FES-Standing and Muscle Spasms: Neurophysiology and Biomechanics

PhD Thesis.

by

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Abstract

Functional Electrical Stimulation (FES) can be used to assist patients with complete paraplegia arising from a traumatic spinal cord injury to stand. In clinical practice the take-up of this technology is poor. It was hypothesised that one potential reason was that the posture during standing was difficult to predict from non-standing biomechanical measures because of the spinal cord's motor responses to standing.

In six patients biomechanical and electrophysiological recordings were made to test whether motor activity arising as a result of standing affected their standing posture. Recordings were made using surface EMG electrodes, force plates and instrumented handles a motion analysis system.

No motor activity that affected the posture of the patients was recorded during standing or when the patients changed their hip or ankle angles.

The act of standing with FES assistance affected spasms in two of the six patients. In one patient his spasms became regularised to a 16s pattern when standing with FES but when standing without FES and in the second patient his spasms were stopped for periods of up to 7 hours. This prolonged cessation only occurred when standing with FES. Mechanically supported standing produced a short (5 minute) cessation in the activity.

The neural activity during the sit-to-stand or steady state standing did not change with increasing experience of standing in one naive subject studied over 6 weeks. The patient used the same strategy for the sit-to-stand as other patients. He improved his performance of this strategy by shortening the phases and the intervals between the phases as well as reducing the safety margin for knee buckling.

The spinal cord when removed from descending inputs is capable of generating rhythmical motor outputs in response to changes in sensory inputs. FES may interact with some of this oscillatory activity.

Preface.

This thesis describes work carried out for my doctoral thesis at University College London. As such the work described within it is my own and where I have collaborated this has been acknowledged within the text. However any period of study such as this cannot be accomplished in isolation, and this is especially true of clinical work, such as that described in this thesis. At this point I therefore wish to thank a number of people. Firstly my two supervisors; Dr Nick Donaldson from the Implanted Devices Group and Dr Brian Day from the MRC Human Movement Group. I have benefited enormously from their experience and this study could not have been completed without their support and encouragement. Nick in particular spent many hours explaining biomechanics to me and Brian was willing to allow his lab to be used and to collaborate on, what was to him, a new area of research. This combination of supervisors made the PhD what it is and I hope they have both benefited from the collaborative experience. Nick and latterly Brian also provided office space.

Two further people deserve special thanks; Dr Duncan Wood, senior clinical engineer at Salisbury District Hospital who took clinical responsibility for the patients and the experiments and controlled the stimulation throughout the experiments and Dr Laura Dekker who ran the 3D whole body scanner and wrote the code for the leg segmentation in the 3D scanning part of the project at UCL and then moved onto 3Q where she has continued to provide advice. Without either of these people the project would not have taken place as successfully as it did.

I also wish to thank the members of the Implanted Devices Group, the Human Movement Group and the Department of Medical Physics and Biomedical Engineering at Salisbury District Hospital for their support and encouragement.

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Lastly and most importantly I must express my grateful thanks and appreciation to the patients who volunteered to take part in this study and gave up their own time for no direct benefit to them. Without their commitment this project would not have taken place.

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List of Abbreviations.

Abbreviation	Use in this Thesis
FES	Functional Electrical Stimulation
SCI	Spinal Cord Injury
COM	Centre of Mass
GRV / HRV	Ground Reaction Vector / Handle Reaction Vector
LARSI	Lumbo-sacral Anterior Root Stimulator Implant
CHRELMS	Control by Handle REaction vectors of Leg Muscle Stimulation

Chapter 1.

Introductory Summary.

Electrical stimulation of the quadriceps of paraplegics to enable them to stand was first proposed by Bajd and Kralj in the 1960s (Kralj & Bajd, 1989). Although considerable man-years have been invested into the development of standing systems for paraplegics using electrical stimulation (Functional Electrical Stimulation, FES) at present there is no system in widespread clinical use. One potential reason for this lack of clinical uptake is that the responses to stimulation during standing may be difficult to predict since the responses in standing and when recumbent or sitting may be different. Since the spinal cord below the lesion in paraplegia remains intact the stimulation to produce standing will also interact with this residual spinal cord. In addition the act of weight-bearing when standing may further complicate prediction of the responses since the spinal cord can generate "support reactions", muscle activity generally in response to lower limb loading (Carpenter, 1996). "Support reactions" is a term that is widely used in some clinical circles but which is very ill-defined. It is generally used to denote persistent non-voluntary muscle activity that acts against gravity and is most commonly used in relation to the ankle where it is thought to "stiffen" the ankle. This study aimed to investigate the functional significance of any naturally occurring, or endogenous, spinal activity during FES-assisted standing in paraplegics.

Endogenous spinal activity which may complicate the responses to FES-assisted standing may arise a) because of the effects of stimulation, b) because of the effects of standing or c) only when the two, stimulation and standing, are combined. In humans the effects of endogenous neural activity during standing can be detected electrophysiologically and biomechanically. The electrophysiological approach, in this study the temporal and spectral analysis of surface electromyographic signals, can identify small signals and give insights into their origins but gives little if any information about the functional significance of the signals whilst the biomechanical approach yields information about the functional effects of signals but gives little information about their origin. In this study both approaches were combined to maximise the data and its interpretation.

This study was set-up to answer the question; does neural activity arising as a result of standing significantly alter the posture and biomechanics of FES-assisted standing in

paraplegics? Given the available apparatus it was not possible to determine any differences in the joint moments between steady-state standing and lying. Activity was found during the sit-to-stand that was not replicated when non-weight bearing. The act of standing also affected spasms in two of the patients.

It was found that spasms may have an inherent oscillatory neural component to them and that non-spasm surface EMG records also showed oscillatory components. The posture dependence of both the spasms and the oscillatory components of the EMG were examined. Given that oscillatory motor activity had been found, and that patients are observed to improve their standing with practice the final question was; is this improvement in standing a result of changes in the neural activity from below the lesion? This was answered in a single patient in whom the biomechanics of the sit-to-stand were also examined for changes within and between sessions that might indicate learning. It was found that there were no changes in motor activity associated with "learning".

In chapter 2 the spinal control of movement, reflexes and neural circuits are introduced along with a brief introduction to rhythmic motor activity, tremor, and some of the sensorimotor consequences of spinal cord lesions. The chapter also includes an introduction to Functional Electrical Stimulation for paraplegic standing.

The methods used in this study are outlined in two chapters, 3 and 4. Chapter 3 describes the technique used in the motion analysis laboratory to determine the leg joint moments, intended to be the primary biomechanical outcome measure and describes previously constructed apparatus, the Multi-Moment Chair System, MMCS, which determines joint moments whilst recumbent. The chapter also describes the use of the instrumented handles and motion analysis system and presents a simple error analysis of the biomechanical measuring system. This error analysis demonstrates that comparing joint moments between standing and lying is not practical since the errors in the MMCS are large. Standard electrophysiological techniques were used in this study and these are also outlined and referenced in this chapter. Chapter 4 presents the details of a new method developed within this study for identifying the mass and centre of mass of the legs of individual subjects, particularly paraplegics. The accurate identification of these mass properties is required for the calculation of the leg joint moments described in chapter 3. The technique uses a 3D whole body surface scanner and the generation of a computer model of the leg with 2 compartments; soft-tissue and bone. This technique offers advantages over both previously used methods of

obtaining this data, which relied either on standardised models, or individual data collected using water-displacement, which is both time-consuming and unpleasant, and impractical for disabled subjects.

The main body of the thesis chapters 5-8 present results from different cohorts of experiments. In chapter 5 data are presented concerning ongoing oscillatory activity recorded from surface EMG signals as a marker of oscillatory activity in the spinal cord during FES-assisted standing. The spectra of the activity changes with postural changes (although there are a number of technical issues associated with interpreting these changes as being neural in origin) and overlaps with those frequencies at which tremor is found.

In contrast to the activity described in chapter 5, chapter 6 presents data from two subjects who have strong intermittent motor activity (spasm) that is modulated by FES-assisted standing. In one patient standing with the aid of FES regularises his spasms into a 16 second cycle which persists for as long as he stands whilst the second patient has intermittent, persistent spasms that are suppressed for up to 9 hours following FES-assisted standing.

In chapter 7 results are presented from two patients who show posture dependent activity during the sit-to-stand phase of FES-assisted standing, but not in other phases of the stand. This activity is clinically observable as rapid oscillatory (8Hz) movements of the legs and can be detected using surface EMG and biomechanical measures. This activity is bilateral and always occurs in the same phase of the sit-to-stand, following knee extension and as the hips are starting to extend and the body weight is starting to be taken through the legs. Spectral analysis of the muscle activity suggests that at least some of this arises from a central oscillator with bilateral projections.

The final results chapter presents a case study of a single patient who, as part of this study, learnt to stand with the aid of FES. He exhibited the 8Hz oscillations described in chapter 7 and these are not re-discussed here. It was initially felt that the improvement in standing ability with practice may be due to changes in neural activity from the spinal cord. There were no changes in neural activity detectable with increasing standing experience. Biomechanically he used the same, previously published (Donaldson & Yu, 1998) strategy for the sit-to-stand as the other patients. With increasing experience, within as well as between sessions, he refined the strategy.

The thesis concludes with a discussion bringing together common elements across the thesis and highlights topics for future research.

Chapter 2.

Introduction: Spinal Injury, the Spinal Cord and Functional Electrical Stimulation.

2.1. Introduction.

Spinal injury has a devastating effect upon the patient and their family and the effects include a loss of voluntary motor control, sensation and many secondary medical complications (Grundy & Swain, 1996). Recent work has started to demonstrate the potential of the intact cord below the lesion e.g. (Barbeau *et al.*, 1999) (Dietz *et al.*, 1994. 1998), (Edgerton *et al* 2001).

Repair to the spinal cord following lesions is looking increasingly possibly, however it is likely that the repair will only be partial (Fawcett & Asher, 1999). After treatment patients with complete lesions are likely to have incomplete lesions, but it is likely to be many years before patients with complete or incomplete lesions return to a normal neurological level following treatment. An understanding of the spinal circuitry that is present is vital not just for adequate, robust control of current FES systems but for a solid scientific foundation for future FES work (Burridge & Ladouceur, 2001), (Barbeau *et al.*, 1999) as well as providing a basis for rehabilitation therapies and for future regeneration or recovery strategies.

Patients with upper motor neurone, UMN, lesions suffer from "spasticity" or UMN syndrome (Hiersemenzel *et al.*, 2000), (Haas & Crow, 1995), (Rothwell, 1994). Spasticity interferes with daily life by making normal voluntary movements difficult to perform, restricting the range of motion of joints and increasing the sensitivity to reflexes. The classical definitions of spasticity consider it to be an increase in the sensitivity of the stretch reflex (Lance, 1980).

However, spasticity also presents with spasms and involuntary muscle movements, classically considered to be a response to a noxious stimulus (Grundy & Swain, 1996). These are poorly understood, but may originate from spinal circuits. This condition is briefly reviewed in terms of possible spinal mechanisms underlying the condition and what this can tell us about the adaptability of spinal circuits.

2.2. The Spinal Cord.

The spinal cord is an integral part of the central nervous system. It originates in the brainstem and continues through the spinal column until the twelfth thoracic

vertebra in man. The cord contains millions of nerves, some travelling virtually the entire length of the cord, such as the cortico-spinal tract neurones, and some only travelling less than a millimetre, short inter-neurones. The ascending and descending fibres are arranged into tracts within the cord. Figure 2.1 illustrates some of the major descending motor pathways from the brain through the spinal cord.

Figure 2.1. The major motor pathways within the brain and the spinal cord. The pathways are bilateral. There are strong interconnections between the various motor pathways prior to the exit of the motor command signal through the anterior horn cells. Taken from Pocock and Richards (1999).

In addition to carrying descending motor command signals from the brain to the periphery the spinal cord also carries ascending sensory signals from the periphery to the brain. As well as acting as the communication pathway between the brain and effector organs and sensors, the spinal cord is also involved in the second-to-second control of some movements.

Below the 12th thoracic vertebra the contents of the spinal canal are the roots which have already left the cord. This area is known as the *cauda equine*. The fibres below this point are lower motor neurones and as such are part of the peripheral nervous system.

2.3. Spinal Cord Injury. An Introduction.

At present the incidence of spinal injury in the UK is 10-15 per million of the population. The majority of the newly injured patients are young, and predominantly male, (4:1, male to female ratio) (Grundy & Swain, 1996)

Spinal cord injury, SCI, causes reduced sensation, voluntary motor control and results in significantly increased health risks. These include an increased risk of coronary heart disease and other cardiovascular problems, depression and many other health problems associated with a lack of mobility and sensation such as pressure sores, breakdown of the skin, increase in body mass, decrease in bone density etc.

There are many ways of classifying the patient with spinal cord injury, depending on level of injury and completeness of the lesion. A truly anatomically complete lesion prevents all neural conduction. The term incomplete describes a continuum from those who are functionally complete, (i.e. are wheelchair bound with little or no sensation or motor control) to those patients who function at or near a normal neurological level (Grundy & Swain, 1996). Patients are defined as complete if they have no sensation below the level of their lesion and no voluntary motor control. Internationally the most widely used scale for classifying injuries is the ASIA (American Spinal Injuries Association) scale. This is a 5-point impairment scale covering the spectrum from complete spinal cord lesion (A) to normal neurological function (E). Table 2.1 shows the scale with a description of each level. As with all ordinal scales the ASIA scale suffers from a lack of sensitivity and there may be a broad spectrum of functional abilities within each band.

ASIA Impairment Level	Description
A	**Complete.** No motor or sensory function is preserved in the sacral segments S4-S5.
B	**Incomplete.** Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4-S5.
C	**Incomplete.** Motor function is preserved below the neurological level, and more than half the key muscles below the neurological level have a muscle grade less than 3.
D	**Incomplete.** Motor function is preserved below the neurological level, and at least half the key muscles below the neurological level have a muscle grade of 3 or above.
E	**Normal.** Motor and sensory function are normal.

Table 2.1. The ASIA impairment scale. This shows a continuum of functional impairment that may not correspond directly with the anatomical state of the injury.

A further neurophysiological classification has been introduced in research in recent years, *discomplete*. The term discomplete was introduced by Dimitrijovic and describes a lesion which is functionally and clinically complete, but which retains fibres that cross the lesion site (revealed using neurophysiological testing) (Dimitrijevic, 1985). It is unclear how many patients are discomplete since the diagnosis is normally only made if they take part in neuroscience experiments and clinically has little, if any, significance at present since it does not alter the treatment of the patient or affect their functionality.

Neuronal regeneration following spinal lesions does not occur naturally. Recent experiments have demonstrated that with appropriate aids such as pharmacological agents, "cell scaffolds", neural implants, etc., fibres can cross the lesion site. Clinical trials of these regeneration strategies may start in the next 5-10 years, but it will be many more years before any of these treatments becomes widespread (Basso, 2000). Even then, the ultimate goal of completely reversing spinal lesions appears out of reach at present. The therapy is likely to restore some fibres, turning patients with complete injuries into patients with incomplete injuries and increasing the number of fibres that cross the lesion in patients with incomplete lesions. A major challenge will be the restoration of functional connections rather than random connections.

Patients with spinal injuries are at an increased risk of premature death when compared with the general population. The major health risks for patients are psychological, cardiovascular and from infectious agents. Many patients also suffer from intractable pain, which may contribute to psychological problems (Grundy & Swain, 1996).

People with SCI are prone to pressure sores because they cannot make the small regular changes in posture using the muscles of the gluteal region that neurologically intact people make. In addition they are unable to sense when they have been in a posture for too long and adjust. The problem is further compounded by the lack of muscle bulk that these patients have, as a result of disuse atrophy, so that the time until tissue damage is significantly lower than in a normal person. This combination of factors means that they are at a high risk of developing pressure sores, which often result in a lengthy recuperation. If the sore becomes open then it is a high-risk area for entry of infectious agents (Grundy & Swain, 1996). Treatment of pressure sores is expensive, time-consuming and unpleasant for the patient.

Lesions in the *cauda equina* result in the dennervation of the muscles supplied below the lesion site. The nerves here are lower motor neurones and as such may regenerate. However the large distances involved mean that in many cases the dennervation is permanent. Lesions here will also result in sensory abnormalities. These may include a loss of sensation or paradoxically a hypersensitivity.

Nociceptive stimuli below the lesion site cannot be felt as pain, since there is no sensory connection with the brain. Spinal reflexes, e.g. the flexion withdrawal reflex, that occur in response to noxious stimuli, may be increased as a result of the loss of descending inhibition and collateral sprouting (Bennet *et al.*, 1999).

2.4. Spasticity.

Spasticity is poorly understood despite its widespread occurrence after upper motor neurone lesions. One reason for the poor understanding may be that the nomenclature is mixed and unclear. Muscle tone and spasticity are used almost interchangeably in some circles, and neither is well defined (Rothwell, 1994). In addition muscle spasms are often considered to be part of spasticity. Spasticity is a major problem for many patients with upper motor neurone lesions, and probably consists of more than one set of neural responses (Lance, 1980), (Pomeroy *et al.*, 2000), (Bajd & Vodovnik, 1984), (Burridge & McLellan, 2000).

Spasticity in spinal patients probably represents the results of a loss of normal, tonic descending inhibition from supraspinal centres onto tonically active spinal circuits (Bennet *et al.*, 1999). The role of new collateral sprouts is also thought to be important, although less well understood. Treatments are primarily pharmacological and are successful in reducing spasticity in many patients but not in all, and only in a small number is the spasticity completely removed (Grundy & Swain, 1996). In addition to the neural changes associated with spasticity there are also changes in the biomechanics of spastic muscle (Pisano *et al.*, 2000).

Muscle spasms are a further feature of "spasticity" and one that many patients with spinal injuries report as having more effect upon their daily lives than joint stiffness, (spasticity). Spasms may be reduced by treatment with Botulinium toxin or baclofen, both of which also have effects upon spasticity. Patients with SCI may find that their spasms are responsible for maintaining some of the bulk of their muscles after injury. Following a spinal injury the muscle fibres convert to a fast fatiguable type and this process may be accelerated and accentuated by spasm activity (Rutherford *et al.*, 1986).

Some patients, particularly those with incomplete lesions, may learn to use their spasms, e.g. to aid in transfers etc. Spasms are responses in one or more muscle(s) to, often, nociceptive stimuli. The responses may be long lasting, several seconds, but are generally considered to be single responses.

A comprehensive study on spasticity was carried out by Dimitrijevic and Nathan in the late 1960s (Dimitrijevic & Nathan, 1967a, b, 1968). These studies revealed the nature of spasms within spasticity in spinal injury. Dimitrijevic and Nathan suggest that the loss of descending inhibition is critical for the generation of "spastic" activity. This loss of inhibition may lead to the exaggerated reflexes and the dis-inhibition of neural networks within the spinal cord. It is further postulated that reducing the inflow from the periphery to the cord may reduce spasticity (Dimitrijevic & Nathan, 1968). Bursting activity in muscles in response to stimulation was reported, but techniques were not available for closer analysis of this activity.

2.5. Spinal Reflexes.

Many reflexes involve a spinal loop, including the tendon-jerk and the H-reflex. In both these cases the sensory stimulus, (pseudo-natural in the tendon jerk or electrical in the H-reflex) travel up a sensory pathway before entering the spinal cord.

Within the spinal cord the sensory fibres synapse onto motor fibres, either directly or through interneurons. The motoneurons may or may not fire depending upon the strength of the input they receive from the sensory fibres and also the state of the motor cell, which will be subject to descending drive that may be either inhibitory or excitatory. A feature of spasticity is the reduction of the descending tonic inhibitory drive leading to an enhanced reflex activity as described above.

Although considered to be monosynaptic these reflexes can be modulated by the state of the subject either via descending control or through spinal segmental circuits. The amplitude of these reflexes can be changed depending upon the state of the muscle (Brooke *et al.*, 1997). There is also evidence that these reflexes can be suppressed during movement to allow smooth movement control during tasks such as locomotion (Brooke *et al.*, 1999). The same study suggested that the site for these modulatory activities is within the spinal cord itself.

In addition to these "simple" reflexes that are often considered to be monosynaptic, more complex reflexes can be generated within the spinal cord. These reflexes are polysynaptic in nature and include reflexes such as the cutaneomuscular reflex (Jenner and Stephens 1982) and long latency stretch reflexes. Although there have been a number of reports in the literature, detailed investigations into these reflexes following spinal injury have not been performed. In normal man these reflexes have been studied and they have also been investigated in patients with upper motor neuron lesions as well as in subjects with sensory neuropathy (Rothwell, 1994). The most complete studies arise from animal work, in particular studies on the cat and to a lesser extent the dog, in which focal, known lesions can be generated and more invasive monitoring and testing methods utilised. It is not known at present how far the results and conclusions from animal studies can be extrapolated into human studies.

Schomburg (Schomburg, 1990) has provided an excellent review of the supraspinal control of reflexes and of polysegmental pathways. The lumbar propriospinal neurones, in the cat at least, are involved in the transmission of signals from the rubrospinal and corticospinal tracts. This convergence and filtering action has been widely studied in the cervical enlargement, but is less well studied in the lumbar enlargement. These pathways may also be involved in the modulation of fast reflexes during movement.

Many, if not all, spinal reflexes are under some element of supraspinal control in normal subjects. Other than the mono-synaptic reflexes such as the H-reflex and the tendon jerk spinal reflexes also involve spinal interneurons. The study of the role of these interneuronal systems in man is tricky and hence most of the work has been carried out in animal models and then extrapolated to man (Jankowska & Hammar 2002). It is widely thought that the cat and human spinal interneuronal system have sufficient similarities to enable transfer of knowledge between species in many cases. Interneurones from group II muscle afferents involved in tri- or di-synaptic pathways may be involved in spasticity since they exhibit the pharmacological properities (depression by α_2 agonists) that are expected of neurones involved in stretch reflex hyperexcitability) (Jankowska & Hammar 2002). Interneurons mediating group II afferent responses are highly likely to be affected by spinal injury (and indirectly by other upper motor neuron lesions) and this disturbance of their normal function may, in part, account for some of the abnormalities seen in locomotion and posture.

One of the most widely studied reflex pathways is the flexion withdrawal reflex which has been the subject of animal and human studies in both normal and neurologically impaired subjects (Rothwell, 1994), (Sherrington, 1910). This is a polysynaptic reflex which as well as flexing the leg on the side of stimulation gives a contralateral extension reflex that serves to stabilise the subject. The responses on both the ipsilateral and contralateral legs are widespread acting at all three joints on the leg, irrespective of the site of stimulation. The stimulation site does however modify the size of the response. The sensitivity of the flexion reflex is increased in patients with spinal cord injury so that non-noxious stimuli are required to elicit the reflex. The reflex is also more widespread and may involve all joints in a limb leading to an exaggerated reflex. It is likely that these changes arise as a result of the loss of descending inhibition within the spinal cord. The widespread nature of the response has lead to its use in rehabilitation studies to promote stepping in subjects with spinal cord injury (Granat *et al.*, 1991), (Ferguson & Granat, 1992) and stroke (Burridge *et al.*, 1997b). The habituation of the reflex has also been studied in patients with upper motor neuron lesions and techniques developed to dis-habituate the reflex (Granat *et al.*, 1991). In contrast to the training of reflexes used within the FES community many physiotherapy approaches work to inhibit reflex pathways (Bromley, 1991).

Electrical stimulation of a motor nerve along its axon will result in both orthodromic and antidromic firing of the fibre. The antidromic fibre will stimulate the cell body of the motor fibre but will also stimulate *Renshaw* cells that receive innervation from the motor axon. During voluntary firing of a motor unit the cell body is depolarised and an action potential is fired along the axon. As the potential passes down the axon a collateral sprouts and synapses onto a Renshaw cell with an excitatory synapse. The Renshaw cell's axon terminates on the same motor neuron as originally fired with an inhibitory synapse. This excitatory/inhibitory combination acts to inhibit a motor neuron immediately after it has fired thereby preventing rapid repeated firing of the same cell. This process is known as *recurrent inhibition*. Not all motor neurones have Renshaw cells associated with them, with the strongest synapses and highest density occurring around the more proximal muscles, suggesting that this mechanism for controlling the firing of motor neurones is more concerned with proximal than distal control (limb vs. digit movement) (Baldissera *et al.*, 1960), (Windhorst, 1996). It is not clear to what extent the motor neurones innervating the trunk receive innervation from Renshaw cells. Recurrent inhibition has the functional effect of "limiting" the firing of the motor neurones. Renshaw cells act therefore as part of a wider gain control system for the motor neuron, but are themselves under descending control.

The actions of the Renshaw cell are comparatively long-lasting with a single excitatory input causing the cell to fire repeatedly, producing many inhibitory post-synaptic potentials, IPSPs in the motor neuron and inhibiting firing over a time course of many milliseconds (Windhorst, 1996). Renshaw cells may also project contralaterally with an excitatory connection. This bilateral inhibition and excitation is believed to be utilised in the control of bilateral reciprocal tasks such as walking (Windhorst, 1996) and see section 2.6 below.

2.6. Spinal Circuitry.

The complexity of spinal circuitry in animals is widely acknowledged by neuroscientists. Decerebrate cats can be trained to walk on treadmills and are remarkably successful at it (Barbeau *et al.*, 1999). Field-Fote has trained decerebrate turtles to do "novel" tasks such as scratching with both legs at once (Field & Stein, 1997a,b). The conventional, simplistic view of the spinal cord as simply a way of

transferring cortical command signals to the periphery cannot accommodate such complex functions.

The most popular views of the spinal circuitry that allows locomotion are the half-centre models, of which there are several variations. This collection of views was first generated by Denny-Brown (Denny-Brown, 1929), (Vilensky & Gilman, 1997) and has subsequently been developed by many neurophysiologists, notably Jankowska (Djouhri & Jankowska, 1998), (Stein *et al.*, 1999). Whilst it is unequivocal that these circuits play a major role in lower vertebrates, e.g. the lamprey, their role and even their existence in higher animals, primates and man, has been questioned (Vilensky *et al.*, 1992).

Work by Dietz and his colleagues has provided some evidence of the existence of central pattern generators in the spinal cords of humans (Dietz *et al.*, 1992, 1994, 1998, 1999). Training of these generators has been moderately successful in patients with incomplete lesions. Patients with complete lesions have shown appropriate modulation of their EMG during the gait cycle more clearly than patients with incomplete lesions but have suffered from low levels of muscle activity. Patients with higher lesions have shown better training effects than those with low lesions, supporting the view that the pattern generators are distributed throughout the spinal cord, and are not concentrated in a few segments (Dietz *et al.*, 1999). The training effects consist of an increase in muscle activity, usually assessed with surface electrodes and a change in the timing of the activity. Whilst the increase in activity may be due to training of the musculature the change in timing is widely taken to represent the training of a spinal circuit for locomotion (Dietz *et al.*, 1998).

To date the functional application of the existence of such complex spinal circuitry has not been widely felt in the field of spinal rehabilitation (Harkema *et al.*, 2000), (Behrman & Harkema, 2000). Partially this is because of the debate over whether man and high primates have as complex circuits as cats and dogs. It is likely that the optimal methods of activating the spinal cord when it is disconnected from higher centres have yet to be found. The treadmill training techniques appear to be a good method of training the spinal cord but have yet to produce functional benefits (although pilot studies from a number of centres including Glasgow have produced promising results Hasler (personal communication 2002)) and are expensive because of the clinician input required (Behrman & Harkema 2000).

Recent work has used spinal reflexes to investigate more complex spinal circuits (Barbeau *et al.*, 1999). Stimulation of these circuits appears a promising approach for FES and has been used to generate functional movements of limbs (Mushahwar *et al.*, 2000) and facilitate micturation through bladder contractions (Grill *et al.*, 1999).

To date these circuits have always been considered in the context of generating functional movements, primarily locomotion. It would seem unlikely that, if these circuits are distributed across many spinal segments (Dietz *et al.*, 1999) that they would not be damaged by the spinal injury. It would therefore be surprising if they were to produce a normal motor output (e.g. locomotion) in every case following spinal injury in man. Many of the studies on spinalised animals have utilised a spinalisation paradigm that results in a "clean", focal lesion. This is not what typically happens in a human injury (Grundy & Swain, 1996). The spread of the injury below the "level of injury" in human injuries may damage any CPGs especially if they are spread over many segments and as argued by Dietz and colleagues (1999) involve cervical segments.

2.7. Spinal Regeneration.

The spinal cord, as part of the central nervous system, is not capable of spontaneous regeneration. Many research groups are working on techniques to allow the cord to regenerate using cell-biology, biochemistry, grafting, pharmacology or other techniques (Bregman, 1998).

Central axons are capable of re-growth following lesions, but are less able than the peripheral axons. Additionally the glial scar that forms following injury inhibits even the limited cell growth (Fawcett & Asher, 1999). Recent work has suggested that the olfactory ensheathing cells may offer great hope for CNS regeneration. These cells may be considered to be halfway between peripheral and central myelinating cells and allow axon re-growth in animal models beyond the dorsal root entry zone (Franklin & Barnett, 2000). Because the adult human continues to make these cells, and the olfactory bulb neurones which they support and ensheath throughout life the possibility exists for auto transplantation, which reduces the chances of immune reactions rejecting the graft. Further work is needed before clinical trials are possible. Other methods of repairing the spinal cord are under investigation including approaches to reduce the size and extent of the scar tissue (Fawcett & Asher 1999).

2.8. Oscillatory Activity in the Motor System.

The healthy motor system produces oscillations and these have been demonstrated in the motor cortex, substantia nigra, cerebellum and peripheral EMG (Brown & Marsden 2001), (Grosse *et al.*, 2002), (Mima & Hallet 1999). Two forms of oscillatory activity are prominent in pathological motor states; tremor and clonus. Around ¼ of the normal population can evoke clonic activity in themselves and this is apparently not pathological. Clonic activity is limited in its bandwidth and although the precise mechanism is not well understood it has been the subject of much work in recent years. Clonic activity is characterised by reciprocal activity in antagonistic muscle pairs around a joint. It is still not clear whether central, i.e. a neural oscillator or peripheral, i.e. persistent and reciprocating stretch reflexes in antagonistic muscle pairs mechanisms are responsible for clonus. In the case of a central mechanism loading the limb would be expected not to alter the frequency of activity whereas in a peripheral mechanism such a procedure would decrease the frequency. Studies have revealed both outcomes to date (Beres-Jones *et al.*, 2003). Rymer and colleagues (Hidler & Rymer, 1999, 2000) have made an extensive study recently of the mechanisms of clonus using simple engineering analysis to determine an origin. This work follows the work of Dimitrijevic and Nathan in the late 1970s (Dimitrijevic *et al.*, 1980). In Dimitrijevic's study the range of clonus is defined as 5-8Hz, although the average was 5.3Hz whilst the Rymer studies found clonus between 3.5 and 5.8Hz with both studies looking at the ankle joint. Dimitrijevic was looking specifically at the ankle although he does argue that the results apply across the rest of the body. Dimitrijevic was unable to alter the frequency of the activity within a single patient by more than 0.7Hz suggesting a fixed mechanism for the rhythm. Dimitrijevic's study concluded that central mechanisms play the major role in clonus (i.e. that clonus was generated by a collection of neurones within the spinal cord). However the Rymer studies propose that the peripheral mechanisms are more important (i.e. that clonus arises as a result of reciprocal activation of antagonistic stretch reflexes) and that through a change in firing threshold within the stretch reflex pathway can explain clonus. Hidler and Rymer (Hidler & Rymer, 1999) suggest that this change in firing pattern may appear similar to a central oscillator. Rymer's study is a simulation study, whilst the work of Dimitrijevic was more clinical in nature. Rymer's subsequent study (Hidler & Rymer, 2000) was more clinical and had similar conclusions to his first.

The most striking difference between the two studies is the frequency range reported. The results from both studies actually show considerable overlap in frequency (~5-6Hz) and more recent studies have also reported clonus within the 3-6Hz range with the frequency being heavily influenced by the path length (Deuschl *et al* 2001), (Rothwell, 1994) but not linearly dependent upon it. This suggests that the peripheral mechanism is more likely to be correct, but that there is some central delay indicative of processing. Clonic activity is an area worthy of further research particularly as many patients (those with stroke and MS) report it as a major hindrance to their daily lives.

Tremor is a broad term that covers a spectrum of rhythmic activity with a range of frequencies. A number of tremors are found in normal subjects, e.g. physiological tremor and therefore not all tremor is considered pathological. A number of recent reviews of tremor have been provided by McAuley and Marsden (McAuley & Marsden, 2000), and Deuschl and colleagues (Deuschl *et al.*, 2001), (Deuschl & Bergman, 2002). Although clonic activity is normally evoked by a specific event, such as a rapid ankle movement, tremor arises spontaneously or with movement, intention to move or changes in posture. Tremors may be peripheral or central in origin with the peripheral tremors showing changes in frequency with changes in the biomechanical properties of the limb. Central tremors in contrast have a fixed frequency irrespective of the biomechanical properties. Central tremors are thought to arise from an oscillating neural network. The location of these networks is uncertain, but many of them are thought to be located in the sub-cortical motor regions (McAuley & Marsden, 2000).

Tremors can be altered by the patient's level of stress, pharmacological agents (particularly alcohol) and their posture. A prime example of a tremor that is posture dependent is primary orthostatic tremor, (Fung *et al.*, 2001). This tremor manifests clinically as a subjective feeling of unsteadiness when standing and can be observed as regular spikes in the surface EMG at a frequency of 16Hz. This feeling is removed when the patient starts to step, and the oscillations in the EMG of a limb disappears when the limb is unloaded. There is no mechanical oscillation in these patients at 16Hz, but the tremor does drop to 8Hz at times and a mechanical oscillation is detectable with an accelerometer. Recent work by Brown has suggested that a 16Hz tremor may be detectable in normal subjects when they are positioned in an unstable

posture (Sharrott *et al* 2003). This tremor may originate within the posterior fossa (Wu *et al.*, 2001).

Oscillatory activity is found widely in both the normal and pathological motor system including the motor cortex (Grosse *et al* 2002), thalamus and cerebellum. Oscillatory activity has also been reported in the neonatal rat spinal cord where it is believed to play a role in motor development (Demir *et al* 2002).

2.9. Functional Electrical Stimulation.

Functional Electrical Stimulation, FES, is a technique for the restoration of muscle function following neurological damage (Rushton, 1997). Damage to upper motor neurones may result in the inability to control a limb(s). However the lower motor neurones may remain intact and capable of carrying action potentials required for muscle contraction. FES provides a method to initiate the action potentials. Artificially generated action potentials, such as those initiated by FES, are in many ways indistinguishable from "natural" action potentials. Action potentials in the periphery are *all or nothing* responses. Therefore outside the region of the direct stimulation the action potential will be identical spatially and temporally to "normal" action potentials. The most fundamental difference between natural action potentials and those generated through FES concerns the timing of the potentials. In a voluntary contraction the axons will fire asynchronously to produce a smooth sustained contraction. In FES-induced nerve firing the axons fire synchronously. This has the potential to lead to more variations in force than during a voluntary contraction as distinct volleys of nerve signals arrive compared to the continuous signal naturally. The low-pass filter characteristics of the muscle act to reduce this variation. Stimulation is generally given at a rate, usually between 20 and 40Hz (Rushton, 1997) which is above that required to generate a smooth, tetanic muscle contraction. These stimulation rates are typically faster than would occur in a normal muscle contraction, (~15Hz for a single fibre) (Rothwell, 1994).

At sub-maximal stimulation levels there is a gradual recruitment of nerve fibres as the intensity of stimulation is increased. Large fibres are recruited before smaller fibres. This is classed as *reverse recruitment* as it is the reverse of the recruitment pattern of normal, voluntary contractions in which the smaller fibres innervating the smaller motor units are recruited first (Rothwell, 1994). The large

nerve fibres innervate fast fatigable muscle in normal subjects. Training can change the fibre type, but fatigue remains a clinical problem with most neuroprosthetic devices (Barr *et al.*, 1990). Fatigue is a further problem because of the conversion of many or all of the muscle fibres to a fatigable type following the injury.

One of the most successful FES devices is the implanted sacral nerve root stimulator developed by Brindley and colleagues (Brindley *et al.*, 1982) with over 2000 users at the time of writing (Information supplied by Finetech Medical Ltd, Welwyn Garden City, UK). The device is known as the Sacral Anterior Root Stimulator (SARSI). In this system the nerve roots are placed in cuff electrodes that are connected to a stimulator that is implanted on the chest wall. The stimulator is powered and controlled through an RF (radio frequency) inductive link. Implanting electrodes whether intra or extra durally, as in SARSI, with a stimulator on the chest wall has proved very successful, with a low failure rate compared to other implant techniques (Brindley 1995). A major limiting factor in its take-up more recently is the requirement that the posterior, sensory, roots are cut to prevent bladder reflexes (Craggs, personal communication).

In the LARSI project, (Lumbo-sacral Anterior Root Stimulator Implant) the lumbar roots are stimulated in addition to the upper sacral roots (Donaldson *et al.*, 1997). The aim of this work is to restore leg function to paraplegics. To date two such implantations have taken place and one experiment in this report was performed on subject 1 with the LARSI. The subject with the 1st implant has stood for over 3 minutes, taken 24 steps and cycled on a modified trike over 1km at over 11km/h (Perkins *et al.*, 1999). However the posture of the subject remains poor despite many attempts to optimise the muscle training. An initial aim of this study was to investigate the reasons for this poor posture.

2.10. FES-Assisted Paraplegic Standing.

Paraplegics with lesions above the T12 spinal level will have many of their lower motoneurons intact. Patients who maintain some level of trunk control, i.e. are not tetraplegics or very high paraplegics may be able to stand using FES using their upper limbs for support. The simplest method to achieve this is through stimulation of the quadriceps muscles by surface electrodes, (i.e. electrodes stuck to the skin overlying the muscles). Stimulation can also be applied to other muscle groups,

(glutei, hamstrings, tibialis anterior etc) but patient compliance is best when only a small number of muscles are stimulated (Wood, 2002 personal communication).

The use of electrical stimulation to assist paraplegics to stand arose from work in Ljubjana, Yugoslavia, (now Slovenia) led by Kralj and Bajd in the 1960's. Since then a number of groups have developed systems to assist paraplegic standing. The effects of endogenous activity within the spinal cord on the posture achieved using FES-assisted standing has been little studied and much of the work done by engineers has taken a simple cable and actuator approach. The work of Kralj and Bajd is one exception (Kralj & Bajd, 1989) although the role of spasticity is discussed the postural effects only get a sentence stating that "Upright posture, for example, doubles the tone of the extensor muscles over that found in the supine patient" p38.

Surface systems have the advantage that they are less invasive, but require external components that must be donned and doffed before and after use. This limits the compliance of the patients and this is one reason for restricting the number of electrodes used. One alternative to allow more electrodes to be used is the use of "electrode garments" which are sometimes used in FES-cycling programmes. The electrode garments have the electrodes sewn into a Lycra or similar item of clothing so that the electrodes are always located in a similar place. This can result in an 80% reduction in donning and doffing time (Perkins, personal communication).

Implanted systems require a greater commitment on the part of the patient, but following surgery the system is quicker to use. A fundamental question for implanted systems is the sighting of the electrodes. The majority of studies have implanted peripherally, essentially using the same approach as the surface systems. This is an area which will become increasingly important in the future.

The benefits to the patient in standing are thought to include an increase in muscle bulk, (with an accompanying increase in limb blood flow and reduction in the risk of pressure sores, especially if the glutei are stimulated), increase stressing of the leg long bones, (leading to a reduction in the rate of mineral loss), and improvements in the functioning of a number of internal organs, (bladder, liver, etc) (Grundy & Swain, 1996). Stefanovska (Stefanovska *et al.*, 1989) reports a decrease in tonic spasticity with use of FES. The tonic spasticity is that present when the tonic component of the stretch reflex predominates over the phasic component. This is an imprecise definition and it is unclear precisely what this decrease in spasticity represents. This decrease may be associated with a decrease in the number of spasms,

although because of the increase in muscle strength and bulk the individual spasms may be stronger. Singer (1987) reports in his review on 4 papers that have used FES to alter spasticity. The results are most striking for their variability. However all of the spinal patients in his review showed some decrease in spasticity. These reports have concentrated on what is termed in this thesis as spasticity as opposed to spasms. This review suggests that there may be fundamental differences between spasticity arising from different pathologies, although there are many other reasons that might explain the differences observed here.

Paraplegics have reduced balance control whilst standing because of their lack of voluntary control of the trunk and leg musculature. Despite attempts at producing controllers to allow hand-free standing (Hunt *et al.*, 1998), (Munih *et al.*, 1997) all the take-home techniques thus far have required the patient to stabilise themselves using at least one hand on a support structure. Figure 2.2 shows a patient from Ljubjana standing in "functional" settings using electrical stimulation whilst having to retain one hand for support.

Figure 2.2. Left) A patient standing at a bar with a drink in one hand and using the other hand for support. Right) the same patient standing with single hand support in a kitchen. Both of these tasks would be considered functional. In both cases the stimulator can be seen slung around the neck of the patient, but the electrodes are hidden beneath the trousers. The stimulation is under open-loop control. Both figures are from Kralj and Bajd (1989).

Functional paraplegic standing is a difficult concept to define. At present the systems in clinical and experimental use require external sensors and at least one hand to be used to maintain balance. This is not functional except for a small number of

tasks in a small proportion of the population. Patients must see a benefit in standing if they are to continue standing and for many of them it appears that a perceived long-term health benefit is not sufficient (Donaldson *et al.*, 2002b). In order to allow more patients to participate in functional standing programmes a better understanding of their spasms, which are a significant reason for non-participation, is needed, which this thesis aims to provide.

In the UK, the Salisbury group use a simple PID, (proportional, integral and derivative) controller based around the knee angle to control the level of stimulation to the quadriceps (and glutei for some patients). The controller is briefly described elsewhere (Wood *et al.*, 1998). Stimulation is kept at a preset minimum level once the patient is upright. Stimulation is increased in response to changes in knee angle, i.e. as the knee flexes. The amount of increase is determined by the weightings given to each of the terms in the controller, which are decided empirically by the clinical engineer (D.Wood in Salisbury). In clinical practice this relatively simple control strategy works sufficiently well to enable 31 patients to stand using the system with 20 using it at home. Figure 2.3 shows a patient standing using this system in the laboratory at Salisbury Hospital. This patient in common with many in the UK requires two hands for postural support.

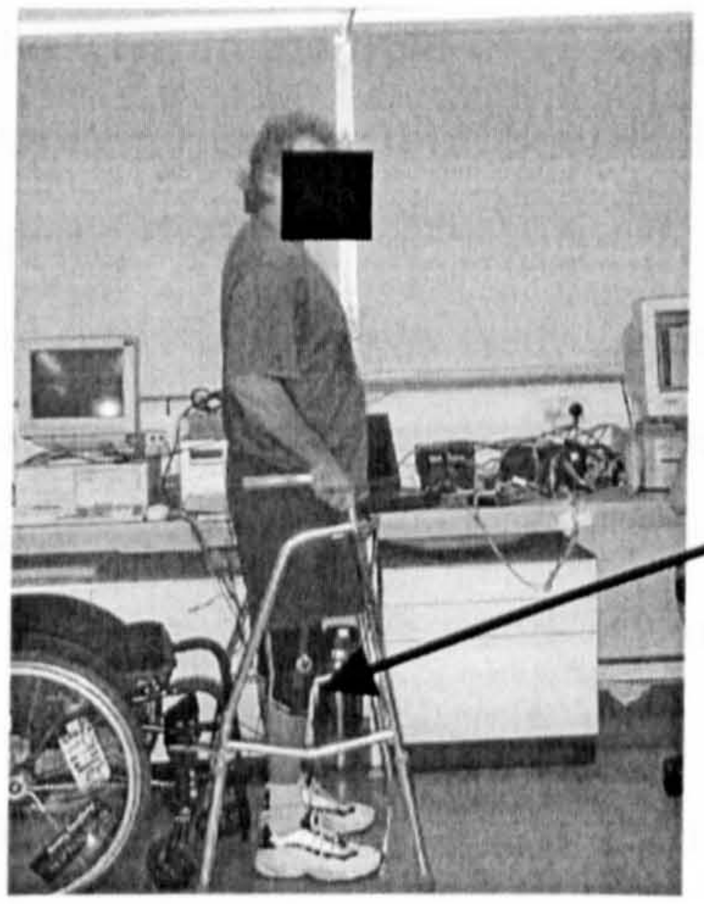


Figure 2.3. A patient standing using the closed-loop PID knee controller system. The electrodes are hidden beneath his shorts and he uses two hands for balance, although he is able to stand using only one hand in periods when he does not spasm. The knee cuffs with the goniometers are visible.

In open-loop control a member of the experimental team controls the stimulation whereas in closed-loop control the stimulation is controlled by the

micoprocessor within the stimulator. The closed-loop control strategy is based upon the measurement of some parameter of the stand, in the Salisbury system this is knee angle. The advantages of closed-loop control of the stimulation include keeping the stimulation levels to a minimum so that when disturbances arise there is spare capacity. The benefits of controllers and how they might be integrated with the intact nervous system was the subject of special issue of the *IEEE Transactions of Rehabilitation Engineering* (*IEEE Trans Rehab Eng, 6(2) 1998*) and falls outside the scope of this thesis.

2.11.Some Comments on Current FES Theories.

Research into FES for standing and walking has traditionally been carried out by engineers. In general, FES has been regarded as an orthosis or brace for paralysed joints in the patient. Some of the earlier papers call the devices "braces" (e.g. see Merletti *et al* in (Taylor *et al.*, 1999)). The traditional view has been that of an engineering model, with motors, the muscles and cables, the nerves. Stimulation of nerve causes a contraction of the muscle and results in a movement of the joint. The use of the flexion reflex to aid in gait for paraplegics (Granit & Rutledge, 1960) is an exception to this general rule. Recently there has been a tendency for engineers to recognise a larger role for the CNS in the field of FES, and a wider range of scientists and clinicians are actively working in the field. Such collaborations are now thought essential (Burridge & Ladouceur, 2001)

This simplistic model described above assumes no ongoing, underlying neural activity, or neural consequence of the stimulation other than muscle contraction, (hereafter described as the *M-wave response*). The majority of the FES standing programmes for spinally injured patients, and even many of the "simpler" programmes such as dropped foot stimulation, exclude patients with spasticity and spasms. This may even be the case when the method is in clinical use, rather than just in preliminary experiments.

In general the historically accepted theories make little or no reference to the nervous system, other than as a conductor to the muscle from the site of stimulation, e.g. (Popovic *et al.*, 1989). One of the aims of this study therefore is to assess the validity of this assumption, (conscious or unconscious) for FES-assisted standing for patients with complete paraplegia.

Chapter 3.

Methods and Materials for Biomechanical and Neurophysiological Assessment of FES-assisted and Passive Standing in Paraplegics.

3.1. Introduction.

This chapter describes the methodology employed in this study. The methodology falls into two sections; electrophysiological and biomechanical. The electrophysiological methodology describes the equipment used to record the EMG signals and the techniques used to analyse the data. Temporal and spectral analysis was used to identify relationships between EMG signals in different muscle groups and compare relationships between conditions.

The biomechanical data was recorded with the patient recumbent in the Multi-Moment Chair System and standing with and/or without FES using force plates, instrumented handles and position measuring systems as appropriate. During FES-assisted standing the hip joint extension moment was calculated in both static and dynamic phases of standing, e.g. steady standing and the sit-to-stand respectively. The effects of endogenous spinal activity are likely to be small and so a clear understanding of the errors arising within the system for measuring the joint moments is needed.

3.2. Joint Moments During Standing.

The hip joint extension/flexion moment is hereafter referred to as the hip extension moment with negative moments being used to signify a flexion moment.

To simplify the equations the patient is considered as a half-man with one leg and arm, the validity of this simplification will be discussed in subsequent chapters. There are two points of support for the patient during supported standing, the foot and hand. The hand is constrained on the handle and can generate turning moments in addition to forces in each of three planes. In normal standing the foot is free and therefore generates forces in each of three planes and there is a resultant point of application of the forces. A representation of this arrangement is shown in figure 3.1.

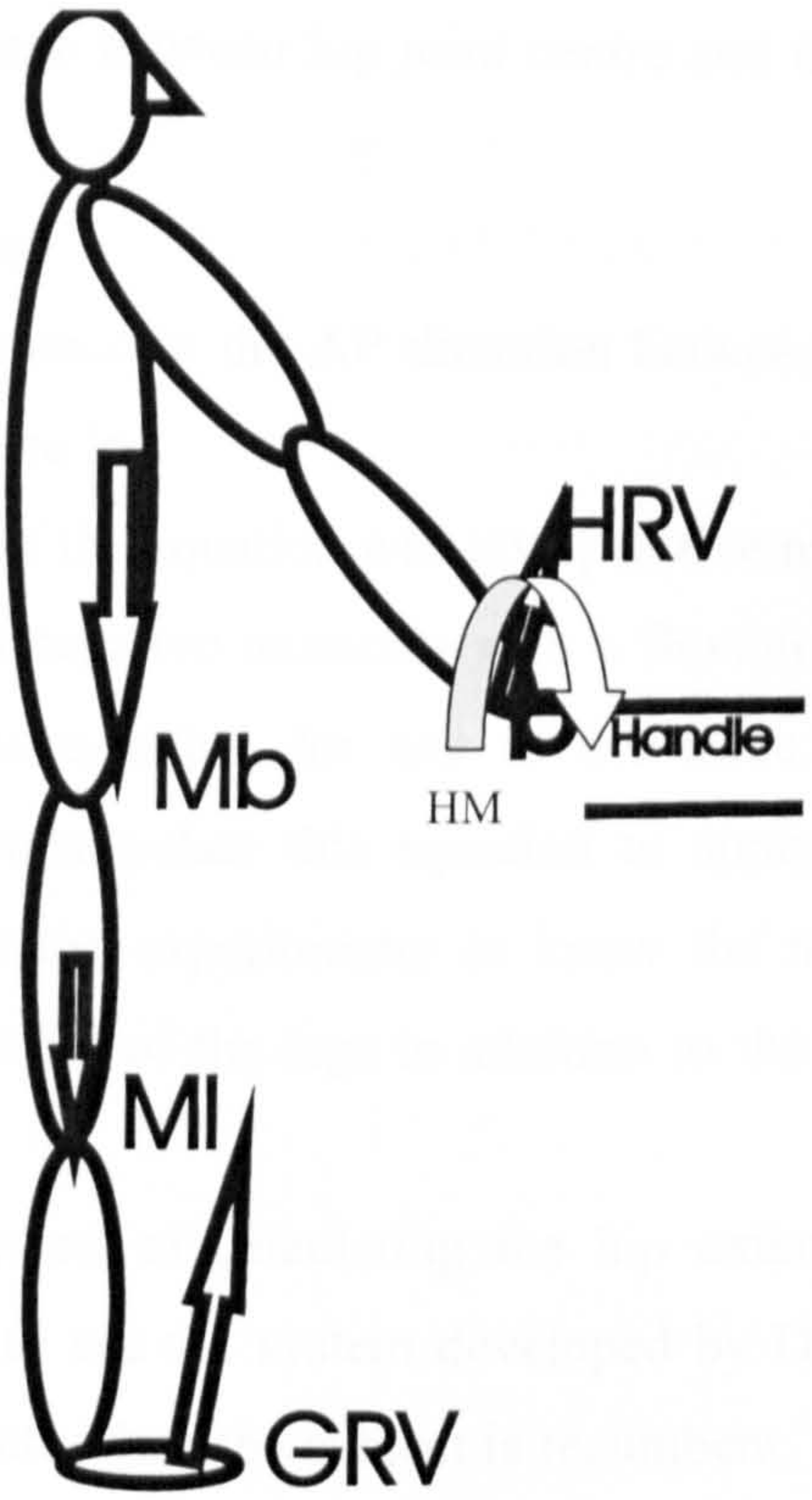


Figure 3.1. A subject standing using handles for support. The mass of the subject is made of two components, the mass of the leg (Ml) acting through the centre of mass of the leg and the mass of the rest of the body (Mb) acting through the centre of mass of the HAT. Reaction forces at the hands (HRV) and ground (GRV) balance these forces so that the subject is stable. The hands also generate a moment about the handle (HM).

To calculate the hip extension moment from the ground up the mass of the legs needs to be known as does the centre of mass of the legs. From the force plates the reaction vector at the ground, GRV, can be measured and split into orthogonal components and the point of application recorded.

The equation to calculate the hip extension moment when the body is static is (based upon (Winter, 1990));

$$He = (GRVhor \times dv) + (GRVvert \times dg) - (Ml \times dh) \quad \text{(eq3.1)}$$

where; He= hip extension moment.

GRVvert = the vertical component of the ground reaction vector.

GRVhor = the horizontal, in the AP direction, component of the ground reaction vector.

dg = horizontal distance in the AP direction between the hip joint centre and the point of application of the GRV.

dl = vertical distance between hip joint centre and the point of application of the GRV.

Ml= mass of the leg.

dh= horizontal distance in the AP direction between the hip joint centre and the centre of mass of the leg.

This arrangement of the equation will give positive moments when the hip has an extension moment and negative moments with a flexion moment. Rearrangement can be performed to this equation for any of the three hip moments and it is comparatively simple to manipulate this equation to apply to the knee joint. This method therefore requires the experimenter to know the mass of the legs and the location of the centre of mass of the legs in addition to the location of the hip joint centre.

An alternative method of calculating the hip extension moment when the subject is not standing is to use the system developed by Donaldson and colleagues for measuring joint moments when the subject is recumbent, the Multi-Moment Chair System, MMCS (Donaldson *et al.*, 1999), (Wood *et al.*, 1999).

During static standing there should be no net joint moment, so any moment generated from the ground up, e.g. by the stimulated legs and "spastic" activity in the case of FES-assisted standing, must be counterbalanced by moments generated by the hands. The hands therefore compensate for deficits in the leg joint moments. Yu and Donaldson (Yu, 1999), (Donaldson & Yu, 1998) developed this into the concept of *leg joint deficits* in their study of paraplegic standing. Leg joint deficits were used as the control signal for their work on the CHRELMS (Control by Handle REactions of Leg Muscle Stimulation) (Donaldson & Yu, 2000).

The two force components of the handle reaction vector in the plane of interest can be combined to give a single reaction vector, as in figure 3.1. Conventionally this vector is drawn originating from the point of application of the forces. This does not include any representation of the moment. In the leg joint deficit representation the vector is drawn offset from the point of application of the forces along a line that is perpendicular to the vector. The distance along this line is determined by the size of the moment divided by the force, (i.e. a moment of 15Nm and a force of 150N would result in an offset of 0.1m). In mechanics it is common to conceptually replace a single force acting at a distance from the centre of object as a force and a moment acting on the centre of the object. The leg joint deficits system works in the reverse

manner and is termed a *resultant force* (Meriam & Kraige, 1998). The vector can then be drawn on the same figure as a stick figure representation of the patient. The vector will pass in front of, behind or through each of the leg joints and its action, (extension or flexion) can be visualised. To calculate the moment generated by this vector the horizontal distance between the vector and the joint centre is multiplied by the size of the vector, (i.e. the force). The calculation of the leg joint deficit also therefore requires knowledge about the position of the joints in relation to the handles. When there is a large moment and a small force the vector is offset by a large distance and the benefits of this representation are greatly diminished. In practice this was not a problem in the CHRELMS study (Donaldson, personal communication).

Leg joint deficits, and joint moments as calculated here, are only valid when the patient is static. During movements, such as sit-to-stand, the static equations should be replaced by dynamic equations. During the CHRELMS study this was not done, and the satisfactory results from that study (Donaldson & Yu, 2000) suggest that is a reasonable assumption to use quasi-static equations for the sit-to-stand.

3.3. Multi-Moment Chair System.

The Multi-Moment Chair System, MMCS, is a device designed to measure isometric joint moments around the axes seven degrees of freedom of each leg. A brief description of the MMCS is given. The MMCS is similar to a "dentist's" chair with an adjustable back rest that can be moved from near vertical to near horizontal. The seat and the backrest are padded to prevent excess pressure and there are shoulder and waist straps to hold the patient in place. The feet of the patient are placed into individual "footboxes" that are mounted on a custom build 6-axis load cell. Each of the footboxes can slide independently and then be locked into position allowing for subjects with an effective leg length discrepancy. The knees are held in place using supporting struts on single axis load cells and lateral motion is prevented through the use of foam padding. The height of the chair can be adjusted allowing the subject's thighs to be horizontal during the recumbent tests.

The Multi-Moment Chair System, MMCS, has been previously described elsewhere (Donaldson *et al.*, 1999) and (Wood *et al.*, 1999). The MMCS is currently housed in Salisbury District Hospital and experiments were performed there on separate occasions to the standing experiments. The MMCS is designed to record the joint moments generated as a result of electrical stimulation. This is not the same as

the total joint moment. The joint moment generated by electrical stimulation is referred to as the differential joint moment and the total joint moment is called the absolute joint moment. The total joint moment during electrical stimulation comprises the muscle activity due to stimulation, muscle activity not due to electrical stimulation and the passive structure of the joint. The MMCS will only measure the effects of the electrical stimulation in its normal operating mode. In this mode the patient is placed into the MMCS and strapped in. The offsets are then removed prior to the onset of stimulation, but any motor effects that are ongoing as a result of being in the MMCS will be removed from the records because of this process. These effects will include both direct M-wave responses as well as reflex and other muscle activity. The MMCS measures isometric joint moments whilst the patient is recumbent with the angles at the hip, knee and ankle being able to be fixed by the user. The footboxes are mounted on slides so that the pressure on the soles of the feet, equivalent to the forces generated during standing, is not accurately replicated. This means that postural support reactions are unlikely to be seen in the MMCS. The MMCS is designed to record the isometric joint moments. To prevent excessive shear forces and pressure on the leg at the support points some padding is provided and this means that movement is inevitable and hence the moments are not truly isometric.

The normal mode of operation for the MMCS is the *differential* mode. In this mode the patient is placed in the MMCS and positioned with the joints at the required angles. Offsets are taken with the patient in position and the stimulation applied. Hence the MMCS measures the difference between the joint moments during stimulation and without stimulation. During the experiments described in this thesis the MMCS was used in *absolute* mode with offsets taken before the patient got into the chair. This allowed the joint moments without stimulation to be recorded in addition to the effects of the stimulation. To accommodate this change the amplifiers on the MMCS were given a negative offset prior to the patient entering the MMCS.

During a recording session with the MMCS the hip joint angle is measured using a Penny and Giles (Penny and Giles, Dorset, UK) goinometer. The goinometer is used during standing to enable a hip angle during "normal" standing to be measured. This allows greater accuracy when comparing the hip angles between standing and the MMCS than when using the standard MMCS measurements. Data is stored on a Teac 145TD digital tape recorder for subsequent analysis in Matlab. The data is sampled at 1 kHz using the Matlab Data Acquisition toolbox.

Data from the MMCS is analysed off-line using custom written scripts in Matlab, to calculate and display the joint moments, in a manner similar to that previously described by Wood and colleagues (Wood *et al.*, 1999).

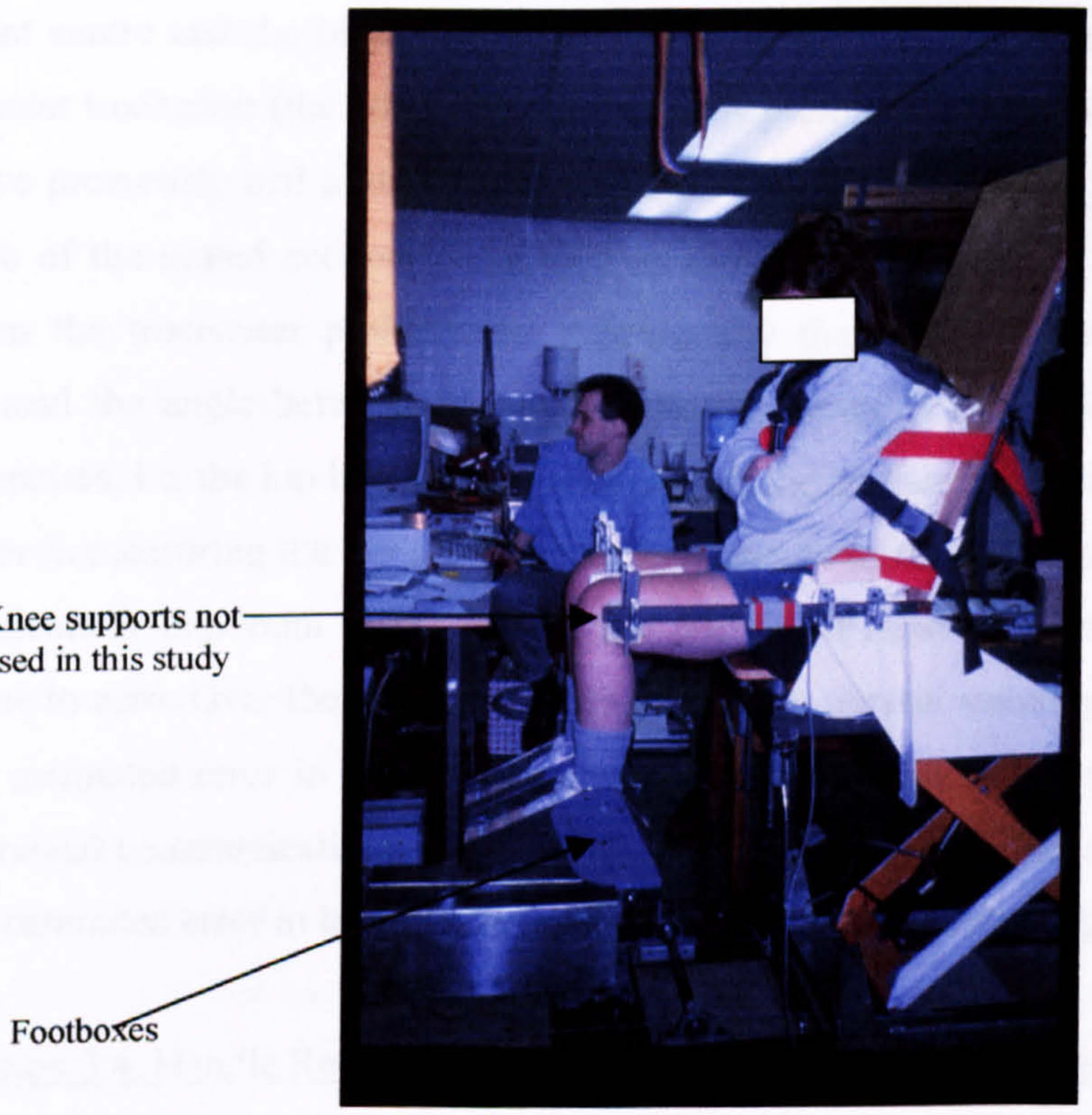


Figure 3.2. The Multi-Moment Chair System. In this figure the system is set to measure moments with the knees flexed. The footboxes are visible as the large blue objects in the bottom at the centre of the figure. The back of the chair is set to be near vertical, i.e. in a normal sitting position. Note that the patient is securely strapped into the MMCS, but that the large amount of padding required will allow some movement.

The errors in the MMCS are set out in the 1999 papers by Donaldson, Wood and colleagues (Donaldson *et al.*, 1999), (Wood *et al.*, 1999). However, the papers only describe the condition when relative joint moments are measured, that is the effects of stimulation. Transducer and amplifier linearity is assumed within the MMCS (Donaldson *et al.*, 1999). If this is not the case then the errors may be increased. To ensure that the amplifiers remain within their normal, calibrated and

validated operating range when measuring the joint moments they are offset prior to testing.

The errors calculated in Wood *et al* (1999) are up to ±5Nm for the hip extension and ±1Nm for the ankle planterflexion. The Wood *et al* paper describes the response of the transducers but not some of the more practical sources of error that arise during use of the MMCS. A major problem arises with the location of the hip joint centre and the hip angle. The location of the hip joint centre in relation to the greater trochanter (the most easily found bony prominence) is known for patients who have previously had a 3D scan and x-ray. The MMCS has a large metal plate at the side of the seated section in addition to some metal bolts etc. This makes locating even the trochanter problematic. Additionally the hip angle cannot be measured. Instead the angle between the hip and lumbar spine is recorded. As the hip angle decreases, i.e. the hip becomes more extended, the amount of pelvic tilt increases. The error in measuring the hip angle therefore increases as the hip angle decreases. This is particularly important since the standing posture of most patients has a hip angle of close to zero. Over the range of hip angles seen in normal standing within this project the estimated error in the measurement of the hip angle within the MMCS is ±10° (personal communications, Perkins and Wood). This value is obtained by combining the estimated error in locating the joint centre, femoral axis and angle at pelvis.

Section 3.4. Handle Reaction Vectors, Ground Reaction Vectors and Posture.

This section describes the instrumentation used to assess posture during standing experiments. It consists of a pair of Kistler force plates to measure the forces and moments applied at the feet, a pair of instrumented handles, (JR3 or custom-made (www.jr3.com JR3, CA, USA or Yu 1999)) and a 3D position measuring system (Selspot or CODA).

The recording of the joint positions and the posture of the patient in 3D space was accomplished using one of two systems, Selspot (Selspot AB, Sweden), (for patients 1 & 3) and CODA (Charnwood Dynamics, Leicestershire, UK), (for all other patients). These two systems give equivalent data. Both systems work by using active markers placed on the skin which are detected by "cameras". The methods of data capture are very different for each system and are not fully discussed. When using the Selspot system data was only captured from one side of the body, whilst bilateral data was collected with the newer CODA system. The CODA system uses up to 56 LEDs

in a single collection. Each LED is plugged into a "control box" which contains a battery to power the LED and is numbered. Boxes can hold either 2 or 8 LEDs. Each LED is therefore given a unique number, which determines when in the strobe cycle it flashes. The CODA then strobes across all 56 possible markers and records the position of any markers within its field of view. The CODA interface is used to allocate positions for each marker (e.g. marker 1 right knee, marker 2 left knee...). Each strobe of the markers takes less than 1ms and so is effectively simultaneous for motion analysis.

The instrumented handles are custom made handles (made by the UCL Medical Physics workshop to a design by the author). These are placed on smooth metal plates that are bolted onto JR3 6-axis load cells. The load cells are powered from the mains and have pre-built strain-gauge amplifiers supplied with them. The output from the amplifiers was fed directly into the PC's AD card and was sampled using the CODA interface. The outputs from the load cells are 6 channels of data which, using a supplied calibration matrix for each cell can be converted to the forces and moments seen about each of 3 pre-defined axes by the cell. Since in this application forces and moments would a) be applied at a distance from the origin of the cell and b) have an offset due to the metal handles additional matrices were calculated for each load cell to allow the forces and moments applied at the centre of the handle to be measured. These new matrices were generated using Matlab (Mathworks, Cambridgeshire, UK). Validation experiments were again carried out using the force plates as references. The signals from the transducers were stable with standard deviations of 2% for one transducer and 1% for the other. The calculated and measured forces and moments agreed very well with differences of less than 1% for both transducers and again the original calibration matrices were used. The results from the calibration and validation of the handles are also included in appendix 1. The responses from the JR3 loadcells are stable with drift of under 2% over a 8 hour session, in line with the manufacturers description.

The handle reaction vector is the sum of the three handle forces and three handle moments. The patient has voluntary control over these forces and moments and generates them to maintain balance and to give external support. The patient may generate more supporting forces than are necessary because they are unaware of the state of their lower body below the lesion. However the vertical forces at the handles

and the vertical forces at the feet will add up to the body weight in a stable, i.e. static, situation.

For both the force plates and the instrumented handles, (both types) the outputs from the transducers are voltages. In the first stage of processing offsets are removed. The resulting voltages are then multiplied within matrices to give forces and moments. The force plate system is entirely self-contained and when integrated into the CODA motion analysis set-up gives forces and moments about each of the three axes automatically. These outputs were calibrated by the manufacturer. Simple validation experiments were performed to confirm the accuracy of the supplied calibration equations. Pure forces, and combined forces and moments using known masses and moment arms were applied at known positions on the plates. The calculated results and generated results were very similar with differences of less than 2.5% over the full range of loads applied. No systematic differences were detected and the errors were randomly distributed either side of the "true" result. The two force plates were also compared. Again the differences were not systematic and appeared random and were very small, (<1.5%) in any direction. It was therefore decided to use the pre-supplied calibration software. The force plates are supplied with charge amplifiers. This type of amplifier is subject to a slow baseline drift. The drift of a force plate amplifier is shown in figure 3.3 in which the plate was loaded with a nominal 10kg weight. To counteract this drift the plates are "reset" after every one or two stands.

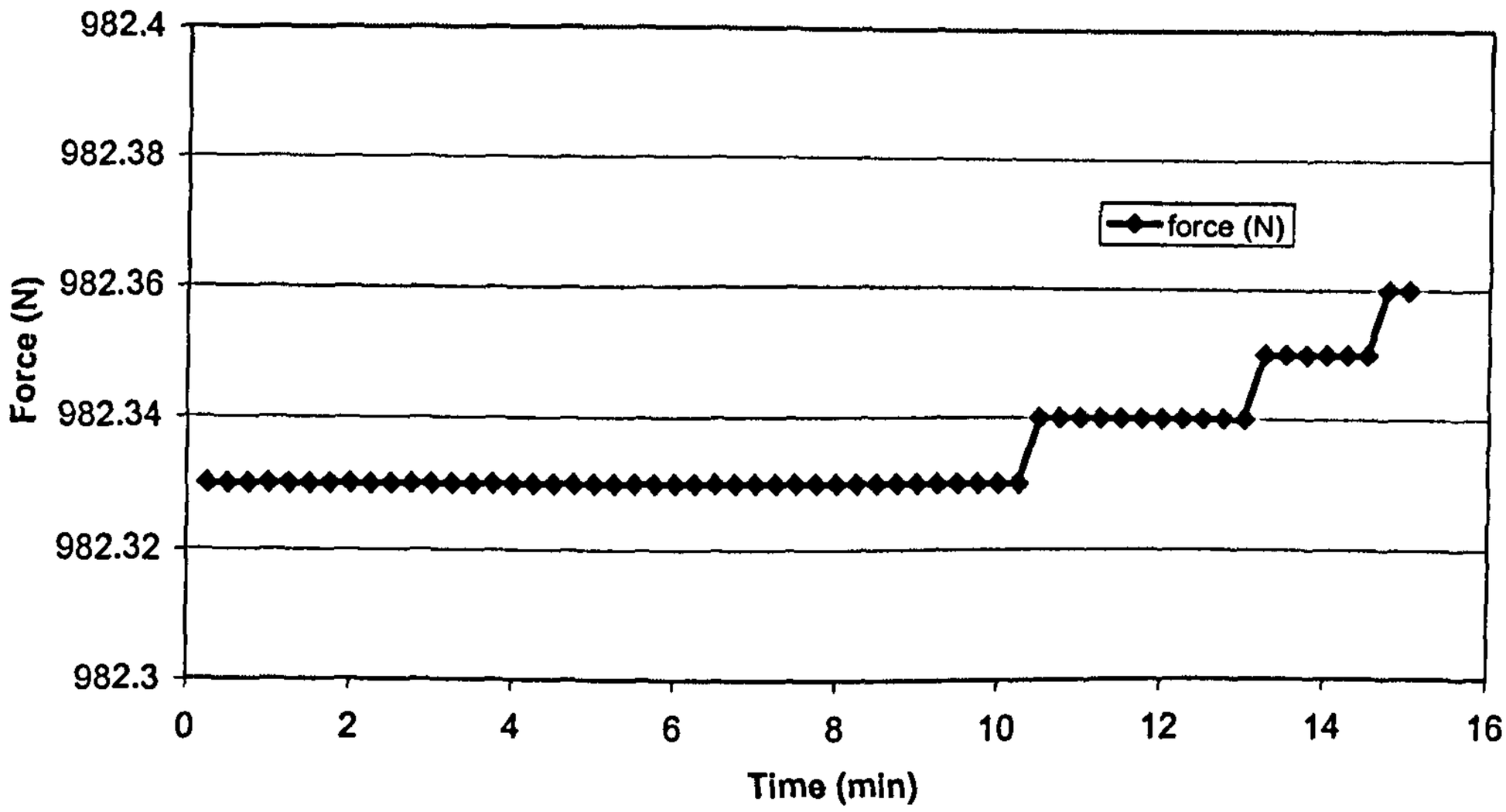


Figure 3.3. The drift of the force plate signals with time when loaded with a nominal 10Kg. Force plates were reset every 5 minutes during the experiments. Even after 15 minutes the drift is only 0.03N.

Prior to each experimental session the CODA system or the Selspot II system is calibrated. This is done using the methods described in the relevant manual. For the Selspot this was done by placing a calibration frame in the field of view at a known position and adjusting the lighting and angle of the cameras to minimise the rms errors (these were automatically calculated in the Selspot software). The CODA system is calibrated by placing two perpendicular lines of LEDs to define a plane. The origin of the coordinate system is then marked using a separate LED. Although the CODA system then checks the errors in position the system was also validated using LEDs at known positions. The calibration is performed in two dimensions on the force plates for the CODA system. The errors in position are a mixture of systematic and random errors. The errors are smaller as the position approaches the position of the calibration grid. Therefore head positions have the greatest error in all three dimensions. At a height of 1.8m this error is up to ±1cm and at hip height it is up to ±0.4cm in each direction.

Figure 3.4 shows the laboratory in a typical set-up for an experiment as described in this thesis. In this instance the patient is wearing knee cuffs, which act as the control signal source for the closed-loop stands that were not part of this study.

Two CODA *boxes* can be seen in the front right of the picture and in the right background of the figure. The patient stands with one leg on each force plate using the handles for support and balance control. The engineer sits in front of the patient to control the stimulation and brace the knees if the patient starts to collapse due to knee buckling. LEDs are placed on the patient and surface EMG (Ag/AgCl) electrodes (Nicolet, Conshohocken, PA, USA) with a pre-amplification of 1000 placed over the major lower leg muscle groups (quadriceps, tibialis anterior and gastrocnemius/solues) as well as over the glutei or paraspinals in some patients. The electrodes are pre-gelled and mounted on an adhesive backing that extends beyond the electrode surface area and is used to fixt the electrodes to the skin. Electrodes are not placed on the hamstrings because experience indicated that these were prone to becoming dislodged during the sit-to-stand, presumably because of being rubbed against the plinth.

