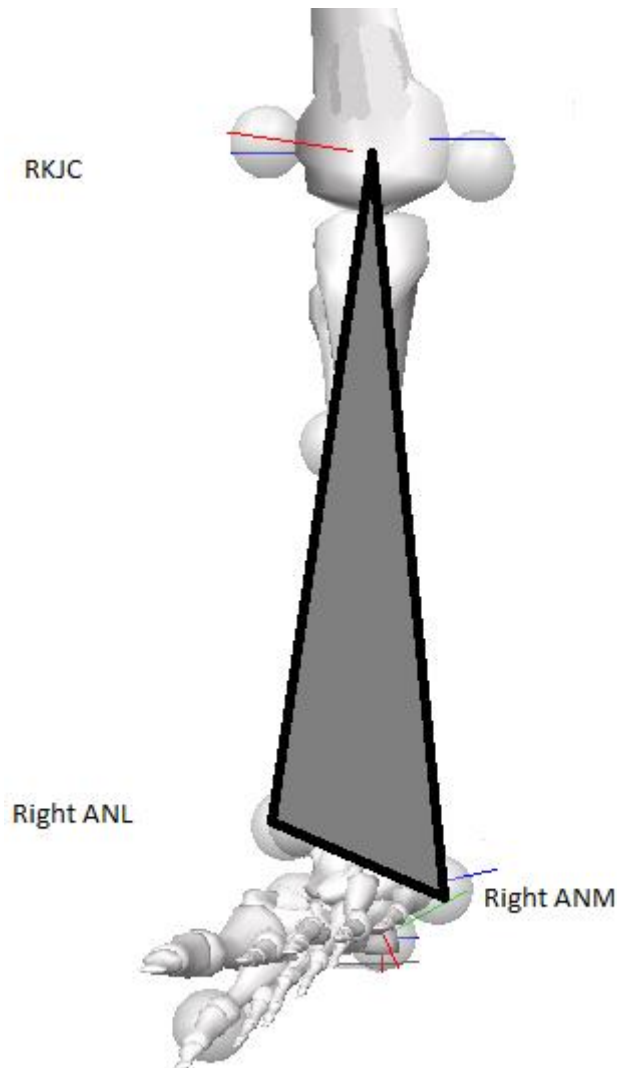
Figure 23 Shank segment definition

3.2.1.2.4. The foot

A foot segment was created for kinematic use only so that the joint angle had a more clinically relevant meaning. The proximal and distal locations of the foot were defined by the heel marker and the metatarsal markers projected to the height of the heel marker. It was tracked by the heel marker and the (non-

projected) metatarsal markers. This segment was adapted from the foot segment defined by Pratt (2012)(foot flat option; Figure 24). The foot flat option sets the longitudinal axis perpendicular to the lab when in the static pose aiding interpretation of extracted angles. This was achieved by projecting all the metatarsal markers to the height of the heel marker during standing. This foot/shoe model has high waveform similarity and correlation (Pratt et al., 2012) with the sagittal and foot rotation angles of the Vicon® Plug-in-Gait foot and with the inversion/eversion angles of the Oxford foot model (Stebbins, Harrington, Thompson, Zavatsky, & Theologis, 2006)).
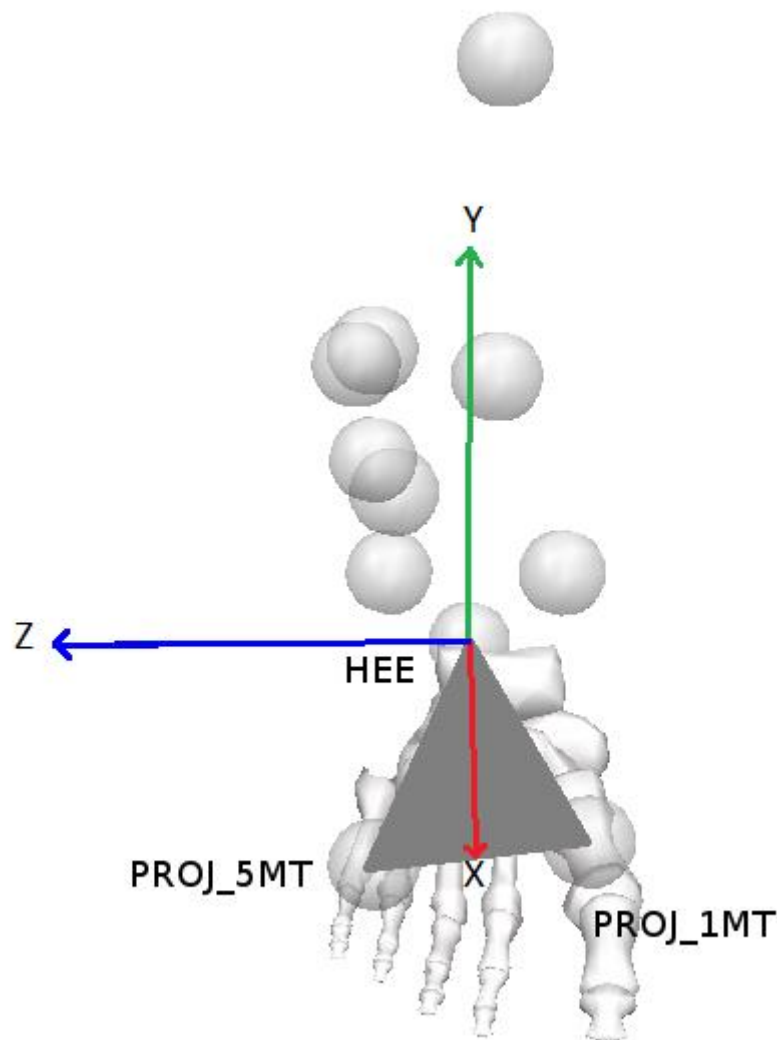
Figure 24 Foot segment definition (kinematics). PROJ_ prefix indicates that markers were projected

A second foot segment was defined for use in kinetic calculations based on a modified Helen Hayes set (Kadaba, Ramakrishnan, & Wootten, 1990). The segment was tracked by the same markers as the kinematic foot (Figure 25). Its definition differs in that the proximal point was defined by the ankle joint centre and distal points by virtual markers estimated to be at the mid-point of each metatarsal head (VMT1 and VMT5). This segment is better suited for inverse dynamics calculations as it follows the dissection positions of Dempster (1955), is defined with the proximal point at the ankle joint centre and removes the foot flat offset used in the kinematic foot.
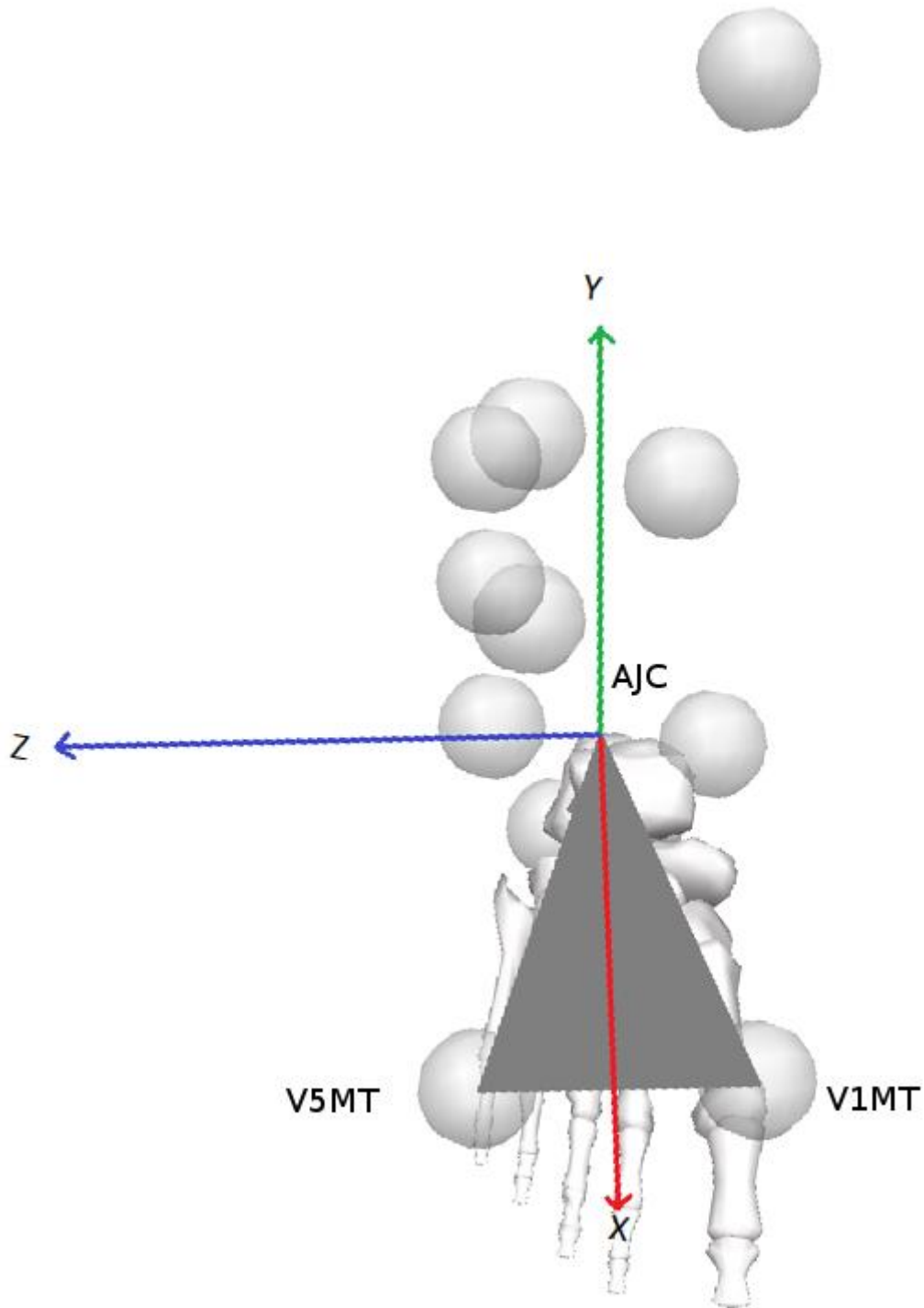
Figure 25 Foot segment definition (kinetic)

3.2.1.2.5. The thorax

The thorax was defined in line with Gutierrez (2003) and Vicon® Plug-in-Gait. The model is very similar to the ISB model except it uses the T10 rather than T8 marker which provide similar results (Armand, Sangeux, & Baker, 2014). The proximal location of the thorax was defined by the midpoint between the

sternum and C7 markers and the distal location was defined by the midpoint between the xyphoid and T10 markers. It was tracked by the C7, sternum, T10 and xyphoid markers. Since the marker set was chosen, a comparative study of thorax models recommended this marker set with one small change: the use of a T2 rather than C7 marker (Armand et al., 2014). C7 was observed to be influenced to a greater extent by isolated head movements; although during ambulation this would not be expected to be a problem

3.2.1.3. Joint centre definitions

A recent comparison of various methods used to define the hip joint centre concluded that the Harrington (2007) regression equations provide the best estimation compared to any other method in populations with reduced hip movement ability (Sangeux, Pillet, & Skalli, 2014). The Harrington (2007) equations placed the hip joint centre on average 1.7 cm away from the gold standard imaged location and were within 3 cm of this location 97% of the time. The equations also compared favourably to functional sphere fitting (mean accuracy 1 cm) in the unimpaired population. During running, better reliability was reported for the anatomical technique than either functional or projection methods (J. Sinclair, Taylor, Currigan, & Hobbs, 2014). The Harrington (2007) equations were therefore chosen due to their good accuracy and reliability in multiple populations and tasks. The additional time required to collect and process the functional methods provided further justification for the use of an anatomical technique.

The knee joint centre was defined as the midpoint between the two knee epicondyles. Dynamic cadaveric data suggests that the transepicondylar axis closely approximates the true flexion axis (Churchill, Incavo, Johnson, & Beynnon, 1998). The location of the epicondylar markers was adjusted to best approximate the flexion axis from visual inspection of the movement.

The ankle joint centre was defined according to the two-marker model as the midpoint between the two ankle malleoli (Davis III et al., 1991; Kadaba et al., 1989). This method has been demonstrated to be superior to the Plug-in-Gait model used by most clinical gait analysis laboratories (Nair, Gibbs, Arnold, Abboud, & Wang, 2010). A correction to the two-marker model has also been proposed, as this model tends to lead to a more proximal location than

expected (Bruening, Crewe, & Buczek, 2008). However the offsets are only small (less than 13 mm) and the authors suggest that it is therefore unlikely to have a large effect on kinematics and kinetics. The original two-marker model was therefore used to allow greater comparability with previous work.

3.2.2. Electromyography

Hair was removed from the EMG testing locations using a surgical razor. The skin was then cleaned using an alcohol wipe and lightly rubbed so that the skin went light red in order to decrease skin impedance (Konrad, 2005). The EMG activity of the TA and gastrocnemius medialis was recorded bilaterally during all movement trials and placed according to the guidelines by Sacco (2009) and the SENIAM project (Stegeman & Hermens, 2007) respectively. The TA EMG locations were determined by measuring one third of the way along a line drawn from the fibular head to the medial malleolus. The gastrocnemius medialis was defined as halfway along a line drawn from the medial margin of the popliteal fossa to the medial insertion of the Achilles tendon at the calcaneus. The sensors were attached using double sided adhesive tape along the longitudinal axis of the muscle. Correct placement and satisfactory signal quality was confirmed by performance of a maximum voluntary contraction of the individual muscle with observation of changes on the monitor in line with guidelines provided by Hislop (1995).

3.3. Assumptions, limitations and sources of error

3.3.1. Marker placement and model definition

Some marker locations can be particularly difficult to palpate. For example the accuracy of locating the correct vertebra level of both C7 and T10 is variable when using surface anatomy as a guide (Shin, Yoon, & Yoon, 2011; Teoh, Santosham, Lydell, Smith, & Beriault, 2009). This is unlikely to result in significant errors as different vertebra can be used while providing similar tracking.

The hip joint centre was used to define the thigh segment and thus errors in its estimation were propagated through to the knee and hip joint angles and moments. The hip moments, in particular the flexion-extension moment, show the most error when the hip joint centre is not located correctly (Stagni, Leardini,

Cappozzo, Grazia Benedetti, & Cappello, 2000). Inaccuracies of 3 cm lead to errors in the moments of more than 22 % of the typical range. The error associated with the hip angle however can be considered negligible with typical errors of less than 1 degree on flexion-extension angle (c. 3% of the typical range) and less than 0.5 degrees on abduction-adduction and internal-external rotation angles (c.5% of the typical range).

Poor definition of the knee joint centre can also have consequences on joint moments. When the KJC is artificially moved 10 mm in the anterior-posterior direction the errors introduced are particularly pronounced at slower walking speeds (Holden & Stanhope, 1998). At normal walking the greatest error is seen in the flexor peak with variation of c.40% of the mean net moment.

3.3.2. Soft tissue artefact

Soft tissue artefact potentially represents the largest source of error in motion capture. Readers are referred to a recent systematic review that discusses the measurement of soft tissue artefact and summarises what is known about this error source (Peters, Galna, Sangeux, Morris, & Baker, 2010). The largest errors are found when markers are placed on bony landmarks such as the lateral epicondyle and lateral malleolus. To reduce the artefact from these markers, these locations were only used as anatomical markers and not used to track the segment. These markers were also placed while the participants were in the same standing posture as was used to calibrate the model. The tracking markers used were generally considered those least susceptible to the effects of soft tissue artefact as described in Chapter 3.2.1.

The measurement of hip and knee rotations seems to be particularly prone to soft tissue artefact. Benoit (2006) performed a relatively large study of knee kinematics during walking and cutting manoeuvres measured using skin mounted markers and bone pin mounted markers. They concluded that the 'repeatable patterns [of the knee] must not be misinterpreted as accurately representing skeletal kinematics, at least beyond the sagittal plane of movement where the error is small relative to the total movement'. This is in agreement with earlier results using external fixators by Capozzo (Cappozzo, Catani, Leardini, Benedetti, & Croce, 1996). During running, consistently larger skin movement errors are present. The measurements of these movements are

similarly limited in the studies presented in this thesis. The anteriorly placed thigh markers have been extensively used in the biomechanics literature (e.g. Sangeux (2011)) and therefore allow comparable results. However, Reinschmidt (1997) suggests that these markers may undergo relatively large movements during running and, in line with the bone pin studies during walking, that only sagittal knee movements can reliably be extracted. Caution is therefore needed when interpreting movements outside of the sagittal plane.

3.3.3. Inverse Dynamics calculations

The calculation of joint moments using inverse dynamics is dependent on both the accurate collection and modelling of kinematic data, the collection of accurate force plate data, and an accurate synchronisation both spatially and temporally of the force and kinematic data. The quality assurance checks were carried out to limit the potential for significant error to arise (Section 3.6). Errors can also be introduced through inaccuracies in segmental parameters such as mass, moment of inertia and the location of the centre-of-mass (Nguyen & Reynolds, 2014). Reduction of these errors was carried out through careful definition of each segment as described in Chapter 3.2.1.2.

Riemer (2008) provides a comprehensive analysis of the errors in calculating joint torques using inverse dynamics. They conclude that the main source of error comes from soft tissue artefact (described in Section 3.3.2). They also state that 'inaccuracies in segment length have minimal contributions to the overall uncertainty'. The errors are propagated up the kinetic chain with a bottom-up approach. The magnitude of expected errors for lower limb joints is well visualised in Figure 26.
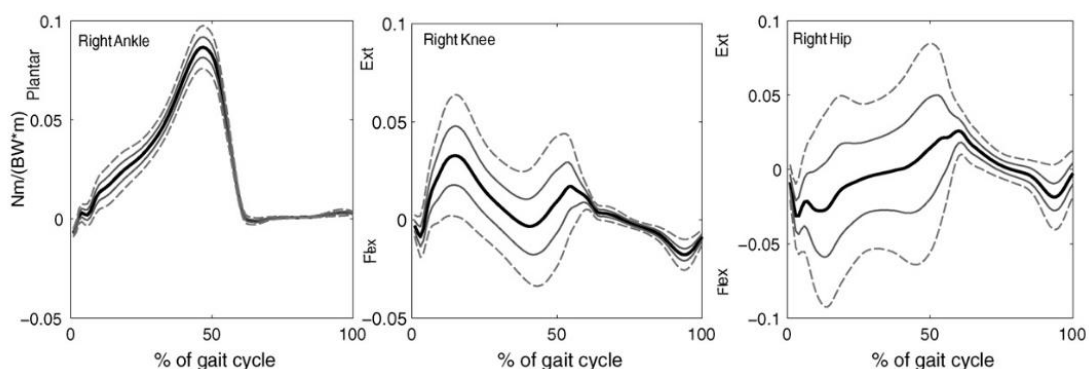
Figure 26 Time varying joint-torque estimates (thick line) and confidence limits derived from two sets of inaccuracy values. The first set represents the lower values of

inaccuracies for each of the variables (thin line) and is probably most representative of the realistic situation. The second set (dashed line) represents the higher values of inaccuracies (the worst case scenario) (Riemer et al., 2008)**.**

The interpretation of joint moments is also limited as they represent the overall moment at a joint and therefore cannot be used to distinguish between a single muscle contracting, multiple muscles contracting or an agonist and antagonist contracting (that would offset one another). Electromyography is currently the best way to aid the understanding of individual muscles contributions (although this technique also has its own limitations as described in Chapter 3.3.4).

3.3.4. Electromyography

The collection of EMG data requires the maximisation of the signal to noise ratio. The reduction of baseline noise and crosstalk is carried out through careful positioning, skin preparation and electrode selection as described for Chapters 7 and 8. In comparison to the commonly used 22 mm spacing single differential sensor, the 10 mm inter-electrode distance and small contact area of the Trigno sensors reduces crosstalk during walking from 23% to 8% (De Luca, Kuznetsov, Gilmore, & Roy, 2012). The lack of sensor leads eliminates their contribution to movement artefact (Odman & Oberg, 1982).

Maintaining signal fidelity can be problematic during vigorous or long-duration activities as contact is lost between the skin and the electrode (Turker, 1993). Skin contact related artefact can be reduced through the use of a strong skin adhesive tape, a contoured sensor design, and without a hydrophilic gel (Roy et al., 2007). These features were all part of the Delsys Trigno system used. Surgical tape was also used for running trials and where the initial adhesion to the skin did not seem adequate to reduce this problem further.

Skin abrasion is known to reduce skin impedance; however its use is controversial (Tam & Webster, 1977). This technique is typically used for passive EMG sensors and their effectiveness for active sensors such as the Delsys Trigno has not been studied. Skin abrasion is not recommended by the manufacturer and was therefore not used in these studies.

Extrinsic sources of noise from power lines and cable motion have been virtually eliminated using the Delsys Trigno sensors. Intrinsic sources of noise either occur in the amplification system, or at the electrode-skin interface.

During activity movement-artefact occurs when the muscle moves under the skin or the forces cause the electrode to move with respect to the muscle; however these artefacts cannot be reduced.

3.3.5. Consequences of marker set restriction and recommendations for future models

As described in Chapter 1.4.1 the marker set used in this thesis was restricted by DMRC. Many of these marker locations are optimal for the reduction of soft tissue artefact, optimal joint centre estimation and correlate with the dissection positions used by Dempster (1955) to determine segment masses (and subsequently used in the model). However, refinements to the model may be of use to improve reliability and validity. The advantages and limitations of the marker set are described below.

The ASI and PSI markers used to define and track the pelvis also provide the best estimation of the HJC (Harrington et al., 2007). However the use of a back cluster for tracking is more reliable in overweight and obese individuals (Borhani et al., 2013). While participants with a high BMI were excluded in the kinematic studies in this thesis, implementation of a back cluster could allow for reliable pelvic motion data across a wider range of participants.

Anterior thigh markers have been observed to result in relatively large soft tissue artefacts during running due to activation of the underlying muscle (Reinschmidt et al., 1997). While the optimal marker set for thigh segment tracking is yet to be determined, the use of a lateral thigh cluster for tracking may be expected to reduce soft tissue artefact. However comparison of a lateral cluster during walking with two marker sets, using single anterior, lateral and posterior markers, suggests that for hip axial rotation at least that there is little difference between these marker sets (Schache, Baker, & Lamoreux, 2008). Alternatively the use of just the distal anterior thigh marker may be preferable as this is less prone to soft tissue artefact than a more proximal marker (Akbarshahi et al., 2010).

The foot is anatomically complex and as such several authors have proposed the use of a multi-segment model that represents foot function in more detail (Bruening, Cooney, & Buczek, 2012; Cobb, Joshi, & Pomeroy, 2016; Oosterwaal et al., 2016; Seo et al., 2014; Stebbins et al., 2006). They are all

limited by the requirement to access the skin for attachment of markers. Despite the ability to generate more complex foot models, the single segment model is still widely used for barefoot analyses (Moore & Dixon, 2014; Nunns et al., 2016; Pasini Neto et al., 2012). This may be due to the need for up to 22 markers per foot in multi-segment models that may cause issues for some camera systems along with increased post-processing time (Deschamps et al., 2011). A single segment model is also the only practical option for shod analyses, as undertaken here, without significantly altering the shoes. Given these issues and the lack of a universally accepted multi-segment model; the selection of foot models should be made on an individual project basis within the MPARL.

3.4. Equipment accuracy

The motion capture system meets the Medical Devices Directive 93/42/EEC (Directive, 1993) and will provide at least a 'resolution of the distance between two static 14 mm spherical markers located within a volume no less than 4 m x 4 m x 1.5 m to within 1 mm mean; 1 mm standard deviation' within the MPARL.

Vibration that can lead to system inaccuracy was minimised through two methods. The air conditioning system leads to visible vibrations in the live view of individual cameras; this was switched off for the duration of testing. Fans and open windows were used instead to ensure a comfortable temperature. The use of the doors was found to cause a vibration effect to cameras mounted nearby. Access was therefore restricted during testing and users were advised to open and close the doors carefully. Segment trajectory data is also affected by missing markers and other sources of noise. The data processing protocols (Section 3.7.1) were designed to minimise the effect of these sources of error.

The force plates are mounted in a first-floor location resulting in the possibility of vibration induced artefact. The force plates and associated amplifiers were therefore designed and set up for low-medium impact activities. For example, the composite top of the force plate reduces vibration induced output by a factor of four in comparison to standard aluminium tops.