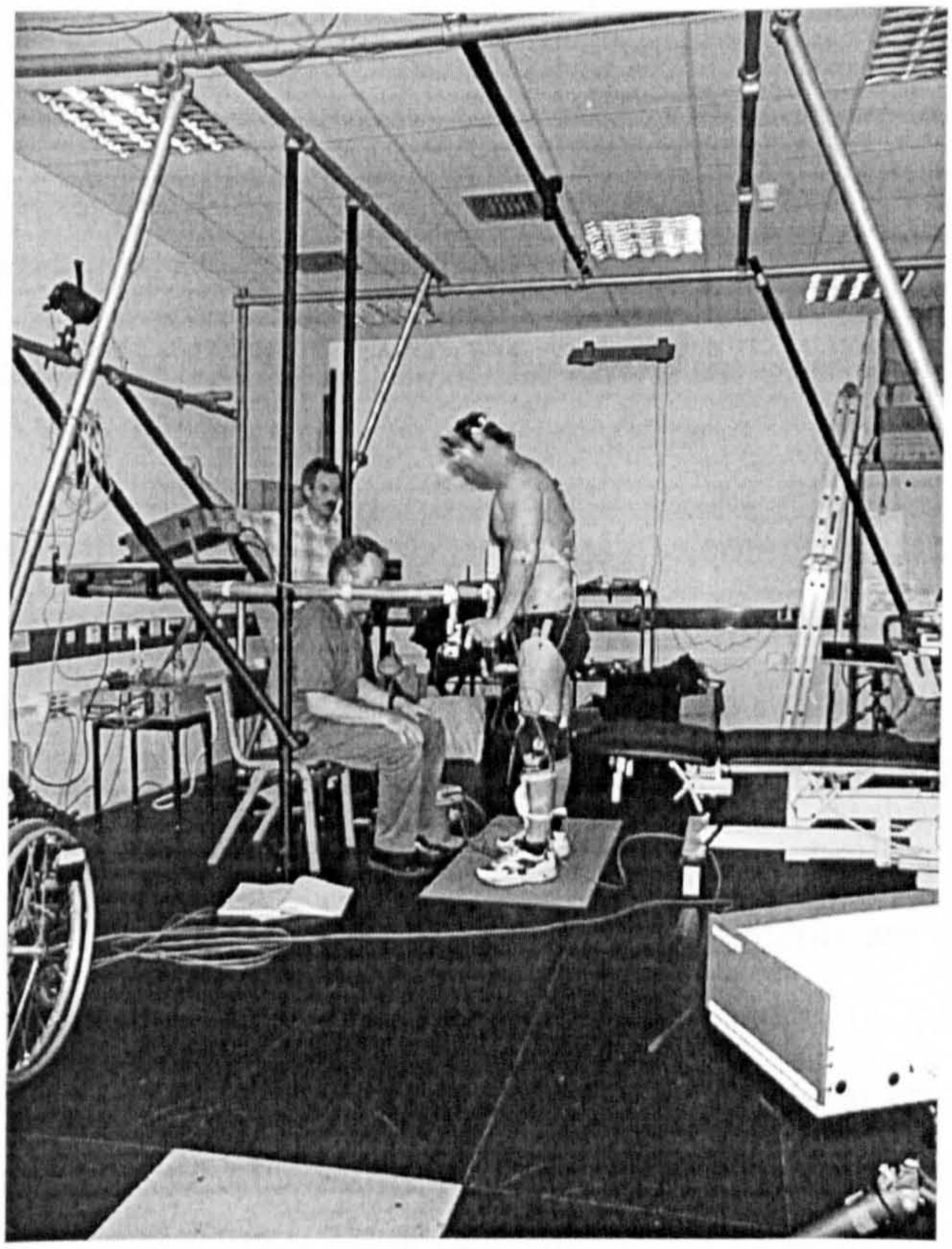


Figure 3.4. The laboratory during an experiment. One CODA *box* is in the foreground, right. The patient is standing on the wooden covers over the force plates. The CHRELMS handles are in use. Although the patient is wearing knee cuffs they were not used for the open-loop experiments described in this thesis.

During the standing experiments surface EMG was recorded from leg and trunk muscle groups. Signals were recorded either using a wire-based system or MIE's wireless system (MT8, MIE Medical Research Ltd, Leeds UK). All signals were amplified and filtered prior to digitisation on a PC at a sampling rate of 1 kHz.

Section 3.5. Biomechanical System Error Analysis.

The errors associated with each component of the biomechanical system have been described individually in the section dealing with each piece of apparatus. In this section the errors are combined and an overall estimate of the error in comparing joint moments at the hip produced. Table 3.1 brings together all of the errors discussed in earlier parts of this chapter.

Source	Error (sd)
MMCS- hip moment	5Nm
MMCS angle measurement	10°
3D scanning	4% in COM
CODA	4mm(horizontal) + 2mm(vertical)
Force Plate	0.1N
Handles	0.1N

Table 3.1. A summary of the errors within each component of the biomechanical system. The origin of the errors are considered in the text throughout this chapter.

The errors in the MMCS are relatively easy to compute using simple addition of errors (Taylor, 1997). Using data from Norton and colleagues (Norton *et al.*, 2000) the change in hip moment with angle, (0.3Nm/°) can be found and this added to the error in the hip moment. The total error in the MMCS is therefore 8Nm.

The error in the standing situation is slightly more complicated because of the increased number of variables and not all of the measurements are easily transferable into Nm. The independent error components will be added in quadrature (Taylor, 1997) and the related errors using arithmetic addition. The total error comes to 4.3% using this method, and is dominated by the error in finding the centre of mass of the leg using the laser scanning. This error translates to an error of ~1.1Nm in a typical posture for the implanted patient.

The original aim of the study was to measure the hip joint moment at a set angle, (or over a range of angles) and compare the moments in the two postures,

(recumbent and standing). As the expected effects are likely to be small they will probably be hidden in the errors associated with the system.

3.6. Neurophysiological Analysis.

The surface electromyogram is recorded using differential amplifiers in the standard manner. For tests with patients Patient 3, Patient 1, Patient 2 and Patient 4 the EMG was collected using a wire-based system. All channels shared a common earth and signals were pre-amplified in a body-worn box before being carried to a second amplifier and the AD card of a PC using a multi-core cable. For Patient 6 and Patient 5 the EMGs were collected using a "wireless" system (MIE MT8, Leeds, UK). In this arrangement each pair of recording electrodes also has its own independent earth electrode. Signals are pre-amplified by a factor of a 1000 by a small box that sits on the earth electrode, i.e. on the muscle in question. Signals are then carried back to a patient worn transmitter using wires. The signal is then transmitted to a remote receiver where it is further amplified and undergoes digitisation within a PC. All EMG data was sampled at 1kHz with a low pass filter of 300Hz and a high pass filter of 0.3Hz. All the EMG data was sampled simultaneously with the CODA and force plate data using the CODA interface and therefore the records were each 16s in length. Electrodes were placed over the belly of the muscle in the "standard" manner and had a electrode separation of 2cm centre to centre. Electrode pairs had a common earth that was positioned between the two recording electrodes.

EMG recordings were made whilst patients were in the MMCS using BEAC (Stradella (PV) Italy) pre-amplifiers and then stored on Teac digital tape recorder (RD-145T, Teac Germany) for later analysis, which was performed using Matlab (Mathworks, Cambridge, UK). Data was poor due to electrical interference in many cases or, not directly comparable with standing data because patients exhibited unusual reactions to being in the MMCS. Patient 4 demonstrated persistent extension spasms whilst strapped into the MMCS, which stopped when the straps were removed, although he remained recumbent.

The EMG signal recorded from the skin consists of the motor unit action potentials from many of the motor units in the muscle(s) near the electrodes. It is therefore a compound recording of the action potentials. A full discussion of the properties of the surface EMG signal is outside the scope of this thesis. The analysis of EMG signals using temporal and spectral analysis is a burgeoning field (Halliday *et*

al., 1995), (Farmer *et al.*, 1997), (Amjad *et al.*, 1997), (Rosenberg *et al.*, 1998), (Cassidy & Brown, 2002).

Spectral analysis of EMG signals relies on the decomposition of the signal into its constituent frequency components. The decomposition can either be performed using the Fourier method or the auto-regressive method (Cassidy & Brown, 2002). In this thesis the Fourier approach used in Matlab was taken. The Fourier method relies upon the stationarity of the signal. During a muscle spasm it may be argued that the signal is not stationary. One approach to this problem is to use short segment lengths. Cassidy and Brown (2002 & personal communication) have shown that this approach is valid with the length of data sets obtained in this thesis. Cassidy has further shown that with the data obtained in this study similar results can be obtained using the auto-regressive moving average technique and the Fourier technique (Cassidy, Personal communication 2002). The equation for the Fourier transform of a signal x is;

$$X(k) = \sum_{j=1}^{N} x(j)\omega_N^{(j-1)(k-1)}$$

eq3.2

where N is the total number of samples and j is the index of the current sample, x is the signal, k is $-1^{0.5}$ and ω is the frequency.

Most mathematical and signal processing texts give further information on this formula, (an online book can be found at http://www.dspguide.com/). To augment this visual inspection the power spectral density was plotted for many of the signals. This revealed the frequency content of the signal in more detail. A Hanning window was used to window the raw signal as outlined in the Matlab guide. The Hanning window is used because of its computational efficiency and good passband and stopband characteristics. However, for applications such as this most of the commonly used windows are adequate (e.g. Hamming, Blackman etc) (Challis & Kitney 1990, 1991) The relationship between two signals in the frequency domain can be examined through examination of the coherence function, which is the frequency domain equivalent to cross-correlation analysis. The Magnitude Squared Coherence, (MSC) is defined with the following equation;

$$MSC = \left|C_{xy}(w)\right|^2 = \frac{\left|G_{xy}(w)\right|^2}{G_{xx}(w)G_{yy}(w)} \quad \text{eq 3.3}$$

which is the equation used within Matlab. $G_{xx}(w)$ is the power spectra of x at frequency w and $G_{xy}(w)$ is the cross power spectra of x and y at frequency w. Coherence is a bounded measure, (between 1 and 0) that plots the relationship between two signals at a given frequency. It is widely used in functional coupling studies in neuroscience since it is believed that a coherent signal, (i.e. above the 95% confidence level, or other level as appropriate) is likely to arise from a common drive (Cassidy & Brown, 2002), (Rosenberg *et al.*, 1998), (Amjad *et al.*, 1997). This assumption should be checked through the use of both phase plots and time-domain methods such as cumulent density plots or cross-correlograms. Coherence at frequencies at which motor units fire spontaneously may represent this unrelated activity rather than a common drive.

The analysis was performed using software provided by Neurospec (www.neurospec.com). The software is a Matlab implementation of the routines developed by Halliday and colleagues (Halliday *et al.*, 1995).

3.7. Patients.

Patients were recruited from Salisbury District Hospital's FES clinic which provides a supra-regional FES service to the Odstock and Stanmore spinal injury units in the south of England. The Salisbury clinic has provided FES-assisted standing to 31 patients of whom 20 have used the system at home over the past 14 years. All patients have used a surface stimulator system and two have subsequently had implanted systems. At the commencement of the project the lead clinical engineer at Salisbury approached all suitable mid-thoracic injury patients and invited them to take part in the project. Patients were suitable if they had a complete injury, were regular FES users, (although one patient had not stood using FES previously he regularly trained his muscles using FES) and were able to commit enough time to the project. A total of seven patients were recruited and one dropped out prior to any standing tests because of both time commitments and an overuse shoulder injury. Subsequently six patients were studied, all with clinically similar lesions. Not all patients completed all parts of the study, primarily because of time constraints.

This study therefore took a primarily "case-study" approach to the patients, particularly as subsequent investigation suggested a large degree of heterogeneity amongst the patients despite their clinically similar lesions. Not all data was available or usable from each part of the study for each patient, either because the patient did not complete that part of the study or because the data was corrupted. Prior to the onset of the study it was not possible to determine what, if any, endogenous spinal activity would be present in each of the patients. Patients were included if they had a stable, complete mid-thoracic spinal cord lesion resulting in complete motor paralysis. Patients had to have completed a training programme to re-strengthen their muscles prior to standing. Patients (except the new standing patient (patient 5)) had to be experienced FES-assisted standers and be able to commit sufficient time to take part in the study. Patients must also be medically stable and have no injections.

Patient 1 is a male patient, aged 40 when he took part in this study, who sustained a complete T10/11 lesion following a crush injury in 1994. Following immediate transfer to a regional spinal injuries unit internal stabilisation (Moss cage) was provided. During the surgical procedure "normal" cord potentials were recorded. These normal potentials below the lesion suggest that the ascending and descending fibres were, at that time, largely intactAt discharge from the spinal injuries unit where he had been treated he was taking Baclofen to reduce his spasms. He continues to take this, and during the period of investigation was taking 60mg/day. The internal fixation remained in place during the investigation.

To improve his bladder management he opted to receive a sacral anterior root stimulator in 1996, implanted as described as elsewhere (Brindley, 1994) As is usual with this procedure he also had a dorsal rhizotomy of the S2-5 roots, (S5 crushed and 2-4 cut). The electrodes were implanted intradurally, in line with standard practice at that time. Three years following the initial implant there was a cable failure within the implant, and 2 new extra-dural electrodes were implanted, leaving the old electrodes in place (Brindley, 1995).

Following the first surgical procedure he experienced a dramatic change in the nature and severity of his spasms. The increase in severity of, and triggers for, spasms meant that the patient was no longer suitable to demonstrate calliper use to new patients. The surgical repair procedure had no significant effect upon the spasms. He reported continuous dorsiflexion whilst sitting that can continue for as long as he remains still, (up to 4 hours is the longest time he has been aware of this). He

sometimes finds moving, either by performing a pressure lift or general change in posture, stops this activity. Typically he will prevent this movement by crossing his legs so that the leg that is moving is now "held in place" by the non-moving leg.

The patient trained his leg muscles, using the Salisbury FES protocol as part of the LARSI project (Rushton *et al.*, 1998) and commenced standing in October 1998. During FES-assisted standing he experiences spasms that appear to be flexor spasms, which occur with remarkable regularity.

Patient 2 has a complete T9 lesion and at the time of investigation he had been regularly standing with FES-assistance over the past 3 years. Following the completion of the first part of the experiment, and prior to the arrangement of a subsequent session he decided to stop standing and start FES-assisted cycling, which he continues to do at the time of writing, (winter 2002).

Patient 3 is a female with a complete T9 spinal cord injury. She has an implanted nerve root stimulator which has previously been described (Donaldson *et al.*, 1997). At the time of the experiments she had been standing with FES-assistance for over 6 years and had had the implant for over 5 years. Clinically her posture was characterised by excessive hip flexion and accompanying lumbar lordosis. Consequently she appeared to take a large proportion of her body weight through her hands (Perkins *et al.*, 1999). This limited her standing time using the implant. She used the implant regularly for exercise and cycle training in addition to the standing training at the time of the study. When standing passively in a standing frame she is able to fully extend her hips suggesting that there is not a major hip contracture present. Patient 3 has been extensively studied in the period leading up to this investigation. With stable stimulation parameters the responses to stimulation and hence her standing remain stable.

Patient 4 is an experienced FES-stander with a complete T11/12 lesion. He has used FES to stand for 2 years.

Patient 5 has a lesion at T7. He had a complete motor lesion but some minor sensory sparing. In practice the sensory sparing was limited to some awareness, (but not pain) of painful stimuli on one portion of one thigh, but not the stimulation. Although he had previously stood using a standing frame, and continued to do so regularly throughout the period of study, he had not previously used FES to stand. He had undergone a 1-year training programme to retrain his quadriceps muscles. The training programme has been described previously (Rushton *et al.*, 1998).

Patient 6 is a 59 year old male with a complete T10/11lesion sustained 20 years ago. He has previously had a Brindley bladder implant and rhizotomy and has been standing with FES for over 13 years. He has previously used FES to step using the flexion withdrawal reflex to initate a swing movement (Granat *et al.*, 1991). Following the implantation of the sacral root stimulator and the rhizotomy he developed persistent, bilateral leg spasms. These did not severely affect his activities of daily living other than to interfere with his sleep.

Patient	Age	Level	Post injury procedures	Scanner	MMCS	Spasm investigation	Stand	Sit-to-stand
1	40	T10/11	SARSI, repair to SARSI	No	Yes	Yes	FES, OSF	No
2	35	T9	None	Yes	Yes	No	FES, hip & ankle movement	Yes
3	42	T9	LARSI	Yes	Yes	No	FES, OSF	No
4	32	T11/12	None	Yes	No	No	FES	Yes
5	35	T7	None	Yes	No	No	FES, OSF, hip & ankle movement	Yes
6	59	T10/11	SARSI	Yes	No	Yes	FES, OSF	Yes

Table 3.2. A summary description of the patients and the tests that they took part in during this study.

3.8. Patient Safety.

All patients had chronic injuries and were therefore familiar with and competent at transferring between their wheelchair and beds and plinths. Each Stanmore stimulator is safety tested prior to its first use by a clinical engineer (D. Wood, Salisbury). The patient is electrically isolated from the mains supply and is only in direct contact with battery powered devices, stimulator and EMG system.

For Patient 5 who was new to standing a safety harness was used to support the patient. The experimenter using the harness reported if he had taken any weight during the test and those tests were checked to confirm a change in the total vertical force between the force plates and handles and discarded from analysis. This happened on one occasion.

All patients took part with informed consent and ethical permission had been obtained from the National Hospital for Neurology and Neurosurgery/Institute of Neurology joint ethics committee, (the standing programme and the use of the MMCS is covered by an ongoing ethical application to Salisbury District Hospital Ethical Committee). Patients were aware that they were free to withdraw at any time, and several patients did not complete the study because they wished to withdraw.

3.9. Conclusions.

The concepts of leg joint moments and leg joint deficits have been defined. The biomechanical instrumentation and techniques that are common to all of the studies have been introduced and an error analysis performed. The error analysis has indicated that to detect differences in joint moments between the two conditions the differences must be larger than 9Nm. The use of signal processing has been introduced and some of the techniques and implications of such analysis highlighted.

Chapter 4.

3D Scanning to Determine the Mass and Centre of Mass of the Leg.

4.1. Why is a New Technique Needed?

The calculation of the joint moments for postural or gait analysis requires that the mass of the patient's leg, the centre of mass, moment of inertia, and centre of rotation are known. In many cases this is not known for the individual and estimates are used. These estimates are based upon population data and so, by definition will not fit the patient. The populations upon which these data are based are essentially drawn from two backgrounds, elderly people who have died (Seidel *et al.*, 1995) and military service personnel (Wright-Patterson Air Force Base, Ohio, USA for example has produced many excellent studies) (Chandler *et al* 1975 cited in (de Leva, 1996)). These studies have been primarily for the field of ergonomics and then applied to general population biomechanics. The majority of the population undergoing clinical biomechanical assessment are elderly, and hence are likely to be better modelled by the cadaver data. However patients are still alive and cover a broader range of ages and body shapes than the cadaver data does. Biomechanical assessment on military personnel is used to optimise and develop military equipment. Stein and colleagues showed that whilst the fit within a population was good, between populations the data were poor at predicting the anthropometric characteristics, i.e. military data was good for military personnel, but poor for all other populations (Stein *et al.*, 1996).

Many disabled patients undergo biomechanical assessment and they will fall into neither of the well-studied population groups. Stein and his colleagues have previously shown that the disabled population is poorly modelled by data obtained in the general population surveys (Stein *et al.*, 1996).

van der Herberg in a M.Sc thesis (1997) looked at two techniques for estimating the mass properties of the leg. The techniques came from two backgrounds, a proportional model and a geometric model and were chosen to represent the two best methods available. Using a paraplegic patient who regularly exercises with FES he arrived at two estimates of the mass which differed by 28% (van der Herberg, 1997).

The majority of clinical biomechanical reports do not include estimates of the errors likely in the calculations due to errors in the estimation of basic parameters (Whittle, 1996) yet, as above they may be large. There is therefore, a case for using

individual, "personalised" data rather than population data. Why has this not been done before?

Essentially the problem has been the time taken to obtain this data from patients. In many cases it is also a relatively unpleasant procedure. Whilst validating the technique described here water displacement was used to compare the mass and locations of the centres of mass for 10 normal subjects. Water displacement is the current "gold standard" for volume estimation of limb segments. This technique involved standing with one leg in a tank of rising water for around 45 minutes. This is not practical for everyday clinical use. It is both too time consuming and unpleasant. In addition it is unlikely that all patients would be able to use this technique.

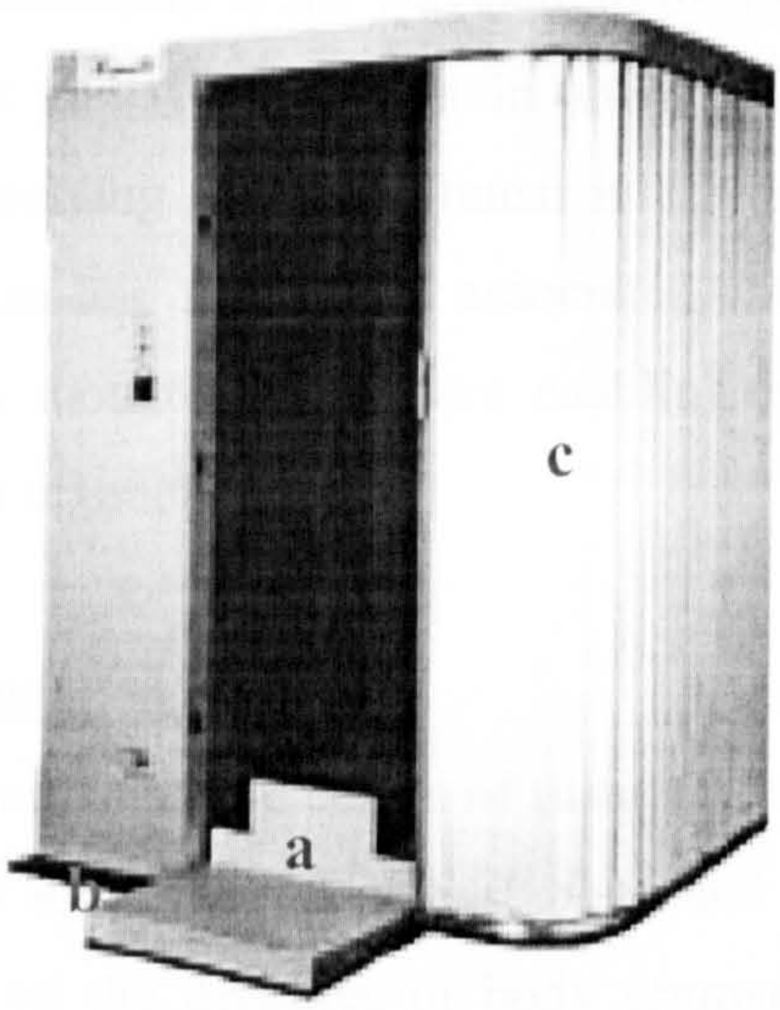
The method described here is based upon the use of a whole-body 3D scanner. The scanner is used to record the external shape of the body. All experiments involved with the calculation of patient's joint moments whilst standing in this study have used this technique. The use of body scanners is not in itself novel, but the extension of their use to the determination of mass properties for the legs is. Jones and Rioux (Jones & Rioux, 1997) have reviewed the use of 3D scanners in the field of anthropometery and concluded that they offer significant advantages over current systems such as speed and ease of use.

Although in this context the use of the scanner is limited to the calculation of the mass and centre of mass of the legs, other date, e.g. radii of gyration may be calculated using the data obtained with this technique.

42.The Scanner and Associated Apparatus.

The scanner used here is the Hamamatsu Photonics Body Lines scanner (Hamamatsu Photonics K.K. Hamamatsu City, Shizuoka Pref., 430-0193, Japan). The scanner occupies a floor area of 1.8 × 1.7 m and is approximately 2.75m tall. In 2000 the scanner cost in the region of US$120,000. The scanner uses near infra-red light, (wavelength 960nm) and scans the body in a *staggered helix* with 256 points in each full revolution. There are 8 scanning heads in the scanner each with 32 emitters and pairs of receivers. The heads move steadily during a scan from head to toe. Each position sample has three space co-ordinates, (x,y,z) which are given in 1/10ths of mm, and an integer representing the reflection intensity. Some post-collection data reduction is used to remove points with low reflection intensities since these are likely to be "aberrant" reflections. A single scan takes around 10 seconds to complete.

Figure 4.1 shows the scanner and an leg modelled in Matlab using data collected from the scanner.



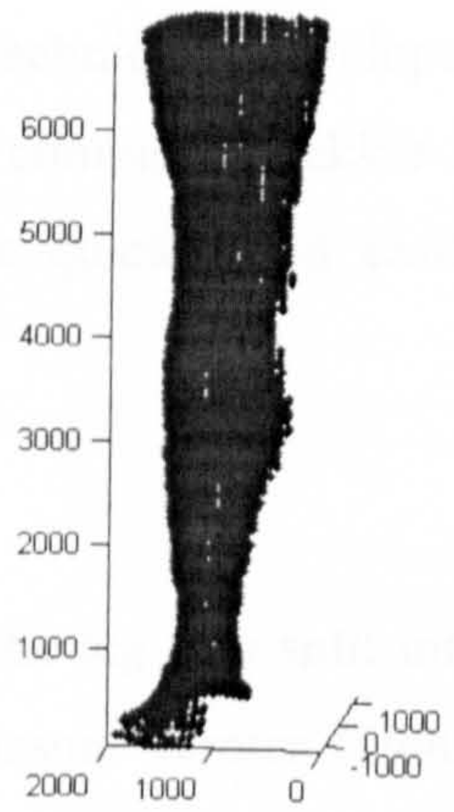


Figure 4.1. Left. A picture of the scanner used in this study. a) the raised platform for normal use, this is replaced by the modified standing frame for paraplegics. b) the IEEE48 cables leaving the scanner. c) the flexible screen which can be pulled around the scanner. Right. An output plot of a leg data set. The axis scales are in tenths of millimetres, as used by the scanner. This image can be rotated in 3D space using Matlab. The points available with the Matlab software are larger than is ideal and can lead to some visual blurring. Bottom. A figure of the patient in the modified frame in the scanner immediately prior to being scanned. The wooden supports are at a distance from the legs and consequently don't interfere with the scanning process. Thin straps are used to minimise the amount of data that is lost because of them.

For use with disabled patients, in particular the paraplegic patients in this study, a modified Oswestry Standing Frame has been developed, see figure 4.1. The frame is raised to place the patient at the same height as the base of the normal

scanner, this gives the scanning heads space for deceleration and stopping. The frame is painted matt-black and its straps are also black. The frame and its associated equipment are therefore absorbent at the wavelength of light used in the scanner. The absorbance of the frame and straps results in small areas of lost data which are corrected for in post-processing using non-linear interpolation techniques developed for this use by Hamamatsu and researchers associated with the company (Dekker *et al.*, 1999). The frame is mounted on castors enabling it to be quickly and easily moved into and out of the scanner.

4.3. Data and Data Manipulation.

To calculate the mass and the centre of mass of the leg the leg was split into two compartments based upon their densities; bone and soft-tissue. Winter (1990) presents composite data on the densities of body segments derived from over 150 years of study. Table 4.1 presents a summary of the data in this report, (table 6-5, p181 in the international edition). The skin, muscle and fat all have similar densities whilst the bone density is larger. The volume of fat and skin within a leg of a trained paraplegic is low (Wood personal communication). The soft-tissue was therefore given an "averaged" density heavily skewed in favour of the muscle density, which also happens to be very close to the average density of skin and fat. Ultrasound scans of patient's legs using FES are routinely carried out in Salisbury to measure muscle thickness. Data previously obtained from these tests was used to determine the ratio of muscle: fat: skin (including all dermal tissue). The final density for the soft-tissue was therefore 1.04Kg/l.

Classification	Component	Ratio	Density (Kg/l)
Soft	Skin	1	1.102
Soft	Muscle	9	1.063
Soft	Fat	3	0.962
Bone	Bone	Na	1.84

Table 4.1. The densities of the components of the legs obtained from Winter (1990). Skin, muscle and fat are all classified as soft-tissue within this thesis and given a composite density, whilst bone is treated separately because of the large volume of bone and its higher density than the other tissues. The ratios of the soft tissue are relative ratios obtained using ultrasound scanning and from Winter (1990).

The bone data was obtained from the US-based Visible Human Project (http://www.nlm.nih.gov/research/visible/visible_human.html) and the bone data was extracted using the University of Texas' UTHSCSA image programme (http://www.uthscsa.edu/). The size and orientation of the bones was adjusted to fit the individual patient using measurements made both on the patient directly and from X-rays. A number of measurements were made; distance between the greater trochanters, distance from the lateral malleolus to the lateral head of fibula and the distance from the lateral malleolus to the greater trochanter. The remaining distance, from the head of fibula to the greater trochanter can be inferred. The bone model was then scaled such that the distances on the model between the boney landmarks was the same as those measured on the patient directly or from the x-ray images that were available for inspection at the patient's hospital. This method undoubtedly introduces some error into the calculation of the bone mass and potentially into the location of the centre of mass. It is impossible to know precisely how large this error is but it is present in both the water-displacement and the scanning technique. Figure 4.2 is taken from an anatomy text book (Moore and Dalley 1992) and shows the bones in the leg with bony landmarks highlighted.

Figure 4.2. The posterior view of the bones in the leg, taken from Moore and Dalley (1992). The major bony landmarks are highlighted including those used in this study to scale the "standard" data to fit the patient. Note that the head of femur and the acetabulum are separated to a much greater extent than is clinically true for ease of viewing.

The output data from the scanner presented as a standard text file. A whole body scan file is around 200Kbytes in size. For this application the leg is segmented using custom written code in Visual C++ and a 3D graphics library. Segmentation occurs in a plane drawn from the crotch point to the superior illiac crest. Each leg is segmented individually (the software to segment the leg was developed jointly by the author and Dr Laura Dekker using the OpenGL 3D graphics language).

Each leg consists of a *non-circular staggered helix* of data points, forming an irregular shape. The volume of the irregularly shaped surface of the scan is calculated using computational integration. Manual smoothing removes points due to aberrant reflections not removed in the automatic cleaning. Each point is then linked to its

neighbour, the point directly underneath it, and its neighbour. This generates a quadrilateral end piece. Consequently some of the curvature of the leg is removed in this process. This is only a very small amount as there are a large number of points in each revolution. Each point in the data set is then connected to the *centroid* by a horizontal line. Each point is also connected to its neighbour in the direction of the helix and their "pairs" on the subsequent revolution of the helix. This process results in a series of *wedges*, see figure 4.3.

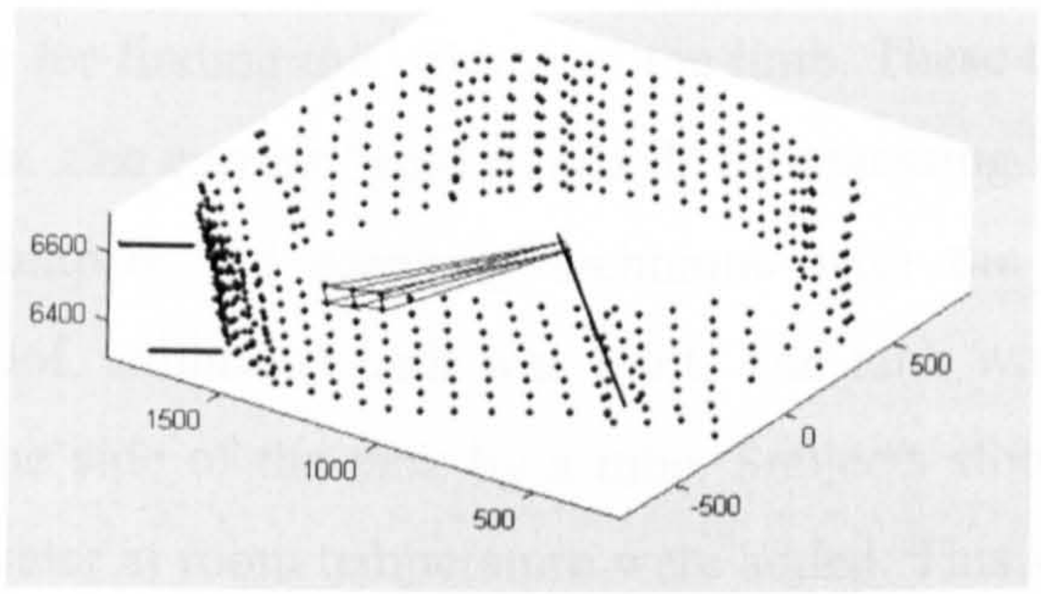


Figure 4.3. A comparison of the two volume measuring techniques. The thick black lines on the left represent the height of water added in one quanta, roughly 20mm. The dots are the output from the scanner and are every 5mm in the z-direction, i.e. 4 times more The thin lines joining the dots represent the "wedges" used in the scanner technique. The long line represents the artificially inserted centroid.

The volume of each of these wedges can be found using integration and the volume of the whole simply requires the summation of these small volumes. Integration is used to find the centre of mass of the shape assuming a uniform density. The mass of the shape is obtained assuming a uniform density of tissue. This density is taken as the density obtained in table 4.1.

- The volume occupied by the bones is calculated in the same manner.
- A 3D representation of the bone is obtained consisting of many points located on the surface of the bone.
- Points are joined to their neighbours to generate wedges.
- The volume of the wedges is found.
- The differential density of the bone compared to the soft-tissue, 0.8Kg/l is added.
- The differential mass of the bones can then be found.

- This is added to the soft-tissue mass to give the mass of the legs.
- The centre of mass of the bones is found in the same manner as for the soft-tissue centre of mass.
- Moments are taken about the two centres of mass to find the centre of mass for the whole leg.

4.4. Technique Validation.

Tests were performed to compare the accuracy of the scanner technique with the current technique for finding the volume of the limb. These tests were carried out using normal subjects. The current "gold standard" for assessing limb volume is water displacement. To compare the scanning technique with the water displacement technique a waterproof, calibrated tank was built. The tank was rectangular with a burette attached to the side of the tank by a tube. Subjects stood in the tank whilst 1000ml aliquots of water at room temperature were added. This volume of water was measured using two calibrated 500ml measuring cylinders. After the addition of each aliquot of water the final height of water in the burette was noted. The subjects were also scanned. The 3D scan data was segmented in a *post hoc* analysis to include only the height of leg that had been measured in the water tank. This resulted in a horizontal plane of segmentation, unlike the transverse plane from the iliac crest to crotch point in the normal scanning procedure used with the patients.

4.5. Validation Results.

	Volume		Difference in Volume	
Subject (ID, sex, (left or right)).	Water (l)	Scanner (l)	Difference(l) Scanner-water	Difference (%)
1F (L)	3.52	3.55	0.03	0.85
2F (L)	4.25	4.23	0.02	0.47
3F (R)	4.30	4.32	0.02	0.46
4M (R)	4.89	4.93	0.04	0.82
5M (R)	4.03	4.04	0.01	0.25
6M (L)	4.41	4.44	0.03	0.68
6M (R)	4.48	4.48	0.00	0.00
7M (R)	3.21	3.18	0.03	0.94
8M (L)	3.34	3.32	0.02	0.75
9F (L)	3.48	3.45	0.03	0.87
Mean (sd)	3.99 (0.57)	3.99 (0.59)	0.023 (0.0116)	0.609 (0.3067)

Table 4.2. The total leg volumes for 10 legs, (9 subjects) obtained using the two methods. The absolute values of the differences are calculated and then the percentage error calculated against the water volume. The means and standard deviations are shown for all values.

The volume of the leg was found in both techniques and compared, table 4.2. The difference between the two techniques across ten legs was 0.61%. The absolute differences ranged from 0.00-0.04l. The cross-sectional area at each measurement height was also compared. The scanner has a vertical pitch of 5mm, so there are areas every 5mm up the leg. In the water displacement technique the height that the water rises depends upon the volume of the leg. There are fewer areas in this technique, but they show less noise than the scanner (figure 4.4). It is assumed that the cross-sectional area is constant for a given aliquot of water although this is actually likely not to be true in the real situation.

Using the technique outlined above it is possible to obtain the mass and centre of mass of the leg using both the scanner and water displacement method. The absolute heights obtained in both methods are displayed in table 4.3 and plotted in figure 4.5 against the height of the leg segment assessed.

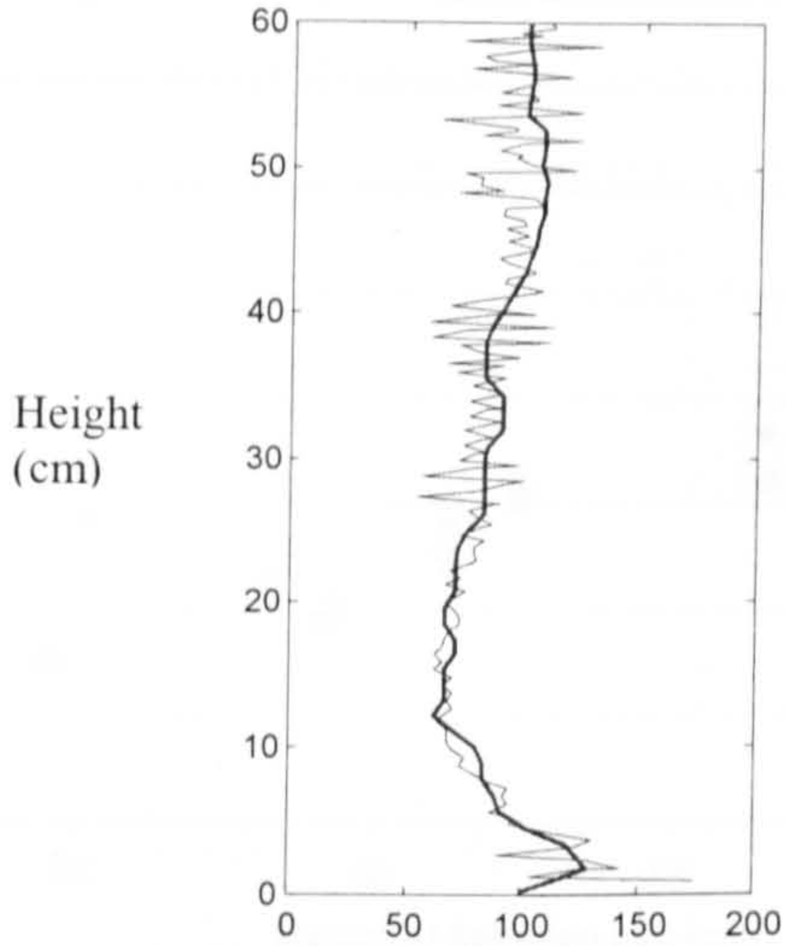


Figure 4.4. The plot shows the cross-sectional areas of a single leg at various heights. The thick line represents the areas obtained using the water displacement technique. The thinner line represents the area obtained with the scanner, at 5mm intervals. The scanner data is noisier than the water data, and has there are more data points with the scanner than the water displacement technique.

	Height		Difference in Height	
Subject (ID, sex, (left or right)).	Scanner (cm)	Water (cm)	Difference (cm)	Difference (%)
1F (L)	23.1	23.0	0.1	0.4
2F (L)	24.1	24.0	0.1	0.4
3F (R)	25.6	26.0	0.4	1.5
4M (R)	25.7	26.7	1	3.7
5M (R)	23.8	23.8	0	0
6M (L)	30.6	31.4	0.8	2.5
6M (R)	31.5	32.0	0.5	1.5
7M (R)	26.5	26.1	0.4	1.5
8M (L)	24.2	24.5	0.3	1.2
9F (L)	24.8	25.1	0.3	1.2
Mean (sd)	26.0 (2.7)	26.3 (2.9)	0.4 (0.30)	1.39 (1.0)

Table 4.3. This table shows the difference in height of the location of the centre of mass from the two techniques. Data is shown for each subject and pooled in the final row.

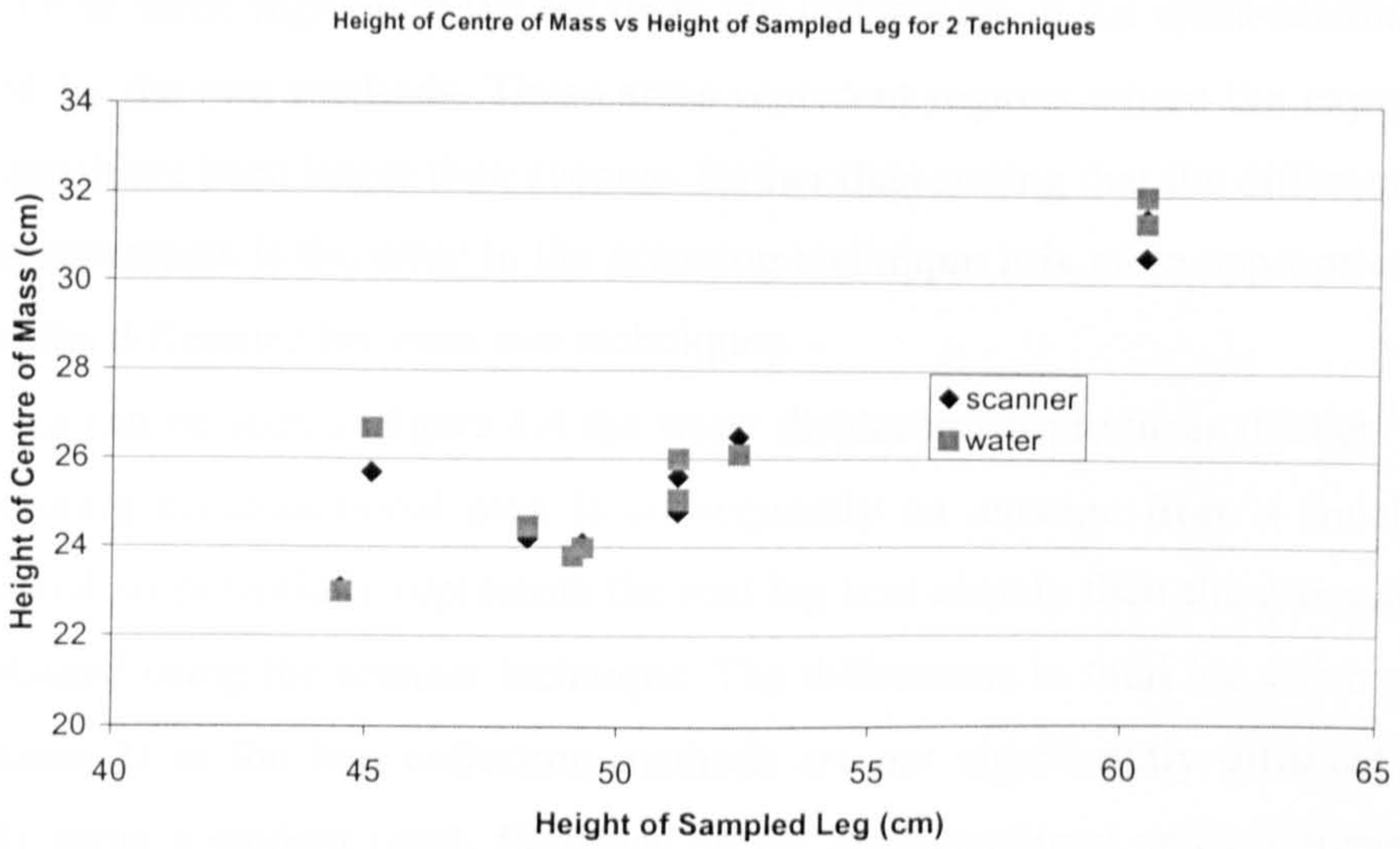


Figure 4.5. The height of the centre of mass obtained by both methods plotted against the height of the leg sampled. There is good agreement between the two methods, as highlighted in table 4.3. The relationship between the height of the leg and centre of mass is complex, depending not only upon the height of the leg, but also the shape of the leg. Note that under the fourth square from the left there is a point from the scanner data set.

Each session with the water tank took in excess of 45 minutes compared to just 10 seconds for a scan, plus time to position the subject in the scanner. With the subjects this never took more than 5 minutes. Consequently the scanner appears to offer a much more practical option for the scanning of individual patients than the use of water displacement.

4.6. Discussion of Results and Technique.

This technique is accurate and quicker to use than water displacement and may improve the determination of the mass properties of individual's legs for use in biomechanical assessment, such as the calculation of joint moments. The major advantage of this system is that it can rapidly acquire individual data, thus eliminating errors that may arise from using population data. Although the scanner is developed, Hamamatsu and its collaborators in many universities worldwide are still developing new algorithms to process the data. These include new techniques to allow the visualisation of the inside of the legs and differential artefact rejection levels depending upon the area of the body being scanned and the level of light on surrounding tissue.

Over some regions of the leg there are differences in the cross-sectional areas obtained by the two methods. These areas represent regions where the experimental errors may have been larger than average. Rather than stating that the difference in the two measurements is the error in the scanning technique it is more appropriate to say that it is the difference between two techniques.

As can be seen in figure 4.4 the water displacement produces thicker "slices". The resulting cross-sectional area is consequently an average from a much larger volume and so potentially represents the real leg less closely than the cross-sectional area obtained using the scanner technique. The differences in total leg volume (Table 4.2 column 3) in the two collection methods are not significantly different from 0 ($p<0.05$) using a student t-test. Statistics on the cross-sectional areas is meaningless since the data overlap within the errors associated with each of the techniques. The scan data is noticeably noisier than data obtained from the water displacement technique. This noise level averages out over a small range, and therefore is not thought to affect the location of the centre of mass.

The scanner system overestimates the size of the leg up to the ankle. This is because of the hollow under the medial arch of the foot, and other areas on the sole of the foot that are raised from the ground are not "seen" by the scanner. The water technique records these volumes. The level of noise in some of the scan data is large, partly due to "outliers". Outliers may arise from aberrant reflections and these have been removed from the data set.

The system offers a number of advantages over the current techniques. It is rapid, non-invasive and gives personalised mass properties, eliminating the gross inaccuracies of using data samples. The estimation of volume is good, (<1%) and hence the estimation of the mass and centre of mass is also likely to be good, although subject to an unknown error due to differences from the published densities and differences from the "stretched" bone from the Visible Human data. If these introduce no error the accuracy will be that shown in table 4.3 (average 1.39%). The system is fast and easy to use when set up, and can be used with those who cannot normally stand by using the Oswestry Standing Frame. It is non-invasive and we have demonstrated its accuracy

The scanner system is capable of measuring the volumes of legs and locating their centres of mass. It is reasonable to assume that the same system could be used for the arms as well. It is unsuitable for calculating the mass properties of the trunk,

although the volume could be calculated, due to the unpredictable densities of the tissues inside the trunk. This is especially true for visceral organs and the lungs which will vary with state of the respiratory system. This type of system is therefore impracticable for calculations of whole body centres of mass, although an approximation could be made. A further problem with the system at present is the initial expense of the scanner. Further uses for this type of system may be found in clinics where knowledge of the shape, surface area and volume of the legs are needed. These might include clinics for lymphodema and the monitoring of joint contractures.

4.7. Future Applications of this Technique.

This technique has been shown to be a reliable method of assessing the volume, mass and centre of mass of the legs. Whilst the present study has limited the application to a biomechanical problem the technique has the potential to be useful in other fields. Patients with lymphodema, following cancer, often have the size of their limbs measured, usually with a tape measure. This technique may offer a quicker and more accurate method of performing this test. Additionally the technique may be useful in monitoring dieting for chronically obese patients.

Whilst the 10 second scan is considerably faster than existing techniques for assessing leg volume it is not fast enough to allow real-time gait analysis. Future work on 3D imaging is aimed at allowing "real-time" imaging with a capture time of around 2ms. At present companies such as 3dMD (Middlesex, UK) are working these techniques but they are still a few years away from a testable system. Additionally work will be needed to enable the reliable marking and tracking of positions, e.g. joint centres in this new arrangement.

For any of these systems to become a reality in clinical practice the price of the imaging system must drop considerably. This is likely to happen as the technology develops and the bespoke clothing industry starts to use the systems for custom clothing.

Chapter 5.

Ongoing Neural Activity During Standing.

5.1. Summary.

Patients with surface stimulation can stand in a satisfactory posture using stimulation of just quadriceps with a small hip extension moment in their normal posture. This is not the case with the LARSI (Donaldson *et al* 1997) system in which the posture is poor and there is a large hip flexion moment. As the posture of patients change, moving around the ankles or hips, support reactions are seen when standing which include oscillatory activity at tremor frequencies. These appear to represent posture dependent, spinally generated tremor.

5.2. Introduction and Brief Methods.

Ongoing or tonic n eural activity during standing may arise from either the spinal cord's response to standing, and any postural changes that take place, or the response to stimulation, if used to assist the stand. The primary aim of the study was to investigate if ongoing neural activity during standing affected the standing of patients using FES and hence all patients described in chapter 3 took part in this section of the study. As described earlier one patient used an implanted nerve root stimulator (Donaldson *et al.*, 1997) and the remaining patients used surface stimulation of the quadriceps via a "Stanmore stimulator" (Phillips GF *et al.*, 1993). Electrodes were placed on the quadriceps muscle group of both legs in all patients. Electrodes were round 2.75cm diameter electrodes (Nidd Valley Medical, UK) and were placed in the optimal position for the patient to generate knee extension with minimal hip flexion. During standing patients were asked to stand in their normal posture. Feedback was not given about the posture that each patient adopted. Recording electrodes were placed over the belly of the muscle longitudinally (except for quadriceps where a latitudal orientation was used as recommended by (Frigo *et al* 2000). Electrodes were placed in pairs with a centre earth electrode and a centre to centre spacing of 3cm, such that the active electrodes were 6cm apart.

If standing produces extra neural activity then by comparing the responses to the same stimulation parameters in two conditions, standing and recumbent, it should be possible to detect differences due to postural changes that are not stimulation dependent. However, as outlined in chapter 3, the errors in the biomechanical

measurement system (especially the MMCS) mean that any biomechanical differences must be large to be detected.

Patient 3 took part in a series of experiments in which the same stimulation parameters were applied in both the MMCS and during standing. The hip angle was varied in both cases, by the experimenters in the MMCS and by Patient 3 during standing. Other patients (Patient 2, Patient 4 and Patient 5) were asked to flex or extend their hips or ankles during a stand, but no direct comparison with data from the MMCS is possible. During the stands in which patients were asked to move the following protocol was used;

- Sit-to-stand. 16 seconds recording.
- Gap in recording due to CODA routine. ~7seconds.
- During gap, patient told which way to move in next recording, i.e. to sway at ankle or hip forwards or backwards. Patients were asked to sway as far as they could whilst remaining confident of standing.
- New recording. 16 seconds.
- ~5 seconds into recording patient asked to move to new position and stays still.
- Gap in recording. ~7 seconds.
- Patient moves back to original position during gap.
- Patient told which way to move in next recording.
- New recording. 16 seconds.
- Patient moves in new direction and stays still.
- Stop recording.
- Patient moves to original position and then sits down.

This protocol was drawn up in consultation with clinicians to take into account the limited standing time of the patients. The limited standing ability of the patients meant that the recording of the return to the original position could not be recorded.

5.3. Results.

5.3.1. Biomechanical Examination of Standing.

Patient 3 had a clinically poor posture during FES-assisted standing which limited her standing time and has been reported elsewhere (Perkins *et al.*, 1999), (Norton *et al.*, 2000). A possible explanation for the poor posture is that there is a hip

contracture, which prevents her from extending her hips fully. Testing in a standing frame without stimulation confirmed that this was not the case and that she could reach the inverted "C" posture with the hips slightly hyper-extended. Other patients in this study were able to achieve a good standing posture with their hips fully extended. Figure 5.1 compares the posture of Patient 3 on the left and Patient 5 on the right during typical stands for both patients.

The hip moment for Patient 3 was calculated using the procedure outlined in chapter 3 and plotted against the hip angle, figure 5.2. This graph shows that there is a flexion moment (negative extension moment) for the majority of the hip angles. The gradient of the slope of the angle/moment graph over the range of hip angles from normal to flexion+, 0.36Nm/°is in line with that expected from typical results from the MMCS, 0.29Nm/°. This value is based only three data points and should be treated with caution. Although the graph appears almost linear over these three points this is over too few points to determine linearity. It is possible that the graph follows a cubic form, although this is of little clinical significance. The clinical interpretation of this graph is that beyond the normal posture it gets increasingly difficult for the patient to extend her hips. Beyond this normal standing posture, however, the graph shows a sudden increase in the moment for only a small change in angle.

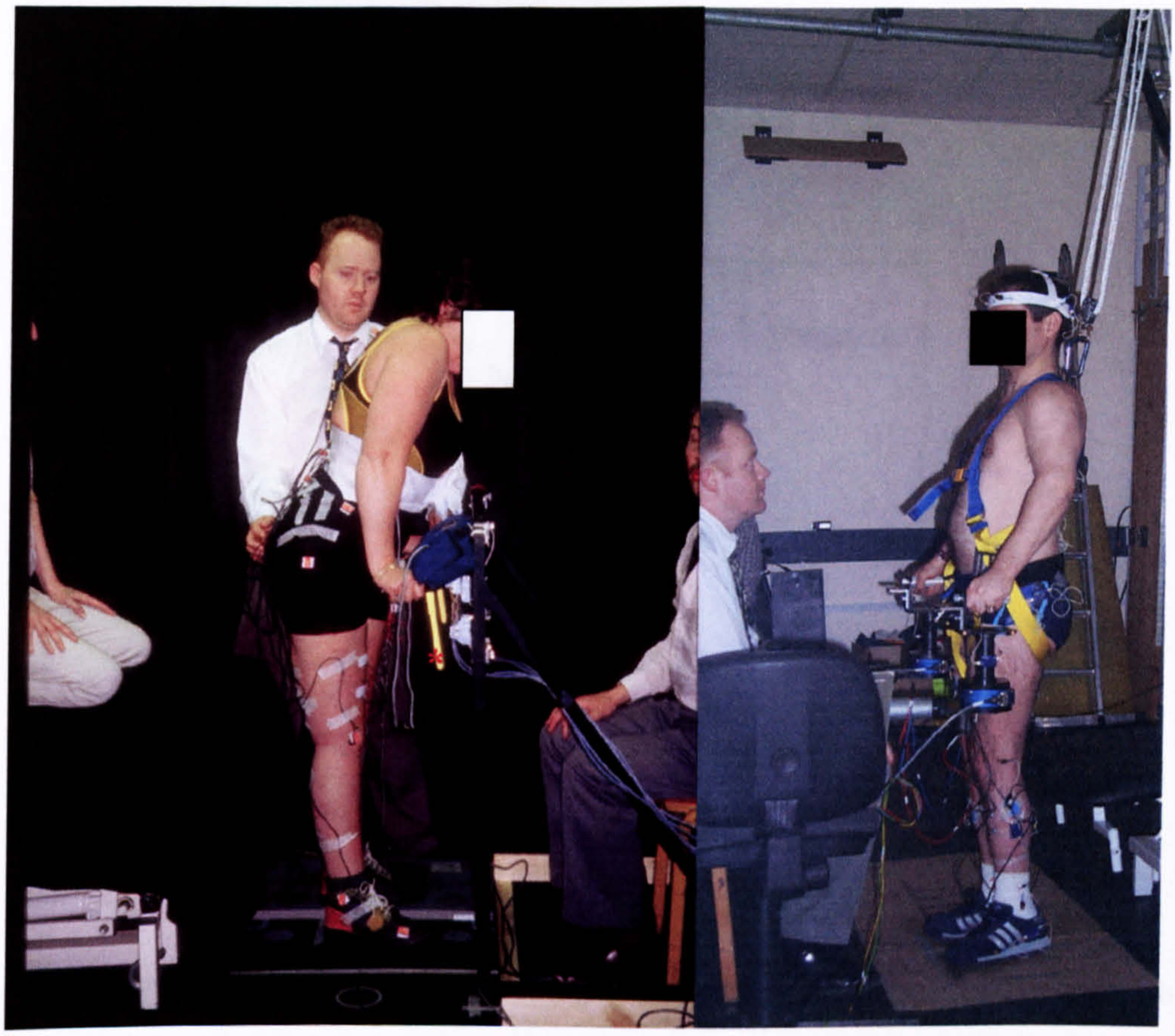


Figure 5.1. Left) Patient 3 standing in a normal posture during the course of the experiments described in this chapter. There is hip flexion and lumbar lordosis throughout the stand. The support handles are CHRELMS handles, and the yellow bars(*) were vertical without any loading. In this posture she is taking ~ 2/3rds body weight through her arms. Right) A patient (Patient 6) standing in a good posture during static standing. Because of the lack of trunk control the stomach bulges giving the appearance of being hyper-extended, whilst actually the hips are straight. The handles are used for balance support and carry some weight, normally just over that expected from the mass of the arms and shoulder girdle.

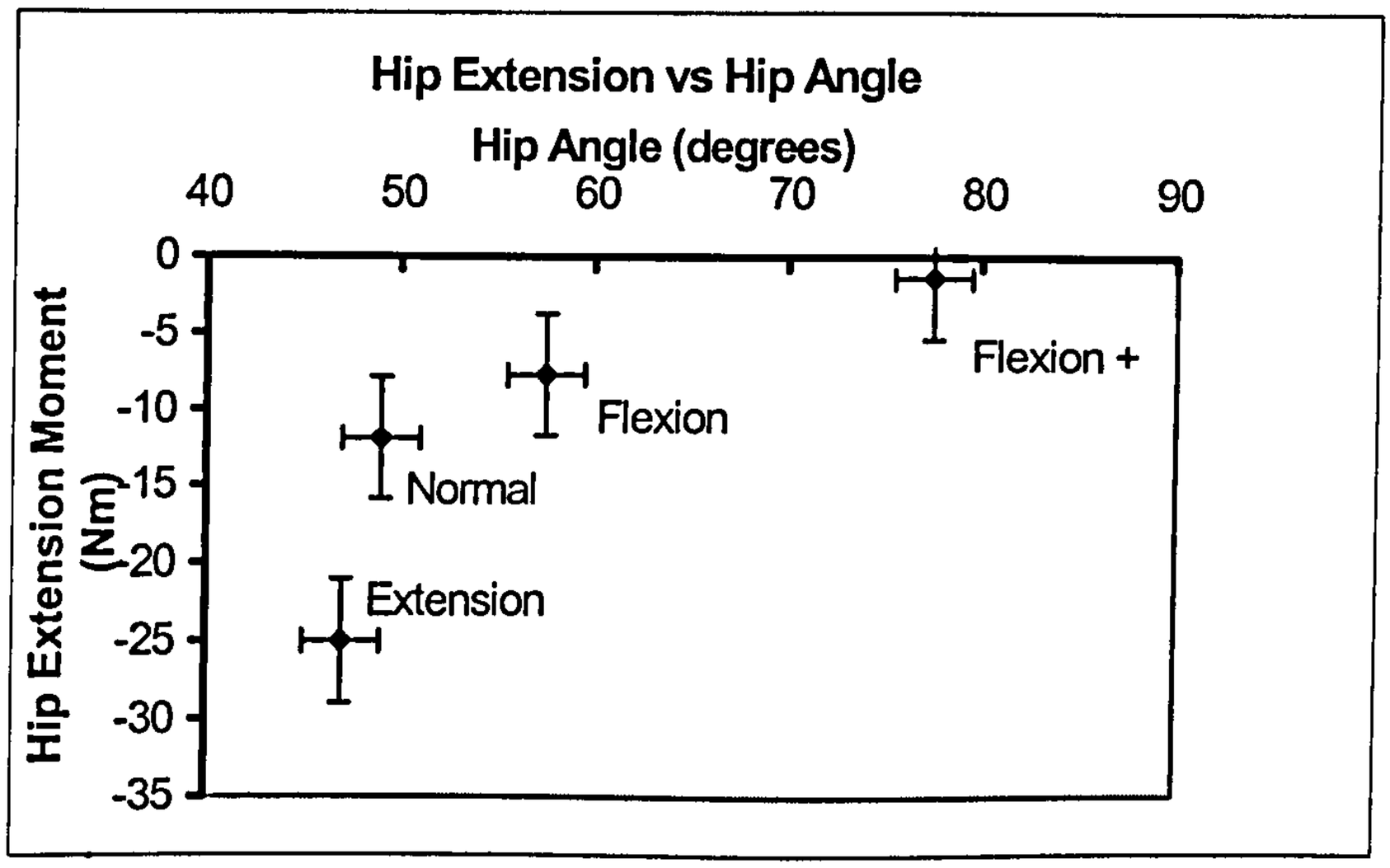


Figure 5.2. The change in hip moment with angle for Patient 3 during standing with normal stimulation parameters using the LARSI system. The more extended the hip the lower the hip angle in this and all other figures. Points show the mean with the standard deviations for both the moment and the angles.

During steady state standing the weight distribution in Patient 3 is poor, with about the weight of each leg, (~9Kg) being taken by each leg. The remaining weight is taken through the arms, figure 5.3. The standing time of the patient is limited by her ability to take this large weight through her arms. The weight is distributed asymmetrically between the hands and the left hand is exerting a rightwards and backwards force in addition to the vertical component. It is not known precisely what muscle groups are activated by stimulation in this patient. Appendix 4 presents a table of muscle groups innervated by each root based on "normal" data. From this table it is expected that both hip flexors and extensors will be stimulated.

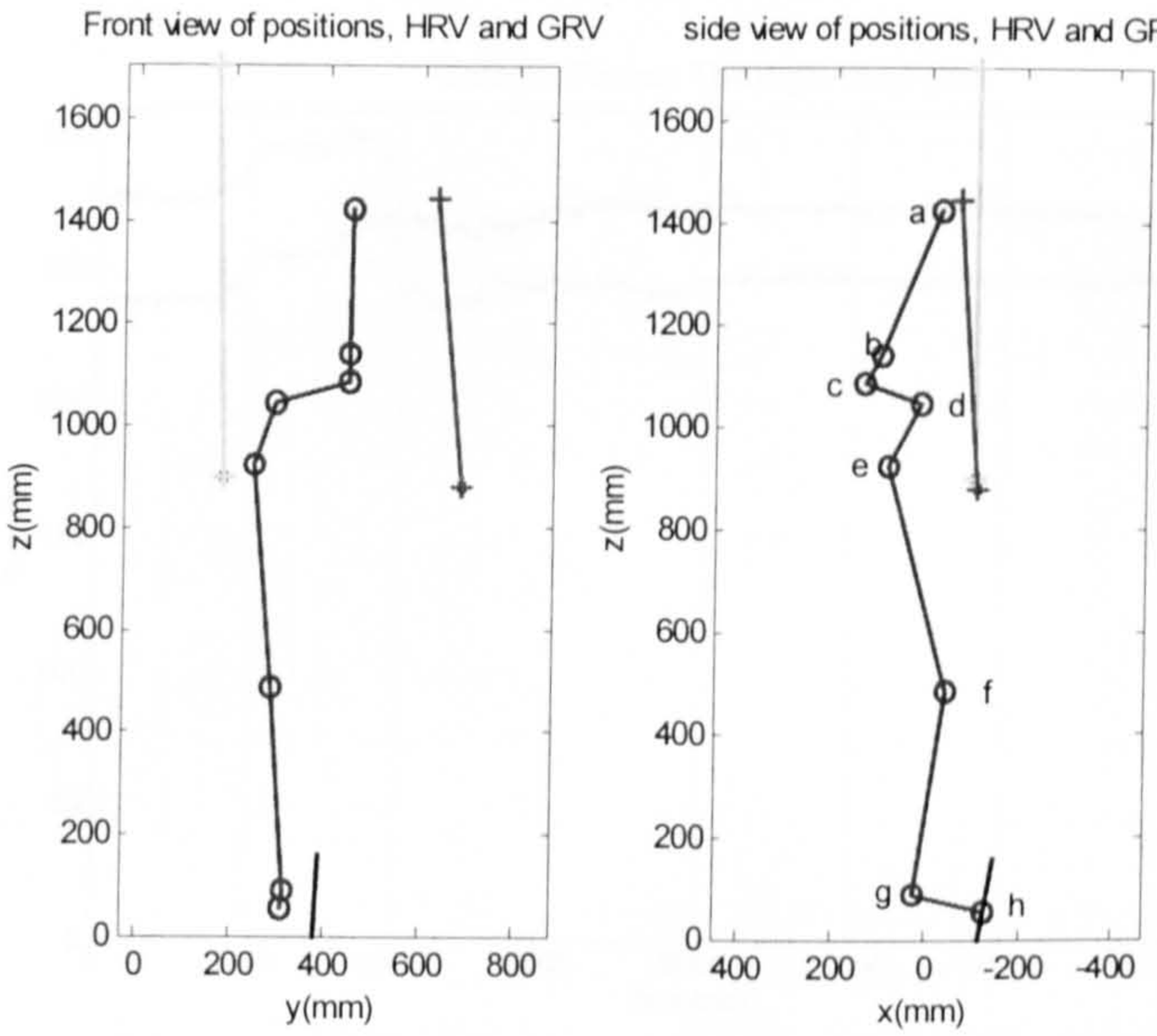


Figure 5.3. The posture and weight distribution of Patient 3 during "normal" standing. The HRVs and the GRV are to the same scale, 0.5N/mm. Only one GRV was recorded. Markers were placed on one side of the body only. There is an asymmetrical weight distribution between the hands. Marker positions; a) T2 vertebrae b) L2 vertebrae, c) back of pelvis, d) front of pelvis, e) greater trochanter, f) knee, g) ankle, h) toe.

The other patients achieve a better posture and carry the majority of their body weight through their legs. Additionally all the other patients have a slight hip extension moment in their normal posture and show a less stiff hip angle/moment relationship. During steady-state standing the patients are very similar and consequently results from one patient will be presented in much of this section for consistency, although where differences are apparent between patients these will be highlighted.

A prominent feature in all patients is the asymmetry of weight distribution between the legs, figure 5.4. This is consistent between stands and stable, but in all cases is not mirrored in asymmetrical weight distribution between the hands. Figure 5.5 shows a period of "steady" standing, although there is a transient increase in the amount of force being taken by the legs at 4 seconds. Despite this change the difference between the two legs remains the same. In this stand, as in all other steady

state stands the vertical force through the hands is small at under 100N per arm. Patients were not given feedback about their weight distribution. The asymmetry was not obvious on clinical examination. In patient 3, figure 5.3 there is also an asymmetry in the size of the handle reaction vectors.

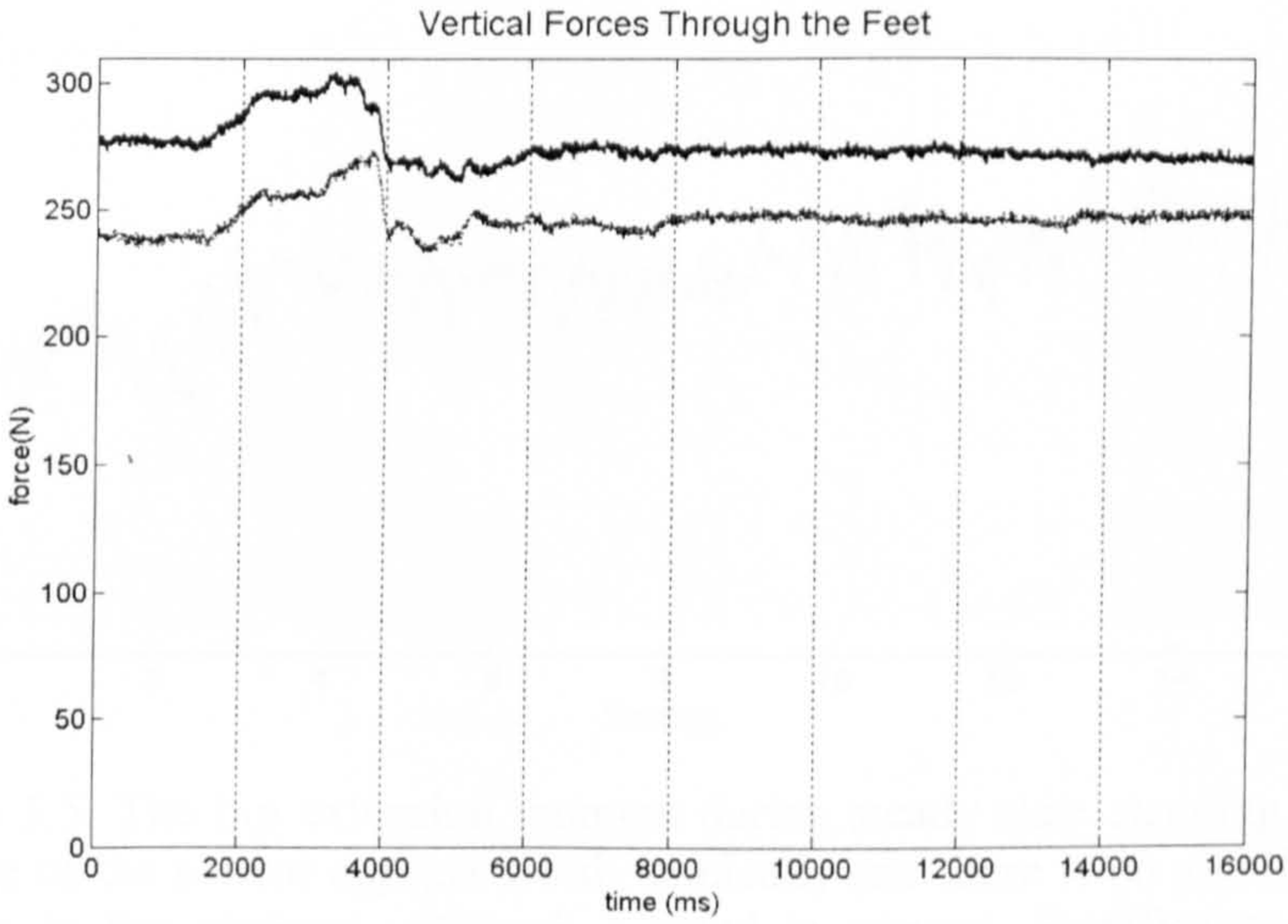


Figure 5.4. The vertical forces taken through the feet during a steady-state stand. The force distribution is asymmetrical and consistent, despite the rise and decrease in force between 2 and 4 seconds. Other than the changes in the 2-4 second period the amount of force being taken through the legs is consistent. Data is from patient 5.

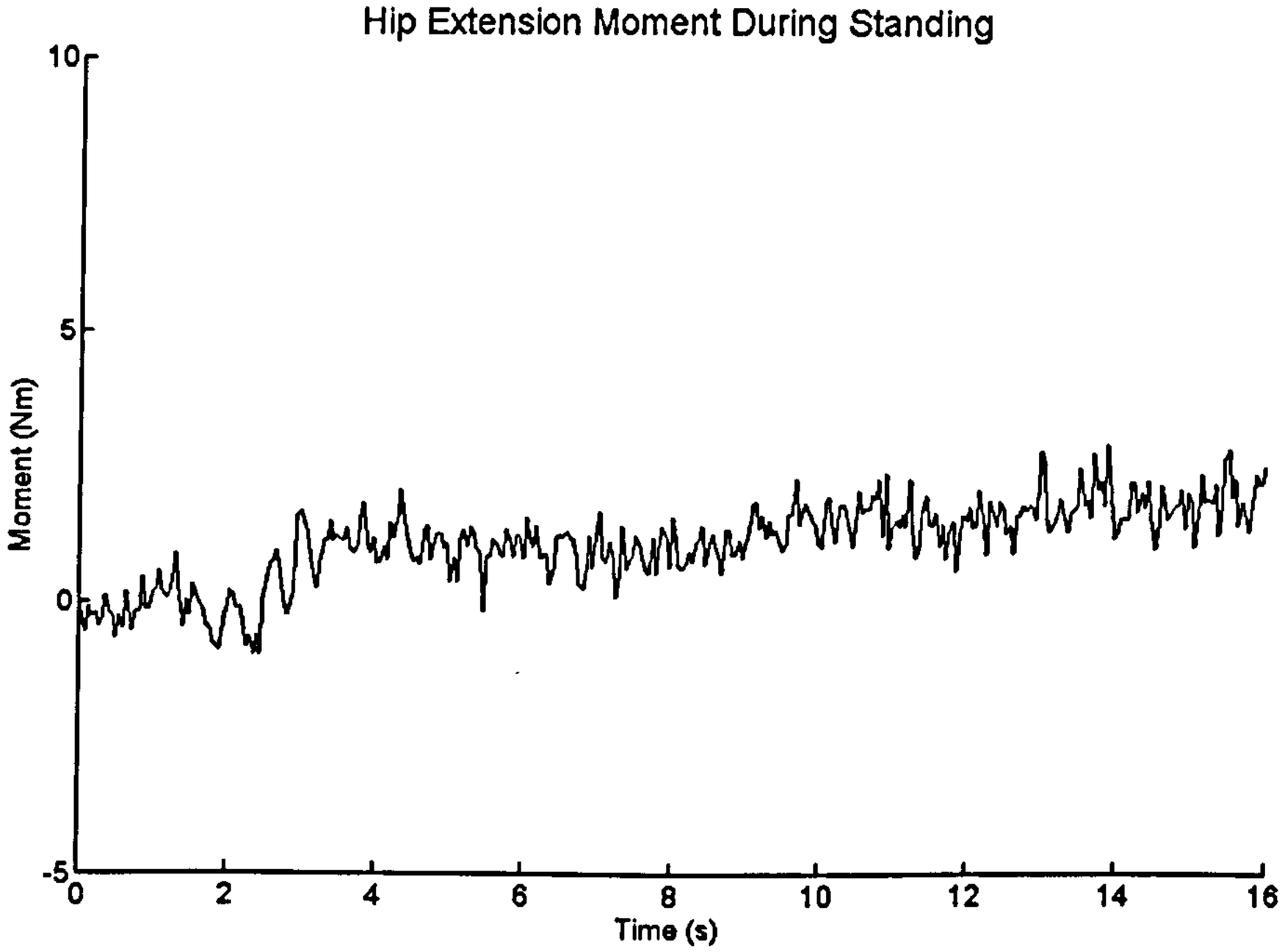


Figure 5.5. The hip extension moment during steady state standing. The posture of the patient appears steady clinically and there is no significant change in the moment, although a trend is present. Significance was assessed by using the limits for each moment calculated in chapter 3. There is a slight flexion moment to start with but after 4 seconds this is an extension moment. Data is from patient 5.

The normal posture of patients standing with FES-assistance is visually similar with the exception of Patient 3 who uses the implanted stimulator. All of the experienced surface stimulation patients were able to stand in the laboratory set-up comfortably for several recording sessions and showed no noticeable changes in their posture. Figure 5.6 shows three of the patients during a normal stand.