The analysis of running gait was restricted to kinematic measurements for two reasons. Firstly, a limited runway length makes it difficult to run naturally due to the inability to accelerate and settle at a set pace before needing to stop (Riley

et al., 2008). Secondly, running is a higher impact activity that may have resulted in force plate data that was significantly affected by vibration.

3.5. Output variable definitions

3.5.1. Gait events and temporo-spatial parameters

The gait cycle was split into several distinct phases based on the timing of initial foot contact and last foot contact. The time between these events was calculated to determine stance time, swing time and step time. Flight time was also calculated for running gait. These parameters are represented in Figure 27 and Figure 28 for walking and running respectively. By definition, greater than 50% of the gait cycle is spent in the stance phase during walking, while the opposite is true for running (Novacheck, 1998). Individual gait cycles were excluded from analysis if a running gait was detected during the walking study and vice-versa. Step length, step width and stride length were calculated based on the position of the foot at these events (Figure 27 and Figure 28). During treadmill running, step length was defined as the anterior-posterior distance from heel strike of one foot to toe-off of the contralateral foot (Owings & Grabiner, 2004).
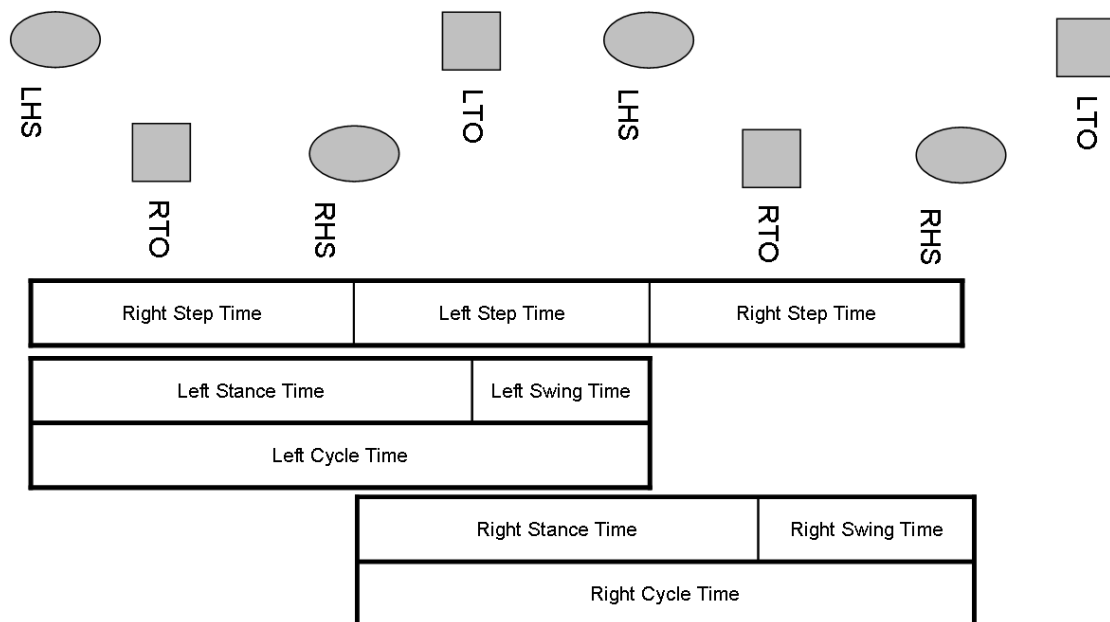
Figure 27 Temporal-spatial variables – Walking . LHS=Left Heel Strike, LTO=Left Toe Off, RHS=Right Heel Strike, RTO=Right Toe Off
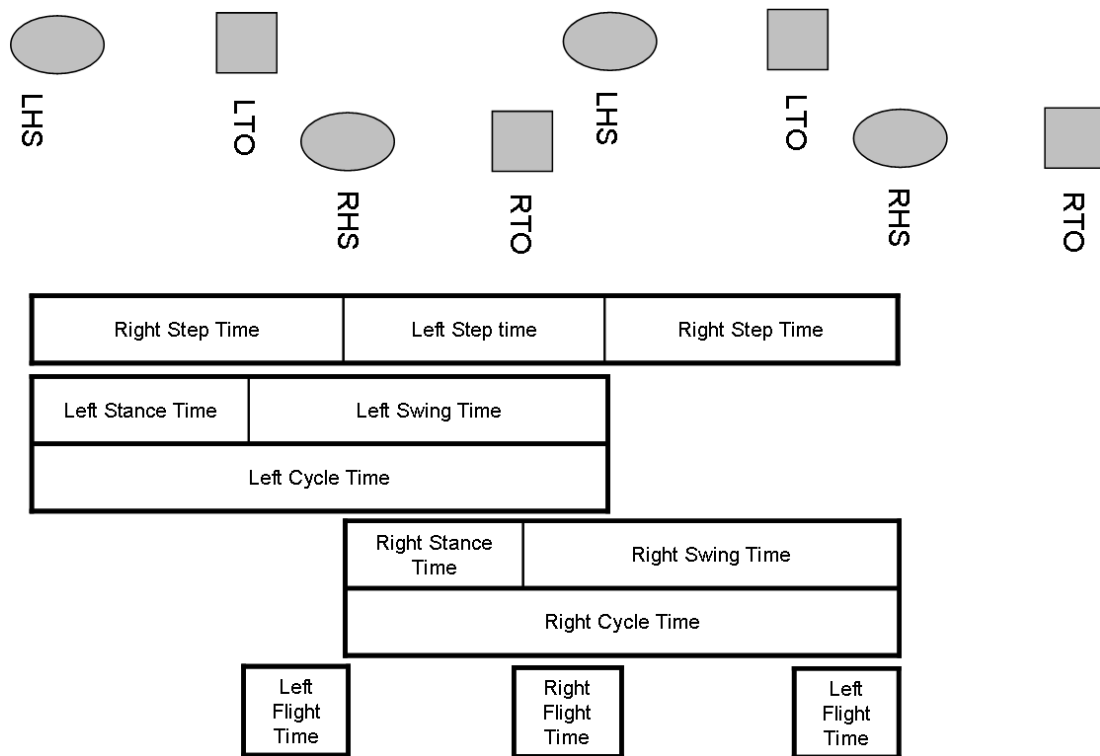
Figure 28 Temporal-spatial variables – Running. LHS=Left Heel Strike (or other foot contact), LTO=Left Toe Off, RTO=Right Toe Off

Initial and last foot contact events have traditionally been defined using force plate data. However these methods limit the number of foot strikes that can be utilised for analysis due to the small area covered by the force plates and the requirement for a 'clean' strike. A 'clean' strike is determined when the only contact with the floor by the foot is on a force plate. Therefore these events were determined visually for kinematic data on the recorded video and algorithmically for kinetic and inverse dynamic data. For kinematic data, initial contact was defined in line with Perry (1992) as the 'moment when the foot just touches the floor'; last foot contact was defined as the last moment before the foot leaves the floor. These events therefore included instances when the foot was not on a force plate. For kinetic and inverse dynamic calculations a 'clean' strike was strictly enforced. First, only gait events occurring on the force plate were identified algorithmically. The contact phase was defined as the period where the unfiltered vertical ground reaction force exceeded 20 N in line with Kristianslund (2012). Second, segments were assigned automatically by Visual 3D™ software (C-Motion, Inc., Rockville, MD, USA) to force plates based on the estimated contact of a segment with the centre of pressure on the force plate.

The force graphs were then checked for outliers and any wrongly assigned contacts manually excluded.

3.5.2. Kinematics

Joint angles and the angles of segments in relation to the lab (aka 'projection angles' or 'segment to vertical angles' or 'inclination angles' (R. Baker, 2013; Owen, 2010; Tong & Granat, 1999)) were defined within Visual 3D™ software (C-Motion, Inc., Rockville, MD, USA). Given the importance of cardan sequences in the description of gait biomechanics (Cole, Nigg, Ronsky, & Yeadon, 1993), the International Society of Biomechanics (ISB) recommended sequence was typically used: flexion/extension, abduction/adduction, and then axial (internal/external) rotation (Wu & Cavanagh, 1995; Wu et al., 2002). Sinclair (2012) demonstrated that these recommendations are also appropriate for non-sagittal plane angles after it had previously been proposed otherwise (Thewlis, Richards, & Hobbs, 2008). The pelvis, which predominantly functions in different planes to the other lower limb segments, was treated differently to ensure consistency with conventional clinical understanding as recommended by Baker (R. Baker, 2001). In this case, the sequence of rotation, obliquity and then tilt was selected.

3.5.3. Joint moments

The internal moment was calculated for each lower limb joint. The choice of reference frames for the expression of joint moments has been suggested by Schache *et al.* (2007), due to the relatively slow speed of gait, to have a greater effect than variability in segmental inertial properties (as described in Section 3.5.2). They examined the effect of using different reference frames (all of which are mathematically correct) on joint moments during gait. They then proposed that 'the non-orthogonal joint co-ordinate system is most logical on the basis of what, biomechanically, the joint moment actually represents'. The same reference frames for joint kinematics and kinetics were therefore used.

3.6. Quality Assurance, Set up and Calibration Procedures

3.6.1. Kinematics

The motion capture cameras were calibrated in accordance with standard Vicon procedures. An active wand was used to calibrate the Vicon system. This

enabled the software to work out the positions, orientations, and lens properties of the motion capture and video cameras. A passive wand was then used to set the origin of the capture volume; positioned in the same location each time to define the lab co-ordinate system (Table 3).

3.6.2. Kinetics

Force plates were switched on at least one hour prior to system calibration and use. An amplitude accuracy test was then performed. Calibrated 25 kg weights were placed on the corner of the force plate nearest to the lab origin and a second time at the centre of the force plate. The measured forces were assessed for accuracy (vGRF within ±2.5 N) and crosstalk (± 2%). If values lay outside of these values the force plates and accompanying software were checked for faults or errors. Force plates were tared on the amplifier and then in the software before data collection started.

3.6.3. Joint Moments/Torques

The accurate definition of the lab co-ordinate system in relation to the position of the force plates is essential for precise calculation of joint moments. This was assessed prior to each testing session using Caltester (C-Motion, Inc., Rockville, MD, USA) using the test proposed by Holden (2003). This test measures the difference in the COP (Centre of Pressure) and force orientation as determined by the force plate and motion capture system. Testing was carried out in the corner of the force plate furthest away from the origin (and therefore expected to be most susceptible to errors (Bobbert & Schamhardt, 1990)). A threshold of 40 N was applied.

Acceptable values in the lateral-medial and anterior-posterior axes were defined according to MPARL protocols as less than 10 mm (mean ± 1 SD). In the vertical axis the acceptable value was less than 5 mm (mean ± 1 SD). The force orientation error was limited at less than 2° (mean ± 1 SD). Systematic changes of 5 mm and 10 mm in the COP in the anterior-posterior direction have been shown to cause on average 7% and 14% changes respectively in maximum joint torque and angular impulse values (McCaw & DeVita, 1995).

3.6.4. Electromyography

Hair was removed from the EMG testing locations using a surgical razor. The skin was then cleaned using an alcohol wipe and lightly rubbed so that the skin goes light red (Konrad, 2005). This has been shown to reduce skin impedance by 90% (Bottin & Rebecchi, 2002). The EMG electrodes were attached using double-sided adhesive tape along the longitudinal axis of the muscle. EMG activity of the TA and gastrocnemius medialis was recorded bilaterally during all movement trials and placed according to the guidelines by Sacco (2009) and the SENIAM project (Stegeman & Hermens, 2007). Prior to the recording the signal was checked for noise and artefact. Electrode position and signal quality was verified by visually inspecting the EMG signals while the participants contracted each instrumented muscle.

The TA EMG locations were determined by measuring 1/3 of the way along a line drawn from the fibular head to the medial malleolus. The gastrocnemius medialis location was standardised as halfway along a line drawn from the medial margin of the popliteal fossa to the medial insertion of the achilles tendon at the calcaneus. In all cases the lower left corner of the electrode was placed at this point. Correct placement and good signal to noise was confirmed by performance of a maximum voluntary contraction of the individual muscle with observation of changes on the monitor in line with guidelines provided by Hislop (1995).

3.7. Data Processing

3.7.1. Kinematics

Missing marker data caused by occlusions or a marker falling off is a common problem impairing data quality. To counteract this, gaps were interpolated using a 3rd order least squares fit. This technique is optimal for gaps of less than 200 ms, although the validity of this technique in motion capture has only been reported for the elbow flexion-extension angle during wheelchair propulsion (Howarth & Callaghan, 2010). A shorter time period (less than 14 frames (117 ms)) was chosen to ensure interpolation would also be valid for other angles during normal gait and to ensure consistency with other MPARL kinematic data. The data was then filtered using a low pass 6 Hz bidirectional Butterworth filter (Winter, Sidwall, & Hobson, 1974).

Segments were excluded from further analysis on a frame-by-frame basis if they contained a tracking marker with a gap greater than 14 frames, with the exception of two markers on the shank (TAP/TAD) and two markers (LASI/RASI) on the pelvis that were occluded regularly. Borhani (2013) demonstrated that tracking the pelvis with a posterior marker cluster had better repeatability than tracking with anterior and posterior markers. This suggests that the posterior markers are subject to less soft tissue artefact. While this information was not available before testing began; loss of a posterior marker was now considered a serious issue. The pelvis segment was therefore only excluded for a particular frame if there was a gap in one of the posterior markers (LPSI/RPSI).

Exclusion of a segment was achieved by replicating the gap in the other tracking markers of the segment, thus preventing the modelling of the segment and its use in calculations. This prevented the artefact that occurs when not all markers are used to track the segment. As the gaps were not always at the same point in the gait cycle, this reduced the variability in segment pose estimation without a loss of data at specific time points.

3.7.2. Forces

Force plate data was filtered using a 50 Hz low pass Butterworth filter. The optimal cut-off frequency for ground reaction forces is dependent on the application. A high cut-off will result in the best force data (Van den Bogert & De Koning, 1996). Although a high cut-off for force data in combination with the low cut off required for marker data can result in artefacts in the moment calculations during impact events (Kristianslund et al., 2012). This is due to the inability of current methods to observe the high frequency components of segment accelerations.

Kristianslund (2012) recommend counteracting these artefacts by matching the force cut-off frequency with that determined for the marker data (i.e. a relatively low frequency). However, Roewer (2014) suggest that this is simply removing physiological information from the force signal due to limitations in the marker data. Their data suggest that the effect is not consistent between subjects and that the use of a high frequency cut-off (50 Hz) still leads to valid results even when the subject is carrying out a high impact activity (drop vertical jump). The

force plates were used in these studies for relatively low impact activities (walking and marching), as such a 50 Hz cut-off frequency was also used to optimise signal to noise ratios within the force data.

3.7.3. Plantar pressure

Each foot was automatically divided into 10 zones by Footscan® (v7.97, RSScan International) software as described by Hagman (2005). In summary, the foot is divided based on anatomical measurements into a rearfoot area of 31%, a midfoot area of 19%, and a forefoot area (containing the metatarsal heads and toes) of 50% relative to foot length (Burns, 2004). The foot axis was then defined as the line from the COP of the rearfoot area to the COP of the forefoot area (Hagman, 2005). The forefoot area is then divided into the metatarsal area and toe area using edge detecting algorithms (Hagman, 2005). The rearfoot, forefoot and toe areas are then divided medio-laterally in the direction of the foot axis: the rearfoot is divided into 2 equal areas; the metatarsals are divided according to the expected proportions of the metatarsal heads and the toe area is divided into the hallux and lesser toes using a custom algorithm.

Data was extracted from Footscan® using the standard exports. These data were then processed within Scilab (v5.3.2; INRIA, France) to generate mean values of each plantar pressure variable for left and right feet.

3.7.4. Electromyography

The data for 5 participants had to be recovered after a bug in an early version of the Vicon Nexus software that resulted in the loss of EMG data following processing. Data that was subsequently recovered required offsetting to match the cropped processed files containing the event identifiers. This was carried out in Visual 3D™ software (C-Motion, Inc., Rockville, MD, USA).

A custom MATLAB (R2015b,Mathworks, Natick,MA) script was used to carry out a wavelet analysis (von Tscharner, 2000); normalise the data temporally to 100% of the gait cycle; and to normalise the wavelet intensity to allow comparison between groups (Federolf & Bakker, 2012). A wavelet analysis allows the power of the EMG signal to be described in both the frequency and time domain, unlike a Fourier transform that can only be used on stationary signals. Low levels of contraction throughout the gait cycle for the TA as

previously described (Reber et al., 1993) meant that the wavelet analysis was also preferred to simple threshold analyses for the identification of timing information.

The R statistical software (v3.2.2, The R Foundation for Statistical Computing, Vienna, Austria) script published by Armstrong (2011) was called by MATLAB to calculate the intensity of 11 wavelets using the EMG-specific parameters defined by von Tscharner (2000). The centre-frequency of these wavelets ranged from 7 Hz to 395 Hz. Normalised wavelet intensity patterns were calculated by dividing the wavelet intensity by the average intensity per gait cycle and the gait cycle duration (Federolf & Bakker, 2012). The normalised wavelet intensity patterns were compared between groups.

3.8. Statistical analyses

A large proportion of biomechanical data is output normalised to the gait cycle. Two options are available for the analysis of this type of data. The first and most widely used involves selecting points of interest either based on specific events (for example, toe-off) or instances of peaks or nadirs. Comparisons between these discrete time points can then be made. However these methods exclude many of the other time points that may be of importance. An alternative is to analyse each individual normalised time point with the t-test (Sharma, Golby, Greeves, & Spears, 2011). A more powerful technique uses bootstrapping for the analysis of gait curves (Lenhoff et al., 1999). The bootstrap method does not assume a particular distribution of the data and can therefore provide more robust results. For the analysis of kinematic, force and EMG data, bootstrapped t-tests were therefore carried out on each individual normalised time point to identify regions within the gait cycle that were significantly different. For temporal-spatial data the bootstrapped t-test was also used to compare groups.

The ability of a statistical test to detect differences between groups can be enhanced if the inter-subject variation can be reduced. For example, variations in height and weight are common in gait studies. Three of the best strategies to reduce global inter-subject variation have been demonstrated to exert similar effects by controlling for these variables (Pierrynowski & Galea, 2001). The method of Hof was chosen for these studies (Hof, 1996).

Differences in speed are commonly found in other case-control studies and 'must be considered when comparing biomechanical findings' (Rodgers, 1988 p. 1823). There were also variations in speed between groups in the study. While attempts were made to control for speed *a priori*, technical issues meant that this was not completely successful. Wilson (2012) summarises the pros and cons of each method for dealing with these differences. When these differences are expected (as in osteoarthritis research) the protocol can be designed with this in mind (either looking for differences in natural gait at a self-selected pace (with variations in speed a limitation); or controlling walking pace (at the expense of a natural gait). Wilson (2012) describes a *post hoc* method of statistically controlling for the confounding effects of speed using analysis of covariance (ANCOVA), but warns of its inappropriateness in certain situations. For example, using a covariate that is affected by the main effect would lead to incorrect conclusions. In the case of CECS this should not be an issue as walking speed has never been assumed to be related to the syndrome until symptoms develop. For temporo-spatial data and other variables that do not change during the gait cycle, an ANCOVA was used to control for leg length and speed.

For analysis of data normalised to the gait cycle an ANCOVA was also carried out with speed as a covariate. The ability to rigorously test all of the assumptions of ANCOVA in such a large dataset is unwieldy however. Only the homogeneity of variance assumption could be easily tested: this was carried out using Levene's test and cross-checked using the variance ratio. Importantly, a recent meta-analysis suggests that ANCOVA remains 'quite robust' to most assumption violations when the design is balanced (Harwell, 2003).

4. Study 1: Clinical characteristics of CECS patients

Roberts, A. J., Hulse, D., Bennett, A., & Dixon, S. J. (In review). Clinical characteristics of patients with chronic exertional compartment syndrome.

4.1. Abstract

Background: Chronic exertional compartment syndrome (CECS) is a common problem within both military and athletic populations that can be difficult to diagnose. Furthermore, it is unclear what causes the development of CECS, particularly in the military population, as personnel undertake a variety of activities that can cause pain with CECS such as fast walking, marching and running. The aim of this study was therefore to describe the clinical characteristics of CECS in a large group of military patients; to provide evidence to support diagnosis and to identify activities associated with the development of CECS.

Methods: 93 service personnel with a clinical diagnosis of anterior CECS participated in a questionnaire study. The questionnaire was developed in consultation with experienced clinicians to assess the natural characteristics of the condition. Participant height and weight were also recorded.

Results: Cases typically presented with bilateral (88%) 'tight' (50%) or 'burning' (28%) pain that they identified on pain diagrams as being in the anterior and lateral compartments (39% and 30% of all identifying marks respectively) of the lower leg that occurred within 10 minutes of exercise (modal response). This pain stopped all cases from exercising during marching and/or running. CECS was associated with other neuromuscular symptoms such as paraesthesia, numbness and foot drop in almost two-thirds of cases.

Conclusion: Although there are many papers on the diagnosis and treatment of patients with CECS, few papers have described in detail the natural characteristics of this condition. This study presents data that will aid the clinician in identifying those patients with CECS. In addition, the observation that pain caused a similarly debilitative effect on marching and running suggests that both these activities should be the focus of future biomechanical studies.

4.2. Introduction

Exercise-induced leg pain is a significant problem within athletic and military populations (Sharma et al., 2011; Willems et al., 2006). It accounts for approximately 13% of all military training injuries (DGAMS, 2013). Management of these injuries has both a significant financial cost along with personnel implications, within the military, as a result of medical downgrading or medical discharge (E. Gibson et al., 2005; Hawley, 2007). Chronic exertional compartment syndrome is a common problem with a reported incidence of 14-27% in those with EILP (Qvarfordt, Christenson, Eklof, Ohlin et al., 1983; Styf, 1988). Differential diagnosis of EILP can be challenging (Gaeta et al., 2008); for CECS the diagnosis is typically made with the measurement of intramuscular compartment pressure (IMCP).

Referral of individuals with chronic exertional leg pain for IMCP testing is based on clinical examination of CECS. In some studies, clinical examination alone has been suggested to provide an accurate diagnosis for referral for surgery (Ali et al., 2013; Orlin et al., 2013; van den Brand et al., 2005). In fact, orthopaedic surgeons that have been in practice longer and seen more patients with suspected CECS are more likely to recommend surgical treatment based on a clinical diagnosis alone (Cruz & Laidlaw, 2015). Since the publication of two systematic reviews criticising the validity of the diagnosis using IMCP (Aweid et al., 2012; Roberts & Franklyn-Miller, 2012) reliance on the clinical diagnosis is likely to have become more prevalent. It is therefore essential that the clinical characteristics of this group of patients are well understood. While the demographics of patients with CECS have been presented (Davis et al., 2013), the clinical characteristics of patients with CECS have never been formally investigated.

Chronic exertional compartment syndrome typically only causes pain during specific athletic activities such as running (Detmer et al., 1985), race walking (Sanzen et al., 1986), skating (Garcia-Mata et al., 2001) or cross-country skiing (Lawson et al., 1992). These activities are therefore often ascribed as the causative factor in the development of the syndrome. In the military population, personnel undertake a variety of activities that can cause pain with CECS such as fast walking, marching and running. It has been reported that 86% of military personnel with CECS have pain during marching and 61% during running

(2004); although it is not clear whether both these activities result in the termination of exercise. It is therefore not clear which military activities may be responsible for the development of CECS.

The aim of this study was to describe the clinical and anthropometric characteristics of anterior CECS in a large cohort of military patients to provide evidence to support diagnosis and to identify activities associated with the development of CECS.

4.3. Methods

The Headley Exertional Leg Pain 8 item questionnaire (HELP-8) (Appendix A: Headley Exertional Leg Pain Questionnaire) was developed in consultation with the clinicians at the Defence Medical Rehabilitation Centre who have a unique exposure to high volumes of exercise-induced leg pain. From this clinical background the specific questionnaire items were developed. Early pilots were tested as part of clinical outcome evaluation at DMRC and then further refined to create HELP-8. The questionnaire has a Flesch Reading Ease score of 80.3 corresponding to a reading age of between 8 and 9.

93 service personnel (6 female) attending a multidisciplinary injury assessment clinic at a tertiary rehabilitation centre with a diagnosis of anterior CECS participated in a questionnaire study. After assessment by the clinical team (n=1-3), who were blinded to the questionnaire answers, a consensus diagnosis was established from typical symptoms, with clinical examination and MRI excluding other pathologies. This diagnosis required agreement of more than 50% of the clinicians on the most likely diagnosis. The clinicians then estimated the confidence of the diagnosis. Clinical diagnoses were defined as having 'good confidence' if the confidence level was greater than 70%. Height and weight were collected using a stadiometer (SECA) and medical grade scales (SECA) respectively. Ethical approval was granted by the MOD Research Ethics Committee.

Analysis of cases was restricted to those where 'good confidence' was present for the diagnosis. The analysis of the pain diagrams was restricted to those presenting with bilateral pain (89%). The number of crosses in each defined region was compared using the Krukal-Wallis test and Dunn's non-parametric comparison test was used to carry out *post hoc* pairwise comparisons.

4.4. Results

Good confidence was present in 96% (n=89) of CECS diagnoses. The estimated likelihood of CECS ranged from 60% (n=4) to 100% (n=61). In one case, tibial stress fracture was also suspected (likelihood=40%) by the primary clinician; in six cases, medial tibial stress syndrome was also suspected (likelihood=10-40%); and, in 1 case popliteal artery entrapment syndrome was also suspected (likelihood=20%). CECS predominately affected both legs (89%; n=83); it presented 10 times unilaterally (9 right, 1 left). Table 4 shows the distribution of height, body mass and age within this study.

Table 4 Distribution of height, body mass and age

	Male (n=87)	Female (n=6)
Height (m)	1.769(0.066)	1.695(0.106)
Body mass (kg)	88.9(12.2)	85.7(11.1)
BMI	28.4(3.4)	29.6(2.2)
Age (years)	28(5)	27 (6)

The presentation of pain was highly variable (Figure 29-Figure 31). The onset of pain was reported to range from immediately to greater than 10 minutes with the modal answer of 'between 6-10' minutes. The settling of pain symptoms was reported to range from immediately to greater than an hour; with the modal value of 'within 30 minutes'. The return of pain after restarting exercise was reported to range from immediately to greater than 10 minutes with the modal answer 'between 1-2 minutes'.
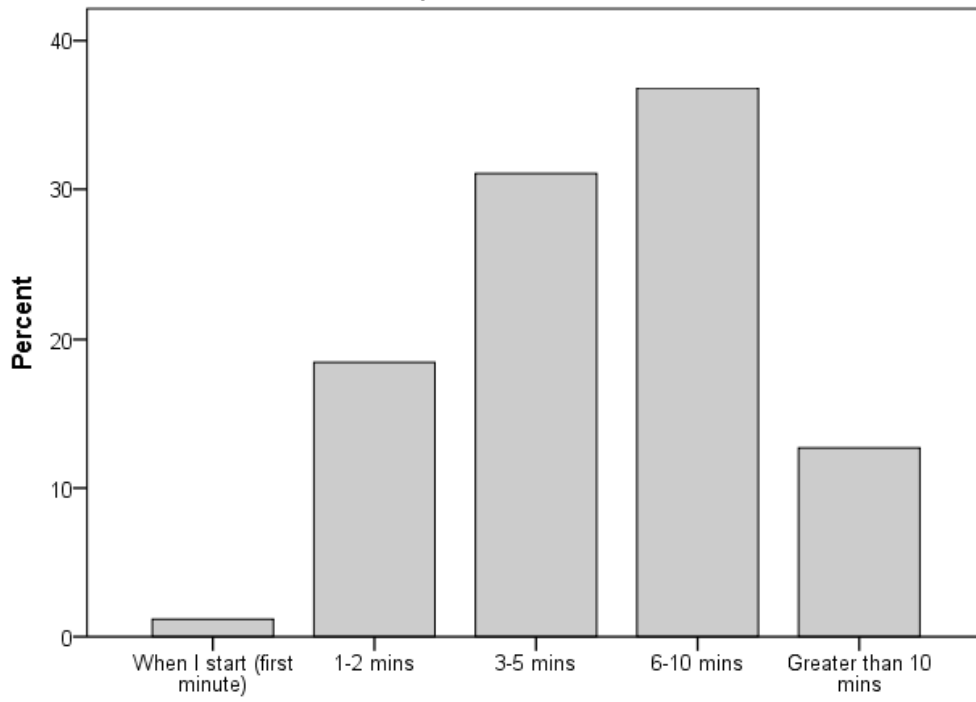
Figure 29 Onset of pain (question 1) percentage frequency distribution
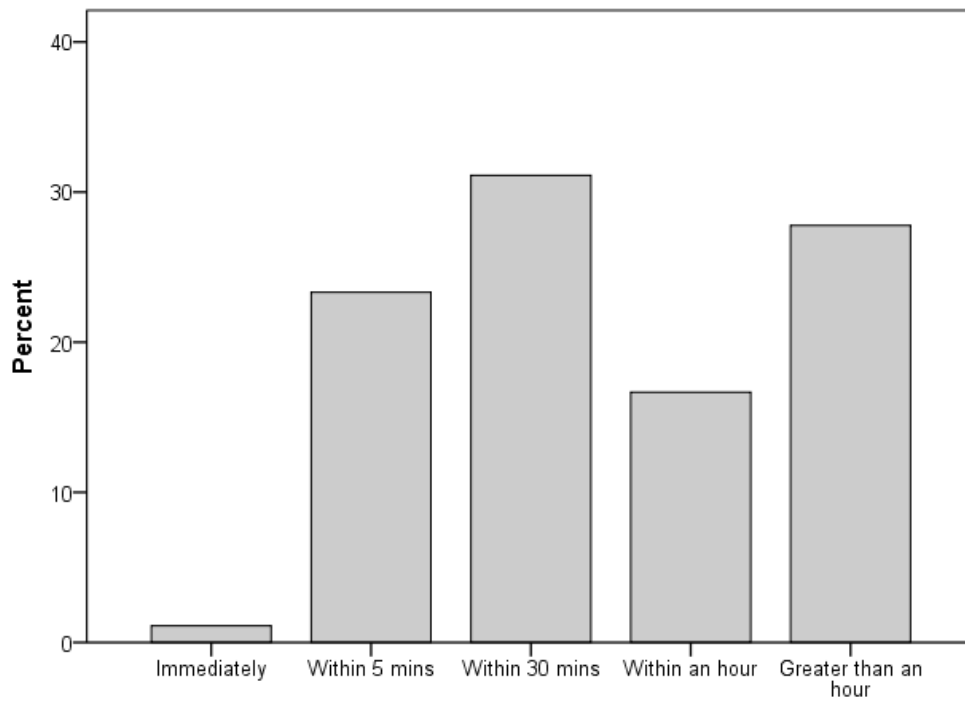
Figure 30 Settling of symptoms (question 2) percentage frequency distribution
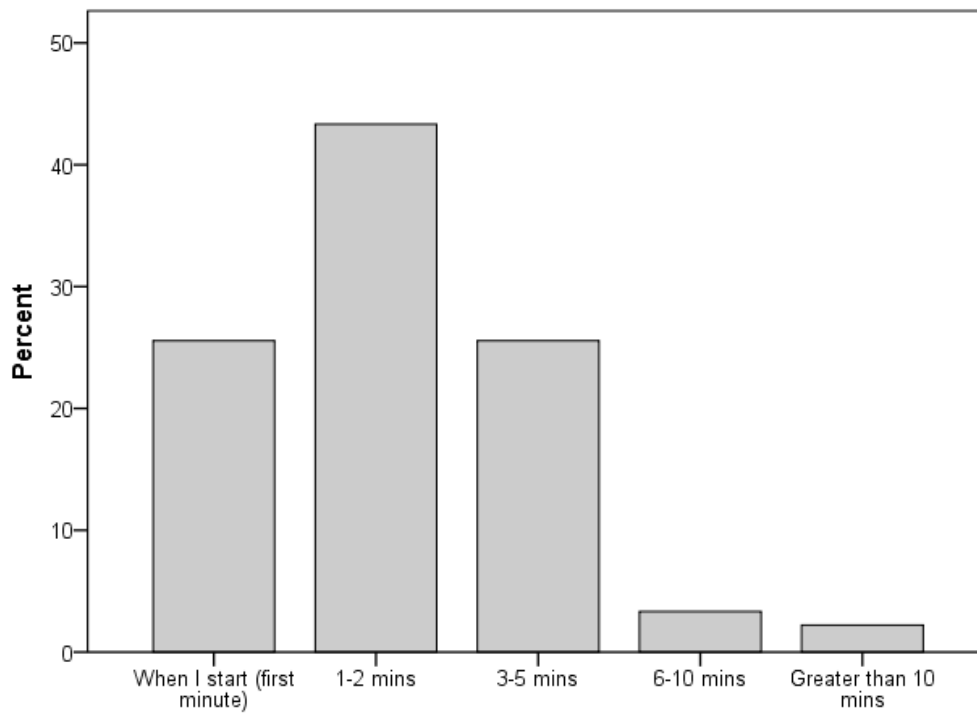
Figure 31 Return of symptoms when recommencing exercise (question 3) percentage frequency distribution

In those with bilateral pain, cases marked significantly more crosses in either the lateral and lateral-tibial zones than any other zone as indicative of where the pain first starts and when the pain is at its worst (Kruskal-Wallis $p<0.001$, Dunn *post hoc* $p≤0.022$). No other differences were apparent; although crosses in the medial tibial and posterior regions accounted for 28% of the total number of crosses (Figure 32).
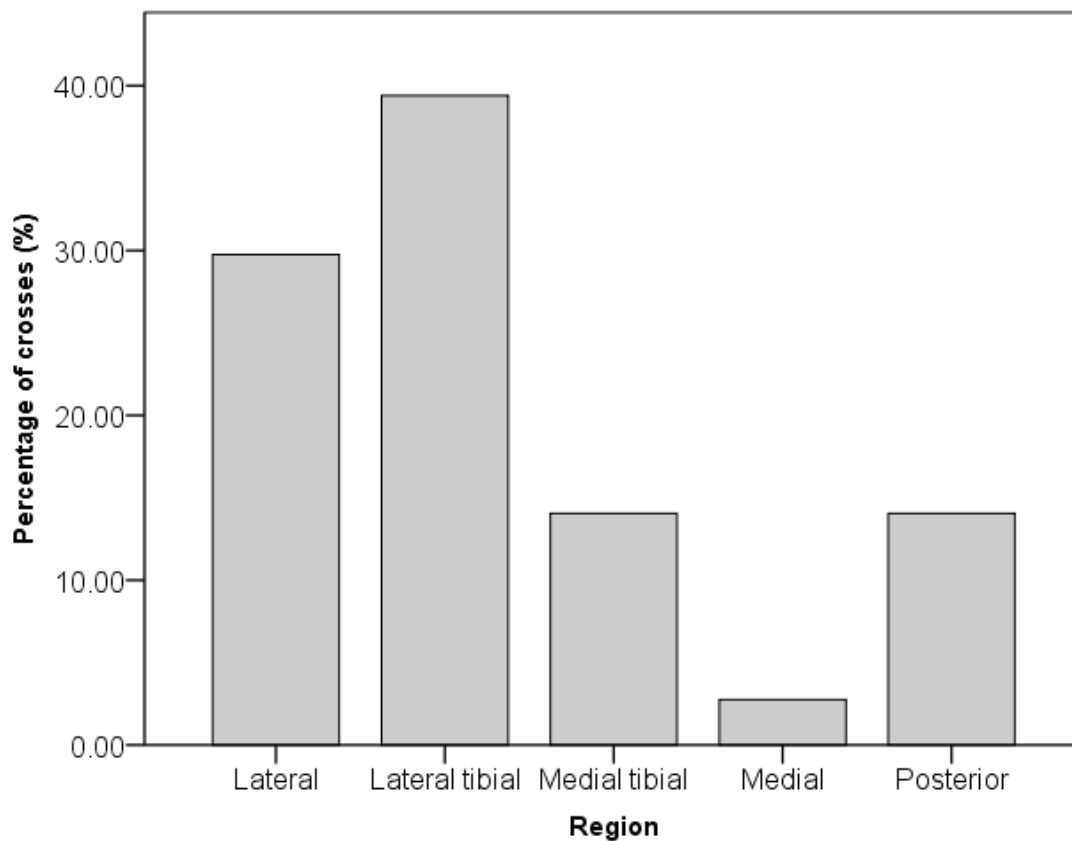
Figure 32 Percentage of crosses placed by cases in the five lower leg regions representing the onset of pain. The left foot only is presented as representative data.

Only 25% of cases described their pain as stopping them from exercising during all activities. Of note, the vast majority (94%) of these cases did not go on to highlight any of the individual activities as stopping them from exercising. Therefore, for the purpose of analysis, these cases were deemed to have selected all subsequent activities as stopping them from exercising. 88% described their pain as stopping them from tabbing or speed marching. 85% described their pain as stopping them from running. 29% described pain stopping them from only one of these activities (Table 5). 58% described their pain as stopping them during impact exercise.

Table 5 Number of cases stopping running or marching due to pain. Brackets indicate adjusted values for those describing pain as stopping them during all activities.

| | | Pain stops cases from tabbing or speed marching | |
		Yes	No
Pain stops cases from running	Yes	41 (67)	15
	No	12	25 (0)

50% reported 'tight' as the term that fits their pain best, with a further 29% reporting a 'burning' sensation. 63% reported experiencing pins and needles in their feet; 45% experienced cramping in their feet; 63% experienced their feet slapping the ground; 30% experienced coldness of feet, with 20% experiencing colour changes; and 41% experienced muscle lumps appearing on their legs.

4.5. Discussion

This study is the first to provide a detailed description of the clinical characteristics of patients with CECS in a military population. While pain presentation was highly variable, 86% of cases experienced the onset of pain within the first 10 minutes of exercise. The results reported here suggest that recommencing exercise then typically brings symptoms on faster than in the fully rested state. The results presented may aid in the referral of individuals with chronic exertional leg pain for IMCP testing. The results may also explain why IMCP between 5 and 10 minutes has been demonstrated to provide improved diagnostic accuracy when compared to other time periods before, during or after exercise (Roscoe et al., 2015).

In agreement with Pedowitz (1990), it was found that CECS patients use a number of terms to describe the pain associated with CECS. The terms 'tightness' or 'burning' were not used by Pedowitz (1990), yet 80% of cases in this study found that these two terms described their pain best. This could potentially be in part due to differences in the location of CECS as only 60% of cases in the earlier study had anterior CECS. Patients describing exertional pain in the anterior compartment with either of these two terms should therefore result in a strong suspicion of CECS.

The identification of similar levels of pain in the lateral and lateral-tibial zones (representing the lateral and anterior compartments respectively) likely explains why both these compartments have been regularly released during operative treatment of anterior CECS (Fronek et al., 1987; Rorabeck, Fowler, & Nott, 1988). However an improved time to return to sports has been reported with just an anterior compartment release prompting the authors to conclude that 'a lateral compartment release is not necessary (Schepsis et al., 1999, p.430). The pain reported in the medial tibial zone may represent locations that were intended by the patient to represent the anterior compartment; or alternatively the presence of pain from other sources such as medial tibial stress syndrome that has been reported in combination with CECS previously (Zimmermann, Helmhout, & Beutler, 2016). Thus pain reported in the lateral compartment is a normal phenomenon and not necessarily an indicator for a lateral release; whereas pain reported in the medial tibial zone should be investigated to rule out other explanations, although could represent a normal presentation.

In the civilian population anterior CECS is most commonly associated with running (Detmer et al., 1985). However in the military population marching is a key component of everyday exercise. Despite this, running has been the focus of biomechanical treatment packages in military populations (Diebal et al., 2011; Diebal et al., 2012; A. R. Gibson, 2013). The results presented here demonstrate that pain is not only present during both these activities but stopped all personnel from exercising during at least one of these activities. Another important finding was that a substantial proportion of cases reported that just one activity, but not the other, would cause them to stop exercising due to pain. These observations suggest that future studies investigating biomechanical characteristics should therefore include the analysis of both marching and running gait in this population.

The finding that marching and running are similarly debilitative is in contrast to those of Verleisdonk (2004), who described a greater proportion of cases reporting pain during marching (86%) than running (61%). These differences may be due to the slight difference in the wording of the questionnaire items (presence of pain vs pain that stops you exercising). It is suggested that future studies should aim to understand any differences in the time of pain onset and subsequent development of pain while carrying out these differing activities.

It has been reported in the literature that, as symptoms progress, paraesthesia and numbness in the deep peroneal distribution, and foot drop or loss of ankle control occur; although the prevalence and magnitude of these issues has not been well documented (Edwards & Myerson, 1996; Gill et al., 2010; Rowdon et al., 2001). The findings presented here suggest that almost two-thirds of patients experience some sort of neuromuscular symptoms. On examination, patients with CECS may have a mild impairment in vibratory sensation in the deep peroneal distribution (Rowdon et al., 2001). No other differences in pre-exercise neuromuscular examinations have been found. Despite this, reduced skin sensation in this distribution using cotton swab and pin prick has been used as part of a diagnostic protocol that excludes IMCP testing (Orlin et al., 2013). While the data presented here helps with the clinical picture, it also suggests that neuromuscular symptoms are unlikely to be suitable candidates for developing a non-invasive diagnosis.

The reports of experiences of cold feet in almost one third of cases are a new finding that has not been linked to CECS previously. This result is surprising as the systolic blood pressure of the hallux is reported to be normal in CECS patients (Qvarfordt, Christenson, Eklof, Ohlin et al., 1983) and foot pulses are reported to be present both before and after exercise (Rowdon et al., 2001) suggesting normal arterial pressure and blood flow within the foot. It is therefore more likely that these experiences could also represent a neurological symptom along with those discussed earlier. Further data in the first instance with a comparative group of controls is required before any firm conclusions can be made.

Cramping of the foot in CECS has been reported previously, but only in deep posterior CECS (Rorabeck et al., 1983) or CECS of the foot (Padhiar et al., 2009). Prior to this study, in anterior CECS, cramping has only been associated with the muscles of the anterior compartment (Orlin et al., 2013; Turnipseed, 2002). The causes of exercise-associated cramps in healthy athletic populations are still unclear despite their high prevalence (Nelson & Churilla, 2016). The explanation for the association of foot cramps with both anterior CECS and deep posterior CECS is therefore also unclear.

The only military study that has reported anthropometrics suggests that CECS patients have a larger BMI and body mass than controls (Birtles et al., 2002).

The results presented here, while lacking a control group, support these findings with male case data demonstrating 3.1 kg higher body mass and 0.7 kg/m^2 higher BMI than those reported in the aforementioned study. The inclusion of 4 females in the earlier study statistics may explain the slight differences in values. The similarity in findings is perhaps not surprising as cases in both studies were recruited from the same rehabilitation centre. It is unclear whether a high body mass and BMI are a result of deconditioning following the development of CECS or a risk factor for the condition itself.

Due to strong evidence that IMCP testing had poor diagnostic validity at the start of this study (Aweid et al., 2012; Roberts & Franklyn-Miller, 2012) the diagnosis of CECS was based on clinical history and not limited to cases that had had IMCP testing. The high level of confidence in diagnosis was therefore reassuring. Recent data has now established that IMCP only has high diagnostic accuracy when it is measured during exercise to the limits of pain tolerance (Roscoe et al., 2015). Future studies would therefore ideally use this new diagnostic method for case selection. This study is also limited with the lack of a comparison group that would enable a better understanding of the questionnaires ability to act as a diagnostic support tool. Nevertheless the results observed provide a useful description of the clinical characteristics of this difficult group of patients that may help clinicians refer patients for IMCP testing and subsequent operative treatment.

In summary this study demonstrates that cases with anterior CECS typically experience 'tightness' or 'burning' pain in the anterior and lateral compartments within 10 minutes of exercise. This is often accompanied by a number of neuromuscular symptoms; although these are unlikely to be able to be used independently for diagnosis. The pain experienced caused all military personnel to stop marching and/or running. In conclusion, the clinical characteristics reported here may improve the ability of clinicians to identify patients with suspected CECS; and given the similar debilitative effect, both ambulatory and running activities should be the focus of future biomechanical studies.

4.6. Progression from Chapter 4 to Chapter 5

Chapter 4 provided the first detailed description of the clinical characteristics of patients with CECS and identified that the condition was aggravated to a similar degree by both ambulatory and running activities. Previous theories have suggested a biomechanical cause for CECS including increased muscle activity and foot pronation (Bates, 1985; Slimmon, Bennell, Brukner, Crossley, & Bell, 2002). In support of these theories, conservative treatment through gait modification has also recently been reported to have promising results (Diebal, Gregory, Alitz, & Gerber, 2011; Diebal et al., 2012; A. R. Gibson, 2013). However there is no empirical evidence of the biomechanical characteristics of cases with CECS. Chapter 5 therefore aimed to investigate plantar pressure variables related to lower limb muscle activity and foot type that may provide insight into this condition.

5. Study 2: Plantar pressure differences between cases with symptoms of chronic exertional compartment syndrome and asymptomatic controls

Roberts, A. J., Hulse, D., Bennett, A., & Dixon, S. J. (In review). Plantar pressure differences between cases with symptoms of chronic exertional compartment syndrome and asymptomatic controls. *Clinical Biomechanics.*

5.1. Abstract

Background: Anterior chronic exertional compartment syndrome of the leg has been hypothesised to develop due to excessive muscle activity and foot pronation. Plantar pressure variables related to lower limb muscle activity and foot type may therefore provide insight into this condition.

Methods: 70 male cases and 70 asymptomatic controls participated. A clinical diagnosis was established from typical symptoms, with clinical examination excluding other pathologies. Plantar pressure variables during walking, hypothesised to be related to foot type, toe extensor activity or had shown predictive validity for general exercise-related lower leg pain, were extracted.

Findings: Cases were shorter in height (mean difference 2.4 cm), had greater body mass (mean difference 4.4 kg) and had reduced ankle dorsiflexion range of motion than controls (mean difference 1.5 cm). Plantar pressure variables indicative of foot-type and toe extensor activity did not differ between groups (P>0.05). The magnitude of medial forefoot loading was the strongest plantar pressure predictor of the presence of chronic exertional compartment syndrome (Odds ratio:0.87, P=0.005). There was also some evidence of greater lateral heel loading at 5% of stance time (P=0.049-0.054).

Interpretation: The lack of association with foot type related and toe extensor activity - related plantar pressure variables suggest that these are not related to the development of chronic exertional compartment syndrome, contrary to earlier hypotheses. The greater lateral to medial loading could theoretically represent increased Tibialis anterior muscle activity at heel strike but a subsequent loss of control as the ankle is lowered. Future studies directly investigating muscle activity and function are now required.

5.2. Introduction

Chronic exertional compartment syndrome (CECS) is an overuse condition presenting as pain in the lower limb. It has been described in numerous compartments of the body, although the anterior compartment of the lower leg is most commonly affected (Reneman, 1975). In up to 98% of cases the condition is bilateral (Reneman, 1975). While the condition is often described as an overuse injury; the mechanism of injury is unclear.

It has also recently been hypothesised to be the underlying cause of pain in CECS rather than a pathological increase in intramuscular compartment pressure (Franklyn-Miller, Roberts et al., 2014; Roberts & Franklyn-Miller, 2012). However, a case-control study has since demonstrated higher resting standing pressures when anterior compartment muscle activity is minimal implying a structural (fascial) aetiology (Roscoe et al., 2015). Nevertheless, excessive anterior compartment muscle activity is still a likely candidate as a risk factor for the development of CECS. Despite this, the function of the anterior compartment musculature during gait has never been investigated in this population.

Plantar pressure measurement provides a method of investigating the impact of both muscle activity and anatomy on the forces applied to the foot. It has previously been demonstrated to be related to lower limb muscle activity (Ferris, Sharkey, Smith, & Matthews, 1995; Morag & Cavanagh, 1999) and foot type (Caravaggi, Giacomozzi, & Leardini, 2014; Cavanagh & Rodgers, 1987; Sánchez-Rodríguez, Martínez-Nova, Escamilla-Martínez, & Pedrera-Zamorano, 2012). Foot type has also been observed to have an effect on Tibialis anterior muscle activity in several studies (Murley et al., 2009). Using plantar pressure, foot type has been directly characterised by the calculation of a dynamic arch index (Cavanagh & Rodgers, 1987). The impulse under all the metatarsals has also been demonstrated to have a strong correlation to two other measures of foot type: medial longitudinal arch range of motion (Caravaggi et al., 2014) and arch height (Teyhen et al., 2009).