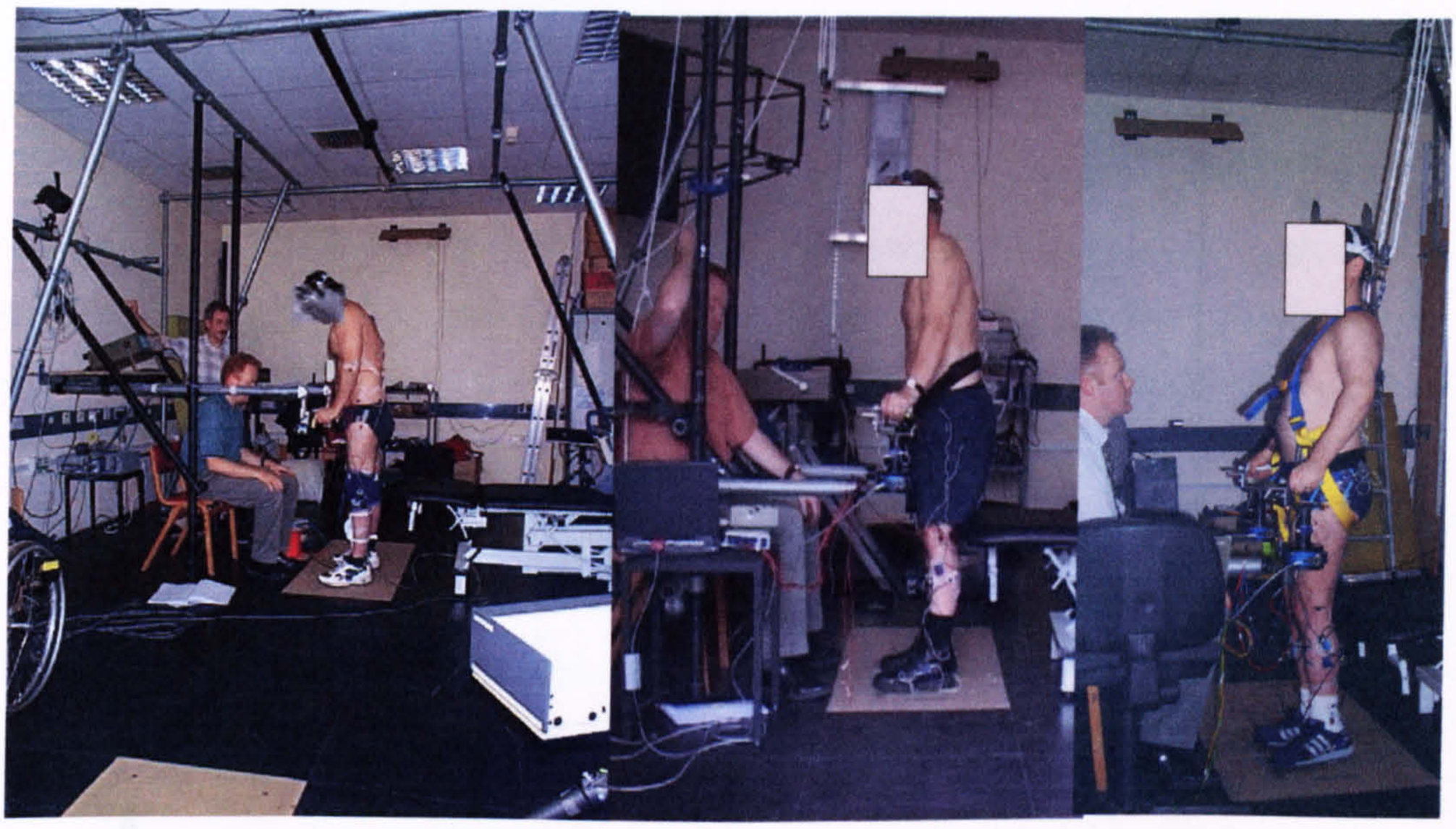
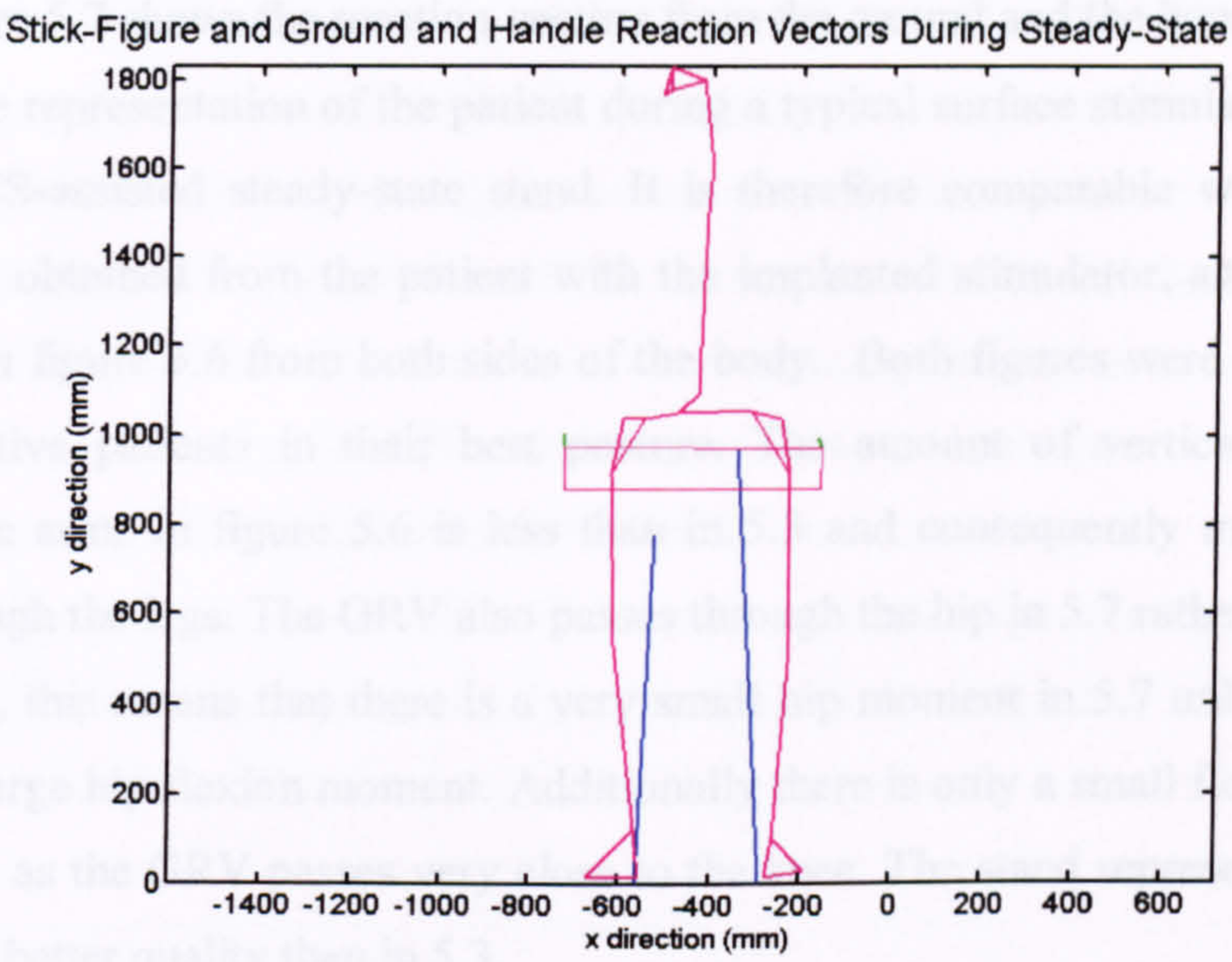


Figure 5.6. Three of the patients (patients 4,6 and 5 from left to right) who stood using surface stimulation in their normal postures. Visually the postures look fairly similar and are quite different to that of patient 3 (figure 5.1).



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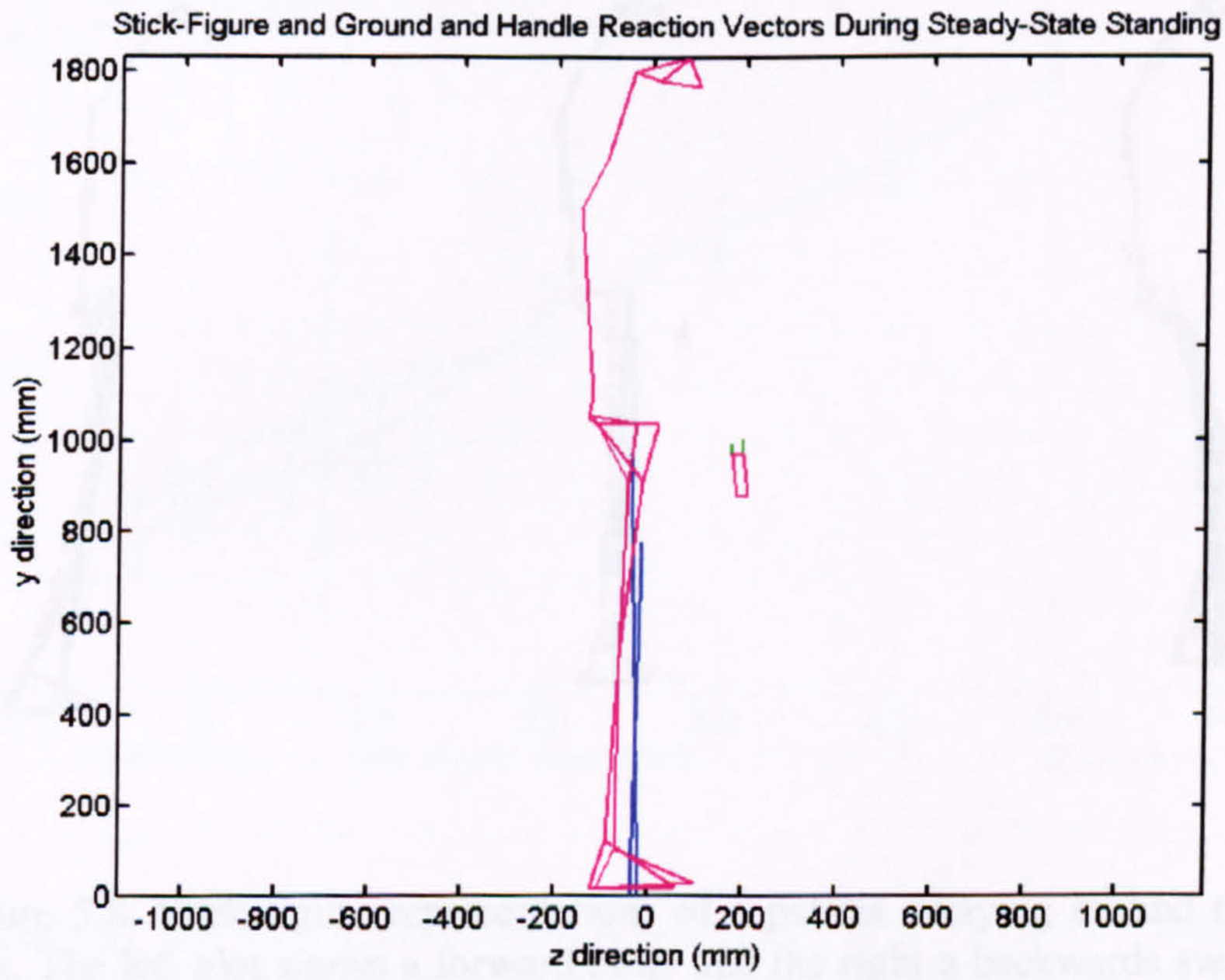


B

Figure 5.7. The Stick Figure representation of a surface stimulation patient (patient 2) standing with FES under open-loop control during steady-state standing. A shows the frontal view whilst B shows the side view. The blue lines are the ground reaction vectors whilst the handle reaction vectors are in green. Markers are positioned on the toe, heel, ankle, knee, greater trochanter, front, middle and back of the pelvis bilaterally, the L2, T10, T3 and C4 vertebrae and four markers are placed on the head at either side, the front and the top of the head. Data is from patient 4.

Figure 5.7 shows the reaction vectors from the ground and the hands as well as a stick figure representation of the patient during a typical surface stimulated open-loop control FES-assisted steady-state stand. It is therefore comparable with figure 5.3 which was obtained from the patient with the implanted stimulator, although data is available in figure 5.6 from both sides of the body. Both figures were obtained with the respective patients in their best posture. The amount of vertical force taken through the arms in figure 5.6 is less than in 5.3 and consequently more weight is taken through the legs. The GRV also passes through the hip in 5.7 rather than in front of it in 5.3, this means that there is a very small hip moment in 5.7 unlike 5.3 where there is a large hip flexion moment. Additionally there is only a small flexion moment at the knee as the GRV passes very close to the knee. The stand represented in 5.7 is therefore a better quality than in 5.3.

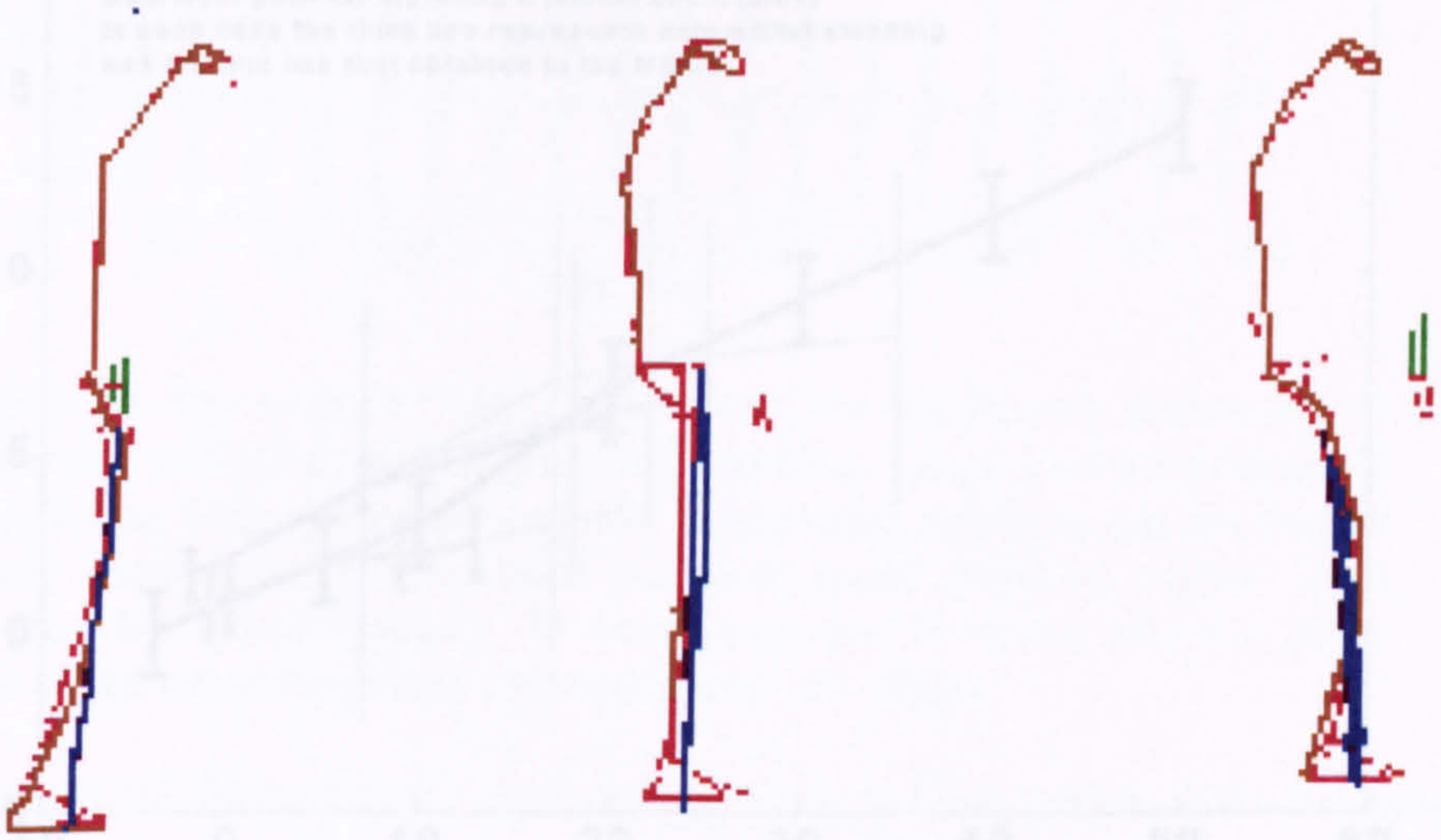


Figure 5.8. Stick figure representations of a patient swaying around the hips. The left plot shows a forward sway and the right a backwards sway with the middle plot showing his "normal" stable posture achieved before and after each sway. During the sways there is more weight bearing through the arms, indicated by the larger green lines from the handles. Although the patient was asked to sway around the hips only there is also some movement at the ankles. The ground reaction vector never passes a long way from the hip joint centre and so the patient never experiences large hip moments during these movements. Data is from patient 4.

During the movement of the hips (figure 5.8) it is possible to calculate the changes in hip extension moment and this is shown in figure 5.9 for surface stimulation patients only. Data was included only if the patient changed their ankle

angle by less than 3° to minimise complication of the results. All patients were asked not to sway at the ankles and restrict the movement to the hips but this was not always the case. Also included in the figure is data from Patient 4 in the MMCS over a comparable range of angles. Patient 5 did not use the MMCS and data from SS was corrupted through electrical interference. Over the range of angles that Patient 4 was tested the results from the MMCS and during standing the error bars overlap and there is therefore no significant difference between the two results.

During tests in the MMCS EMG was recorded from the leg muscles (see chapter 3). This activity was also analysed but no activity other than 20Hz stimulation effects were found on either temporal or spectral analysis.

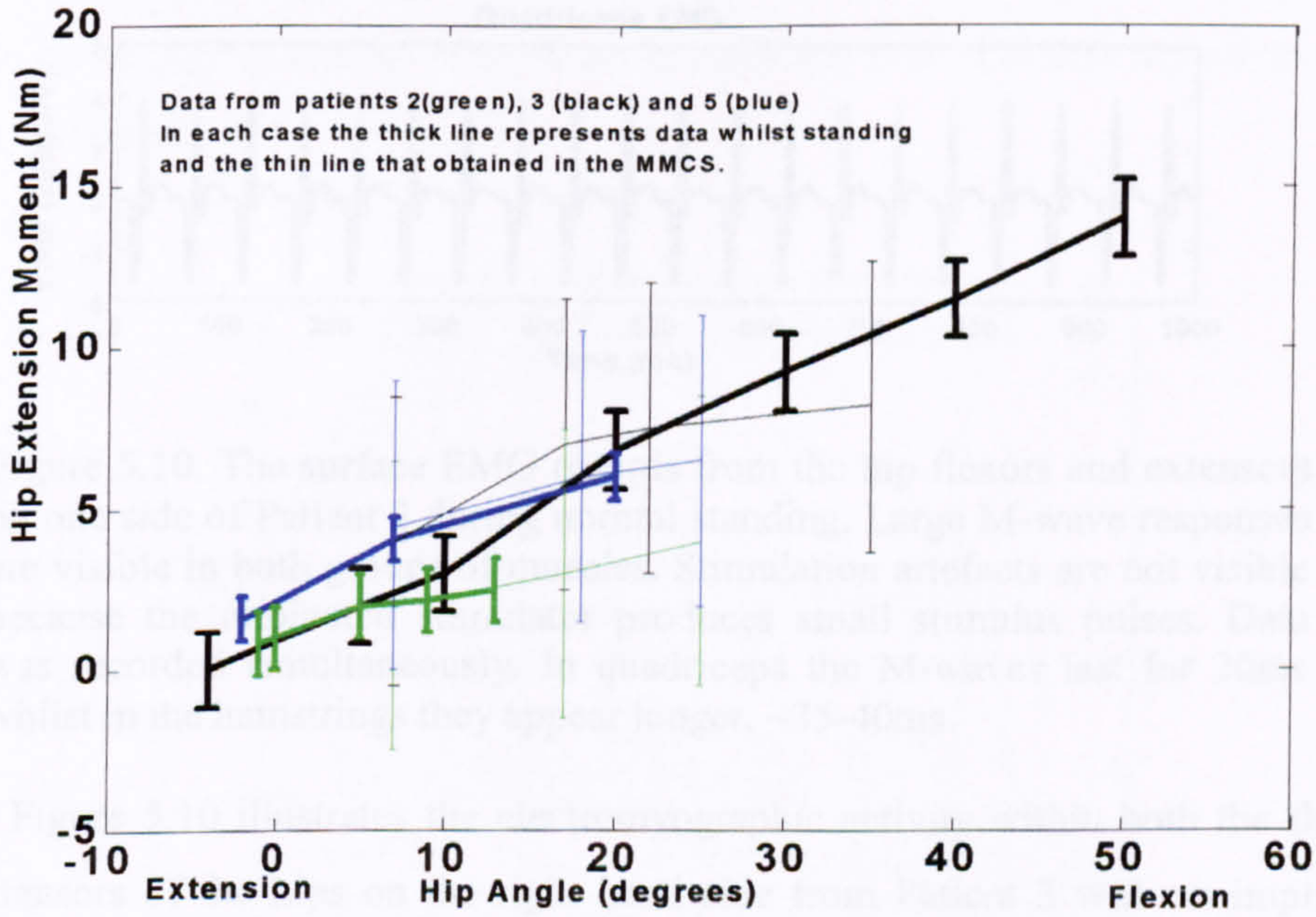


Figure 5.9. The Hip angle/moment relationship for the patients standing using surface stimulation who achieved some deliberate change in hip angle whilst standing. Also included for comparison are data from SS using the MMCS over a wider range of angles than during standing. Data from Patient 5's sit-to-stand is included, but not from other subjects who did not have this recorded. Over the normal range of standing angles ~10-0° the lines for all patients are similar within the errors of the system, outline in chapter 3. Data has only been included when there has been under 3° of ankle movement.

5.3.2. Electrophysiology of Standing.

During standing with stimulation large muscle contractions are present in those muscles that are stimulated. This occurs whether the stimulator is implanted or a surface stimulator. The implanted stimulator stimulates more muscles and has smaller stimulation artefacts than the surface stimulator because smaller currents (and hence voltages) are required to generate muscle contractions.

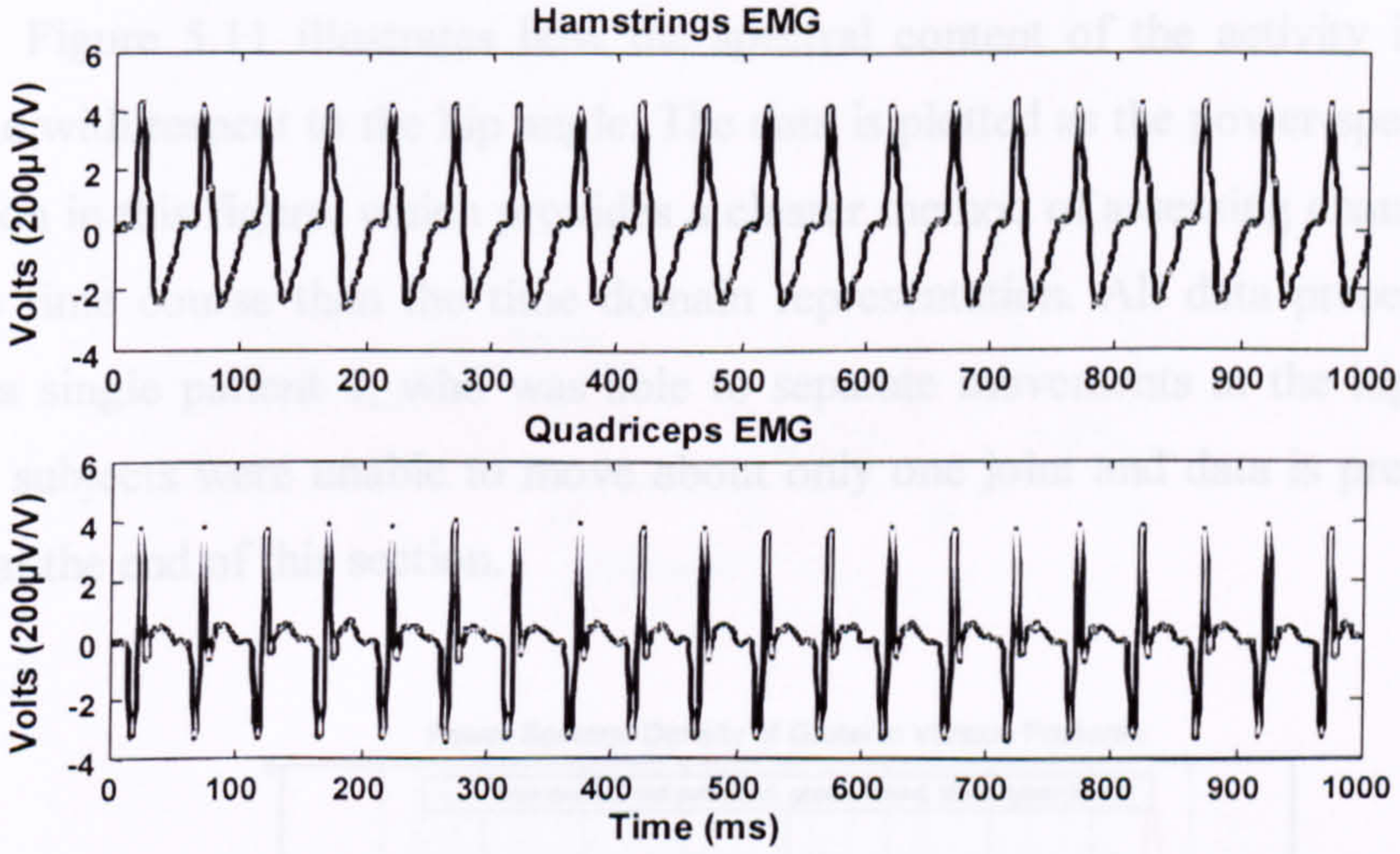


Figure 5.10. The surface EMG records from the hip flexors and extensors on one side of Patient 3 during normal standing. Large M-wave responses are visible in both groups of muscles. Stimulation artefacts are not visible because the implanted stimulator produces small stimulus pulses. Data was recorded simultaneously. In quadriceps the M-waves last for 20ms whilst in the hamstrings they appear longer, ~35-40ms.

Figure 5.10 illustrates the electromyographic activity within both the flexors and extensors of the hips on the right hand side from Patient 3 with an implanted stimulator. Large responses are visible in both groups of muscles that would serve to stiffen the hip. The direct M-wave responses which are seen in figure 5.10 are the result of stimulation of nerve roots which contain fibres innervating many muscles. In collaboration with Perkins a chart of the lumbo-sacral innervation has been developed and is included in Appendix 4.

In contrast, the patients with surface stimulation have large M-wave responses to stimulation in the quadriceps at a very short latency as the electrodes are placed over the muscle belly. In many cases it is not possible to determine the latency of the responses because the stimulus artefact is very large with this type of stimulation and may last for many ms depending upon the characteristics of the amplifiers used. As stimulation is only applied to the quadriceps muscles, M-wave responses are only

seen in the quadriceps. Stimulation artefacts are seen in all of the leg muscle groups with surface stimulation because of the large voltages generated by the stimulator.

5.3.3. Changes in Posture.

Some of the data from Patient 3 has been presented in section 5.3.1 (figure 5.2). The levels of activity in the hip flexors and extensors did not change with hip angle. Figure 5.11 illustrates how the spectral content of the activity in the glutei change with respect to the hip angle. The data is plotted as the power-spectral density function in this figure, which provides a clearer method of assessing changes over the whole time course than the time domain representation. All data presented here is from a single patient 4, who was able to separate movements at the hip and ankle. Other subjects were unable to move about only one joint and data is presented from them at the end of this section.

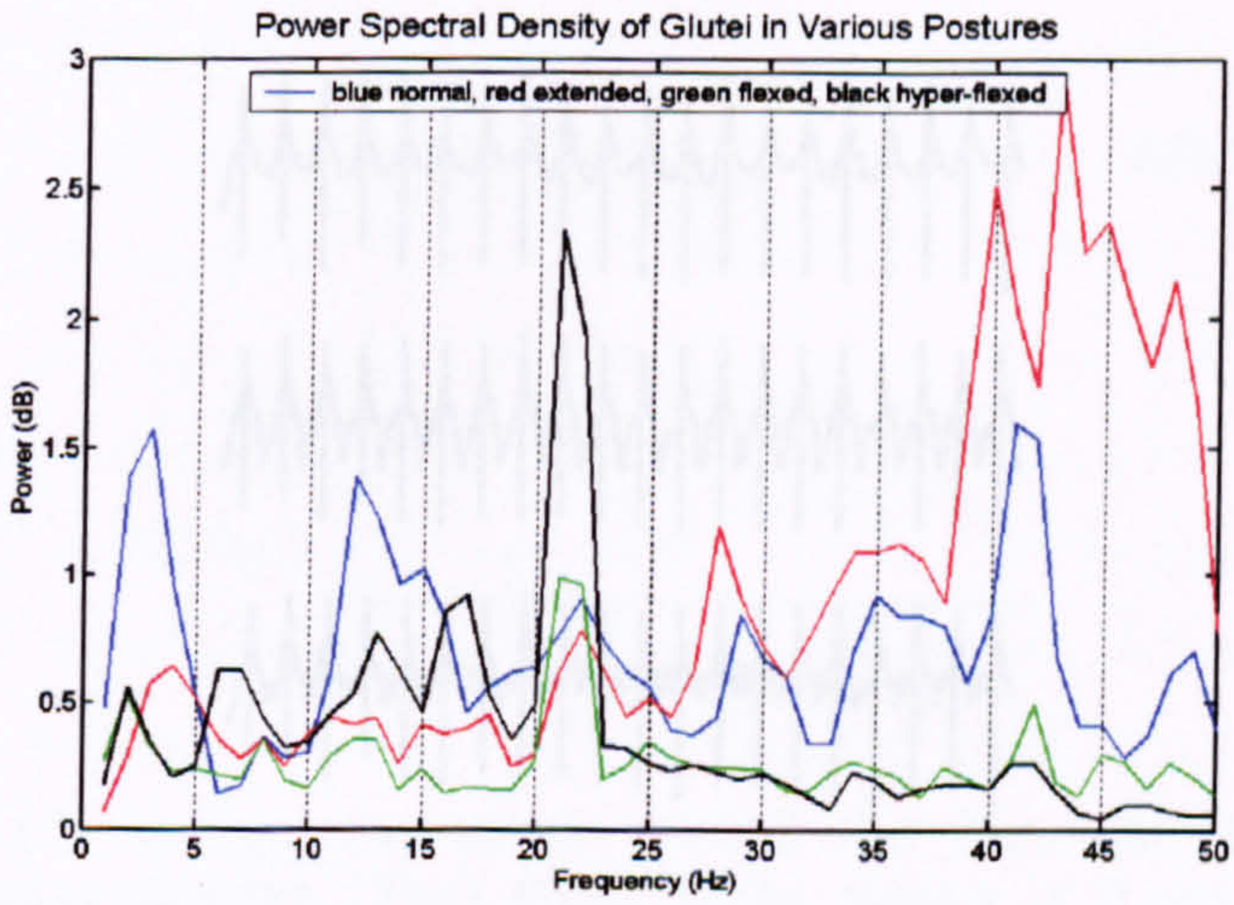
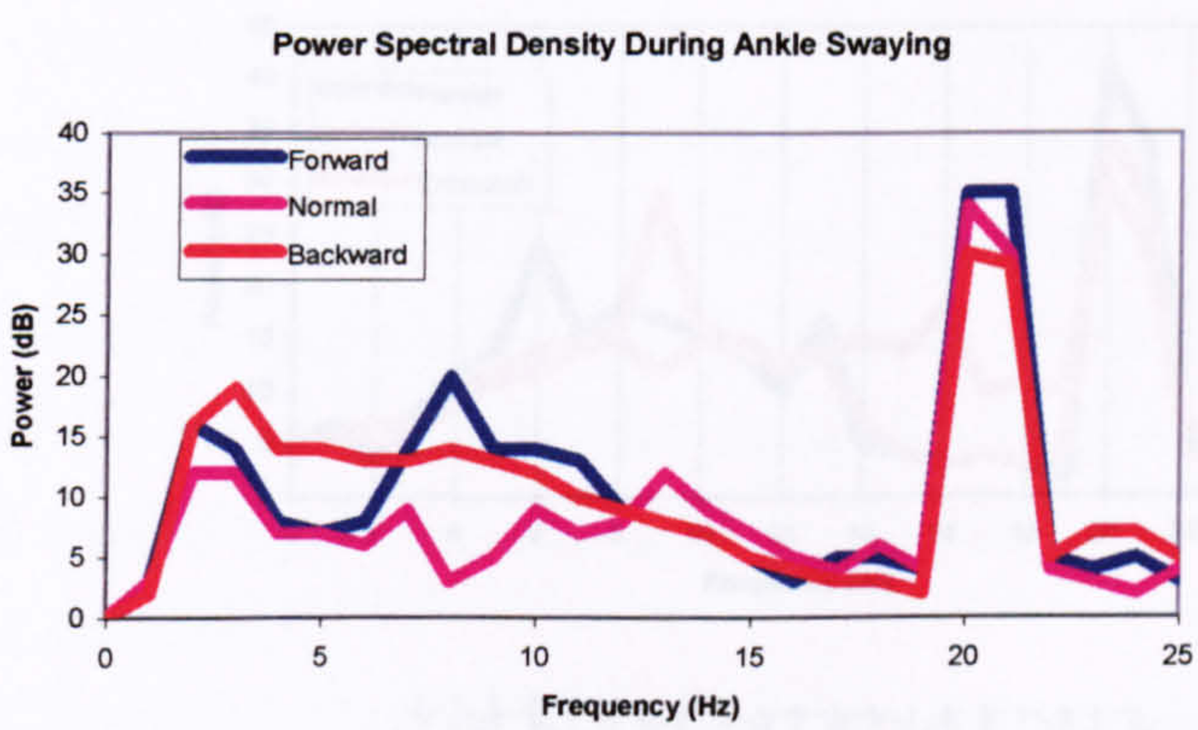


Figure 5.11. The power spectral density obtained from the glutei during FES-assisted standing, with an implanted nerve root stimulator. The patient was asked to stand in four postures, characterised by different hip angles. The postures were self-selected by the patient. The large peaks at both 20 and 40Hz are generated by the stimulus pulses and stimulus-locked events. Because of the movements generated during these tasks the relationship between the electrodes, (on the surface) and the muscle may not be fixed and hence changes in the power content, or in the temporal analysis of the results may be seen which are not due to neural changes.

The raw EMG records obtained during surface stimulated standing are heavily contaminated with stimulus artefact which makes the interpretation and examination of the records complex. However, stimulus driven effects are locked to the stimulus

frequency of 20Hz. Simple spectral analysis, comparing the frequency components in different postures, is used to highlight changes in muscle activity patterns. Changes in reflexes from the stimulation will not be discernable in this technique, but non 20Hz effects will be highlighted.



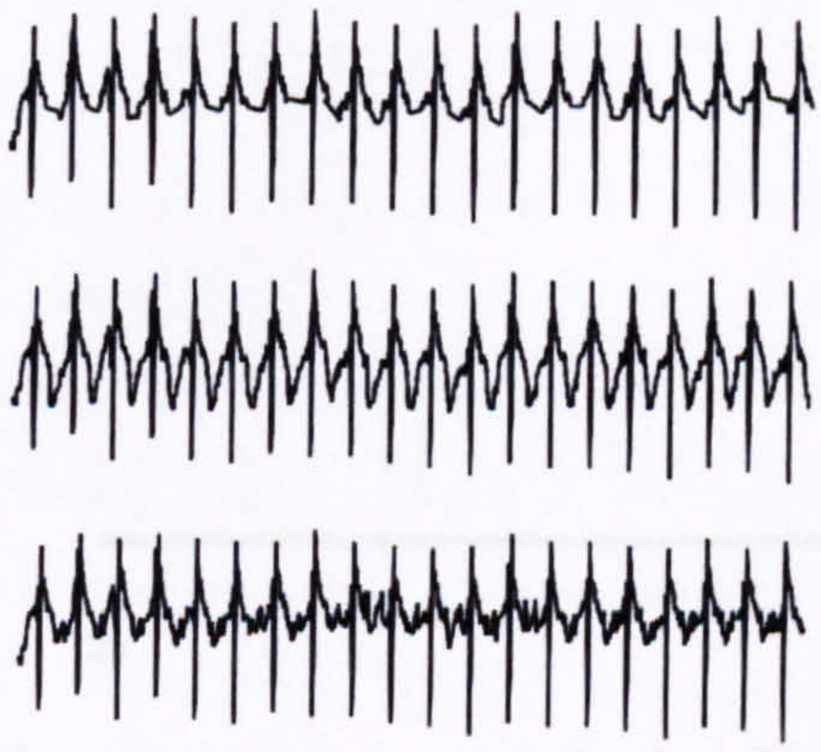


Figure 5.12. (Top). Variations in the power spectral density of EMG from the gastrocnemius as the patient sways around his ankles. The angle is measured as the deviation from his normal angle. When the subject sways forward at the ankles activity at 8Hz appears more prominently than at rest or when the patient sways backward. (Bottom). The raw EMG during each condition (top forward, middle normal and bottom backward) looks very similar and differences are hard to determine.

Activity in the glutei may serve to stabilise the hip. Figure 5.10 shows the changes in spectra as the hip moves from hyper-flexion through to extension. There isn't a linear progression in the spectra from hyper-flexion to extension. In the hyper-flexed position there is a large 20Hz artefact and also a peak at around 16-17Hz,

which is not present in any of the other postures. During normal standing there is a large peak at low frequencies (2-3Hz) and also a broad region of activity between 12-16Hz. The higher frequencies are more prominent in the extended posture.

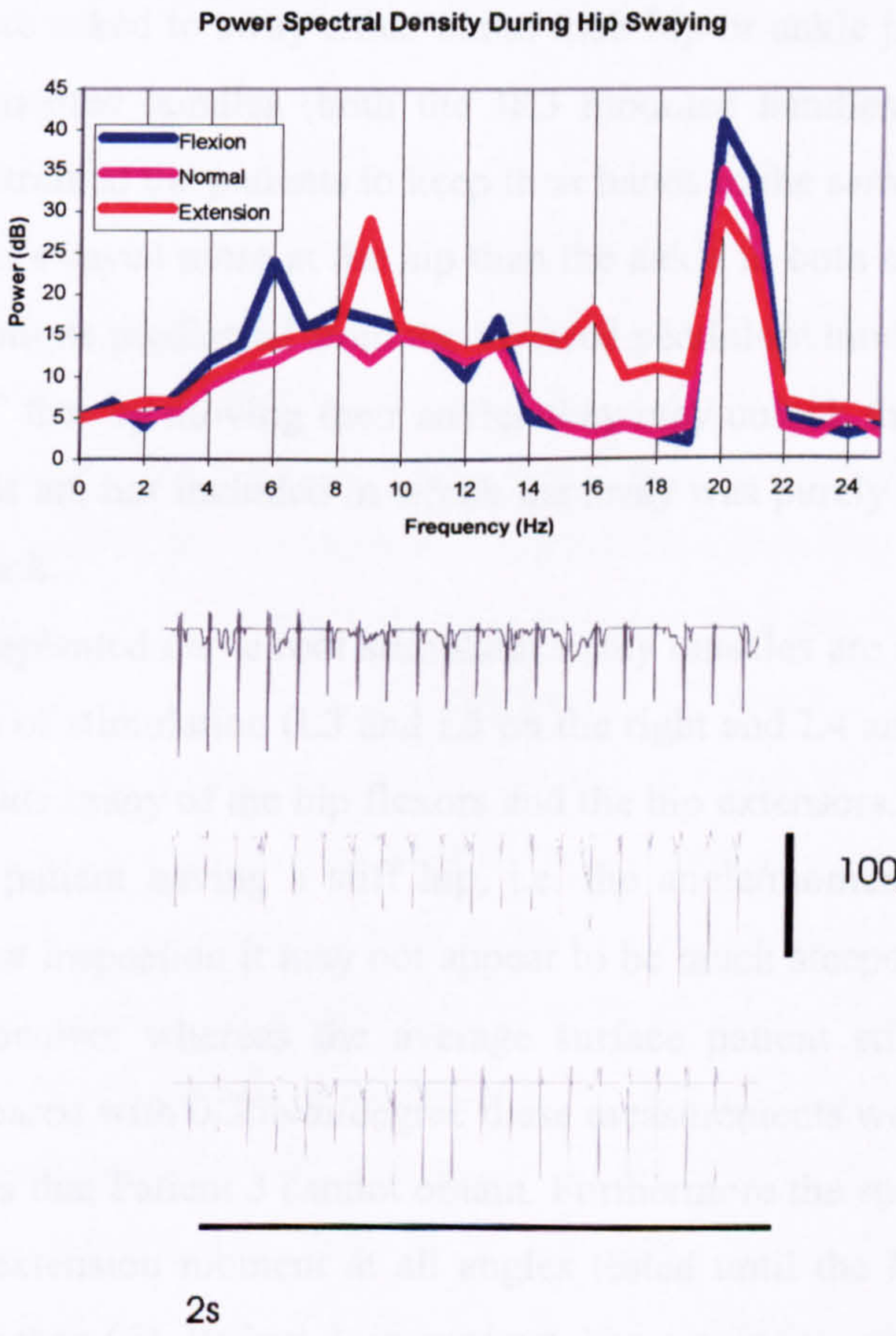


Figure 5.13. During movement around the hip, activity in the gastrocnemius changes. (Top) Peaks in the spectra at 9 and 16Hz are present more prominently when the hips are extended than when they are flexed. (Bottom) The raw EMG during forward (top), normal (middle) and backward (bottom) shows some changes in activity however the majority of the changes are obscured in the time domain by the large stimulus artefacts.

Activity in the gastrocnemius also shows some postural changes with both ankle, figure 5.12, and hip, figure 5.13, movements. A peak at 8Hz is seen during forward sway at the ankles (figure 5.12) which is not present during the backward sway where a peak at 3Hz is present. However, overall the two spectra appear very similar. During movement of the hip (figure 5.13) peaks appear again during forward

sway, which extends the hips, this time at both 9 and 16Hz. When swaying backwards there is a peak at 12Hz, which is not present in other conditions.

5.4. Discussion.

Patients were asked to sway either about their hip or ankle joints during some stands. The instrumented handles (both the JR3 mounted handles and the custom-build handles) constrained the patients to keep their hands in the same position.

Patients also swayed more at the hip than the ankle in both conditions. This is in line with expectations predicated from the inverted pendulum model (Winter 1990). Patients may "fear" that by moving their ankles they may unlock their knees causing them to fall. Results are not included in which the sway was purely or predominantly generated by the trunk.

Using the implanted nerve root stimulator many muscles are stimulated within the standing pattern of stimulation (L3 and L5 on the right and L4 and S1 on the left). These muscles include many of the hip flexors and the hip extensors. These combined effects lead to the patient having a stiff hip, i.e. the angle/moment curve is steep, figure 5.2. Upon first inspection it may not appear to be much steeper than that in the surface patients, however whereas the average surface patient stiffness is around 0.2Nm/degree compared with 0.36Nm/degree these measurements were obtained over a range of hip angles that Patient 3 cannot obtain. Furthermore the surface stimulation patients had a hip extension moment at all angles tested until the hips were hyper-extended (angle less than 0°). Patient 3, in contrast, has a negative moment unless her hips are flexed to a large degree, about 50°. Yu (1999) and Donaldson (Donaldson & Yu, 1998, 2000) developed the concept of joint deficits as "the effective moments at the leg joints owing to the forces at the handles. The upper body is supplementing the inadequately stimulated leg muscles by these deficits." Although in the CHRELMS framework "inadequately stimulated" was taken to mean that the stimulation level was not high enough (and therefore this was part of the input signal to the controller) in the LARSI experiments joint deficits can also be calculated and these arise because of *relative inadequate stimulation*. Relative inadequate stimulation is used as the term here because the stimulation to the quadriceps may be sufficient to extend the knees but causes flexion of the hip, whilst hamstring stimulation causes hip extension but weakens the knee extension. Consequently the effective hip extension stimulation

(quadriceps-hamstrings) is inadequate. Hip extension deficits can then be calculated during steady-state standing as well as the sit-to-stand. In this study the sit-to-stand was not examined but Donaldson and Yu, (1998) have previously studied Patient 3 during the sit-to-stand as well as the early phase of steady standing (figure 3, Donaldson and Yu 1998). During steady state standing they found a hip joint deficit of ~25Nm.

A fundamental question within the LARSI project, and the starting point for this study was the question; "is there a reason why Patient 3 can't stand straight with LARSI stimulation"? The answer to the question is that the stimulation delivered via the implant stimulates both extensor and flexor muscles leading to co-contraction of the muscles and consequently a very stiff hip. As the hip becomes more extended, the hip extensors have increasingly short moment arms. This means that the joint moment they can exert for a given force of contraction becomes smaller. It can therefore be concluded within this study that standing using the LARSI is not feasible for Patient 3 because of the polymyal innervation from the anterior nerve roots. This conclusion is line with the findings from an *in vivo* animal study (Stein *et al.*, 2002). Stein *et al* report that ventral root stimulation will not produce a full range of limb movements and therefore is unsuitable for stimulation. However in their paper, Stein and colleagues do not consider the use of stimulation for cycling, which has been shown to be successful in one patient (Perkins *et al.*, 1999). The joint moments measured in the MMCS in this study are larger than those previously measured and the posture that might be predicted from these moments is in line with that seen clinically. The difference in joint moments was due to the removal of offsets prior to the patient entering the MMCS which suggests that there might be some low level motor activity or a small hip contracture.

Previously it had been hoped that selective training of muscle responses might lead to suitable muscle contractions for standing (Rushton *et al.*, 1997). This is not the case for Patient 3 and as she started training for cycling (Perkins *et al.*, 1999) the clinically observed quality of her standing decreased. Hip flexion is crucial during cycling and therefore it is not unexpected, although disappointing that it is not possible to train adequately for both standing and cycling.

In contrast to Patient 3 the patients who stand with the use of surface stimulation to the quadriceps all achieve a satisfactory posture. The posture of these patients is characterised by knee extension, ankles at around 90° and straight hips.

During steady-state normal standing at least 2/3 of the body weight is taken through the legs and in many cases, patients 1,2 and 5 this is around 90%. The patients report that standing "feels comfortable" and that they enjoy it, although given that all the patients, except Patient 5 were experienced standers this is perhaps not surprising since they might have stopped standing if they did not enjoy it. None of the patients regularly stimulated their gluteal muscles and all achieved a satisfactory posture using just quadriceps stimulation. This might be surprising since the quadriceps (rectus femorus), in addition to extending the knee, which is why they are stimulated, also act to flex the hips. *Rectus Femoris* is the main muscle that is stimulated using surface stimulation as it is close to the stimulation electrodes. It is a bi-articular muscle with two insertion points in the bone, the proximal serving to flex the hip and the distal to extend the knee. By teaching the patients to place the electrodes over the lower portion of the muscle it is possible to minimise the hip flexion and thereby achieve satisfactory standing. During this type of standing there is a very small hip extension moment which tends to reverse into a flexion moment as the hips hyper-extend, in line with expectations based upon the anatomy of the hip and the biomechanics of standing. The exact angle at which this switch takes place appears to be different for each subject. However there are errors associated with each measurement both of joint moment and hip angle. In addition each patient's anatomy, points of muscle insertion etc., will vary and therefore some variation is to be expected between patients.

Movement during steady-state standing did not affect the biomechanics of standing, other than changes in the joint extension moments which altered in line with expectation and as discussed above. At a functional level it therefore appears as if there is little effect of changing the posture. Comparing the results from the MMCS and during standing (figure 5.8) the joint moments fall within the expected limits for each system, implying that there is no measurable difference in joint moments between standing and lying.

Although the affect biomechanically upon the stand of changing the posture is small there may be electrophysiological effects associated with the changes in posture described in this chapter. Whilst standing with stimulation the EMG is dominated by 20Hz activity that arises either from direct muscle contraction or as stimulus artefact. The stimulus artefacts are large because of the large stimulation voltages that are used to stand the patients. Examination of the raw EMG is therefore complex. Low-pass or band-pass filtering might be thought of to improve the situation; however 20Hz is a

frequency at which neural activity is expected to be found, both naturally and in response to the stimulation. The filter would also remove large amounts of activity in the region around 20Hz. Therefore low-pass or band-pass filtering is not a feasible option for these data. Spectral analysis provides an interesting approach to examining data of this type. In this analysis the changes in the spectral content can be analysed against changes in posture.

Previous studies (Buneo *et al.*, 1997), (Denny-Brown, 1929), have identified the muscles around the ankle as being the muscle groups most likely to show postural "support reactions". These muscles are also less affected by the stimulation pulses as they are further away from the stimulating electrodes than the thigh muscles. In this study changes have also been found in the ankle musculature and in the glutei. What is the functional significance of this posture dependent activity? The amount of activity seen is not large, figure 5.10. The level of activity recorded with surface EMG is difficult to interpret because of the many confounding factors involved (Hallet *et al.*, 1994); impedance of skin, distance between electrodes, distance from muscle to electrode etc. The situation here is further compounded by the large stimulus artefacts that are present in all recordings obtained with surface stimulation from all muscle groups. The recorded activity may be sufficient to help stabilise the hips and ankles but is unlikely to be sufficient on its own to provide support to the body. Support reactions and postural reflexes are thought to help stabilise the body rather than provide all of the support (Carpenter, 1996). These responses may therefore be classified as support reactions under that description and it can be concluded that there is posture dependent spinal activity.

The level of activity seen is low and there were no biomechanical effects of the activity during either FES-assisted standing or passive standing that were detectable using the current system. The support reactions were, in these instances, therefore very limited and would have provided no support to the patient. However, it is significant that there is activity that is posture dependent, and future FES-controllers may be able to use this activity to control stimulation to maintain a set posture.

The changes observed in the spectra of the surface recorded EMG in each posture might actually reflect artefactual changes rather than neurophysiological phenomena. The stimulation artefacts on the raw records run into each other making sensible interpretation of them virtually impossible. A future way around this might

be to use a charge balanced stimulator and to develop a programme to control the stimulator in which 2 or 3 stimulus pulses were missed every 2-3 seconds. Unfortunately therefore it is not possible to state with certainty whether the observations here represent neurophysiological changes or an artefact of the recording system.

5.5. Conclusions.

During FES-assisted standing the patient with the nerve root stimulator stands in a poor posture because of direct stimulation to both hip flexors and extensors which leave her with a net hip flexion. Other patients, using surface stimulation, are able to achieve a good posture without a hip moment in their final upright posture. Non-stimulus driven activity was seen in all patients during standing. This was not observed to have any effect upon their posture, as recorded biomechanically. The joint moments during standing and whilst recumbent were the same within experimental limits, indicating that there were no large postural reactions to standing.

Chapter 6.

Intermittent Neural Activity During Standing.

6.1. Summary.

The spinal cord receives many sensory inputs during standing. This chapter presents results from two patients in whom standing produces clinically diametric effects upon their spasm activity. FES-assisted standing for Patient 1 produces regular spasms that severely impinge upon his standing ability whilst for Patient 6 FES-assisted standing produces long-lasting suppression of tonic spasm activity. Unstimulated standing for Patient 1 also produces spasms, but these have a variable inter-spasm interval that is similar to that seen in Patient 6 at rest, 3-30 seconds. It is therefore proposed that similar neural mechanisms may underlay the production of the spasms in both instances.

These spasms, or motor outputs, are similar in nature to those seen in the developing spinal cord. It is therefore possible that these motor outputs arise because of changes in the spinal cord as a result of the loss of descending inputs.

The results of the interaction between the oscillators in the spinal cord, standing up and the FES are very different in the two patients. The differences may arise because of differences in the site and extent of the lesions. This chapter provides further evidence of the spinal cord's ability to change its motor output as a result of standing up.

6.2. Introduction and Methods.

Two patients outlined in chapter 3 have unusual and persistent "spasm" activity associated with standing. Spasms have been discussed in chapter 2 and are generally not thought to be ongoing in nature unless there is a persistent stimulus. The two patients, Patient 6 and Patient 1 are both patients who have had a sacral root stimulator implanted for bladder control and an accompanying posterior rhizotomy of sacral roots S2-5 (Brindley *et al.*, 1982). Both patients are established and were continuing users of the Salisbury FES-assisted standing system at the time of the study.

The effects of FES upon spasms are unclear and have been mentioned in chapter 2 and were reviewed by Alfieri recently (Alfieri, 2001).

Experiments with Patient 1 were carried out in two sessions; in the first the effects of FES-assisted and passive standing on his spasms were recorded in a manner similar to that described in chapter 3. The second session consisted of neurophysiological testing of the completeness of the lesion. These tests were performed because of some potential confusion in the medical notes concerning the lesion level. The extensive orthopaedic implant to stabilise the lesion site together with the implanted nerve root stimulator prevented the use of MR imaging of the injury site. Neurophysiological tests of descending motor pathways were carried out with the patient standing in an Oswestry Standing Frame. Transcranial Magnetic Stimulation, TMS, was applied over the leg area of the primary motor cortex. Stimulation was applied using a Magstim200 (the Magstim company, Dfyyed, Wales) and a figure of 8 coil with the vertex positioned over Cz and the stimulator turned up to 100% of its output. Surface EMG electrodes were placed over the leg muscles on both legs and on the arm to confirm that the stimulation was working. Electrodes were in a standard configuration with an inter electrode distance of 3cm and using a common earth electrode. Signals were amplified using Digitimer D150 (Digitimer UK) amplifiers (amplification 1000, band pass filter 0.3-300Hz). 15 trials were presented per leg and analysed individually and then averaged for each leg and combined legs. The number of stimuli presented was limited by the patient's tolerance of the stimulation at such a high level, which produced widespread muscle contractions in the upper limb and face that the patient found unpleasant. Because of his lesion he was unable to provide any background EMG.

Further descending pathways were examined through the use of Galvanic Vestibular Stimulation, GVS, and the startle reflex. These responses are thought to be mediated via pathways other than the cortico-spinal pathway. During GVS (Day 1999) a bipolar arrangement was employed, with the anode on the sterno-mastoid process behind one ear and the cathode behind the other ear. Anode and cathode were alternated on a pseudo-random basis. Square waves of 1.5mA were applied for 3seconds. EMG responses were collected from the leg and upper arm muscles. A total of 30 stimuli were applied and average results were analysed for each polarity and across polarities.

The startle reflex (Kimura *et al* 1994) was tested by the use of a sudden loud tone applied to the patient who was wearing ear-phones. As this reflex is known to habituate rapidly the tone was only applied three times (Nieuwenhuijzen *et al.*, 2000).

Responses were analysed individually. During the motor pathway testing care was taken to test the responses between spasms.

The sensory pathways were assessed by trying to elicit somatosensory evoked potentials, SEPs. As the patient could not feel any stimuli on his legs we used a mixed (motor and sensory) nerve, the common peroneal for the tests. Stimulation was applied through a Digitimer stimulator (DS3), and at a level which gave a clear motor response (dorsiflexion) in both legs this was a current of 40mA and a pulsewidth of 0.5ms. This level was chosen as the motor threshold is typically higher than the sensory threshold. Scalp electrodes were placed over the sensory cortex, C3, C4 Cz, CP4, CP3 and CPz (using the 10-20 system of naming (American Electroencephalographic Society 1994)) referenced to linked earlobes. 250 stimuli were presented on each leg and the data were collected and averaged using Spike2 software (CED, Cambridge, UK). These responses were collected with the patient recumbent. It was felt that there would be too much activity from the upper body associated with standing to allow the collection of data whilst standing.

In all of the neurophysiological tests for completeness the analysis of the results was concerned with the identification of responses that had traversed the lesion. Responses were analysed visually to determine if there were any changes in the EMG level following the stimulation. Had responses been found, the responses would have been measured for amplitude, latency and variability.

Further experiments were planned with Patient 1, but these were prevented by the occurrence of a post-traumatic syringomyelioma, (syrinx) which was finally treated with a partial cordectomy. This treatment resulted in the loss of lower motor neurones and consequently Patient 1 was no longer able to stand. The treatment also resulted in the removal of the part of the spinal cord we believed responsible for the observations reported here.

Experiments with Patient 6 were also carried out on two occasions. On the first occasion a series of recordings of the spasms present at rest and during passive standing were recorded. The second session also recorded spasms at rest to assess their variation between sessions and also recorded the effects of FES-assisted standing on the spasm activity.

6.3. Results.

The two patients in this chapter have contrasting clinical effects from FES-assisted standing; Patient 1 develops very regular spasms and Patient 6's spasms cease for a prolonged period of time. The results from each of the patients will therefore be considered independently.

6.3.1. Patient 1. Regular Spasms when Standing.

6.3.1.1. Completeness of Lesion.

No responses below the lesion were seen in any of the tests of the descending pathways nor above the lesion for the SEP tests. These results suggest that there is no neural conduction across the lesion site. The neurophysiological testing of the extent of the lesion, indicated that the lesion was both motor and sensory complete. A recent physiotherapy assessment prior to the commencement of the study reached the same conclusion and classified the lesion as T10 on the right and T11 on the left. Although neither the physiotherapy nor physiological testing provides proof of the status of the lesion it is assumed throughout the remainder of this work that the lesion is complete.

6.3.1.2. Spasms During Passive Standing.

The patient experiences spasms of varying severity during standing in a supporting structure like an Oswestry Standing Frame. The inter-spasm interval for these events is variable between 3-30 seconds in the records obtained in the present study (figure 6.1), as assessed by the onset of EMG activity in the Tibialis Anterior muscle.

Spasms during passive standing are observed to be unilateral in nature. Using surface EMG electrodes it is possible to observe the pattern of muscle activity during a spasm, and in the period between spasms.

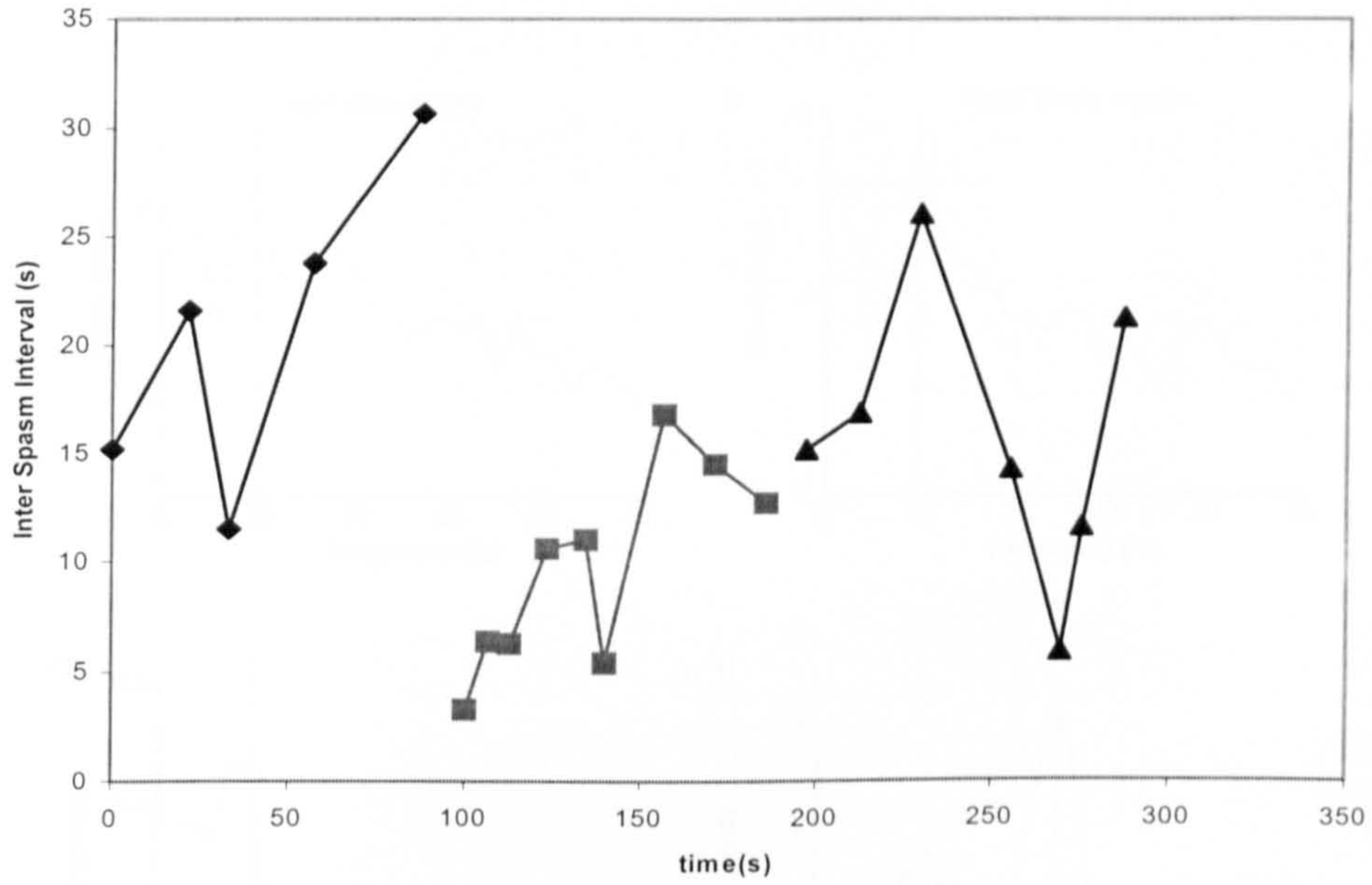


Figure 6.1. The inter-spasm interval during passive standing, in an Oswestry frame. The data was recorded in two separate periods separated by a couple of seconds, (this is a result of the operating system used to collect the data). The period between the spasms is irregular, varying between 3 and 32 seconds. The timing is taken from the onset of EMG activity in the Tibialis Anterior muscle, but all recorded muscles were active during the spasms. The timing was started after the initial sit-to-stand and when the patient felt comfortable in the frame. The spasms looked to be similar in size to one another, but motion analysis was not used because of the interference caused by the standing frame.

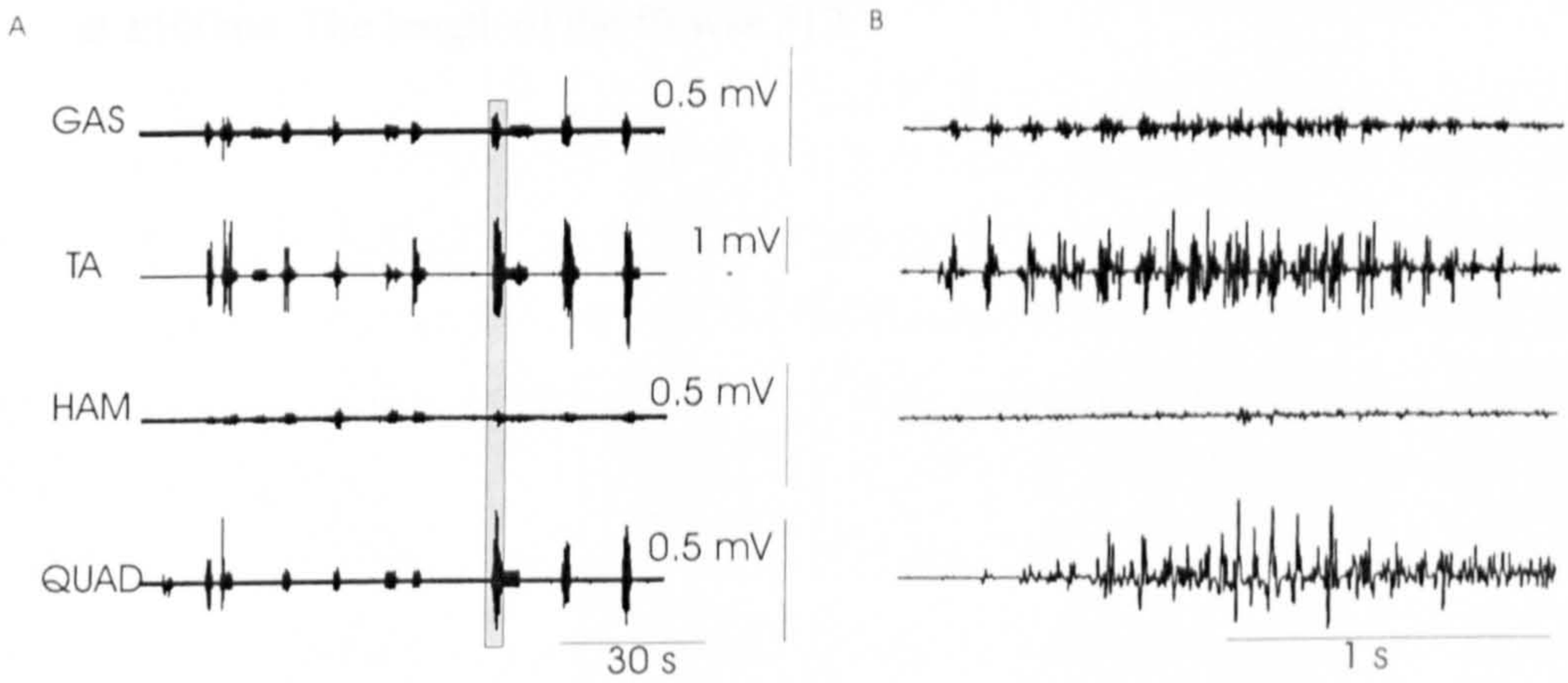


Figure 6.2. Left. The surface EMG record during a passive (unstimulated) stand in an Oswestry Standing Frame. Irregular bursting activity is seen in all muscle groups, all from the same side. These appear to occur concurrently across muscle groups. Right. The area shaded in grey is expanded. The bursting activity during a spasm is clearly shown. Regular activity at 10Hz is observable in Tibialis Anterior.

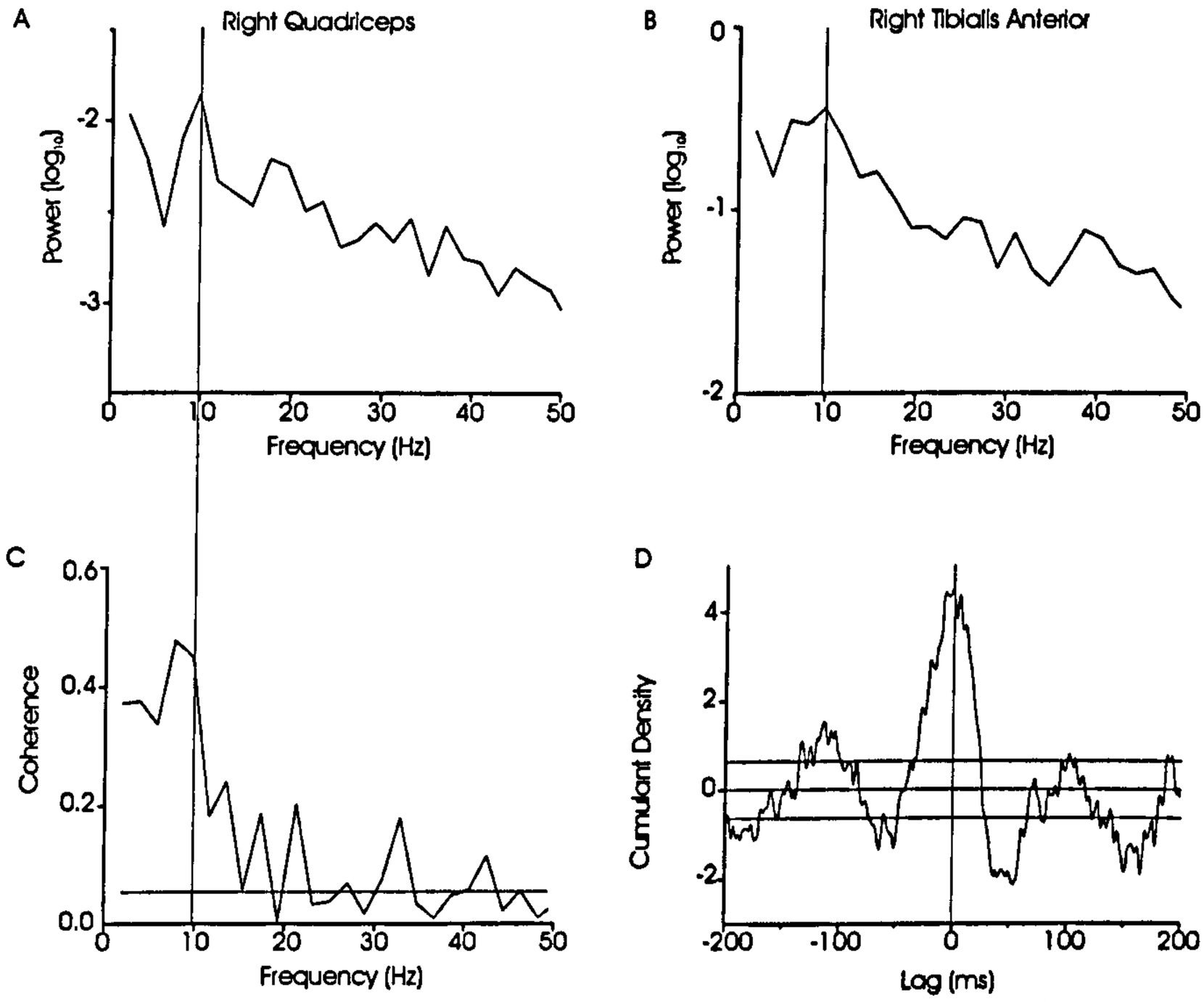


Figure 6.3. The top two plots show the Fourier transform of the EMG during a spasm from the Quadriceps, top left, and the Tibialis Anterior, top right, muscle groups. There is a large peak at 10Hz in the quadriceps and a less prominent peak in the tibialis anterior. Coherence analysis between the two muscles, bottom left, shows a peak in the 8-10Hz range. This 10Hz coherence is further confirmed by cumulant density between the muscles, bottom right. There is a peak at around 0ms, with side peaks at ±100ms. The length of the fft was 512.

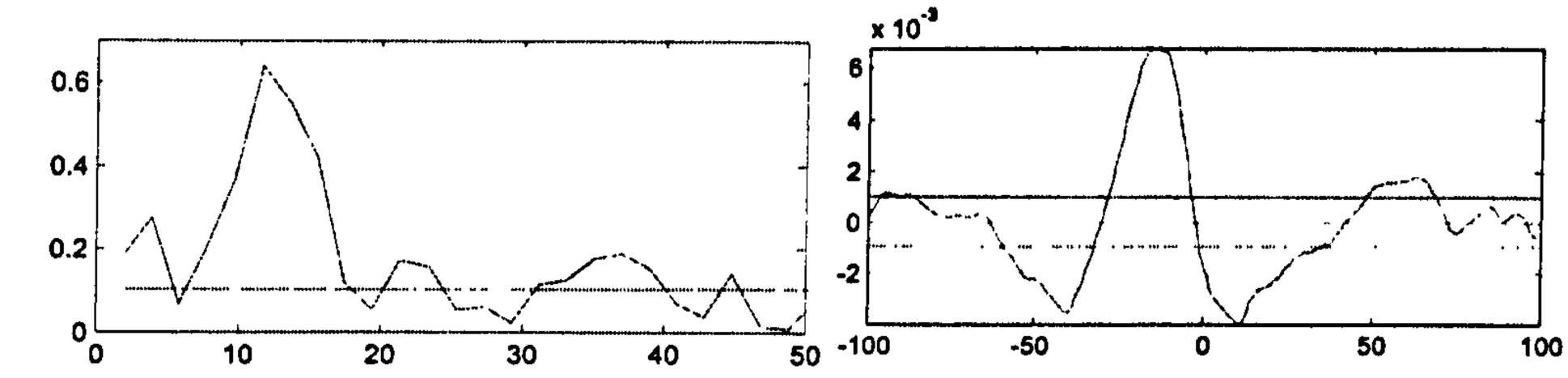


Figure 6.4. The coherence (A & C) and cumulent densities (B & D) between Gastrocnemius and Tibialis Anterior (A & B) and Gastrocnemius and Quadriceps (C & D). Both coherence plots show a peak at 10Hz, mirroring that in figure 6.3. Both cumulent densities also show a peak at around zero lag, although for the pair of muscles at the ankle (B) this is offset with tibialis anterior leading gastrocnemius.

The figure (figure 6.2) shows apparently synchronous bursts of activity across muscle groups. Activity appears synchronous between tibialis anterior and gastrocnemius. This argues against the activity being clonic in nature. Using electrical stimulation of single muscles it was possible to record activity in just one channel for each of the channel. This suggests that the activity is not due to electrical cross talk either within the amplifiers or between the electrodes. Figure 6.3 shows temporal and spectral analysis of the spasms. Data was concatenated from individual spasms. Fourier analysis shows a peak in activity at 10Hz in all of the muscle groups, to a greater or lesser extent. Coherence analysis between the quadriceps and tibialis anterior muscle also shows a peak at 10Hz. When the temporal relationship is plotted between the two muscles there is a central peak at ~0ms, with lobes at ±100ms. The actual peak is at -3ms, indicating that the quadriceps lead the tibialis anterior by 3ms, roughly what might be expected to be the conduction delay between the muscles. The peaks at ±100ms provides further confirmation of the 10Hz finding in the spectra and coherence analysis.

It is unlikely that this result is due to cross-talk either from the recording electrodes since each muscle could be stimulated individually using electrical stimulation and activity was not seen in other muscles. Since the muscles illustrated were separated by the knee joint it is further unlikely that the activity is due to cross-talk. Regular checks were made of the equipment by the technical staff at the Institute of Neurology and the isolation between channels was over 2kV thereby making electrical cross-talk within the amplifiers very unlikely.

The activity reported here is not clonic in nature since antagonistic pairs had activity at the same time (clonic activity is typically reciprocal between antagonistic muscle pairs). Clonus could be evoked around the ankle in this patient comparatively easily (as it can in many patients with spinal cord injuries) and showed reciprocal activity between tibialis anterior and gastrocnemius.

The data shown here (figure 6.3) is typical of that seen between other muscle pairs, although the coherence is the strongest in the example shown.

6.3.1.3. Spasms during FES-assisted Standing.

In common with many FES-standers this patient is able to stand for prolonged periods using FES. The limiting factor in the standing time, reported by the patient, is fatigue in the arms caused by weight-bearing during spasms. During the sit-to-stand a mild flexor spasm occurs that passes very quickly and is presumably due to changes in muscle length and loading. This type of spasm is not uncommon in patients and is relatively simplistic and is not the same as the spasms described in detail in chapter 7. However, as mentioned in the introduction the patient experiences severe spasms at regular intervals during FES-assisted standing. Figure 6.4 shows two photos of the patient with him in a good posture on the left and during a spasm on the right. These spasms lasted for around 3-5 seconds when observed clinically. A plot of the inter-spasm interval is shown in figure 6.5. The 16s regularity, with the exception of the two 8s spasms, is striking. Although only a short time period is shown, the patient reports that the spasms seem to him to remain with the same regularity for long periods of time (up to 30 minutes).