Activity of the toe extensor muscles may also be characterised by plantar pressure. Pressure underneath the toes has previously been demonstrated to be affected by simulated flexor hallucis longus and flexor digitorum longus activity (Ferris et al., 1995). It seems reasonable to assume that activity of the

antagonists located in the anterior compartment (extensor hallucis longus and extensor digitorum longus) would have a similar effect (i.e. reduction of toe pressures).

One previous study has investigated plantar pressure in 20 patients with CECS (Roscoe et al., 2016). They observed reductions in stance time and the time from initial foot contact to initial full forefoot contact that may be a result of alterations in anterior compartment activity/function. A greater understanding of foot function related to ankle dorsiflexor and toe extensor activity in this condition is now needed.

This study therefore aimed to compare, in a case-control study, the plantar pressure variables described above that have previously been associated with foot type, toe-extensor activity or had shown predictive validity for all-cause exercise-related lower leg pain (Willems et al., 2006). A secondary aim was to compare the variables investigated by Roscoe et al. (2016) in a larger cohort. It was hypothesised that those plantar pressure variables indicative of: a more pronated foot type, greater toe-extensor activity and the development of all-cause exercise-related lower leg pain would be greater in cases with CECS than healthy controls.

5.3. Methods

70 male cases with symptoms consistent with CECS of the anterior compartment of the leg and 70 asymptomatic controls participated following informed consent. A consensus diagnosis of CECS was established from typical symptoms, with clinical examination excluding other pathologies. Controls were recruited from the British Armed forces. Cases were recruited from two military rehabilitation centres. Ethical approval was granted by the MOD Research Ethics Committee.

Cases required the following: symptoms of exercise-induced leg pain consistent with a diagnosis of anterior compartment CECS; no diagnosis other than CECS more likely; absence of multiple lower limb pathologies; and, no previous lower limb surgery. While intramuscular compartment pressure measurement is considered the gold standard for diagnosis (Roscoe et al., 2015); clinical examination alone has been suggested to provide an accurate diagnosis for referral for surgery (Ali et al., 2013; Orlin et al., 2013; van den Brand et al.,

2005). As pressure measurement was not available for this study, a clinical diagnosis was used. Controls were included when they had no history of musculoskeletal leg pain in the previous 12 months; and no current pain at any site, including during exercise activities.

Participants completed the Short Pain Inventory that measures both current physical pain and the emotional consequences of pain (Kilminster & Mould, 2002). Participant age, height (stadiometer; SECA, Birmingham, UK)) and body mass (medical grade scales; SECA, Birmingham, UK) were recorded. A weight-bearing dorsiflexion device (Jones, Carter, Moore, & Wills, 2005) was used to measure the anterior-posterior distance between the knee and the hallux during a weight-bearing lunge; anatomical parameters that could influence this distance were therefore also recorded (UK shoe size/lower leg length (tibial tuberosity to lateral malleolus)).

5.3.1. Plantar pressure measurement and data extraction

Participants were asked to walk over a 2 m x 0.4 m x 0.02 m pressure plate (RSScan International, Olen, Belgium) fitted flush to the floor of the laboratory; and were free to choose the order of foot placement. Participants completed a dynamic calibration and familiarisation traverses of the laboratory. Data was then collected at a natural, relaxed, self-selected walking velocity until a minimum of 3 valid foot contacts for both left and right feet had been captured at 125 Hz (De Cock, Willems, Witvrouw, Vanrenterghem, & De Clercq, 2006). Each foot was automatically divided into 10 zones (Hallux (T1), lesser toes, metatarsals 1-5 (M1,M2,M3,M4,M5), midfoot, medial/lateral heel (HM/HL)) by Footscan® (v7.97, RSScan International) software; these were used to calculate all loading-related variables. Data was extracted from Footscan® using the default exports. These data were then processed within Scilab (v5.3.2; INRIA, France) to generate mean values of each plantar pressure variable described below for left and right feet.

5.3.1.1. Primary variables

1. Arch index
2. Impulse under all the metatarsal zones
3. Toe contact area at mid-stance
4. Peak force and impulse under the hallux

5. Peak force and impulse under the lesser toes

6. Medio-lateral centre of force (COF) position at last foot contact

7. Antero-posterior COF position at initial foot contact

8. Medio-lateral pressure ratio during forefoot contact phase (initial metatarsal contact to first instant all metatarsals make contact)
   a. $[(HM+M1+M2)-(HL+M4+M5)]/(HM+HL+M1+M2+M3+M4+M5+T1)$

Primary variables 1-2, 3-5 and 6-8 are indicative of foot type, greater toe-extensor activity and the development of all-cause exercise-related lower leg pain respectively.

5.3.1.2. Secondary variables

1. Stance time

2. Foot progression angle

3. Mean medial-lateral displacement of COF during stance

4. Time from initial foot contact to initial full forefoot contact

5. Medial-lateral distribution of pressure under the heel at at initial foot contact, 5% of stance time and time of initial full forefoot contact
   a. $HM/(HM+HL)$

6. Mean ratio between 1st and 5th metatarsal loading during stance
   a. $[(M1-M5)/((M1+M5)/2)]*100$

5.3.2. Statistical analysis

Bootstrapped t-tests were carried out on all variables using the bias-corrected and accelerated method (Efron, 1987). Significant variables were then entered into a forward stepwise multinomial logistic regression model. The statistic (Likelihood ratio, Wald statistic, and conditional statistic) used in the test for variable inclusion did not affect the variables in the final model. Means and 95% CIs are reported unless otherwise stated. SPSS (v21; SPSS Inc, USA) was used for all analyses with alpha set to 0.05.

5.4. Results

Cases reported relatively low levels of pain (mean severity score 0.66 out of 4) at rest although significantly more than controls (t=5.09, P=0.001). This was accompanied with reports of significantly greater sadness (mean difference in z-score=0.53, t=2.53, P=0.016) and anxiety (mean difference in z score=0.49,

t=2.21, *P*=0.028) than cases. Pain was not reported to be aggravated by cases or controls during testing demonstrating that sufficient rest was provided between each traverse.

Cases (28(5) years) were marginally younger than controls (32(6) years). Cases (1.759(6.8) m) were 2.4 cm shorter than controls (1.783(7.3) m) although this was marginally higher than the accepted level of significance (P=0.051). Cases (85.8(12.3) kg) were 4.4 kg heavier (P=0.026) than controls (81.4(10.4) kg). Weight-bearing dorsiflexion range of motion was significantly lower (95% CI of difference [-26.7,-3.5], *P*=0.012, Cohens d=0.4) in cases (113(40) mm) than controls (128(30) mm). There were no differences (*P*>0.3) in shoe size (cases 9.0(1.3) vs controls 9.2(1.4)) or lower leg length (cases 35.8(2.1) cm vs controls 36.2(2.5) cm).

The primary analysis did not find any significant differences for any of the plantar pressure variables (Table 6). The secondary analysis demonstrated significantly greater medial forefoot loading (*P*=0.019-0.020); and borderline significantly greater lateral heel loading at 5% of stance time (*P*=0.049-0.054) and greater overall medial COF (*P*=0.013-0.086) in cases. The results of the primary analysis suggest that the differences observed in the medial-lateral COF normalise by last foot contact. No other significant differences were observed (Table 7).

Table 6 Differences between cases and controls in the primary analysis . 95% CIs and p-values are bootstrapped. Degrees of freedom = 138 for all plantar pressure variables.

Variable	Mean difference (95% CI)	T-value	*P*-value
Weight-bearing dorsiflexion range of motion (mm)	-15.0 (-26.7,-3.5)	-2.52	0.012
Arch index	0.0015 (-0.0153,0.016)	0.184	0.835
Impulse: metatarsal zones (Ns)	6.71 (-15.3,27.8)	0.653	0.533
Toe contact area at midstance (as percentage of toe contact area during stance phase)	1.29 (-1.29,3.9)	0.964	0.346
Peak force: hallux zone (N)	11.8067 (-14.7578,38.7605)	0.851	0.418
Peak force: lesser toes (N)	-4.2064 (-12.1415,3.4802)	-1.056	0.297
Impulse: hallux zone (Ns)	3.99 (-0.74,8.94)	1.579	0.125
Impulse: lesser toes (Ns)	-0.67 (-2.13,0.58)	-0.984	0.345
Medio-lateral centre of force position at last foot contact (mm)	-0.0069 (-0.0372,0.0264)	-0.413	0.682
Antero-posterior centre of force position at initial foot contact (mm)	-0.0012 (-0.0053,0.0035)	-0.488	0.645
Medio-lateral pressure ratio during forefoot contact phase	-0.0908 (-3.3108,2.9767)	-0.062	0.947

Table 7 Differences between cases and controls in the secondary analysis . 95% CIs and p-values are bootstrapped. Degrees of freedom = 138 for all plantar pressure variables.

Variable	Mean difference (95% CI)	T-value	*P*-value
Stance time (ms)	0.08(-0.06,0.21)	1.17	0.27
Foot progression angle (°)	-0.63(-2.90,1.33)	-0.63	0.54
Mean medial-lateral displacement of COF during stance (mm)	0.74(-0.05,1.51)	1.85	0.09
Time from initial foot contact to initial full forefoot contact (IFFC; ms)	8.32(-6.24,23.2)	1.41	0.15
Medial-lateral heel pressure at initial foot contact	-0.02(-0.04,0.005)	-1.65	0.11
Medial-lateral heel pressure at 5% of stance time	-0.02(-0.04,0.0006)	-2.08	0.054
Medial-lateral heel pressure at time of IFFC	-0.01(-0.03,0.001)	-1.96	0.058
Overall medial-lateral forefoot loading	1.92(0.37,3.49)	2.50	0.02

Logistic regression demonstrated that height, mass and medial-lateral forefoot loading were the best predictors of group membership. No other variables added any further predictive value and were not entered into the logistic regression model (Table 8). The goodness-of-fit test indicated that the logistic regression model does not misrepresent the data (*P*=0.967).

Table 8 Logistic regression analysis results [a]

Predictor[b]	Regression Coefficient (SE)	Wald Statistic	Odds Ratio	*P*-value
Height	0.150	14.4	1.16	<0.001
Mass	-0.105	18.3	0.900	<0.001
Overall medial-lateral forefoot loading	-0.136	7.82	0.873	0.005
Intercept[c]	-17.9	9.63	<0.001	0.002

[a]Pseudo R^2 = 0.223-0.298, [b]For each predictor, df=1, [c]The constant in the model representing the log odds when all predictors are 0

5.5. Discussion

In this study, it was investigated whether anthropometry, ankle range of motion and plantar pressure variables differ between cases and controls. The results show that cases appear to be shorter in height with a greater body mass and reduced ankle dorsiflexion range of motion. There were no differences in the plantar pressure variables chosen as indicative of foot type and toe extensor activity; but differences in the medial-lateral distribution of pressure under the heel and forefoot were apparent.

The identification of small stature as a risk factor for the development of CECS supports previous findings for military patients (Roscoe et al., 2015) strengthening the evidence for this measure. This larger study does however suggest that the effect size may be smaller than originally thought. Shorter stature may result in an increased stride length during marching that could cause an increased demand on Tibialis anterior and subsequent development of CECS (Roberts, Roscoe, Hulse, Bennett, & Dixon, 2016b).

Two military studies have also observed greater body mass in cases (Birtles et al., 2002; Roberts, Roscoe, Hulse, Bennett, & Dixon, 2016a). Small effect sizes that were not statistically significant have also been observed in two additional studies (Rorabeck et al., 1988; Varelas et al., 1993). It is unclear whether this is

a result of deconditioning following the development of CECS or a risk factor for the condition itself.

Controls demonstrated similar ankle dorsiflexion range of motion values to those previously published (Bennell et al., 1998). Previous studies have reported that long distance runners have tighter plantarflexors and hamstrings than untrained individuals (Kubo et al., 2015; S. S. Wang, Whitney, Burdett, & Janosky, 1993). Similarly, tendon stiffness is increased by resistance training (Kubo, Kanehisa, & Fukunaga, 2002). A greater body mass index is also associated with decreased joint mobility (Soucie et al., 2011). The finding presented here may therefore be a reflection of greater usage of the plantarflexors in this population due to the greater body mass and reduced stature, necessitating a relatively longer stride (Roberts, Roscoe, Hulse, Bennett, & Dixon, 2016b), of cases. Alternatively this finding could be theorised to result in increased anterior compartment activity during swing phase due to the resistance of the flexors. Further research is required to confirm this.

The results suggest that foot type is not related to the development of CECS. This is surprising given that Tibialis anterior muscle activity is modulated by foot type, and over-activity of this muscle is proposed to be key to the development of CECS (Tweed & Barnes, 2008). These results may help explain the poor efficacy of conservative treatment such as the provision of foot orthoses (Fronek et al., 1987; Martens et al., 1984; Sebik & Dogan, 2008; Wiley et al., 1987). Alternatively, it is possible that the differences in medial-lateral foot pressure observed could represent differences in foot type. However, both medial and lateral heel forces (peak and mean) and impulse are positively correlated with arch height (Teyhen et al., 2009). Similar results were also reported at the forefoot, although the strength of the correlation appeared to be lower in the medial regions; however it is not clear if the slope of the regression lines follw the same pattern. Direct measurement of foot type to confirm these findings is warranted in future studies in this population.

To the author's knowledge, no previous studies have quantified toe extension during gait in a healthy population. The results presented here suggest that some toe extension at mid-stance is a normal occurrence. This is evidenced by the observation that only 10% of all the sensors identified as being under the toes were active at mid-stance in both groups. Clinical observations of

'persistent toe extension at mid-stance' have previously been described in patients with CECS (Franklyn-Miller, Roberts et al., 2014). However the findings presented here do not suggest that there is over-activity of these muscles during stance.

The variables previously identified as predictive of all-cause exercise-related lower leg pain (Willems et al., 2006) did not differ between cases and controls. This emphasises the need to identify gait-related risk factors for individual conditions, injury locations and populations. The risk factors identified by Willems (2006) are therefore likely to be most predictive of the most common injury observed. Unfortunately the injury distribution was not reported for the Willems (2006) study; although the focus on medial tibial stress syndrome in the discussion suggests that CECS may not have been the primary diagnosis. An automatic zoning method was also used that resulted in larger zones than the semi-automatic identification method used by Willems (2006) that may contribute to the difference in results.

The secondary analysis found differences in variables that had not been identified in the earlier smaller study of plantar pressure in this population (Roscoe et al., 2016). The results presented here provide some evidence that patients with CECS walk with greater lateral pressure under the heel and stronger evidence that this is followed by greater medial pressure under the forefoot, although this is not associated with variables indicative of a more pronated foot type. It is suggested that these differences were not identified in the earlier study due to the lower sample size. The differences observed in this study may be due to differences in Tibialis anterior activity and function. For example, a medial shift in heel loading at initial contact has been simulated when the force output of Tibialis anterior is reduced (Gefen, 2001). The greater lateral heel loading at the beginning of stance in cases may therefore be due to increased Tibialis anterior activity. The greater transfer of forces medially however may indicate that the subsequent control of ankle movement is impaired.Direct observations of the activity and function of Tibialis anterior are required to confirm this hypothesis.

The study design is limited in its ability to distinguish between cause and effect of injury; the findings would therefore ideally be confirmed in a further longitudinal study. It is not possible to rule out the possibility that the age

differences observed could also reflect a longer exposure to military tasks such as marching that may have influenced the results. There is no evidence of age-related differences in plantar pressure variables and whereas range of motion is more likely to be reduced in the older group than the younger cohort found here (Vandervoort et al., 1992). Diagnosis of CECS was based on a clear clinical history rather than IMCP measurement due to strong evidence that IMCP testing had poor diagnostic validity at the start of this study (Roberts & Franklyn-Miller, 2012). The relatively low pain levels at rest observed are in agreement with the typical description of CECS as a type of exercise-induced leg pain (Willems et al., 2006). Recently published data now demonstrates that the diagnosis can only be made accurately using IMCP when it is measured during exercise to the limits of pain tolerance (Roscoe et al., 2015). Future studies would therefore ideally use this new diagnostic method for case selection.

In summary, this study demonstrates differences in anthropometry and joint mobility that provide evidence that small stature may be a key risk factor for the development of CECS in this population. The lack of association with plantar pressure variables indicative of foot type, toe extensor activity and the development of all-cause exercise-related lower leg pain suggest that these are not related to the development of CECS, contrary to earlier hypotheses. Having established these differences for walking, future studies should expand their investigation to marching and running gait. These studies should directly investigate the kinematic and kinetic characteristics and the associated lower limb muscle activity that may be responsible for the development of CECS.

5.6. Progression from Chapter 5 to Chapter 6

Chapter 5 identified that plantar pressure variables related to anterior compartment muscle activity, foot type and the development of all-cause exercise induced leg pain were not associated with CECS during walking. However, plantar pressure does not provide a full biomechanical picture as it is limited to forces at the foot. Furthermore, the results reported in Chapter 4 also demonstrate the need to investigate the biomechanics of CECS during other aggravating activities. Chapter 6 therefore aimed to investigate the kinematic and kinetic characteristics of cases with CECS during both walking and marching.

6. Study 3 (Part 1): Biomechanical differences between cases with CECS and asymptomatic controls during walking and marching

6.1. Abstract

Chronic exertional compartment syndrome is a significant problem in military populations that may be caused by specific military activities. This study aimed to investigate the kinematic and kinetic differences in military cases with chronic exertional compartment syndrome and asymptomatic controls.

20 males with symptoms of chronic exertional compartment syndrome of the anterior compartment and 20 asymptomatic controls were studied. Three-dimensional lower limb kinematics and kinetics were compared during walking and marching.

Cases were significantly shorter in stature and took a relatively longer stride in relation to leg length than controls. All kinematic differences identified were at the ankle. Cases demonstrated increased ankle plantarflexion from mid-stance to toe-off. Cases also demonstrated less ankle inversion at the end of stance and early swing phases. Lower ankle inversion moments were observed during mid-stance.

The anthropometric and biomechanical differences demonstrated provide a plausible mechanism for the development of chronic exertional compartment syndrome in this population. The shorter stature in combination with the relatively longer stride length observed may result in an increased demand on the anterior compartment musculature during ambulation. This difference is proposed to be a result of the requirement to achieve a required speed and cadence for group marches. The results of this study, together with clinical insights and the literature suggest that ambulating near to or above the walk-to-run transition speed during group marches may play a significant role in the development of chronic exertional compartment syndrome within a military

population. The differences in joint angles and moments also suggest an impairment of the muscular control of ankle joint function, such as a reduced effectiveness of tibialis anterior. It is unclear whether this is a cause or consequence of chronic exertional compartment syndrome.

6.2. Introduction

Chronic exertional compartment syndrome of the leg was first described in 1956 (Mavor). It is an overuse condition presenting as pain in the lower limb, associated with the muscles contained within the myofascial compartments of the shank. The anterior compartment is most frequently affected (Reneman, 1975). While numerous studies have attempted to understand the pathophysiology of CECS (Barbour et al., 2004; Evers et al., 1997; Hurschler et al., 1994; Turnipseed et al., 1995), few studies have identified potential risk factors. Chronic exertional compartment syndrome poses a significant clinical burden in the military making this population suitable for investigating these potential factors (Waterman et al., 2013).

The North Atlantic Treaty Organization (NATO) recently identified walking and marching as key common tasks performed in recent and current military missions (Jaenen, 2009). As such these activities are also commonly performed during military training. These tasks have also previously been associated with CECS (de Fijter et al., 2006; Trease et al., 2001; Waterman et al., 2013). The exact definition of a march varies; however it typically requires a fast walking gait with a set stride length and cadence to allow the movement of a group of individuals at a set pace. Personnel often undertake organised group marches that prepare them for deployment and the completion of the annual fitness tests that, for example in the Army and Royal Marines, require 2-3 hours of marching at 1.8 m/s (Ministry of Defence, 2015a; Ministry of Defence, 2015b). A large proportion of military training also involves walking between other planned activities (Trank, Ryman, Minagawa, Trone, & Shaffer, 2001; Wilkinson, Rayson, & Bilzon, 2008).

Chronic exertional compartment syndrome has been defined as a condition where elevated intramuscular compartment pressure (IMCP) during exercise impedes local blood flow leading to ischaemia and impaired neuromuscular function within the compartment (Styf, Korner et al., 1987; Zhang, Jonasson, &

Styf, 2011). Intramuscular compartment pressure can be increased through changes in compartment compliance, compartment fluid content or muscle activity (Hile et al., 2006; Sporrong & Styf, 1999a; Turnipseed et al., 1995). However there has been only limited investigation into these factors within CECS.

Biomechanical factors related to muscle activity have been considered to play a role in the development of CECS for a long time (Bates, 1985; Franklyn-Miller, Roberts et al., 2014); however these have never been directly studied. The aim of this study therefore was to examine potential biomechanical differences during walking and marching between cases and controls to provide evidence regarding the role of biomechanical factors in the aetiology of this condition. The anterior compartment musculature is responsible for movements at the ankle; these angles and moments were therefore of prime interest. As this was the first study to examine the biomechanics of CECS patients the angular and moment data of joints further up the kinetic chain was also explored. These more proximal joints have also been the subject of recent biomechanical interventions for CECS (Diebal et al., 2012; Franklyn-Miller, Roberts et al., 2014; Helmhout et al., 2015). Based on these studies it was hypothesised that cases would demonstrate increased ankle dorsiflexion around heel strike, associated with an increased ankle dorsiflexion moment, with no differences further up the kinetic chain.

6.3. Methods

20 male cases (PT) with symptoms consistent with CECS of the anterior compartment of the leg and 20 asymptomatic controls (CON) participated following informed consent. The diagnosis of CECS was established from typical symptoms, with clinical examination and MRI excluding other pathologies. All participants were recruited from the UK armed forces with significant experience of marching. Cases were recruited from the Lower Limb Pain clinic at the Defence Medical Rehabiltation Centre. Ethical approval was granted by the MOD Research Ethics Committee.

The inclusion criteria were: Male; Aged 18-40 (representing the typical age-range of UK military service personnel); BMI<35; and, no true leg length discrepancy >2 cm. Cases required the following: symptoms of exercise-

induced leg pain consistent with a diagnosis of anterior compartment CECS; a negative MRI of the affected limb(s) and lumbar spine; no diagnosis other than CECS more likely; absence of multiple lower limb pathologies; and, no previous lower limb surgery. Cases had higher IMCP than controls (114±32 mmHg vs 68.7±22 mmHg) and reported pain (scale: 0-10) in the anterior compartment of 5.1±2.6 within 10 minutes of loaded marching as previously reported (Roscoe et al., 2015). Controls were included when they were able to run for a minimum of 20 minutes and had: no lower limb pain in the previous 12 months; no current pain at any site, including during exercise activities; and no reliance on orthotics.

Measurements of leg length, height and body mass were performed using a tape measure, stadiometer (SECA, UK) and medical grade scales (SECA, UK) respectively. The same operator, using the same landmarks and techniques assessed all subjects.

6.3.1. Motion capture

Fifteen body segments (feet, shank, thigh, pelvis, trunk, head, upper arm, forearm and hand) were defined using retro-reflective markers placed on specific anatomical landmarks by the same operator. The head, upper arm, forearm and hand were not analysed as part of this study. Data were collected using a 10 camera (4xT160, 4xT40-S, 2xT10) 3D motion analysis system (Vicon MX system, Oxford Metrics Ltd., Oxford, England) at a sampling frequency of 120 Hz. Ground reaction forces were collected using three force plates (AMTI, OR-6, USA) at a sampling frequency of 1200 Hz.

Following a static calibration trial, participants performed traverses of the laboratory while walking and marching until a minimum of 10 complete cycles for each leg had been captured (Monaghan, Delahunt, & Caulfield, 2007). Following familiarisation, participants were asked to walk at their natural pace (expected speed c.1.4 m/s) and march 'as if they were doing their military fitness test' (expected speed c.1.8 m/s). They were then asked to adjust their speed between trials if they were outside (±0.1 m/s) of the expected pace.

Shod and barefoot trials were captured resulting in a total of 4 conditions: walk and march; and, shod and barefoot. Participants wore military issue training shoes (Silver Shadow, Hi-Tec™) for collection of shod trials over the force

plates. Training shoes were chosen for testing over military boots primarily to allow direct marker placement on the ankle malleoli. Participants were discouraged from targeting the force plates. A recorded trial was deemed suitable if it had minimal marker dropout, full clean contact of the foot within the boundary of the force plates (minimum 5 clean strikes for each side) and no major gait inconsistency on the part of the subject as judged by an observer, e.g. stopping or stumbling.

The pelvis and thigh segments were defined according to Wu (2002), the shank segments were defined according to Peters (2009) and tracked using the marker cluster recommended by Manal (2000), the foot segments were a modified version of the foot flat option defined according to Pratt (2012). The thorax was defined according to Gutierrez (Gutierrez et al., 2003). An additional foot segment was created for the calculation of joint moments based on a modified Helen Hayes set (Kadaba et al., 1990). This segment is considered better suited for inverse dynamics calculations as it follows the dissection positions of Dempster (1955). It is defined with the proximal point at the ankle joint centre and removes the foot flat offset used in the kinematic foot. Internal moments were calculated for each lower limb joint.

6.3.2. Data processing and statistical analysis

Gaps smaller than 14 frames in the raw marker data were interpolated using a 3rd order least squares fit (Howarth & Callaghan, 2010). In the case of larger gaps the whole segment was excluded from analysis at these time points. The marker data was then filtered using a 6 Hz low pass bidirectional Butterworth filter (Winter et al., 1974). Force plate data were filtered using a 50 Hz low pass Butterworth filter (Roewer et al., 2014). Gait data were normalised to body size as recommended by Hof (1996) and Pierrynowski (Pierrynowski & Galea, 2001) (Table 9).

Table 9 Normalisation of gait parameters . Symbols: l_0, leg length; m, body mass; g, acceleration due to gravity (9.81 m/s^2).

Quantity	Dimensionless number
Length, distance (l)	$\dfrac{l}{l_0}$
Time (t)	$\dfrac{t}{\sqrt{l_0/g}}$
Force (F)	$\dfrac{F}{mg}$
Moment (M)	$\dfrac{M}{mgl_0}$

Kinematic and kinetic data were normalized to 100% of the gait cycle and stance phase respectively. This resulted in 101 individual time points for each movement plane where heel strike (HS) occurs at time points 0 and 100. Bootstrapped t-tests on each individual normalised time point were carried out to identify regions within the gait cycle that were significantly different (Lenhoff et al., 1999). Joint (segment-segment) and segment-lab angles were analysed independently. Reference values for peak joint angles, and time to peak for sagittal lower limb angles are presented as supplementary data in Appendix B.

An attempt was made to control for speed a priori, however technical failure of light gates meant that this was not completely successful. Consequently, speeds were higher and more variable between participants than intended. Military training typically involves walking and marching at a fixed pace. ANCOVA was therefore used to control for speed in the temporal-spatial data. Multiple ANCOVAs were also carried out to cross-check that controlling for the variations in speed would not alter the interpretation of the original analysis of gait curves. Alpha for all analyses was set to 0.05. SPSS (v18; SPSS Inc, USA) and Matlab (v2014a; MathWorks, USA) were used for all analyses.

6.4. Results

Cases ranged in age between 21-40 years (mean=27.5 years, sd=4.9 years); controls between 19-40 years (mean=28.3 years, sd=7.4 years).

No pain was reported by cases or controls during testing demonstrating sufficient rest was provided between traverses.

Cases (mean height 1.71 m; sd 0.13) were significantly shorter (p=0.002) than controls (1.81 m; 0.06) although there were no differences in weight or height-to-leg length ratio.

6.4.1. Kinematics

The mean (sd) speed was 1.8 (0.2) m/s for walking and 2.1 (0.2) m/s for marching. There were no differences in normalised step time, stance time or swing time. A significantly longer stride length (relative to leg length) was observed for cases in the shod condition only (Table 10).

Table 10. Comparison of differences in temporal-spatial data between groups (*P<0.05). Differences for the left-side only are presented as there were no differences between left and right-sided data. N.b. All variables are normalised according to Hof and therefore do not have units. BF=Barefoot.

Hof-normalised variable	BF/ SHOD	Condition	F	P	Mean (CON)	SE (CON)	Mean (PT)	SE (PT)	Mean Diff
Stride Length	BF	Walk	1.6	0.22	1.76	0.02	1.80	0.02	0.042
		March	2.7	0.11	1.90	0.03	1.96	0.03	0.063
	SHOD	Walk	6.6	0.01*	1.79	0.02	1.86	0.03	0.068
		March	4.3	0.05*	2.00	0.03	2.08	0.03	0.076
Step time	BF	Walk	0.06	0.80	1.52	0.01	1.51	0.01	0.005
		March	0.01	0.91	1.40	0.02	1.39	0.02	0.002
	SHOD	Walk	0.03	0.88	1.61	0.01	1.61	0.01	0.003
		March	0.01	0.93	1.46	0.02	1.46	0.02	0.002
Stance time	BF	Walk	1.42	0.24	1.78	0.02	1.75	0.02	0.027
		March	3.02	0.09	1.60	0.02	1.56	0.02	0.040
	SHOD	Walk	0.34	0.56	1.96	0.02	1.95	0.02	0.013
		March	0.48	0.49	1.72	0.02	1.71	0.02	0.016
Swing time	BF	Walk	0.23	0.64	1.26	0.02	1.27	0.02	0.011
		March	0.72	0.40	1.20	0.02	1.22	0.02	0.024
	SHOD	Walk	1.69	0.20	1.25	0.02	1.28	0.02	0.028
		March	0.54	0.47	1.20	0.02	1.21	0.02	0.020

Toe-off occurred between 58-60% of the gait cycle for both the walking and marching conditions. The position of toe-off is therefore marked at 59% on all

gait curves. Each kinematic and kinetic variable is presented graphically highlighting regions of data that differ significantly (p<0.05) between the two groups.

Significantly greater ankle plantarflexion was measured in cases from mid-stance to toe-off with a maximum difference of 6.3° at 55% of the gait cycle (Table 11 and Table 12). When the effect of speed was controlled for (using the ANCOVA) the difference observed was less but the relationship to the gait cycle described above remained. Ankle flexion total range of motion ranged from 24°-26° in controls and 25°-29° in cases.

Table 11. Angular measurements from bootstrapped t-test data of maximal significant differences between controls and cases (Left shod-marching).

Joint	Movement (% of gait cycle)	Mean (sd) angle (°)		Difference (°)
		Control	Cases	
Ankle	Inversion (64%)	6.5 (3.1)	2.7 (4.8)	-3.8
Ankle	Plantarflexion (55%)	1.6 (6.8)	-4.7 (5.9)	+6.3

Significantly less ankle inversion was observed in cases at the end of stance and beginning of swing with a maximum difference of 3.8° at 64% of the gait cycle. This consistent difference persisted, after statistical control for the effect of speed, for almost 10% of the gait cycle. A summary of the significant differences for kinematic data is presented in Table 12.

Table 12. Time points of significant differences in angular and moment data (all conditions).

Joint	Movement	Angle/Moment	Bootstrapped t-test (%)	ANCOVA (%)	Direction of effect
Ankle	Inversion	Angle	63-70	62-69	CON>PT
Ankle	Plantarflexion	Angle	55-57	-	PT>CON
Ankle	Inversion	Moment	34-67	37-65	CON>PT
Ankle	Dorsiflexion	Moment	6-13, 51-61	9-10, 59-61	PT>CON
Hip	Abduction	Moment	19	31-39, 92-94	CON>PT
Knee	Internal rotation	Moment	82-85	-	CON>PT

In view of the consistency of the results reported in Table 12, graphs of the original data (i.e. unadjusted for speed) are presented (Figure 33). Graphs for left-sided shod-marching are presented as there were no differences between left and right-sided data.
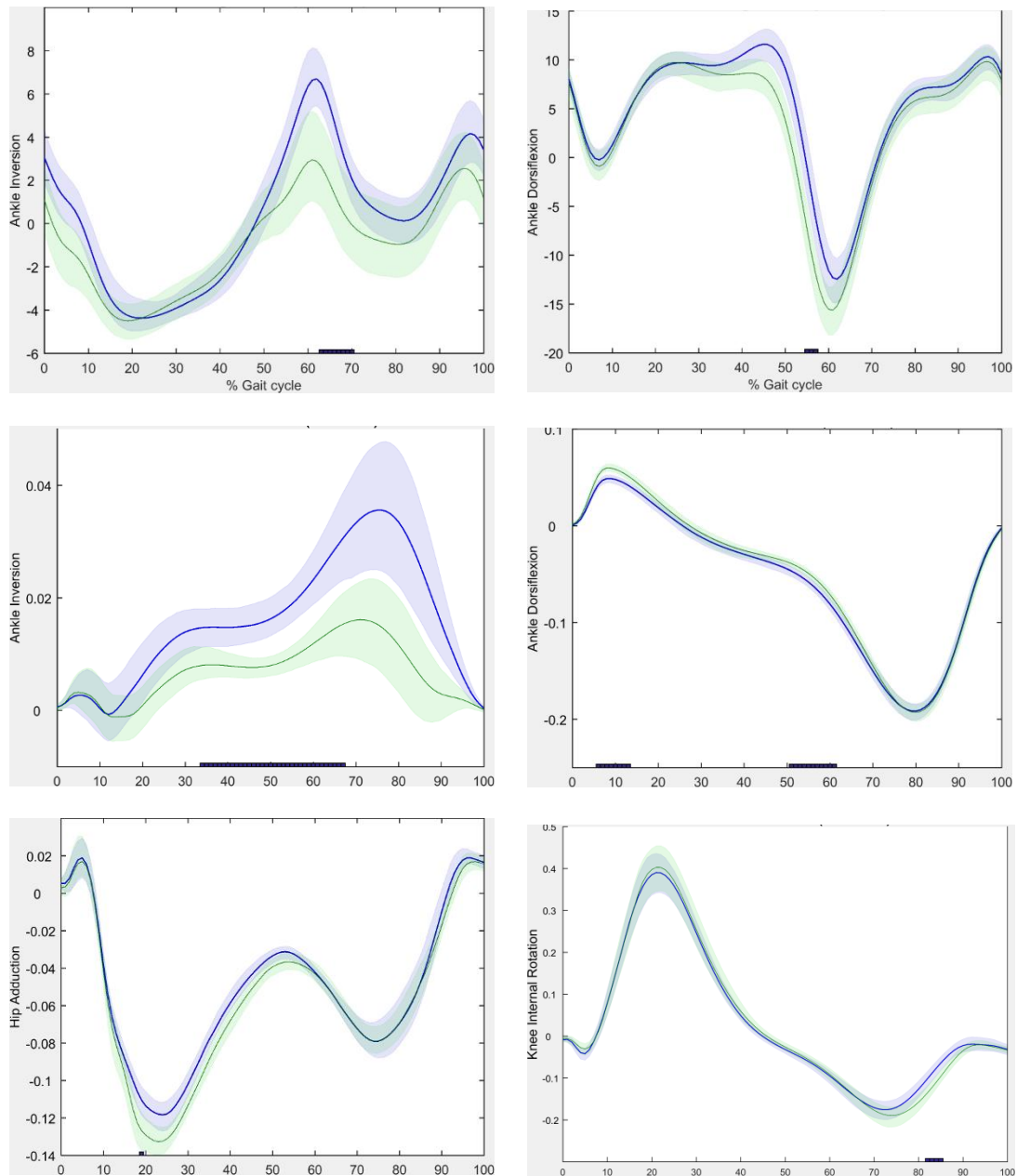
Figure 33. Differences in ankle angles (top row) during the gait cycle and ankle and hip moments (2nd and 3rd rows) during stance phase from left shod-marching data. Blue lines represent CON group, green PT group. Shaded areas represent bootstrapped 95% confidence intervals. The bar along the x-axis indicates those time points where all conditions were significantly (P<0.05) different. The graphs show both dorsiflexion and inversion but the movements in these planes are predominantly negative indicating plantarflexion and eversion respectively.

6.4.2. Forces and joint moments

When controlled for speed there were no consistent differences in any of the ground reaction forces. Consistent differences were found in the joint moments and are summarised in Table 11. Cases demonstrated lower ankle inversion moments during the majority of mid-stance; and greater ankle dorsiflexion moments during small sections of early stance and around the time of heel-off. Hip abductor moments were lower in cases during early mid-stance and during terminal stance. Representative graphs are presented in Figure 33.

6.5. Discussion

This study demonstrates a number of differences in biomechanical measurements between cases with CECS and asymptomatic controls. These differences were consistent during walking, marching, barefoot and shod gait. The shorter stature, with no differences in body proportions, seen in this cohort has not previously been discussed in a biomechanical context. This difference has not been demonstrated in a civilian population (Rorabeck et al., 1988) and has only been reported in the military once (Roscoe et al., 2015). The implications of the observed shorter stature are discussed throughout this Chapter.

During the completion of this study many participants reported having previously experienced the urge to transition to run in order to alleviate their pain. The transition from walking to running (WRT) has been suggested to transfer the work from the dorsiflexor muscles to the larger proximal muscles (such as gluteus maximus, rectus femoris, vastus lateralis, and vastus medialis) (A. Hreljac, 1995). The speed at which both humans and quadrupeds begin to transition to running also appears to be dependent on stature; resulting in a transition at the same Froude number (c.0.5; speed in relation to leg length). In humans, this corresponds to a WRT speed of around 2 m/s (the marching speed in this study) depending on leg length (A. Hreljac et al., 2007). The degree of tibialis anterior activation has been identified as a key determinant of the speed at which the WRT is triggered (Malcolm et al., 2009). The short stature found for cases in this study may therefore have important implications on the requirements of tibialis anterior and the subsequent development of CECS.

The muscles of the anterior compartment in healthy individuals perform close to maximum capacity during fast walking (A. Hreljac, 1995). This is amplified in shorter individuals during level walking (Sheehan & Gottschall, 2014) and is even less advantageous during ambulation on an incline as greater propulsion and toe clearance are required. The shorter stature found for cases in this study therefore likely demands increased activation of tibialis anterior, that may be represented here as an increased ankle dorsiflexor moment, and plays a significant role in the development of CECS. Further work to test this hypothesis is needed. This may also explain reported findings of greater pain levels and better diagnostic value of IMCP when marching on an incline compared to level ground, owing to the relationship between muscle activation and IMCP (Roscoe et al., 2015).

The relatively longer stride of shorter personnel, when normalised to leg length, may reflect ingrained changes induced by military training; whereby all personnel are required to move at a uniform cadence and speed. In order to maintain this relationship, shorter personnel can only achieve this through an increase of stride length relative to taller peers. This is likely to be the adaptation to allow ambulation at a higher Froude number. Cases increase speed through an increase in ankle plantarflexion at toe-off, resulting in an increased stride length, rather than a change in cadence. Experimental data also indicates that increasing stride length at a fixed speed increases the stress to the dorsiflexor musculature (Seay, Frykman, Sauer, & Gutekunst, 2014). The greater ankle dorsiflexion moment observed in this study further supports this theory. This homogenisation of gait may be a key factor in the development of CECS in the military population.

The results of the current study suggest that the homogenisation of marching gait also has a similar effect on the slower walking gait. The over-striding in late stance, which is required by shorter personnel during marching, may then become ingrained into everyday walking gait in this population. It is suggested that, along with learning to adapt their stride, cases have been required to walk at speeds closer to the WRT than their taller peers.

Discomfort in the anterior compartment muscles has been reported in healthy individuals during fast walking (A. Hreljac, 1993) and pain has also been described when the speed exceeds the WRT speed but subsides on

transitioning to running or cessation of activity (Bartlett & Kram, 2008). The continued excessive demand on the anterior compartment due to marching close to or above the WRT may be the trigger for the development of CECS and/or symptoms of CECS in this population and could account for the higher reported prevalence of CECS in the military. The observation that kinematic differences of the lower limb only occur at the ankle joint and, that kinetic differences are present at the ankle joint also supports the suggestion of excessive demand on the anterior compartment. This is also in line with the symptomatology. The lower ankle inversion moments in cases from mid-stance to toe-off suggests that, in CECS, tibialis anterior is operating at a mechanical disadvantage. This may be due to an inability to generate the force required for inversion, due to intrinsic weakness (Birtles et al., 2002; Varelas et al., 1993) or neuromuscular fatigue. It could also occur as a result of failure to effectively transfer the force generated by tibialis anterior contraction due to tendon lengthening or stretch. This effect could also be produced by an external barrier, such as through compressive footwear, to the normal stretch of the extensor retinaculum at the ankle during tibialis anterior contraction (Maganaris et al., 1999). Reduced force transmission through the tibialis anterior tendon would reasonably account for the differences observed in the ankle inversion angles in this study.

The reduced hip abductor moments observed in this study have also been identified in other patient populations including those with iliotibial band syndrome and knee osteoarthritis (Chang et al., 2005; Fredericson et al., 2000). This has been suggested to be as a result of weakness of the hip musculature. Of note, hip joint moments are the most susceptible to errors in the calculation of joint moments as these are propagated up the kinetic chain (Riemer et al., 2008). The reasons for these differences are therefore unclear and warrant further investigation to determine the role of the hip abductors, if any, in this condition.

This study provides evidence of biomechanical factors associated with CECS in males that are unlikely to be a protective mechanism; further investigation is required to confirm that these same factors apply to females. Furthermore the assessment of biomechanical differences in non-military populations is also required. Future work is also needed to investigate the activity of tibialis anterior

in these populations. The technical issues experienced in the control of speed also could have affected the results. It was therefore reassuring that both the bootstrapped t-test and ANCOVA gave predominantly the same results. Finally, the case-control design of the current study identifies key aspects of gait specific to those with CECS. Acknowledging the limitations of this approach, the results of this study identify height, stride length and ankle biomechanics for potential inclusion in a prospective study. Nevertheless, this study is the first to describe biomechanical differences in this population, and the results provide new insights into this condition.

6.5.1. Perspectives

In summary, this study demonstrates differences, which are present prior to the onset of painful symptoms, in height and biomechanical measurements during ambulation. These data can not confirm whether the biomechanical differences are a cause or consequence of CECS. However, these data do provide potential mechanisms underpinning the development of CECS in this population: The changes in joint angles and moments may indicate an impairment of either the muscle or tendon of tibialis anterior. The shorter height necessitates an increased stride length that likely results in an increased demand on tibialis anterior during ambulation. This disadvantage may be further amplified when individuals are required to march at speeds close to the walk-to-run transition speed or when ambulating on gradients. This may be a vital factor in the development of CECS in the military. Shorter personnel in military populations will continue to be required to march at prescribed speeds to fulfil occupational requirements; biomechanical interventions for CECS are therefore unlikely to be efficacious within this population.

6.6. Progression from Chapter 6 to Chapter 7

Chapter 6 identified anthropometric, kinematic and kinetic characteristics associated with CECS during walking and marching gait. The differences observed suggest that there may be increased activity of Tibialis anterior and that the muscle may also be impaired. However, these data do not provide direct evidence of a difference in muscle activity. Furthermore, the results reported in Chapter 5 suggested that plantar pressure variables related to foot type, that has been reported to modify Tibialis anterior activity, and related to

toe extensor activity were no different to controls. Chapter 7 therefore aimed to directly investigate the muscle activation characteristics of cases with CECS during the same activities.

7. Study 3 (Part 2): Differences in muscle activation in chronic exertional compartment syndrome during walking and marching

Roberts, A. J., Roscoe, D., Hulse, D., Bennett, A., & Dixon, S. J. (In review). Differences in muscle activation in chronic exertional compartment syndrome during walking and marching.

7.1. Abstract

Chronic exertional compartment syndrome (CECS) is a common problem within the military population that is associated with increased intramuscular compartment pressure (Roscoe et al., 2015). Over-activity of Tibialis anterior has previously been hypothesised to be a causative factor in the development of CECS (Tweed & Barnes, 2008) or the main cause of pain in anterior CECS (Franklyn-Miller, Roberts et al., 2014; Roberts & Franklyn-Miller, 2012). This study aimed to investigate the differences in muscle activation between cases with CECS and asymptomatic controls.

Surface electromyography (EMG) of Tibialis anterior and Gastrocnemius medialis of 20 male cases with anterior CECS and 20 pain-free controls was measured during walking and marching. Differences in EMG intensity during the gait cycle were compared in the frequency and time domain using wavelet analysis. There were no consistent differences in EMG intensity for Tibialis anterior between cases and controls at any timepoint or in any frequency band. Cases had significantly greater intensities within the medium-high frequency wavelets between 25 and 40% of the gait cycle for Gastrocnemius medialis than controls.

The similarity in Tibialis anterior activation during walking and marching suggests that a structural difference, such as increased fascial stiffness, is the cause of increased IMCP in CECS patients. Over-activity does not contribute to the higher IMCP observed in CECS; and over-activity is unlikely to be a risk factor for the development of CECS. The increased gastrocnemius activity may be related to the previously observed increase in stride length for this population; but is unlikely to be the direct cause of the increased IMCP.

7.2. Introduction

Chronic exertional compartment syndrome (CECS) is a cause of exercise-induced leg pain that predominantly affects the anterior compartment of the lower leg in athletes and military personnel (Almdahl & Samdal, 1989; Detmer et al., 1985; Reneman, 1975). Intramuscular compartment pressure (IMCP) during exercise is much higher in the Tibialis anterior muscles of patients with CECS than controls (Roscoe et al., 2015); however the reasons for the rise in IMCP in this muscle are unclear. Evidence for raised IMCP before exercise (during standing) suggests that a structural element, such as increased fascial stiffness, plays a part. However it is also known that the degree of muscle contraction is directly related to the IMCP (Sporrong & Styf, 1999b). Given this relationship, some authors have suggested that increased muscle activity rather than increased IMCP is the main cause of pain in CECS (Franklyn-Miller, Roberts et al., 2014; Roberts & Franklyn-Miller, 2012).

Tibialis anterior is the largest and strongest muscle of the anterior compartment (Silver et al., 1985) and generally accepted to be primarily a dorsiflexor of the foot in addition to its inversion role. In non-weight-bearing it is most active during a dorsiflexion movement when the foot is inverted (Houtz & Walsh, 1959). The most accurate estimates of the dorsiflexion moment arm suggest it is c.32-43 mm long (longer in dorsiflexion); in comparison to its inversion moment arm which is c.4 mm long (Klein et al., 1996). During walking, the Tibialis anterior typically becomes active prior to toe-off and remains active throughout the swing phase and into the first 10% of the next cycle. However, there is much variability in activation, even within the same subject (Di Nardo et al., 2014).

The medial Gastrocnemius has been described as the true antagonist of Tibialis anterior due to the reciprocal innervation between them (Wolf & Kim, 1997). It works as part of the Triceps surae (Soleus and medial/lateral Gastrocnemius) which act primarily as plantarflexors through a common insertion into the Achilles tendon. The Gastrocnemius also generates knee flexion moments as it is biarticular. During gait Gastrocnemius activity contributes to forward propulsion (Francis et al., 2013). It may also cause dorsiflexion during mid-stance, when the knee flexion moment induces ankle dorsiflexion motion of greater magnitude than the plantarflexion motion induced by the moment

generated at the ankle (Lenhart et al., 2014; Stewart et al., 2007). The inversion/eversion moment arm of the Triceps surae changes depending on the position of the ankle (Klein et al., 1996; R. Wang & Gutierrez-Farewik, 2011). As such, activation could be expected to always return the ankle back towards a neutral position.

Co-contraction of Tibialis anterior and Gastrocnemius during cross-country skiing has been suggested to occur more in a small sample of CECS patients than controls (Federolf & Bakker, 2012). However no evidence exists of the activity of these muscles during natural gait. Co-contraction of the muscles in the adjacent superficial and deep posterior compartments is associated with small increases in IMCP in the anterior compartment (Maton, Thiney, Ouchene, Flaud, & Barthelemy, 2006); although it was not clear from that study whether the IMCP rise was simply due to the collinearity with anterior compartment contraction. Experimental evidence suggests that raised IMCP in one compartment can result in raised IMCP in another. Increasing the deep posterior IMCP by 100 mmHg can cause the anterior IMCP to increase by 25 mmHg (Seel, Wijesinghe, & O'Connor, 2005), or raising anterior IMCP by 100 mmHg can cause a 6.7 mmHg rise in the superficial IMCP (Sellei et al., 2014). Contraction of muscles in adjacent compartments is therefore likely to have a small but significant effect on IMCP. EMG activity of both Tibialis anterior and Gastrocnemius medialis is therefore of interest for this condition.