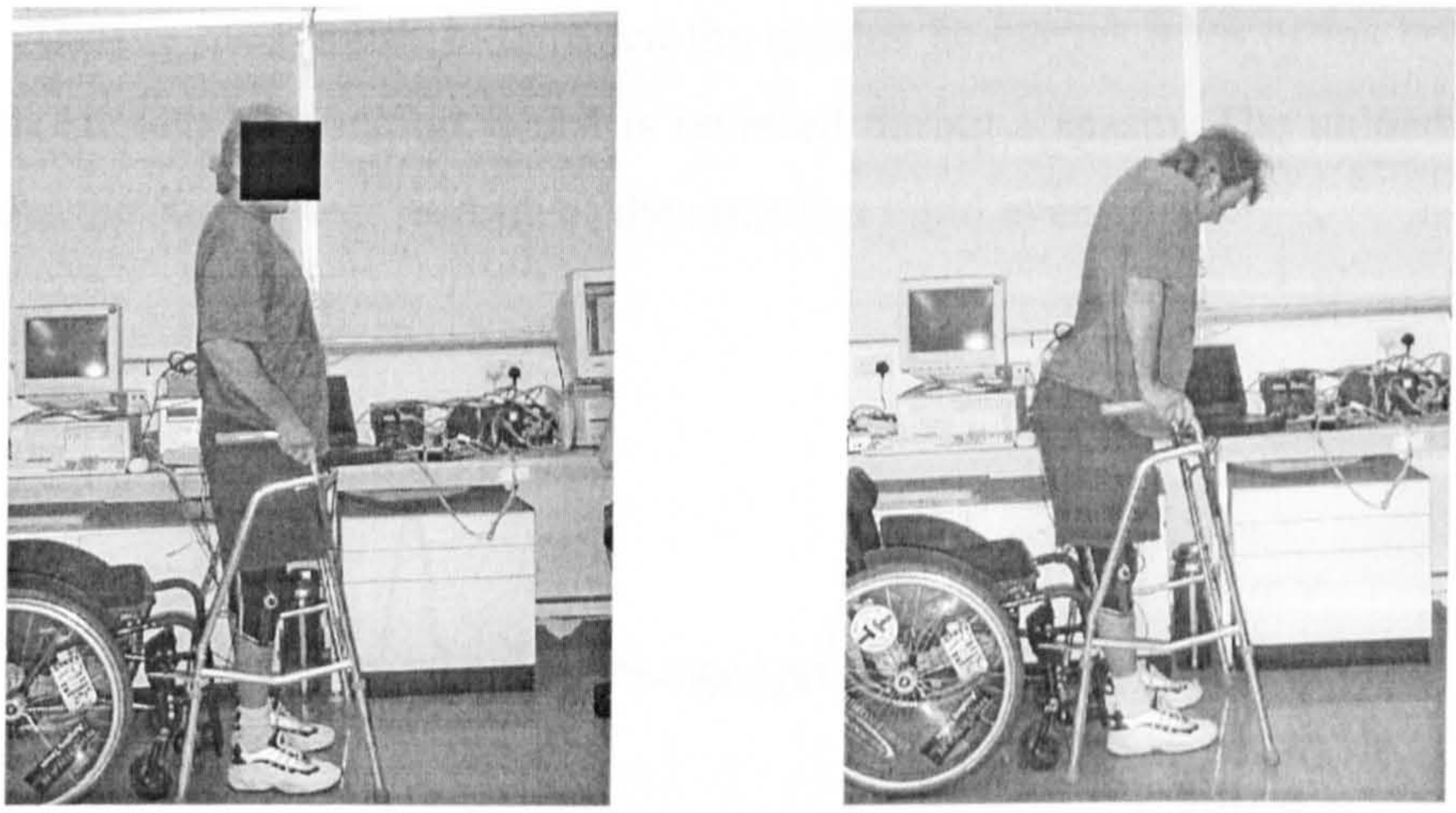


Figure 6.5. The patient standing using closed-loop control of FES to the quadriceps muscle. Stimulation is controlled using a PID controller using the knee-angle as a control signal. The patient is standing between spasms on the left and during a spasm on the right. The change in posture between the two conditions is characterised by hip flexion and the transference of weight bearing to the arms. On the left the patient is holding on to the vertical supports, whilst during the spasm the patient uses the horizontal supports so that he can carry the weight of his body through his arms.

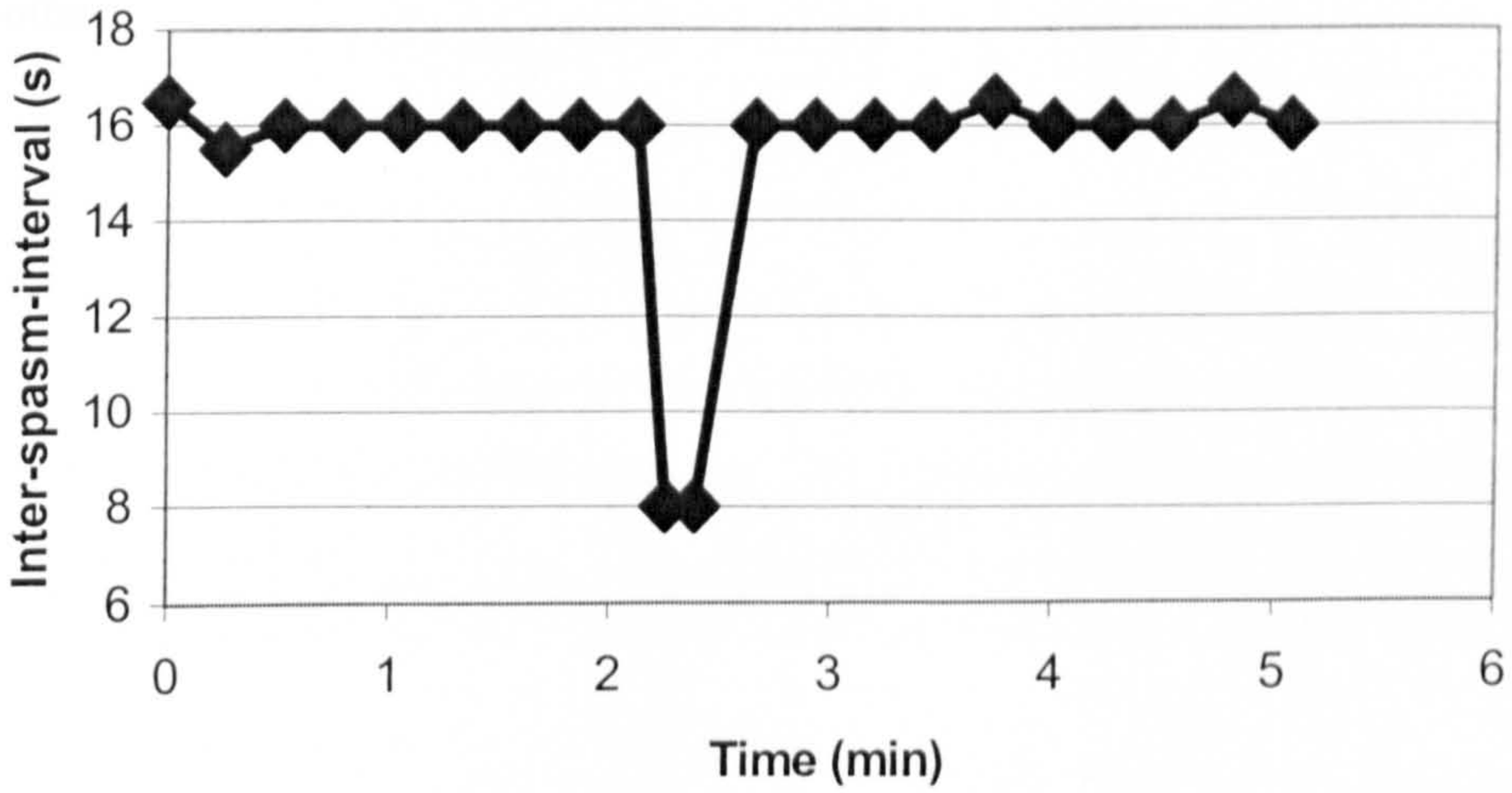


Figure 6.6. The inter-spasm interval during FES-assisted standing. This was recorded from a video record of the stand and therefore only spasms in which there was a movement of the body were recorded. The spasms are at regular 16 second intervals, with the exception of the two spasms at 8 second intervals, which observationally appeared to be smaller than the other spasms, i.e. the movement of the trunk was less.

During the periods in-between the spasms he carries most of his body weight through his legs, a situation which is reversed during a spasm. The unloading of the legs, and the consequent loading of the arms is a rapid event.

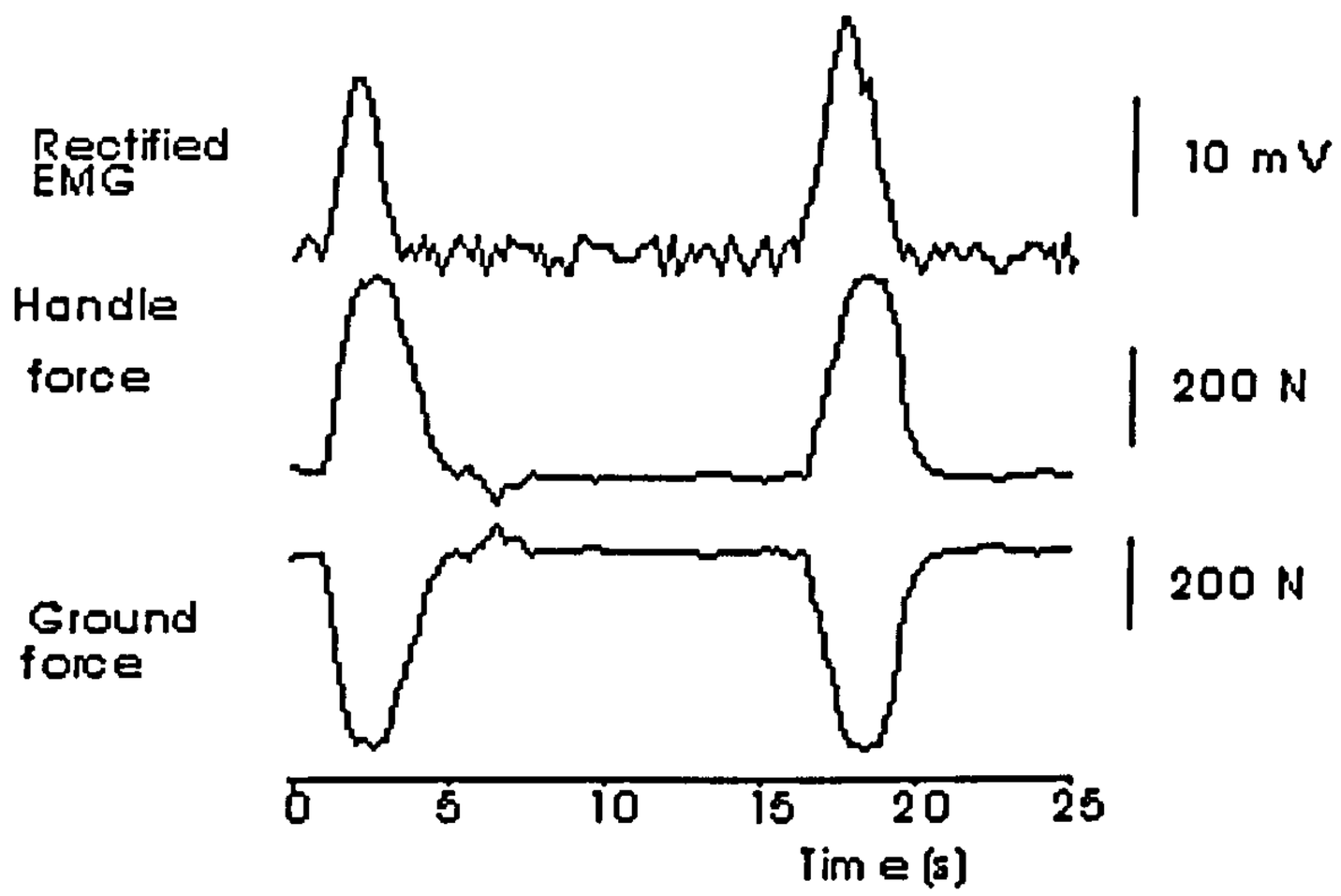


Figure 6.7. Top plot. The rectified EMG from the Hamstrings muscle group, after passing through a low pass filter. Bottom two plots. The vertical components of the ground and handle vertical reaction vectors during 2 spasms. The ground and handle reaction vectors mirror each other.

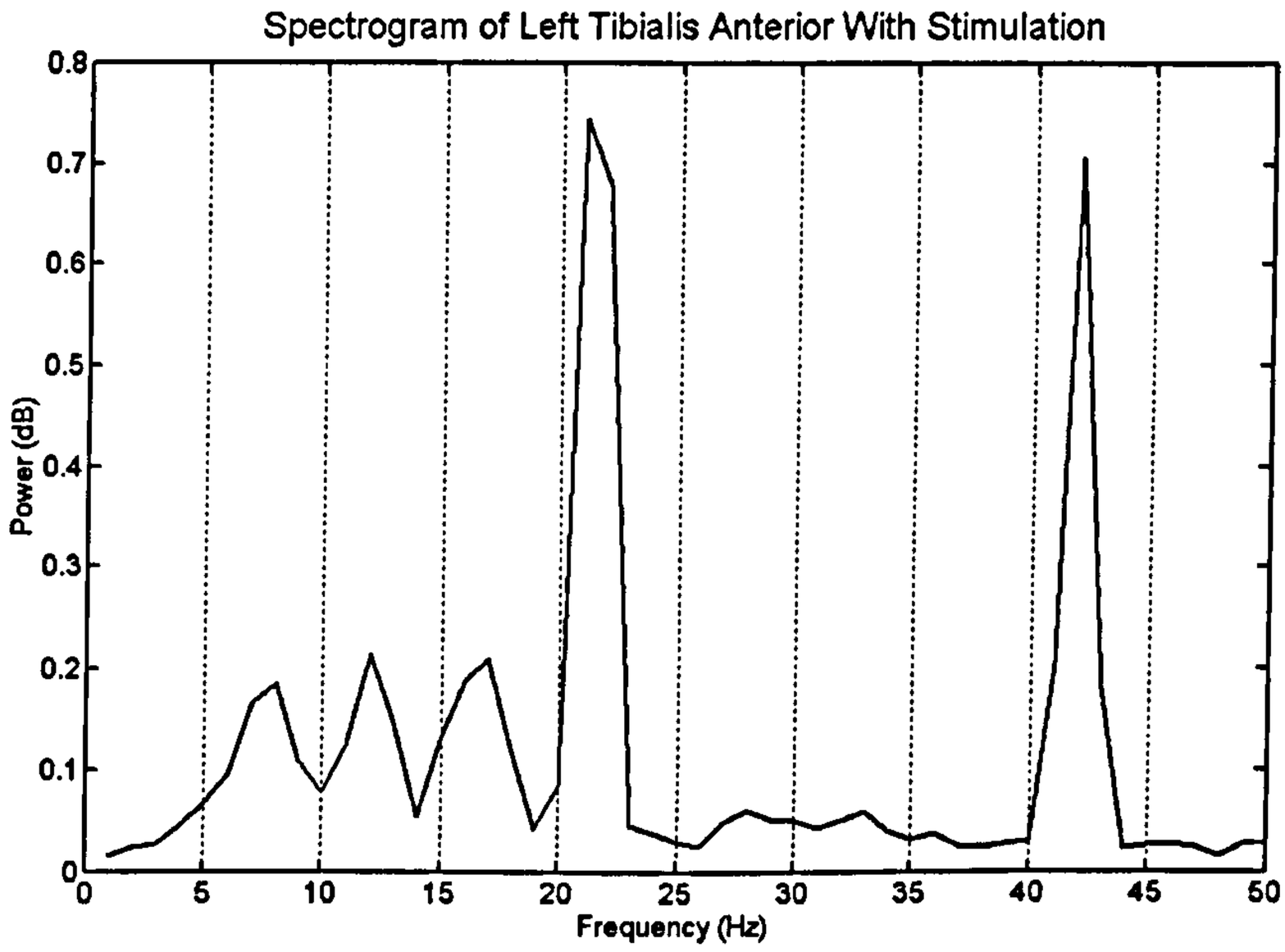


Figure 6.8. A spectra of the EMG signal from the tibialis anterior. This record was taken during a stimulated stand. Stimulation is applied at 20Hz and the peaks at 20 and 40Hz are artefacts of this stimulation. At low frequencies there are peaks at 8, 12 and 16Hz. The length of the fft was 512.

During stimulation there is activity that is time-locked to the stimuli in all of the muscles, especially the quadriceps and hamstrings. However, the activity in the tibialis anterior and gastrocnemius can be interpreted. When the signals are analysed in the frequency domain it can be seen that in addition to the 20Hz and other stimulation artefactual effects there is activity at low frequencies in distinct bands. Coherence analysis reveals that there is significant coherence between the two lower leg muscles, although they are antagonists. The coherence falls into two bands, figure 6.8, the first around 8Hz and the second around 17Hz. Bands around 20 and 40Hz are due to the stimulation.

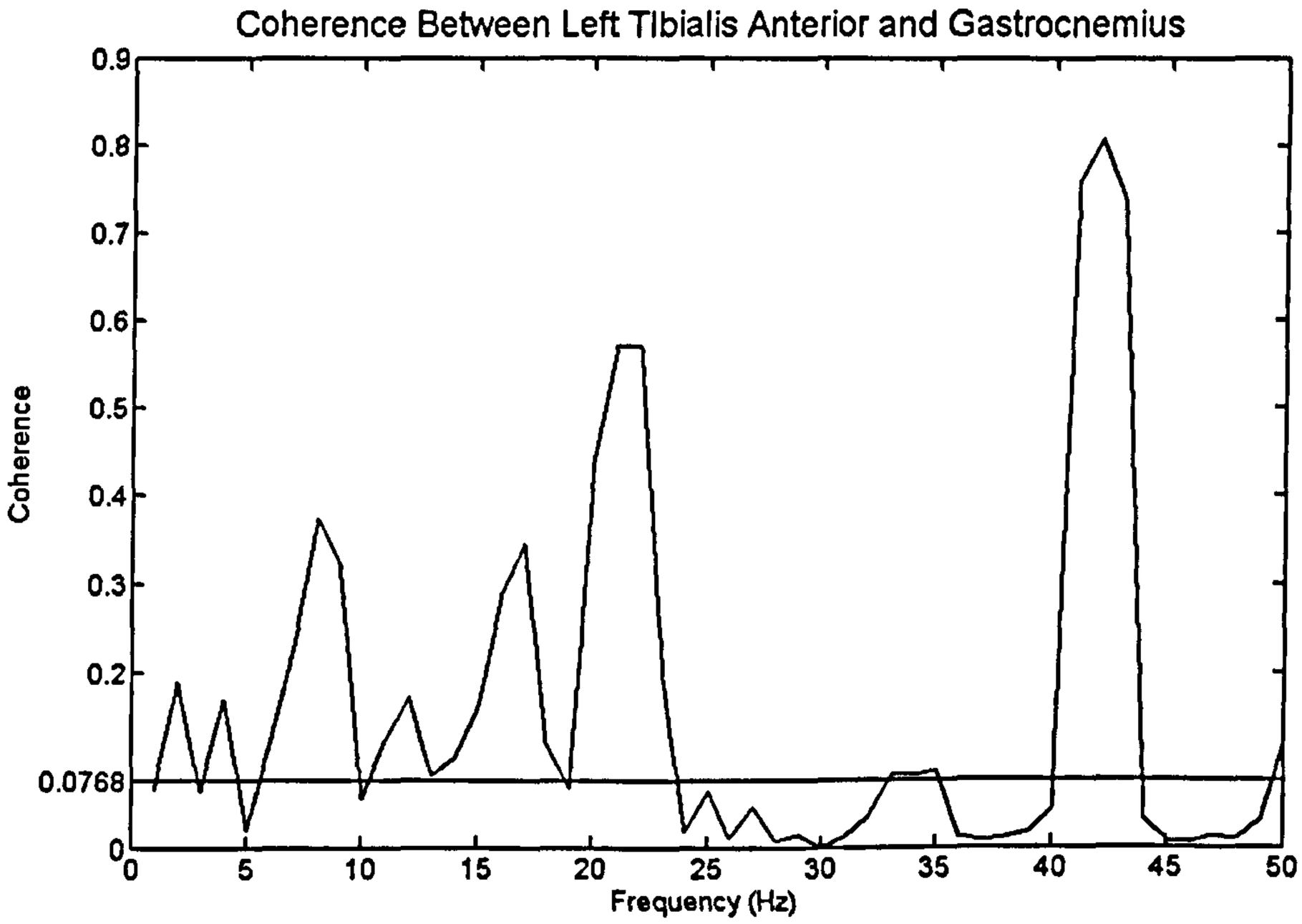


Figure 6.9. The coherence between the tibialis anterior and gastrocnemius on the left leg during stimulation. Peaks are present at 20 and 40Hz representing coherence generated by the stimulation. Peaks are also noticeable at 8 and 16Hz, as in the spectrogram above, figure 6.7. The black line represents the 95% confidence level. The coherence is generated with a segment length of 60000, nfft = 1024.

6.3.2. Patient 6. Cessation of Spasms During FES-Assisted Standing.

6.3.2.1. Neurophysiological Description of Spasm Activity.

When Patient 6 is at rest he experiences regular spasms in both his legs. These spasms persist for many hours and are both regular and consistent. The spasms appear clinically as dorsiflexion and are bilateral. Movement, such as from a wheelchair to a plinth, appears to stop the spasms temporarily but they reappear within 2 minutes.

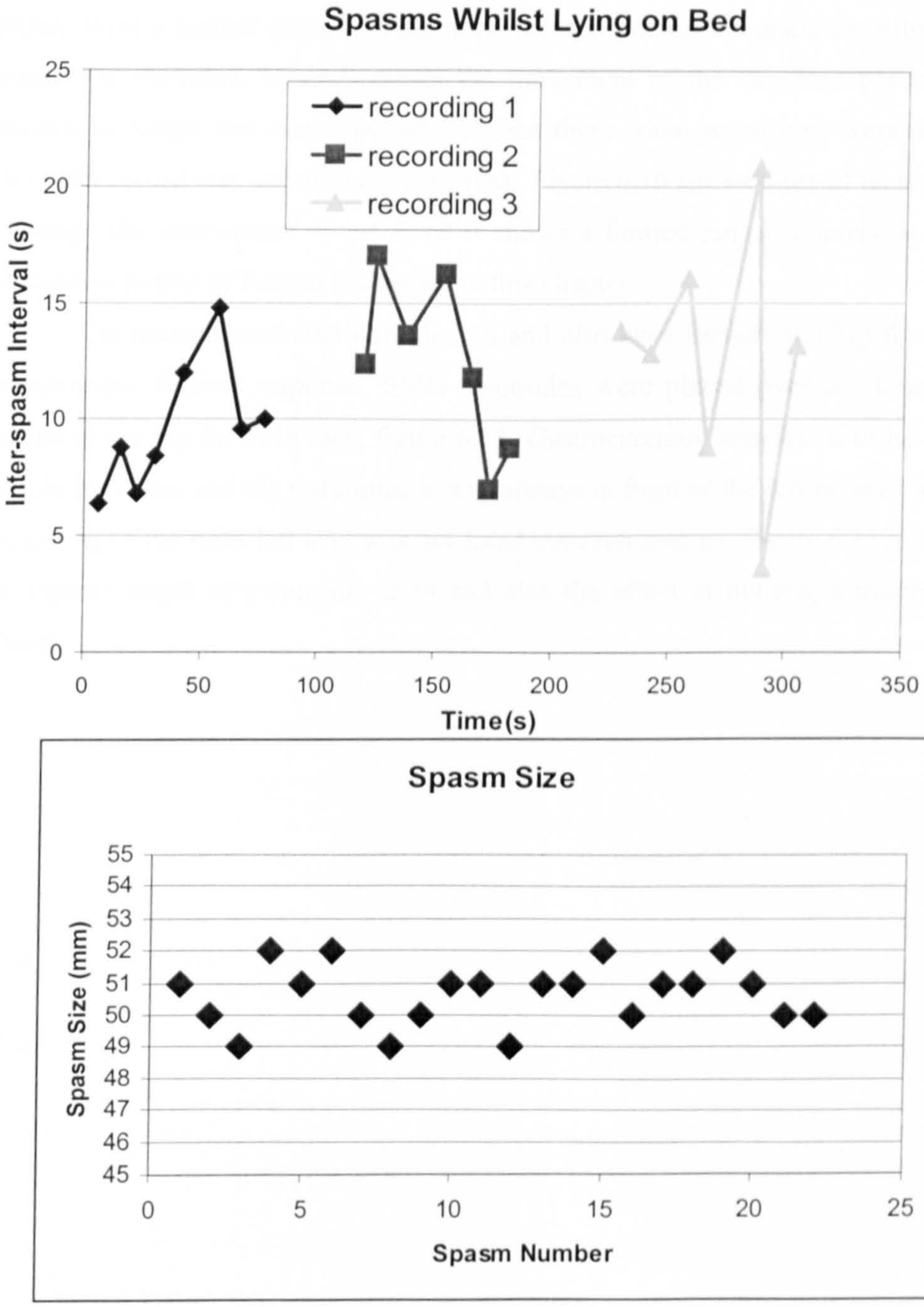


Figure 6.10. Top. The time course of the spasms with the patient on the bed. Several records were combined to produce this figure. In between records gaps are inserted. The inter-spasm intervals shown here are typical, and were never seen to be longer than 30s. Bottom. The size of the spasms, measured by the movement of a marker on the great toe relative to a marker on the ankle. There is little variation in the size of the movement and no apparent correlation with the inter spasm interval.

Regular spasms were recorded from this patient whilst he lay recumbent on the bed. Spasms were recorded using the CODA system to detect motion of the ankles. With a marker placed on the great toe and one on the ankle the effect of the spasm was recorded. In each spasm the movement of the two Records were 100 seconds in length and had a period between them when recordings were not made whilst the record was saved to the hard-disk. Figure 6.10 shows three of these records. Although the inter-spasm is not fixed it shows a limited range of intervals and has similarities to that of Patient 1's earlier in this chapter.

The spasms generated dorsiflexion and also knee flexion and hip flexion in a characteristic flexion response. EMG electrodes were placed over the four muscle groups in the leg for both legs, figure 6.11. Gastrocnemius was found to be the lead muscle by 15ms, and the right muscle was always in front of the left muscle, although the timing of the right-left lead was not fixed between spasms. Figure 6.11 also shows the typical length of a spasms ~2-3s and also the effect at the toe, a movement of 50mm.

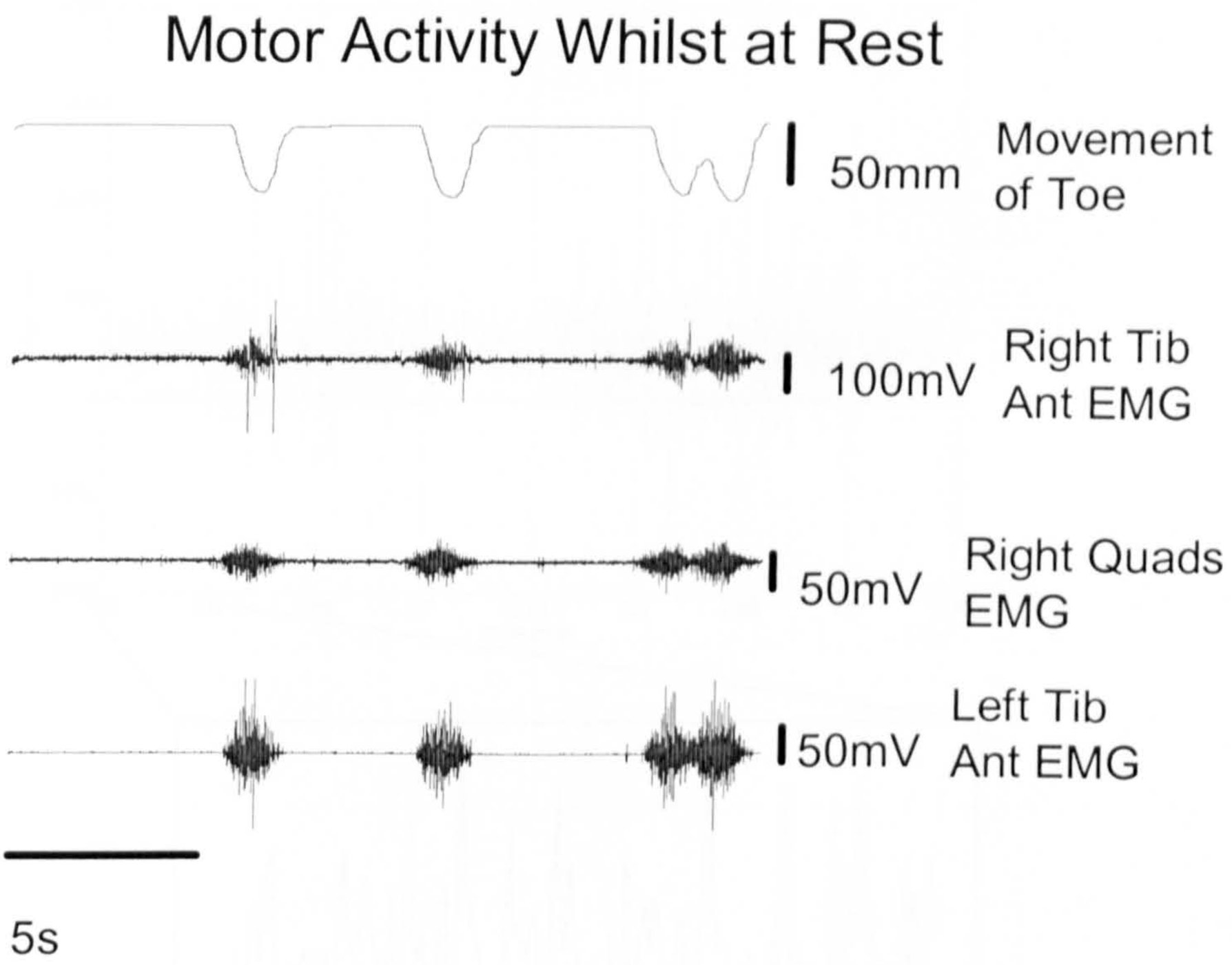


Figure 6.11. Motor activity at rest. The top plot shows dorsiflexion of the foot, indicated by the movement of a marker on the toe towards the nose of the patient. The movement is calculated by measuring the distance between the toe and the ankle, so whole leg movements are not included. EMG is shown from the right and left tibialis anterior and the right quadriceps. Activity in both legs and both muscle groups occurs with the movement.

The firing pattern within each of the spasms was similar within a muscle and tibialis anterior is a good example muscle as clear records were obtained without movement artefacts that interfered with the records from the back of the leg. The firing pattern within the tibialis anterior muscle is fractionated (occurs in bursts) and shows fast activity at 15-16 peaks per second (figure 6.12). This record is highly characteristic of the activity seen in this patient and was time invariant. It was possible to electrically stimulate each muscle individually and activity was not seen in other muscle groups indicating that the activity does not arise as a result of cross-talk.

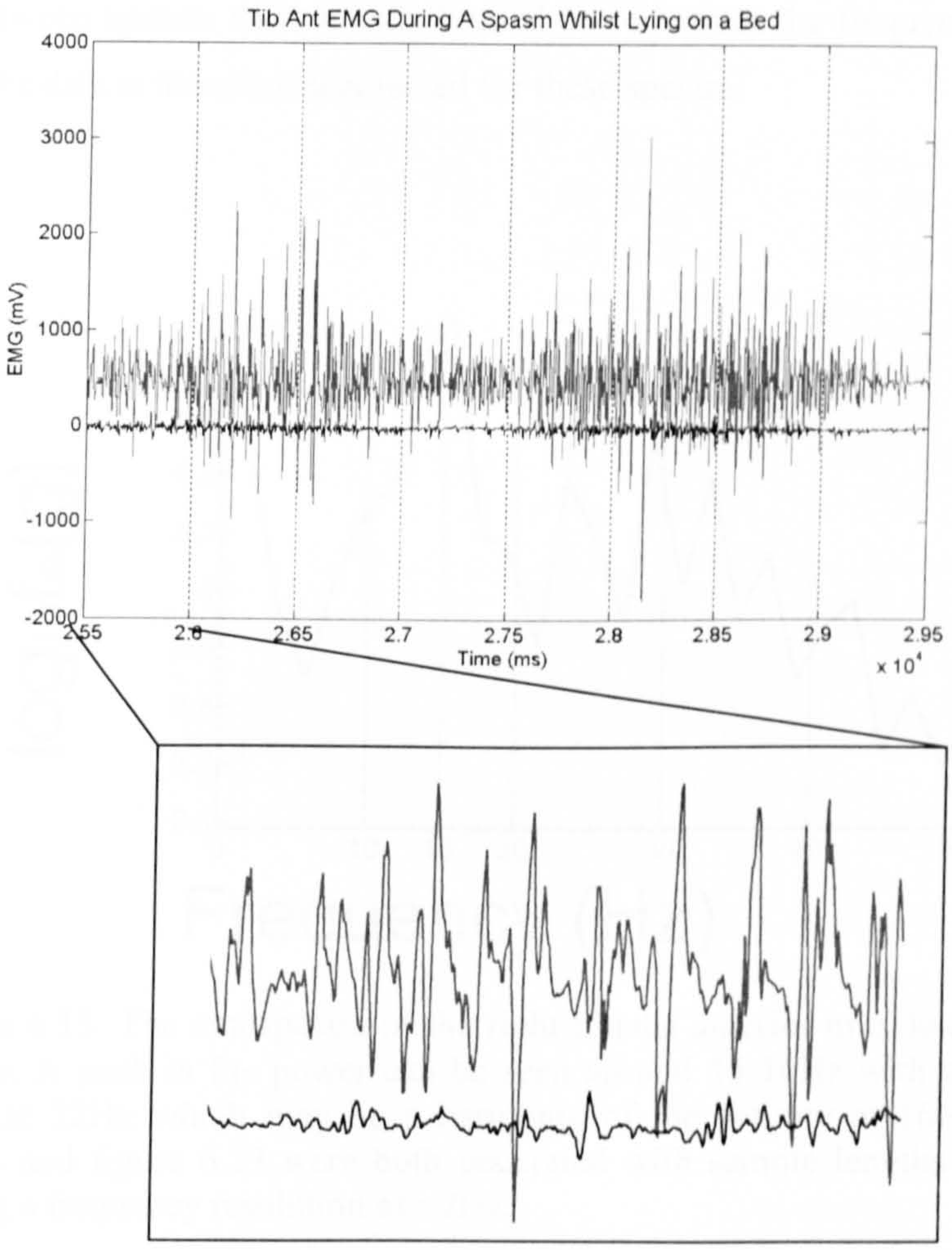


Figure 6.12. The last spasm in figure 6.11 expanded. The activity on the left shown in red is much larger than on the right, but both sides show this activity.

The fractionated (showing distinct bursts of activity) activity present in figure 6.12 suggests a rhythmic nature to the activity and figure 6.13 illustrates the power spectral density obtained from the tibialis anterior during the muscle spasms. The bursting visible in the raw trace at 16 bursts a second is prominent in figure 6.13 as a peak at 16Hz. There is little activity below 20Hz other than this 16Hz peak, but there is activity at a broad range of higher frequencies.

Both the quadriceps and tibialis anterior also show a peak in the power spectral density at around 14-16Hz, figures 6.13 and 6.14. The gastrocnemius also shows a large low frequency component, although the scales on the two plots are not the same. The spectra in figures 6.13 and 6.14 are all taken during spasms, in the

periods between spasms there is only limited power across the frequency range in the figures. The data is therefore segmented for these spectra.

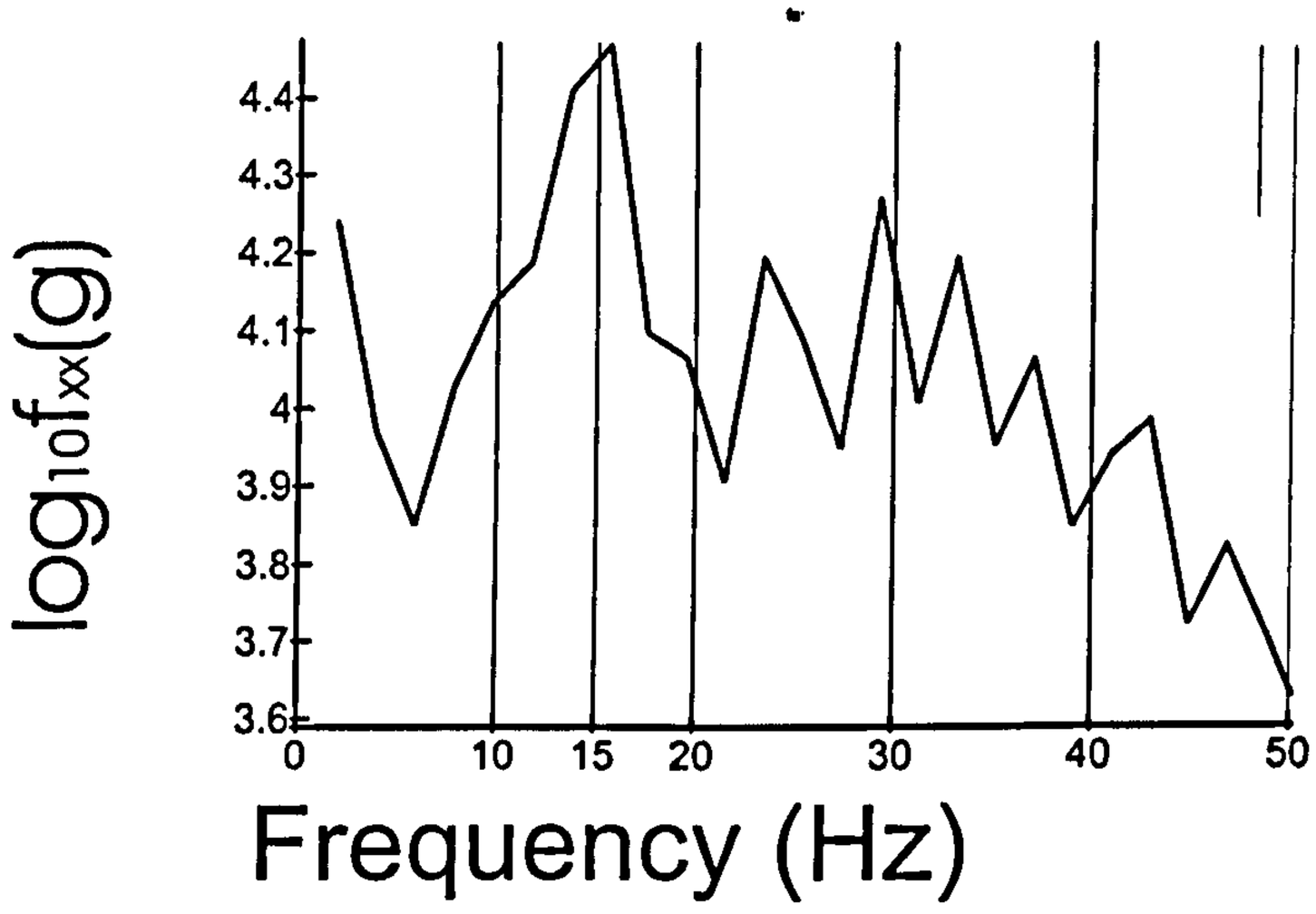


Figure 6.13. The autospectra of the right tibialis anterior muscle during a spasm. A peak in the power can be seen around 15-16Hz with a further peak at 32Hz which may be a harmonic of the activity at 16Hz. This figure and figure 6.13 were both generated with sample lengths of 512, giving a frequency resolution of <2Hz.

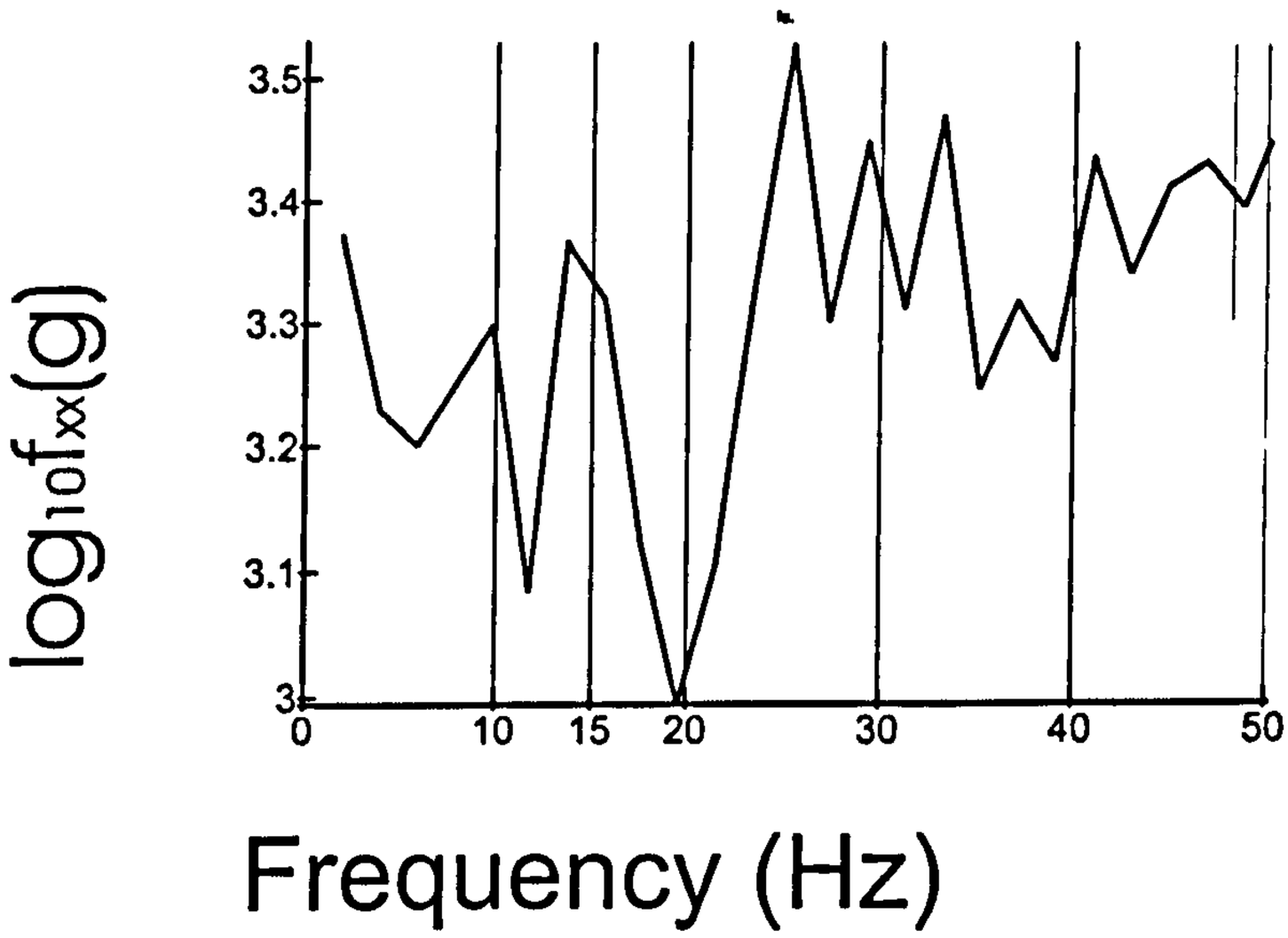


Figure 6.14. The autospectra of the right quadriceps during a spasm. A peak is visible at around 14Hz with a broad region of activity above 25Hz.

Figure 6.15 shows the coherence between the two tibialis anterior muscles during spasms. There is little coherence above the 95% confidence level across the range of frequencies in the figure. This indicates that the two legs are generally independent of each other in terms of frequency content. Peaks are present at both 8 and 13Hz suggestive of a bilaterally organised component at these frequencies, which lie within the expected range of tremor frequencies. At 16Hz, which has previously been shown to be a prominent frequency during spasms, there is no coherence between the legs.

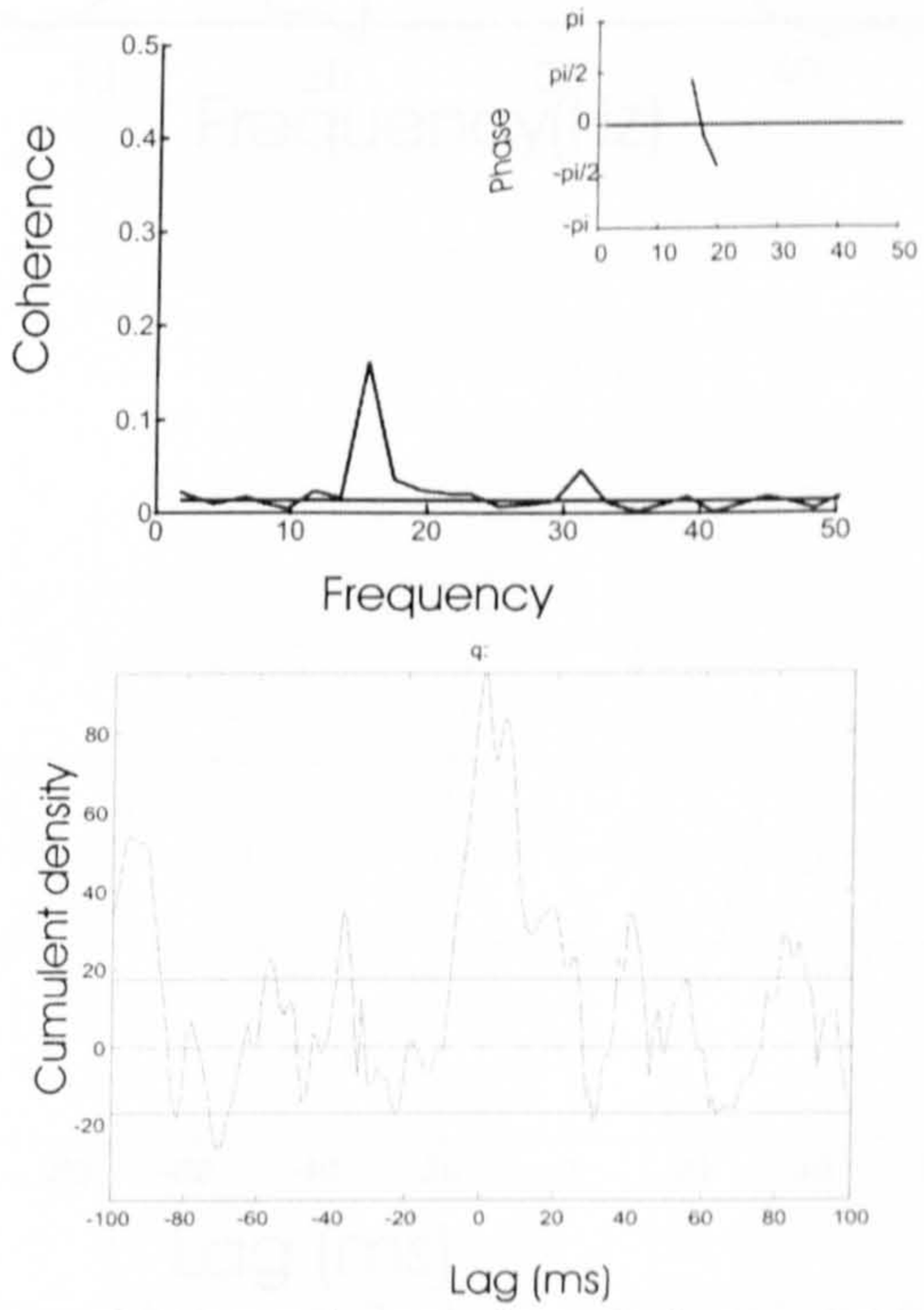


Figure 6.15. Coherence between the two legs during muscle spasms. The horizontal line represents the 95% confidence interval. There is a peak in the coherence at 16Hz in addition to low frequency coherence and additional peaks around 20Hz and 28Hz. Peaks at higher frequencies may represent harmonics of these lower frequencies. Coherence was calculated with segments of length 512, giving resolution of <2Hz. The phase is shown in the upper right hand corner of the coherence plot over the regions in which there is significant coherence. This provides evidence that the coherence is not due to cross-talk since there is a consistent, non-zero phase lag between the channels. The cumulent density also shows a peak at zero which provides further evidence for the coupling between these channels. The broadness of the peak also suggests that it is not artefactual in nature.

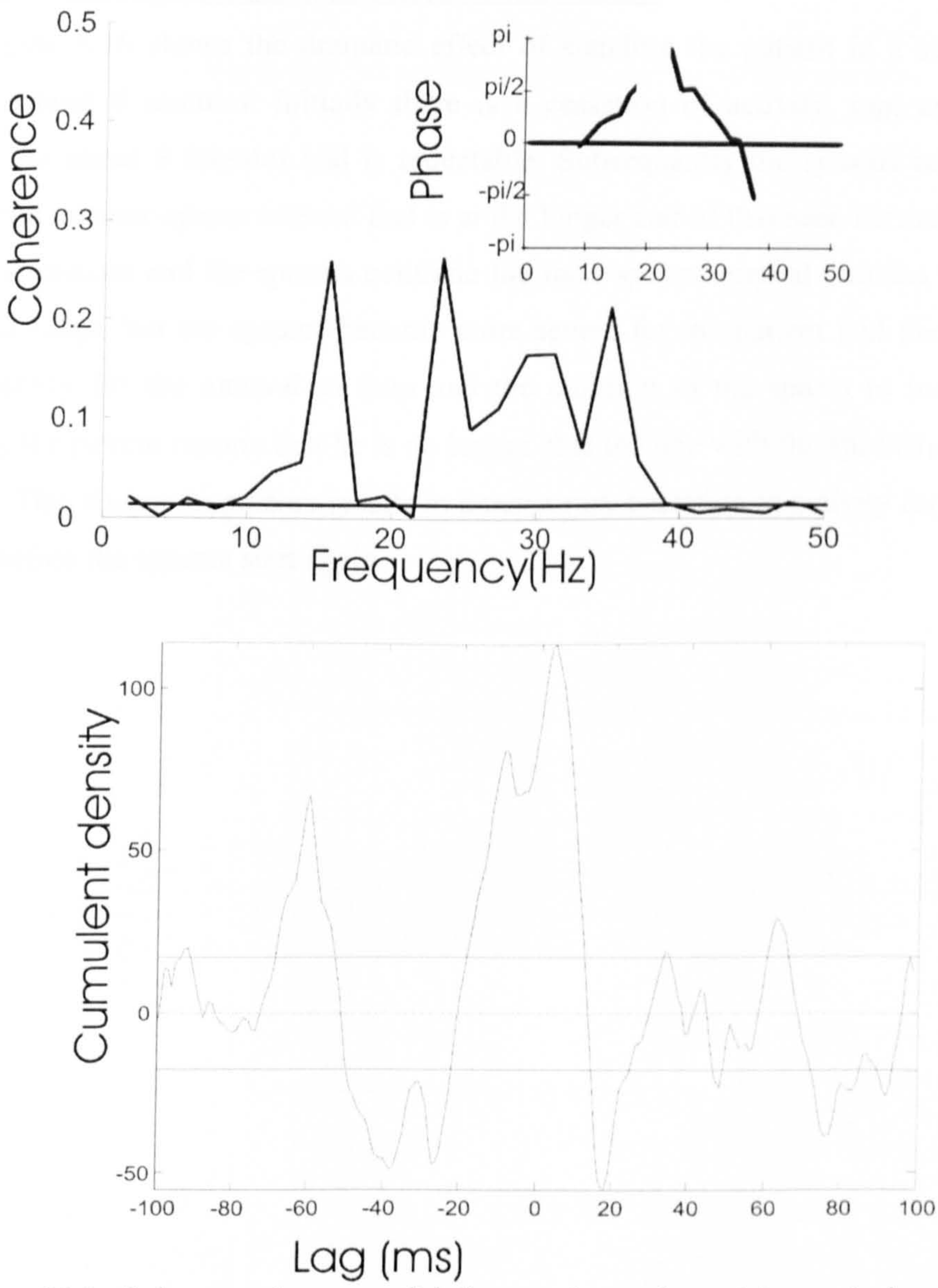


Figure 6.16. Coherence between tibialis anterior and quadriceps during muscle spasms. The horizontal line represents the 95% confidence level. A peak in the coherence is present at 16Hz and a further broad region of coherence between 25 and 35Hz. The phase plot in the upper right hand corner of the coherence shows two distinct components, both of which are non-zero but temporally stable over the region in which there is coherence. The cumulent density also shows a peak at 0ms with lobes at ±62ms indicative of 16Hz activity.

6.3.2.2. Spasms Temporarily Stopped by Passive Standing.

Figure 6.16 shows the dramatic effect of standing the patient in a standing frame for about 8 minutes. Initially there is a cessation of activity, top, and this continues for about 5 minutes and is repeatable. Subsequently the spasms reappear initially with an inter-spasm interval that is at the longer end of that seen normally. As the stand continues and the spasms continue the inter-spasm interval remains within the normal range, but the spasms become more severe for the patient and there is a slight tendency for the interval to drop and the duration of the spasm to increase. Eventually the patient reports that he is no longer able to cope with the spasms and he sits down. This change in posture results in a temporary cessation in activity for about 1 minute before the spasms start again.

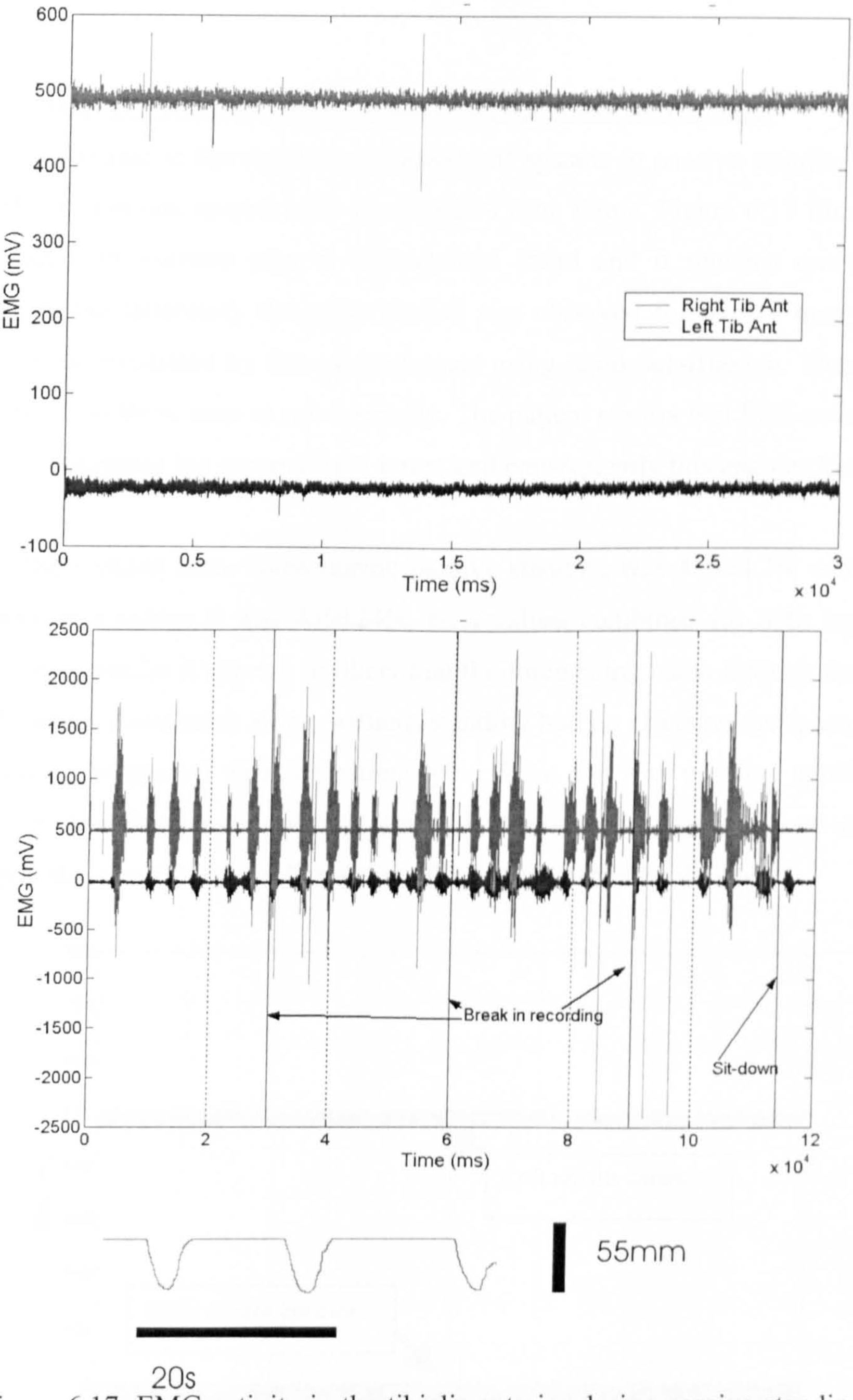


Figure 6.17. EMG activity in the tibialis anterior during passive standing. The top record shows 30 seconds at the start of the record and the bottom plot shows 2 minutes at the end of the stand. There is a gap of 6 minutes between the two plots, the spasms started 1 minute before the start of the bottom record. The patient sat at the end of the record because he could no longer cope with the spasms. The bottom trace shows the movement of the foot in a series of spasms following a passive stand. The arrangement is the same as for figure 6.10. Movement of the toe relative to the ankle is shown.

6.3.2.3. Long-term Suppression of Spasms by FES-Assisted Standing.

In contrast to the rapid re-appearance of spasms in passive standing, standing with FES suppresses spasms over an extended time frame. Figure 6.17 illustrates the EMG taken 45 minutes after a FES-assisted stand and it remains quiet with no spasms. In the laboratory this quiet period was observed for over 1 hour and then spasms were reinitiated by the experimenters using rapid dorsiflexion. These spasms were similar to those seen at rest normally. The patient reports that FES-assisted stand typically suppresses his spasms for 7 hours and consequently this enables him to sleep well.

The vertical force taken during passive standing was 410±4.7N while during FES-assisted standing it was 459±24N, both values combined for both legs. These values are so similar it appears unlikely that the force being taken through the feet is a critical factor. Stimulation alone, without standing had no effect on the spasms. When stimulation was applied with the patient lying down and with pressure applied to the soles of the feet through the patient's shoes by an experimenter pushing, no effect was seen upon the spasms. It is unlikely that 400N were applied to the feet.

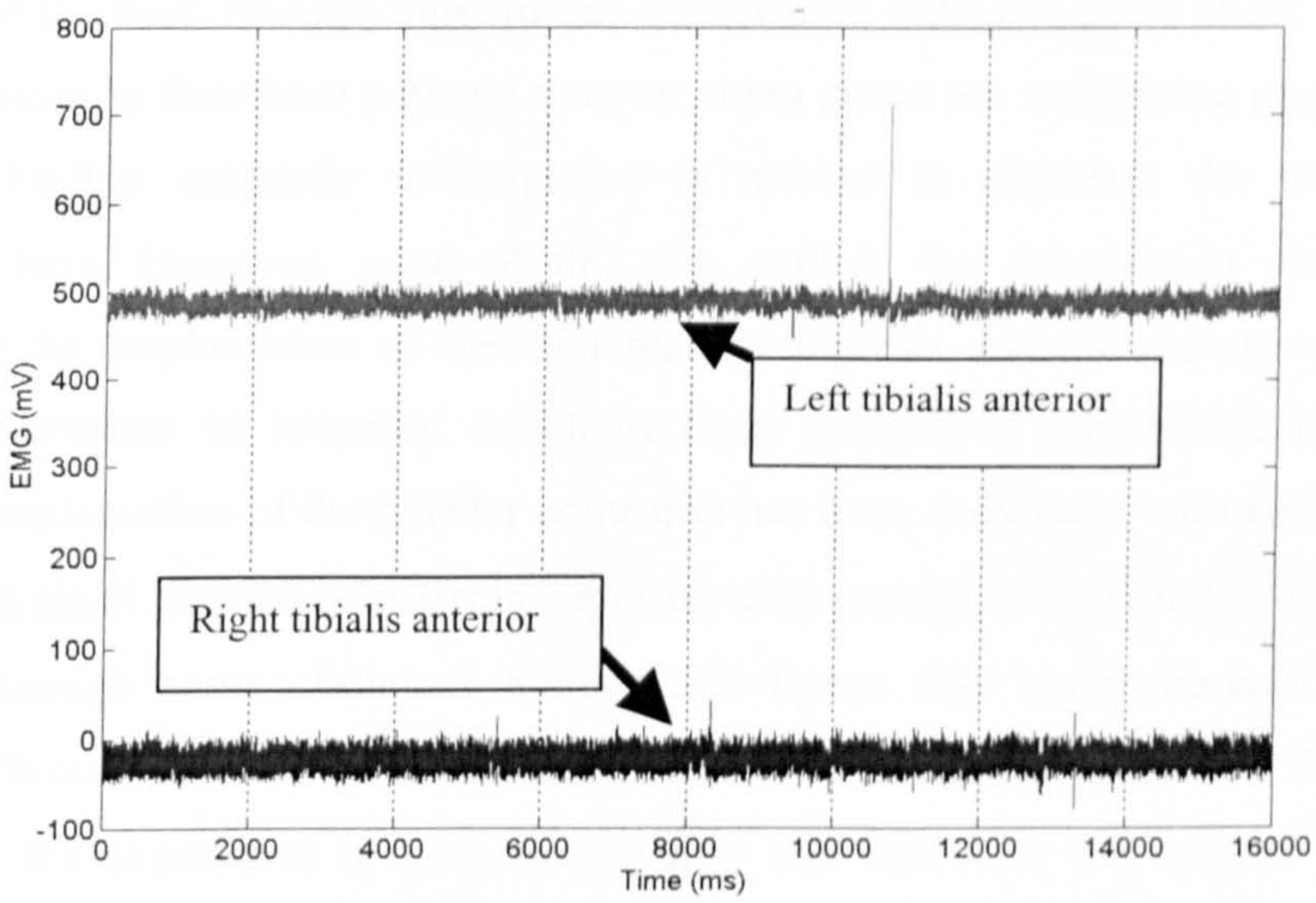


Figure 6.18. EMG activity in the tibialis anterior following an FES-assisted stand. This record was recorded 45 minutes after the end of the stand. No activity is present. This continued until the spasms were re-initiated using rapid dorsiflexion as a stimulus. The y-axis is shown after an amplification of 1000.

6.4. Discussion.

The spasm activity presented in this chapter is unusual in many respects including the prolonged nature of the activity and the pattern of activity within each spasm. Although the effects of electrical stimulation and standing upon the spasms of the two patients are different the activity at rest in Patient 6 and during passive standing in Patient 1 appear similar. Posterior rhizotomy's are performed in conjunction with the Brindley bladder implant to prevent dysnnergia in the bladder and reflex bladder contractions (Brindley, 1994), (Brindley & Rushton, 1990). This appears to have been successful in these patients. Rhizotomies also used to reduce spasticity and spasms, particularly in patients with cerebral palsy, although the roots cut are usually higher roots, extending up to L3. This is a controversial procedure which is rarely performed in the UK, although more common in the US (Steinbok, 2001). Recent work from the Craggs group in London (Craggs *et al.*, 2000a,b) suggests that stimulation of the same posterior roots as are usually cut in the bladder implant implantation procedure, S3 in particular, may relieve spasms in some patients. The mechanisms underlying this observation are unclear, especially as the S3 sensory root innervates a small portion of the buttocks and possibly a very small portion of the dorsum of the foot. Possibly this limited observation indicates more about the trigger for the spasm in this/these patients than anything about the underlying physiology of spasms. Further scientific investigation is needed to elucidate the mechanisms involved here. However, none of this can explain the increase in spasms seen following the implantation of the first bladder implant and the rhizotomy. It is of course impossible to ascertain which of these procedures caused the increase in spasms. Implantation of the bladder controller has been associated with an increase in spasm in a small number of patients, reported to be around 14% (Brindley & Rushton, 1990), although some clinicians believe this figure may under-represent the true number, (Wood, personal communication). However, Rushton reports that Patient 1 is unique in his experience in both the severity and extent of the spasms (Rushton, personal communication).

6.4.1. Irregular but Persistent Spasm Activity.

It is highly unusual to find persistent spasm activity without an obvious trigger. In Patient 1 the spasms started after a quiet period of standing and in Patient 6,

although rapid dorsiflexion did re-start the spasms it was not clear what normally triggered the spasms. Although the inter-spasm interval is not fixed in these conditions it is very frequent and regular compared to the normal pattern of spasm activity in paraplegics.

The spasms recorded during the passive stands of Patient 1 have distinct similarities with two movement disorders that arise as a result of spinal cord pathology, restless leg syndrome and stiff limb syndrome. Stiff limb syndrome (Brown *et al.*, 1997) is a clinically distinct condition from stiff man syndrome and progressive encephalomyelitis (Barker *et al.*, 1998). Stiff limb syndrome has a number of defining characteristics; i) normal descending fibres, (not present in this patient due to the original spinal injury) ii) continuous motor unit activity, (10Hz pattern seen in gastrocnemius in this patient), iii) tendency to grouped repetitive discharges of motor units during a spasm, (10Hz peaks in EMG spectra during spasms in this patient) and iv) abnormal cutaneomuscular reflexes, (in this patient mild stroking of the sole of the foot, or leg evoked a strong reflex response). The patient demonstrated a clear positive Babinski sign with an upward going toe to stroking of the sole of the foot. In addition to this classically sign of upper motor neuron syndrome mild stroking, which did not produce a Babinski sign resulted in a withdrawal response which is interpreted as an abnormal cutaneomuscular reflex in this study. However in the study by Brown and colleagues (1997) they recorded electrically triggered reflexes, which was not done in this study.

Stiff man and stiff leg syndrome may both be immune-mediated chronic encephalomyelitis (Meinck & Thompson 2002). In these conditions the immune system may attack the patient's own spinal cord resulting in the various pathologies seen in the conditions. Biochemical diagnosis is not possible at the present time and clinical diagnosis is performed electrophysiologically.

Periodic Leg Movements, PLM, and Restless Leg Syndrome, RLS, are both characterised by spasms in the legs or movements of the legs at irregular intervals but typically with a mean inter-spasm/movement interval between 10 and 20s, 13.6s as seen in this patient therefore falls into this range. Patients with spinal lesions can experience PLM as well as patients who are otherwise neurologically normal. However both these conditions appear when patients are asleep and descending tonic inhibitory control onto spinal circuits may be less than normal (Provini *et al.*, 2001).

In these patients (Patient 6 and Patient 1) the partial deafferentation and loss of descending inputs may account for the similarities with these pathologies.

Each of the spasms in passive standing appears to be a well-ordered event, and not just a reflex response to a noxious stimulus. The autospectra for the four muscle groups on one side of the body all show a peak at around 10Hz, which falls well outside the typical range considered as clonus (Hidler & Rymer, 2000), (Dimitrijevic *et al.*, 1980). This 10Hz rhythm is strongly coherent between pairs of muscles, and presumably therefore sustained by activity in a common spinal network. However, tremor was not visible in this patient to the naked eye. Previous work has suggested that motor unit may fire spontaneously at ~10Hz (Gorassini *et al.* 2002a,b) and therefore it is possible that this activity arises from the excitability of the anterior horn cell. However the activity shows temporal and spectral characteristics (coherence and time-locking) that suggest that the activity is being driven at least in part from a common source.

Although it is unclear what initiates the spasms they are maintained by spinal circuits. The peaks in the spectra from individual muscles suggest that there are circuits responsible for generating particular frequencies of activity rather than "random" activity. Individual motor units can fire at around 10Hz in spinal patients (Gorassini *et al.*, 2002a). In the spasms described in this chapter peaks are found at 16Hz, 20Hz although this does not imply that individual motor units are firing at these frequencies.

The coherence spectra reveal further insights into the organisation of the neural activity within the spasms. Activity that is coherent between legs, possibly representing bilateral outflow is centred around two frequencies in the low frequency range, 8 and 13Hz, both of which are within the range expected for tremor. Higher frequency components have been found in motor signals. Although these are generally believed to originate in the motor cortex and supraspinal centres they have not been studied in the spinal cord (Cassidy *et al.*, 2002), (Marsden *et al.*, 2000).

Within a leg there is coherent activity at around 16Hz between tibialis anterior and both quadriceps and gastrocnemius. This strongly suggests that this activity within the leg arises from a neural oscillator with a widespread ipsilateral output. Between the two antagonistic muscles around the ankle there is little coherent activity below this 16Hz band. Above this band however there are a number of further bands of activity that, as above, may represent complex and/or comparatively fast neural

oscillators within the cord. Between muscles at the front of the leg, figure 6.18 there is a peak at 8Hz. Coherent activity at this frequency was also seen between legs and this widespread activity implies a more central oscillator with outputs onto many regions of the cord and ultimately motor neurones. A striking feature of these spasms is the consistency with which peaks are seen at around 16Hz both in spectra, coherency spectra and even in temporal relationships such as the cross-correlograms.

One mechanism that may be responsible for the maintenance of the organised is the generation of plateau potentials (Kiehn & Eken 1998). These are the result of the cell membrane exhibiting bistability, i.e. being stable at two membrane potentials, a resting membrane potential and a plateau potential. The plateau potential is a partially depolarised potential and may lead to "spontaneous" firing of action potentials (Gorassini *et al.* 2002a,b), (Collins *et al* 2002). However recent comments by Gorassini (personal communication 2002) has suggested that this may not be as widespread in humans as earlier thought.

6.4.2. Regularisation of Spasm Activity During FES-Assisted Standing.

In contrast to the frequent, but comparatively irregular spasms seen during passive standing, those seen during FES-assisted standing in patient 1 are particularly remarkable for their regularity. This suggests, therefore, that in some way the stimulation is defining the inter-spasm interval. The spasms also appear in unstimulated muscle and this suggests that there is a general increase in the level of excitability of the spinal cord during a spasm.

One possible mechanism for the regular spasms during FES-assisted standing is that the spasms are reflex responses to the stimuli. Following each response there might be inhibition of the motoneurons in the spinal cord. As this inhibition is reduced the response reappears. However, this argument suggests that the spasms with and without stimulation are dissimilar since the unstimulated responses occur more regularly than 16s. A further argument against this theory is that stimulation in the absence of standing failed to produce responses such as those seen when standing.

The regularity of the spasms may arise because of entrainment of neural oscillators by the stimulation. The 10Hz oscillations recorded during the passive stands suggests an underlying oscillator with a frequency around 10Hz. The stimulation is applied at 20Hz and therefore 10Hz is the first sub-harmonic of the stimulation frequency. If the oscillations were not exactly at 10Hz, but very close to it,

then they would be expected to come into phase with the 20Hz stimulation at regular intervals. If the oscillator was 0.06Hz away from this 10Hz frequency, a change undetectable using either Fourier or auto-regressive techniques with the sample lengths generated during spasms, then the two oscillations would come into phase every 16s. The spasms might therefore arise when the two circuits come into phase, and generate long lasting, many seconds, changes in the excitability of the cord. However, this explanation does not explain why the two spasms were seen at 8s intervals. It is possible that being 180° out of phase may also be a strong enough stimulus to trigger a spasm in some cases, possibly depending upon the state of the cord. The most obvious method of testing this hypothesis is to stand the patient and adjust the stimulation frequency. However the patient's spinal syrinx prevented him from standing due to pain, and this progressive condition has damaged increasingly large parts of the cord. The patient recently had radical surgery to drain the syrinx and concurrently a large part of the spinal cord was removed, including the part which it is expected would have contained the oscillatory circuits. This procedure also resulted in severe denervation of the patient's legs, meaning it is highly unlikely that he will be able to stand again.

6.4.3. Cessation of Spasm Activity by FES-assisted Standing.

The use of electrical stimulation for the modulation of the symptoms of upper motor neuron lesions is not new and has been reviewed several times in the past (Daly *et al.*, 1996), (Alfieri, 2001), (Singer, 1987), (Bajd *et al.*, 1985). However these reviews and papers have concentrated on spasticity rather than muscle spasms.

The effect of weight bearing through the feet on the size and latency of spinal reflexes has been studied for both standing and stepping in normal and spinal patients. Applying force to the metatarsal region reduces the size of the H-reflex in both populations although the relationship between force and decrease is not clear (Knikou & Conway, 2001). In this study the application of pressure to the soles of the feet was not measured. This pressured combined with electrical stimulation of the quadriceps also produced no changes to the spasms. Although the force applied to the feet is unknown it is reasonable to assume that the force was less than 100N.

The effect of standing, without stimulation, was to temporarily suppress the spasms. Movements, such as from plinth to wheelchair, also suppressed the spasms although not for as long as standing did. When the spasms re-started there was no

gradual build up, they suddenly started with the same severity as previously, both when standing or following movement. During standing the patient reported that the spasms got much worse and that he had to sit down. This is not obvious from the data although the spasms may be getting more frequent for the patient as they get slightly longer and the period without spasms gets shorter. It is not clear why standing should suppress the spasms for so long or why they should get longer when they reappear. The suppression may be the result of additional sensory input from the soles of the feet as discussed in (Knikou & Conway, 2001). Although Knikou and Conway waited after the application of each pressure before testing the reflex the time taken was always under 60s. Knikou and Conway suggest that there may be spinal mechanisms responsible for the suppression of the motoneurons excitability, at least as measured by the size of the H-reflex. Some of the mechanoreceptors that respond to skin indentation and pressure, such as Merkel cell and Ruffini's corpuscles, are slowly adapting (Johnson, 2001), (Kandell *et al.*, 1991). Sensory input from the cord from these receptors may act to suppress the spasm activity temporarily. When their input stops or decreases below a certain level the spasm activity restarts. Joint angles can be sensed in a number of ways using cutaneous, myo or other soft tissue receptors. Evidence from studies on the flexion reflex has shown that hip angle in particular is able to modulate the size of the reflex (Knikou & Rymer 2002). This suggests that the spinal cord is able integrate the polymodal sensory inputs concerning joint angle and uses this information to modulate the excitability of anterior horn cells and other motor cells in the spinal cord. At present it is not clear which of the inputs is critical to this modulation. Providing mis-matched information (to the spinal cord may elicit this information.

Standing with stimulation stops the spasms for a prolonged period of time, even if the stand is only for a minute or so. The mechanism for the suppression of spasms suggested above may explain the initial suppression but not the longer term effect. The spasm suppression therefore appears to be the result of two sensory inputs combining and having a bigger effect than either individually or would be expected when added together. The suppression of spasms for many hours is a previously unreported effect from such a stimulus as FES-assisted standing. Theories that might explain the neuromodulation seen by Craggs (Craggs *et al.*, 2000a) such as sensory disruption of an oscillating network (further discussed in chapter 9) are unlikely to be able to explain multi-hour spasm suppression. One possible explanation is that the

combined stimuli of standing and stimulation causes the production and release of endogenous opioids, which have a half-life of 3-6 hours. If this is part of the mechanism of action then it is unclear why the nociceptive stimulation arising from the rapid dorsiflexing of the foot should be able to restart the spasms. Knikou and Conway (2002) have demonstrated that there is a decrease in the size of the H-reflex, possibly reflecting a decrease in the excitability of the motoneurons or an increase in the inhibition of the cells mediated via interneuronal pathways.