Despite the known relationships between IMCP, torque and EMG; the effect of co-contraction on IMCP; and the general belief that CECS is an overuse injury, no studies have investigated muscle activity during gait in cases with CECS. This study therefore investigated the intensity and frequency content of the EMG signal of injured and uninjured military personnel during two aggravating activities: walking and marching. Based on the findings of Federolf and Bakker (2012) it was hypothesised that cases would demonstrate both increased tibialis anterior and gastrocnemius muscle activity. Furthermore the increase in tibialis anterior activity was hypothesised to occur mainly around heel strike.

7.3. Methods

20 male cases with symptoms consistent with CECS of the anterior compartment of the leg and 20 asymptomatic controls were recruited. The diagnosis of CECS was established from typical symptoms, with clinical examination and MRI excluding other pathologies. Controls were recruited from the UK armed forces. Cases were recruited from the Lower Limb Pain clinic at the Defence Medical Rehabilitation Centre, Headley Court. The Ministry of Defence Research Ethics Committee provided ethical approval.

The inclusion criteria were: Male; Aged 18-40 (representing the typical age-range of UK military service personnel); BMI<35; and no lower limb length discrepancy >2 cm. Cases were included if they had: symptoms of exercise-induced leg pan consistent with a diagnosis of anterior compartment syndrome; a negative MRI of the affected limb(s) and lumbar spine; no diagnosis other than CECS more likely; absence of multiple lower limb pathologies; and, no previous lower limb surgery. Controls were included if they were able to run for up to 20 minutes and reported: no lower limb pain in the previous 12 months; no current pain at any site, including during exercise activities; and no reliance on orthotics.

Electromyographic (EMG) data were collected using 4 wireless Trigno (Delsys Inc., Boston, MA, USA) sensors (16-bit Resolution; four 5 mm x 1 mm silver contacts; fixed 10 mm inter electrode distance) at a sampling frequency of 1200 Hz. Hair was removed from the EMG testing locations using a surgical razor. The skin was then cleaned using an alcohol wipe and lightly rubbed so that the skin went light red in order to decrease skin impedance (Konrad, 2005). EMG activity of the Tibialis anterior and Gastrocnemius medialis was recorded bilaterally during all movement trials and placed according to the guidelines by Sacco (2009) and the SENIAM project (Stegeman & Hermens, 2007) respectively. The Tibialis anterior EMG locations were determined by measuring one third of the way along a line drawn from the fibular head to the medial malleolus. The Gastrocnemius medialis was defined as halfway along a line drawn from the medial margin of the popliteal fossa to the medial insertion of the Achilles tendon at the calcaneus. The sensors were attached using double sided adhesive tape along the longitudinal axis of the muscle. Correct placement and satisfactory signal quality was confirmed by performance of a

maximum voluntary contraction of the individual muscle with observation of changes on the monitor in line with guidelines provided by Hislop (1995).

Participants performed traverses of the laboratory while walking and marching until a minimum of 10 complete cycles for each leg had been captured. 3D kinematics, kinetics and plantar pressure were also collected and have been reported elsewhere (Roberts, Roscoe, Hulse, Bennett, & Dixon, 2016b; Roscoe et al., 2016). Following familiarisation, participants were asked to walk at their natural pace (expected speed c.1.4 m/s) and march 'as if they were doing their military fitness test' (expected speed c.1.8 m/s). They were then asked to adjust their speed between trials if they were outside of the expected pace. Shod and barefoot trials were captured resulting in a total of 6 conditions: left and right leg; walk and march; and, shod and barefoot. Participants wore military issue training shoes (Silver Shadow, Hi-tec^{TM}) for collection of shod trials.

A custom MATLAB (R2015b,Mathworks, Natick,MA) script was used to carry out a wavelet analysis (von Tscharner, 2000), normalise the result to 100% of the gait cycle, and perform bootstrap t-tests on each wavelet and individual time point to identify regions with the gait cycle that were significantly different (Lenhoff et al., 1999). A wavelet analysis allows the power of the EMG signal to be described in both the frequency and time domain, unlike a Fourier transform that can only be used on stationary signals. The R statistical software (v3.2.2, The R Foundation for Statistical Computing, Vienna, Austria) script published by Armstrong (2011) was called by MATLAB to calculate the intensity of 11 wavelets using the EMG-specific parameters defined by von Tscharner (2000). The centre-frequency of these wavelets ranged from 7 Hz to 395 Hz. The time normalisation resulted in 1000 individual time points where heel strike occurs at time points 1 and 1000. The wavelet intensity patterns were normalised as per Federolf (2012) by dividing the power (at each centre-frequency and time point) by the average power per step and the step duration.

An attempt was made to control for speed *a priori*, however technical failure meant that this was not completely successful. Consequently, there were unintended variations in speed. ANCOVA was therefore used to control for speed and cross-check the original analyses for EMG duration. These cross-checks confirmed the validity of the original analyses; as such only the original analyses are presented in the results. Alpha for all analyses was set to 0.05.

7.4. Results

Cases ranged in age between 21 and 40; controls ranged between 19 and 40. Service personnel below officer status ('other ranks' as defined by NATO) were most commonly affected by CECS (n=18); two were officers. The control group was well matched to rank and consisted of 14 other ranks and 6 officers. Cases were significantly shorter than controls, although there were no differences in weight or the height: leg length ratio as reported previously (Roscoe et al., 2015). As such there were no differences in body mass index. These descriptive statistics are summarised in Table 13. No pain was reported by cases or controls during testing.

Table 13 Sample descriptives using bootstrapped t-test for equality of means. SD=standard deviation, t=t-statistic, df=degrees of freedom.

Variable	Cases Mean (SD)	Controls Mean (SD)	t (df)	p
Age	26.8 (5.0)	27.9 (7.6)	0.54 (38)	0.591
Height (m)	1.81 (0.06)	1.71 (0.13)	3.16 (38)	0.010
Body mass (kg)	79.4 (12.8)	82.0 (10.3)	0.69 (38)	0.488
BMI	27.5 (6.9)	24.9 (2.6)	-1.57 (38)	0.215

Cases had greater intensities within the low frequency EMG wavelets (1-4) between 90% and 5% of the gait cycle (i.e. before and after heel strike) for Tibialis anterior. Cases also had greater intensities within wavelets 6-8 between 93% and 98% of the gait cycle. However in both sets of wavelets the significance of these differences was not consistent between footwear, mode of locomotion and left/right muscles (Figure 34).
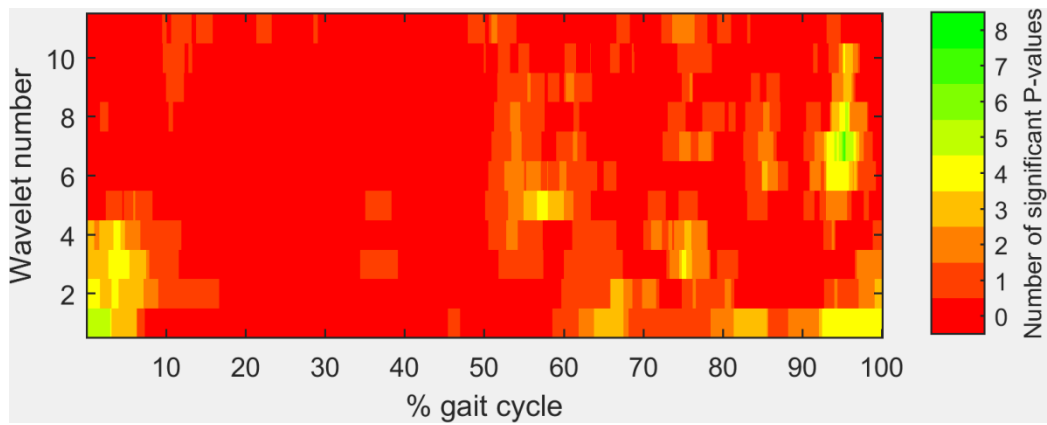
Figure 34 Number of significant differences between wavelet intensities across the gait cycle for Tibialis Anterior. Red represents no significant differences ranging to green representing 8 significant differences for all combinations (left/right x walk/march x shod/barefoot).

Cases had significantly greater intensities within the medium-high frequency wavelets (6-11) between 15 and 30% of the gait cycle for Gastrocnemius medialis. During this period all 8 combinations were significantly different (Figure 35). Increased activity of this muscle was also observed in lower frequency wavelets (2-4) between 30% and 40%; however the significance of these differences was not as consistent.
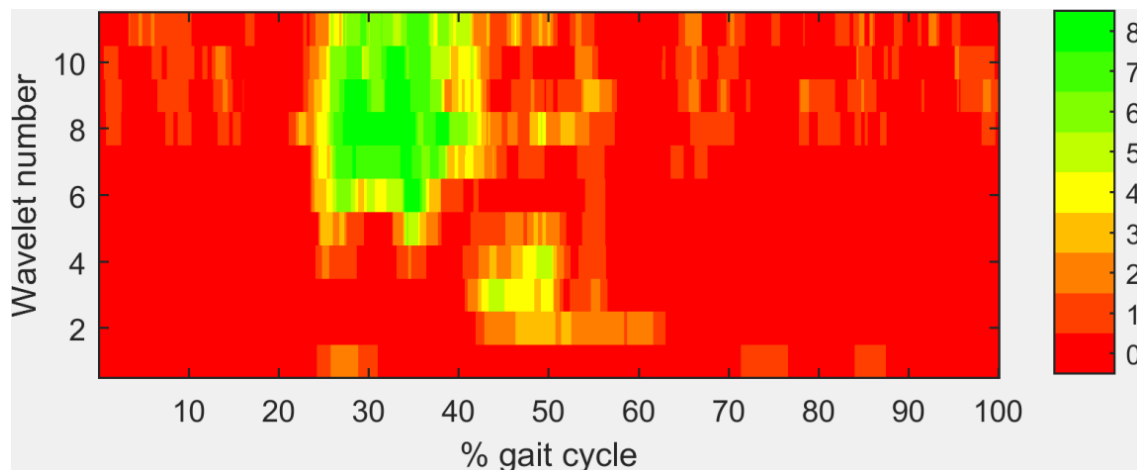
Figure 35 Number of significant differences between wavelet intensities across the gait cycle for gastrocnemius medialis. Red represents no significant differences ranging to green representing 8 significant differences for all combinations (left/right x walk/march x shod/barefoot).

7.5. Discussion

This is the first study to describe differences in muscle activity in patients with CECS during gait. The only previous study that has attempted to detect differences in movement strategies was carried out in a small sample (5

patients/4 controls) of cross-country skiers (Federolf & Bakker, 2012). They reported increased intensity of tibialis anterior, peroneus longus and gastrocnemius lateralis in CECS patients. However, given the small sample size and different mode of locomotion the results presented here cannot be considered to be comparable.

The typical description of CECS is as a condition caused directly by increased intramuscular compartment pressure (Roscoe et al., 2015). Although over-activity of Tibialis anterior has been hypothesised to be the main cause of pain in CECS (Franklyn-Miller, Roberts et al., 2014; Roberts & Franklyn-Miller, 2012). More recent evidence suggests a structural aetiology (Roscoe et al., 2015); although structural changes could theoretically also be caused through increased muscle activity (Stecco et al., 2014). The results presented here do not support over-activity of Tibialis anterior during walking and marching as either the main cause of pain in CECS; or as a risk factor for the development of CECS (assuming that the development of CECS does not result in muscle activity returning to normal levels).

The increased ankle dorsiflexor moment observed in Chapter 6 also suggested increased activation of Tibialis anterior. However, this interpretation does not fit with the electromyographic data. The differences in the ankle dorsiflexor moments are therefore suggested to be due to shortening of the moment arm associated with the increased plantarflexion observed.

The relationship between muscle contraction and IMCP was first described by Baskin (1967) in association with the changes in volume that occur with muscle contraction. Since then IMCP has been shown to correlate well with torque production during eccentric and concentric contractions of tibialis anterior (and soleus); and even demonstrating better correlations than EMG during eccentric torque production (Ballard et al., 1992; Sporrong & Styf, 1999b). However the IMCP:torque ratio is lower during eccentric contraction (Crenshaw et al., 1995; Styf et al., 1995). The results presented here suggest that the greater IMCP observed in CECS patients during marching, that has excellent diagnostic value (Roscoe et al., 2015), is not due to greater anterior compartment muscle activity. Thus this study provides further evidence to support the suggestion that CECS is caused by structural differences such as a less compliant fascia.

Reports of outcomes following conservative treatment of CECS through gait modification, aimed at reducing anterior compartment muscle activity, have suggested positive results (Breen, Foster, Falvey, & Franklyn-Miller, 2015; Diebal et al., 2011; Diebal et al., 2012; Helmhout et al., 2015). However these studies have only modified running gait despite predominately being carried out in military populations. This is surprising as within the military, marching has been reported as provoking greater levels of pain than running (Verleisdonk et al., 2004). While the results presented here are limited to walking and marching gait, the lack of a difference in Tibialis anterior muscle activity emphasises the need to carry out similar comparative studies during running.

Increased stride length has previously been demonstrated in cases with CECS in this population (Chapter 6). This is accompanied by increased ankle plantarflexion at toe-off during walking and marching (Roberts, Roscoe, Hulse, Bennett, & Dixon, 2016b). During marching ankle plantarflexion range of motion has been shown to increase with experimentally enforced over-striding (Seay et al., 2014). The triceps surae are also recognised as the main contributors to increased stride length during running (Dorn, Schache, & Pandy, 2012) and likely play a similar role during walking and marching gait. The individual roles of gastrocnemius and soleus during gait may differ despite similar EMG profiles and distal insertions (Lenhart et al., 2014; Stewart et al., 2007). For example, electrical stimulation of the gastrocnemius or soleus muscles during gait results in a decrease or increase respectively in ankle plantarflexion at toe-off (Stewart et al., 2007). The increased gastrocnemius activity observed in this study from mid-stance to toe-off is therefore unlikely to result in an increase in stride length without co-activation of soleus.

Given the strong relationship between gastrocnemius and soleus activity; and the overall greater strength of the soleus muscle (Silver et al., 1985) an increase in triceps surae EMG activity could be expected to lead to an increase in plantarflexion rather than dorsiflexion. Thus greater activation would facilitate the increase in stride length. Future studies should include the soleus when testing EMG in this population to confirm this hypothesis. Furthermore, the increased activity of the triceps surae (and resultant increase in superficial IMCP) is unlikely to be the major cause of the observed higher anterior IMCP in

CECS (Roscoe et al., 2015), given the small effect size observed experimentally (Seel et al., 2005; Sellei et al., 2014).

The differences and similarities in the EMG signal presented in this study are limited to males with and without CECS. Females have been observed to exhibit greater Tibialis anterior muscle activity and ankle motion than males during gait at the same speed (Chiu & Wang, 2007). These differences in activation suggest that confirmation of these results in a female cohort is therefore required. After exercise, CECS patients have an increase in Tibialis anterior muscle thickness (Rajasekaran et al., 2013) likely as a result of increased fluid content that may have affected the low-pass filtering of the EMG signal by the tissue (Stegeman, Blok, Hermens, & Roeleveld, 2000). However fluid shift does not appear to alter the EMG variables of interest in this study including amplitude and frequency (von Walden, Pozzo, Elman, & Tesch, 2008), providing confidence in the study observations. The technical problems experienced in the regulation of speed could also have adversely affected the results. It was therefore reassuring that inclusion of speed as a covariate gave similar results to the original analysis.

7.5.1. Conclusions

In summary, this study demonstrates no consistent differences in the activity of Tibialis anterior; and increased activity of the Gastrocnemius medialis muscle in cases with CECS. These results provide insight into the pathology of CECS and help explain the increased stride length previously reported in these patients. The similarity in Tibialis anterior activation during walking and marching suggests that a structural difference is the only cause of increased IMCP in CECS patients. Based on these findings, over-activity does not contribute to the higher IMCP observed in CECS; and over-activity is unlikely to be a risk factor for the development of CECS. The increased gastrocnemius activity is likely related to the increased plantarflexion required to increase stride length; but is unlikely to be the direct cause of the increased IMCP.

7.6. Progression from Chapter 7 to Chapter 8

Chapter 7 did not identify any consistent evidence that Tibialis anterior muscle activity was associated with CECS during walking and marching gait. This was in agreement with the findings presented in Chapter 5 on plantar pressure; and

questions the role of muscle activity and ambulatory activities in the development of CECS. In civilian cases, CECS most commonly develops during running activity. As presented in Chapter 4 the pain from CECS also aggravates military personnel to a similar extent during running. Thus the development of CECS in military and civilian cases may have a common biomechanical cause. Chapter 8 therefore aimed to investigate the kinematic and muscle activation characteristics of CECS during running gait.

8. Study 4: Biomechanical differences between cases with CECS and asymptomatic controls during running

Roberts, A. J., Roscoe, D., Hulse, D., Bennett, A., & Dixon, S. J. (In review). Biomechanical differences between cases with chronic exertional compartment syndrome and asymptomatic controls during running. *Gait & Posture*.

8.1. Abstract

Chronic exertional compartment syndrome (CECS) has been hypothesised, following clinical observations, to be the result of abnormal biomechanics predominantly at the ankle. Treatment of CECS through running re-education to correct these abnormalities has been reported to improve symptoms. However no primary research has been carried out to investigate the running movement patterns of those with CECS. This study aimed to compare the running kinematics and muscle activity of cases with CECS and asymptomatic controls.

20 men with bilateral symptoms of CECS of the anterior compartment and 20 asymptomatic controls participated. Barefoot and shod running 3D kinematics and muscle activity of the left and right legs; and anthropometry were compared.

Cases displayed less anterior trunk lean and less anterior pelvic tilt throughout the whole gait cycle and a more upright shank inclination angle during late swing (peak mean difference 3.5°, 4.1° and 7.3° respectively). Cases demonstrated greater step length and stance time, although this was not consistent across analyses. There were no consistent differences in Tibialis anterior or Gastrocnemius medialis muscle activity. Cases were heavier (mean difference 7.9 kg, p=0.02) than controls with no differences in height (p>0.05)

These differences only partially match the clinical observations previously described. However, no consistent differences were found at the ankle joint suggesting that current running re-education interventions which focus on adjusting ankle kinematics are not modifying pathological aspects of gait. The longer step length is a continuing theme in this population and as such may be a key component in the development of CECS.

Keywords: exercise-induced leg pain; chronic exertional compartment syndrome; biomechanics; anthropometry; military training.

8.2. Introduction

Chronic exertional compartment syndrome was first described in 1956 (Mavor). It is an overuse condition presenting as pain in the lower limb, associated with the muscles contained within the myofascial compartments of the shank. The anterior compartment is most frequently affected (Reneman, 1975). While numerous studies have tried to understand the pathophysiology of CECS (Barbour et al., 2004; Evers et al., 1997; Hurschler et al., 1994; Turnipseed et al., 1995), few studies have tried to identify potential risk factors for CECS. The higher reported incidence of CECS in the military compared to civilian practice makes this population ideal for testing potential factors.

CECS is commonly defined as a condition where elevated intramuscular compartment pressure (IMCP) during exercise impedes local blood flow leading to ischaemia and impaired neuromuscular function within the compartment (Styf, Korner et al., 1987; Zhang et al., 2011). Two systematic reviews recently questioned the role of IMCP and the validity of its use in diagnosis (Aweid et al., 2012; Roberts & Franklyn-Miller, 2012). However, much improved diagnostic criteria for CECS have since been reported using continuous IMCP measurement during exercise, thus confirming the intrinsic role of IMCP in this condition (Roscoe et al., 2015).

IMCP can be increased through changes in compartment compliance, compartment content or muscle activity (Hile et al., 2006; Sporrong & Styf, 1999a; Turnipseed et al., 1995). It has recently been reported that IMCP in patients is elevated on standing prior to exercise. This suggests that a structural component, presumably increased fascial stiffness, results in reduced compartment compliance (Roscoe et al., 2015). Biomechanical factors have been considered to play a role in the development of CECS for a long time (Bates, 1985). More recently CECS has been hypothesised, following clinical observations, to be the result of abnormal biomechanics predominantly at the ankle (Franklyn-Miller, Roberts et al., 2014). However, only one other group has investigated the role of movement patterns and muscle activity in the pathology and aetiology of CECS (Federolf & Bakker, 2012). This study was focussed on

skiing biomechanics and had a very limited sample (n=5 cases); limiting the applicability to the wider population.

Conservative treatment through gait modification has recently been promoted as a viable option for CECS (Franklyn-Miller, 2014; Franklyn-Miller, Roberts et al., 2014; Helmhout et al., 2015). Forefoot running was first described as a possible treatment in a case report by Cunningham (2004) that may reduce the anterior compartment muscle activity (Jerosch et al., 1989) and therefore pain. This has since been followed up by further case reports and a case series of ten US military patients (Diebal et al., 2011; Diebal et al., 2012; A. R. Gibson, 2013).

The kinematic and kinetic differences between CECS patients and controls during walking and marching have recently been reported (Chapter 7). Patients had greater ankle plantarflexion at toe-off, generated lower ankle inversion moments and greater ankle dorsiflexion moments in early stance than healthy controls. However, patients typically also complain of pain during running; indeed running is the most common cause of pain within civilians (Detmer et al., 1985). All of the military patients questioned at this centre described their pain as stopping them from either marching or running; while 30% of these individuals describe pain stopping them from only one of these activities (unpublished data; Chapter 4). This study therefore aimed to identify the differences in the running biomechanics between patients with CECS and healthy controls; and investigate the temporal spatial and kinematic differences previously identified (Chapter 6). In line with the clinical observations described previously (Franklyn-Miller, Roberts et al., 2014) it was hypothesised that, in comparison to controls, cases would demonstrate increased ankle dorsiflexion around heel strike associated with increased tibialis anterior muscle activity; reduced ankle plantarflexion at toe off associated with reduced gastrocnemius medialis muscle activity; increased knee flexion during swing phase; and no differences higher up the kinetic chain.

8.3. Methods

20 male cases with symptoms consistent with CECS of the anterior compartment of the leg and 20 asymptomatic controls were recruited. The diagnosis of CECS was established from typical symptoms, with clinical

examination and MRI excluding alternative pathologies. Controls were recruited from the UK armed forces. All participants gave informed consent. Cases were recruited from the Lower Limb Pain clinic at the Defence Medical Rehabilitation Centre prior to the provision of any gait advice. Ethical approval was granted by the MOD Research Ethics Committee.

The inclusion criteria were: Male; Aged 18-40 (representing the typical age-range of UK military service personnel); BMI<35; and no lower limb length discrepancy >2 cm. Cases required the following: symptoms of exercise-induced leg pain consistent with a diagnosis of anterior compartment CECS; a negative MRI of the affected limb(s); no diagnosis other than anterior CECS more likely, and the ability to run for short periods without pain limiting performance. All patients were assessed in a multidisciplinary clinic by a consultant in sport and exercise medicine and senior physiotherapist. This specialist clinic was specifically for patients presenting with exercise induced leg pain. Detailed history taking, including direct questioning and physical examination were used to determine the exact localisation of the patients' pain. This often included a symptom provocation test on a treadmill. Patients were only included in the study if their symptoms were purely localised to the anterior myofascial compartment. Controls were included when they were able to run for at least 20 minutes and had: no lower limb pain in the previous 12 months; no current pain at any site, including during exercise activities; and no reliance on orthotics.

Measurements of leg length, height and body mass were performed using a tape measure, stadiometer (SECA, UK) and medical grade scales (SECA, UK) respectively.

8.3.1. Kinematics and electromyography

Retro-reflective markers were placed on specific anatomical landmarks to form 15 body segments including the feet, shank, thigh, pelvis, trunk, head, upper arm, forearm and hand by the same operator. The head, upper arm, forearm and hand were not analysed as part of this study; these were not considered further. Data were collected using a 10 camera (4xT160, 4xT40-S, 2xT10) 3D motion analysis system (Vicon MX system, Oxford Metrics Ltd., Oxford,

England) at a sampling frequency of 120 Hz. A static calibration trial was first collected.

Participants walked barefoot on the treadmill for familiarisation, once happy the participant directed a member of the research team to increase the speed until they were at a comfortable running pace that they felt could be sustained for 15-30 minutes under normal circumstances. Once at the chosen speed this was maintained for a further 2 minutes. Only the final minute was used for analysis in order to allow gait to normalise to the running environment as much as possible. Five trials of five seconds of data were collected at five-second intervals in accordance with a similar previous study (Loudon & Reiman, 2012). This process was repeated with participants provided with military issue training shoes (Hi-Tec Silver Shadow). Orthotics were not used during testing. A recorded trial was deemed suitable if it had minimal marker dropout and no major gait inconsistency on the part of the subject as judged by an observer, e.g. stopping or stumbling.