6.5. Conclusions.

Two patients have been presented, in some detail, who experience regular, persistent and ongoing "spasms". Investigation of the spasms has suggested that at least in part they are driven by spinal, neural oscillators. Regular electrical stimulation (at 20Hz) combined with standing has profound effects upon both patients. In one patient the spasms become locked into a 16s cycle and in the other the spasms are stopped for periods in excess of 6 hours (as reported by the patient). These results suggest that the neural oscillators can be influenced by external, regular peripheral stimulation. The actions of this stimulation may be to either suppress the oscillations or to drive the oscillations.

Chapter 7.

Intermittent Neural Activity During the Sit-to-Stand.

7.1. Summary.

This chapter describes a fast oscillatory motor event that occurs during the sit-to-stand in two of the four patients in whom the procedure was studied. The activity occurs after the initial rising phase and during the period in which the legs are taking load. The activity has a frequency around 8Hz in both patients and is found in both legs during both passive and FES-assisted standing. The persistence and frequency content of the activity is unlike conventional spasms and is more like that known as tremor. The results suggest that this activity arises from a central source and is a novel form of posture dependent tremor.

7.2. Introduction and Brief Methods.

Spasms and other neural activity, such as that described in the preceding chapters are unexpected during "steady-state" conditions. Spasms are known to occur during dynamic tasks such as standing up as a result of the changes in sensory input. Typically these spasms are considered to be exaggerated stretch reflexes (Rack *et al.*, 1984), arising because of the loss of descending inhibitory input.

The act of standing up involves a number of changes in sensory input to the spinal cord; change in load distribution, change in joint angles and, during FES-assisted standing, muscle contractions. All of these inputs might be expected to trigger spasms or other forms of motor activity. These would be short lasting effects and re-occur consistently with repeated presentation of the stimuli, provided the presentation rate was slow enough to avoid habituation (Rothwell *et al.*, 1986).

The work presented in this chapter examines a further type of neural activity that is inherently oscillatory in nature. Reflexes were not seen during the steady state standing of patients examined in this chapter.

Four patients were studied during their sit-to-stand using the techniques and methods described in chapter 3. Patients stood using open-loop FES control with stimulation applied to the quadriceps. Patients stood with one foot on each of the two force plates and using the instrumented handles (JR3) for support. Surface EMG electrodes were placed over the bellies of the quadriceps, tibialis anterior and soleus/gastrocnemius muscle groups on both legs. Patients were instructed to stand in

their normal manner. Of the four patients studied, two showed similar oscillatory activity that is described in this chapter. Stands were performed with and without stimulation, using a standing frame for support in the unstimulated stands.

7.3. Results.

This section contains a brief description of the biomechanical events during a sit-to-stand. A fuller description of the biomechanical events is presented in the following chapter in which the issue of learning to stand and therefore controlling this procedure is considered in more detail.

During the sit-to-stand the patient must extend their hips and their knees and planterflex their ankles to an angle of around 90°. At the conclusion of the procedure the patient should be taking the majority of their body weight through their legs and their arms should be providing balance support and only minimal weight support. The profile of the vertical forces taken through the feet shows a polyphasic profile with an initial increase followed by a rapid decrease and a subsequent slower increase in the vertical force, figure 7.1. The figure also shows a stick-figure representation of a patient during the sit-to-stand. The knees are extended before the hips, and this is described in more detail in chapter 8. Chapter 8 also describes the variations in the force profile. This strategy is in contrast to the approach adopted by paraplegic patients using a standing frame or neurologically normal subjects. When paraplegic patients use a standing frame to stand there is a mechanical support provided at knee level. Although I know of no analysis of the techniques by which patients stand observations suggest that patient use the knee strap to take some body weight as they extend their hips and then use their upper body strength to extend their knees once their hips are straight. In contrast, neurologically normal subjects stand by extending both their hips and their knees at the same time.

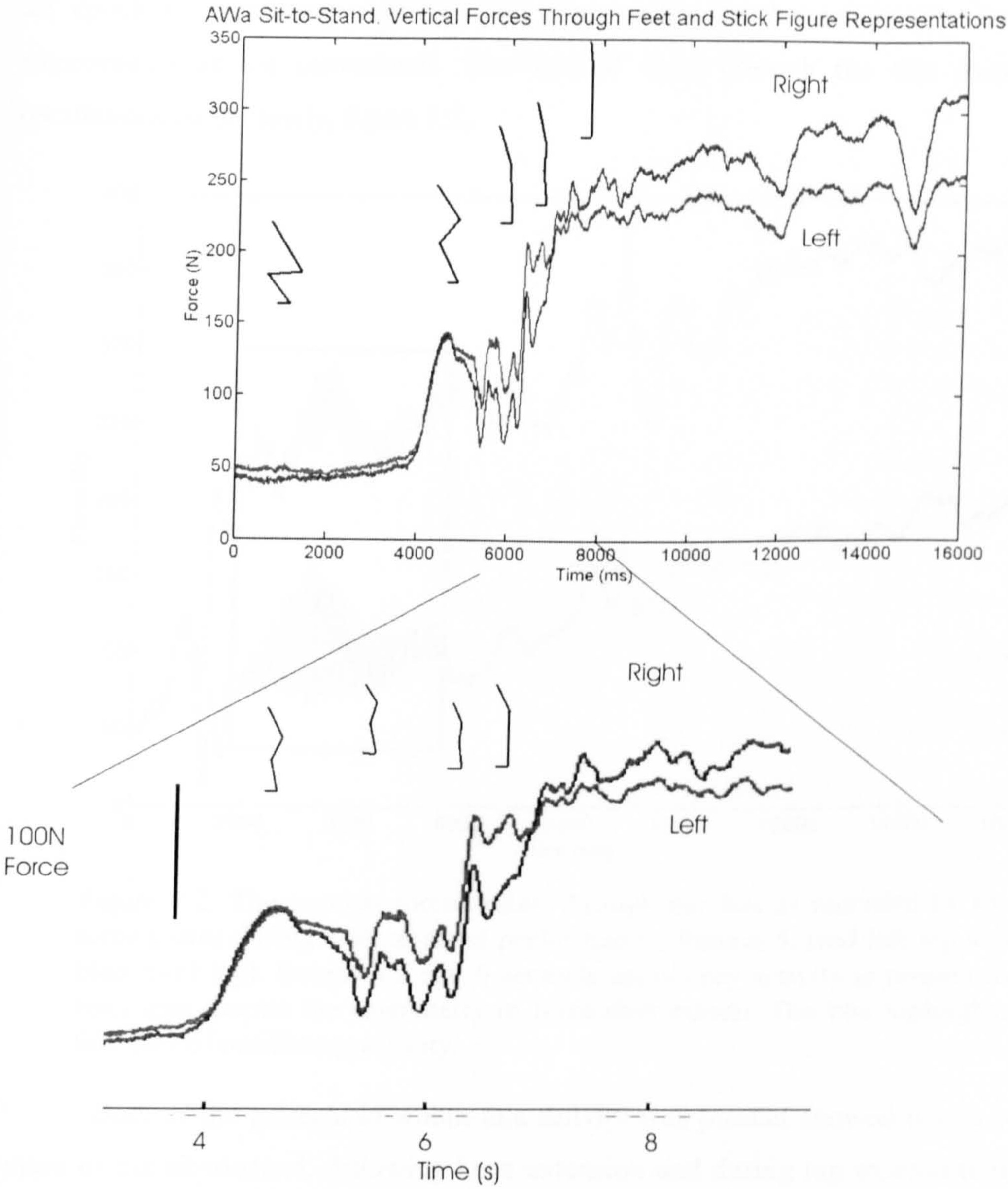


Figure 7.1. The vertical force profile and stick figure representations of a sit-to-stand. Top) the whole process showing hip and knee flexion at the start of the process and then knee extension before hip extension. Bottom) the region of the stand in which the knees become fully extended and "locked" is expanded. During this period there is a transfer of weight to the hands and a vertical acceleration. Patients lift themselves up and allow their knees to extend under them without any weight being taken by them.

Two of the four patients studied showed a further feature during the sit-to-stand. In the final part of the sit-to-stand, when the hips are nearly extended there was an epoch of oscillatory activity. This was visible to the naked eye during the experiments as leg movements. The vertical force through the feet showed the oscillations most clearly, figure 7.2.

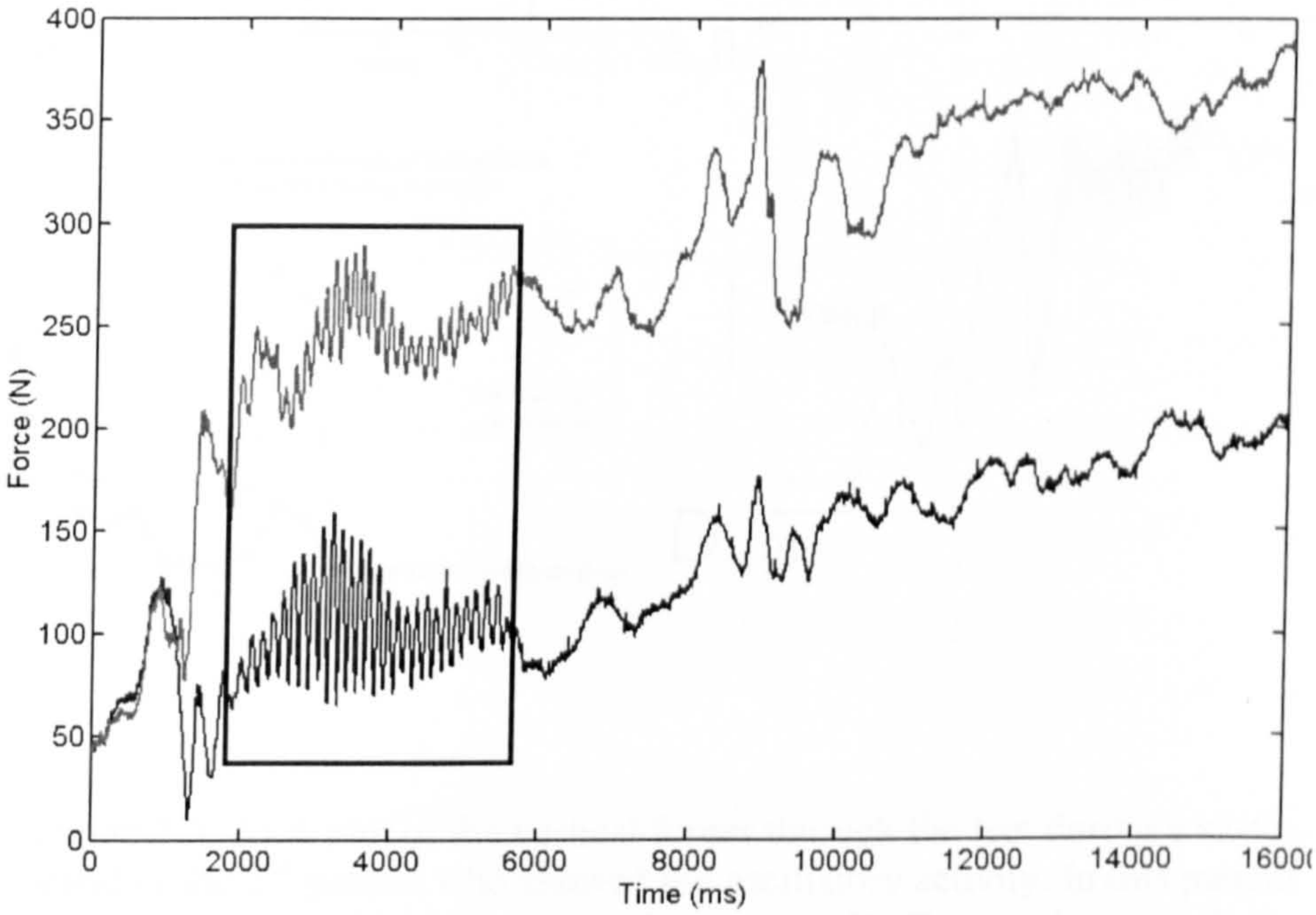


Figure 7.2. The vertical forces taken through the feet as recorded by the force plates during a sit-to-stand performed by Patient 5, (red left leg and blue right leg). Between 2 and 6 seconds oscillatory activity is present in both legs despite the asymmetry in force distribution. The box highlights this area of oscillatory activity.

Both of the patients in whom this activity was present showed it in a similar phase of the sit-to-stand, following knee extension and during hip extension and leg loading. Patient 5 attended more experimental sessions and most of the data in this chapter is taken from him. In figure 7.3 the vertical forces taken through the feet during one of his typical stands are plotted. The oscillations are expanded in part B of the figure and the spectrum of the oscillation plotted in part C. The expanded raw trace and the spectrum both illustrate the rhythmicity of the oscillation and its frequency, 8Hz.

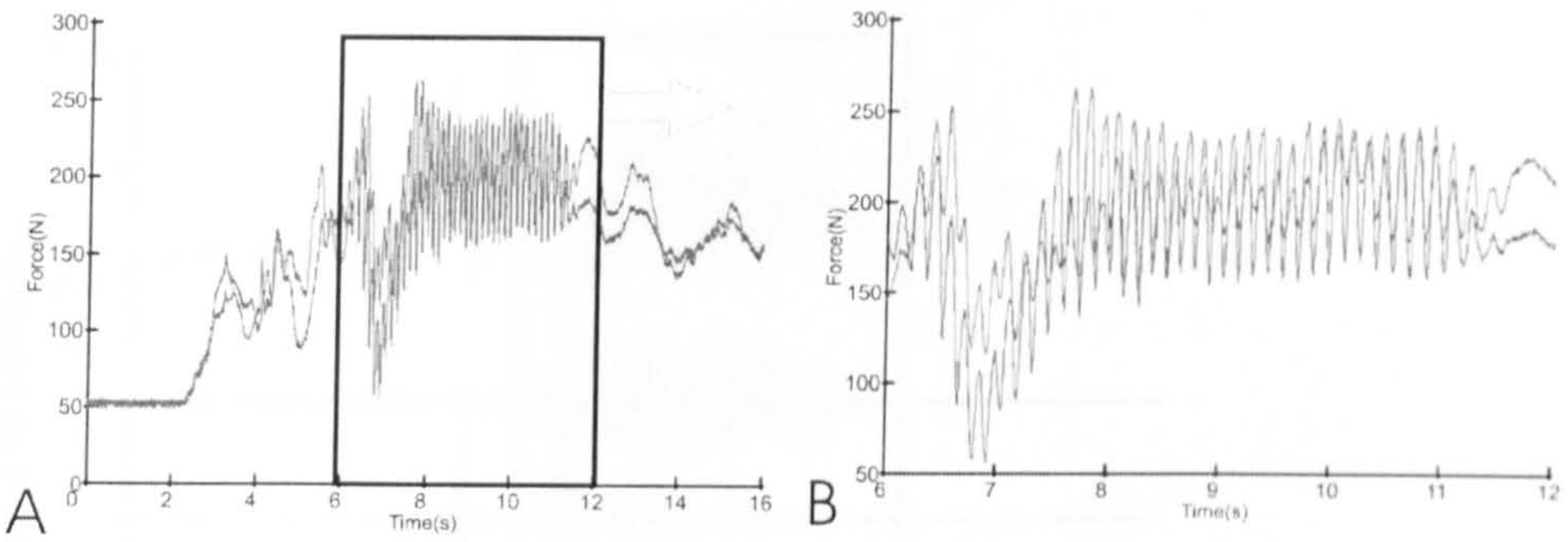


Figure 7.3. A) A plot of the vertical forces through the feet during a sit-to-stand of the 2nd patient who showed the oscillatory activity. In this patient the activity occurs later than in the first patient. B) The epoch in which the oscillatory activity occurs is expanded and C) a Power Spectral Density Plot of the vertical components of the force plate data for the stand shown in B). The spectrum was calculated over the time period in which there was oscillatory activity in the vertical component of the force plate signal. A peak in the spectra at 8Hz is clear in both legs. In the raw signal the oscillations are observed to have a frequency of 8Hz and this is confirmed in this figure. D shows the knee angle during a sit-to-stand and this also shows an 8Hz oscillation between 8 and 10s at the same time as the oscillations recorded from the force plate. This figure was obtained during a stand with stimulation.

The oscillatory activity in the force profile is accompanied by changes in the angles and moments of the hip and knee (an example, knee angle is shown in figure 7.3). These changes are also manifested in EMG activity. It is not possible to determine whether the EMG activity is purely reflex or driving the oscillatory activity. Clonus, when evoked in Patient 5 occurred at a frequency of 4Hz. Figure 7.4 shows the force profile and the EMG activity from the tibialis anterior and gastrocnemius from one side of the body.

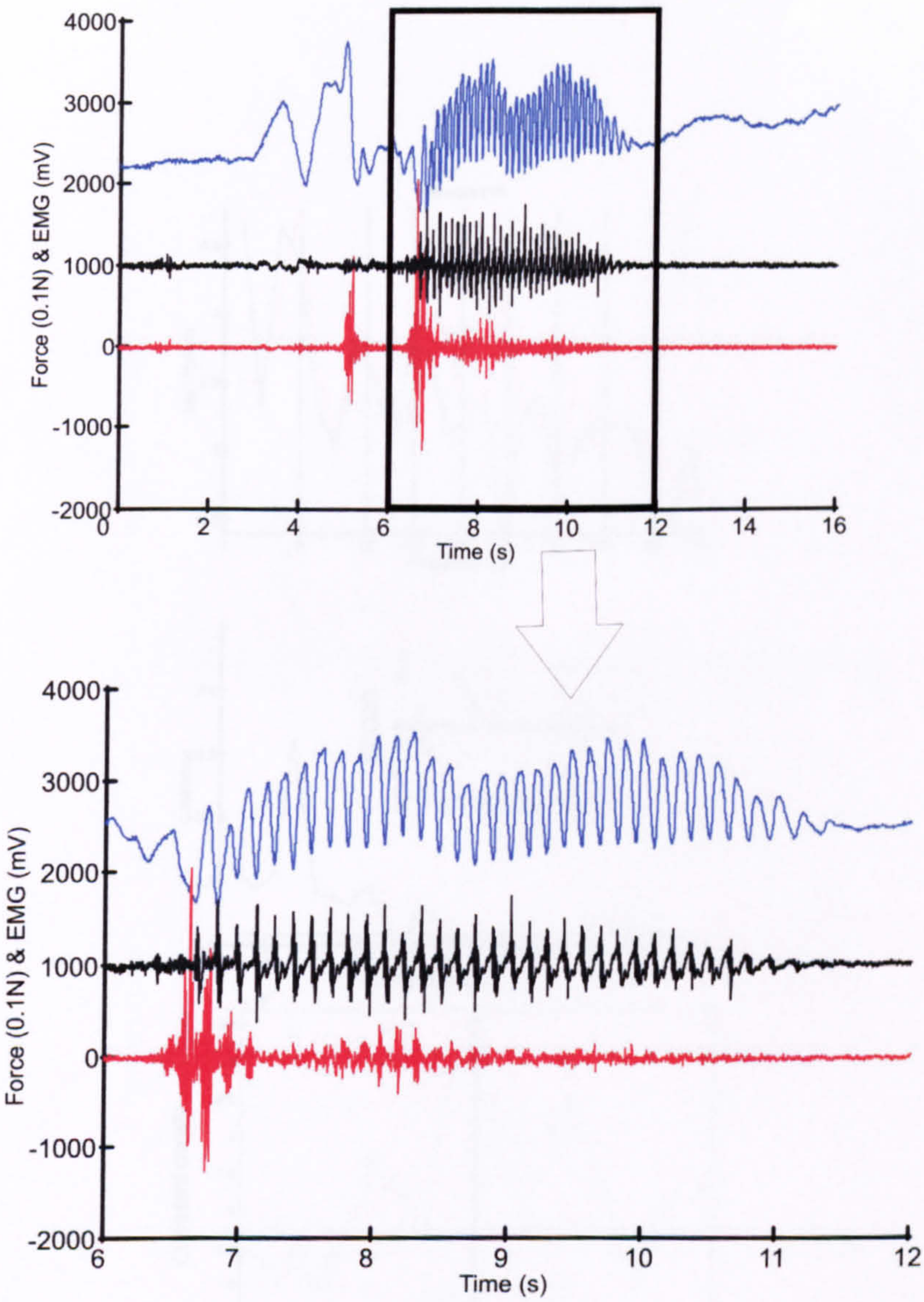


Figure 7.4. EMG activity from the Tibialis Anterior (black) and Gastrocnemius (red) from one side of the body and the vertical force profile. Activity in the tibialis anterior occurs in phase with the oscillatory activity in the force profile. There also appears to be some movement artefact on both the EMG records. The activity in gastrocnemius is less clear, but also is related to oscillatory activity. This figure was obtained during a stand without stimulation, as can be seen by the lack of artefacts from the stimulation in the EMG records.

The EMG activity showed a peak in the auto-spectra at 8Hz in both muscle groups, figure 7.5.

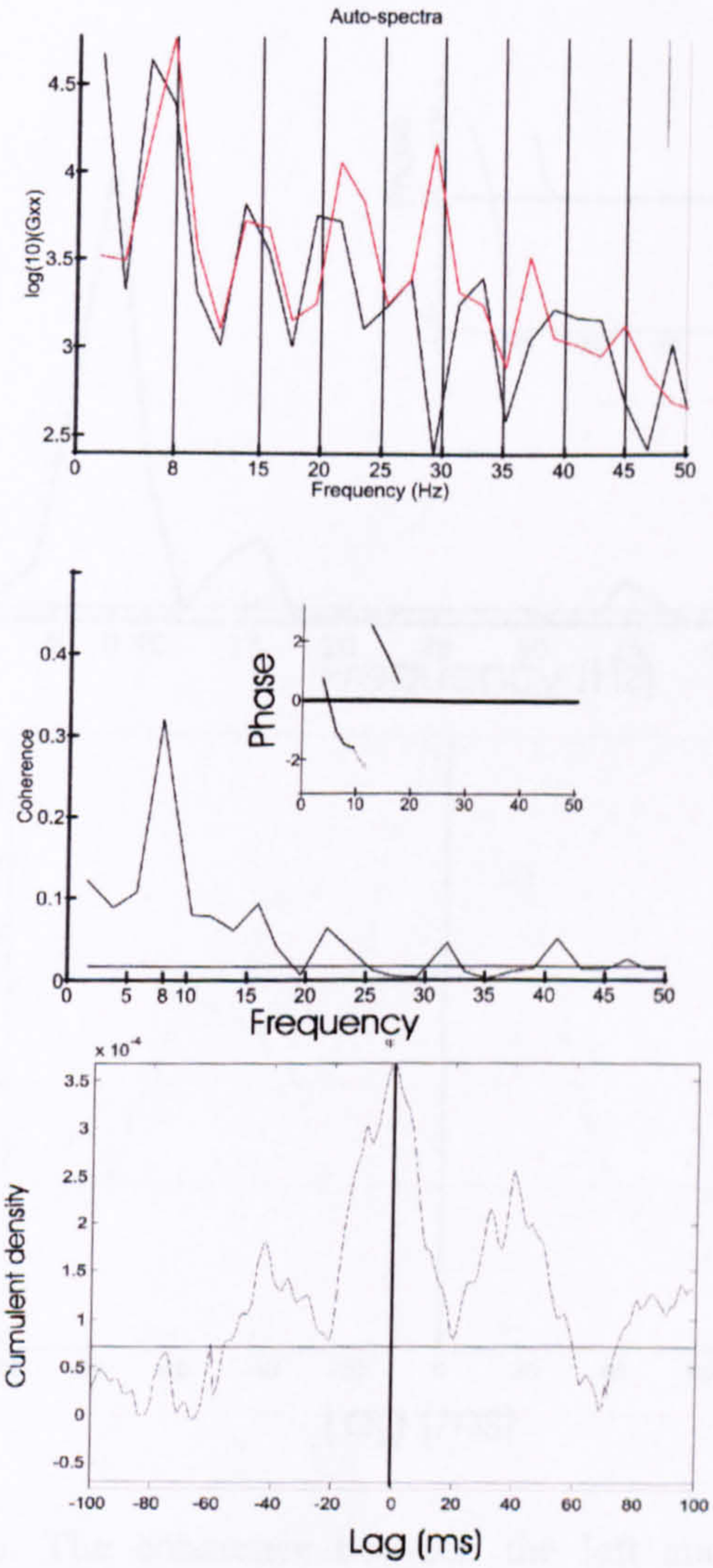


Figure 7.5. Top) the auto-spectra of the EMG activity from the tibialis anterior (black) and gastrocnemius (red) during the oscillation. Both muscles show activity at 8Hz. Middle) the coherence between the two muscle groups during the oscillation. Activity below 14Hz is coherent between the muscles, particuarly at around 10Hz. The horizontal line is the 95% confidence level. Segment lengths were 512 in both autospectra and the coherence estimate. The phase plot in the upper right corner shows a consistent non-zero time lag between the muscles in the regions of significant coherence. Peaks in the cumulent density (bottom) provide further evidence of functional coupling and the 8Hz rhythmicity.

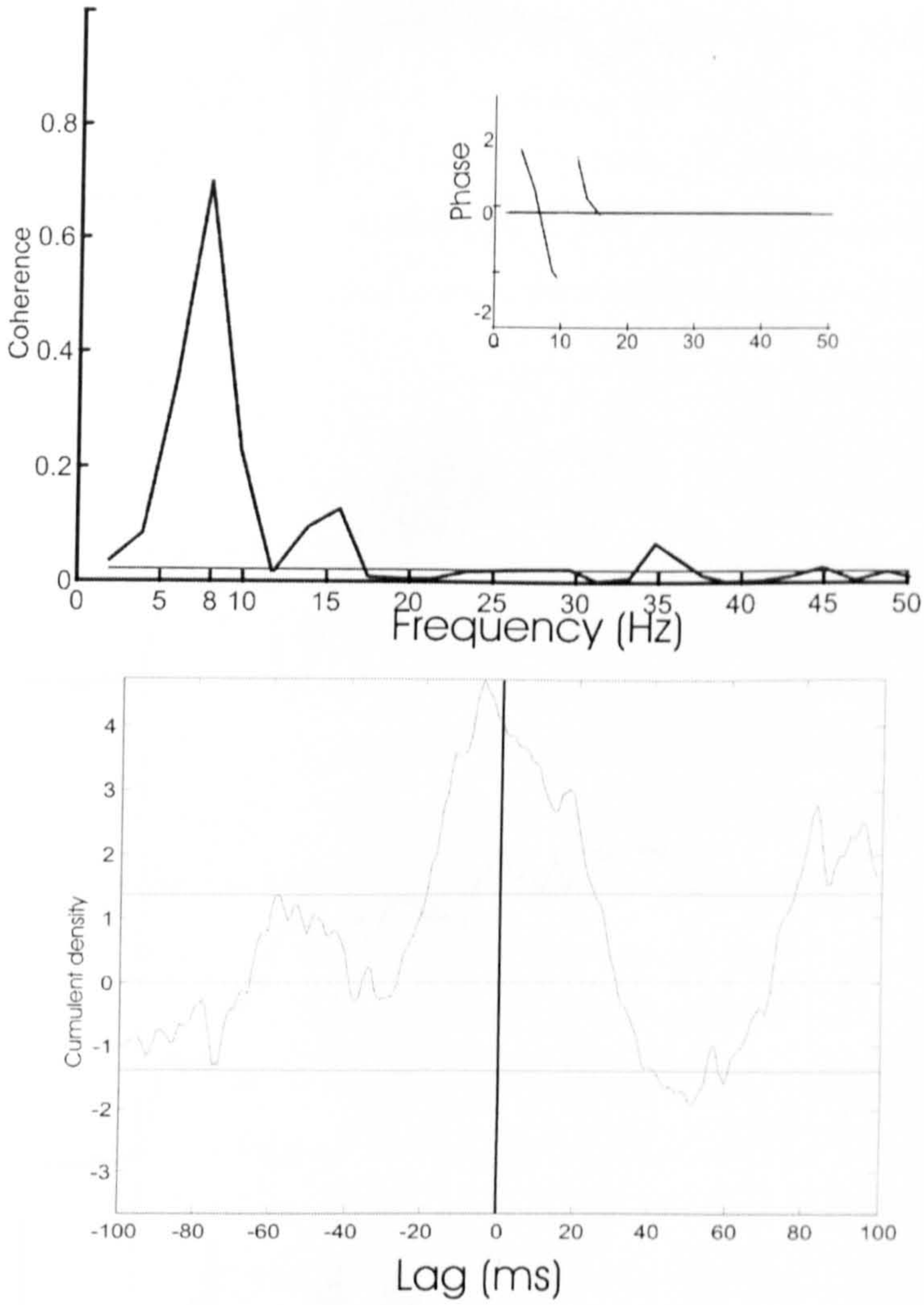


Figure 7.6. The coherence between the left and right tibialis anterior during an oscillation. A large peak is visible at 8Hz with a harmonic at 16Hz. The horizontal line is the 95% confidence interval, calculated over segment lengths of 512.

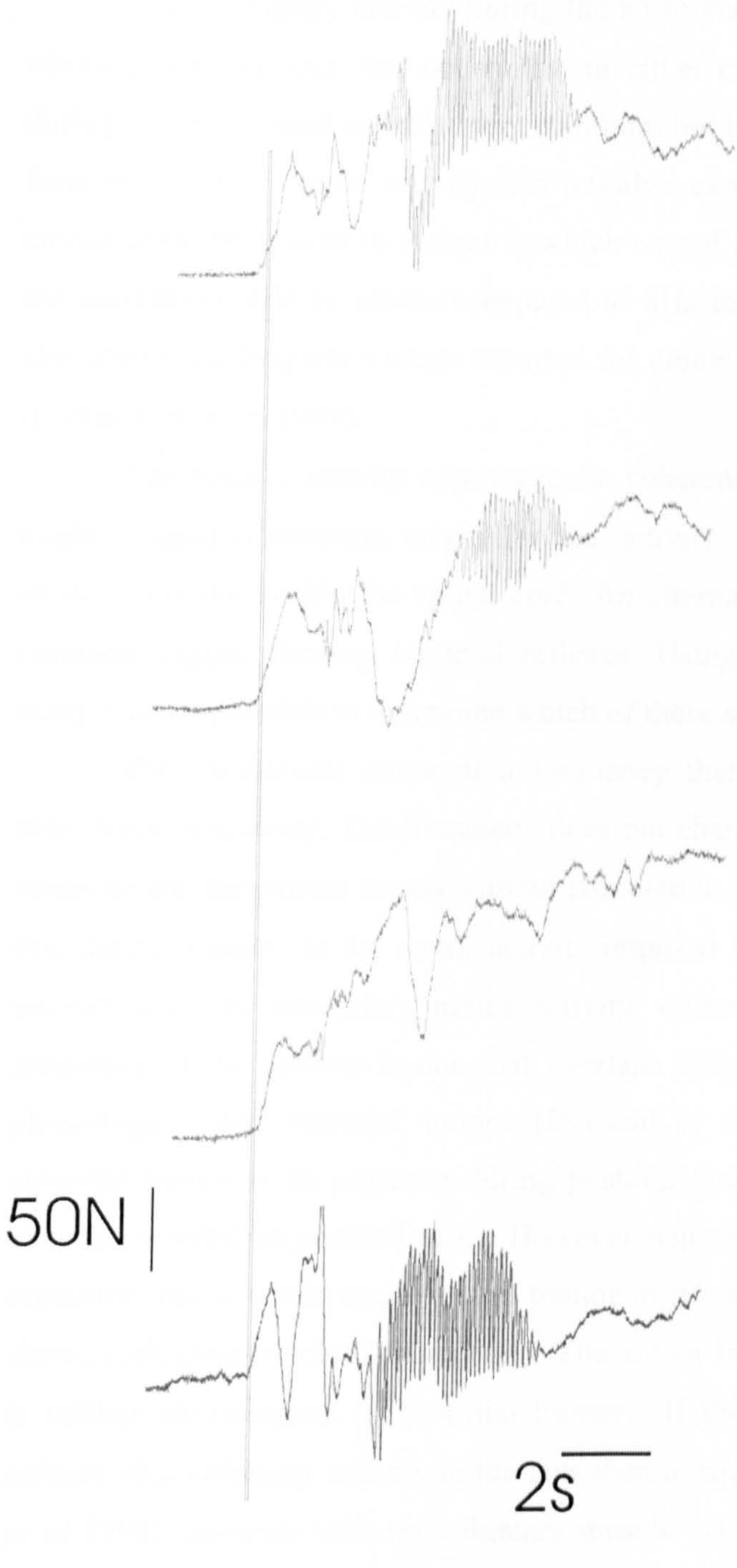


Figure 7.7. The time course of the oscillatory activity. The first three stands (top three plots) were performed with minimal rest periods. The amount of oscillatory activity decreases between each of the stands. The bottom plot was obtained after a 10-minute rest period. The oscillations have returned and are of a similar size to those seen in the original trace. The frequency of the oscillation in all the records is the same.

7.4. Discussion.

The oscillatory activity during the sit-to-stand is persistent in both patients in whom it was obvious, but not visible in either of the other two patients. Reflexes during the sit-to-stand are relatively common, but have not been observed to take this form previously. Clonic activity is a possible explanation for this activity however clonus could be evoked in Patient 5, which was of a lower frequency than that seen in the oscillation, 4Hz in clonus compared to 8Hz in the oscillation. The oscillation is also above the frequency range reported for clonic activity by Rymer and colleagues (Hidler & Rymer, 1999).

The muscle activity appears to be coherent within and between legs, which might suggest a common origin for the activity. This common origin might be a neural oscillator within the spinal cord. An alternative explanation is that there is a common trigger eliciting bilateral reflexes. Using the techniques available in this study it is not possible to determine which of these alternatives is correct.

The oscillations occur at a frequency that is not obviously related to the stimulation frequency. The frequency does not change from 8Hz when stimulation is removed and the patient stands without stimulation, figures 7.3 and 7.4. This suggests that the oscillations in the motor activity imposed by the stimulation do not directly interact with the oscillatory motor activity, either reflex or centrally driven. The frequency of the activity is one that overlaps with a number of tremors, including physiological and essential tremor (Deuschl *et al* 1998). A defining feature of essential tremor is its presence during postural tasks and physiological tremor may also be manifest in postural tasks. However neither of these tremors habituate with repetition and it is not usual to find tremor in the legs during the sit-to-stand which shows such clear synchronous activity. The author therefore believes that this activity is neither physiological or essential tremor. If this type of activity occurred in a subject with voluntary activity in the legs then it might be an *action tremor* (Deuschl *et al* 1998), however with no voluntary muscle activity in these patients one of the defining features of an action tremor is missing.

Oscillatory motor activity is found in muscles during fatigue (Gandevia 2001). However in those instances the oscillatory activity represents a decrease in the firing rate of voluntarily active muscle probably as a result of central fatigue. In this instance it is unlikely that the activity is fatigue related since it appears in the first stand on

each occasion, decreases with repeated stands (which might be expected to further fatigue the muscle) and stops during the stand.

It is unclear what the trigger is for the activity. The sit-to-stand involves a number of changes of sensory input to the spinal cord. The joint angles and muscle lengths may change as well as a redistribution of weight onto the feet. The activity does not occur when the patients undergo the same angle changes in a simulated stand whilst they are lying on a plinth. The activity does occur when the patients are standing without stimulation. This suggests that the act of standing is required to trigger the activity. The largest difference between simulated and actual standing is the change in weight distribution. However, the amount of weight being taken through the feet cannot be the sole trigger in a simple model since the oscillations occur with the feet taking less weight than they had previously before the knees were locked, figure 7.1 and chapter 8. In a simulated stand the changes in joint angles are not exactly those seen in a real stand, as both joints extend at the same time. The trigger for the oscillatory activity may be a combination of stimuli, such as the hip angle and the weight distribution. Previous studies have emphasised the role of hip angle in determining the amplitude and latency of spinal reflexes in both normal subjects and those with spinal injury (Knikou & Rymer, 2002a,b). Other studies have demonstrated similar effects with pressure on the sole of the foot (Knikou & Conway, 2001). A combination of these inputs therefore seems a likely trigger for the oscillatory activity seen here.

There are several mechanisms in which the weight distribution might be sensed including within joints or through cutaneous receptors. Neither of the patients who showed the activity had previously suffered any nerve damage, e.g. a rhizotomy accompanying a SARSI implant (chapter 2), which might dennervate either their gluteal region or a portion of the sole of their foot (Brindley GS, 1994). Within the current experimental setting it is not possible to determine which of the neural receptors is relevant in this situation.

The time course of the activity between stands is interesting in that it shows habituation with repeated, regular standing. This is similar to the pattern seen in spinal reflexes. If there is a pause in the presentation of the trigger, the sit-to-stand, then the response re-appears again. This is again similar to the pattern previously seen in spinal reflexes. The pattern of habituation of spinal reflexes has been studied for the stretch (Rothwell *et al.*, 1986), flexion withdrawal (Nicol *et al.*, 1998) and

cutaneomuscular reflexes (CMR) (Harrision *et al.*, 2000). All show an exponential decay with re-appearance of the reflex at or close to its original size if the stimuli are stopped briefly. Pilot data suggests that for the CMR this need only be a single missing stimulus in a train of many hundred at 9Hz (Harrison, Norton & Stephens. Unpublished observation and Norton B.Sc dissertation 1997). This provides further evidence for the reflex nature of the event as a whole, e.g. oscillatory motor output in response to a trigger or stimulus arising from standing up. It does not explain the generation of the oscillatory motor output.

7.5. Conclusions.

Two of the patients exhibit rhythmical motor activity during the final phase of the sit-to-stand. It is not clear what triggers the activity, but a combination of sensory inputs such as joint angle and weight distribution is possible. The origin of the oscillations in the motor system is unclear. It may be reflex or centrally driven but is unaffected by the stimulation. The oscillatory motor response shows a pattern of habituation that is typical of that seen in spinal reflexes.

Chapter 8.

Does the Neural Activity Associated with Standing Change with Standing Experience?

8.1. Summary.

A naïve paraplegic subject was taught to stand using surface FES. Reflex and oscillatory motor activity remained stable over the 6 weeks in which experiments were performed. With increasing experience it was found that he took more weight through his legs during steady-state standing such that at the end of the period he was using his arms for balance and they were carrying under 5% of his body weight. With increasing experience he also modified his strategy during the sit-to-stand so that he extended his knees earlier in the stand, extended his hips more quickly and reduced the margin of safety for his knee extension during the hip extension phase of the sit-to-stand. Although he modified and refined his strategy during the sit-to-stand with experience it remained, in essence the same strategy as he used at the beginning and has previously been reported to be used by two experienced FES-assisted standers.

8.2. Introduction and Brief Methods.

8.2.1. Introduction.

Learning to stand with FES assistance is likely to be a difficult procedure for the patient. Clinical experience suggests that many patients are able to "learn" how to perform this task with just a few standing sessions spread over one or two months (Wood, personal communication). The subjective observation of improvement is based upon an increase in standing time for the patients and the clinician's view that the patient is taking more of their body weight through their legs rather than their arms. Sometimes the clinician reports an improved posture, typically a straighter hip.

An improvement in the "quality" of the stand may arise because of an improvement in the confidence of the patient or in their skill level or in both. When standing with FES the patient will be standing for the first time since their injury without mechanical supports. The patient must learn to trust their own muscles, both leg and upper body which will be providing balance and some weight support as well as the team responsible for providing the FES service.

When standing with FES the patient is supported by his or her own leg muscles. These have unknown, dynamic properties, e.g. fatigue which the patient

must learn to understand and take account of, probably subconsciously. Additionally the lack of mechanical supports during FES-assisted standing means that the patients must learn to stand up in a different way to that used in a standing frame in which the knee support is used to provide some weight bearing assistance whilst the body is extended.

The process of learning to stand with FES assistance has not previously been studied and it is unclear what parameters of the stand change with increasing experience and if these correlate to an "improvement" in the stand. This study used a single case study approach with a patient who had previously trained his muscles in accordance with the previously published protocol and was now ready to commence open-loop standing trials (Rushton *et al.*, 1998). To be ready to commence open-loop standing the patient had to have knee extension moments, when seated and with the knee at 90° that were at least 1Nm per Kg of body weight.

The study set out to answer four questions;

- Does the patient improve his stand? This would primarily be assessed by measuring the vertical forces through the feet during steady state standing since clinically this is believed to be a useful measure of the quality of the stand.
- Does the spinally generated endogenous neural activity during steady-state standing or the sit-to-stand change with increasing experience?
- Does the patient use the same strategy as previous subjects for the sit-to-stand?
- If the patient does use the same strategy for the sit-to-stand during learning, what changes in the strategy?

8.2.2. The Motor Task: FES-Standing with Upper Body Support.

The moments acting about the leg joints will arise from the weight of the body and the action of the hands on any supporting structure. In general the equation can be written as; $M=L\cdot F+w\cdot P\cdot W$ from equation 1 in Donaldson and Yu (1998). In this equation M is the leg joint extension moment, F is the forces and moments applied at the handles, L is the perpendicular distance from the handle reaction vector to the joint, w is the total body weight, P is the position of the centre of mass of the body segment above the joint, in this case the HAT (head, arms and trunk) and W is the proportion of the body weight in the segment above the joint. If no handle supports

are used then the internal extension moment arising from muscle contractions, and passive components within the joint must equal the externally acting moments arising because of the segment masses and positions. This is the case when neurologically normal people stand up, or hold a particular posture. If support handles are used then the moments that are required from the muscles, under voluntary or artificial control, may be reduced for any given posture. The component in the equation $L \cdot F$ is the deficit, and is generated by the action of the hands on the handles, termed M_{def} by Donaldson and Yu (1998). The concept of a joint deficit is novel to the work of Donaldson and Yu and has not been expanded upon by other groups. Donaldson and Yu used joint deficits as a control signal in their CHRELMS controller (Donaldson and Yu 2000). The significance of the concept in this discussion is that it offers a way of understanding what the action of the handle reaction vector will be at a number of joints. If the vector passes through a joint centre then the vector will generate no moment about the joint. If the vector acts along a line that does not pass through a joint then the vector will exert a moment about that joint. The magnitude of the vector can be found by multiplying the size of the vector by the perpendicular distance between the vector and the joint centre as outlined in chapter 3 and Meriam and Kraige (1998). An upward vector passing in front of the knee and behind the hip joint will flex the joints and one passing behind the knee and in front of the hips will extend them, table 8.1.

	Upward Acting Vector	
Joint	In Front of Joint	Behind Joint
Hip	Extend	Flex
Knee	Flex	Extend

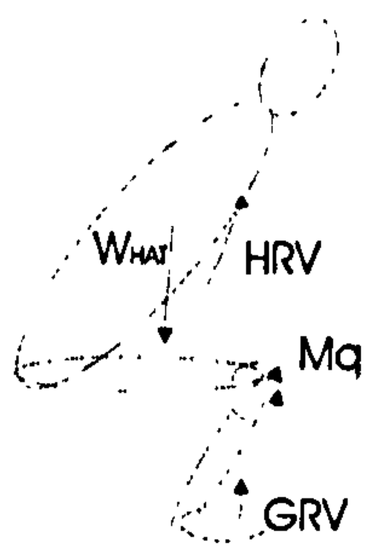
Table 8.1. A summary of the actions of an upward vector about the hip and knee joints. The size of the moment will depend upon the distance from the joint to the line of the vector.

The line of action of the handle reaction vector is under the patient's control, (either implicitly or explicitly). By adjusting the line of action of the vector he is able to adjust the moment it generates at a joint. The problem is; what vector can, with the internal moments, cause the desired movement or maintain the desired posture?

8.2.3. A Strategy for Standing-up.

When patients perform the sit-to-stand with FES-assistance they must adopt a different strategy then when they stand with mechanical support with their knees fixed or prevented from flexing. When there is mechanical support patients are able to use the supports to take some of their body weight. Without those supports patients must find a different strategy to perform the sit-to-stand. Donaldson and Yu have suggested a strategy they call *quick knee locking* (Donaldson & Yu, 1998). In this strategy the patients extend their knees so that they are fully, or close to fully extended before their hips are extended. This reduces the number of degrees of freedom within the leg making it more controllable. The knee can be held extended by the electrical stimulation to the quadriceps and the action of the weight of the upper body.

The stimulation starts to extend the knee, Mq. There is a small GRV and HRV and the weight of the body, WHAT, passes in front of the hip and behind the knee.



A

B

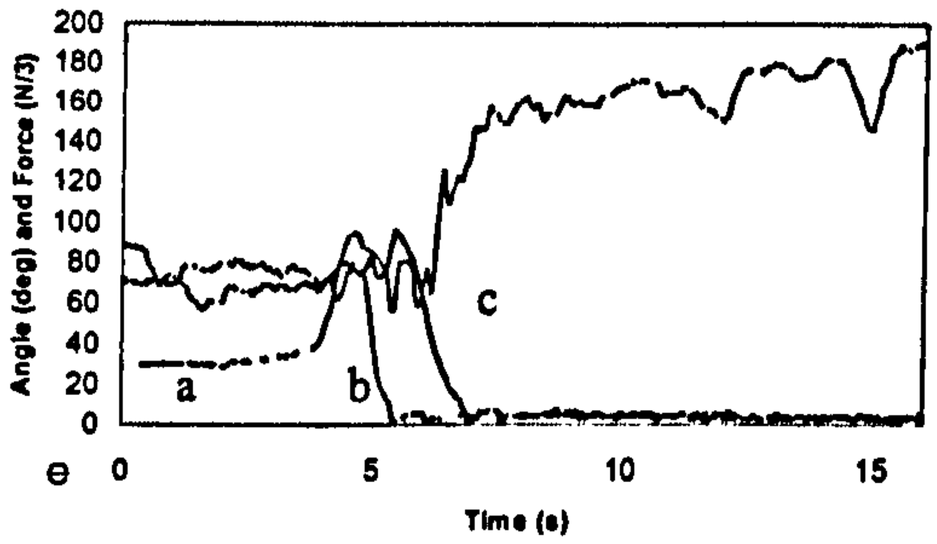
The knees are more extended, but still producing an extension moment. The GRV is growing. The HRV is also passing in front of the hips and behind the knees.

The knees are straight so Ml arising from the ligaments counteracts the extension from the stimulation. The HRV is still extending the hips, but now is flexing the knee, but as the knee is locked no flexion takes place.

C

D

The patient is upright and using their hands for balance. The knees remain locked.



e

Figure 8.1. Figures a-d show in cartoon form the four stages of the sit-to-stand using the quick knee locking strategy. As the knees become straight in c and d a flexion moment from the ligaments is generated. In e data is presented from an experiment in this study, which confirms that, the knees extend before the hips and then the majority of the weight is transferred to the legs. A shows the weight being taken through the legs, b shows the knee angle and c shows the hip angle.

Figure 8.1 shows the posture of the patients adopting the quick knee locking, QKL, strategy in each of four phases of the sit-to-stand. The phase that is unusual in this strategy is illustrated by part c of the figure in which the knees are extended but the hips are still being extended. Normal subjects extend their hips and knees simultaneously to achieve their final posture. Both joints start extending together and finish extending together. Normative data has been presented by Kralj and colleagues (Kralj *et al.*, 1990). Normal subjects elongate phase b in which both joints are being extended until they are in the posture illustrated in part d. Part e of the figure shows how, in the subject in this study, the joint angles change with time and with the forces being taken through the feet. This is in contrast to figure 4a in (Kralj *et al.*, 1990) which shows the knees and hips extending together.

Donaldson and Yu did not provide precise definitions of the strategy in their paper. In this study QKL is taken to have occurred if the patient has extended his knee to within 5% of the steady state angle before the hips are extended by 20%. The definition is arbitrary. The hips initially start to extend with the knees before the knees are locked, figure 8.1.b. Therefore the hips will be extending as the knees are being locked.

Using the QKL strategy for the sit-to-stand there are four phases to the sit-to-stand;

- Initial movement; this occurs from the onset of the movement from the chair until the knees are 50% extended.
- Knee locking; this phase extends the knees and is short in the QKL strategy. The knees move from 50% to 95% extended.
- Hip extension; in this phase the knees are at least 95% extended but may be continuing to extend. The hips are extending up to their final position.
- Weight bearing; in this phase, which may occur during or after the hip extension phase, the patient takes an increasing amount of body weight through their legs.

8.2.4. Joint Moments.

Joint moments have been previously described in chapter 3. The moments about the knee, (or any joint) will consist of internal moment and external moments. The internal moments will consist of the moment generated by muscle contractions, in

this case electrically stimulated contraction of the quadriceps or endogenous activity and moments generated by internal, "passive" structures such as ligaments. For the knee joint the ligaments will generate moments only when the knee is extended.

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Figure 8.2. Left. The knees are extended enabling the mass of the body to pass behind the joint in the model. If the mass of the body passes close to the joint it generates only a small moment since the moment arm is small. Right. A patient standing in a typical posture with both hips and knees extended similar to that shown on the left. Both figures from (Kralj A & Bajd T, 1989).

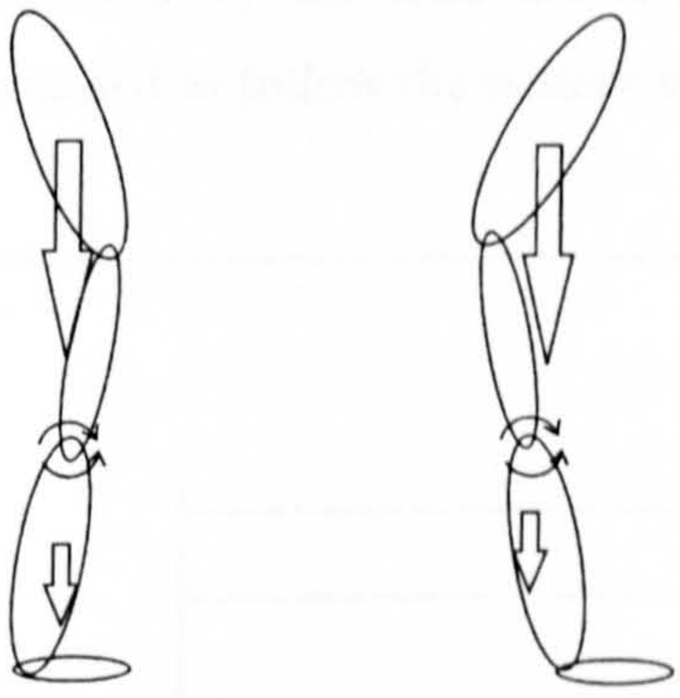


Figure 8.3. A cartoon model of two conditions in which a patient is balanced around the ankle joint and will not need to apply a HRV. On the left the hips are extended and the weight of the trunk and thigh pass behind, but close to the ankle. The weight of the shank passes in front of the ankle. On the right the situation is reversed. The right hand posture is obtained during the sit-to-stand and the left hand posture is a steady standing posture. How does the patient move between the two postures?

Figure 8.2 shows a patient standing using electrical stimulation in an inverted "C" posture. This posture is represented in cartoon format in figure 8.3 (left) along with the "reverse" position in which the joints are flexed slightly (figure 8.3 right).

At any position with the knees extended the total clockwise moment about the knee from the stimulated quadriceps and the upper body is;

Mq+What*dhat. (1).

Where Mq is the moment due to the stimulation of the quadriceps, What is the mass of the head, arms, trunk and thigh and dhat is the distance from the What vector to the joint centre.

This must be opposed by the knee ligaments so;

Ml = Mq+What*dhat (2)

Where Ml is the moment due to the ligaments.

In the right hand posture in figure 8.3 Ml is large. As the patient changes posture towards that seen on the left Ml gets smaller as dhat goes from positive to negative. Ml must be greater than or equal to zero. When Ml becomes 0 then 2 can be rewritten as;

0= Mq+What*dhat. (3).

Or;

Mq=- What*dhat (4).

Because Mq is determined by the stimulation it is assumed to be constant. The internal moment is assumed to follow the pattern seen in figure 8.4.

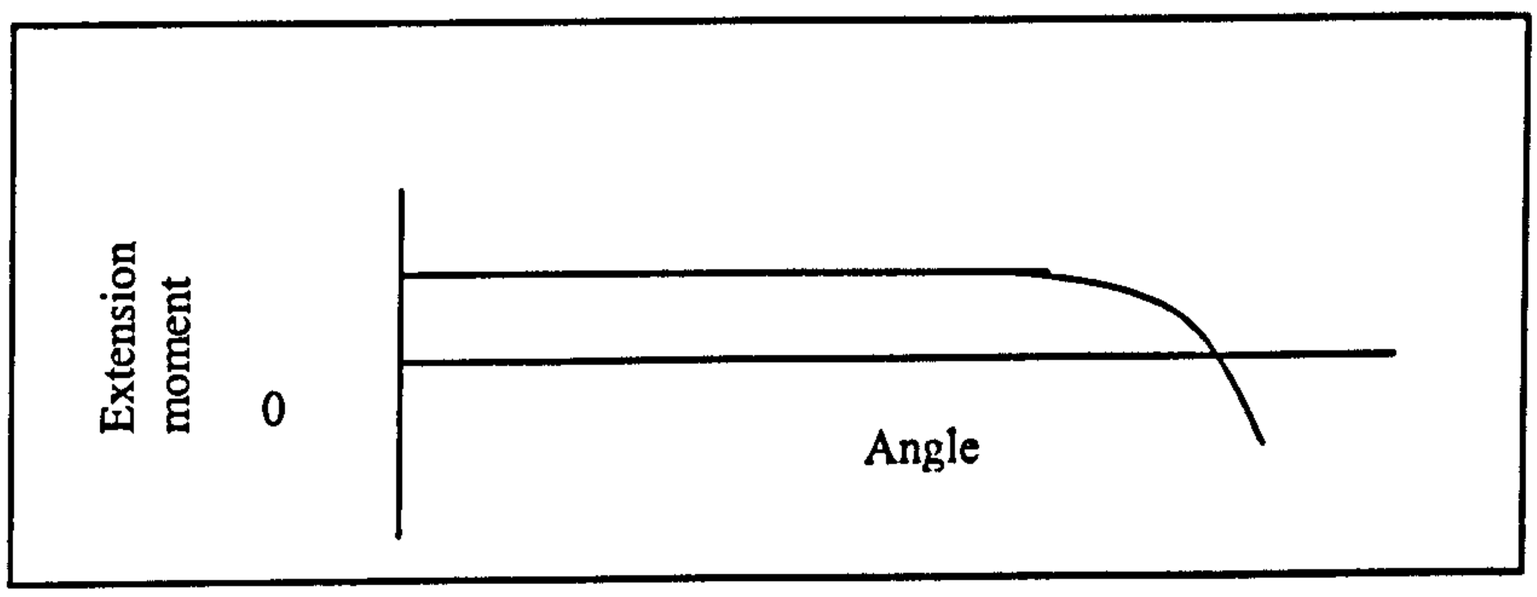


Figure 8.4. A schematic representation of the angle/internal moment curve for the knee. The turning point occurs around the point in which the knee is straight, but is undefined as is the slope of the curve.

When the internal moment is Mq any further movement of the line of action of What, (i.e. making dhat more negative) will cause the knees to buckle. This model

assumes no stiffness within the quadriceps and also fails to account for any neural activity arising as a result of buckling, it is solely concerned with detecting the onset of buckling.

How can this posture be detected? The internal moment can be calculated from the lower leg in a ground-up manner. This is preferably to the top down approach since the mass and centre of mass of the trunk are unknown, whereas these properties are known for the lower leg.

The internal moment Mi can be found;

$$Mi=Mq-Ml \quad (5).$$

But also;

$$Mi=GRV*dgrv+Wshank*dshank \quad (6).$$

At the point of collapse;

$$Mi=Mq \quad (7).$$

Since Ml=0.

Mq is an unknown, however it can be estimated to be at least 15Nm per leg. If during the hip extension phase Mi is less than 10Nm then the posture can be considered safe. Moments larger than this might lead to buckling. The smaller or more negative the moment, the greater the margin of safety.

8.2.5. Experimental Set-up.

All experiments were carried out in the laboratory described in chapter 3. Recordings were made of the forces and moments applied by the hands, the forces exerted by the feet and the position of the body as well as EMG recordings from the leg muscles. For safety reasons the patient wore a support harness connected to a pulley system that was kept just slack by a member of the experimental team. The harness was used on all occasions but weight was only taken through it on two occasions, once during a sit-down that was not recorded and once during a sit-to-stand, the data for which has not been included in the analysis here. The patient stood on four occasions in the laboratory, the first three were each separated by a week and the last occasion was three weeks after the previous session.

During the experimental sessions the number of stands was chosen by the experimental team based upon estimates of how many stands the patient would be able to perform before fatiguing and was agreed before the experimental session started with the patient. Throughout the experiments the patient was free to stop the

session for any reason. The total time of each stand was also determined by the experimenters based upon the number of 16s records required. Typically stands lasted for a total of a minute. On day 1 the patient stood 9 separate times, on days two and three 7 times and day four 6 times.

8.3.Results.

Data was analysed from all sessions and all stands with the exception of aborted stands where body weight was taken through the support harness. Most of the analysis was performed on stands in session 2 which had a number of both bad and good stands and in which the data was the most complete.

8.3.1. Did he Improve?

The initial measure of the quality of the stand was the amount of vertical force being taken through the feet during the steady-state part of each stand. Figure 8.5 illustrates how over the first session the amount of vertical force taken by each foot increased. Figure 8.6 shows that as well as a general increase within a session in the amount of vertical force being taken through the feet there was a trend between sessions towards increasing force being taken by the feet. In none of the tests was it possible for the subject to see the forces being taken through his legs.

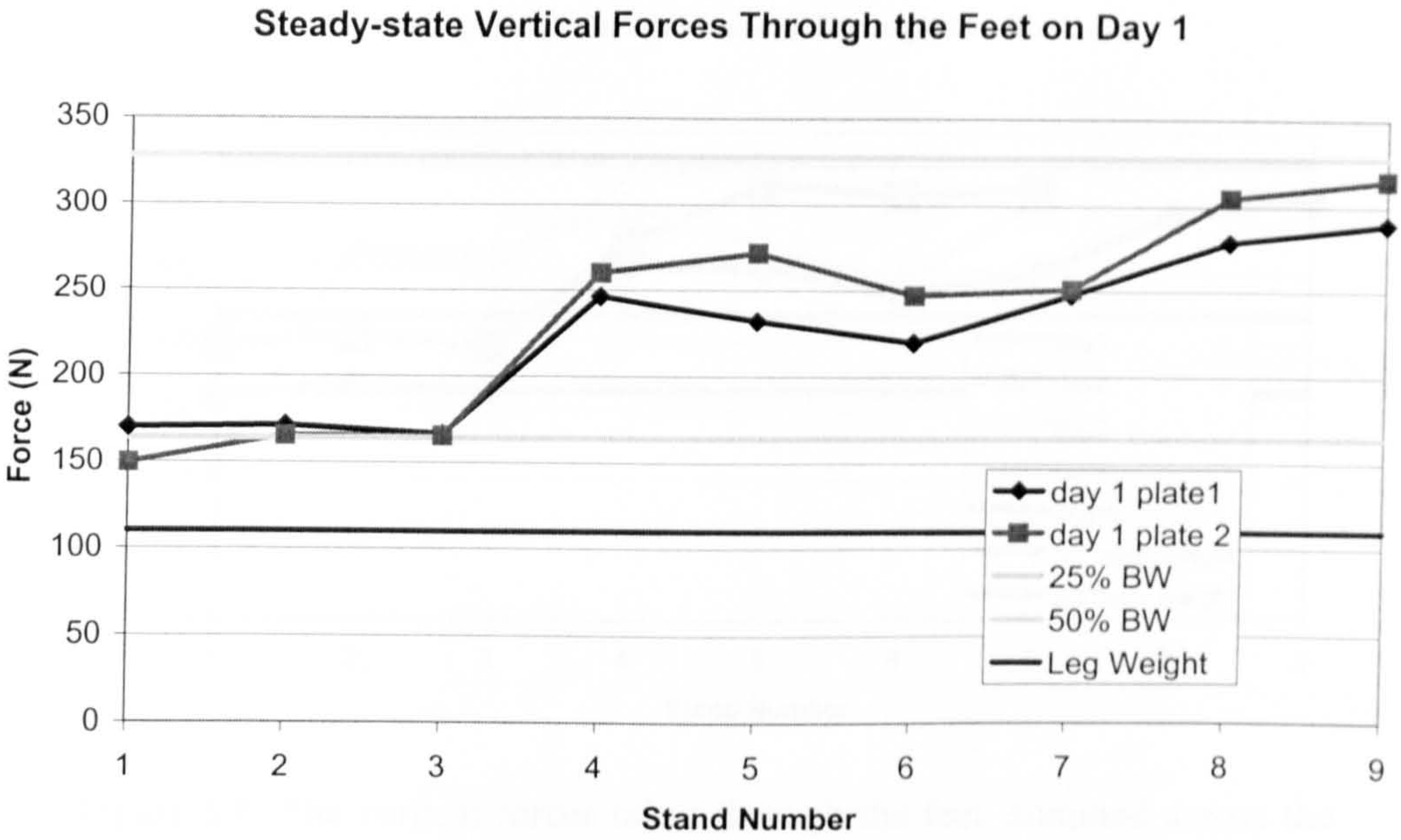


Figure 8.5. The vertical force being taken through the feet in each of 9 successive stands. Values are the mean of the 1s period at the end of the sit-to-stand recording which lasted 16s. There is a trend towards increasing force in each leg, particularly prominent between the 3rd and 4th stand. Even on day one there is a slight asymmetry between legs.

The patient's total body weight was 656N, and by the final stand on day 1 he is taking nearly 50% of his body weight, 328N, through each leg. However for the first 3 stands he is taking only about ½ his body weight through his legs with the remainder being taken through the arms. There is an increase in the amount of force being transmitted through the feet between the 3rd and 4th stands. The patient reported that the 4th stand "felt right" whereas the previous stands had not felt as comfortable. He was unable to explain what he had done differently and no feedback or advice had been given to him by the experimenters. On subsequent visits the patient stood for the first three occasions without verbal feedback. The amount of vertical force transmitted at the same stage of the stand is shown in figure 8.6. There is an increase between days 1 and 2 and 4. On day 3 the patient reported feeling "under the weather" and had fallen out of his chair in the morning whilst being carried down some steps. These factors may explain why the starting level on day 3 is lower than on the previous occasions.

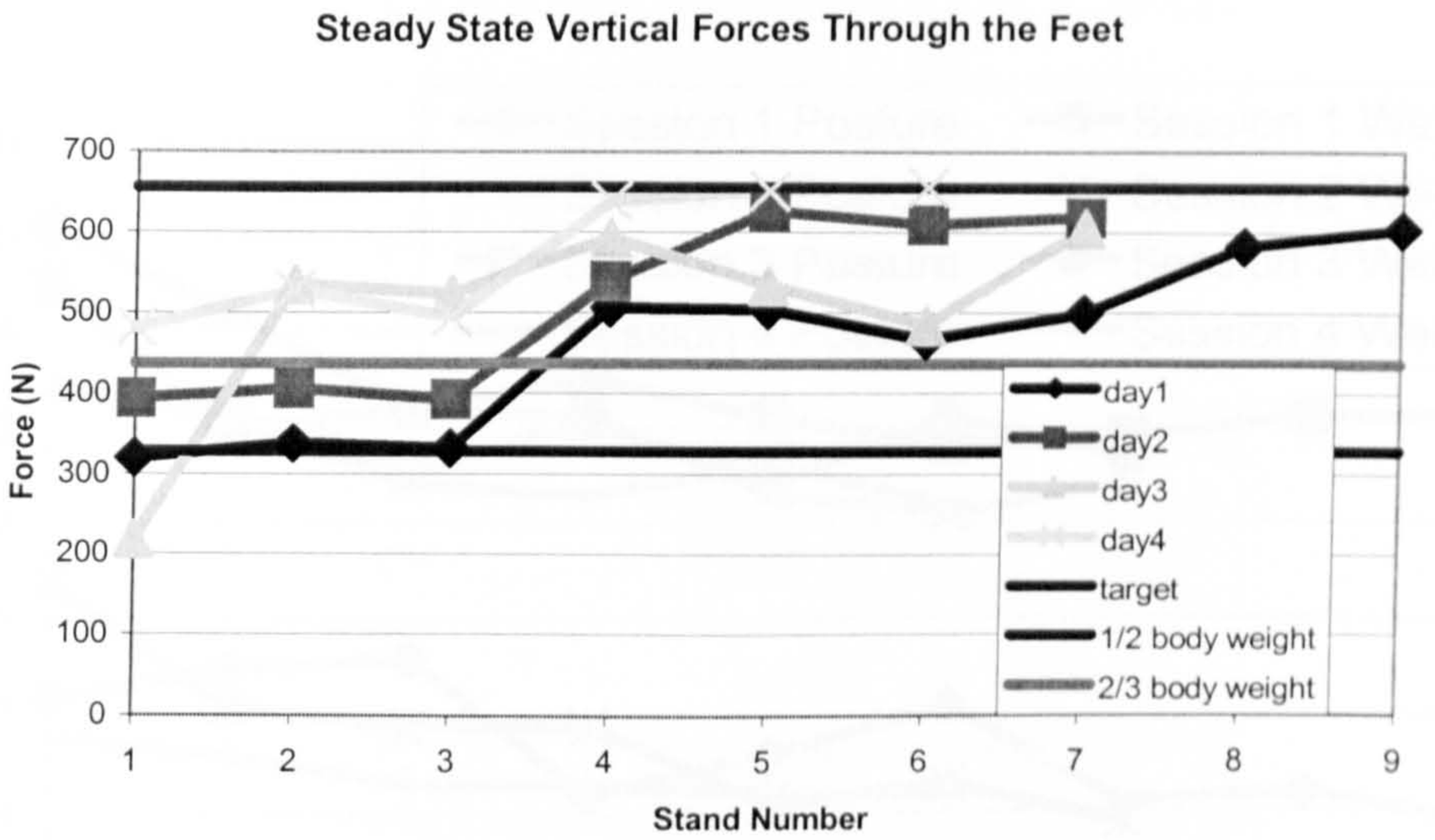


Figure 8.6. The vertical forces taken through the feet, summed across the two legs during steady-state standing, plotted against the stand number for successive days, typically separated by a week. The target is set at the patient's body weight.

Using a simple classification based upon the amount of weight being taken through the feet it is possible to separate the stands into "good" and "bad" stands. A threshold force distribution has been arbitrarily set, if the patient is taking less than of his body weight through his legs it is a "bad" stand. The first three stands on the first two sessions and the first stand on the third session are all "bad", whilst the remaining stands are "good".

Further assessment of the stand quality was based upon the time to perform the sit-to-stand. The sit-to-stand was split into two phases for this measure; the time for the posture to settle, in this case for the hips to get to 95% of their final angle and the time for the body weight to settle, to get to 95% of its steady-state level.

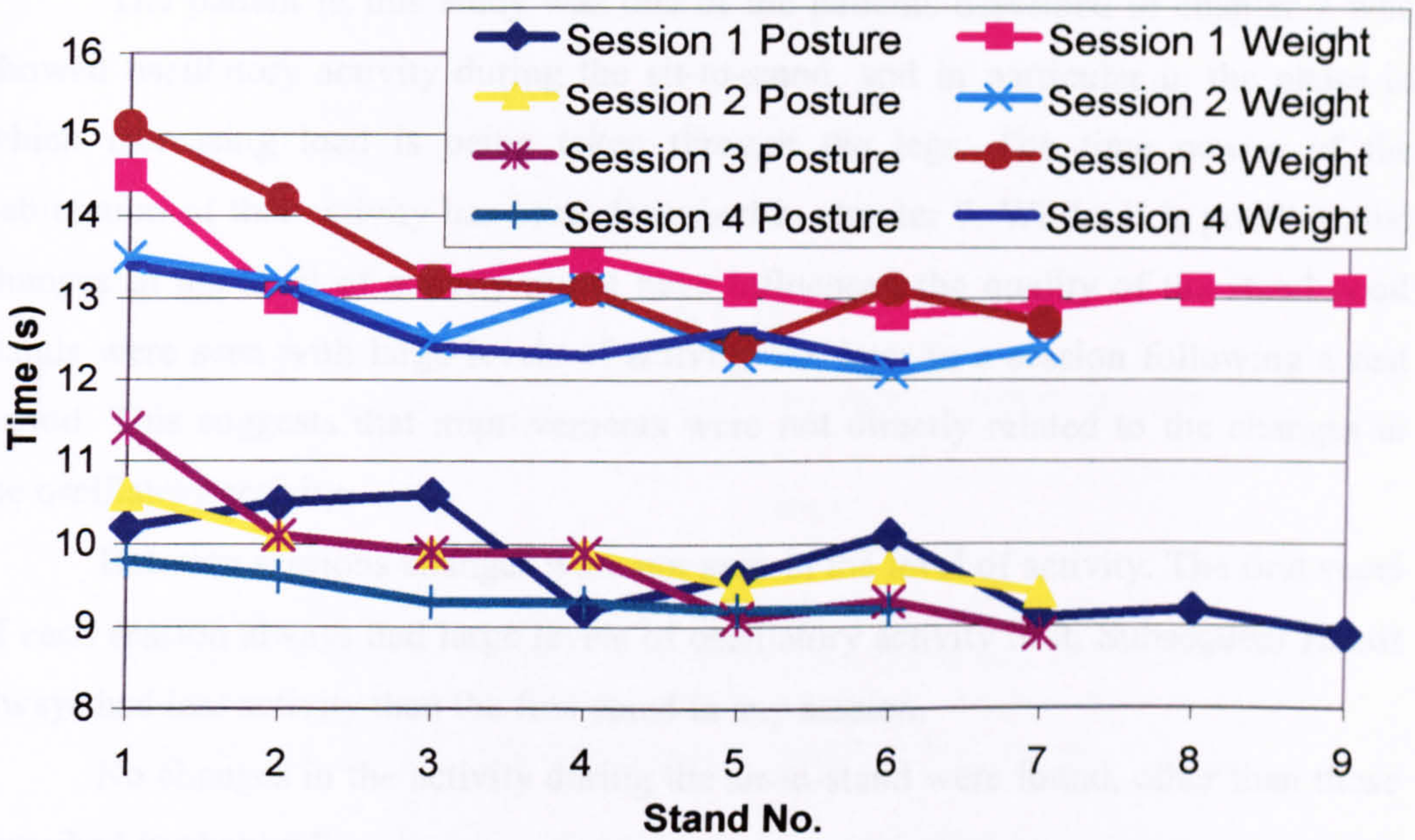


Figure 8.7. The time taken for the patient to reach his steady state posture and weight distribution for each stand on each session. There is a general decrease within and between sessions for both measures. There is a high degree of variability in both of the measures. Both measures were timed from the onset of the movement initiating the sit-to-stand.

Figure 8.7 shows that the time taken by the patient to reach his steady-state posture and weight distribution decreases with increasing experience. These measures are highly variable but do show a general decrease with increasing experience for both the time to reach a steady posture and to reach a steady weight distribution.

8.3.2. Are There Changes in the Neural Activity During Steady-State Standing?

Using surface EMG recordings it was not possible to record any neural activity during steady-state standing that was not directly attributable to the stimulation. Therefore it is not possible to state whether there were any changes in the activity. Any changes that did occur were so small as to be undetectable and therefore unlikely to result in changes in the quality of the stand.

8.3.3. Are There Changes in the Neural Activity During the Sit-to-Stand?

The patient in this study was one of the patients described in chapter 7 who showed oscillatory activity during the sit-to-stand, and in particular in the phase in which increasing load is being taken through the legs. The time course of the habituation of that activity has been described in chapter 7. Whilst it is possible that changes in the level of activity might have influenced the quality of the stand good stands were seen with large levels of activity, i.e. later in a session following a rest period. This suggests that improvements were not directly related to the changes in the oscillatory activity.

Between sessions changes were not seen in the level of activity. The first stand of each session always had large levels of oscillatory activity in it. Subsequent stands always had less activity than the first stand in any session.

No changes in the activity during the sit-to-stand were found, other than those described in chapter 7.

8.3.4. Are There Changes in the Timing of the Phases?

Some preliminary evidence has been provided in 8.3.1 showing that the time to achieve a steady posture and steady weight distribution decreases with increasing experience. In this section the timing of the phases will be presented in some more detail. For all the figures t=0 is the start of the recording. The start of the stand was defined as the onset of movement by the patient. Timings between phases and of the onset of QKL are taken from the onset of the stand, not t=0 on the plots.

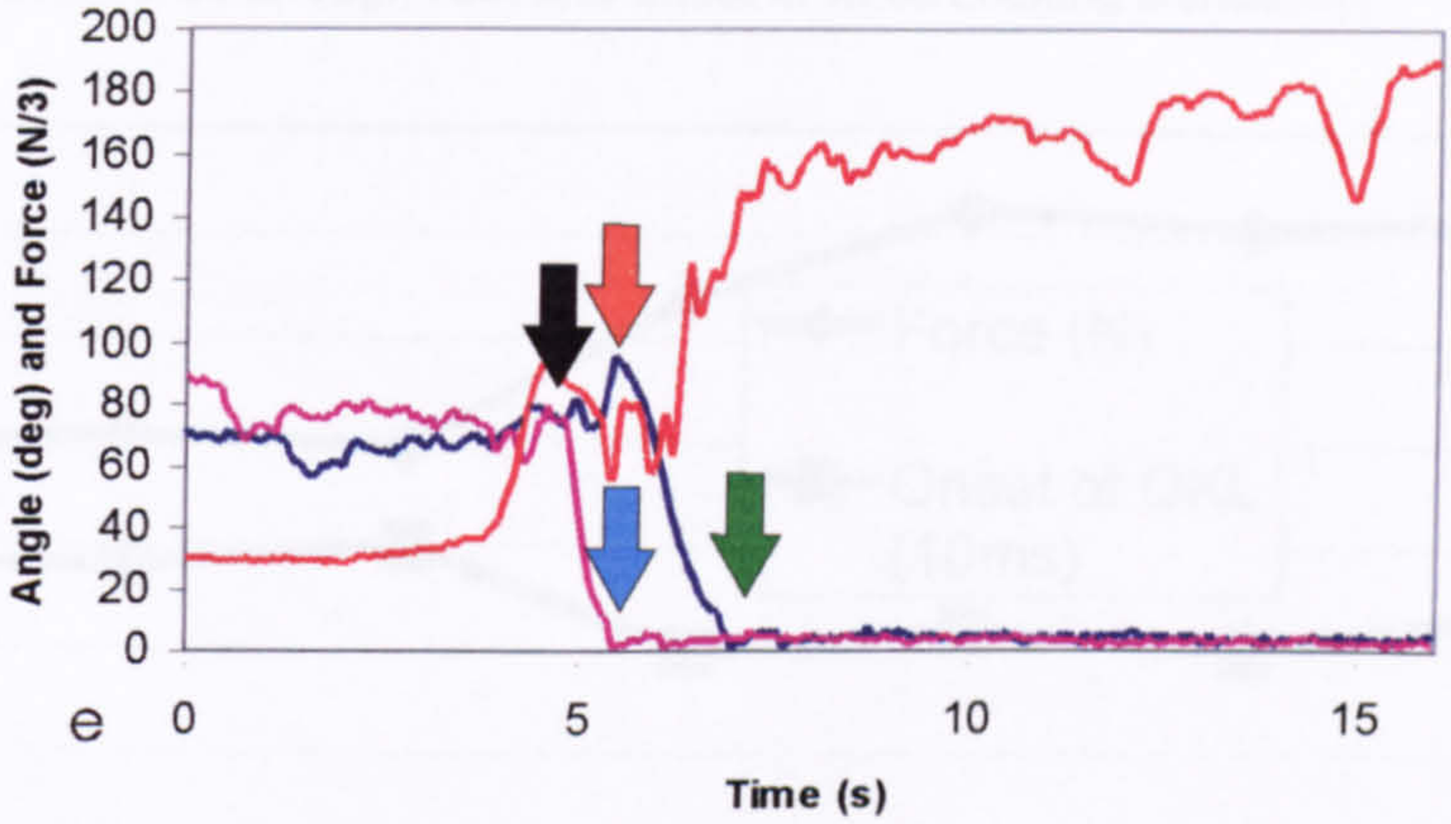


Figure 8.8. Part e of figure 8.1 repeated. The red line represents the vertical force profile, the mauve line the knee angle and the blue line the hip angle. Changes in the angle of both joints start before extra weight is taken through the feet. The hip then extends after the knee has extended.