The pelvis and thigh segments were defined according to Wu (2002), the shank segments were defined according to Peters (2009) and tracked using the marker cluster recommended by Manal (2000), the feet segments were a modified version of the foot flat option defined by Pratt (2012). The thorax was defined according to Gutierrez (Gutierrez et al., 2003).

Electromyographic (EMG) data were collected using 4 wireless Trigno (Delsys Inc., Boston, MA, USA) sensors (16-bit Resolution; four 5 mm x 1 mm silver contacts; fixed 10 mm inter electrode distance) at a sampling frequency of 1200 Hz. Hair was removed from the EMG testing locations using a surgical razor. In order to reduce skin impedance, the skin was cleaned using an alcohol wipe and lightly rubbed so that the skin went light red (Konrad, 2005). EMG activity of the Tibialis anterior and Gastrocnemius medialis were recorded bilaterally during all movement trials and sensors placed according to the guidelines by Sacco (2009) and the SENIAM project (Stegeman & Hermens, 2007). The Tibialis anterior EMG sensor locations were determined by measuring 1/3 of the way along a line drawn from the fibular head to the medial malleolus. The Gastrocnemius medialis was defined as halfway along a line drawn from the medial margin of the popliteal fossa to the medial insertion of the Achilles tendon at the calcaneus. In all cases the lower left corner of the electrode was

placed at this point in order to improve standardisation. The sensors were attached using double sided adhesive tape along the longitudinal axis of the muscle. Correct placement and satisfactory signal quality was confirmed by performance of a maximum voluntary contraction of the individual muscle with observation of changes on the monitor in line with guidelines provided by Hislop (1995).

8.3.2. Data processing and statistical analysis

Gaps smaller than 14 frames in the raw marker data were interpolated using a 3rd order least squares fit (Howarth & Callaghan, 2010). In the case of larger gaps the whole segment was excluded from analysis at these time points. The marker data was then filtered using a 6 Hz low pass bidirectional Butterworth filter (Winter et al., 1974). Gait data were normalised to leg length as recommended by Hof (1996) and Pierrynowski (Pierrynowski & Galea, 2001).

Kinematic and kinetic data were normalized to 100% of the gait cycle and stance phase respectively. Bootstrapped t-tests on each individual normalised time point were carried out to identify regions within the gait cycle that were significantly different (Lenhoff et al., 1999).

A custom MATLAB (R2015b,Mathworks, Natick,MA) script was used to carry out a wavelet analysis (von Tscharner, 2000), normalise the result to 100% of the gait cycle, and perform bootstrap t-tests on each wavelet and time point to identify regions within the gait cycle that were significantly different (Lenhoff et al., 1999). A wavelet analysis allows the power of the EMG signal to be described in both the frequency and time domain. The R statistical software (v3.2.2, The R Foundation for Statistical Computing, Vienna, Austria) script published by Armstrong (2011) was called by MATLAB to calculate the intensity of 11 wavelets using the EMG-specific parameters defined by von Tscharner (2000). The centre-frequency of these wavelets ranged from 7 Hz to 395 Hz.

Running speed was self-selected by the participants. Consequently there were variations in speed between participants. ANCOVA was therefore used to cross-check that controlling for the variations in speed would not alter the interpretation of the original analyses. Alpha for all analyses was set to 0.05. SPSS (v18; SPSS Inc, USA) or Matlab (v2014a; MathWorks, USA) were used for all analyses.

8.4. Results

Cases ranged in age between 18-37 (M=27.5, sd=5.2); controls between 18-36 (M=25.0, sd=6.1). No significant pain was reported during testing.

Cases (M=84.1 kg, sd=10.0 kg) were heavier (p=0.02) than controls (M=76.2 kg, sd=11.4 kg). There were no significant differences in height (Cases: M=1.77 m, sd=0.05 m; controls: M=1.79 m, sd=0.09 m). Cases (M=26.9, sd=2.7) also had a larger body mass index (BMI; p<0.001) than controls (M=23.6, sd=2.5).

Self-selected speed was slightly faster (p<0.05) for cases (M=11.0 kph, SD=1.1 kph) than controls (M=10.1 kph, SD=1.2 kph). When speed was controlled for, no consistent differences were seen in the temporal-spatial variables. As such there were no consistent differences in normalised step time, stance time, swing time or flight time. The faster speed necessitated a significantly longer step length (relative to leg length), as shown in the uncorrected data, for cases. This difference was generally no longer significant when speed was controlled for; although was still significant in the left shod condition. These differences are summarised in Table 14.

Table 14. Comparison of differences (ANCOVA) in temporal-spatial data between groups (*P<0.05). N.b. All variables are normalised to leg length and therefore do not have units.

Normalised variable	BF/ SHOD	L/R	F	P	Mean (Controls)	SE (Controls)	Mean (Cases)	SE (Cases)	Mean Diff
Step Length	BF	L	1.612	0.212	0.599	0.010	0.618	0.011	-0.019
		R	0.960	0.334	0.604	0.008	0.616	0.009	-0.012
	SHOD	L	4.720	0.036*	0.608	0.009	0.638	0.010	-0.030
		R	0.003	0.959	0.635	0.010	0.634	0.010	0.001
Step time	BF	L	0.015	0.903	1.148	0.012	1.150	0.012	-0.002
		R	0.050	0.825	1.185	0.013	1.181	0.013	0.004
	SHOD	L	2.621	0.114	1.154	0.013	1.186	0.013	-0.032
		R	0.760	0.389	1.230	0.014	1.212	0.014	0.018
Stance time	BF	L	2.170	0.149	0.764	0.013	0.792	0.013	-0.028
		R	4.254	0.046*	0.733	0.012	0.771	0.012	-0.038
	SHOD	L	0.565	0.457	0.821	0.015	0.837	0.015	-0.016
		R	4.418	0.042*	0.774	0.015	0.821	0.015	-0.047
Flight time	BF	L	2.225	0.144	0.422	0.016	0.388	0.016	0.034
		R	3.243	0.080	0.414	0.014	0.378	0.014	0.036
	SHOD	L	1.677	0.203	0.409	0.018	0.376	0.018	0.033
		R	0.397	0.533	0.381	0.017	0.365	0.017	0.016
Swing time	BF	L	0.910	0.346	1.570	0.023	1.538	0.023	0.032
		R	1.332	0.256	1.599	0.024	1.559	0.024	0.040
	SHOD	L	0.060	0.807	1.551	0.029	1.561	0.029	-0.010
		R	0.702	0.407	1.610	0.027	1.577	0.027	0.033

Normalisation to the gait cycle resulted in 101 individual tests for each movement plane where heel strike (HS) occurs at time points 0 and 100 and toe-off occurs between 32-35% of the gait cycle for both the barefoot and shod conditions. All participants had initial contact with the heel. The mean position of Toe-Off (TO) of 33% is marked on all gait curves. Key kinematic variables are presented graphically highlighting regions of data that differ significantly (p<0.05) between the two groups (Figure 36).
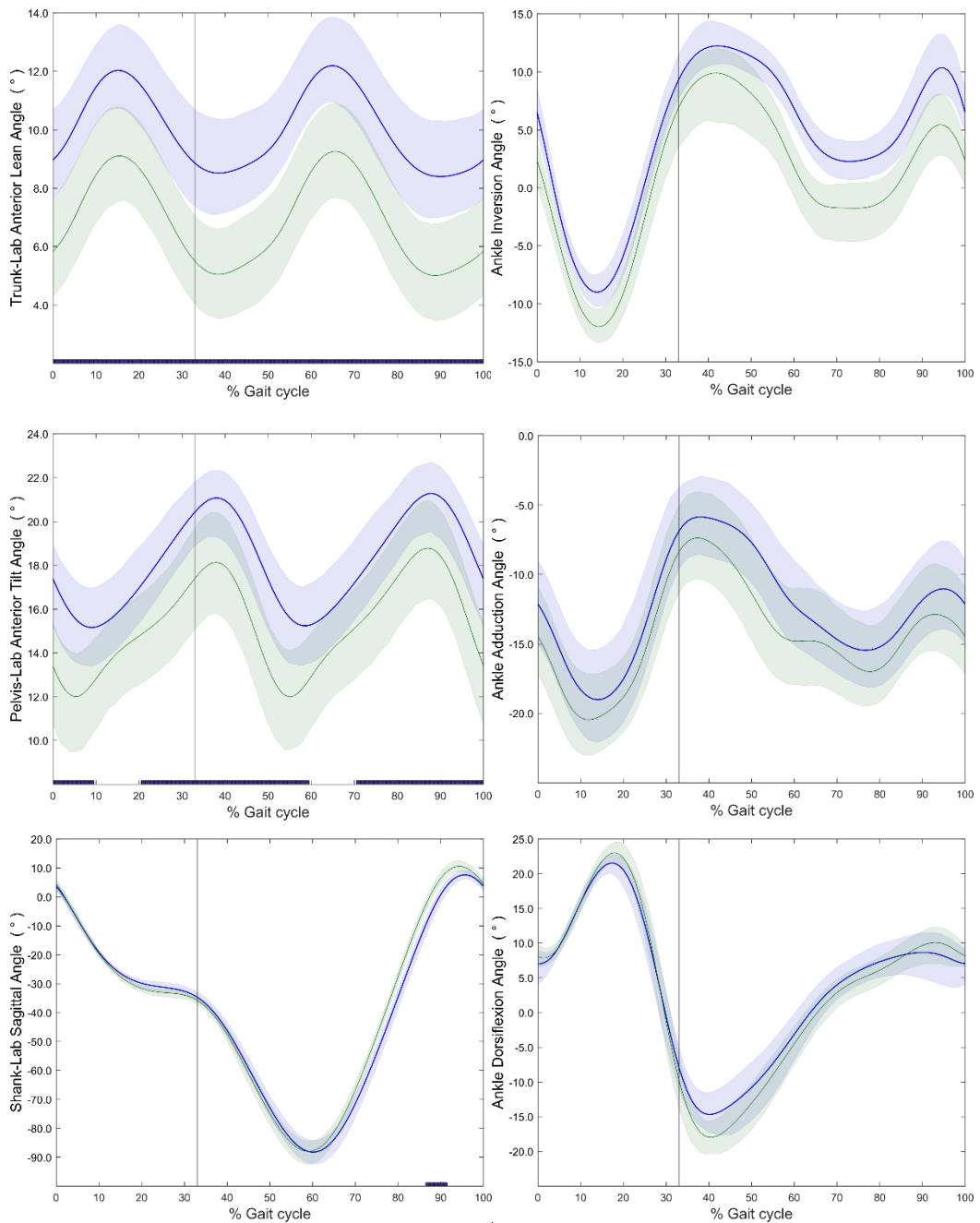
Figure 36. Angular data for joints demonstrating significant differences in the ANCOVA for all four experimental conditions (blue bar on x-axis indicates significance). From top to bottom: Trunk lean, pelvic tilt and shank inclination. Blue lines represent control group, green case group. Shaded areas represent bootstrapped 95% confidence intervals.

Cases displayed less anterior trunk lean and less anterior pelvic tilt throughout the whole gait cycle. During the late swing phase, cases had a more upright shank inclination angle. There was also some evidence that cases had less hip flexion during early swing phase (and terminal stance); although these differences were not apparent when speed was controlled for. A summary of the significant differences for kinematic data is presented in Table 15. Four different combinations of experimental condition were defined (Left / Right; Barefoot / Shod). There was some evidence of increased ankle plantarflexion between 39-43% and reduced ankle inversion between 62-69%; however only three of four conditions were significant at these time points (left shod plantarflexion and right barefoot inversion were the exceptions). Ankle flexion total range of motion ranged from 36°-41° in controls and 41°-44° in cases.

Table 15. Time points of significant differences (all conditions) and representative values of maximal differences between cases and controls (left shod).

Angle	Angular values of maximal differences (left shod)				Time points of significant differences (all conditions)	
	Time point of maximum difference	Mean angle (sd) Controls	Mean angle (sd) Cases	Mean difference	Bootstrapped t-test (%)	ANCOVA (%)
Trunk inclination	87%	8.6° (3.9°)	5.1° (3.4°)	3.5°	0-100	0-100
Pelvis tilt	51%	16.9° (4.5°)	12.9° (5.4°)	4.1°	0-6,44-56,92-100	0-9,21-59, 71-100
Hip flexion	33%	1.3° (4.7°)	-4.7° (5.4°)	6.0°	30-47	NONE
Shank inclination	83%	-22.8° (7.4°)	-15.6° (4.8°)	-7.3°	81-96	87-91

In view of the consistency of the results (with the exception of the hip angle) reported in Table 15, graphs of the original data (i.e. unadjusted for speed) are

shown (Figure 36). Graphs for the left-sided shod condition are shown as there were no differences between left and right-sided data. The magnitudes of the differences in angular measurements are presented in Table 15 and summarised in Figure 37.
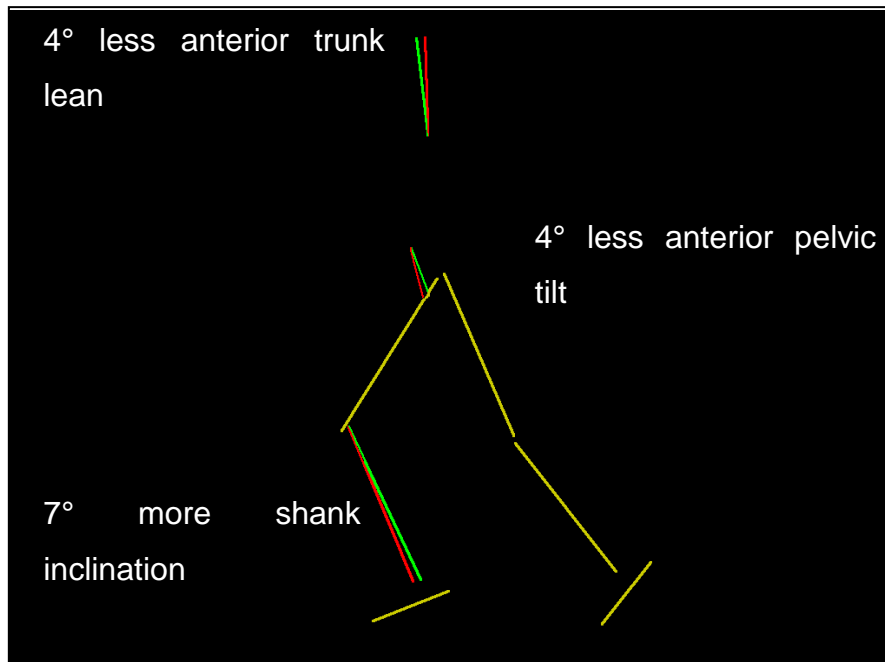
Figure 37. 2D representation of kinematic differences during the late swing phase. Yellow lines represent segments where no significant differences were found. Font size is representative of the number of significant time points in the gait cycle for that angle. Red and green lines represent segments for cases and controls respectively.

There were no consistently significant differences in any of the wavelet intensities or time points of the gait cycle for Tibialis anterior or Gastrocnemius medialis (Figure 38).
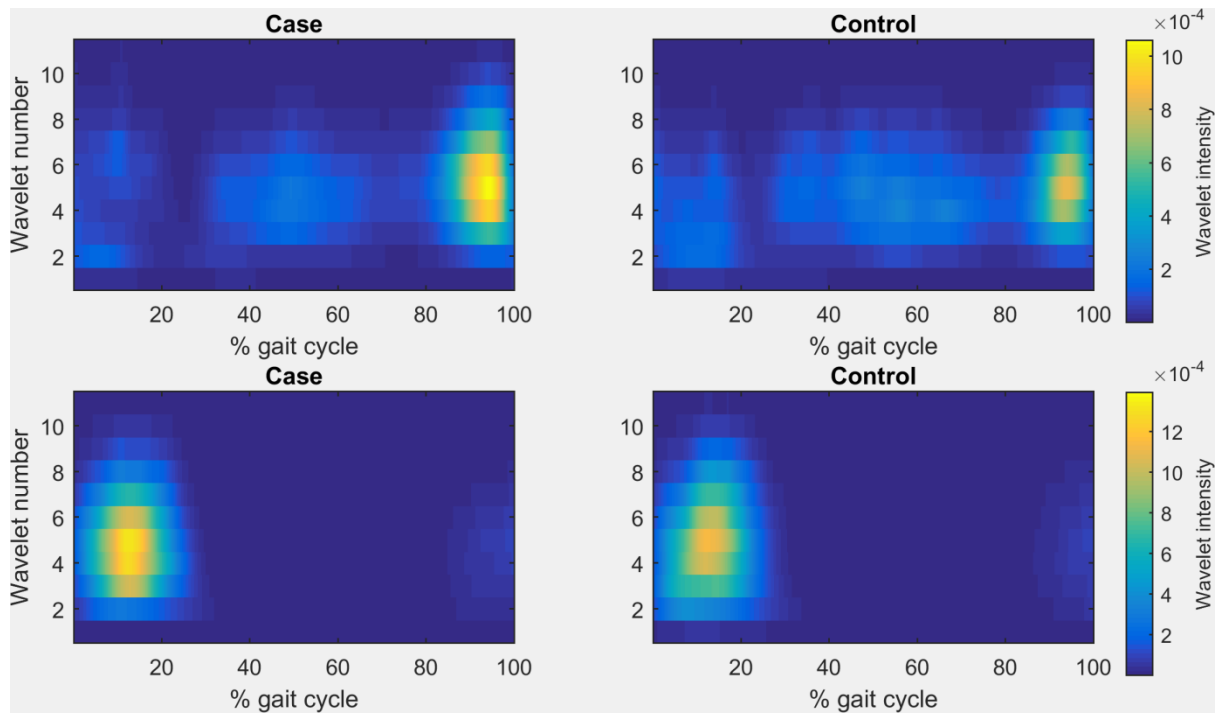
Figure 38. Mean EMG wavelet intensities for Tibialis anterior (top) and Gastrocnemius medialis (bottom). Left shod data only is shown as representative.

8.5. Discussion

This study demonstrates a number of key differences in biomechanical variables between CECS cases and asymptomatic controls. Anthropometric findings contrast with a recent study that demonstrated that cases in that cohort were on average 10 cm shorter than controls (Chapter 6); with no significant differences in mass (Roscoe et al., 2015) or BMI (unpublished data). As such, it has previously been suggested that smaller stature may be a risk factor for CECS in the military. The results of the current study suggest that a prospective study is now needed to provide more robust data on this theory.

The findings presented here are the first to demonstrate that patients with CECS run with a different gait pattern to asymptomatic controls. The results complement the differences found in the earlier study (Roberts et al., 2016) demonstrating that CECS patients have different ankle mechanics during walking and marching; but no differences occur further up the kinetic chain. The localisation of these differences to the planes of motion controlled by Tibialis anterior suggested that this muscle is functionally disadvantaged in these patients. However, during running, the main differences occur at the trunk with these differences then appearing to be propagated but diluted down the kinetic chain. It is feasible that the reduced requirements of Tibialis anterior during

running compared to fast walking (A. Hreljac, 1995) explain why the disadvantage is not apparent during running. Studies directly testing the strength, endurance and mechanical properties of Tibialis anterior are therefore required. It is also possible that there is a separate aetiology for CECS developing for an athletic/running population versus a fast walking/marching population. Comparisons between the biomechanics of civilian and military populations are therefore required.

Modifications to running style that have been used in an attempt to reduce the anterior compartment muscle activity of CECS patients have typically encouraged greater forward lean; along with changing from a heel strike to a forefoot strike, increasing cadence and reducing step length (Helmhout et al., 2015). Clinical observations have also suggested that patients have abnormally high levels of ankle dorsiflexion throughout the gait cycle and 'reduced heel lift during swing phase' (Franklyn-Miller, Roberts et al., 2014). While the differences in shank inclination observed during late swing phase (87-91% gait cycle) in the current study would result in the heel being closer to the ground, strong evidence for any differences at the ankle joint was not found. Similarly there was no evidence of altered ankle muscle activity. This is surprising as an expected consequence of less heel lift would be increased ankle dorsiflexion during the swing phase to allow foot clearance.

The similarity in ankle joint kinematics observed between cases and controls suggests that it is unlikely that running technique alone is the sole cause of CECS development. Thus current running re-education interventions which focus on adjusting ankle kinematics do not focus on modification of pathological aspects of gait; yet have been reported to reduce CECS complaints in soldiers for up to one year (Diebal 2012). Given the reports of reduced anterior compartment muscle activity in forefoot runners in healthy populations (Yong, Silder, & Delp, 2014), these interventions may simply be an option for activity modification that has not previously been explored. A resulting reduction in anterior compartment muscle activity would also explain the differences in IMCP observed after exercise following the intervention (Diebal et al., 2012; Hargens et al., 1989). The ability of these interventions to provide a lasting solution to military personnel that also need to regularly walk and march at a fast pace while carrying load is unclear.

The observations of increased ankle plantarflexion and reduced ankle inversion matched those described in Chapter 6 during walking and marching. However the inconsistency of these differences during running suggests that there is less of a difference in mechanical load of the anterior compartment musculature (and therefore fascia through myofascial force transmission) during running in this population. The electromyographical data also provides further evidence that the fascia is not additionally loaded through increased muscle activity. Military personnel typically experience pain that causes them to stop both marching and running (as reported in Chapter 4). Although the pain from CECS is more prevalent and of greater intensity during marching than running activities (Verleisdonk et al., 2004). Replication of these results within the civilian athletic population is therefore warranted.

The temporal-spatial results in the current study are very similar to those reported in the walking/marching study (Roberts et al., 2016). The increased stride length (relative to leg length) during walking/marching was suggested to reflect ingrained changes induced by military training; whereby all personnel are required to move at a uniform cadence and speed. During running, cases also ran with a significantly longer step length (relative to leg length), although this was only significant in the left shod condition when speed was controlled for. Ingrained movement strategies are believed to explain the differences in gait seen between trained distance runners and sprinters running at the same speed (Bushnell & Hunter, 2007). A similar mechanism could be occurring in this population whereby the increased stride length ingrained during walking and marching becomes translated into running gait.

Three prior studies comparing body mass and/or BMI between cases and controls have reported mixed findings (Birtles et al., 2002; Rorabeck et al., 1988; Varelas et al., 1993). The reasons for this are not clear, although some of the differences may be due to study design. For example, the comparisons in two of these studies may not be entirely valid as they were made between groups that consisted of both male and female subjects (Birtles et al., 2002; Rorabeck et al., 1988). The study by Varelas (1993) is also not directly comparable as they recruited an all-female cohort (Varelas et al., 1993). It is unclear whether the greater body mass observed in military studies is a result of

deconditioning following the development of CECS or a risk factor for the condition itself.

This study was limited to an all-male sample. This eliminated the influence of gender-related anatomical differences in the interpretation of the results; although for this reason may limit the translation of the results to females. The cases were also selected based on a clear clinical history rather than IMCP measurement due to strong evidence that IMCP testing had poor diagnostic validity at the start of this study (Roberts & Franklyn-Miller, 2012). A recent study now reports that IMCP can only provide an accurate diagnosis when it is measured during exercise to the limits of pain tolerance (Roscoe et al., 2015). Future studies would therefore ideally use this new diagnostic method for case selection.

The differences in speed selected also could have affected the results. It was therefore reassuring that both the bootstrapped t-tests and ANCOVA tests gave predominantly the same results. In order to prevent the onset of pain during testing, the familiarisation period at the selected speed could not be as long as generally recommended. However, even after just two minutes of familiarisation, the measurements can be considered to have high reliability (Lavcanska, Taylor, & Schache, 2005). In light of this, and due to the constancy of this period for all participants, it is unlikely that this would have adversely affected the results. However this condition did not allow the investigation of the biomechanics of muscle activity during a longer time period and after the onset of fatigue when the development of this condition may be expected to occur. Finally, to differentiate between cause and association it is acknowledged that these results would ideally be confirmed in a prospective longitudinal study.

In summary, this study demonstrates differences in the running biomechanics of cases with CECS that are present prior to the onset of notable symptoms. These differences match to some extent the clinical observations previously described (Franklyn-Miller, Roberts et al., 2014). However the lack of differences in ankle kinematics and anterior compartment muscle activity suggests that current running re-education interventions do not focus on modifying pathological aspects of gait. The increased step length is a continuing theme in this population and as such it is considered that this may be a key component in the development of the condition.

9. General Discussion

In this thesis the clinical characteristics and biomechanical factors associated with chronic exertional compartment syndrome were studied. While CECS has typically been described as an overuse injury; only a few theories have been proposed regarding its aetiology. Despite numerous publications on CECS, the clinical characteristics of this patient group have never been systematically described; knowledge of which may aid the selection of patients for diagnostic testing. Within military populations it was also unclear which activities were affected by CECS or may have a role in its development. Knowledge of this is important as the prevention of CECS will only be possible by reducing the exposure of personnel to the risk factors associated with its development. This therefore provided the rationale for study 1. Reductions in these risk factors may also play a role in the treatment of CECS to either reduce the risk of re-occurrence or as a first-line treatment. Prior to the work presented in this thesis there was only very weak evidence of the existence of biomechanical factors associated with CECS; thus the ability to make evidence-based decisions in this regard has not been possible.

9.1. Summary of the main findings

The overarching aim of this PhD research programme was to improve diagnosis, optimise treatment and identify potential factors that may cause CECS. Four studies were designed and carried out to address the questions detailed in Section 1.5.

The aim of study 1 was to provide information on the characteristics of CECS in the military population. The results of this study will help improve diagnosis through the identification of the clinical observations that best characterise CECS. The systematic characterisation of these clinical observations has produced clear evidence of the key features of this condition in this population. This knowledge will enable clinicians to better select patients for diagnostic testing, reducing unnecessary costs. Determination of the activities most affected by CECS in the military, and therefore the activities most likely to be involved in the development of the condition, provided the rationale for testing walking, marching and running gait in the later studies.

The data reported in the earlier systematic review (Roberts & Franklyn-Miller, 2012) suggested that IMCP may simply be considered a measure of muscle contraction force and duration and therefore a higher IMCP in CECS patients may represent over-activation of the muscles of the anterior compartment. Furthermore, the primary treatment for CECS at DMRC was changed to a biomechanical intervention focussed on changing running gait. However the results of study 1 demonstrated that running and marching both caused levels of pain that prevented continuation of the activity; and that there was no single aggravating activity. The reasons for the development of pain during these activities and the reasons for the preliminary encouraging results of the biomechanical intervention were poorly understood. Prior to the studies described in this thesis there had been no studies examining the biomechanical differences between CECS patients and controls.

The biomechanics of cases with CECS was therefore compared to asymptomatic controls in three separate studies investigating varying aspects of gait. Each biomechanics study had the joint aim of improving the understanding of the pathology and to identify potential risk factors for CECS. The ultimate aim of these three studies was to acquire information that would improve the treatment of patients with CECS and provide potential mechanisms to reduce injury occurrence.

9.1.1. What are the clinical observations that best characterise CECS and which activities may lead to the development of CECS in the military?

Study 1 demonstrated that cases with anterior CECS typically describe experiencing 'tightness' or 'burning' pain in the anterior and lateral compartments within 10 minutes of exercise. This was accompanied by a number of neuromuscular symptoms in almost two thirds of patients; although these are unlikely to be able to be used independently for diagnosis. Only 41% reported experiencing muscle lumps appearing on their legs. Pain then typically settled within 30 minutes. However descriptions of pain were highly variable reflecting the reported difficulty in establishing a diagnosis. The pain experienced caused all military personnel to stop marching and/or running; causing a similar debilitative effect for each activity. Biomechanical

measurements during walking have also been reported to be predictive of other sources of exercise-induced leg pain within the military (Franklyn-Miller, Bilzon, Wilson, & McCrory, 2014; Sharma et al., 2011) and in other running related overuse injuries (Barton, Levinger, Crossley, Webster, & Menz, 2012). Walking, marching and running were therefore chosen as the focus of the biomechanical studies.

9.1.2. What plantar pressure variables related to lower limb muscle activity and foot type are associated with CECS?

Study 2 demonstrated differences in anthropometry and joint mobility that provide evidence that small stature may be a key risk factor for the development of CECS in this population. The lack of association with foot type and toe extensor activity - related plantar pressure variables suggest that these are not related to the development of CECS, contrary to earlier hypotheses. The greater lateral to medial loading could theoretically represent increased tibialis anterior muscle activity at heel strike but a subsequent loss of control as the ankle is lowered.

9.1.3. What kinematic, kinetic and muscle activation variables are associated with CECS during walking and marching?

Study 3 demonstrated differences in the biomechanics and stature of patients that provide potential mechanisms for the development of CECS in this population. The reduced stature in combination with an increased stride length may result in an excessive load on tibialis anterior, when walking/marching at high speeds. Previous literature suggests that tibialis anterior activity may also be increased if an individual is unable to transition to a run as experienced within the military training environment. The changes in joint angles and moments were also indicative of an impairment of the function of tibialis anterior. However no differences were observed in tibialis anterior muscle activity. The increased gastrocnemius activity is likely related to the increased plantarflexion required to increase stride length; and could also explain the earlier return of the ankle back towards a neutral (less inverted) position.

9.1.4. What kinematic and muscle activation variables are associated with CECS during running?

Study 4 demonstrated differences in the running biomechanics of cases with CECS that are present prior to the onset of notable symptoms. These differences matched to some extent the anecdotal observations previously described; however the lack of differences in the ankle kinematics and muscle activity was notable. The increased stride length was a continuing theme in this set of studies and as such may be a key component in the development of the condition. The results complement the previous findings on walking and marching gait.

9.2. Potential insights into the development of CECS

Prior to this set of studies, there was very little evidence on the anthropometry of CECS cases. In the civilian population two studies reported no difference in height or body mass between civilian CECS cases and controls (Rorabeck et al., 1988; Varelas et al., 1993). The only military study that had reported anthropometrics suggested that patients have a larger BMI and body mass than controls (Birtles et al., 2002). Study 1 provided further evidence that CECS cases were overweight; although the design precluded a comparison to the normal population. Cases were also significantly heavier than controls in studies 2 and 4; while a lower body mass was observed in study 3. In the three case-control studies cases were shorter than controls. The large difference in height in study 3 accounted for the lower body mass observed. As such higher BMI was observed in all three case-control studies.

The anthropometric characteristics observed may provide insight into the development of the condition. It is unclear whether the increased weight is a result of deconditioning following the development of CECS or a risk factor for the condition itself. If the development of CECS were due to over-activity of the TA as previous theories have suggested; it would be reasonable to hypothesise that being overweight may increase the activity of the TA, and therefore the development of CECS. However ambulation with additional load does not appear to have an effect on TA activity (Ghori & Luckwill, 1985; Harman et al., 1992). Alternatively it is possible that it is the underlying cause of weight gain or its consequences that results in an increased risk of CECS. If this were the

case, this could explain the reports of CECS in diabetic non-athletic populations. These populations could also provide insights into potential weight-related mechanisms (D. Edmundsson et al., 2007; D. Edmundsson, Svensson, & Toolanen, 2008).

In all three case-control studies presented in this thesis, cases were shorter in height than controls ranging from a 2-10 cm difference in group means. Given that height will generally not change after the end of puberty this factor may play a key role in the development of CECS in this population. Reduced stature results in a reduced orthostatic response that would be expected to reduce leg blood volume and therefore IMCP (Arvedsen, Damgaard, & Norsk, 2012; Truijen et al., 2012); whereas patients with CECS have increased IMCP upon standing (Roscoe et al., 2015). The reduced height must therefore increase IMCP through an alternative mechanism. Studies 3 and 4 suggest that the reduced height interacts with the strict requirements of military activities resulting in an environment that increases the risk of developing CECS through altered biomechanics.

There was strong evidence from study 3 that cases had greater relative stride lengths than controls during marching gait. This was achieved through an increase in ankle plantarflexion during late stance and a concomitant increase in triceps surae muscle activity. Given the differences in height observed, this may reflect ingrained alterations in gait resulting from military training; whereby all personnel are required to move at an even cadence and speed. These differences in stride length were also observed in walking and running gaits although to a lesser extent. This suggests that the ingrained changes in marching gait are then translated into walking and running gait.

The localisation of kinematic differences to the ankle in study 3; the lack of differences in ankle kinematics in study 4; and the likely translation of differences observed during marching to other gaits suggest that marching is the main activity responsible for the development of CECS in this population. Two potential aetiological mechanisms based on these findings are:

1. Increased tibialis anterior muscle activity causing increased fascial loading
   a. The differences observed in ankle joint kinematics and kinetics may indicate an impairment of either the muscle or tendon of tibialis anterior that may require compensatory muscle activity.
   b. The shorter height necessitates an increased stride length that likely results in an increased demand on tibialis anterior during ambulation. This disadvantage may be further amplified when individuals ambulate at fast speeds or on gradients.
2. Increased passive load on the anterior compartment structures
   a. The increased plantarflexion angle will result in passive tension of the structures of the anterior compartment including the surrounding fascia. This may result in a positive feedback loop whereby the stretch increases ankle plantarflexion range of motion that could then amplify the movement.

These mechanisms could both feasibly increase IMCP through fascial remodelling resulting in a decrease in compliance in response to the increased load. Thickened fascia in other conditions (as described in more detail in Section 2.1.2) has been proposed to be caused by increased mechanical loading (Langevin et al., 2009; Stecco et al., 2014). There is conflicting evidence on the properties of fascia in CECS that may be due to limitations in sample size and the selection of suitable control groups (Section 2.2.5.1).

The increased muscle activity described in the first mechanism has been tested empirically in this thesis. There was no evidence from the EMG data that patients with CECS had greater TA activation than controls during any activity tested. There was also no evidence of differences between groups in plantar pressure derived measures of foot type, which are associated with TA activity. Similarly there was no evidence of differences in plantar pressure variables associated with toe extensor muscle activity. In contrast, the differences in

medio-lateral loading observed in Study 2 were theoretically linked with increased Tibialis anterior muscle activity at heel strike. Despite this last observation, overall increased muscle activity of the anterior compartment musculature does not appear to be associated with CECS.

Given the lack of evidence for increased muscle activity the increased passive load described in the second mechanism may therefore be considered more likely. Placing the ankle in full plantarflexion is not observed to increase IMCP directly (Gershuni et al., 1984; Tsintzas et al., 2009). However empirical evidence demonstrates that repeated stretching of the fascia leads to an increase in stiffness in a process known as strain hardening (Schleip et al., 2012; Yahia et al., 1993). This process appears to be related to a super-compensatory increase in tissue hydration following decreases in hydration during the stretch (Schleip et al., 2012). It is not clear however whether this process is transient or could lead to permanent changes in fascial stiffness that would be needed for CECS to develop. The increased ankle plantarflexion observed in Study 3 would be expected to strain the longitudinal axis of the anterior crural fascia to a greater extent than the transverse axis. However transverse stiffness may play a larger role in modulating IMCP than axial stiffness (Pavan et al., 2015). It is therefore clear that questions still surround the exact mechanism by which CECS develops. Nevertheless, the studies presented in this thesis provide evidence that the interaction, between individuals of shorter height and the specific requirements of marching, is the initial trigger for its development.

9.3. Implications for prevention

The symptoms of CECS were reported to have a similar debilitating effect on both running and marching. Preventative strategies may therefore need to focus on both these elements to have maximum effect. However the similarity in TA muscle activity and ankle kinematics between cases and controls during running suggests that alterations in running gait are unlikely to be the main cause of CECS within the military. A focus on the requirements of marching is therefore recommended.

This thesis presents strong evidence that short height is a risk factor for CECS within the military. This is likely to be a risk factor due to the increased stride length required to meet the occupational requirements of marching at a constant speed and cadence; or as a consequence of marching close to the walk to run transition speed. Preventative strategies that reduce the amount or speed of marching; or allow marching with a natural gait may therefore help reduce the incidence of CECS.

A number of studies have investigated the efficacy of foot orthoses as a method of preventing injuries in the military and other populations (Franklyn-Miller, Wilson, Bilzon, & McCrory, 2011; Hume et al., 2008; Larsen, Weidich, & Leboeuf-Yde, 2002). Foot orthoses typically attempt to re-establish normal biomechanics of the foot and ankle (Hume et al., 2008). The data, presented in this thesis, does not suggest that foot orthoses would be a useful prevention strategy for this condition. Firstly the similar levels of TA muscle activity and similar foot types between CECS cases and controls suggests that these are not abnormal. Secondly the key biomechanical differences observed are caused by the military environment rather than internal factors and as such would not be a suitable target for foot orthoses.

The results presented provide insights into the development of CECS in a military population due to marching. However they do not identify any potential running-related factors at the ankle joint in this population. There may therefore be a separate aetiology for CECS in running only populations. Alternatively over-striding could also plausibly be a factor in the development of CECS in the civilian population. This would suggest that running with a higher cadence at a given speed may be an appropriate preventative strategy; however biomechanical studies in the civilian population are needed to confirm this.

9.4. Implications for treatment

The lack of evidence for an increase in muscle activity, an association with foot type, or biomechanical differences during running that had previously been described anecdotally, has important implications for the treatment of CECS. The recent reports of positive results following treating CECS conservatively (Diebal et al., 2011; Diebal et al., 2012; A. R. Gibson, 2013) or of diagnosing it as a new syndrome (Franklyn-Miller, Roberts et al., 2014) have implied

biomechanical abnormalities in running gait. The lack of differences in the ankle kinematics and TA muscle activity observed in study 4 suggests that the outcomes were not a result of modifying pathological gait. Given the likely changes in TA muscle activity of changing from a heel to forefoot strike; these treatment options may simply act by modifying the activity rather than treating the underlying cause. While this may be sufficient for some civilian patients; military personnel will continue to be required to march at prescribed speeds to satisfy occupational requirements. Biomechanical interventions for CECS, such as a change in foot strike or the use of foot orthotics, are therefore unlikely to be efficacious within this population. Surgical intervention is therefore recommended as the primary treatment in this population.

9.5. Limitations and future directions

The main limitation of these studies was the use of a cross-sectional study design. It is well established that case-control studies play an important role in the evidence-base, particularly when populations are relatively rare as this prevents the execution of a longitudinal cohort study from being cost-effective (Manolio, Bailey-Wilson, & Collins, 2006). As such it was not possible to infer whether the biomechanical and anthropometric differences observed were the cause of CECS or developed as a result of the condition. The exception to this is height as this parameter generally will not change after the end of puberty. Acknowledging the limitations of this approach, the results of these studies identified height; stride length and ankle biomechanics for potential inclusion in a prospective study. Furthermore additional evidence is required to better understand the effect of height on gait in the military population, particularly during group marches.

These studies were limited to the laboratory setting. A future prospective study would ideally measure the variables identified in this thesis within the field setting. While this would be challenging on a logistical and technical level it would provide the best confirmatory evidence of the factors aetiologically related to CECS. The utilisation of wearable technology, that can measure these variables during arduous activities, may represent the best way of implementing this type of study. However, validation of the output from these new technologies is only just beginning to be made during activities that can't easily be replicated in the laboratory. The relatively low incidence of CECS also

means that a large initial population would be required to enable a prospective study to be successfully carried out. This therefore may only be achieved if the technology develops such that all soldiers can become instrumented (through reductions in cost and weight) thus allowing cost-effective large scale studies that can examine the effect of these factors on the risk of developing CECS and other conditions. This would also provide further benefits such as the ability to explore training load exposure and the effect of training programmes on these factors.

A limitation (and strength) of these studies was the investigation of a single diagnostic entity. While a focus on a single diagnosis allowed an in-depth exploration of CECS in males; the insights gained and implications for prevention are limited to this condition and gender. It is therefore difficult to predict the effects that these preventative measures would have on the overall incidence of injury. Given this limitation the implementation of the preventative strategies is not recommended until these effects have been investigated.

This thesis was limited to the assessment of military personnel. The assessment of biomechanical and muscle activation characteristics in non-military populations is now required. Future studies in both populations should include the soleus when testing EMG and the direct measurement of foot type to confirm hypotheses generated in this thesis. Investigators should also aim to understand any differences in the time of pain onset and subsequent development of pain while carrying out differing activities. These clinical characteristics may impact on the accuracy of diagnosis if the activity is not standardised. The novel reports of cold feet in CECS cases also requires further investigation including comparison to a control group.

The potential aetiological mechanisms described in chapter 9.2 assume that the fascia will respond to repetitive loading through remodelling resulting in an increase in stiffness. While an increase in stiffness has been demonstrated in the short term due to changes in tissue hydration; studies providing longitudinal evidence of longer term changes is required. Direct measurement of the effect of differing actively and passively generated forces on the strain in the fascia is also required to provide further strength to this theory. Shear-wave ultrasound elastography has been used to measure strain in a number of tissues *in vivo.*

Further investigation of this relatively new technique is required to validate its utility to measure stress in the fascia.

Marching is often carried out while carrying load. These studies did not include load carriage as this would have resulted in the occlusion of the markers required for defining and tracking the pelvis and trunk. As described in Chapter 1.4.1 the use of a pre-selected marker set was required by DMRC and the tracking of these segments was considered to be important in the exploration of this condition. Given the lack of an effect of load carriage on TA activity during ambulation this was not considered key to the study hypothesis (Ghori & Luckwill, 1985; Harman et al., 1992). However the studies in this thesis have presented strong evidence that reduced height is a risk factor for CECS. Reduced height has also been demonstrated to increase TA activity to a greater extent when walking on slopes; and affects the walk to run transition speed that is determined by the degree of TA muscle activity. Future research investigating the effect of load carriage on TA activity while accounting for the interactions with height, slope and speed would therefore be of interest; and may provide further insight into the mechanisms proposed in this thesis for the development of CECS.

9.6. Final conclusions

The purpose of this thesis was to identify the biomechanical, muscle activation and clinical characteristics of chronic exertional compartment syndrome. The findings have demonstrated key anthropometric differences; important biomechanical and muscle activation differences and similarities during aggravating activities; and key clinical characteristics of the condition. The evidence in this thesis suggests that the interaction between the requirements of marching and personnel of shorter stature is the initial trigger for its development. Based on the results, preventative strategies should focus on the requirements of marching, while in this population surgical intervention is recommended to be the primary treatment modality.

10. Appendices

Appendix A: Headley Exertional Leg Pain Questionnaire

Headley Exertional Leg Pain Questionnaire (HELP-8)

1. When you start to exercise, how many minutes until your pain starts?
    A. When I start (first minute)
    B. 1-2 mins
    C. 3-5 mins
    D. 6-10 mins
    E. Greater than 10 mins

2. How quickly do your pain symptoms settle on stopping exercise?
    A. Immediately
    B. Within 5 mins
    C. Within 30 mins
    D. Within an hour
    E. Greater than an hour

3. If you start to recommence exercise, how quickly do your symptoms return?
    A. When I start (first minute)
    B. 1-2 mins
    C. 3-5 mins
    D. 6-10 mins
    E. Greater than 10 mins

4. Please mark with **crosses** the area/areas on the diagram below that corresponds to the region **where your pain first starts when you get it**?*
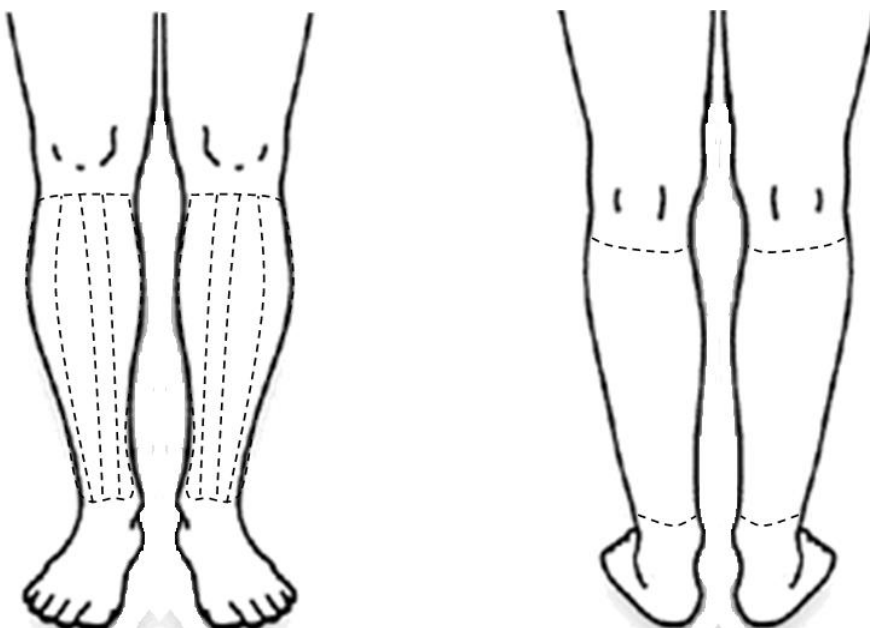
5. Please mark with **crosses** the area/areas on the diagram below that corresponds to the most painful area **when the pain is at its worst**?*
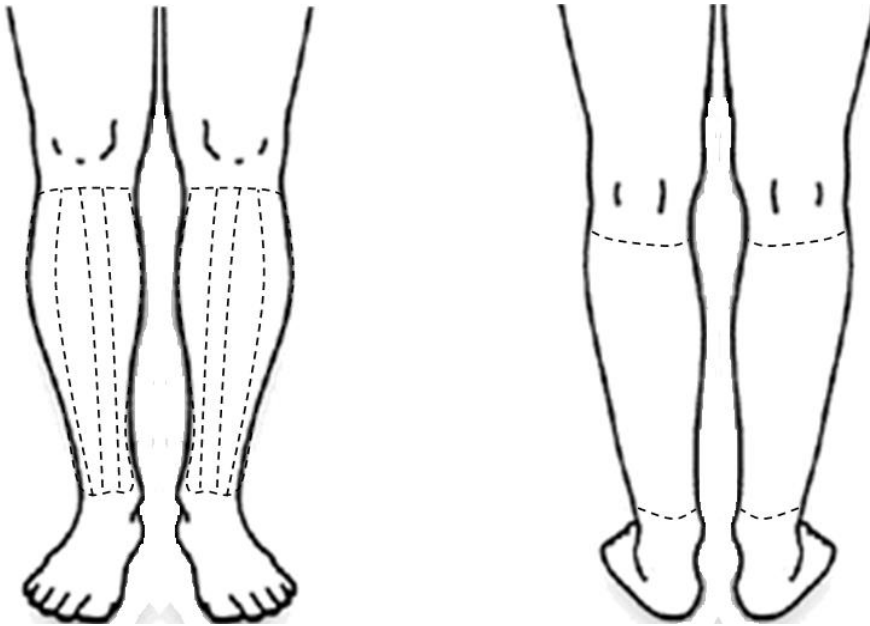
6. During which activities does the pain stop you exercising? (circle those that apply)

    A. All activities

    B. When Tabbing or Speed marching

    C. When running

    D. During impact exercise

7. When describing the pain which term fits your pain best?

    A. Sharp

    B. Tight

    C. Dull

    D. Tearing

    E. Burning

8. Do you experience (delete as appropriate)

    A. pins and needles in your feet?   Yes / No

    B. cramping in your feet?   Yes / No

    C. your foot slapping the ground when running?   Yes / No

    D. coldness of feet?   Yes / No

    E. colour changes?   Yes / No

    F. muscle lumps appearing on your legs?   Yes / No

Appendix B: Supplementary data table study 3

Peak angles from left shod marching data. Joint angles with consistent prominent peaks are presented. Time to peak is expressed as a percentage of the gait cycle.

Joint angle	Peak angle° (mean(sd))		Time to peak (mean(sd))	
	Controls	Cases	Controls	Cases
Ankle plantarflexion	-13.2(5)	-16.1(5.7)	62.7(1.8)	61.5(1.4)
Ankle inversion	-4.7(1.5)	-5.1(2)	62.7(1.8)	61.5(2.9)
Knee flexion	69.4(3)	70.1(4.4)	70.9(1.3)	70.8(1.1)
Hip flexion	39.8(5.3)	39.4(5.8)	99.6(5.2)	97.1(7.1)
Hip extension	-13.5(4.7)	-16.8(5.6)	49.7(1.2)	49.7(1.3)
Hip abduction	-10.1(3.3)	-10.7(2.9)	66.0(1.9)	68.0(7.3)
Hip adduction	6.7(3)	6.9(2.5)	19.3(3.8)	20.7(3.5)

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