Figure 8.8 shows the angle plots for the knee and hip joints during a good stand. Arrows positioned on the plot mark the start and stop of the knee extension (black-blue) and hip extension (red-green) phases.

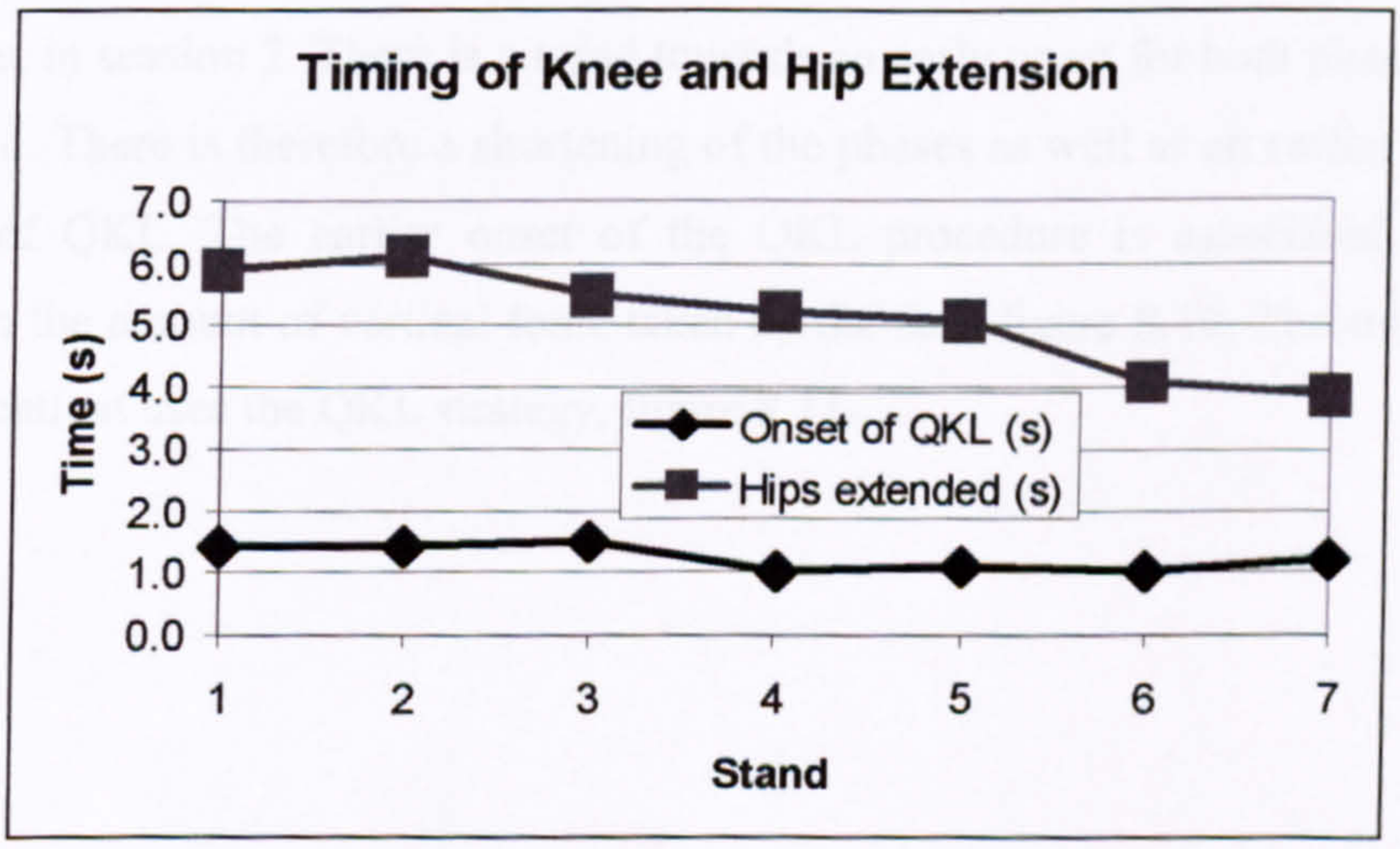


Figure 8.9. The timing of the completion of the hip extension against stand number, with the timing of the onset of the quick knee locking superimposed. Although there is a sudden change in the onset of the quick knee locking after the 3rd stand, this is not present for the completion of the hip extension. The timing of the completion of the hip extension shows a gradual decrease with increasing stands. All stands are from the 2nd session.

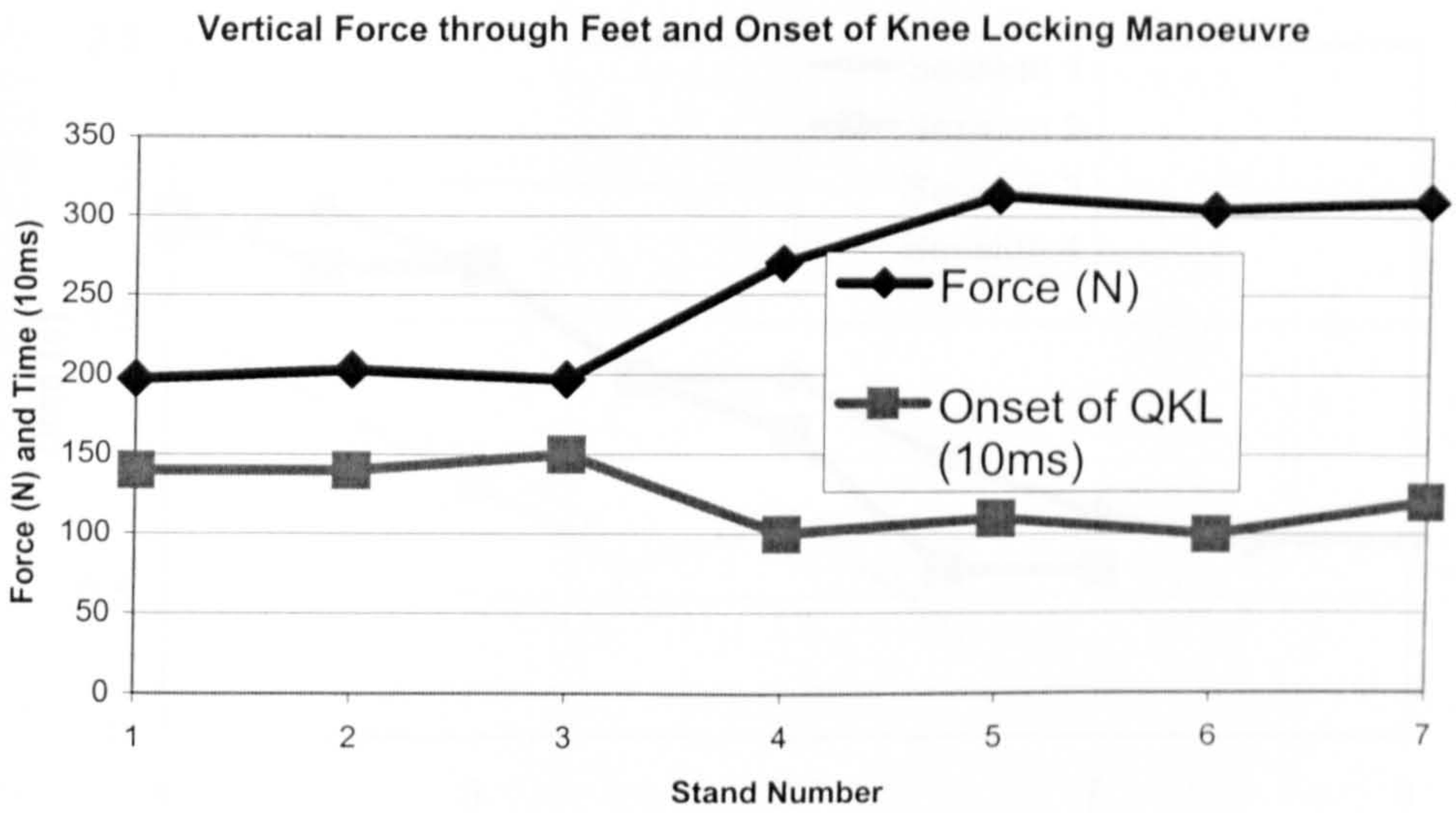


Figure 8.10. The timing of the onset of quick knee-locking during the 2nd session and the amount of weight being taken through the feet during the final steady state standing condition. The increase in force through the feet occurs as the onset time of the quick knee locking decreases, at the 4th stand of this session.

Figure 8.19 shows the timing of the onset of these events, i.e. the black and the red arrows, in session 2. There is a trend towards an early onset for both phases of the sit-to-stand. There is therefore a shortening of the phases as well as an earlier onset of the start of QKL. The earlier onset of the QKL procedure is associated with an increase in the amount of vertical force taken by the feet, figure 8.10. Throughout the study the patient uses the QKL strategy, figure 8.11.

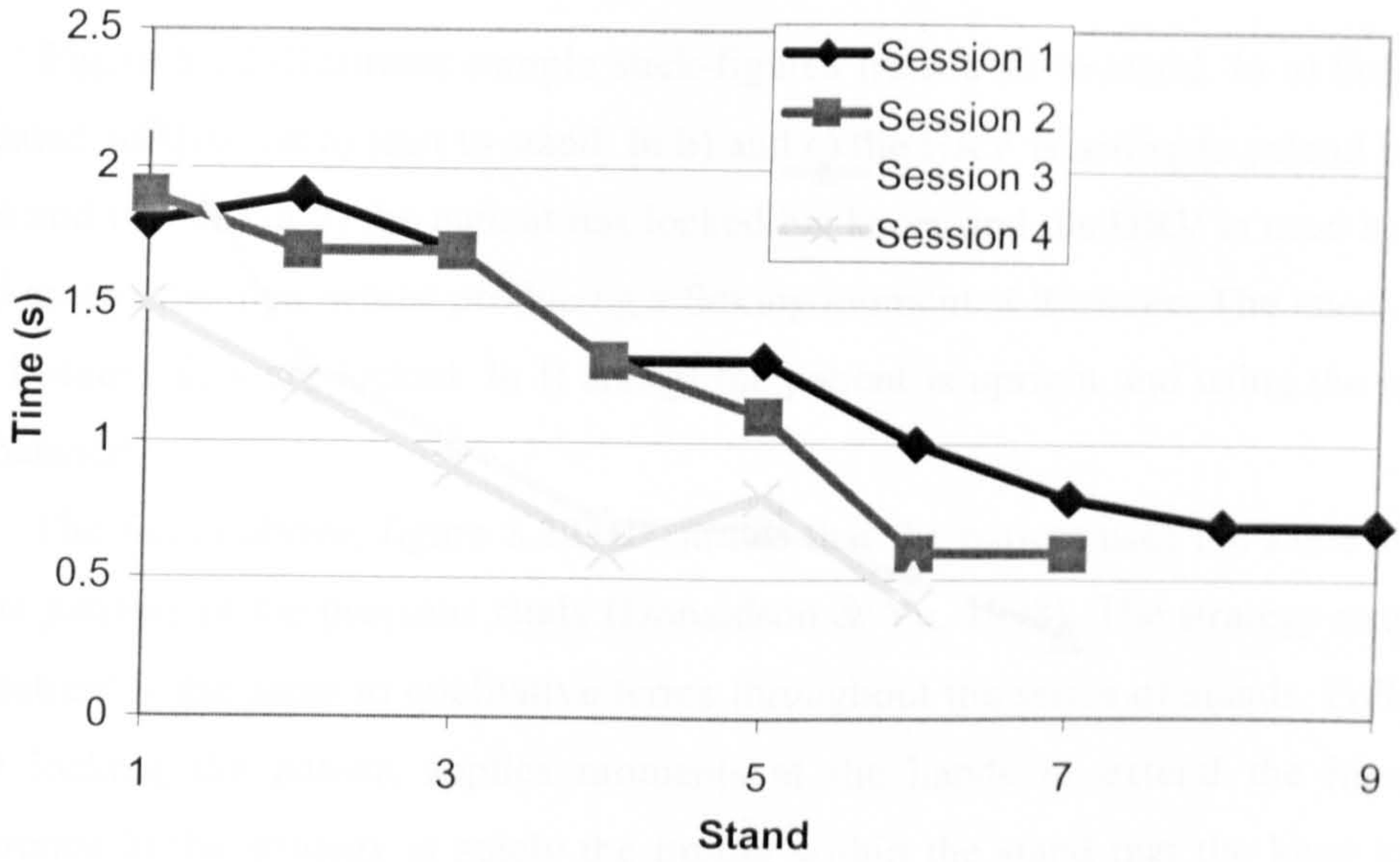


Figure 8.11. The interval between the end of knee extension and the start of the hip extension phase, as defined using the definition at the start of this chapter. Although the intervals are short at the end of the sessions, and increasingly so they are never negative indicating that the patient does adopt the QKL strategy throughout.

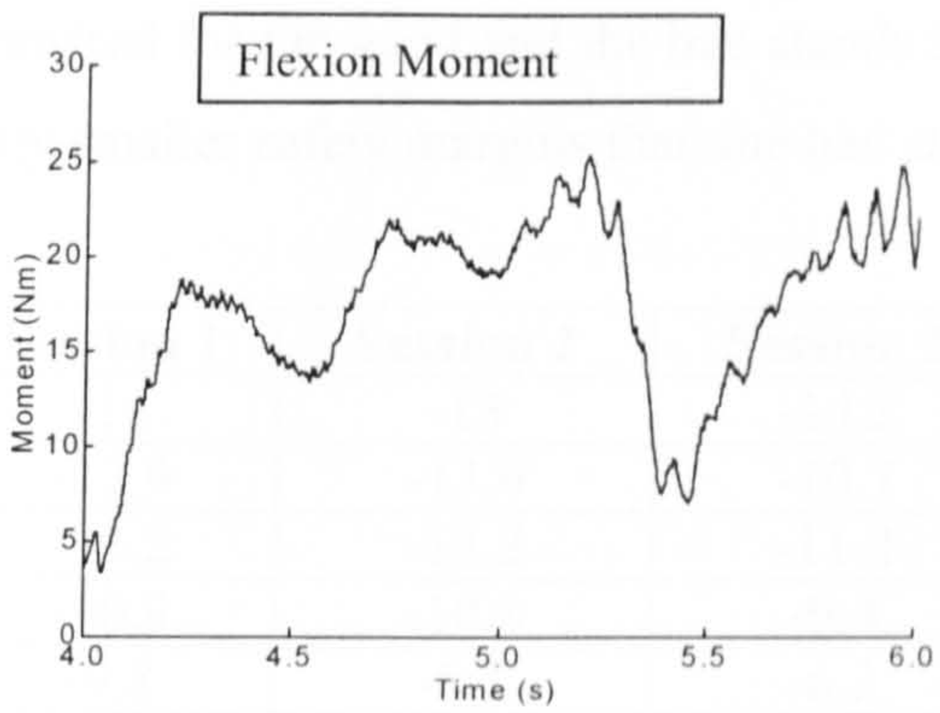
8.3.5. Are There Changes in the Margin of Safety at the Knee.

Figure 8.12. Stick figure representations of the posture of the patient at t=1, 2, 2.5, 3, 3.5, 4 and 4.5 seconds into a stand. Also plotted are the ground and handle reaction vectors offset to take into account the moment arms. The subject can bee seen to be in phase B of figure 8.1 for the first three figures. The knees then straighten and he is in phase C before moving into phase D for the last two figures. In each plot the hip is marked by a star. Markers are positioned as described in chapter 3 and 5.

Figure 8.12 illustrates sample stick-figures from a sit-to-stand. In a) the patient is seated and has yet to start to stand. In b) and c) the HRV is acting to extend both the knee and the hip. In d) the patient has locked his knees and the HRV is used in d) and e) to extend the hips, whilst producing a flexing moment at the knee. The knees do not flex because they are locked. In f) and g) the patient is upright and using the handles for balance.

The figure above, figure 8.12, illustrates that the patient uses the same strategy as the patients in the previous study (Donaldson & Yu, 1998). The strategy employed the patient is the same in qualitative terms throughout the series of stands. Following knee locking the patient applies moments at the hands to extend the hips. The difference in the strategy is solely the timing within the stand that the knee locking starts.

Given that the patient adopts this strategy does he change the margin of safety at the knee? Although it is not possible to calculate the safety margin of the knees, the size of the moment before the knees buckle, as described in the introduction to this chapter it is possible to measure the internal moment during standing with the knee straight. Since it is not possible to know where the centre of mass of the upper body is this calculation is performed from the ground-up.



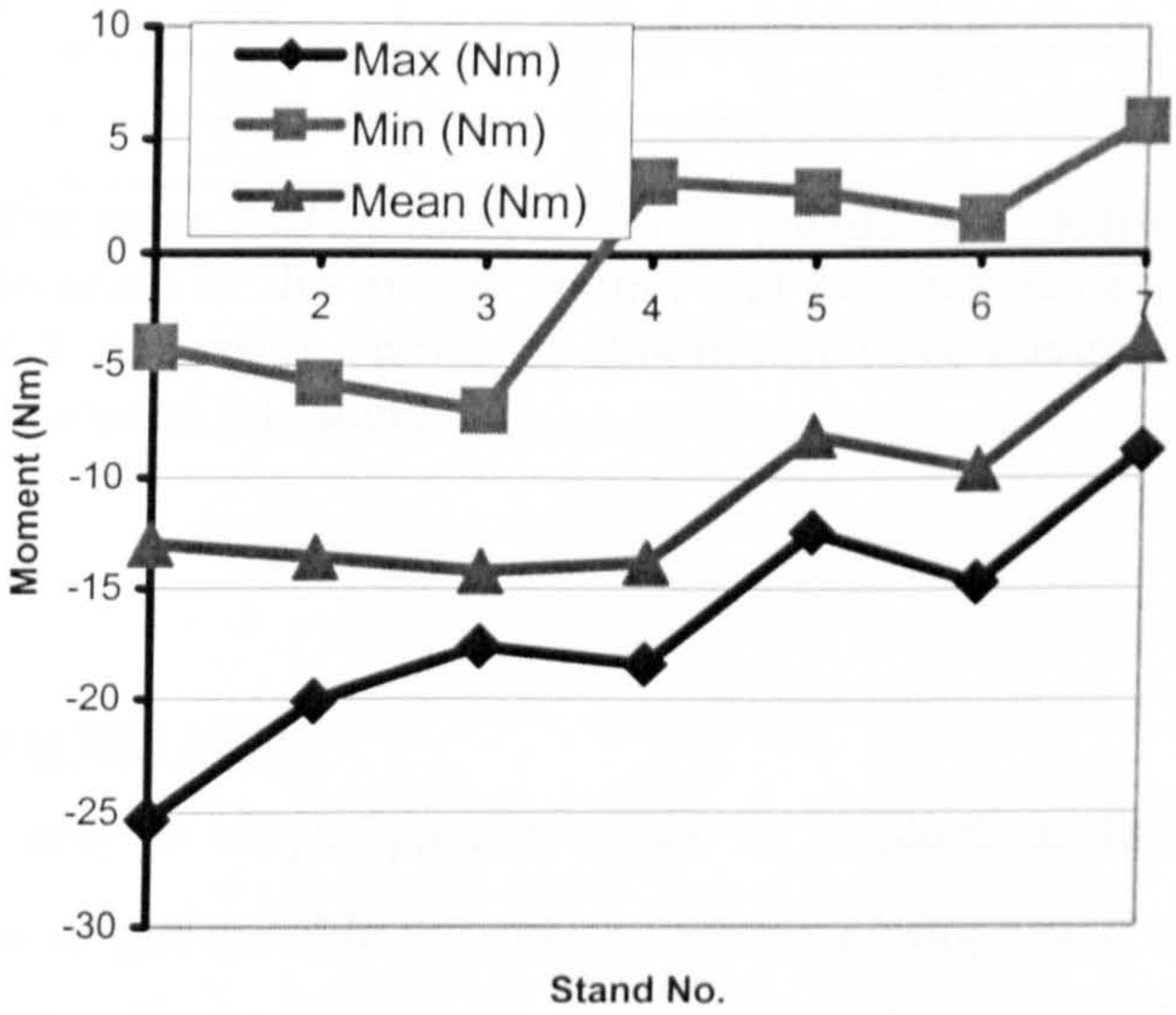


Figure 8.13. The internal knee moment during the hip extension phase of the sit-to-stand. **Top:** a single trial (trial 1) showing the variation in the moment as the subject extends his hips. The moment is shown as a flexion moment. **Bottom:** data from all trials showing a general trend towards reducing the knee moment, and hence the safety margin. In contrast to the top plot the bottom plot shows the moment with an extension moment shown as a positive moment.

Within a single stand the safety margin is variable and shows a general decrease in the size of the safety margin. This suggests that there is increase in the confidence of the patient. Between sessions there is also a general decrease in the mean safety margin, table 8.2 and the reduction within a session is present in all session. Data presented in figure 8.13 is from session 2 in the table 8.2.

Using the criteria outlined earlier to determine good and bad stands the first three stands in the first two sessions and the first stand in the third session were categorised as "bad" stands with all other stands classed as "good" stands. When the

safety margins are compared for the good and the bad stands it is found that the good stands have significantly smaller safety margins than the bad stands, ($P<0.05$).

	Session 1	Session 2	Session 3	Session 4
Stand 1	-14	-13	-14.2	-9.6
Stand 2	-12.9	-13.6	-10.7	-7.8
Stand 3	-13.2	-12.2	-11.2	-6.9
Stand 4	-10.9	-10.8	-9.4	-5.4
Stand 5	-9.8	-8.1	-6.2	-4.9
Stand 6	-9.8	-9.6	-5.4	-3.5
Stand 7	-8.8	-3.9	-4.8	X
Stand 8	-8.6	X	X	X
Stand 9	-7.2	X	X	X

Table 8.2. The mean "safety margin" for all stands in all sessions. There is a general decrease in the margin within and between sessions. The first stand of the third session shows an abnormally large margin, in common with all measures of this stand.

8.4. Discussion.

8.4.1. Does learning take place?

Although only a single patient could be studied in this study as it is comparatively rare to get suitable patients a number of important observations have been made concerning the process of learning to stand. A number of trends were seen which might indicate improvement. These were;

- An increase in weight bearing through the legs.
- A decrease in safety margin at the knee during hip extension.
- A decrease in the time taken to reach a steady posture and weight distribution.
- A decrease in the time between the knee reaching near full extension and the onset of hip extension.

There are many potential factors that may influence the ability of patient to stand with FES-assistance. The first question to ask therefore is; does the patient's ability to stand with FES-assistance change with increasing experience? The pattern of weight distribution between the hands and the feet changes with experience within a session. This might indicate a short-term learning process. There appeared to be little difference between the 1st and 2nd session. Whilst the first stand on the third session was poor, low percentage of body weight being taken by the feet, subsequent stands were better, and did not require the three stands to get started that the first 2

sessions had required. From the fourth session he was able to stand with a high percentage of body weight being taken by his legs from the first stand in the session. If the amount of weight taken through the feet determines the "goodness" of the stand then the first three stands on the first two sessions and the first stand on the third session were "poor" and the remainder were "good". There appears to be "learning" taking place over two time scales, firstly intra-session learning and secondly inter-session learning.

8.4.2. Are there changes in the neural activity?

The oscillatory activity is present in the first stand of the first session and undergoes changes within a session with a trend towards a decrease in the size of the oscillations. However between sessions there do not appear to be any changes indicating that there is an experience driven change in the neural activity. The activity is present at the start of each session and there is no formal correlation between the oscillation size and the amount of bodyweight taken through the legs. The same size oscillation can occur with different amounts of body weight being taken through the feet and the same amount of body weight can produce different, (either larger or smaller) size oscillations.

The changes within a session follow a general trend with a decrease in the size of the oscillations as the session progressed. However, if there was a long pause in the session, e.g. to have lunch, the first stand after the break had a much larger oscillation than previously. A number of previous studies have demonstrated that habituation of reflex activity can occur within the spinal cord (Rothwell *et al.*, 1986), (Harrision *et al.*, 2000). Although the fast oscillations are complex reflexes, or tremor and therefore not directly comparable to those reflexes previously studied the changes in the size of the response within a session are more likely to represent habituation of the response than any learning.

The fast oscillation appears to represent a response of the spinal cord to the sit-to-stand procedure that is present in some patients. It is not specific for FES-assisted standing although the stimulation may have an influence upon the frequency of the oscillation. Since the oscillation is not specific to FES-assisted standing but also takes place during passive or mechanically supported standing it may be a response that has developed over time as a result of repeated standing sessions. During these experiments no changes in the activity representing learning were detected.

8.4.3. What changes in the sit-to-stand strategy?

When the knee locking starts early in the stand the patient is able to take an increased load through his legs and there is also a decrease in the hip flexion angle, i.e. he stands straighter. The term quick knee locking does not specifically imply when during the stand the knees are locked, it rather refers to the relative timing compared to the hips being extended. It therefore appears that the patient uses the same strategy from the first stand, and that essentially the strategy is the same as that used by the other, more experienced patients (Donaldson and Yu 1998).

There is a change in the timing of the quick knee locking as stands progress within a session and between sessions. The procedure is one that is driven by the upper, neurologically intact body. To facilitate the knee extension the patients unload their legs so that they are taking a large proportion of their body weight through their arms. This makes the manoeuvre easier, but will also impose other demands on the upper body of the patient. Patients therefore choose an acceptable level of upper body weight bearing for them, and this varies between patients and within patients depending upon their fatigue amongst other issues. During the knee locking procedure the accelerations of the joints are large, but this is a temporary situation, which once the knees are locked stopped leaving negligible joint moments and the quasi-static assumption become valid again.

The act of locking the knees and turning the legs into "struts" means that a critical stage has been passed in the sit-to-stand. The patient can no longer just sit back down again, but must first unlock the knees before he is able to sit. As described in the methodology to this chapter an advantage of extending the knees before the hips is that greater moments can be generated by the hands during hip extension. These moments generate a flexion moment at the knee, which if the knee were not straight might cause it to buckle. The action of moments generated at the handles on other joints was termed *deficits* by Donaldson and Yu (Donaldson & Yu, 1996). This action is strictly valid only when the situation is static. However, the sit-to-stand can be modelled as a *quasi-static* process since the vertical acceleration forces are small, <10% of body weight.

There is a change in the quality of the stand with increased experience of FES-assisted standing over the first month of training. This improvement is most clearly seen in the increase in the weight bearing through the feet. The improvement is not associated with changes in neural activity, which remains similar throughout the

training period, but is likely to be associated with an increased confidence in the system. This increase in confidence manifests itself in a number of inter-related ways; firstly the onset of the knee-locking is earlier within a stand, secondly the hips are more extended during "confident" stands and finally there are large hip extending, (and knee flexing) moments applied during a "confident" stand. All patients in this study adopt the strategy previously proposed by Donaldson and Yu (1998) of quick knee locking, which enables them to extend their hips without flexing their knees. As in the Donaldson and Yu study the vector from the handles passes in front of the hip and behind the knee. This results in a knee flexion moment, which is counteracted by an extension moment generated from the ground up.

Exerting moments at the hands to extend the hips can generate flexion moments at the knee. By having the knees straight the patient is able to resist this moment. Figure 8.4 shows schematically that as the knee becomes straighter the measured moment becomes more negative. At some, unknown point, the knee will flex, but only when the knee's internal moment is an extension moment, i.e. when the knee is no longer straight or hyper extended. The size of the moment gives an indication of the margin of safety, the more negative the moment the greater the safety margin. A positive moment does not mean that the knee will flex, but does mean that the safety margin against flexing is small.

This study, presented for the first time the concept of the safety margin, which is an extension of the work developed by Donaldson on joint deficits (Donaldson and Yu 1998). Both within and between sessions there is a decrease in the safety margin with increasing experience. Although the patient is probably unaware of the concepts involved this result provides evidence of learning. The patient is willing to take a greater risk as he becomes more confident in the FES system and team and gains an understanding of the dynamics involved in the sit-to-stand. Future studies on this topic may explore whether all patients reduce the safety margin or whether it only occurs with "good" standers and what the limit on the safety margin is for individuals and group of patients. In this study the limit appeared to be around -2.5Nm as a mean value, although there were occasions within most of the stands in which moments more positive than this were recorded. The exact moment at which buckling would occur is unknown but is likely to be around +30Nm. The patient therefore maintains a large safety margin in all stands compared to this value. The concept of the safety margin may also be thought of as a method of the patient improving the efficiency of

the sit-to-stand. However, in this context it is more likely that this parameter is determined by the patient's confidence in the system than their desire for an efficient stand and therefore safety margin is probably a better term than efficiency.

Kralj and Bajd (1980) suggest therapists encourage their patients to adopt a "C" posture. Many therapists standing patients with spinal injuries adopt this approach when using FES or a standing frame. The posture hyperextends the hips and moves the weight of the trunk behind the hip joint. The knees are kept straight by the strength of the quadriceps stimulation. Data from this study suggests patients take about 3 sessions to learn to adopt this posture. The main adaptations in the learning process concern an increase in confidence in the system and can be seen by decreases in the delay between knee and hip extension and in reducing the safety margin.

What are the clinical implications of this study? Although measurement of Mi is a very useful clinical measure that indicates the susceptibility of buckling, it is not likely to be a clinically convenient measure since the mass and centre of mass of the lower leg need to be known and the direction and size of the GRV in addition to knowing the position of the knee joint accurately. The amount of weight being taken by the feet is a comparatively easy measure to record clinically. It appears to offer a simple measure of the quality of the stand. Changes in the amount of weight being taken by the feet are mirrored by improvements in other parameters. I am not aware that the Salisbury group, or other clinical groups, regularly record this parameter.

8.5. Conclusions.

Changes seen during the process of "learning" to stand with FES centre predominantly on confidence in the system and the clinical team. This enables the patient to extend their knees earlier in the stand. The patient used the same strategy throughout the study and it is the same strategy as that used by all patients in this study and the two previously studied patients (Donaldson & Yu, 1998). A simple method of objectively measuring the stand quality would be to record the amount of weight being taken through the feet.

Chapter 9.

Discussion.

9.1. Introduction and Summary.

This was an observational study into the neural activity that arose in the spinal cords of paraplegics during FES-assisted standing and its biomechanical effects. Most of this study took a case-study approach because of both the small number of available patients and the heterogeneity of the population. Considerable care must therefore be exercised to prevent over-generalising the results and conclusions from this work. The final section of this chapter suggests some areas for future research that I feel would be worthwhile on the basis of this preliminary data. In the introduction a number of questions were posed that this study set out to answer. They were;

- Is there endogenous neural activity present during paraplegic FES-assisted standing?
- If there is, does it affect the posture of the patient?
- Does the neural activity change with experience of standing with FES-assistance?

The results of this study can be summarised by answering each of the questions in turn;

- There is endogenous, non-stimulus driven, neural activity in the paraplegics in this study when they stand with FES-assistance. This is present in both steady-state standing and the sit-to-stand phase.
- Endogenous neural activity may arise as a result of changes in posture. During steady-state standing ongoing activity does not affect the posture of the patient, whilst intermittent activity (spasms) may affect the patient's posture.
- The neural activity does not appear to change with increasing experience of FES-assisted standing.

The major conclusions from this study are;

- There is endogenous neural activity, which is oscillatory in nature when recorded with surface EMG electrodes, during paraplegic FES-assisted standing.
- In some patients (50% in this study) there is neural activity at around 8Hz during the sit-to-stand phase. The activity is visible to the naked eye and in biomechanical as well as electrophysiological records.
- Some spasms in paraplegics appear oscillatory in nature when recorded using surface EMG electrodes and may show coherence within and between legs. This suggests a central circuit may drive some spasm activity.
- During steady state, paraplegic, FES-assisted standing there is an asymmetry in the weight distribution between the legs.
- A naive patient uses the same strategy for the sit-to-stand as more experienced standers. "Improvements" are seen with increasing experience.

Most of these conclusions have been commented on in the chapters in which they arise. Two of these conclusions (asymmetrical standing and oscillatory spasms) arise from results spread across a number of chapters and will be discussed further in this chapter.

9.2. Asymmetrical Weight Distribution During FES-Assisted Standing.

All of the patients in this study stood with an asymmetrical distribution of weight. This is a previously unreported finding in the literature and persisted irrespective of the whether the stimulation was applied through a surface or implanted system or whether the patient was an experienced or naïve stander. None of the patients were aware that they were standing in an asymmetrical manner and its presence in Patient 5 from the first stand suggests that it is not a learned response. All of the patients were able to stand satisfactorily in their opinion and therefore can be assumed to have coped with the asymmetry.

These patients were drawn from the UK population of FES-standers and had all except Patient 6 had been trained in Salisbury although not always by the same members of the team. All of the experiments reported here were performed under open-loop control. However a companion experiment performed under closed-loop control with Patient 4 continued to show the asymmetry. The controller measures

knee angles and since in all stands the knee was straight during standing it is unlikely that this can explain a difference in the symmetry of standing. There is therefore no reason to suspect that the asymmetry is an artefact of open-loop rather than closed-loop stimulation.

Mathematical and biomechanical models of FES-assisted standing are widely used to study the control of standing and develop new control strategies (Reiner R, 1999). All of these models assume that there is symmetry about the mid-line. In none of the patients in this study was this assumption valid. Two questions arise; a) why has this not been reported before? and b) is it important?

Previous studies examining the kinematics of FES-assisted standing have used a single force plate and assumed symmetry about the midline e.g. (Triolo *et al.*, 2001). Yu (1999) studied the act of standing up with FES assistance and averaged the forces and moments recorded from both support handles to generate joint deficits and control the stimulation to both legs. Using these approaches the asymmetry described in this study would not have been detected. A bilateral recording approach is therefore required to examine fully the effects of FES-assisted standing.

The importance of the asymmetry is unclear. For the development of models it is important to recognise that there is asymmetry in patients. Many of the current models used in research don't take this into account (Soetanto *et al.*, 2001). This is often the case even when "complex" models are developed which have more than one muscle group per leg etc. However, the models are estimates of parameters and so apply over a range of values. A potential problem arising from the use of modelled data on asymmetrical patients is that excessive forces and/or moments may need to be generated by one leg to compensate for "deficits" in the other leg.

9.3. The Oscillatory Nature of Some Spasm Activity in Paraplegics.

9.3.1. Spasms and Other Oscillatory Motor Outputs.

Spasms are normally considered to be motor responses in direct response to a stimulus. In this study spasms have been studied that do not fit into this simple definition. The spasms have arisen without a directly preceding trigger and in some cases have been persistent. Indirect triggers have been found, e.g. standing for patient 1 but in that instance he has a period of spasm free standing prior to the onset of spasms.

During postural changes, e.g. hip or ankle movement or the sit-to-stand oscillatory motor activity has been found in most of the patients in this study. The oscillatory nature of the motor output was detectable in both the raw records and the spectra of the individual muscles. Components of this activity were found to be coherent within and sometimes between legs. This suggests that at least some of the activity may arise as a result of neural oscillator. The oscillator may be a network of neurones with an output cell that has projections onto many motor neurons (directly or indirectly), which may be ipsilateral or contralateral.

It is not usual to analyse spasm with Fourier techniques since the stationarity condition required for the Fourier method is not meet in spasms. However, tremor has regularly been assessed using Fourier methods and also fails to meet the stationarity condition because of the movements involved. Tremor in many cases is similar to the spasms seen in this study. Auto-regressive moving average (arma) techniques may be more valid for this type of data but are not widely available. A simple comparison between the two techniques performed by Cassidy using sample data from this study showed the two approaches give similar results.

9.3.2. Orthostatic and Other Tremors.

Fast oscillatory motor output is often called tremor. Not all oscillatory motor activity is in this category however as activities such as walking and swimming may be considered to be an oscillatory motor activity. In these instances however the oscillations are at a much lower frequency than those seen in this study. Tremor is not necessarily pathological in nature although a number of pathologies, e.g. Parkinson's disease are characterised by specific tremors. The sites of origin of tremors are varicd but some do have a spinal component, e.g. physiological tremor (Deuschl *et al.*, 2001). One method of characterising tremor is based upon the frequency of the oscillations in either the EMG record or of the movement (McAuley & Marsden, 2000).

Primary Orthostatic Tremor is an uncommon tremor that is clinically characterised by a persistent feeling of increasing unsteadiness when standing which is relieved when walking. Neurophysiological examination reveals a 16Hz pattern to the EMG records that is coherent within and between legs (McAuley *et al.*, 2000). The tremor may also be found in upper limb and cranial muscles (Deuschl & Bergman, 2002). This, coupled with functional imaging data has lead one group to

suggest that this tremor arises in the posterior fossa (Wu *et al.*, 2001). The tremor is not normally seen in force-plate recordings but may be discernable in severe cases (Yarrow K *et al.*, 2001). Orthostatic tremor is a postural tremor with an as yet unknown mechanism of action. Recent reports (Sharrott *et al* 2003) have suggested it may be an exaggerated response to unsteadiness and may be mediated via the reticulo-spinal tract.

Within the spasms reported in this study activity at 16Hz has been found on a number of occasions. These occurrences were always in response to changes in the sensory input to the spinal cord as a result of changes in posture. Since the patients all had complete spinal lesions the activity at 16Hz must have been generated within the spinal cord in response to the changes in sensory input. Drawing a direct comparison between orthostatic tremor and the events recorded in this study would be unjustified. However, it is of considerable interest that the isolated spinal cord can generate oscillatory motor outputs in response to changes in sensory inputs and that these oscillations may be similar to other pathological conditions.

Two other frequencies appeared in the spectral analysis regularly, 8Hz and 13Hz. Tremor is commonly seen at 8Hz, again though it is not justifiable to extrapolate from these observations directly to tremor. The current study does provide evidence that the spinal cord is capable of generating rhythmical motor outputs in response to sensory inputs.

There was within this study a tendency for the frequencies of 8, 13 and 16Hz to be found in a number of conditions. It is unclear what this signifies. It may be coincidence or it may be as a result of the organisation of neural networks within the cord.

9.3.3 Spinal Neural Oscillators: Is Locomotion the Only Output?

Much work has concentrated on the locomotor capacity of the isolated or damaged spinal cord and its potential for rehabilitation (Edgerton *et al.*, 2001). Dietz defines a *central pattern generator*, CPG, as; A neural circuit that produces self-sustaining patterns of behaviour independently of sensory input (Dietz, 2002). Most training regimes with humans, including Dietz's, do not take place in the absence of sensory input, although animal studies have shown a regular rhythmical output in the absence of sensory input. Previously, only locomotor output has considered in relation

to CPGs and a view has become widespread that locomotion is the only motor output from human CPGs.

The evidence from this study suggests that "spasms" in spinal patients are clearly organised and self-sustaining thereby fulfilling many of the criteria of the output from a CPG. Sensory input has been shown to alter the pattern of the output. The activity was not locomotor like in character. If the spasm activity arose from a CPG then this suggests that either there is at least one CPG in the human spinal cord which generates a non-locomotor motor output or that the CPG for locomotion is damaged in these patients and the motor output seen in this study is the result of a partial or incomplete CPG for locomotion. None of the patients in this study have had treadmill training which might be expected to potentate the effects of a locomotor CPG.

9.3.4. Spasm Timing.

In both Patient 1 and Patient 6 the interval between the spasms varied between 3 and 30 seconds. This interval is a long time period in neurophysiology and few mechanisms act over this time-course. The isolated neonatal rat spinal cord exhibits a bursting motor output with a similar time course to that seen in these patients. Furthermore within the bursts of activity, activity is found at similar frequencies to those found in this study (Beato & Nistri, 1999), (Marchetti *et al.*, 2001), (Dougherty *et al.*, 2001, 2002).

The neonatal spinal cord has fewer descending inputs than the mature spinal cord, (Kandell *et al.*, 1991). The maturation of the brain leads to the development of more descending pathways and this helps to drive the maturation of the spinal cord. The neonatal spinal cord also contains more gap junctions than are found in the mature spinal cord (Dougherty *et al.*, 2002). These enable the development of the bursting patterns seen in the neonatal rat spinal cord (Dougherty *et al.*, 2001). Pharmacological manipulation may also be required to set-up the bursting pattern in the isolated neonatal rat spinal cord (Marchetti & Nistri, 2001) and (Nistri 2002 personal communication).

The descending inputs into the spinal cord from higher centres may be responsible for the maintenance of the mature spinal cord. If this is true, then the loss of these inputs following spinal injury may lead to a more neonatal like spinal cord and a proliferation of gap junctions and other proteins etc. which are rarely seen in the

mature spinal cord. The bursting patterns of motor activity were seen most clearly in patients with sacral dorsal rhizotomies and sacral anterior nerve root stimulator implants (Brindley *et al.*, 1982). Clinical observation has suggested that it is not limited to these patients (Wood personal communication 2002), but may be more pronounced in these patients. It is therefore possible that either the act of the stimulator implantation or the dorsal rhizotomy leads to the release of pharmacological agents that increase the likelihood of this bursting pattern.

If the spinal cord does become more like that of the neonate following spinal injury this may have important implications for future rehabilitation studies. The process of the developing of new networks and expression of new proteins will take time and therefore even chronic animal models which are typically a few months post injury may be too acute to detect these changes. In humans however, who may be many years post injury such observations may be possible. There may also be an increased tendency for the residual neurons to form oscillatory networks. Rehabilitation may be able to take advantage of these networks, either through gait retraining (Pinter & Dimitrijevic, 1999), (Behrman & Harkema, 2000) or direct stimulation of the networks (Barbeau *et al.*, 1999).

9.3.5. Some Comparisons between the Oscillatory Motor Activity in Paraplegics and that seen in Neurologically Normal Subjects.

Although tasks such as walking and swimming are oscillatory motor activities in this section I shall concentrate on faster oscillations, i.e. above 2-3Hz. During walking in normal subjects oscillatory motor activity can be observed. Halliday and colleagues (2003) and Hansen and colleagues (2002) report on the coupling between motor units during gait in normal subjects. Their results show limited coupling between antagonistic muscle pairs around the ankle during a co-contraction either when the co-contraction is maintained by alternating bursts of activity in the antagonistic pair or ongoing activity in both muscles. Both the coherence and cumulent density show only single peaks that are significant (e.g. figure 1 in Hansen *et al* 2002). In contrast this study has shown broader bands of coherence and peaks in the cumulent densities, chapters 6 and 7. One difficulty in comparing these studies is that the amount of EMG activity in the studies on normal subjects will be much higher than that seen in this study with paralysed patients. The patterns seen in this patient represent the outputs from the spinal cord. The temporal analysis suggests that there

might be less temporal focussing of these signals, broader peaks in the cumulent densities. The tight temporal relationships seen in normal subjects might arise in part because the supraspinal centres don't send synchronous signals but stagger the signals such that they arrive at the muscle synchronously irrespective of the pathlength.

The broader coherence seen in this study than in the normal studies suggests that when spinal networks are responsible for generating the motor output the network outputs project across more muscle groups than is the case when supraspinal centres are controlling the motor output.

9.4. Conclusions and Further Work.

A new technique for determining the mass and centre of mass of the legs has been presented and used in the calculation of joint moments during standing. Within the experimental limits the joint moments calculated whilst standing and when recumbent are the same although there is more EMG activity, particularly oscillatory in nature when standing.

The 3D surface scanning system for finding the mass and centre of mass of the legs is not in widespread use and requires development from the hardware manufacturer to reduce the cost to one that a biomechanics laboratory could afford. At present the system is highly over-specified for these measurements being capable of whole body scanning and reconstructing clothing etc. A biomechanical version could be a significantly cut-down version of the current model and software. A further development from this work is the development of real-time 3D surface scanning (www.3dmd.com). This offers the possibility of real-time maker-less 3D motion analysis.

This study has been novel in asking questions about the interactions between FES, standing and residual nervous system. The results have, in general, indicated that during clinical application of FES, the traditional approach, of considering the stimulation electrodes, the nerve and muscle only, is valid. The study on learning to stand revealed for the first time some previously assumed facets of the process of learning to stand. As the patient becomes more experienced at standing he is able to lock his knees earlier in the stand. Increasing experience also leads to a decrease in the amount of time taken to extend the hips.

Throughout this study the number of patients has been low, despite recruiting from two spinal injury units in southern England. There is therefore a need to repeat all of these experiments in larger studies. In particular the learning to stand experiment and the effects of stimulation on paraplegic spasms require expansion before generalisations can be made to the paraplegic population at large. A major contributing factor to the low patient numbers in any group is the heterogeneity of the population despite the similarities in lesions (all were mid-thoracic complete paraplegics).

It has been shown that for the development of standing programmes using FES assistance a device such as the MMCS, in which the joint moments are measured in the recumbent posture, provides a satisfactory method of estimating the joint moments whilst standing. However, fine tuning of the stimulation parameters and testing the quality of the stand requires a laboratory with two force plates and instrumented handles and a motion capture system capable of recording the movement of both sides of the body. Comparisons between different control strategies will need to be carried out in laboratories such as the one used in the current study.

This thesis has demonstrated the capacity of the spinal cord when disconnected from descending inputs because of a spinal lesion to generate rhythmic motor patterns that are posture dependent in nature. The relationship between the spinal cord and oscillatory motor outputs, which has been hinted at by this study, requires further investigation.

The presence of posture dependent oscillatory activity within the spinal cord means that the spinal cord can, to some extent, assess the posture of the patient. From this study it is unclear whether this is related to joint angles, the location of the centre of pressure on the feet, some combination of these signals or something else is unclear and worthy of further study. A potential control signal for stimulator systems might be the presence or absence of this oscillatory system although clinical systems operate best with simple controllers and this would appear to be a rather complex control signal. The signal is also rather small and potentially variable between as well as within patients.

The interaction between electrical stimulation and spontaneous bursting activity within the cord is complex, in one patient regularising the activity and in a second patient when combined with load-bearing standing stopping the bursting. The spontaneous bursting is similar to that seen in neonatal rat spinal cords and further

investigation is needed to determine the long-term effects of deprivation of descending input to the cord and effects of dorsal rhizotomies. In particular it is clinically important to try to understand why the bursting activity starts and what happens to the human cord in the long-term when it is disconnected from the descending inputs from the brain. This is not practical in animal studies, which are tricky to maintain in a spinalised condition beyond 6 months because of both practical considerations (e.g. infections and muscle wastage) and ethico-legal concerns and these patients were many years post injury (20 years in one case). Neuromodulation of spasms by electrical stimulation has been reported previously (Craggs *et al* 2002 a & b). This study has provided further evidence that peripheral as well as more central stimulation can affect spasms, although no broad conclusions can be drawn from this study as stimulation both stopped and regularised the spasms in different patients.

Although much work has been carried out on spasticity, muscle and joint stiffness, little has been done on muscle spasms. This study has revealed, in addition to a bursting pattern of spasms in some patients, fractionated and co-ordinated bursting within spasms. This co-ordinated activity between muscles implies that some parts of the spasm have a common drive and are therefore organised within the spinal cord. A more systematic study of spasms and their organisation in spinal cord injury and other neurological conditions is required. A better understanding of the organisation of spasms may lead to improved treatment of the condition.

Reference List

- Alfieri V (2001). Electrical Stimulation for Modulation of Spasticity in Hemiplegic and Spinal Cord Injury Subjects. *Neuromodulation* 4, 85-92.
- Amjad AM, Halliday DM, Rosenberg JR, & Conway BA (1997). An Extended Difference of Coherence Test for Comparing and Combining Several Independent Coherence Estimates: Theory and Application to the Study of Motor Units and Physiological Tremor. *Journal of Neuroscience Methods* **73**, 69-79.
- Bajd T, Gregoric M, Vodovnik L, & Benko H (1985). Electrical Stimulation in Treating Spasticity Resulting from Spinal Cord Injury. *Archives of Physical Medicine and Rehabilitation* **66**, 515-517.
- Bajd T & Vodovnik L (1984). Pendulum Testing of Spasticity. *Journal of Biomedical Engineering* **6**, 9-16.
- Baldissera F, Hultborn H, & Illert M (1960). Integration in Spinal Neuronal Systems. In *Handbook of Physiology: Section 1: Volume II Motor Control. Part I*, eds. Brookhart JM & Mountcastle VB, pp. 509-595.
- Barbeau H, McCrea DA, O'Donovan MJ, Rossignol S, Grill WM, & Lemay MA (1999). Tapping into Spinal Circuits to Restore Motor Functions. *Brain Research Reviews* **30**, 27-51.
- Barker RA, Revesz T, Thom M, Marsden CD, & Brown P (1998). Review of 23 Patients Affected by the Stiff Man Syndrome: Clinical Subdivision into Stiff Trunk (Man) Syndrome, Stiff Limb Syndrome and Progressive Encephalomyelitis with Rigidity. *Journal of Neurology, Neurosurgery and Psychiatry* **65**, 633-640.
- Barr FMD, Moffat B, & Phillips GF (1990). Clinical Problems with Programmes of Functional Electrical Stimulation for Paraplegic Patients. *Advances in the External Control of Human Extremities* **10**, 197-203.
- Basso DM (2000). Neuroanatomical Substrates of Functional Recovery after Experimental Spinal Cord Injury: Implications of Basic Science Research for Human Spinal Cord Injury. *Physical Therapy* **80**, 808-817.
- Beato M & Nistri A (1999). Interaction Between Disinhibited Bursting and Fictive Locomotor Patterns in the Rat Isolated Spinal Cord. *Journal of Neurophysiology* **82**, 2029-2038.
- Behrman A & Harkema SJ (2000). Locomotor Training after Human Spinal Cord Injury: A Series of Case Studies. *Physical Therapy* 80, 688-700.
- Bennet DJ, Gorassini M, Fouad K, Sanelli L, Han Y, & Cheng J (1999). Spasticity in Rats with Sacral Spinal Cord Injury. *Journal of Neurotrauma* **16**, 69-84.
- Beres-Jones JA, Johnson TD & Harkema SJ (2003). Clonus After Human Spinal Cord Activity Cannot be Attributed Solely to Recurrent Muscle-Tendon Stretch. *Experimental Brain Research* **149**, 222-236.
- Bracci E, Beato M, & Nistri A (1997). Afferent Inputs Modulate the Activity of a Rhythmic Burst Generator in the Rat Disinhibited Spinal Cord In Vitro. *Journal of Neurophysiology* **77**, 3157-3167.
- Bracci E, Beato M, & Nistri A (1998). Extracellular K+ Induces Locomotor-Like Patterns in the Rat Spinal Cord In Vitro: Comparison with NMDA or 5-HT Induced Activity. *Journal of Neurophysiology* **79**, 2643-2652.

- Bregman BS (1998). Spinal Regeneration. *Current Opinion in Neurobiology* **8**, 800-807
- Brindley GS (1994). The first 500 Patients with Sacral Anterior Root Stimulator Implants: General Description. *Paraplegia* **32**, 795-805.
- Brindley GS (1995). The first 500 Patients with Sacral Anterior Root Stimulators Implant Failures and their Repair. *Paraplegia* **33**, 5-9.
- Brindley GS, Polkey CE, & Rushton DN (1982). Sacral Anterior Root Stimulators for Bladder Control in Paraplegia. *Paraplegia* **20**, 365-381.
- Brindley GS & Rushton DN (1990). Long-Term Follow-up of Patients with Sacral Anterior Root Stimulator Implants. *Paraplegia* **28**, 469-475.
- Bromley I (1991). *Tetraplegia and Paraplegia: A Guide for Physiotherapists.*
- Brooke JD, Cheng J, Collins DF, McIllroy WE, Misiaszek JE, & Staines WR (1997). Sensori-Sensory Afferent Conditioning with Leg Movement: Gain Control in Spinal Reflex and Ascending Paths. *Progress in Neurobiology* **51**, 393-421.
- Brooke JD, McIllroy WE, Staines WR, Angerilli PA, & Perirtore GF (1999). Cutaneous Reflexes of the Human Leg During Passive Movement. *Journal of Physiology* **518**, 619-628.
- Brown P & Marsden J (2001). Cortical Network Resonance and Motor Activity in Humans. *The Neuroscientist* **7** 518-526.
- Brown P, Rothwell J, & Marsden CD (1997). The Stiff Leg Syndrome. *Journal of Neurology, Neurosurgery and Psychiatry* **62**, 31-37.
- Buneo CA, Soechting JF, & Floeter MK (1997). Postural Dependence of Muscle Actions: Implications for Neural Control. *Journal of Neuroscience* **17**, 2128-2142.
- Burke JE (1999). The Use of State-dependent Modulation of Spinal Reflexes as a Tool to Investigate the Organization of Spinal Circuitry. *Experimental Brain Research* **128**, 263-277.
- Burridge JH & Ladouceur M. Clinical and Therapeutic Applications of Neuromuscular stimulation- A Review of Current Use and Speculation into Future Developments. 2001. Cleveland, *IFESS*.
- Burridge JH & McLellan DL (2000). Relation Between Abnormal Patterns of Muscle Activation and Responses to Common Peroneal Stimulation. *Journal of Neurology, Neurosurgery and Psychiatry* **69**.
- Burridge JH, Taylor PN, Hagan S, & Swain ID (1997a). Experience of Clinical Use of the Odstock Dropped Foot Stimulator. *Artificial Organs* **21**, 254-260.
- Burridge JH, Taylor PN, Hagan S, Wood DE, & Swain ID (1997b). The Effects of Common Peroneal Stimulation on the Effort and Speed of Walking: A Randomized Controlled Trial. *Clinical Rehabilitation* **11**, 201-210.
- Capaday C (2002). The Special Nature of Human Walking and its Neural Control. *Trends in Neuroscience* **25**, 370-376.
- Carpenter RHS (1996). *Neurophysiology*, 3 ed. Arnold.
- Cassidy MJ & Brown P (2002). Hidden Markov Based Autoregressive Analysis of Stationary and Non-stationary Electrophysiological Signals for Functional Coupling Studies. *Journal of Neuroscience Methods* **116**, 35-53.
- Cassidy MJ, Mazzone P, Oliviero A, Insola A, Tonali P, Di Lazzaro V, & Brown P (2002). Movement-related Changes in Synchronization in the Human Basal Ganglia. *Brain* **125**, 1235-1246.

- Craggs M, Knight S, Kirkham A, Casey A, & Middleton F. Sacral Nerve Neuromodulation for Lower Spasm and Spasticity in Spinal Cord Injury. 2000a. London, Spinal Injury Conference.
- Craggs M, Knight S, Kirkham A, Casey A, & Shah J. The Stanmore SPARSI. 2000b. London, Spinal Injury Conference.
- Daly JJ, Marsolais EB, Mendell LM, Rymer WZ, Stefanovska A, Wolpaw JR, & Kantor C (1996). Therapeutic Neural Effects of Electrical Stimulation. *IEEE Transactions on Rehabilitation Engineering* 4, 218-230.
- Day BL (1999). Galvanic Vestibular Stimulation: New Uses for an Old Tool. *Journal of Physiology* **517** 631.
- de Leva P (1996). Joint Center Longitudinal Positions Computed from a Selected Subset of Chandler's Data. *Journal of Biomechanics* **29**, 1231-1233.
- Dekker L, Douros I, Buxton BF, & Treleaven P (1999). Building Symbolic Information for 3D Human Body Modelling from Range Data. *IEEE Computer Society* 388-397.
- Demir R, Gao BX, Jackson MB & Ziskind-Conhaim L (2002). Interactions between Multiple Rhythm Generators Produce Complex Patterns of Oscillation in the Developing Rat Spinal Cord. *Journal of Neurophysiology* **87,** 1094-1105.
- Denny-Brown D (1929). On the Nature of Postural Reflexes. *Proceedings of the Royal Society of London* **104**, 252-301.
- Deuschl G & Bergman H (2002). Pathophysiology of Nonparkinsonian Tremors. *Movement Disorders* **17**, 41-48.
- Deuschl G, Raethjen J, Lindmann M, & Krack P (2001). The Pathophysiology of Tremor. *Muscle & Nerve* **24**, 716-735.
- Dietz V (2002). Proprioception and Locomotor Disorders. *Nature Reviews Neuroscience* **3**, 781-790.
- Dietz V, Colombo G, & Jensen L (1994). Locomotor Activity in Spinal Man. *Lancet* **344**, 1260-1263.
- Dietz V, Curt A, & Colombo G (1998). Locomotor Pattern in Paraplegic Patients: Training Effects and Recovery of Spinal Cord Function. *Spinal Cord* **36**, 380-390.
- Dietz V & Duysens J (2000). Significance of Load Receptor Input During Locomotion: A Review. *Gait and Posture* **11**, 102-110.
- Dietz V, Golhofer A, Lieber M, & Trippel M (1992). Regulation of Bipedal Stance: Dependency on "Load" Receptors. *Experimental Brain Research* **89**, 229-231.
- Dietz V, Nakazawa K, Wirz M, & Erni T (1999). Level of Spinal Cord Lesion Determines Locomotor Activity in Spinal Man. *Experimental Brain Research* **128**, 405-409.
- Dimitrijevic MR. Residual Motor Functions in Spinal Cord Injury. 1985. Ref Type: Unpublished Work
- Dimitrijevic MR & Nathan PW (1967a). Studies of Spasticity in Man. *Brain* **90**, 1-30.
- Dimitrijevic MR & Nathan PW (1967b). Studies of Spasticity in Man II. *Brain* **90**, 333-358.
- Dimitrijevic MR & Nathan PW (1968). Studies of Spasticity in Man III. *Brain* **91**, 349-368.

- Dimitrijevic MR, Nathan PW, & Sherwood AM (1980). Clonus: The Role of Central Mechanisms. *Journal of Neurology, Neurosurgery and Psychiatry* **43**, 321-332.
- Djouhri L & Jankowska E (1998). Indications for Coupling Between Feline Spinocervical Tract Neurones and Midlumbar Interneurones. *Experimental Brain Research* **119**, 39-46.
- Donaldson N, Munih M, Perkins TA, & Wood DE (1999). Apparatus to Measure Simultaneously 14 Isometric Leg Joint Moments. Part 1. Design and Calibration of Six-Axis Transducers for the Forces and Moments at the Ankle Joint. *Medical and Biological Engineering and Computing* **37**, 137-147.
- Donaldson N, Rushton DN, Perkins TA, Wood DE, Norton JA, & Krabbendam A (2002a). Recruitment by Motor Nerve Root Stimulators: Significance for Implant Design. *Medical Engineering and Physics* **Accepted.** In press (Medical Engineering & Physics).
- Donaldson N, Rushton DN, & Tromans AM (1997). Neuroprothesis for Leg Function after Spinal Cord Injury. *Lancet* **350**, 711.
- Donaldson N, Wood DE, & McFadden C. Functional Standing for Paraplegics: Is it a Sensible Goal? 9-11. 2002b. Ljbujana, IFESS.
- Donaldson N & Yu Ch (1996). FES Standing: Control by Handle Reactions of Leg Muscle Stimulation. (CHRELMS). *IEEE Transactions on Rehabilitation Engineering* **4**, 280-284.
- Donaldson N & Yu Ch (1998). A Strategy Used by Paraplegics to Stand-up Using FES. *IEEE Transactions on Rehabilitation Engineering* **6**, 162-167.
- Donaldson N & Yu Ch (2000). Experiments with CHRELMS Patient-driven Stimulator Controllers for the Restoration of Function to Paralysed Legs. *Proceedings of the Institute of Mechanical Engineers* **214**, 1-20.
- Dougherty KJ, Aduonum AD, Machacek DW, & Hochman S. Unconventional Synaptic Mechanisms Recruited by the Isolated Spinal Cord During Synchronous Motor Bursting. Federation of European Neuroscience Societies Abstracts . 2002.
- Dougherty KJ, Aduonum AD, Machacek DW, Hochman S, & Cowley KC. Coordinated Motor Bursts Throughout the Isolated Spinal Cord in the Absence of Conventional Synaptic Mechanisms. Society for Neuroscience Abstracts. 2001.
- Edgerton VR, de Leon RD, Harkema SJ, Hodgson JA, London N, Reinkensmeyer DJ, Roy RR, Talmadge RJ, Tillakaratne N, Timoszyk W, & Tobin A (2001). Retraining the Injured Spinal Cord. *Journal of Physiology* **533**, 15-22.
- Farmer SF (1998). Rhythmicity, Synchronization and Binding in Humans and Primate Motor Systems. *Journal of Physiology* **509**, 3-14.
- Farmer SF, Halliday DM, Conway BA, Stephens JA, & Rosenberg JR (1997). A Review of Recent Applicationss of Cross-Correlation Methodologies to Human Motor Unit Recording. *Journal of Neuroscience Methods* **74**, 175-187.
- Fawcett JW & Asher RA (1999). The Glial Scar and Central Nervous System Repair. *Brain Research Bulletin* **49**, 377-391.
- Ferguson ACB & Granat MH (1992). Evaluation of Functional Electrical Stimulation for an Incomplete Spinal Cord Injured Patient. *Physiotherapy* **78**, 253-256.

- Field EC & Stein PSG (1997a). Spinal Cord Co-ordination of Hindlimb Movements in the Turtle: Interlimb Temporal Relationships During Scratching and Swimming. *Journal of Neurophysiology* **78**, 1394-1403.
- Field EC & Stein PSG (1997b). Spinal Cord Co-ordination of Hindlimb Movments in the Turtle: Interlimb Temporal Relationships During Bilateral Scratching and Swimming. *Journal of Neurophysiology* **78**, 1404-1413.
- Franklin RJM & Barnett SC (2000). Olfactory Ensheathing Cells and CNS Regeneration: The Sweet Smell of Success? *Neuron* **28**, 15-18.
- Frigo C, Ferrarin M, Frasson W, Pavan E & Thorsen R (2000). EMG Signals Detection and Processing for on-line Control of Functional Electrical Stimulation. *Journal of Electromyography and Kinesology* **10**, 351-360.
- Fung VSC, Sauner D, & Day BL (2001). A Dissociation Between Subjective and Objective Unsteadiness in Primary Orthostatic Tremor. *Brain* **124**, 322-330.
- Gandevia SC (2001). Spinal and Supraspinal Factors in Human Muscle Fatigue. *Physiological Reviews* **81**, 1725-1789.
- Gorassini M, Yang JF, Siu M, & Bennett DJ (2002a). Intrinsic Activation of Human Motoneurons: Possible Contribution to Motor Unit Excitation. *Journal of Neurophysiology* **87**, 1850-1858.
- Gorassini M, Yang JF, Siu M & Bennett DJ (2002b). Intrinsic Activation of Human Motoneurons: Reduction of Motor Unit Activation Thresholds by Repeated Contractions. *Journal of Neurophysiology* **87**, 1859-1866.
- Granat MH, Nicol DJ, Baxendale RH, & Andrews BJ (1991). Dishabituation of the Flexion Reflex in Spinal Cord-Injured Man and its Application in the Restoration of Gait. *Brain Research* **559**, 344-346.
- Granit R & Rutledge LT (1960). Surplus Excitation in Reflex Action of Motoneurones as Measured by Recurrent Inhibition. *Journal of Physiology* **154**, 288-307.
- Grill WM, Bhadra N, & Wang B (1999). Bladder and Urethral Pressures Evoked by Microstimulation of the Sacral Spinal Cord in Cats. *Brain Research* **836**, 19-30.
- Grosse P, Cassidy MJ & Brown P 2002). EEG-EMG, MEG-EMG and EMG-EMG Frequency Analysis: Physiological Principles and Clinical Applications. *Clinical Neurophysiology* **113**, 1523-1531.
- Grundy D & Swain A (1996). *ABC of Spinal Cord Injury*, 3 ed.
- Haas BM & Crow JL (1995). Towards a Clinical Measure of Spasticity. *Physiotherapy* **81**, 474-479.
- Hallet M, Berardelli A, Delwaide P, Freund HJ, Kimura J, Lucking C, Rothwell J, Shahani BT, & Yanagisawa N (1994). Central EMG and Tests of Motor Control. Report of an IFCN Committee. *Electroencephalography and Clinical Neurophysiology* **90**, 404-432.
- Halliday DM, Rosenberg JR, Amjad AM, Breeze P, Conway BA, & Farmer SF (1995). A Framework for the Analysis of Mixed Time Series/Point Process Data- Theory and Application to the Study of Physiological Tremor, Single Motor Unit Discharges and Electromyograms. *Progress in Biophysics and Molecular Biology* **64**, 237-278.
- Halliday DM, Conway BA, Christensen LOD, Hansen NL, Petersen NP & Nielsen JB (2003). Functional Coupling of Motor Units is Modulated During Walking in Human Subjects. *Journal of Neurophysiology* **89** 960-968.

- Hansen S, Hansen NL, Christensen LOD, Petersen NT & Nielsen JB (2002). Coupling of Antagonistic Ankle Muscles During Co-contraction in Humans. *Experimental Brain Research* **146** 282-292.
- Harkema SJ, Dobkin BH, & Edgerton VR (2000). Pattern Generators in Locomotion: Implications for Recovery of Walking After Spinal Cord Injury. *Topics in Spinal Cord Injury Rehabilitation* **6**, 82-96.
- Harrision LM, Norton JA, & Stephens JA (2000). Habituation of Cutaneomuscular Reflexes Recorded from the First Dorsal Interosseous and Triceps Muscle in Man. *Journal of the Neurological Sciences* **177**, 32-40.
- Hidler JM & Rymer WZ (1999). A Simulation Study of Reflex Instability in Spasticity: Origins of Clonus. *IEEE Transactions on Rehabilitation Engineering* **7**, 327-340.
- Hidler JM & Rymer WZ (2000). Limit Cycle Behaviour in Spasticity: Analysis and Evaluation. *IEEE Transaction on Biomedical Engineering* **47**, 1565-1575.
- Hiersemenzel LP, Curt A, & Dietz V (2000). From Spinal Shock to Spasticity. Neuronal Adaptations to a Spinal Cord Injury. *Neurology* **54**, 1574-1582.
- Hunt KJ, Munih M, Donaldson N, & Barr FMD (1998). Optimal Control of Ankle Joint Moment. Towards Unsupported Standing in Paraplegia. *IEEE Transactions on Automatic Control* **43**, 819-832.
- Jankowska E & Hammar I (2002). Spinal Interneurons; How can Studies in Animals Contribute to the Understanding of Spinal Interneuronal Systems in Man? *Brain Research Reviews* **40** 19-28.`
- Johnson KO (2001). The Roles and Functions of Cutaneous Mechanoreceptors. *Current Opinion in Neurobiology* **11**, 455-461.
- Jones PMR & Rioux M (1997). Three-dimensional Surface Anthropometry: Applications to the Human Body. *Optics and Lasers in Engineering* **28**, 89-117.
- Kandell ER, Schwartz JH, & Jessel TM (1991). *Principles of Neural Science*, 3rd ed. Appleton & Lange.
- Kiehn O & Eken T (1998). Functional Role of Plateua Potentials in Vertebrate Motor Neurons. *Current Opinion in Neurobiology* **8**, 746-752.
- Kiehn O & Katz PS (1990). Making Circuits Dance: Neuromodulation of Motor Systems. In *Beyond Neurotransmission, Neuromodulation.*
- Kimura J, Daube J, Burke D, Hallet M, Cruccu G, Ongerboer de Visser BW, Yanagisawa N, Shimamura M & Rothwell J (1994). Human Reflexes and Late Responses. Report of an IFCN Committee. *Electroencephalography and Clinical Neurophysiology* **90** 393-403.
- Knikou M & Conway BA (2001). Modulation of Soleus H-reflex Following Ipsilateral Mechanical Loading of the Sole of the Foot in Normal and Complete Spinal Cord Injured Humans. *Neuroscience Letters* **303**, 107-110.
- Knikou M & Rymer WZ (2002). Effects of Changes of Hip Joint Angle on H-reflex Excitability in Humans. *Experimental Brain Research* **143**, 149-159.
- Kralj A & Bajd T (1989). *Functional Electrical Stimulation: Standing and Walking after Spinal Cord Injury* CRC Press.
- Lance JW (1980). The Control of Muscle Tone, Reflexes and Movement. *Neurology* **30**, 1303-1313.

- Marchetti C, Beato M, & Nistri A (2001). Alternating Rhythmic Activity Induced by Dorsal Root Stimulation in the Neonatal Rat Spinal Cord *in Vitro*. *Journal of Physiology* **530**, 105-112.
- Marchetti C & Nistri A (2001). Neuronal Bursting Induced by NK3 Receptor Activation in the Neonatal Rat Spinal Cord In Vitro. *Journal of Neurophysiology* **86**, 2939-2950.
- Marsden JF, Werhahn KJ, Ashby P, Rothwell J, Noachtar S, & Brown P (2000). Organization of Cortical Activities Related to Movement in Humans. *Journal of Neuroscience* **20**, 2307-2314.
- McAuley JH & Marsden CD (2000). Physiological and Pathological Tremors and Rhythmic Central Motor Control. *Brain* **123**, 1545-1567.
- Meinck HM & Thompson PD (2002). Stiff Man Syndrome and Related Conditions. *Movement Disorders* **17** 853-866.
- Meriam JL & Kraige LG (1998). *Engineering Mechanics: Statics*, 4 ed. Wiley.
- Mima T & Hallet M (1999), Corticomuscular Coherence: A Review. *Journal of Clinical Neurophysiology* **16** 501-510.
- Munih M, Donaldson N, Hunt KJ, & Barr FMD (1997). Feedback Control of Unsupported Standing in Paraplegia- Part II. Experimental Results. *IEEE Transactions on Rehabilitation Engineering* **5**, 341-352.
- Mushahwar VK, Collins DF, & Prochazka A (2000). Spinal Cord Microstimulation Generates Functional Limb Movements in Chronically Implanted Cats. *Experimental Neurology* **163**, 422-429.
- Nieuwenhuijzen PHJA, Schillings AM, Van Galen GP, & Duysens J (2000). Modulation of the Startle Response During Human Gait. *Journal of Neurophysiology* **84**, 65-74.
- Norton JA, Donaldson N, Day BL, Dekker L, Perkins TA, Rushton DN, Tromans AM, & Wood DE. The Determinants of Posture in Paraplegics Standing Using Functional Electrical Stimulation. IFESS 2000, 478-481. 2000.
- O'Sullivan JD, Rothwell J, Lees AJ, & Brown P (2002). Bilaterally Coherent Tremor Resembling Enhanced Physiological Tremor: Report of Three Cases. *Movement Disorders* **17**, 387-391.
- Ogawa H (1996). The Merkel Cell as a Possible Mechanoreceptor Cell. *Progress in Neurobiology* **49**, 317-334.
- Perkins TA, Donaldson N, Harper VJ, Norton JA, Rushton DN, Tromans AM, & Wood DE. Standing, Stepping and Cycling for a T9 Paraplegic with a Lumbo-sacral Anterior Root Stimulator Implant. 1999. Proceedings of the Lurcene Neuromodulation Conference and IFESS CD-ROM.
- Phillips GF, Adler JR, & Taylor SJG. A Portable Programmable Stimulator for Surface FES. 166-168. 1993. Ljubjana, IFESS.
- Pinter MM & Dimitrijevic MR (1999). Gait After Spinal Cord Injury and the Central Pattern Generator for Locomotion. *Spinal Cord* **37**, 531-537.
- Pisano F, Miscio G, Conto CD, Pianca D, Candeloro E, & Colombo R (2000). Quantitative Measures of Spasticity in Post-stroke Patients. *Clinical Neurophysiology* **111**, 1015-1022.
- Pocock G & Richards CD (1999). *Human Physiology. The Basis of Medicine*, 1 ed. OUP, Oxford.

- Pomeroy VM, Dean D, Sykes L, Faragher EB, Yates M, Tyrell PJ, Moss S, & Tallis R (2000). The Unreliability of Clinical Measures of Muscle Tone: Implications for Stroke Therapy. *Age and Ageing* **29**, 229-233.
- Popovic D, Tomovic R, & Schwirtlich L (1989). Hybrid Assistive System - The Motor Neuroprosthesis. *IEEE Transaction on Biomedical Engineering* **36**, 729-737.
- Pressel T & Lengsfeld M (1998). The Function of Hip Joint Muscles. *Medical Engineering and Physics* **20**, 50-56.
- Provini F, Vetrugo R, Meletti S, Plazzi G, Solieri L, Lugaresi E, Coccagna G, & Montagna P (2001). Motor Patterns of Periodic Limb Movements During Sleep. *Neurology* **57**, 300-304.
- Rack PMH, Ross HF, & Thilmann AF (1984). The Ankle Stretch Reflex in Normal and Spastic Subjects. *Brain* **107**, 637-654.
- Reiner R (1999). Model Based Development of Neuroprosthesis for Paraplegic Patients. *Philosophical Transactions of the Royal Society of London (B)* **354**, 877-894.
- Rosenberg JR, Halliday DM, Breeze P, & Conway BA (1998). Identification of Patterns of Neuronal Connectivity- Partial Spectra, Partial Coherence, and Neuronal Interactions. *Journal of Neuroscience Methods* **83**, 57-72.
- Rothwell J (1994). *Control of Human Voluntary Movement*, 2 ed. Chapman & Hall, London.
- Rothwell J, Day BL, Berardelli A, & Marsden CD (1986). Habituation and Conditioning of the Human Long Latency Stretch Reflex. *Experimental Brain Research* **63**, 197-204.
- Rothwell J, Traub MM, Day BL, Obeso JA, Thomas PK, & Marsden CD (1982). Manual Motor Performance in a Deafferented Man. *Brain* **105**, 515-542.
- Rubinstein JT & Miller CA (1999). How Do Cochlear Prostheses Work? *Current Opinion in Neurobiology* **9**, 399-404.
- Rushton DN (1997). Functional Electrical Stimulation. *Physiological Measurement* **18**, 241-275.
- Rushton DN (2002). Electrical Stimulation in the Treatment of Pain. *Disability and Rehabilitation* **24**, 407-415.
- Rushton DN, Barr FMD, Donaldson N, Harper VJ, Perkins TA, Taylor PN, & Tromans AM (1998). Selecting Patients for a Lower Limb Stimulator Implant Programme: A Patient Centered Approach. *Spinal Cord* **36**, 303-309.
- Rushton DN, Perkins TA, Donaldson N, Wood DE, Harper VJ, Tromans AM, Barr FMD, & Holder DS (1997). LARSI: How to Obtain Favourable Muscle Contractions? *IFESS 1997* 163-164.
- Rutherford OM, Jones DA, & Newham DJ (1986). Clinical and Experimental Application of the Percutaneous Twitch Superimposition Technique for the Study of Human Muscle Activation. *Journal of Neurology, Neurosurgery and Psychiatry* **49**, 1288-1291.
- Schomburg ED (1990). Spinal Sensorimotor Systems and Their Supraspinal Control. *Neuroscience Research* **7**, 265-340.
- Seidel GK, Marchinda DA, Dijkers M, & Soutas-Little RW (1995). Hip Joint Center Location from Palpable Boney Landmarks A Cadaver Study. *Journal of Biomechanics* **28**, 995-998.

- Sharrott A, Marsden J & Brown P (2003). Primary Orthostatic Tremor is an Exaggeration of a Physiological Response to Instability. *Movement Disorders* **18** 195-199.
- Sherrington CS (1910). Flexion-reflex of the Limb, Crossed Extension-reflex and Reflex Stepping and Standing. *Journal of Physiology* **40**, 28-121.
- Singer B (1987). Functional Electrical Stimulation of the Extremities in the Neurological Patient: A Review. *The Australian Journal of Physiotherapy* **33**, 33-42.
- Soetanto D, Kuo CY, & Babic D (2001). Stabilization of Human Standing Posture using Functional Neuromusular Stimulation. *Journal of Biomechanics* **34**, 1589-1597.
- Stefanovska A, Vodovnik L, Gros N, Rebersek S, & Acimovic-Janezic R (1989). FES and Spasticity. *IEEE Transaction on Biomedical Engineering* **36**, 738-745.
- Stein PSG, Grillner S, Selverston AI, & Stuart DG (1999). *Neurons, Networks, and Motor Behavior*, 1 ed.
- Stein RB, Aoyagi Y, Mushahwar VK, & Prochazka A (2002). Limb Movements Generated by Stimulating Muscle, Nerve and Spinal Cord. *Archives Italiennes de Biologie* **140**, 273-281.
- Stein RB, Zehr P, Lebiedowska MK, Popovic D, Schiner A, & Chizeck HJ (1996). Estimating Mechanical Parameters of Leg Segments in Individuals with and without Physical Disabilities. *IEEE Transactions on Rehabilitation Engineering* **4**, 201-211.
- Steinbok P (2001). Outcomes after Selective Dorsal Rhizotomy for Spastic Cerebral Palsy. *Child's Nervous System* **17**, 1-18.
- Taylor JR (1997). *An Introduction to Error Analysis*, 2nd ed. University Science Books, California.
- Taylor PN, Burridge JH, Dunkerely AL, Wood DE, Norton JA, Singleton C, & Swain ID (1999). Clinical Use of the Odstock Dropped Foot Stimulator: Its Effect on the Effort and Speed of Walking. *Archives of Physical Medicine and Rehabilitation* **80**, 1577-1583.
- Triolo R, Wibowo M, Uhlir J, Kobetic R, & Kirsch RF (2001). Effects of Stimulated Hip Extension Moment and Position on Upper-limb Support Forces During FNS-Induced Standing - A Technical Note. *Journal of Rehabilitation Research and Development* **38**, 545-555.
- van der Herberg E. Leg Joint Moments During Paraplegic Standing with Lumbar Root Stimulation. 1997. UCL and Twente. M.Sc Thesis.
- Vilensky JA & Gilman S (1997). Positive and Negative Factors in Movement Control; A Current Review of Denny-Brown's Hypothesis. *Journal of the Neurological Sciences* **151**, 149-158.
- Vilensky JA, Moore AM, Eidelberg E, & Walden JG (1992). Recovery of Locomotion in Monkeys with Spinal Cord Lesions. *Journal of Motor Behaviour* **24**, 288-296.
- Whittle MW (1996). *Gait Analysis. An Introduction*, 2 ed. Butterworth-Heinemann.
- Windhorst U (1996). On the Role of Recurrent Inhibitory Feedback in Motor Control. *Progress in Neurobiology* **49**, 517-587.
- Winter DA (1990). *Biomechanics and motor control of human movement.*

- Wood DE, Donaldson N, & Perkins TA (1999). Apparatus to Measure Simultaneously 14 Isometric Leg Joint Moments. Part 2. Multi-Moment Chair System. *Medical and Biological Engineering and Computing* **37**, 148-154.
- Wood DE, Harper VJ, Barr FMD, Taylor PN, Phillips GF, & Ewins DJ. Experience in Using Knee Angles as Part of a Closed Loop Algorithm to Control FES Assisted Paraplegic Standing. 137-140. 1998. Vienna, 6th Vienna International Workshop on Functional Electrostimulation.
- Wu YR, Ashby P, & Lang AE (2001). Orthostatic Tremor Arises from an Oscillator in the Posterior Fossa. *Movement Disorders* **16**, 272-279.
- Yu Ch. New Method for Restoring Standing to Paraplegics: Control of Leg Muscle Stimulation by the Handle Support Reactions. 1999. UCL. PhD Thesis.

Appendix 1.
Calibration of the JR3 Multi-axis Load Cells.

The early experiments in this thesis were performed using handles made by Yu for support. Yu describes the calibration and validation procedure in his thesis, (Yu C-h 1999). These handles were not suitable for the majority of the patients in this study who exerted large turning moments and vertical forces during the sit-to-stand in particular. New handles were made which were mounted on JR3 six-axis transducers. The transducers are supplied with a 6x6 calibration matrix. A further matrix was generated to account for the forces and moments applied by the handles and a second extra matrix generated to allow for the offset in the application of the forces and moments.

The forces and moments applied at the handles are calculated by; multiplying the 6 channels of output by the calibration matrix to obtain 3 forces and 3 moments in the correct order, subtracting the offsets and then multiplying by the "transformation" matrix to translate the forces and moments measured at the transducer into those applied at the handles. All forces and moments are assumed to be applied at the centre of the handle, which is located above the centre of the transducer.

To validate these matrices known force/moment combinations were applied to the handles and compared to the measured outputs. The force/moment combinations were referenced against a force-plate that was assumed to have no error or noise.

Forces and moments were applied up to 200% of that expected to be applied throughout the study (actually 175% of those generated). The transducers were linear in all axes.

Table A1 shows samples of the grouped data obtained during a steady-state loading condition for the right transducer. The values shown are mean ± standard deviation and all values are shown in Newtons for forces and Newton metres for the moments.

Condition	Fx	Fy	Fz	Mx	My	Mz
981N Fx	981.1±0.02	0.08±0.02	0.12±0.05	0.00±0.002	0.01±0.01	0.08±0.02
981N Fz	0.05±0.002	0.02±0.02	980.9±0.1	0.02±0.002	0.49±0.04	0.0±0.0
50N Fy & 10Nm Mz	0.5±0.05	50.0±0.05	0.1±0.01	0.02±0.01	0.0±0.01	10.0±0.02
50N Fx&Fy	50.1±0.05	50.0±0.05	0.0±0.02	0.0±0.0	0.0±0.02	0.1±0.02
25Nm My	0.02±0.00	0.01±0.01	0.3±0.08	0.0±0.001	24.9±0.2	0.01±0.01

Table A1. Sample, grouped data from the calibration of the first of the JR3 loadcells, connected to the right handle. The data is typical of that obtained during the calibration and shows good resolution, and low cross-talk between channels.

Condition	Fx	Fy	Fz	Mx	My	Mz
981N Fx	981.2±0.04	0.08±0.04	0.12±0.07	0.01±0.002	0.01±0.02	0.08±0.03
981N Fz	0.05±0.005	0.02±0.01	981.1±0.1	0.02±0.004	0.49±0.03	0.0±0.0
50N Fy & 10Nm Mz	0.5±0.05	50.0±0.05	0.1±0.02	0.01±0.01	0.0±0.01	10.0±0.02
50N Fx&Fy	50.1±0.06	50.0±0.05	0.0±0.02	0.0±0.01	0.0±0.02	0.1±0.02
25Nm My	0.02±0.00	0.01±0.01	0.1±0.01	0.0±0.00	24.9±0.2	0.01±0.01

Table A2. Sample, grouped data from the calibration of the second of the JR3 loadcells. This cell was connected to the left handle.

Appendix 2.
Calibration of the CODA Position Measuring System.

During the experiments in this thesis two CODA "boxes" were used, which were co-registered, using the standard CODA technique. This gives both boxes the same coordinate system and origin which was also defined to be the same as the force-plate coordinates. Therefore there is a single origin for all components of the system and the coordinate system is common across the force plates and the CODA systems.

The force plates had been previously calibrated and validated as part of my Master of Research Degree, (1999) and subsequently re-validation had taken place by Dr Day following a relocation of his laboratory. Since that work was not carried out as part of the PhD study it is not included in this thesis.

The CODA calibration procedure is outlined in detail in the documentation accompanying the system. Briefly 4 LEDs are arranged to give a perpendicular grid. This grid is then defined to be in a plane. The perpendicular plane is then defined within the CODA system automatically and the origin of the system set in a separate procedure by placing a LED at the user defined origin.

To validate the system in a "real-life" situation using markers not in a plane a frame was constructed which had a wide base and a narrow top. The base extended to a height of 1m and the top was a further 75cm tall giving a total height of 1.75m. This configuration was designed to simulate a person.

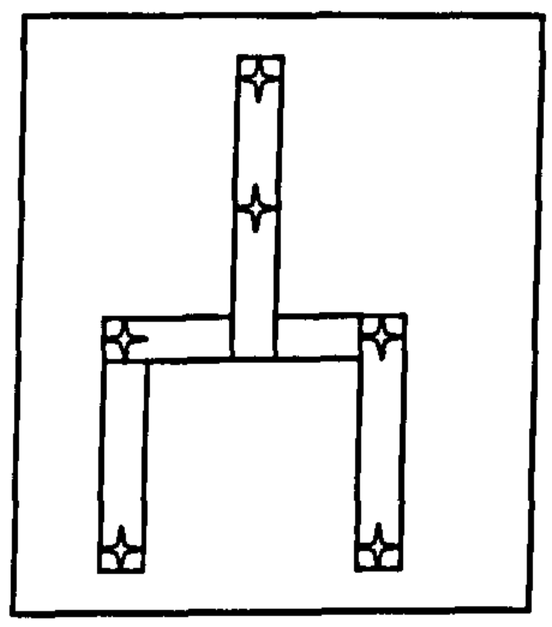


Figure A2.1. A cartoon of the structure used to validate the CODA calibration. The structure simulated a person in the general layout of the LEDs and had not dissimilar proportions. LEDs were position at the points marked by the stars.

Throughout the validation two measures were of interest; the position of the LED recorded using the CODA system and the variations in the reported position with time, i.e the accuracy and consistency of the system. Both the accuracy and consistency of the system decreased with distance away from the plane in which the calibration was carried out. A summary of the results is provided in the main body of the thesis. A fuller summary is provided here.

Manually Measured Position (mm)	Direction	CODA Measured Position (mm)	CODA Noise. Standard Deviation	Number of samples.
1740	Z	1741.8	0.89	1280
0	Y	0.1	0.01	1280
-50	X	-47.9	0.45	1280
1436	Z	1434.8	0.24	1280
0	Y	-0.1	0.08	1280
-49	X	-47.1	0.19	1280
1000	Z	1001	0.88	1280
25	Y	24.2	0.05	1280
0	X	0	0.07	1280
998	Z	998.5	0.04	1280
10	Y	10	0.04	1280
-50	X	-50.1	0.06	1280
100	Z	99.9	0.05	1280
35	Y	34.9	0.04	1280
-6	X	-6	0.02	1280
102	Z	102.5	0.03	1280
-100	Y	-100	0.05	1280
82	X	82	0.02	1280

Appendix 3.
Matlab Scripts.

3.1. Script for plotting Moments and Angles.

```
%awimoments.m

% to plot moments from AWi during good and bad sit-to-stands.
% Created by Jonathan Norton on implant-lap on 16th August 2002 at UCL.
clear
load g:\wishart\AWi4mar02\awib20.txt   \asc
data=awib20(1:16000,:);
clear awib20

for n=1:320
   mean_data(n,:)=mean(data((n*50)-49:n*50,:));
end
data=mean_data;

  Fx1=[data(:,122)];     % xforce
   Fy1=[data(:,123)];     % yforce
    Fz1=[data(:,124)];     % zforce
    Fx2=[data(:,125)];     % xforce
    Fy2=[data(:,126)];     % yforce
    Fz2=[data(:,127)];    % zforce

   W=10.79*9.81;
HCx=0.02;
%*************************************************************************************
% Force plate 1 is for right, plate 2 for left.
% Force plate 1 is the larger plate with the origin at its' centre.


for n=1:length(data)
HPx(n,1)=(data(n,53)/1000);      %y hip position 53 for left 30 for right
HPz(n,1)=(data(n,25)/1000)+0.05;                    % z hip postion 25 for left 32 for right

My2(n,1)=(Fz2(n)*((data(n,121)-data(n,42))/1000));
E(n,1)=-My2(n)-(-Fz2(n)*HPx(n))+(Fx2(n)*HPz(n))-(W*HCx);


HPxr(n,1)=(data(n,49)/1000);      %y hip position 49 for left 77 for right
HPzr(n,1)=(data(n,21)/1000)+0.05;                    % z hip postion 20 for left 21 for right
My1(n,1)=(Fz1(n)*((data(n,119)-data(n,38)))/1000);
Er(n,1)=-My1(n)-(-Fz1(n)*HPxr(n))+(Fx1(n)*HPzr(n))-(W*HCx);
%Er(n,1)=Er(n,1)*(-n/10);
Hip_data=[data(n,11),data(n,39), data(n,21),data(n,49), data(n,16),data(n,44)];

X3=Hip_data(1,3)-Hip_data(1,1);
X4=Hip_data(1,5)-Hip_data(1,3);
Y3=Hip_data(1,4)-Hip_data(1,2);
Y4=Hip_data(1,6)-Hip_data(1,4);
R=(X3*X4)+(Y3*Y4);
S=sqrt(((X3)^2)+((Y3)^2));
T=sqrt(((X4)^2)+((Y4)^2));
H=R/(S*T);
Ha(n,1)=acos(H);
Ha(n,1)=Ha(n,1)*360/(2*pi);
end
E=-E;
```

```
Er=-Er;
Fz1=Fz1/10;
E=E-E(1);
Er=Er-Er(1);




figure(1);plot(Ha,Er)
title('Hip extension during Stand')
ylabel('Moment (Nm)')
xlabel('Angle')
legend(' Right Moment')
figure(2);plot(data(:,1),Er)
return
clear
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
% good stand data.
load f:\wishart\AWid8may02\jndata\awid18a.txt   \asc
data=awid18a(1:16000,:);
clear awid18a

Fx1=[data(:,7)];    % xforce
  Fy1=[data(:,6)];    % yforce
   Fz1=[data(:,5)];    % zforce
   Fx2=[data(:,4)];    % xforce
   Fy2=[data(:,3)];    % yforce
   Fz2=[data(:,2)];    % zforce

   W=10.79*9.81;
HCx=0.02;
%*******************************************************************************
% Force plate 1 is for right, plate 2 for left.
% Force plate 1 is the larger plate with the origin at its' centre.


for n=1:length(data)
HPx(n,1)=(data(n,76)/1000);     %y hip position 76 for left 30 for right
HPz(n,1)=(data(n,104)/1000)+0.05;                       % z hip postion 104 for left 32 for right
%My2(n,1)=(Fz2(n)*((data(n,121)-(data(n,42)))/1000);
My2(n,1)=(Fz2(n)*((data(n,8)-data(n,87))/1000));
E(n,1)=-My2(n)-(-Fz2(n)*HPx(n))+(Fx2(n)*HPz(n))-(W*HCx);

HPxr(n,1)=(data(n,80)/1000);     %y hip position 80  for right
HPzr(n,1)=(data(n,108)/1000)+0.05;                      % z hip postion 108 for right
My1(n,1)=(Fz1(n)*((data(n,10)-data(n,91)))/1000);
Er(n,1)=-My1(n)-(-Fz1(n)*HPxr(n))+(Fx1(n)*HPzr(n))-(W*HCx);
end
E=-E;
Er=-Er;
Fz1=Fz1/10;
E=E-E(1);
Er=Er-Er(1);
figure(1);subplot(2,1,2);plot(data(:,1),E,''); hold on; plot(data(:,1),Er,'--')
xlabel('Time (s)')
ylabel('Moment (Nm)')

return
```

3.2. for calibrating the handles.

```
% handlecalib.m
% Created by Jonathan Norton 14th Dec 2001.
% Created on main lab computer (Black in rack).
% to put handle data through calibration matrices to get forces and moments out.

% The left handle is the original JR3 and the right the new one.

% There is an offset as a result of the handle and a translation.
% These will be dealt with seperatly.
% general formulae will be; [data]-[offset]=[new_data]
% [calib]*[new_data]=[f,m]
% [f,m]*[translation]=[F,M]

load c:\Matlabr12\work\jonathan\cal02.txt   \asc
data=cal02(:,5:21);      %load and pull out handle data. must be 12 columns
clear cal02
data_l=data(:,1:6);
data_r=data(:,7:12);       % seperate out left and right data.

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
left_calib=[74.396 0.835 -0.294 -1.164 -0.048 0.579;...
      -0.109 73.875 0.298 0.350 0.719 2.351;...
      1.518 0.050 147.587 -3.393 -2.616 3.119;...
      -0.037 0.078 -0.030 8.157 -0.037 -0.099;...
      -0.075 -0.051 -0.073 0.049 8.126 0.001;...
      0.034 0.062 0.007 0.022 -0.010 8.565];

right_calib=[76.3304 0.1249 -0.2799 -0.3720 0.2975 -0.8257;...
      -0.0245 75.8098 0.1382 0.6449 -1.0409 -0.5066;...
      -2.5941 -0.3564 159.9452 -0.8235 4.1034 6.7240;...
      -0.2299 0.0369 0.0988 8.8537 -0.0109 0.3781;...
      0.0778 0.0180 0.1149 0.0216 8.4296 0.0759;...
      -0.0133 -0.0145 0.0145 0.0396 -0.0045 8.4294];
% These matrices are taken from the JR3 calibration data sheets.
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
[offset_l]=[-217.7377 -67.7111 -511.7819 -2.2695 185.3550 -0.9931];
[offset_r]=[29.0262 -92.0168 -392.594 -57.9434 -289.4080 -1.5051];
% these are the means of data with just the handles attached.


new_data_l(:,1)=data_l(:,1)-offset_l(:,1);
new_data_l(:,2)=data_l(:,2)-offset_l(:,2);
new_data_l(:,3)=data_l(:,3)-offset_l(:,3);
new_data_l(:,4)=data_l(:,4)-offset_l(:,4);
new_data_l(:,5)=data_l(:,5)-offset_l(:,5);
new_data_l(:,6)=data_l(:,6)-offset_l(:,6);

new_data_r(:,1)=data_r(:,1)-offset_r(:,1);
new_data_r(:,2)=data_r(:,2)-offset_r(:,2);
new_data_r(:,3)=data_r(:,3)-offset_r(:,3);
new_data_r(:,4)=data_r(:,4)-offset_r(:,4);
new_data_r(:,5)=data_r(:,5)-offset_r(:,5);
new_data_r(:,6)=data_r(:,6)-offset_r(:,6);

new_data_l=new_data_l';
```

```
new_data_r=new_data_r';

fml=left_calib*new_data_l;
fmr=right_calib*new_data_r;
fmr=fmr';
fml=fml';
return
% the effect of the translation is to add a moment to all fx, My. Therefore to allow for this
% the effect the Fx*handle offset must be subtracted from the My.  It is therefore a single
dimension change.
%[FL,ML]=[fl,ml]+[translation_l];
%[FR,MR]=[fr,mr]+[translation_r];
return
```

3.3

```
%sol_stand1_force.m
% A script to plot forces from force plates generated by Sol during OL standing.
% This version to show 1st stand.
% Aim to plot movie with HRV & GRV.
% Created by Jonathan Norton. 30th July 2001.
% Created on implant-lap.
clear
load d:\Jonathan\Control_of_standing\ss\sol\sol01a.txt  \asc

data=sol01a;

clear sol01a

%plotting GRV from plate 2.
%MM=moviein(160);          %No longer needed in this version of Matlab
%MM=zeros(length(getframe),length(data));
 sc=0.5;     % number of newtons per metre on graph
     fig=figure;
       set(fig,'DoubleBuffer','on');
       set(gca,'xlim',[-80 80],'ylim',[-80 80],...
             'NextPlot','replace','Visible','off')
       mov = avifile('sol1(side).avi')
for n=1:65:16001
%n=10001;
    h2=[data(n,93)];     % xforce
    m2=[data(n,94)];     % yforce
    v2=[data(n,95)];     % zforce
    %mag2=sqrt((h^2)+(m^2)+(v^2));
    x_foot2=[data(n,4)];     % xorigin
    y_foot2=[data(n,5)];     %yorigin

    line_foot2=[x_foot2, y_foot2, 0];
    line_tip2=[x_foot2+(h2/sc), y_foot2+(m2/sc), (v2/sc)];
line2=[line_foot2;...
        line_tip2];
% now to plot for plate 1
    h1=[data(n,90)];     % xforce
    m1=[data(n,91)];     % yforce
    v1=[data(n,92)];     % zforce
    %mag1=sqrt((h^2)+(m^2)+(v^2));
    x_foot1=[data(n,2)];     % xorigin
    y_foot1=[data(n,3)];     % yorigin

    line_foot1=[x_foot1, y_foot1, 0];
    line_tip1=[x_foot1+(h1/sc), y_foot1+(m1/sc), (v1/sc)];
```

```
line1=[line_foot1;...
       line_tip1];

% now to attempt to do the handles
sensl=[-0.0157  -0.2863  -0.0029   0.0367   0.2790   0.0702
   0.0146   0.0058  -0.2409   0.0130  -0.0069  -0.0003
   0.0002   0.0192   0.0347   0.0009   0.0161  -0.0006];
sensr=[-0.0166  -0.2654   0.0083   0.0180   0.2658   0.0702
  -0.0100  -0.0061   0.2413  -0.0098   0.0061   0.0014
   0.0043   0.0185  -0.0348   0.0048   0.0179   0.0001
];
%the outputs from this are Fx, Fz, My.
LHF=sensl*data(n,104:109)';
RHF=sensr*data(n,110:115)';
LHFx=LHF(1,1);
LHFz=LHF(2,1);
LHMy=LHF(3,1);
RHFx=RHF(1,1);
RHFz=RHF(2,1);
RHMy=RHF(3,1);
l_hand_origin_x=[data(n,72)];
l_hand_origin_y=[data(n,73)];
l_hand_origin_z=[data(n,74)];
r_hand_origin_x=[data(n,78)];
r_hand_origin_y=[data(n,79)];
r_hand_origin_z=[data(n,80)];

l_hand_origin=[data(n,72), data(n,73), data(n,74)];
r_hand_origin=[data(n,78), data(n,79), data(n,80)];
line_foot_3=[l_hand_origin];
line_foot_4=[r_hand_origin];
line_tip_3=[l_hand_origin_x+(LHFx/sc), l_hand_origin_y, l_hand_origin_z+(LHFz/sc)];
line_tip_4=[r_hand_origin_x+(RHFx/sc), r_hand_origin_y, r_hand_origin_z+(RHFz/sc)];

line3=[line_foot_3;
   line_tip_3];

line4=[line_foot_4;
   line_tip_4];

% Now to plot the CODA markers.
mark1=[data(n,6), data(n,7), data(n,8)];
mark2=[data(n,9), data(n,10), data(n,11)];
mark3=[data(n,12), data(n,13), data(n,14)];
mark4=[data(n,15), data(n,16), data(n,17)];
mark5=[data(n,18), data(n,19), data(n,20)];
mark6=[data(n,21), data(n,22), data(n,23)];
mark7=[data(n,24), data(n,25), data(n,26)];
mark8=[data(n,27), data(n,28), data(n,29)];
mark9=[data(n,30), data(n,31), data(n,32)];
mark10=[data(n,33), data(n,34), data(n,35)];
mark11=[data(n,36), data(n,37), data(n,38)];
mark12=[data(n,39), data(n,40), data(n,41)];
mark13=[data(n,42), data(n,43), data(n,44)];
mark14=[data(n,45), data(n,46), data(n,47)];
mark15=[data(n,48), data(n,49), data(n,50)];
mark16=[data(n,51), data(n,52), data(n,53)];
mark17=[data(n,54), data(n,55), data(n,56)];
mark18=[data(n,57), data(n,58), data(n,59)];
mark19=[data(n,60), data(n,61), data(n,62)];
```

```
mark20=[data(n,63), data(n,64), data(n,65)];
mark21=[data(n,66), data(n,67), data(n,68)];
mark22=[data(n,69), data(n,70), data(n,71)];
mark23=[data(n,72), data(n,73), data(n,74)];
mark24=[data(n,75), data(n,76), data(n,77)];
mark25=[data(n,78), data(n,79), data(n,80)];
mark26=[data(n,81), data(n,82), data(n,83)];
mark27=[data(n,84), data(n,85), data(n,86)];
mark28=[data(n,87), data(n,88), data(n,89)];
line5=[mark1;
   mark2;
   mark4;
   mark1;
   mark4;
   mark3;
   mark1;
   mark3;
   mark13;
   mark27;
   mark28;
   mark14;
   mark8;
   mark7;
   mark6;
   mark5;
   mark15;
   mark16;
   mark18;
   mark17;
   mark16;
   mark15;
    mark5;
    mark7;
    mark8;
    mark12;
    mark11;
    mark10;
    mark9;
    mark19;
    mark20;
    mark21;
    mark22;
    mark20;
    mark19;
    mark9;
    mark11;
    mark12];
line6=[mark23;
   mark24;
   mark26;
   mark25;
   mark23];
% These lines actually plot the forces.
%subplot(1,2,1);
plot(line2(:,2), line2(:,3)); hold on;
%subplot(1,2,1);
plot(line4(:,2),  line4(:,3),'g')
%subplot(1,2,1);
plot(line3(:,2),  line3(:,3),'g')
%subplot(1,2,1);
```

```
plot(line1(:,2),  line1(:,3))
%subplot(1,2,1);
plot(line6(:,2),  line6(:,3), 'm')
%subplot(1,2,1);
plot(line5(:,2),  line5(:,3), 'm');hold off
%subplot(1,2,2);plot(line2(:,2), line2(:,3)); hold on;
%subplot(1,2,2);plot(line4(:,2),  line4(:,3),'g')
%subplot(1,2,2);plot(line3(:,2),  line3(:,3),'g')
%subplot(1,2,2);plot(line1(:,2),  line1(:,3))
%subplot(1,2,2);plot(line6(:,2),  line6(:,3), 'm')
%subplot(1,2,2);plot(line5(:,2),  line5(:,3), 'm');hold off;

%plot3(line2(:,1), line2(:,2), line2(:,3)); hold on;
%plot3(line4(:,1),  line4(:,2), line4(:,3),'g')
%plot3(line3(:,1),  line3(:,2), line3(:,3),'g')
%plot3(line1(:,1),  line1(:,2), line1(:,3))
%plot3(line6(:,1),  line6(:,2), line6(:,3), 'm')
%plot3(line5(:,1),  line5(:,2), line5(:,3), 'm');hold off;

frame_string=['frame number' ,num2str(n)];
xlabel('x direction (mm)')
ylabel('y direction (mm)')
zlabel('Force (0.5N/mm)& z direction (mm)')
axis equal
%title('10001st frame 2nd1/2 1st stand')
 %MM(:,n) = getframe;%(gcf,rect);
        F = getframe(gca);
        mov = addframe(mov,F);
end

%       N = 1;
%       FPS = 1;
%       movie(gcf,MM,N,FPS,rect)
mov=close(mov);
%movie(MM,1,1)
return


%plot(data(:,1),data(:,103));% hold on;
%plot(data(:,1),data(:,95),'--'); hold on;
%xlabel('time (s)')
%ylabel('EMG (mV)')
%title('Sol 1st stand, sit-to-stand, EMG')
%legend('plate 1 solid Right   plate 2 -- Left')

%Fs=1000;
%blocksize=3500;
%[f,mag]=daqdocfft((data(2000:5500,103)),Fs,blocksize);
%figure(2);
%plot(f,mag)
%grid on
%ylabel('Magnitude (dB)')
%xlabel('Frequency (Hz)')
return
```

Appendix 4.

Lumbo-sacral Anterior Root Innervations.

Stimulation responses to be expected with LARSI: based on the following anatomical texts:-

'g': Gray's Anatomy ('Classic' edition 1977) ISBN 0-517-23651, pp415-441.
'p': Palastanga, Field & Soames, 'Anatomy & Human Movement', 1997 reprint, ISBN 0-7506-0970-2, pp326-393.
's': Stone & Stone, 1990, 'Atlas of skeletal muscles'ISBN 0-697-10618-7, pp179-188.
cf Liguori R., Krarop C. & Trojaborg W. (1992) "Determination of the segmental sensory and motor innervation of the lumbosacral spinal nerves." Brain **115**, pp. 915-934.

This may not be an absolute or exhaustive list, but it is intended to list the muscles innervated from each of the roots. Based upon wall chart at UCL, Medical Physics, initially prepared by Alan Worley (from Stone and Stone) and cross checked against Gray's and Palastanga by Jonathan Norton and Tim Perkins. Where the texts give slightly different innervation the additional root is given. There were no instances spotted where the texts differed by more than one root. Further information on the spread or variability of innervation has been seen in Liguori *et al* (1992). In general, it is not unexpected to find roots innervation from one root higher or lower than is listed here. In addition to the inter subject variability hinted at here there is also a degree of asymmetry in the majority of patients. Broadly the lumbar roots innervate the anterior and medial aspects of the leg and the sacral roots the posterior and lateral. Some posterior innervation is received from L4 and more from L5.
[NB Erector Spinae (expected segmentally, posterior rami): given only because observed in one of Giles Brindley's patients as well as the first Salisbury patient.]

Source	Root	Muscles	Actions
g,p,s	L2	Psoas Major	Hip and vertebral column flexor
g,p,s		Iliacus	Thigh flexor (at hip)
g,p,s		Sartorius	Hip flexion, lateral rotation & medial knee rotation
g,p,s		Rectus Femoris	Knee extension & hip flexion
g,p,s		Vastus	Knee extension
p,g		Lateralis/Medialis/Intermedius	Knee flexion, Hip adduction (+ medial rotation)
p,g		Gracilis	Hip adduction and flexion
p,g		Adductor Longus/ Brevis	Hip adduction (+ lateral rotation)
g,		Adductor Magnus	Lateral thigh rotation
		Obturator externus	Extension (lordosis) and lateral flexion of spine)
s,g		Erector Spinae	Hip adduction, flexion and medial rotation
		Pectineus	

g,p,s	L3	Psoas Major	Hip and vertebral column flexor
g,p,s		Illiacus	Thigh flexor (at hip)
g,p,s		Obturator Externus	Lateral thigh rotation
g,p,s		Sartorius	Hip flexion, lateral rotation & medial knee rotation
g,p,s		Rectus Femoris	Knee extension & hip flexion
g,p,s		Vastus	Knee extension
g,p,s		Lateralis/Medialis/Intermedius	Hip adduction and knee flexion
g,p,s		Gracilis	Hip adduction and flexion
g,p,s		Adductor Longus/ Brevis	Hip adduction (+ lateral rotation)
g,s		Adductor Magnus	Hip adduction, flexion and medial rotation
		Pectineus	
g,p,s	**L4**	Obturator Externus	Lateral thigh rotation
g,p,s		Gluteus Medius/ Minimus	Hip abduction and medial rotation
g,p,s		Tensor Fascia Latae	Hip flexion, abduction and medial rotation
g,p,s		Rectus Femoris	Knee extension & hip flexion
g,p,s		Vastus Lateralis/	Knee extension
g,p,s		Medialis/Intermedius	Hip adduction and flexion
g,s		Gracilis	Hip adduction, (+ lateral rotation & extension)
g,p,s		Adductor Magnus	Hip adduction and flexion
g,p,s		Adductor Longus/ Brevis	Dorsiflexion & ankle inversion
g,p,s		Tibialis Anterior	Plantarflexion (+ knee flexion)
g,s		Plantaris	Plantarflexion & foot eversion
g,s		Peroneus Longus/ Brevis	Big toe extension, dorsiflexion & foot inversion
s,g		Extensor Hallucis Longus	Toe extension, dorsiflexion & eversion
s,g		Extensor Digitorum Longus	Hip adduction, flexion and medial rotation
g,s		Pectineus	Dorsiflexion and eversion
s,g		Peroneus Tertius	Lateral thigh rotation
p,		Quadratus Femoris	Planterflexion (+ankle inversion)
p,		Tibialis Posterior	Lateral thigh rotation
p,		Gemellus Inferior	Hip flexion, lateral rotation & medial knee rotation
g		Sartorious	

g,p,s	L5	Obturator Internus	Lateral thigh rotation (at hip)
g,p,s,		Quadratus Femoris	Lateral thigh rotation
g,p,s		Gluteus Maximus	Hip extension and lateral rotation (+ adduction)
g,p,s		Gluteus Medias/ Minimus	Hip abduction and medial rotation.
g,p,s		Tensor Fascia Latae	Hip flexion and medial rotation
p,s		Biceps Femoris	Knee flexion and hip extension
p,s		Semitendinosus	Knee flexion & medial rotation and hip extension
p,s		Semimembranosus	Knee flexion and hip extension
g,p,s		Tibialis Anterior	Dorsiflexion & ankle inversion
g,s		Plantaris	Plantarflexion (+ knee flexion)
g,p,s		Tibialis Posterior	Plantarflexion & ankle inversion
g,p,s		Peroneus Longus/ Brevis	Plantarflexion & foot eversion
g,s		Flexor Hallucis Longus	Big toe flexion, plantarflexion & foot inversion
g,p,s		Flexor Digitorum Longus	Toe flexion, plantarflexion & foot inversion
p,s		Extensor Hallucis Longus	Big toe extension, dorsiflexion & foot inversion
p,g		Extensor Digitorum Longus	Toe extension & dorsiflexion (+ eversion)
p,s,g		Peroneus Tertius	Dorsiflexion and eversion
p,g		Gemullus Superior/Inferior	Lateral thigh rotation
g		Soleus	Planterflexion

p,s,g	S1	Obturator Internus	Lateral thigh rotation (at hip)
p,s,g		Quadratus Femoris	Lateral thigh rotation
p,s,g		Gluteus Maximus	Hip extension and lateral rotation (+ adduction)
p,s,g		Gluteus Medias / Mininus	Hip abduction and medial rotation
s,g		Tensor Fascia Latae	Hip flexion and medial rotation

p,g,s,		Biceps Femoris	Knee flexion and hip extension
p,s,g		Semimembranosus	Knee flexion and hip extension
sg		Tibialis Anterior	Dorsiflexion & ankle inversion
p,g,s		Gastrocnemius	Plantarflexion and knee flexion
p,s,g		Soleus	Plantarflexion
p,s,g		Plantaris	Plantarflexion (+ knee flexion)
s,g		Tibialis Posterior	Plantarflexion & ankle inversion
p,g,s		Peroneus Longus/ Brevis	Plantarflexion & foot eversion
p,s,g		Flexor Hallucis Longus	Big toe flexion, plantarflexion & foot inversion
p,s,g		Flexor Digitorum Longus	Toe flexion, plantarflexion & foot inversion
p,s,g		Extensor Hallucis Longus	Big toe extension, dorsiflexion & foot inversion
p,s,g		Extensor Digitorum Longus	Toe extension & dorsiflexion (+ eversion)
p,s,g		Peroneus Tertius	Dorsiflexion and eversion
p,s,g		Semitendinous	Knee flexion & medial rotation and hip extension
p,g		Gemullus Superior/Inferior	Lateral thigh rotation

p,s,g	S2	Obturator Internus	Lateral thigh rotation (at hip)
p,s,g		Gluteus Maximus	Hip extension and lateral rotation
p,s,g		Biceps Femoris	Knee flexion and hip extension
p,sg		Semitendinosus	Knee flexion & medial rotation and hip extension
p,sg		Semimembranosus	Knee flexion and hip extension
p,sg		Gastrocnemius	Plantarflexion and knee flexion
p,sg		Soleus	Plantarflexion
p,sg		Flexor Hallucis Longus	Big toe flexion, planterflexion & foot inversion
p,		Plantaris	Plantarflexion (+ knee flexion)
p,		Flexor Digitorum Longus	Toe flexion, plantarflexion & foot inversion
p,g		Gemullus Superior	Lateral thigh rotation

Appendix 5.

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3D Whole Body Scanning to Determine Mass Properties of Legs.

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Keywords: Anthropometry, 3D scanning, mass properties.

Abstract.

We describe a novel method of measuring the mass properties of the limbs, specifically legs. We use the method to obtain the mass and centres of mass of the legs which enables us to calculate the leg joint moments from measurements of ground reaction forces using force plates. The data is obtained by using a 3D whole body scanner to obtain a data set representing the surface of both legs. The bones are significantly denser than the soft tissue so their mass is calculated. Textbook values for the densities of bone and soft tissue are used. The actual bones are approximated by stretching appropriate bone shapes to fit the x-ray of the subject. Numerical integration is then used to obtain the mass and centre of mass of the limb. The system is fast and reliable and allows an individual's mass properties to be measured rather than relying upon population surveys which may be biased, particularly when the subject is atypical by being disabled. Paraplegics can be measured in the scanner using a modified Oswestry Standing Frame. When compared with a water displacement method, for 10 legs the errors in the total leg volume using this method are less than 1% and in the location of the centre of mass less than 4%.

Introduction.

The accurate determination of the mass properties of the body segments for an individual has been a long-standing problem in biomechanics. Generally estimates for an individual have been related to sample data contained in tables because individual measurement has not been practical. Traditionally these tables have been derived from two major populations, cadavers which have typically came from persons over the age of 65, (e.g. Seidel *et al* 1995) and military personnel, (e.g. Chandler *et al* 1975). Neither of these groups represents accurately the majority of the population today, nor the disabled population. A substantial proportion of the subjects undergoing biomechanical analysis are likely to suffer from some disability, and therefore are unlike "normals" in biomechanical terms. A survey by Stein and colleagues (Stein *et al* 1996) has shown that the disabled population is poorly modelled by data obtained in these surveys.

A previous attempt using both a proportional body model, (De Lava 1996) and a geometric model, (Yeadon 1990) in van der Herberg (1997), arrived at 2 estimates of the masses of the leg for one person that differed by 28%, (see the Appendix for further information). Other papers do not assess the likely error arising from using tabulated data. More importantly, we believe that the majority of gait labs do not include error analysis in a typical report (Whittle 1996).

The method we describe here is based upon the use a 3D whole body scanner to measure the external shape of the body. We have previously mentioned this technique, Norton *et al* (2000). Whilst whole body scanners are not novel, use of the scan data to calculate the mass and centre of mass of the legs is unpublished. The use of 3D body scanners within the field of anthropometry has been reviewed by Jones and Rioux (1997) who concluded that such scanners offer the opportunity to study the

human body in more detail and that there are many potential applications of such techniques, e.g. Rigotti *et al* (1998). Pearsall and Reid (1994), have provided a review of the use of body segment parameters in biomechanics. Here we describe a technique which we have used to calculate the mass and centre of mass of legs, although other uses are possible with this technique.

Methods and Materials.

The Scanner.

3D whole body scanners are under development by a number of companies, primarily for use in the bespoke clothing industry, or to provide data for computer animations. We are currently using a Hamamatsu (Hamamatsu Photonics K.K. Hamamatsu City, Shizuoka Pref., 430-0193, Japan) Body Lines scanner, which uses near infra-red light. The scan heads move vertically and the body is scanned in a staggered helix. The helix has a pitch of 5mm and in each revolution of the helix there are 256 position samples, each with 3 co-ordinates, (x,y,z) and a reflection intensity. The scan takes 10 seconds to complete. Some data reduction is used to remove points with a low intensity, because the co-ordinates of those points tend to be inaccurate (Horiguchi 1998). The scanner currently costs in the region of $120,000 and occupies an area of 1.8×1.7m and is 2.75m high.

For use with disabled subjects (paraplegics) we have developed a modified Oswestry Standing Frame. The frame is shown in figure 1. The frame has a raised base, so that the subject stands at the same height as a normal subject in the scanner. The frame is mounted on castors and so can be easily moved into the scanner when the subject is positioned in the frame. The frame and the straps are painted matt black, absorbent to infra-red light. This results in small lost areas in the data set, which we correct by interpolation between points on the surrounding surface before calculating the volume.

Figure 1. A paraplegic stands in the Oswestry frame inside the scanner. The scanner heads are located at the front and back of the scanner, consequently this design of frame has very little structure in the viewing fields of the heads over the required area, the legs.

Data is output from the scanner software as a standard text file. It is segmented using custom written code written in Visual C++ (Microsoft Corp, 1 Microsoft Way, Richmond WA, USA) and a 3D graphics library, (www.tgs.com/Products/openinv-index.html), Dekker *et al* (1999). The leg is segmented by a plane through the crotch

point and the superior iliac crest. The points of segmentation are chosen on a case by case basis. Numerical integration using Matlab, (The MathWorks UK, Matrix House, Cowley Park, Cambridge, CB4 0HH. UK.) is used to calculate the volume, mass and centre of mass of the leg. A typical file containing text data from one leg will be around 200kbytes.

The leg data consists of a non-circular helix of points. To calculate the volume of this irregular object it is treated as a large number of "wedges", see figure 2. These are formed as follows. An artificial mid-line is generated along the longitudinal axis of the leg which joins the centroids of the cross-sections. Adjacent points of the helix are joined. Each point in the helix joined to its closest neighbour in the row below. The leg is thus divided into wedges, all of whose volumes are calculated. This method is described more fully in Yamanaka (1998).

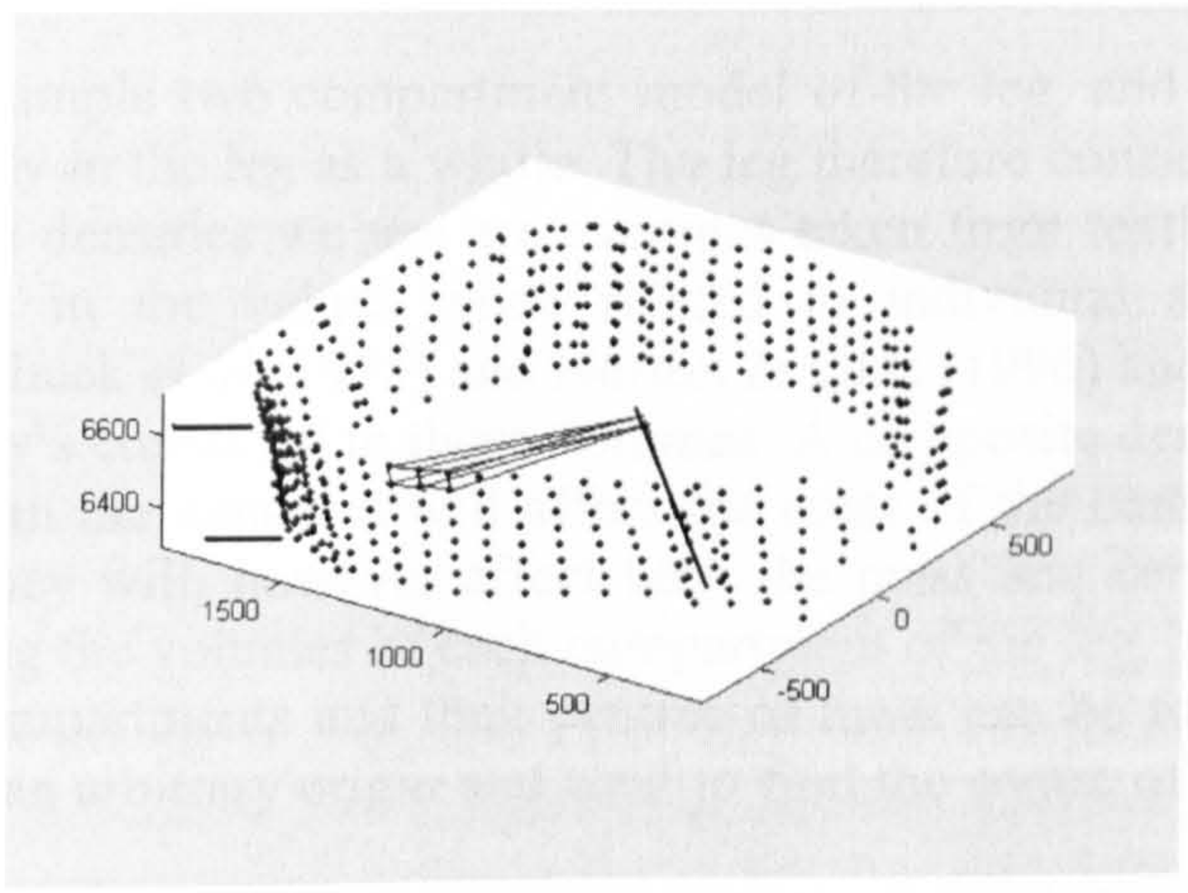

Figure 2. A comparison of the two volume measuring techniques. The thick black lines on the left represent the height of water added in one quantum. The thin lines joining the dots represent the "wedges" used in the scanner technique. The long line represents the artificially inserted centroid.

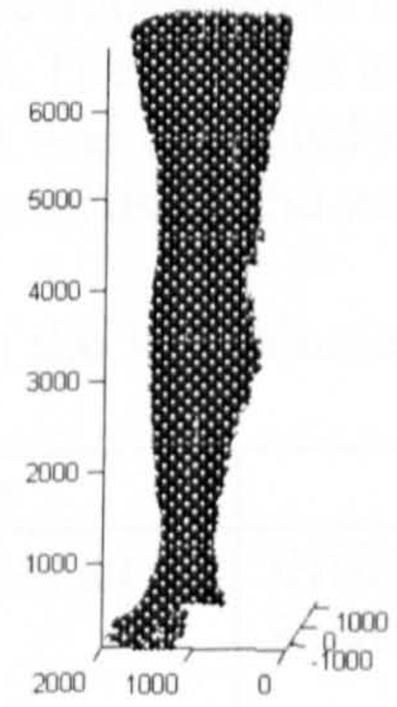

Figure 3. An output plot of a leg data set. The axis scales are in tenths of millimetres, as used by the scanner. This image is can be rotated in 3D space using Matlab. The points available with the Matlab software are larger than is ideal and can lead to some visual blurring.

Bone Data

The National Institutes of Health has placed on the Internet images from cadavers from two "normal, healthy" subjects[1]. By obtaining slices through a leg it is possible to reconstruct a data set representing the lower limb skeleton of the individual. Using distances measured from a lower limb X-ray the bones of the NIH data are re-scaled to fit the dimensions of the patient. This is done using Matlab. The following anatomical landmarks are used to rescale the NIH data:

- Greater Trochanter separation;
- Greater Trochanter to Lateral Malleoli;
- Greater Trochanter to Superior Patella;
- Superior Patella to Lateral Malleoli (inferred from the two distances above).

We use a simple two compartment model of the leg, and in the initial study were interested only in the leg as a whole. The leg therefore consists of bone and soft tissue. Because the densities we use are averages taken from textbooks there will be some inaccuracies in the values when related to individual subjects. Data was obtained from Roebuck *et al* (1975) and Norton & Olds (1996) and was based upon a collection of survey's contained in those volumes. A composite density is used for the soft tissue. Errors in the densities will affect the mass of the component, but not its centre of mass. They will, however affect both the mass and centre of mass of the whole leg. Knowing the volumes of each compartment of the leg, bone and non-bone, the mass of the compartments and their centres of mass can be found. Moments are then taken around an arbitrary origin and used to find the centre of mass of the whole leg.

Volume Validation.

The scanner is only used to find the volume of the leg. To validate this method we compared the volume obtained in 10 "normal" legs (9 subjects, 5 male) from the scanner, with that obtained using a water displacement method. All subjects volunteered and gave verbal informed consent. The experiments were therefore carried out in accordance with the Declaration of Helsinki (1964). The subject stood with one leg in a waterproof tank and 500 or 1000ml quanta of water were added. The rise in height of the water was noted after each quantum. The tank was calibrated before use, i.e. quanta of water were added to the tank with no leg in it and the rise in height noted using the same burette. The subjects were also scanned whilst standing in a normal posture. The scan data set was truncated in *post hoc* analysis to include only the height of the leg that was measured using the water displacement method.

Results.

The results from comparing the leg volume measured in the two methods are shown in table 1.

	Volume		Difference in Volume	
Subject (ID, sex, (left or right)).	Water (l)	Scanner (l)	Difference(l) Scanner-water	Difference (%)
1F (L)	3.52	3.55	0.03	0.85
2F (L)	4.25	4.23	0.02	0.47
3F (R)	4.30	4.32	0.02	0.46

[1] The Visible Human Project: http://www.dhpc.adelaide.edu.au/projects/vishuman2/index.html is the site used in the current study but others are available. For more information see: http://www.nlm.nih.gov/research/visible/visible_human.html

4M (R)	4.89	4.93	0.04	0.82
5M (R)	4.03	4.04	0.01	0.25
6M (L)	4.41	4.44	0.03	0.68
6M (R)	4.48	4.48	0.00	0.00
7M (R)	3.21	3.18	0.03	0.94
8M (L)	3.34	3.32	0.02	0.75
9F (L)	3.48	3.45	0.03	0.87
Mean (sd)	3.99 (0.57)	3.99 (0.59)	0.023 (0.0116)	0.609 (0.3067)

Table 1. The total leg volumes, (litres) for 10 legs, (9 subjects) obtained using the two methods. The absolute values of the differences are calculated and then the percentage error calculated against the water volume. The means and standard deviations are shown for all values.

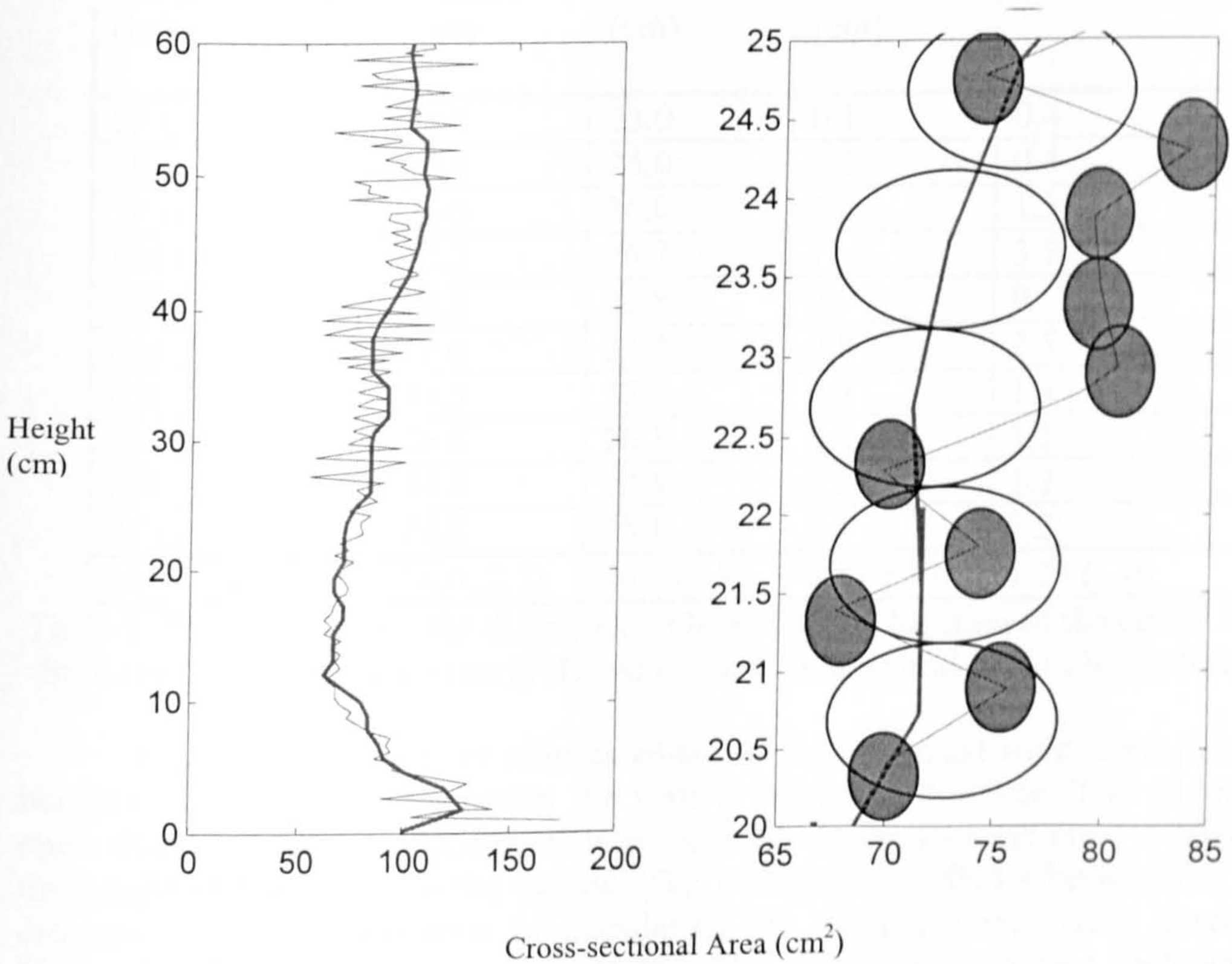

Figure 4. The left hand plot shows the cross-sectional areas of a single leg at various heights. The thick line represents the areas obtained using the water displacement technique. The right hand plot is an enlarged area from the left with error ellipses added representing the measurement and calculation errors in each technique. The open ellipses and thick line represent the water displacement technique.

For each revolution of the helix of data the average cross-sectional area was calculated. The results are plotted in figure 4. There are many more areas calculated for the scan data than for the water data. The height of the error ellipses is determined

by the sampling frequency, i.e. fewer samples leads to a greater height of the ellipse. The width of the ellipse is dependent upon the estimated error in measurement techniques. For the scanning technique this is based upon data from previously published data. For the water technique this is based upon errors in recording the height of water in the burette and measuring cylinder. This is because of the increased vertical resolution of the scanner compared with the water method, using 500ml quanta of water. Using the cross-sectional areas the vertical position of the centre of mass for each leg was calculated from both techniques. The equation used to locate the centre of mass with each technique was;

$Z_0 = \frac{\sum A\delta Z.Z}{\sum A\delta Z}$, where A= cross-sectional area of each "slice", δZ = the thickness of the "slice" (not constant) and Z = the height of the "slice" from the origin. Since we are measuring the accuracy of the volume measurement using the scanner we neglect variations in the density of the tissues. The results of these calculations are shown in table 2.

	Height		Difference in Height	
Subject (ID, sex, (left or right)).	Scanner (cm)	Water (cm)	Difference (cm)	Difference (%)
1F (L)	23.1	23.0	0.1	0.4
2F (L)	24.1	24.0	0.1	0.4
3F (R)	25.6	26.0	0.4	1.5
4M (R)	25.7	26.7	1	3.7
5M (R)	23.8	23.8	0	0
6M (L)	30.6	31.4	0.8	2.5
6M (R)	31.5	32.0	0.5	1.5
7M (R)	26.5	26.1	0.4	1.5
8M (L)	24.2	24.5	0.3	1.2
9F (L)	24.8	25.1	0.3	1.2
Mean (sd)	26.0 (2.7)	26.3 (2.9)	0.4 (0.30)	1.39 (1.0)

Table 2. This table shows the difference in height of the location of the centre of mass from the two techniques. Data is shown for each subject and pooled in the final row.

Figure 4 has had error ellipses added to the expanded right hand panel. The height of these ellipses represents the vertical height of the slice. The width of the open ellipses, (water displacement) is an estimate of the average error in measuring the height of the liquid on the burette. The width of the filled ellipses (scan), is an estimate of the average error in calculating the cross-sectional areas based upon Horiguchi (1998) and Yamanaka (1998). The water displacement technique has particularly large errors since the rise in the burette was small compared to the height of the meniscus.

Discussion.

Over some regions of the leg there are differences in the cross-sectional areas obtained by the two methods. These areas represent regions where the experimental errors may have been larger than average. Rather than stating that the difference in the two measurements is the error in the scanning technique we feel that it is more appropriate to say that it is the difference between two techniques.

As can be seen in figure 2 the water displacement produces thicker "slices". The resulting cross-sectional area is consequently an average from a much larger volume and so potentially represents the real leg less closely than the cross-sectional area obtained using the scanner technique. The differences in total leg volume (Table 1 column 3) in the two collection methods are not significantly different from 0 ($p<0.05$) using a student t-test. Statistics on the cross-sectional areas is meaningless since as can be seen, the data overlap within the errors associated with each of the techniques. The scan data is noticeably noisier than data obtained from the water displacement technique. This noise level averages out over a small range, and therefore is not thought to affect the location of the centre of mass.

The scanner system overestimates the size of the leg up to the ankle. This is because the hollow under the medial arch of the foot, and other areas on the sole of the foot that are raised from the ground are not "seen" by the scanner. The water technique records these volumes. The level of noise in some of the scan data is large, partly due to "outliers". A method of "cleaning" the data to remove outliers left in the data set by the scanner has been developed which, if implemented, would reduce the noise level. Outliers may arise from aberrant reflections. Using the current volume estimation technique apparent points also arise if the scanner records data points that overlap with existing points. This problem is eliminated in the new cleaning technique and has been reduced in the total leg volume estimation using manual cleaning. It is possible to remove some of the noise in the scan data using processing techniques, not utilised in this study.

The effect of the density upon the location of the centre of mass is shown in the table 3. As well as the obvious effect on the overall mass of the leg, and each of its components it will also affect the location of the centre of mass.

Parameter	Change per unit change in bone density	Change per unit change in soft tissue density	Units
Leg mass	1.3	9	$\frac{kg}{kg/l}$
Location of mass centre (x)	0.0005	0.004	$\frac{m}{kg/l}$
Location of mass centre (y)	0.005	0.009	$\frac{m}{kg/l}$
Location of mass centre (z)	0.0025	0.0015	$\frac{m}{kg/l}$

Table 3. The effect of changing the density of each of the compartments and the surface measured volume on the four main outputs.

Table 3 shows the rate of change of the 4 outputs, mass and 3D location of the centre of mass, with changing densities of the two compartments. The standard deviations of these densities are small, less than 0.05kg/l typically.

The system offers a number of advantages over the current techniques. It is rapid, non-invasive and gives personalised mass properties, eliminating the gross inaccuracies of using population data samples. The estimation of volume is good, (<1%) and hence the estimation of the mass and centre of mass is also good subject to an unknown error due to differences from the published densities and differences from the "stretched" bone from the Visible Human data. If these introduce no error

the accuracy will be that shown in table 2, (average 1.39%). The system is fast and easy to use when set up, and can be used with those who cannot normally stand by using the Oswestry Standing Frame. It is non-invasive and we have demonstrated its accuracy.

Although the cost of the scanner is high at present it is expected that this will fall in the future as such scanners become more common in the high-end fashion retail sector. Because the subject has to stand still for 10 seconds for the scan it is not applicable for all subjects, e.g. those with severe tremor, or those unable to stand. The modified Oswestry Frame we describe may help with some of these patients.

Although we have not discussed the influence of this technique upon biomechanical properties other than the centre of mass, e.g. the moment of inertia, we believe that it will improve such measures.

The scanner system is capable of measuring the volumes of legs and locating their centres of mass. It is reasonable to assume that the same system could be used for arms as well. It is unsuitable for calculating the mass properties of the trunk, although the volume could be calculated, due to the unpredictable densities of the tissues inside the trunk. This is especially true for visceral organs and the lungs which will vary with state of the respiratory system. This type of system is therefore impracticable for calculations of whole body centres of mass. A further problem with the system at present is the initial expense of the scanner. Further uses for this type of system may be found in clinics where knowledge of the shape, surface area and volume of the legs are needed. These might include clinics for lymphodema and the monitoring of joint contractures.

Acknowledgements:

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References:

- Chandler RF, Clauser CE, McConville JT, Reynolds HM & Young JW. 1975. *Investigation of Inertial Properties of the Human Body.* AMRL TR 69-70 Wright-Patterson Air Force Base, Ohio. (cited in de Lava P.1996 *Joint Center Longitudinal Positions Computed from a Selected Subset of Chandler's data.* Journal of Biomechanics. 29(9) 1231-1233.)
- Dekker L, Douros I, Buxton BF & Treleaven P. 1999. *Building Symbolic Information for 3D Human Body Modeling from Range Data.* Proceedings of the 2nd International Conference on 3-D Digital Imaging and Modeling. IEEE Computer Society. Ottawa, Canada.
- De Leva P. 1996. *Adjustments to Zatsiorsky-Seluyanov's Segment Inertia Parameters.* Journal of Biomechanics. 29. 1223-1230.
- Horiguchi C. 1998. *BL (Body Line) Scanner. The Development of a new 3D Measurement and Reconstruction system.* International Archives of Photogrammetry and Remote Sensing. 32(2) 421-429.
- Jones PMR & Rioux M. 1997. *Three-dimensional Surface Anthropometry: Applications to the Human Body.* Optics and Lasers in Engineering. 28. 89-117.
- Norton JA, Donaldson NdeN, Day BL, Dekker L, Perkins TA, Wood DE, McFadden C & Tromans AM. 2000. *The Determinants of Posture in Paraplegics Standing using Lumbar Anterior Root Stimulation.* Proceedings of the

International Functional Electrical Stimulation Society. Aalborg, DK. ISBN 87-90562-01-1 p478-481.

- Norton K & Olds T. 1996. *Anthropometrica. (A textbook of body measurements for health and sports courses).* University of New South Wales Press. ISBN 0868402230.
- Pearsall DJ & Reid JG. 1994. *The Study of Human Boy Segment Parameters in Biomechanics. An Historical Review and Current Status Report.* Sports Medicine. 18(2). 126-140.
- Rigotti C, Ferrigno G, Aliverti A & Pedotti A. 1998. *Surface Scanning: An Application to Mammary Surgery.* Journal of Biomedical Optics. 3(2). 161-170.
- Roebuck JA, Kroemer KHE & Thomson WG. 1975. *Engineering anthropometry methods.* Wiley Series in Human Factors. P179. ISBN 0471729752.
- Seidel GK, Marchinda DM, Dijkers M & Soutas-Little RW. 1995. *Hip Joint Centre Location from Palpable Bony Landmarks – a Cadver Study.* Journal of Biomechanics. 28 995-998.
- Stein RB, Zehr EP, Lebiedowska MK, Popovic DB, Scheiner A & Chizeck HJ. 1996. *Estimating Mechanical Parameters of Leg Segments in Individuals with and without Physical Disabilities.* IEEE Trans. Rehab. Eng. 4(3). 201-211.
- Van der Herberg E. 1997. *Leg Joint Moments during Paraplegic Standing with Lumbar Root Stimulation.* M.Sc Thesis, University College London, UK and Universiteit Twente, NL.
- Whittle MW. 1996. *Gait Analysis an Introduction.* 2nd edition. Butterworth Heinemann. ISBN 0-7506-222-9.
- Yamanaka D. 1998. *Segmentation, Volume and Surface Area Calculations in a 3D Human Body Model.* M.Sc. Thesis, University College London, UK.
- Yeadon MR. 1990. *The Simulation of Aerial Movement-II. A Mathematical Inertia Model of the Human Body.* Journal of Biomechanics. 23 67-74.

Appendix:

Mass Estimates by Two Different Methods, Applied to a Single Subject

Van der Herberg (1997) used a proportional method and a geometric method to estimate the mass and centre of mass of a patient's legs. The proportional method, (deLeva 1996) assumes that the segment mass is a fixed function of the body mass, and that the location of the centre of mass, COM, is at a fixed function of the length of the limb. Table A1 is taken from van der Herberg and illustrates the potential errors with conventional techniques. Distances to the COM are from the proximal locations.

Table A1. The Proportional model for a 2 segment leg in both male and female subjects. From van der Herberg(1997), based upon de Leva (1996).

The geometric model used was that described by Yeadon (1990). In this model the leg is divided into 5 truncated, non circular cones by planes perpendicular to the

longitudinal axis of the leg. Planes are placed at the ankle, knee and hip joint centres, maximum calf and thigh diameter and the crotch. The mass and COM is calculated assuming a homogenous density by integration. Yeadon claimed a maximum error of 2.3% when calculating whole body mass of normals.

Van der Herberg applied both of these methods, geometric and proportional, to the thighs and shanks of a paraplegic patient. The two methods gave mass estimates that differed by 28%. The techniques were also used to estimate the centres of mass of the two leg segments. For each segment the difference in the results obtained using the two techniques was 10% of the distance from the proximal joint centre to the COM. This is despite the techniques having been chosen to represent the better of the available methods.

Appendix 6.

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Spinally Generated EMG Oscillations and Spasms in a Low Thoracic Complete Paraplegic.

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Abstract:

An investigation into severe lower limb spasms experienced by a low-thoracic complete paraplegic during standing.

Completeness of the lesion was tested using standard neurophysiological techniques. EMG was recorded from the leg muscles whilst the patient stood passively in a standing frame. Frequency and coherence analysis was performed on these EMG data. The patient also stood using Functional Electrical Stimulation, FES, while ground and handle reaction force vectors were measured together with EMG activity.

During passive standing spasms appeared simultaneously in all leg muscle groups on one side. The interval between spasms varied between 3 and 30s. The spasms were inherently oscillatory. Within the spasms there was a tendency of repetitive grouped discharge of motor units as well as a strong 10Hz component in the EMG that was coherent across ipsilateral muscle groups. During FES assisted standing the interval between spasms was remarkably constant at around 16s. There are similarities between this patient's spasms and other pathological states that are thought to be of spinal origin.

Keywords: Spinal Oscillations, Paraplegia, Spasms.

In spinal cord injured human subjects the most common, clinically observed motor activity in muscles below the level of the lesion takes the form of either spasticity or spasms[1]. These forms of motor output are the result of intrinsic or reflex activity of the spinal cord since they may be present in patients with clinically complete lesions[1]. Spasms are typically triggered by a noxious stimulus and will normally last for a few seconds.

The ability of the decerebrate or spinalised cat to produce rhythmic motor output has been known since the time of Sherrington[2]. Studies following peripheral deafferentation or peripheral paralysis (fictive locomotion) in spinalised cats and other species suggest that this oscillatory activity is centrally generated within the spinal cord. The neural circuits underlying the production of this rhythmic activity have been referred to as central pattern generators[3]. Although spinal pattern generators are typically considered in relation to locomotion, they may be responsible for any rhythmical output from the spinal cord.

Spasms are not conventionally thought of as rhythmic motor outputs arising from spinal pattern generators. In the present paper we present results from a patient with a low, complete spinal cord lesion in whom spasms occur both rhythmically and spontaneously i.e. in the apparent absence of noxious stimuli. Further we provide evidence for oscillatory activity within each spasm.

METHODS

Subject

The patient (male, aged 40 at the time of the study) suffered a crush injury in October 1994 resulting in an asymmetric complete spinal cord lesion, T10/11. Following transfer to a regional spinal injuries centre the lesion was decompressed

and normal cord potentials were recorded intra-operatively below the lesion. A Moss cage and plate were used to stabilise the lesion site at the time of injury, these remain *in situ*.

Standing in callipers and an Oswestry Standing Frame was good, despite some initial hip stiffness on sit-to-stand. At discharge the patient was on Baclofen for lower limb and abdominal muscle spasms and spasticity (currently 60ml/day). The patient continued to use callipers.

In August 1996 he had a sacral anterior root bladder stimulator implanted[4]. Roots S2-4 were trapped in 3 intra-thecal electrodes. Concurrently he had a bilateral posterior rhizotomy of roots S2-5, (S2-4 cut and S5 crushed). The implant worked well for three years and then "failed" so that it worked only intermittently. In November 1999 a new two-channel stimulator was implanted with extradural electrodes. The old electrodes were not removed.

Immediately following the implantation of the first bladder stimulator, with its accompanying rhizotomy, there was a marked increase in the severity of spasms and the number of triggers for spasms. The spasms were usually observed when standing in callipers and because of these spasms the patient subsequently discontinued calliper standing.

FES-assisted standing[5] was commenced in October 1998 and by February 1999 he was able to balance using a single arm for support. During FES standing the patient experiences a series of spasms that is remarkably consistent. Following a period of approximately two minutes hip and trunk flexion spasms subsequently occur around every 16 seconds whilst the stand continues. Finally, on completion of the stand another spasm appears consisting of strong isolated ankle dorsiflexion activity with a period of about 20 seconds. The patient reports that the dorsiflexion activity is also present without prior stimulation and can persist for up to 4 hours, (the longest time the patient has sat without moving).

In this paper we describe only spasms that occur during either FES-assisted standing or passive standing in an Oswestry Standing Frame.

Experimental Procedures

The patient gave fully informed written consent and the experiments were approved by the local ethical committee. The spasms were investigated because they were interfering in the patient's functional activities.

Tests for Completeness of Lesion

In 2000, (6 years post injury), we reassessed the patient to determine if the lesion was complete. Repeated physiotherapeutic assessment, performed by an experienced spinal physiotherapist, indicated that the lesion had remained stable, T10 on the right and T11 on the left. The therapist was of the clinical opinion that the lesion was complete.

To further assess the completeness of the lesion a number of standard neurophysiological tests were performed. All data were collected on a PC using a CED 1401+ interface and Spike2 software, (both from Cambridge Electronic Design, Cambridge, UK).

Sensory pathways were assessed using cortical somatosensory evoked potential testing. Since the patient reported no sensation we used a mixed nerve, (Common Peroneal) so that the motor response could be used as a guide to appropriate stimulation levels. Stimulation was provided through a Digitimer, (Digitmer Ltd, Welwyn Garden City, UK), stimulator. 250 stimuli were presented and averaged for each leg. To assess the integrity of the corticospinal motor pathway we

stimulated over motor cortex with transcranial magnetic stimuli, (TMS)[6], using a Magstim200, (The Magstim Company, Dyfed, Wales). Galvanic vestibular stimulation, GVS, was used to assess further descending motor pathways. GVS is believed to activate descending motor pathways through modulation of vestibular afferent activity[7&8]. Flexible, self-adhesive 2.5 cm diameter round electrodes (PALS, Nidd Valley, Knaresborough, UK) were fixed to both mastoid processes. With the patient standing in an Oswestry frame 1.5mA constant current stimuli of 200ms duration were applied between the electrodes

Standing Experiments

The sacral root stimulator is only turned on for bladder emptying[4] and consequently was turned off throughout all the experiments described here. EMG electrodes were placed over quadriceps, hamstrings, tibialis anterior and gastrocnemius bilaterally. Silver/silver chloride and/or steel mesh, (PALS) electrodes were used. EMG was amplified and filtered prior to sampling. The patient stood in an Oswestry Standing Frame. We define this as passive standing. No biomechanical data was recorded during these stands because of the presence of the frame. No stimuli were applied and the patient stood for 10 minutes during which time a number of separate recordings of the EMG were made. All EMG data was sampled at 1kHz using custom written code in LabVIEW, (National Instruments, Austin, Texas, USA.).

The patient also stood using his surface FES system, defined as FES-assisted standing. FES-assisted standing is achieved in this patient by stimulation of the quadriceps muscles with electrodes placed on the skin. Stimulation is applied at 20Hz, with a pulse width of 300μs and an amplitude of 80V. In these experiments he stood on a pair of force plates, (Kistler Instruments AG Winterthur, Switzerland) and used a custom made pair of handles with 6-axis force transducers for support[9]. His posture was recorded using a Selspot system, (Selspot AB, Sweden). The patient stood in his normal standing posture for a period of time determined by the experimenter. This was timed to include several spasms on each occasion, but not to be so long as to fatigue the patient. The stand was repeated 3 times and each stand typically lasted 5 minutes.

Biomechanical data was sampled at 50Hz. All data was analysed off-line using custom written code in Matlab, (The Math Works Inc, Cambridge, UK). Coherence analysis was performed using software written by David Halliday (York University).

RESULTS

Tests for Completeness of Lesion

Cortical sensory evoked potentials to common peroneal nerve stimuli were absent despite good motor responses. Because the patient had no voluntary motor control he was unable to produce any background muscle activity during the TMS study. With stimulation at 100% of the stimulator's output responses were seen in the arms and facial muscles at appropriate latencies, indicating cortical current spread. No responses were seen in the leg muscles in individual sweeps or in averaged data. No responses to GVS were seen.

All of these tests support the clinical impression that the lesion is complete. Unfortunately MR imaging was not performed in this patient due to the presence of the nerve root stimulator[10] and the internal metal stabilisation around the lesion site.

Spasms During Passive Standing

When the patient is not receiving stimulation he can stand within a standing frame. Most of the time only minimal EMG activity is observed, with gastrocnemius tending to show low-level continuous motor unit activity. Spasms appear as large bursts of activity simultaneously across all leg muscle groups on one side of the body at a time (figure 1A). The inter-spasm interval during the passive stand is quite variable ranging from approximately 3 to 30s (figure 1C).

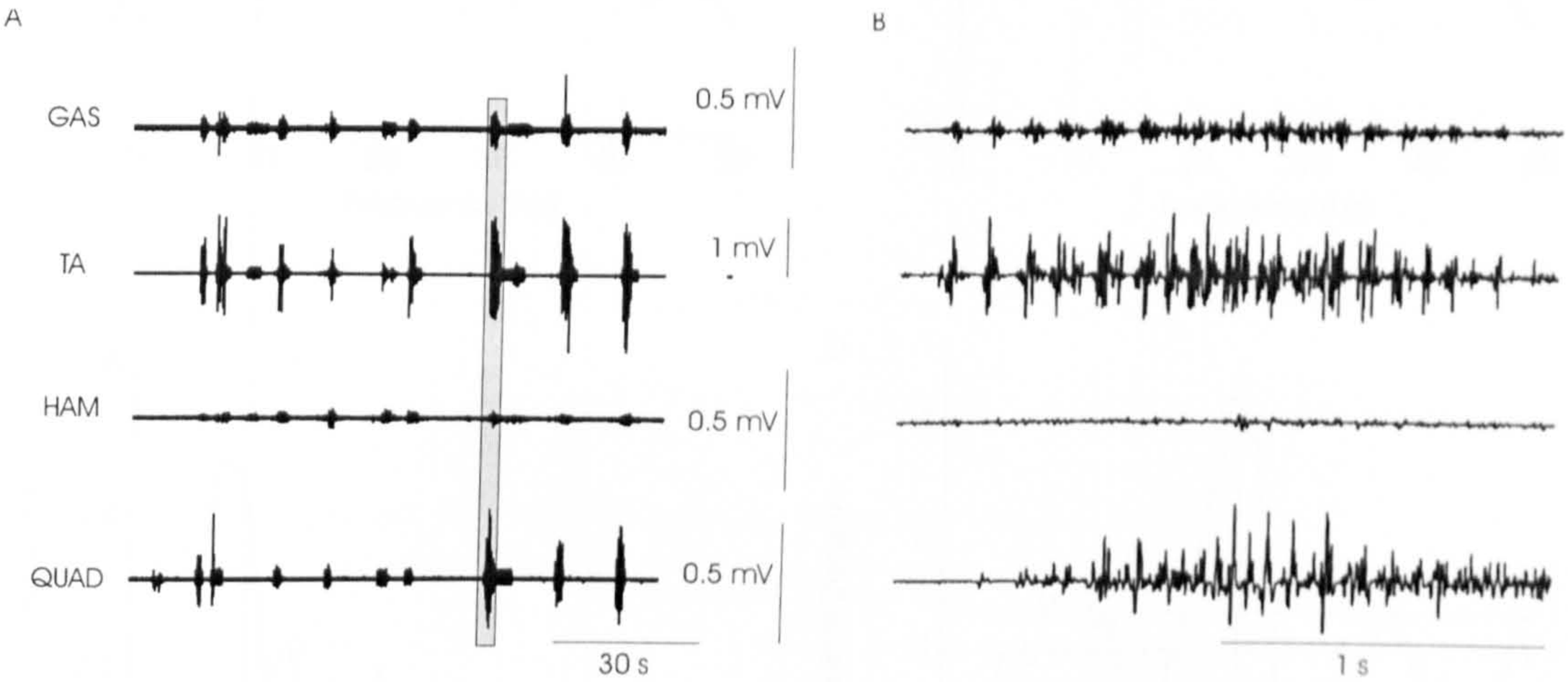

Figure 1: A plot of the EMG activity in Tibialis Anterior, Gastrocnemius, Quadriceps and Hamstrings during a passive stand (**A**). In **B** part of the plot from **A** (highlighted) is expanded. **C** shows the inter-spasm-interval during a passive stand recorded in two segments during a single stand. Spasms were defined as the onset of the EMG activity in Tibialis Anterior.

In figure 1B a segment of the plot is expanded and shows that, within a spasm, there are segmented bursts of muscle activity that often appear synchronously across leg muscles.

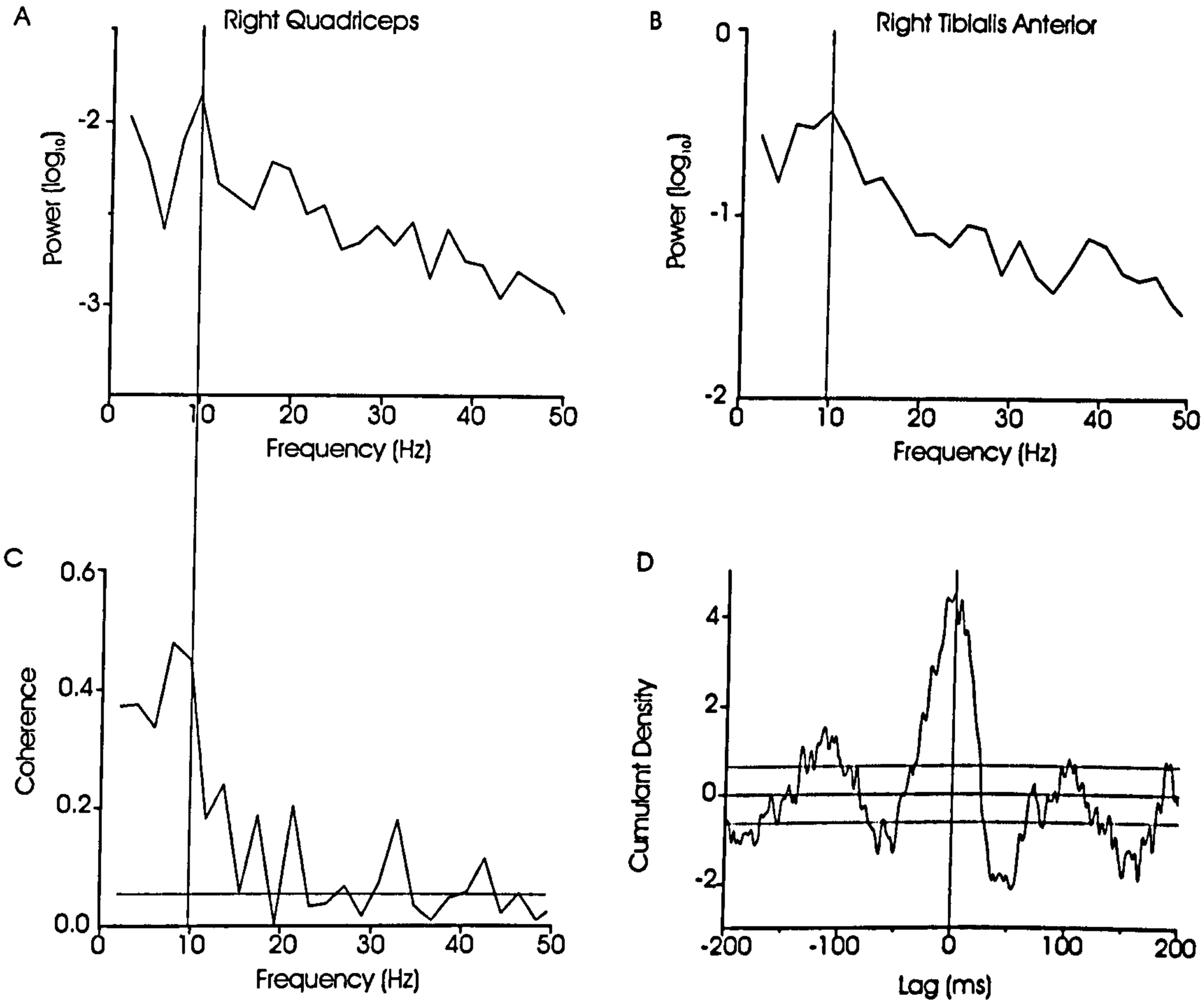

Figure 2. **A & B** show the autospectra for the Quadriceps (**A**) and Tibialis Anterior (**B**). A line is drawn through each spectra at around 10Hz, highlighting the similarity in the peaks. **C** shows the coherence between the two muscles, again the line is at around 10Hz. The dotted line represents the 95% confidence interval. The spectra and coherence were calculated using 54 segments of length 512 samples. **D** illustrates the lag between the muscles in the time domain. The dotted lines represent the 95% confidence interval. The peak at around time 0 shows the coherence between the muscles, and the prominent sidelobes at ~±100ms highlight the ~10Hz rhythmicity.

In the raw data it is often possible to see the bursts within the spasms occurring at approximately 10Hz (figure 1B). This is reflected in the autospectra of the EMG which shows a peak at around 10Hz in all muscles during a spasm (figure 2A&B). Coherence analysis[11] demonstrates a peak at similar frequencies between all pairs of ipsilateral muscles during the spasms (figure 2C). The relationship between quadriceps and tibialis anterior in the time domain is shown in figure 2D. The quadriceps appear to lead the Tibialis Anterior by ~3ms. The 10Hz rhythm is demonstrated by the noticeable sidelobes at ~±100ms. During passive standing the spasms are unilateral in nature in this patient, therefore we are unable to comment on possible coherence between legs.

Spasms During FES-Assisted Standing

The patient is able to stand for prolonged periods of time using FES. Throughout this time he experiences regular spasms.

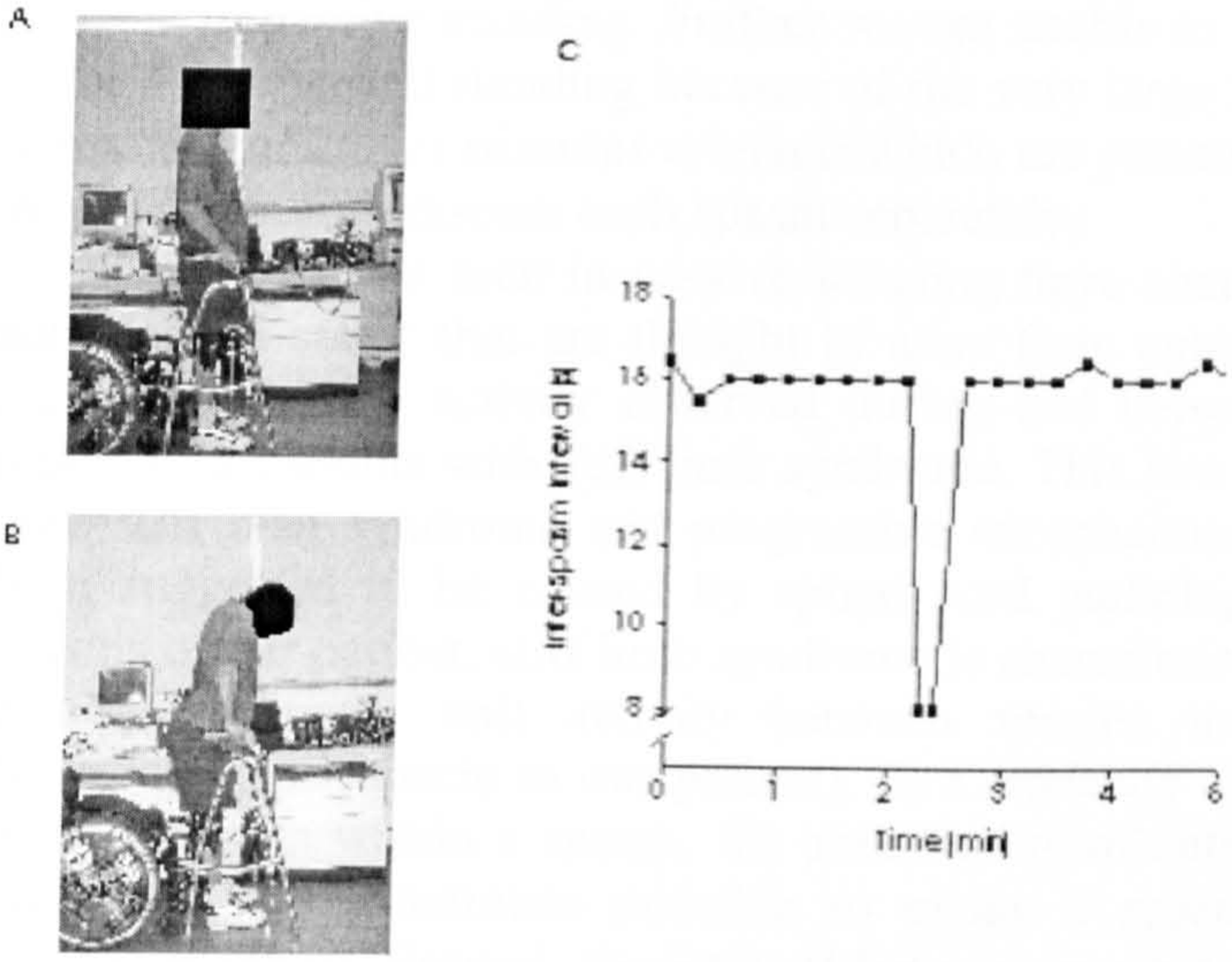

Figure 3: **A** shows the patient during a period of spasm free FES-assisted standing. **B** illustrates the change of posture during a spasm. **D** shows the inter-spasm-interval during FES-assisted standing.

The patient is shown both in a spasm-free standing posture (figure 3A) and during a trunk/hip flexor spasm (figure 3B) in which the patient is thrown forward at the waist. During spasm-free FES-assisted standing the patient appears relaxed and is carrying little weight through the arms. In contrast during a spasm there is a transfer in weight bearing from the lower to the upper limbs[12]. The occurrence of the spasms is rhythmic, with the majority of inter spasm intervals being very close to 16 seconds although occasionally this would halve (figure 3C).

Unstimulated muscles show an increase in muscle activity for the duration of the clinically observable spasm. The behaviour of stimulated muscle (quadriceps muscle groups) is different. In stimulated muscle there is a short latency reflex component of muscle activity that starts concurrently with the onset of the spasm, but outlasts the clinically observed spasm.

DISCUSSION

The rhythmicity and severity of the spasms experience by this patient are unusual. The patient had a rhizotomy accompanying his first sacral root bladder implant. Such procedures may be used to reduce spasticity and spasms, [13 & 14]. In this patient, although the rhizotomy prevented dyssynergic bladder problems, the total surgical procedure resulted in increased spasms. Similar results have been reported in a few (7/50) patients undergoing implantation of a sacral root stimulator which is normally accompanied by a posterior rhizotomy[15]. Clinically, his lesion is complete and remained stable from the time of the original injury until the development of the syringomyelia, (after the completion of the study reported here). Although it is impossible to rule out totally the possibility of some fibres crossing the lesion site[16] all of the stimulation tests we performed support the view that the lesion is complete.

We recorded spasms under two different conditions; FES-assisted standing and passive standing. Although behavioural responses to the spasms in these two standing conditions appear clinically similar it is uncertain whether they share the same mechanism. The inter spasm interval is regular in FES-assisted standing and

variable in passive standing. Further we are unable to assess intra-spasm rhythmicity in the FES-assisted standing because of the very large 20Hz (and harmonics and sub-harmonics of 20Hz) stimulus artefacts which are present even in unstimulated muscle. We will therefore discuss each spasm separately.

The spasms seen in passive standing have characteristics that resemble other pathological states that are thought to arise from spinal cord dysfunction. First, the pattern of muscle activity observed during and between spasms is similar to that reported in patients with stiff limb syndrome. This is a syndrome that is distinct from both stiff man syndrome and progressive encephalomyelitis with rigidity[17] and has been suggested to be caused by spinal cord pathology[18&19]. In common with the spasms of our patient, stiff limb syndrome is characterised electrophysiologically by i) continuous motor unit activity between spasms in at least one limb muscle (gastrocnemius muscle in our patient), ii) a tendency of repetitive grouped discharge of motor units within a spasm, iii) abnormality of cutaneomuscular reflexes (in our patient it was sometimes possible to evoke a spasm by presumed non-noxious cutaneous input). Second, the interval between spasms, which is 13.6s on average in our study, is similar to that seen in periodic leg movements during sleep (PLM) and restless leg syndrome. These involuntary leg movements tend to occur with a frequency of 0.1 – 0.05Hz and are thought to originate in the spinal cord. Patients with spinal lesions experience PLM[20] and both of PLM and restless leg syndrome are more common during sleep in otherwise neurologically normal subjects when central descending inhibition onto spinal circuits may be reduced[21]. Presumably, similarities in our patient to these different pathological states could arise from partial deafferentation and loss of descending propriospinal and/or supraspinal control of the lower spinal cord.

Within the spasm recorded during passive standing the autospectra of the EMG of all four muscle groups studied show a peak at around 10Hz, which seems too high a frequency for it to be classified as clonus[22]. This 10Hz rhythm is strongly coherent between any ipsilateral pair of muscles and presumably is sustained by activity solely in spinal networks. This raises the interesting possibility that oscillations of similar frequency seen in intact subjects may also be spinal in origin. For example, Masani and colleagues, (Personal communication.) have shown in healthy subjects a similar pronounced ~9Hz component in ankle extensor muscles during quiet standing. The 10Hz component also overlaps with the common frequencies for both essential tremor and enhanced physiological tremor[23].

Why do the spasms arise so regularly in this patient during FES-assisted standing? We suggest that the regular stimulation entrains the neural circuits that generate the spasms. One possibility is that this occurs through the interaction of two oscillators, one within the network of the spasm generator and the other through the fixed stimulation cycle. An underlying spinal oscillation may be inferred from the data obtained during passive standing. The spasms may arise when the stimulation and spinal oscillations are in phase and inhibited when out of phase. However, if this is true then it might be expected that a change in the stimulation frequency would lead to a change in the frequency with which the patient experiences spasms during FES-assisted standing. Unfortunately we were unable to test this prediction before the patient had a partial cordectomy as treatment for a syringomyelia which developed after the experiments described here.

The unusual and highly stereotyped and rhythmical spasms experienced by this patient offer an insight into the potential of the isolated spinal cord for generating oscillations and interpreting sensory information.

Acknowledgements

We wish to thank our patient for his time and input into these experiments. We would like to acknowledge the help of Carol McFadden in performing the repeat assessment of the patient and Dr Nick Donaldson and Mr Tim Perkins with some of the experiments. Dr Jonathan Cole provided advice. A UCL Graduate School Research Scholarship supported JAN. We acknowledge financial support from the MRC and the Wellcome Trust.

REFERENCES

1. Grundy D, Swain A. *ABC of Spinal Cord Injury*. BMJ publications, London. 1996.
2. Sherrington CS. Flexion-reflex of the Limb, Crossed Extension Reflex, and Reflex Standing and Stepping. *Journal of Physiology* 1910; 40: 28-121.
3. Grillner S and Wallen P. Central Pattern Generators for Locomotion, with Special Reference to Vertebrates. *Annual Reviews of Neuroscience* 1985; 8: 233-261.
4. Brindley GS, Polkey CE, Rushton DN (1982) Sacral Anterior Root Stimulators for Bladder Control in Paraplegia. *Paraplegia* 1982; 20: 365-381.
5. Wood DE, Harper VJ, Barr FMD, Taylor PN, Phillips GF, and Ewins DJ. Experience in Using Knee Angles as Part of a Closed Loop Algorithm to Control FES Assisted Paraplegic Standing. *Proceedings of the 6th Vienna International Workshop on Functional Electrostimulation.* 1998; 137-140.
6. Rossini PM, Barker AT, Berardelli A, Caramia MD, Caruso G, Cracco RQ, Dimitrijevic MR, Hallet M, Katayama Y, Lucking CH, Maertens de Noordhout AL, Marsden CD, Murray NMF, Rothwell J, Swash M, Tomberg C. Non-invasive Electrical and Magnetic Stimulation of the Brain, Spinal Cord and Roots: Basic Prinicples and Procedures for Routine Clinical Application. Report of an IFCN Committee. *Electroencephalography and Clinical Neurophysiology* 1994; 91: 79-92
7. Britton TC, Day BL, Rothwell J, Thompson PD, Marsden CD. Postural eletromyographic responses in the arm and leg following galvanic vestibular stimulation in man. *Journal of Physiology* 1993. 94: 143-151.
8. Goldberg JM, Smith CE, Fernandez C. Relation between discharge regularity and responses to externally applied galvanic currents in vestibular nerve afferents of the squirrel monkey. *Journal of Neurophysiology.* 1984. 51: 1256.
9. Donaldson N, Yu Ch. FES Standing: Control by Handle Reactions of Leg Muscle Stimulation. (CHRELMS). *IEEE Transactions on Rehabilitation Engineering* 1996; 4: 280-284.
10. Brindley GS. Surgeon's and Physician's Notes for Guidance on the Finetech/Brindley Sacral Root Stimulator. Finetech. 1998.
11. Halliday DM, Rosenberg JR, Amjad AM, Breeze P, Conway BA, Farmer SF. A framework for the analysis of mixed time series/point process data--theory and application to the study of physiological tremor, single motor unit discharges and electromyograms. *Progress in Biophysics and Molecular Biology* 1995; 64(2-3): 237-78.
12. Wood DE, Norton JA, Day BL, Marsden J. Flexor spasms observed in a low thoracic complete paraplegic. Proceedings of IFESS 2002, Ljubjana, Slovenia. Accepted. In press 2002.

13. Fukuhara T, Najm IM, Levin KH, Luciano MG, Brant CL. Nerve Rootlets to be Sectioned for Spasticity Resolution in Selective Dorsal Rhizotomy. *Surgical Neurology* 2000; 54: 126-133.
14. Eschenfelder S, Habler HJ, Janig W. Dorsal Root Section Elicits Signs of Neuropathic Pain Rather than Reversing them in Rats with L5 Spinal Nerve Injury. *Pain* 2000; 87: 213-219.
15. Brindley GS & Rushton DN. Long Term Follow-up of Patients with Sacral Anterior Root Stimulator Implants. *Paraplegia* 1990; 28(8): 469-475.
16. Kakulas BA. A Review of the Neuropathology of Human Spinal Cord Injury with Emphasis on Special Features. *Journal of Spinal Cord Medicine* 1999; 22: 119-124
17. Barker RA, Revesz T, Thom M, Marsden CD & Brown P. Review of 23 Patients Affected by the Stiff Man Syndrome: Clinical Subdivision into Stiff Trunk (Man) Syndrome, Stiff Limb Syndrome, and Progressive Encephalomyelitis with Rigidity. *Journal of Neurology, Neurosurgery and Psychiatry* 1998; 65: 633-640.
18. Brown P, Quinn NP, Barnes D, Wren DR & Marsden CD. Spinal Rigidity Following Acute Myelitis. *Movement Disorders* 1997; 12(6): 1056-1059.
19. Brown P, Rothwell JC & Marsden CD. The Stiff Leg Syndrome. *Journal of Neurology, Neurosurgery and Psychiatry* 1997; 62: 31-37.
20. Hartmann M; Pfister R; Pfadenhauer K. Restless Legs Syndrome Associated with Spinal Cord Lesions. *Journal of Neurology Neurosurgery and Psychiatry* 1999; 66: 688 689
21. Allen RP, Earley CJ. Restless Leg Syndrome. A Review of Clinical and Pathological Features. *Journal of Clinical Neurophysiology* 2001; 18(2): 128-147.
22. Hidler JM, Rymer WZ. Limit Cycle Behaviour in Spasticity: Analysis and Evaluation. *IEEE Transactions on Biomedical Engineering.* 2000;47(12): 1565-1575.
23. McAuley JH, Marsden CD. Physiological and Pathological Tremors and Rhythmic Central Motor Control. *Brain* 2000; 123: 1545-1567.

Appendix 7.

Presented at the IFESS conference in Aalborg, DK, June 2000.

The Determinants of Posture in Paraplegics Standing using Lumbar Anterior Root Stimulation

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Abstract

We have measured the hip extension moment in a patient standing using anterior nerve root stimulation. We present a novel method for calculating the mass properties of the leg using a 3D laser scanner.

The joint moments when standing are not significantly different from those recorded in the recumbent posture. We asked the patient to alter the hip angle and present data that suggests that the poor standing posture of the patient may partly be due to a sharp increase in the flexion moment as the hip extends.

Only slight changes in both M-wave and non M-wave activity were seen in a number of muscles. As such we believe that the primary reason for the poor posture seen in this patient is biomechanical rather than neurophysiological in nature.

Keywords: LARSI, joint moments, laser scanning,

1.Introduction

One of the difficulties of using nerve root stimulation to restore leg function to paraplegics is the complexity of the responses to the stimuli, [3,7]. In the British project we have previously described a system for measuring 14 isometric leg joint moments whilst the patient is seated or recumbent, [2,10], the MMCS. Relating these measures to the standing posture is not easy.

The subject stands with excessive lordosis and carries a lot of weight through her hands. This occurs even when our best stimulation pattern is used. What can we do about this? Can we be confident that any future surgical procedure will improve the situation?

We hypothesised that there could be one or more causes for the poor posture; (1) the flexibility of the abdomen between the stimulated legs and the neurologically intact upper body, the subject is a T9 paraplegic; (2) that it is impossible for her to apply forces at the support handles so as to improve her posture; and (3) that there is non M-wave activity, both reflex and of other origin, within the paralysed muscles.

To investigate these possibilities, we calculated joint moments, measured joint angles and recorded EMGs, when standing and compared them to those obtained when recumbent.

2. Method.

2.1. The Subject.

Patient 1 in the British project has been described elsewhere, (see for example [6]). She is a complete T9 paraplegic who had Lumbo-sacral Anterior Root Stimulator Implant, LARSI, implanted in December 1994. The roots L2-S2 bilaterally were placed in tripolar electrode books, [3]. Standing with the implant is not functional because of apparent excessive hip flexion and lordosis. However, passive standing using an Oswestry Standing Frame gives a good posture, indicating that there is no skeletal problem that prevents good standing. She has previously demonstrated the ability to take up to 24 steps in the laboratory (with assistance because of excessive adduction); also the ability to tricycle over 1km on road, [6]. We have previously demonstrated a significant innervation to the hip flexor muscles from roots used in the standing pattern in this patient using needle EMG, [7].

2.2. Calculation leg mass and centre of mass.

One of the besetting problems within biomechanics has been the accurate calculation of the mass and centre of mass of subjects' limbs. The traditional route to solve this problem has been the use of tabulated data from extensive surveys. Within each study there is good agreement upon the results, but there is poor agreement between studies, indicating that the selection of population is important. However, this method also has a problem when considering individuals. It assumes that people conform to the average population. When considering the disabled population this problem is accentuated. In fact studies have shown how poorly the disabled (SCI) population fit the existing tables, [8]. For the subgroup of patients who use FES, and are therefore unlike the "normal" disabled population in terms of leg mass and muscle bulk, an interesting question arises: will they be better served by a "disabled" model or a "normal" model? Since the differences in leg joint moments between the recumbent and standing positions are likely to be small, an accurate method of calculating the mass properties of the leg was needed. A previous study using two established methods has found estimates of the leg mass of this subject of 9.19kg and 11.75kg respectively, [9]. This size of error, (28%) is unacceptably large for this type of work.

If we could individually determine the mass of the leg and its centre of mass we would not have to rely upon sampled population data. To do this a fast, (at least for the patient), non-invasive technique is needed. The method we have chosen utilises a 3D near infra-red whole-body laser scanner[2] [4].

The use of such a technique is not entirely new, (cf Jones & Rioux [5]). However its use to calculate the mass properties, mass and centre of mass, of the leg is novel. To achieve steady standing subjects stand in a specially constructed mobile Oswestry Standing Frame, OSF. They therefore stand passively, not using FES.

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[2] Hamastua's Body Lines Scanner. Japan,

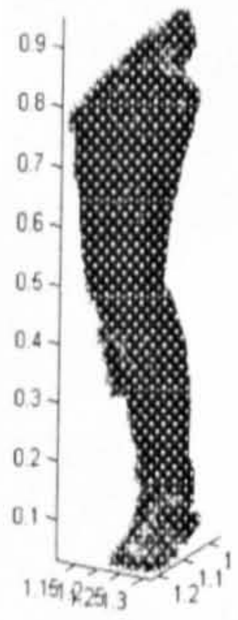

Figure 1. The reconstructed, sliced leg from the laser scanner data set.

Several scans are taken and the data set is output as a text file. The images are visually inspected and rotated to ensure completeness and absence of movement artefact. Each scan takes just 10 seconds, short enough to allow a paraplegic to stand steadily in an OSF for several scans at a time.

The mass properties are calculated by numerical integration and using published densities for soft tissue and for bone. The size of the bones is estimated from the female data in the Visible Human Project[3]. This is digitally re-scaled to fit the x-ray image and scan size of the patient.

2.3 Standing experiments.

The subject had surface EMG electrodes applied to muscles on the right side: Paraspinals, Glutei, Rectus Femoris, Hamstrings, Gastrocnemius and Adductors. Muscle activity during stimulation with the standing pattern, whilst the subject is extended on a physiotherapy plinth, was recorded. EMG is also recorded whilst the subject stood without stimulation in an OSF.

[3]URL:http://www.dhpc.adelaide.edu.au/projects/vishuman2/index.html

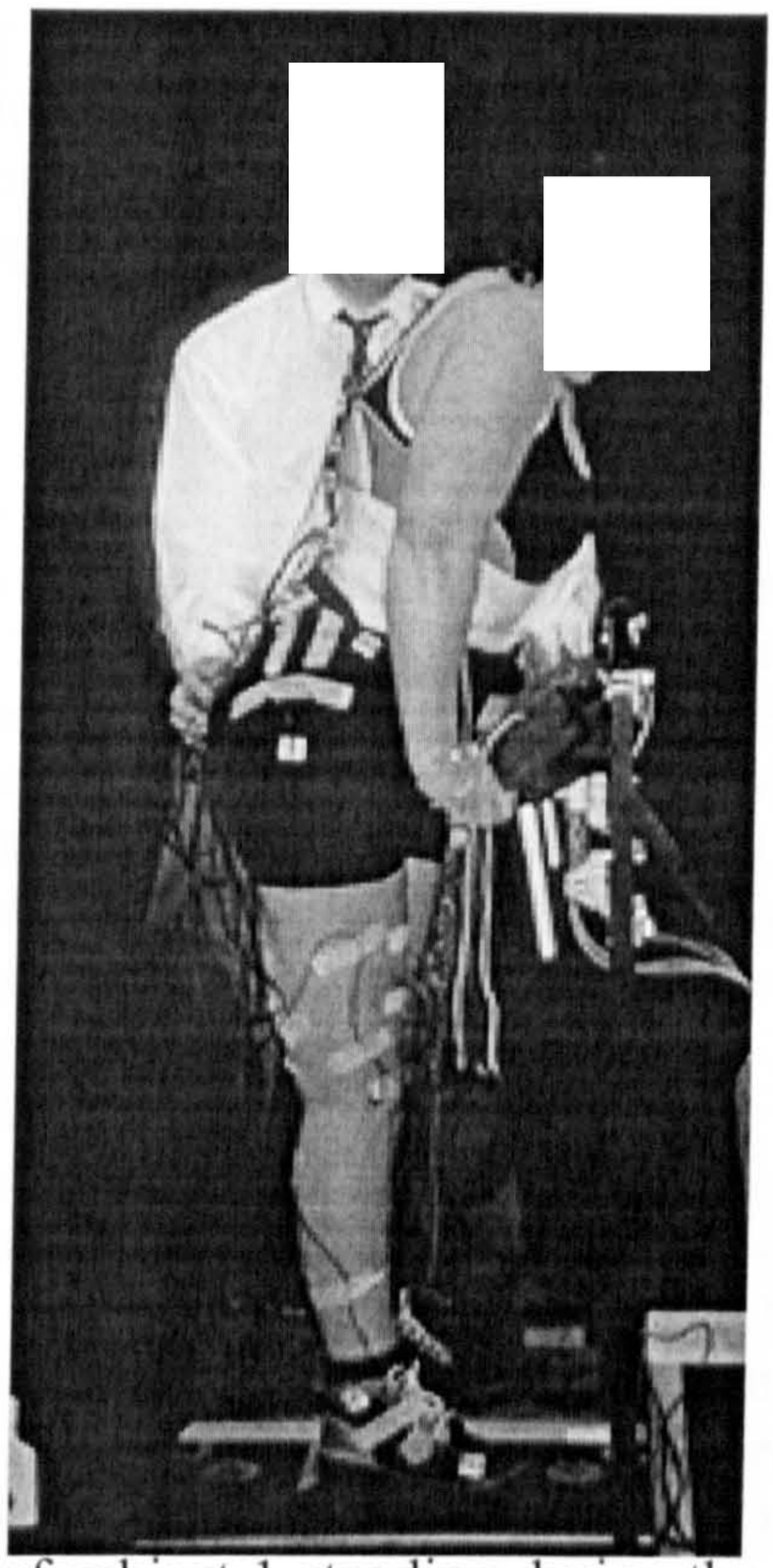

Figure 2. A photo of subject 1 standing during the experiment. The LEDs and EMG electrodes can be clearly seen. This figure is represented in figure 3. Note the deflections on the handles indicating the amount of force being carried by the arms.

A position-measuring system, Selspot, is used to record the patient's posture in 3D space. Infra-red LEDs were placed over the leg joints and the spine of the subject. The positions marked were; T2, (a) and L2, (b) vertebrae, the front, (d) and back, (c) of iliac crests, the greater trochanter, (e), knee, (f), ankle, (g), (lateral malleoli) and the little toe, (h) on the right. All of the stands using FES were performed with the same stimulation pattern. This has been selected on the basis of the joint moments recorded in the MMCS. The primary consideration is to obtain the maximum knee extension to hip flexion ratio, that is the maximal amount of knee extension with the least amount of hip flexion, and without unwanted responses, e.g. inversion, [7].

During these tests the patient stands with each leg on a force platform[4]. The patient uses handles for support, which contain six-axis load cells, as described by Donaldson and Yu [1].

2.4. Results analysis.

EMG records were sampled at 1kHz (passband 16Hz-300Hz). Forces and moments from the handles were also sampled at 1kHz. The force plate and position data was sampled at 50Hz. The two recording computers were synchronised to within 2ms over the test period. The force data was plotted using Matlab[5] and displayed as a "movie" to allow a visual inspection of the changes in the forces and the posture to be seen. Joint moments were calculated at typical periods for each stand. The handle

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[4] Kistler force plates. Kistler Instrumente AG
Winterthur CH.

[5] The Maths Works inc. supplied by Cambridge Control Ltd, Cambridge, UK.

reaction vectors, [1], and the ground reaction vector for the right leg were plotted on the same axes as the positions of the LEDs.

Visual analysis of the EMGs was carried out to prevent loss of non-time locked data through averaging.

3. Results.

3.1 Biomechanical results.

The validation of the laser scanning method for determining mass centres will not be presented here. The worst case error in calculating the hip joint extension moment using the laser scanner, force plate and Selspot system is less than 4Nm.

The patient carries a large proportion of her body weight through her arms. The right arm carries significantly more than the left, which corresponds to a clinical finding that the left leg is less flexed than the right. The right GRV only has just enough vertical force in it to correspond to the mass of the leg, suggesting that the rest of the ½ body weight is carried through her arms. This explains why the patient gets tired very quickly when standing

When the joint moments are calculated, they are very similar to those seen in measurements taken in the MMCS. Three out of the previous 4 tests with this pattern have given a joint moment of between 10 and 15Nm of hip flexion. The exception came during a test in which it was noted that the subject was extremely fatigued.

The hip angle in figure 4 is the angle between the vectors fe and ed in figure 3. An angle of around 35° would be expected for full hip extension in a normal standing posture.

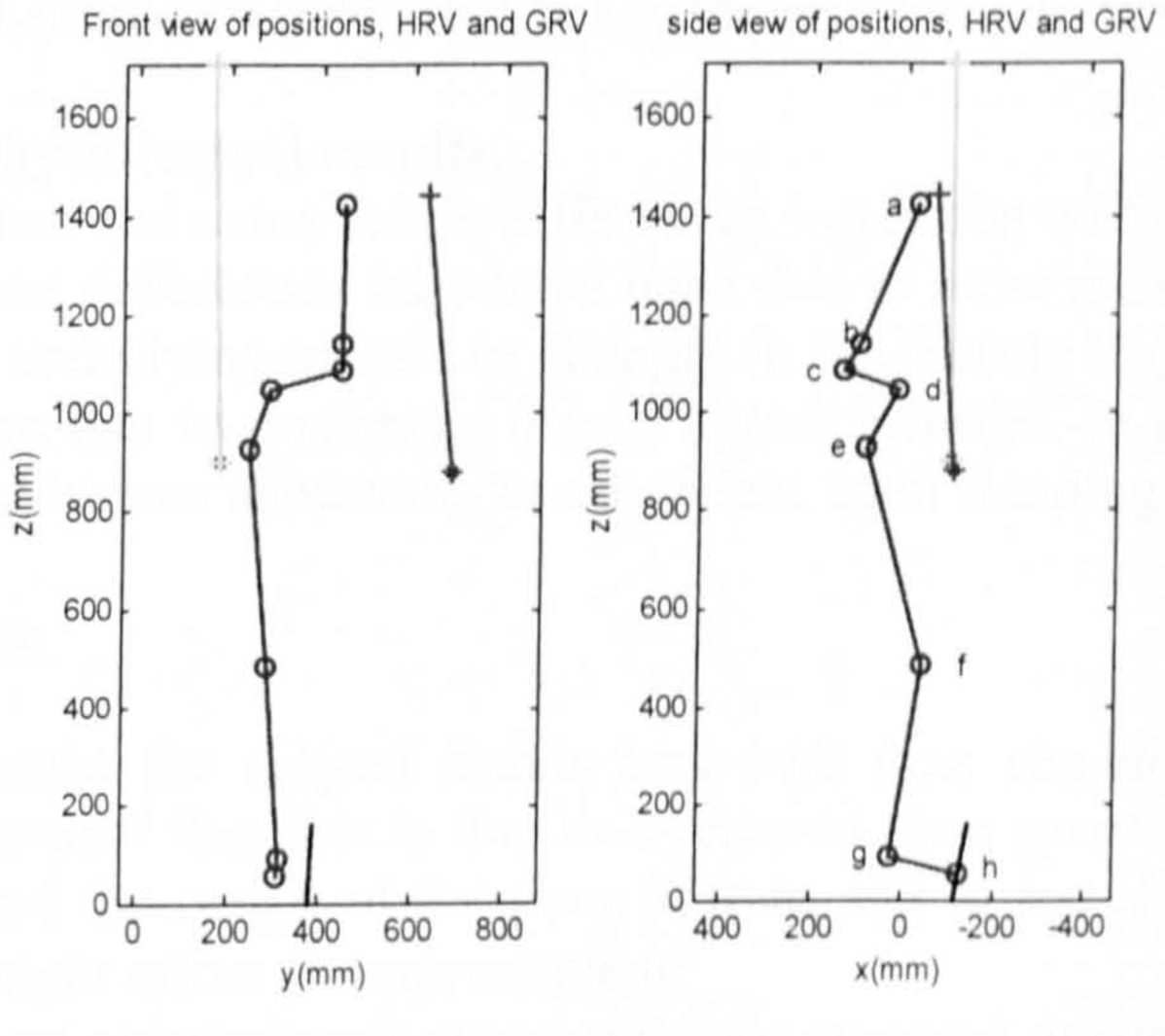

Figure 3. A plot of the posture of the patient (o-), and the ground reaction vector and the two handle reaction vectors. Note only one GRV is plotted. The scale for the GRV and the HRVs are 0.5N/mm.

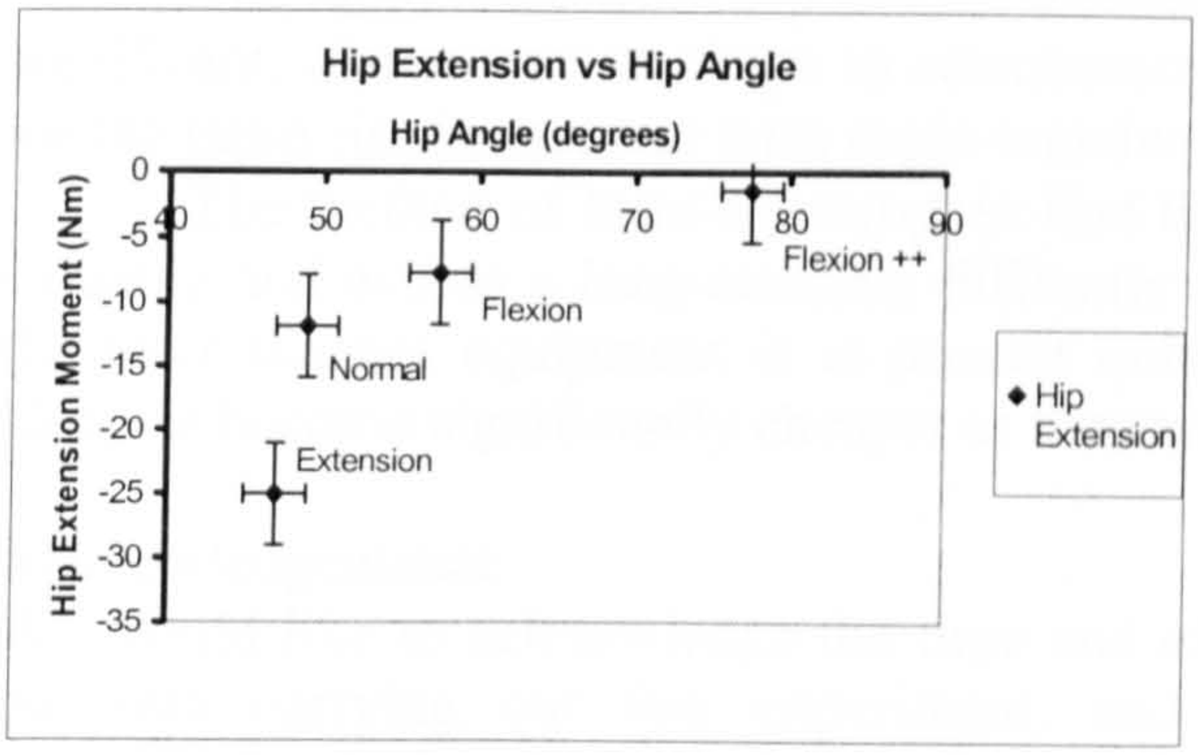

Figure 4. Plot of the Hip angle against the Hip Extension Moment. Note that all the moments are negative, meaning that the moment is flexing the hip. Error bars give the max and min measured result, with the mean as the point, samples of 3 for each angle, with a corresponding moment.

The hip flexion moment (figure 4) decreases as the amount of hip flexion increases. The gradient gives the change in moment per degree change in hip angle. To the right of the "normal" standing posture this is 0.36Nm/°. This compares with a value of 0.29Nm/° recorded in the MMCS. However when the patient tries to extend her hips beyond "normal" the amount of flexion moment increases dramatically, by about 10Nm. Such an increase would significantly hinder her ability reaching a better posture, but it should be noted that this is the result of only one experiment.

3.2. Electrophysiological results.

Some minor and some subtle differences were seen with the change from lying to standing. Minor differences may have been due to movements of the electrodes with respect to the underlying muscle or changes in the muscle lengths. Some subtle effects may have been due to posturally driven spinal reflexes. In particular an extra 10Hz reflex in the adductors appears to be dependent upon standing posture.

4. Conclusions.

At present the subject stands less well than she did at one time with the implant. We expect that this is due to a reduced time spent exercising. Nevertheless we wish to find the origin of the poor posture and to see if any medical or surgical intervention might effect an improvement.

Her short standing endurance and poor standing posture are accompanied by a significant right hip flexion moment. However, we have found that this moment is not greater than we measure in the MMCS while she is recumbent. Furthermore, we saw no significant non-M-wave EMG activity in Rectus Femoris or in Iliacus (at an earlier experiment, not reported here) which would have caused greater hip flexion moment. We therefore conclude that the third hypothesis, listed in the Introduction, is untenable: the cause of her poor posture is essentially biomechanical rather than physiological in nature. We will use this data to investigate the first two hypotheses.

The rapid increase in hip flexion moment, seen only in this experiment, is very significant, if true, and we hope to corroborate it. What muscle could be responsible for the rapid rise in moment with angle remains a matter of conjecture.

The method of laser-scanning, to find the leg mass properties of individuals is valuable and avoids a long-standing difficulty in experimental biomechanics. While the laser scanner equipment is at present quite expensive (circa £40,000), they are likely to become significantly cheaper as they are adopted by bespoke tailors.

Acknowledgements.
We would like to acknowledge the time and effort that our subject and her husband put into carrying out this experiment, and thank her husband for taking the photographs during the experiment. We would also like to thank Jon Marsden and Celia Coutinho of the HMBU for providing practical support during the experiment. J. Norton is supported by a Graduate School Research Scholarship from University College London. Some of the support came from the NHS Executive; the views expressed here are those of the authors and not necessarily those of the NHS Executive.

References.

1. Donaldson N & Yu C-h. (2000). Experiments with CHRELMS patient-driven stimulator controllers for the restoration of function to paralysed legs. *Proc. Instn. Mech Engrs Part H.* 214. 1-20
2. Donaldson NdeN, Munih M, Perkins TA & Wood DE. (1999). Apparatus to measure simultaneously 14 isometric leg joint moments. Part 1: Design and calibration of six-axis transducers for the forces and moments at the ankle. *Med Biol Eng Comp.* 37. 137-147.
3. Donaldson N, Rushton D & Tromans T. (1997). Neuroprosthesis for leg function after spinal-cord injury. *Lancet* 350 711.
4. Horiguchi C. (1998). BL (Body Line) Scanner. The development of a new 3D measurement and reconstruction system. *Int. Arch. Phot Rem. Sens.* 32(5) 421-429.
5. Jones PRM & Rioux M. (1997). Three-dimensional Surface Anthropometry: Applications to the Human Body. *Optics and Lasers in Engineering.* 28 89-117
6. Perkins TA, Donaldson NdeN, Harper VJ, Norton J, Tromans AM, Wood DE & Rushton DN. (1998). Standing, stepping and cycling for a T9 paraplegic with a Lumbo-sacral Anterior Root Stimulator Implant. *IFESS CDROM & Proc of IFESS ('98).*
7. Rushton DN, Perkins TA, Donaldson NdeN, Wood DE, Harper VJ, Tromans AM, Barr FMD & Holder DS. (19997). LARSI. How to obtain favourable muscle contractions? *Proc. IFESS ('97).* 163-4.
8. Stein RB, Zehr P, Lebiedowska MK, Popovic DB, Scheiner A & Chizeck HJ. (1996). Estimating Mechanical Parameters of Leg Segments in Individuals with and without Physical Disabilities. *IEEE Trans Rehab Eng.* 4(3) 201-211.
9. Van der Herberg E. (1997). Leg joint moments during paraplegic standing with lumbar root stimulation. *M.Sc Thesis. (Universiteit Twente and University College London).*
10. Wood DE, Donaldson NdeN & Perkins TA. (1999). Apparatus to measure simultaneously 14 isometric leg joint moments. Part 2: Multi-moment chair system. *Med. Biol. Eng. Comp.* 37 148-154.

Appendix 8.

Presented at the Federation of European Neuroscience Societies, Paris, FR, July 2002.

Load-Dependent Spinal Oscillations During Functional Electrical Stimulation-Assisted Standing in Paraplegics.

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2. Implanted Devices Group, Department of Medical Physics and Bioengineering University College London, London, UK and
3. Department of Medical Physics and Biomedical Engineering, Salisbury District Hospital, Salisbury, UK.

Following a complete spinal cord transection the cord below the lesion remains intact and plastic and is capable of generating muscle activity either intrinsically or reflexively. We have investigated the oscillatory behaviour of such activity in two paraplegic subjects when they stand using Functional Electrical Stimulation (FES). Subjects stood either with the aid of FES or passively in a standing frame. During FES-assisted standing they stood on a pair of force plates and used instrumented handles for balance and for extra support. The position of their body was recorded in 3D space (CODA or Selspot) and surface EMG records were taken from major leg muscle groups.

In one subject, with a complete T10/11 lesion, spasms were observed regularly every 16s during FES-assisted steady-state standing. Spasms also occurred, although less regularly, during passive standing. During a spasm, frequency domain analysis of the EMG records demonstrated a 10Hz peak that was coherent between muscles. In the second subject, with a complete T10 lesion, spasms occurred only during the dynamic sit-to-stand procedure. These spasms resulted in large 8Hz oscillations that were conspicuous in EMG records and also in vertical and horizontal forces applied through the feet and hands. These spasms lasted for 3 to 5 seconds and were not present during the remainder of the stand. They were not observed when the same stimulation parameters and stretching procedures were carried out with the patient recumbent.

We conclude that the isolated spinal cord of paraplegics exhibits the potential to generate significant muscle activity that is rhythmic in nature. Part of this oscillatory activity appears to be dependent upon loading of the legs and may occur during dynamic or static loading in different subjects.

We wish to thank the subjects and the rest of the teams in London and Salisbury. Financial support is acknowledged from the UCL Graduate School, Wellcome Trust and the MRC.

Appendix 9.

Presented at the Physiological Society UCL, December 2002. Proceedings of the Physiological Society 547P C147.

Cessation of Paraplegic Spasms by Combined Neuromuscular Stimulation and Standing.

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3. Department of Medical Physics and Biomedical Engineering, Salisbury District Hospital, Salisbury, Wilts. UK.

Patients with complete paraplegia frequently suffer from muscles spasms and spasticity. Electrical stimulation of the posterior nerve roots has been demonstrated to stop spasms in a paraplegic patient in a pilot study, (Craggs *et al* 2000).

In this study we used peripheral electrical stimulation to investigate neuromodulation of spasms. The patient, a 59 year old male, had a complete spinal cord lesion at the 9th thoracic level of 20 years duration and a S2-5 posterior rhizotomy. Peripheral stimulation was applied at 20Hz using a Stanmore stimulator (Phillips *et al* 1993). All experiments were approved by the local ethics committee and the patient gave informed consent.

The patient experienced ongoing dorsiflexion spasms at rest. These slow events had a characteristic pattern of onset and an interspasm interval of between 3 and 30 seconds. Figure 1 shows surface EMG recorded from the lower leg with the patient at rest.

Stimulation of the quadriceps to produce a muscle contraction did not affect the spasms. Passive standing within a standing frame stopped the spasms, but they reappeared after 5 minutes. When pressure was applied to the soles of the feet and stimulation applied there were no changes in the spasms. Standing with stimulation stopped the spasms entirely. The vertical force taken by the legs was 410±5N during passive standing and 459±24N (mean±sd) during FES-assisted standing. The patient reports that such a procedure typically stops the spasms for 7 hours. Rapid dorsiflexion restarted the spasms with the same pattern and frequency as before the stimulated stand.

This study further demonstrates, in one patient, the potential of neuromodulation as a technique for spasm suppression in paraplegic patients.

Craggs M, Knight S, Kirkham A, Casey A and Middleton F (2000). Sacral Nerve Neuromodulation for Lower Spasm and Spasticity in Spinal Cord Injury. *Spinal Injury, New Horizons Conference.*
Phillips GF, Adler JR &Taylor SJG (1993). A Portable Programmable Stimulator for Surface FES. *International FES Society Conference.* 166-168.

We wish to thank our patient. This work was supported by the UCL Graduate School, MRC and Wellcome Trust.

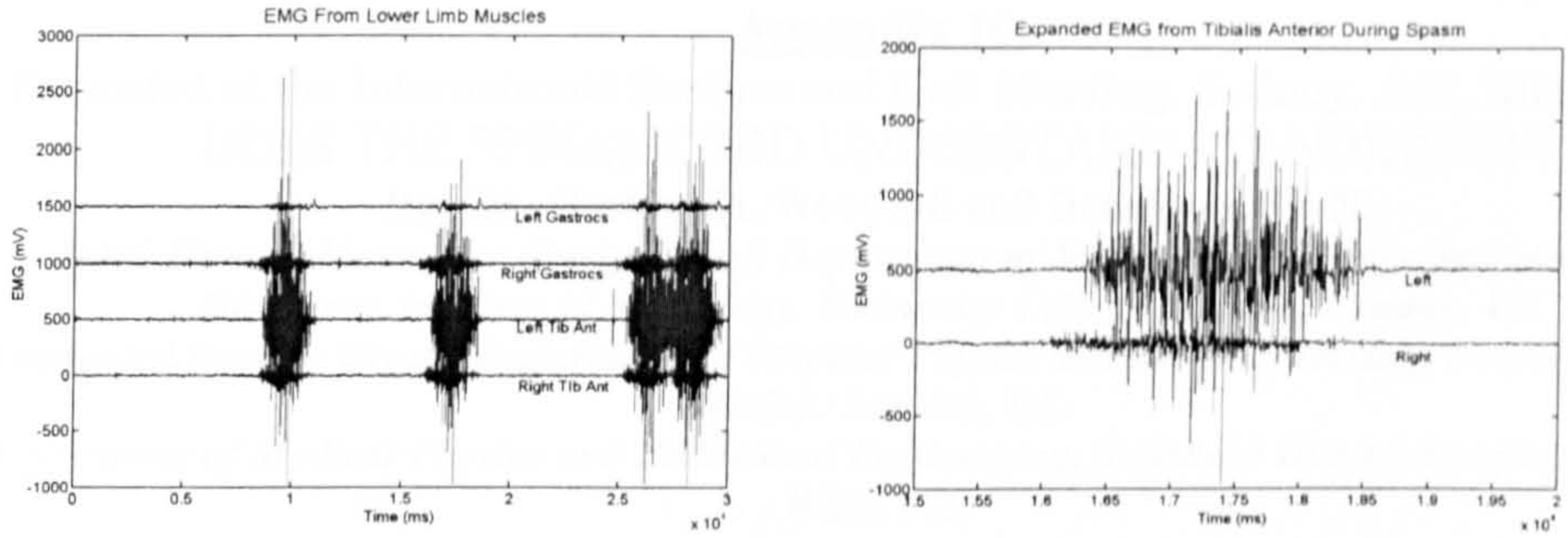

Figure 1. Surface EMG from lower leg muscles. A shows a 30 second record illustrating the spasms as discrete events between quiet periods. In B a spasm is expanded for the tibialis anterior muscle. The right tibialis anterior muscle leads the left and the EMG is fractionated.

Appendix 10.

Presented at the International Posture and Gait Meeting, Sydney, Aus, March 2003.

DOES THE SPINAL CORD UNDERSTAND STANDING UP?

Day BL, Norton JA, Wood DE and Donaldson NdeN.

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Introduction:

Paraplegics can be assisted to stand with Functional Electrical Stimulation (FES) of the quadriceps to provide knee extension [1]. During a stand, the spinal cord receives a unique pattern of somatosensory input produced by the posture, the body weight and the peripheral stimulation all of which may influence the state of the spinal cord [2]. Below the level of the lesion the spinal cord operates on this input in isolation from higher centres. In the present study we have investigated whether the isolated spinal cord is capable of responding to the stand-related input by measuring changes in muscle activity and forces from the lower limbs in a group of paraplegic subjects.

Methods:

Experiments were carried out with local ethical committee approval and all subjects gave fully informed consent. Four paraplegics with complete motor lesions were recruited from a supra-regional FES centre. Three were experienced FES-users. Subjects started from a sitting posture and with the aid of 20Hz stimulation of quadriceps muscles pulled themselves into a standing posture using handles mounted on 6-axis force transducers (JR3). The ground reaction forces were recorded separately under each foot using 2 force plates (Kistler). The posture and leg muscle activity were recorded using CODA and a MIE-8 telemetry system respectively.

Results:

Three distinct phenomena were observed all of which were specific to the act of standing and involved oscillatory muscle activity. 1) In 2 subjects a large bilateral 8 Hz leg tremor appeared at a fixed point of the dynamic sit-to-stand phase. The tremor lasted for a variable period (max 10 s) becoming progressively shorter on subsequent stands of a session. 2) In 1 subject steady-state FES standing induced spasms which occurred cyclically every 16s. Spectral analysis of EMG revealed oscillatory activity (dominant frequency 10Hz) within each spasm. 3) 1 subject experienced regular spasms (every 3 to 30 s) when seated or supine. These spasms, which had oscillatory characteristics, (dominant frequency 8Hz both within and between legs), were abolished by FES standing. FES alone, or standing alone failed to abolish the spasms in the same manner.

Discussion and Conclusions:

The results suggest that oscillatory sensorimotor networks exist in the spinal cord. Somatosensory input interacts with these networks. The interaction seems to require the specific patterns of afferent input produced by standing since we have not been able to reproduce the effects by other means. When the stand is performed with FES the additional somatosensory inputs arising from the stimulation further alter the outputs of these sensorimotor networks. This raises the question of whether spinal cord oscillatory networks contribute to the control of normal standing.

References:

1. Wood DE, Harper VJ, Barr FMD, Taylor PN, Phillips GF & Ewins DJ. Proceedings of 6th Vienna International Workshop on Functional Electrostimulation. 1998. 137-140.

2. Dietz V & Duysens J. Gait Posture. 2000 11. 102-110.

Appendix 11.

Presented at the British Society for Clinical Neurophysiology, London, July 2001.
Published in Clinical Neurophysiology 112(12). 2331-2332.

EMG Responses to Chronic Anterior Nerve Root Stimulation in a Paraplegic,

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4. Department of Medical Physics and Biomedical Engineering, Salisbury District Hospital.

Abstract.

We are investigating the feasibility of lumbar-sacral anterior nerve root stimulation for the restoration of leg function in complete, mid-thoracic paraplegics. The patient described here is the first patient with this system and functional results, (including preliminary EMG results) from this patient, and a description of the system have been reported elsewhere[1,2,3].

As expected, a prominent feature of root stimulation is the co-activation of many muscle groups, often including antagonistic pairs. Muscle innervations were found to be asymmetrical in this patient, and more diffuse, (typically one root in either direction), than textbook values. Although reflexes and spinally generated EMG rhythms are seen, these are modest when compared to the M-wave responses of the stimulation. The responses have been stable for over 6 years.

The patient uses the system to maintain fitness and for recreational tricycling.

Reference List

1.Donaldson N, Rushton DN, Tromans AM. Neuroprothesis for Leg Function after Spinal Cord Injury. *Lancet* 1997;**350**:711.

2.Norton JA, Donaldson N, Day BL, Dekker L, Perkins TA, Rushton DN, Tromans AM, and Wood DE. The Determinants of Posture in Paraplegics Standing Using Functional Electrical Stimulation. IFESS 2000; 478-481.

3.Rushton DN, Perkins TA, Donaldson N, Wood DE, Harper VJ, Tromans AM, Barr FMD, Holder DS. LARSI: How to Obtain Favourable Muscle Contractions? *IFESS 1997* 1997;163-4.

Appendix 12.

Is the spinal cord the generator of 16Hz orthostatic tremor?

Norton JA, Wood DE & Day BL.

Submitted to the Annals of Neurology 2003.

Abstract:
Muscle activity at 16Hz is characteristic of primary orthostatic tremor. It has been suggested that this tremor originates in the brain. This view is questioned by findings from a patient with complete paraplegia who experiences intermittent leg spasms at rest. The electromyographic activity within the spasms showed a strong 16Hz component that was coherent between muscles unilaterally and bilaterally. This raises the possibility that orthostatic tremor arises in the spinal cord.

Tremors are commonly characterised by the frequency of their oscillations. Often there is overlap in the range of tremor frequencies found in different diseases[1]. However, there is one tremor syndrome, primary orthostatic tremor, with a frequency that is virtually pathognomonic. Primary orthostatic tremor is associated with synchronised bursting of muscle activity at a remarkably fast rate of around 16Hz [2]. Because of its high frequency the tremor is difficult to see with the naked eye but has a devastating effect on the patient in whom it produces a profound and disabling sense of unsteadiness when standing[3,4]. Patients are compelled to sit down or walk after a short time ranging from a few seconds to a few minutes depending upon the severity of the condition[4]. Although orthostatic tremor is generally thought to arise from a central oscillator it is not known where in the nervous system the oscillator is located. A number of reports have suggested possible supraspinal sites as the origin of this activity[5-9], including the brain stem[7], the motor cortex[8] and the pons and cerebellum[9]. Our present results question this view by showing that the human spinal cord, when disconnected from the brain, is capable of generating 16 Hz motor oscillations that are coherent between leg muscles.

With local ethical committee approval and the patient's informed consent we investigated muscle spasms in a patient with paraplegia arising from trauma over 20 years ago. The patient has a complete T10/11 lesion (confirmed radiologically and clinically) resulting in the total absence of sensation and voluntary motor activity below the level of the lesion. At rest (either seated or recumbent) he experiences intermittent spasms that last for 1-2s and occur every 1-30s. All spasms are bilateral and produce ankle dorsiflexion, knee flexion and hip flexion. Surface-recorded electromyographic activity showed synchronous bursts of muscle activity on both sides of the body during a spasm but no activity in the periods between spasms. Figure 1 illustrates the activity recorded from a unilateral pair of muscles separated by a joint (quadriceps and tibialis anterior from the right hand side) and a bilateral pair of muscles (left and right tibialis anterior). These muscles were chosen as illustrative but all muscle groups (right and left quadriceps, tibialis anterior and gastrocnemius) showed a similar pattern of activity.

Figure 1 near here.

Closer inspection of the EMG activity during a spasm often revealed fluctuating or oscillatory behaviour. Figure 2 shows an example of raw EMG (MIE Medical Ltd,

Leeds UK) and rectified, low-pass filtered EMG (low-pass at 50Hz) from the right tibialis anterior during a spasm. Oscillations are evident in the filtered signal. To study these oscillations further the EMG activity recorded during spasms was spectrally analysed using a Fourier approach[10]. Signals were sampled at 1kHz and analysis was performed on 124 non-overlapping samples of length 512, giving a frequency resolution of 1.95Hz. Analysis was performed using Matlab (Mathworks, Cambridge, UK.) and Neurospec (www.neurospec.org). Confidence limits were estimated using the approach described by Halliday *et al*[10].

Figure 2 near here.

Autospectra of the electromyographic activity from the right quadriceps and the right and left tibialis anterior are shown in figure 3. Clear peaks of activity at around 16Hz can be seen in muscles of the right leg. Also shown in figure 3 is the coherence between pairs of muscles. Coherence is a measure of the correlation between signals in the frequency domain and is measured on a scale from 0 (no correlation) to unity (perfect correlation) in each frequency bin. The EMG activity was coherent at 16Hz both between the unilateral muscle pair and between the bilateral muscle pair. Coherence at 16 Hz was evident between all combinations of muscles pairs studied. Phase plots showed that there was a consistent time lag between each pair of muscles in each band of coherence indicating that the activity did not arise from electrical cross-talk. Coherence was also found between the unilateral muscle pair in the 25-35Hz band.

Figure 3 near here.

In a different paraplegic patient with a complete T10-11 lesion, we previously showed that his muscle spasms have an oscillatory component that may arise from a spinal cord oscillator[11]. In that case the spasms were only seen during standing and had an oscillatory component at around 10 Hz. The manifestation of spasms in the present patient was different. His spasms occurred when lying or sitting and they had an oscillatory component at 16 Hz, a frequency that is characteristic of orthostatic tremor. Also, his 16Hz activity was coherent between muscles both within and between legs, again a characteristic of orthostatic tremor[5,6]. It is unusual for orthostatic tremor to be present unless the patient is standing (but see Boroojerdi *et al*[12]). However, the atypical expression of 16Hz oscillations in the current patient need not imply a different mechanism but may relate to his complete absence of descending control of the spinal cord.

The pattern of coherence seen here and in studies on primary orthostatic tremor, suggests that a proportion of the 16Hz activity arises from a common source. In our patient with a T10/11 spinal cord lesion the source is likely to be within the lumbosacral spinal cord.
This raises the possibility that 16Hz orthostatic tremor also originates from the spinal cord, although its expression may depend on abnormal descending control of the cord from supraspinal centres.

Acknowledgements.
We wish to thank the patient for taking part in this study. We would like to thank Dr Peter Brown for helpful discussions concerning this patient and manuscript and Dr Mike Cassidy for assistance with the spectral analysis. JAN was funded by the UCL Graduate School.

References

1. Deuschl G, Bain P, Brin M et al. Consensus Statement of the Movement Disorders Society on Tremor. Movement Disorders. 1998; 13:2-23
2. Thompson PD, Rothwell J, Day BL et al. The Physiology of Orthostatic Tremor. Archives of Neurology. 1986; 43:584-587
3. Heilman KM. Orthostatic Tremor. Archives of Neurology. 1984; 41:880-881
4. Fung VSC, Sauner D, Day BL. A Dissociation Between Subjective and Objective Unsteadiness in Primary Orthostatic Tremor. Brain. 2001; 124:322-330
5. McAuley JH, Britton TC, Rothwell J et al. The Timing of Primary Orthostatic Tremor Bursts has a Task-Specific Plasticity. Brain. 2000; 123:254-266
6. Koster B, Lauk M, Timmer J et al. Involvement of Cranial Muscles and High Intermuscular Coherence in Orthostatic Tremor . Annals of Neurology. 1999; 45:384-388
7. Wu YR, Ashby P, Lang AE. Orthostatic Tremor Arises from an Oscillator in the Posterior Fossa. Movement Disorders. 2001; 16:272-279
8. Tsai CH, Semmler JG, Kimber TE et al. Modulation of Primary Orthostatic Tremor by Magnetic Stimulation over the Motor Cortex. Journal of Neurology, Neurosurgery and Pyschiatry . 1998; 64:33-36
9. Benito-Leon J, Rodriguez J, Orti-Pareja M et al. Symptomatic Orthostatic Tremor in Pontine Lesions. Neurology. 1997; 49:1439-1441
10. Halliday DM, Rosenberg JR, Amjad AM et al. A Framework for the Analysis of Mixed Time Series/Point Process Data- Theory and Application to the Study of Physiological Tremor, Single Motor Unit Discharges and Electromyograms. Progress in Biophysics and Molecular Biology. 1995; 64:237-278
11. Norton JA, Wood DE, Marsden JF et al. Spinally Generated Electromyographic Oscillations and Spasms in a Low-Thoracic Complete Paraplegic. Movement Disorders. 2003; 18:101-106.
12. Boroojerdi B, Ferbert A, Foltys H et al. Evidence for a Non-Orthostatic Origin of Orthostatic Tremor. Journal of Neurology, Neurosurgery and Pyschiatry. 1999; 66:284-288

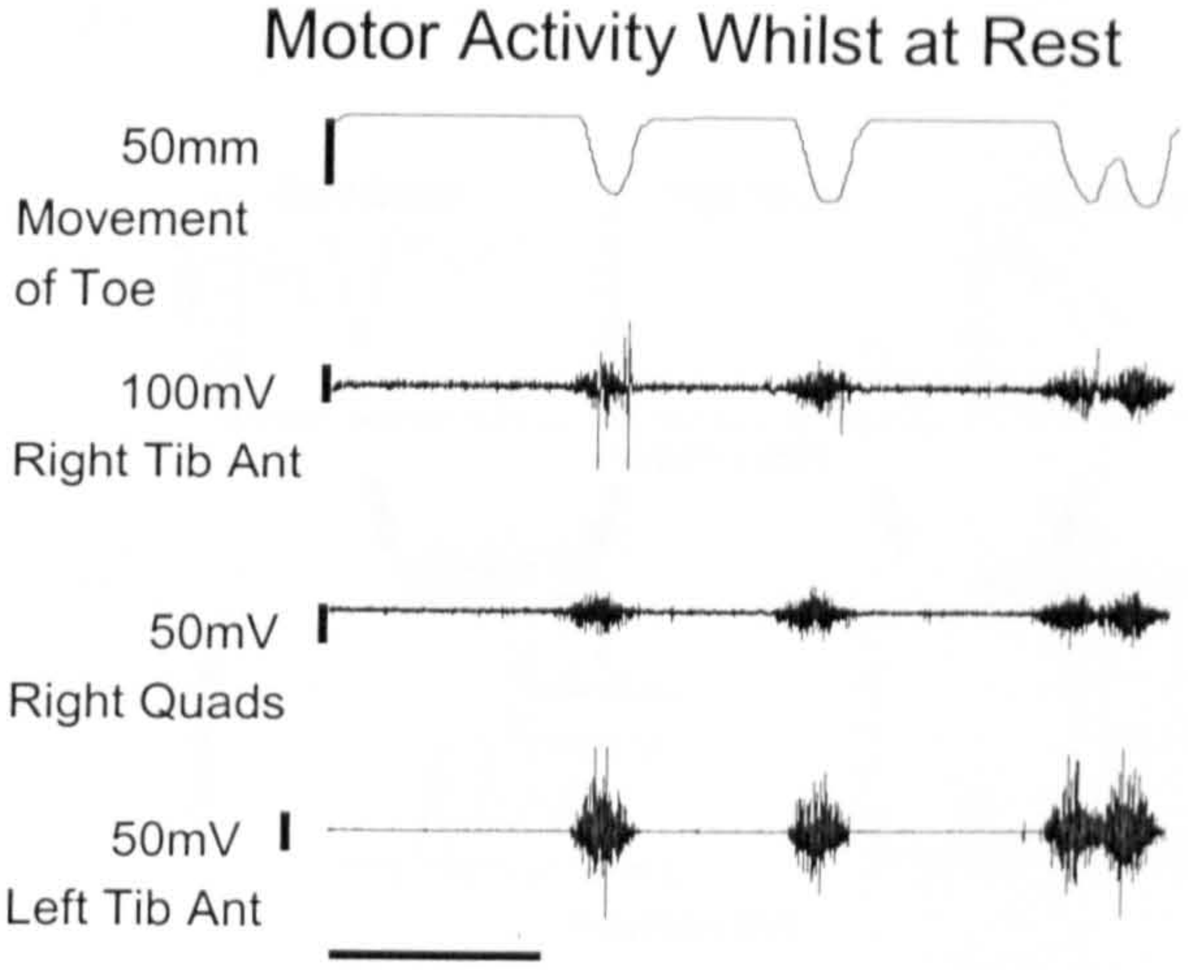

Figure 1. Movements and muscle activity during spasms recorded with the patient recumbent. Movements were recorded using a contact-less opto-electronic measurement system (CODA, Charnwood Dynamics, Leicester, UK) Top trace shows foot movement which was obtained by measuring the movement of a marker placed on the great toe relative to another placed on the ankle. The negative-going deflections indicate a movement of the foot towards the knee. Bottom three traces show electromyographic activity from three sample muscles of the right and left legs.

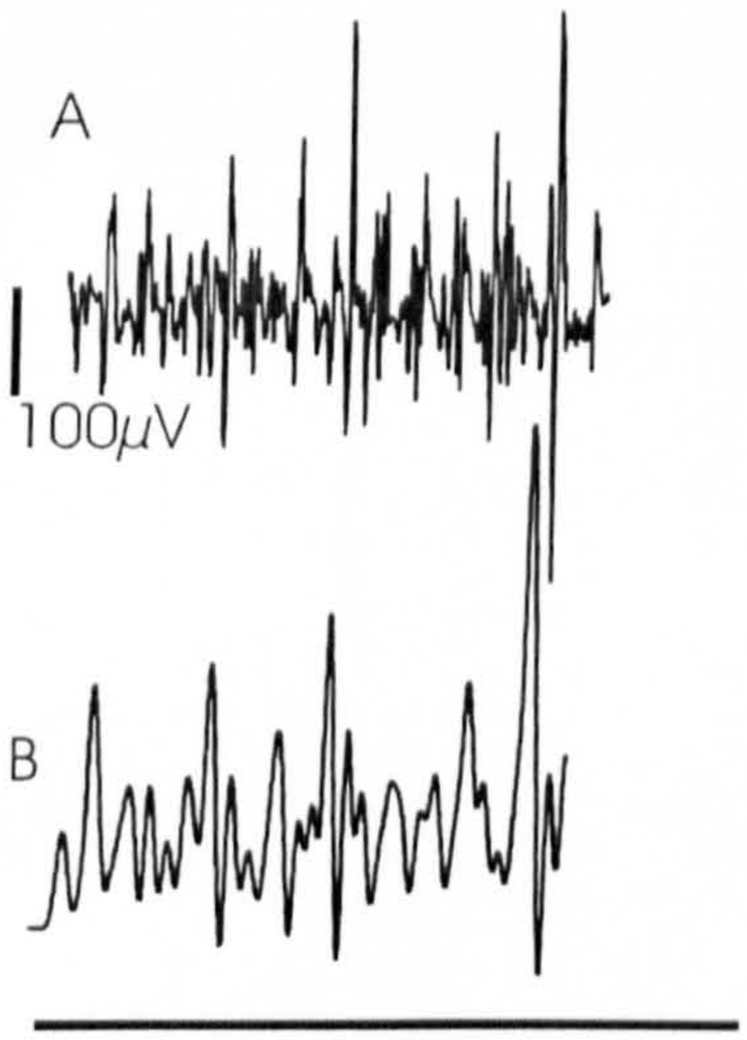

Figure 2. Raw (A) and rectified and smoothed (B) EMG from the right tibialis anterior muscle during a spasm. Clear oscillatory activity is visible in the rectified and smoothed trace (low-pass filtered at 50Hz, there is also a short time delay at the start of the record caused by the filter characteristics). Similar oscillatory behaviour was visible in the muscle groups recorded in this study.

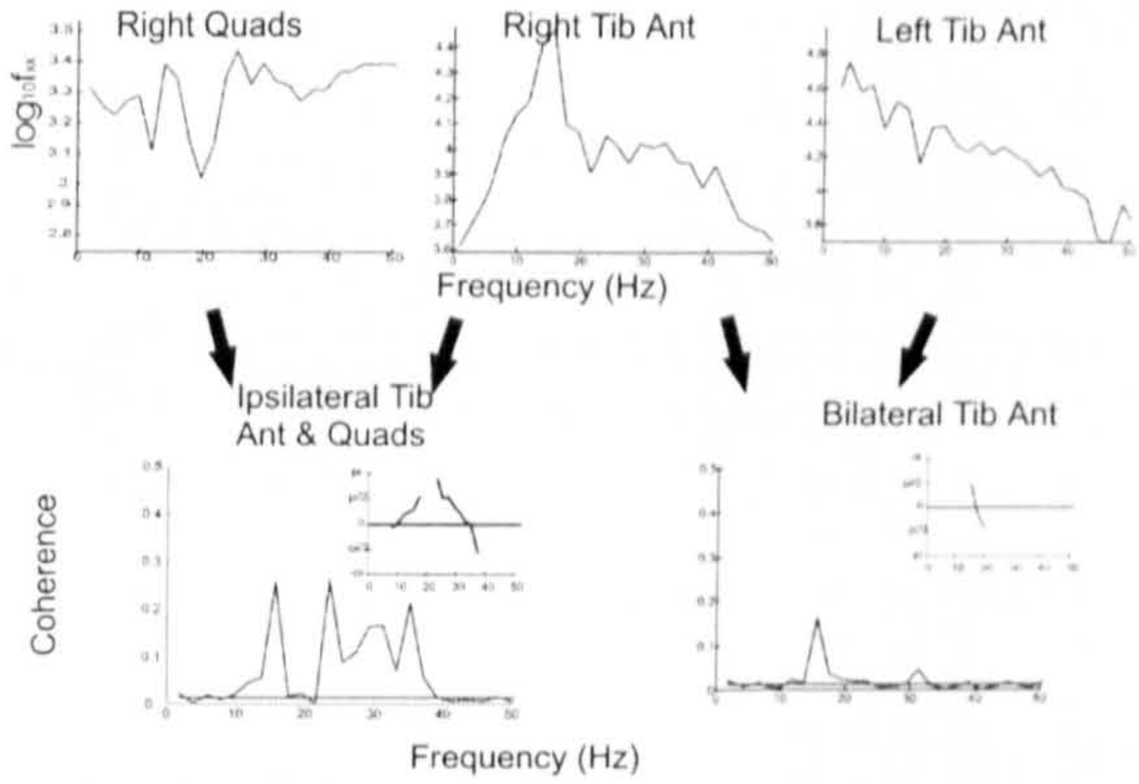

Figure 3. Auto spectra (top row) of muscle activity from the right quadriceps and left and right tibialis anterior during a muscle spasm from patient 1. There is a peak in the spectra at ~16Hz in both the right quadriceps and tibialis anterior. This peak is not as prominent in the left tibialis anterior. The coherence (bottom row) between the muscles shows that both ipsilaterally (left) and bilaterally (right) there is significant coherence at 16Hz. The horizontal line in both plots indicates the 95% confidence level. The phase plots in the top right hand corner of the coherence plots both indicate a steady, non-zero phase relationship between the muscles in the region of significant coherence indicating that the coherence is not a result of electrical cross-talk. This record was obtained with the patient seated, at rest (in the absence of electrical stimulation) with his legs extended. No stimuli were given to provoke the activity. Records were obtained from 124 segments each of length 512.