

**A STUDY OF THE FEASIBILITY OF USING NERVE CUFF
SIGNALS AS FEEDBACK FOR MAINTENANCE OF POSTURE IN
PARAPLEGIC SUBJECTS**

by

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ABSTRACT

Standing in paraplegics can be restored using Functional Electrical Stimulation (FES) to activate paralyzed muscles below the spinal cord lesion. However, reliable balance control with FES will also require sensory feedback. Suitability of electroneurographic (ENG) signals from nerve cuff electrodes as feedback for controlling FES was studied in awake swine during postural sway. Tibial nerve ENG signals were recorded using implanted amplifiers, and pressure distribution under both hind feet was simultaneously monitored. Comparisons were made between pressure changes under the feet of swine and human subjects. During human sway in eight directions, average pressure in loaded foot-sole regions increased by $72\pm 24\%$. In swine subjects, comparable pressure changes were detected from the ENG signals with 94% accuracy, and 84% of all swine postural sway events were detectable from ENG signals. Results from this study suggest that closed-loop control of paraplegic posture using nerve signals to monitor center-of-pressure displacements may be feasible.

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LIST OF ABBREVIATIONS AND ACRONYMS

CNS – Central Nervous System

COM – Centre of Mass

COP – Centre of Pressure

CT – Region innervated by the Calcaneal branch of the Tibial nerve

CWRU – Case Western Reserve University

EMG – Electromyograph

ENG – Electroneurograph

FA – Rapidly Adapting cutaneous receptor

FES – Functional Electrical Stimulation

FES – Functional Neuromuscular Stimulation

FFT – Fast Fourier Transfer

LP – Region innervated by the Lateral Plantar nerve

LPR – linear para-radicular electrodes for stimulation of the sacral roots

LSU-RGO – Louisiana State University Reciprocal Gait Orthosis

MCC – Multi Channel Cuff

MP – Region innervated by the Medial Plantar nerve

PC – Pacinian Corpuscle

RF – Radio Frequency

SA – Slowly Adapting cutaneous receptor

SCI – Spinal Cord Injury

SW – Swine subject

VA – Veterans Association

INTRODUCTION

The mechanisms employed by the central nervous system (CNS) to control upright bipedal posture in humans are incredibly complex. The system is continually adapting to compensate for repositioning, length-tension and force-length characteristics, joint angle changes, muscular fatigue, hysteresis of muscles, tendons and receptors, changes in the characteristics of the base of support, and the influence of external perturbations. To monitor these factors, the CNS must simultaneously integrate a massive volume of sensory data from various receptors, in order to influence and ultimately maintain balance via muscular contractions. In addition, to further complicate the problem, the fundamentals of the human system require that a high centre of mass is balanced above a small support base.

This thesis examines some of these intrinsic problems of controlling posture, in particular, for subjects with spinal cord injury (SCI) and will examine the use of functional electrical stimulation (FES) as a means of replacing the lost functions of standing and balancing. The main focus is on the possible use of nerve cuff electrodes to record electroneurographic (ENG) signals, to provide information about the changing state of the system in order to influence the ongoing control, for use in future FES prostheses. The long-term goal is to track the movement of the centre of pressure (COP) within the base of support of paraplegic subjects during FES-assisted standing, so as to initiate corrections in the delivery of FES when stability is threatened.

Objectives

The ultimate goal of this thesis was to determine the feasibility of providing control signals for a closed-loop system, which incorporates natural sensory feedback recorded using nerve cuff electrodes placed around peripheral nerves. Specifically, the study was focused on recording ENG signals from peripheral nerves as a means to provide sufficient feedback for the control of balance in future FES systems for standing. The swine was used as a model to extract nerve signals evoked as a consequence of pressure changes during postural perturbations. In addition, analysis of human stance was conducted to collect data regarding pressure changes that occur on the soles of the

human feet during standing. The major objectives of the study were to try to answer the following questions:

1. What is the relationship between the change in pressure on the mechanoreceptors of the hind foot of the swine during postural perturbations and the resultant electroneurographic (ENG) signals recorded using nerve cuff electrodes placed around the Tibial nerve?
2. How does the pressure distribution on the soles of human feet during stance relate to the innervation of sensory nerve receptive fields?
3. How do typical ground contact pressure changes that occur during standing compare between humans and swine? Are relative differences likely to influence the usefulness of ENG signals?
4. Are there advantages in using bilateral versus unilateral ENG signal analysis to monitor stance perturbations in swine?

Overview

The underlying concepts of this thesis were based on a review of many years of research in the field of FES. This overview will examine developments within the field, and justification for the assumption that a neural prosthesis for balance using information gleaned from cutaneous sensory receptors may be feasible.

Functional Electrical Stimulation

The evolution of FES over the past few decades has involved the development of many new techniques, and as a result many FES systems have been designed for use across the medical field. These systems include those for bladder and bowel voiding (Creasey, 1993), Phrenic nerve stimulation for diaphragmatic pacing (Glenn, 1985), and control of grasp for quadriplegics (Peckham *et al.* 2001) amongst others.

The first FES systems developed for skeletal muscle stimulation used simple external electrodes with only one or a few stimulation channels. One example was the work by Liberson *et al.* (1961), to help subjects suffering from a dropped foot; this also saw the introduction of external switches as sensors. It was quickly realized that sensors were required in order to negate some of the problems of open-loop systems, such as over stimulation and consequent premature muscle fatigue (Hoffer *et al.* 1996) and in

addition, to control the timing of stimulation. The Liberson system employed a footswitch to trigger stimulation of the Common Peroneal nerve, in order to elicit a flexion withdrawal reflex and dorsiflex the foot during the swing phase of gait. This was successful but the sensor was simply a switch, rather than providing continual feedback, and it was externally mounted. External sensors are well documented as having problems associated with donning and doffing, calibration time, cosmetics and mechanical vulnerability (Hoffer *et al.* 1996). Liberson stated after his early work that a fully implanted device using natural sensors for feedback was the solution, if FES systems were to be widely accepted (Liberson *et al.* 1961). Meanwhile, several researchers have since used implanted artificial sensors, such as the Hall Effect sensor used in the Freehand® system (Johnson MW *et al.* 1999), developed at Case Western Reserve University (CWRU). Problems with such implantable sensors to control upright stance include the requirement for calibration but more importantly it is presently not possible to use implantable sensors to monitor the movement of the COP. To date there are no implantable pressure transducers available and the required information cannot be determined from joint angle changes. Implantable pressure sensors that may be developed in the future will have to be designed such that they circumvent the inevitable issues of infection and pressure sores due to friction. Consequently, other solutions have been sought.

One rather appealing solution is to extract information from the body's natural sensors, as Liberson mentioned. This option of recording afferent sensory output from receptors, obviously involves a direct interface with the nervous system. Implanted nerve interfaces may be used to both stimulate (to produce muscle contraction and/or sensations), and/or to record neural activity (afferent and/or efferent).

In terms of stimulation capabilities, early FES systems were limited by a small number of channels and poor recruitment properties. Most early implantable electrodes were intramuscular. Intramuscular electrodes are selective, but require large current amplitude when compared to neural stimulation, can rarely recruit the entire muscle, are prone to electrode migration and lead breakage, and multiple electrodes are required for smooth or complex recruitment.

A number of attempts have been made to develop electrodes that will alleviate some of these problems by stimulating and recording directly from peripheral nerves. These

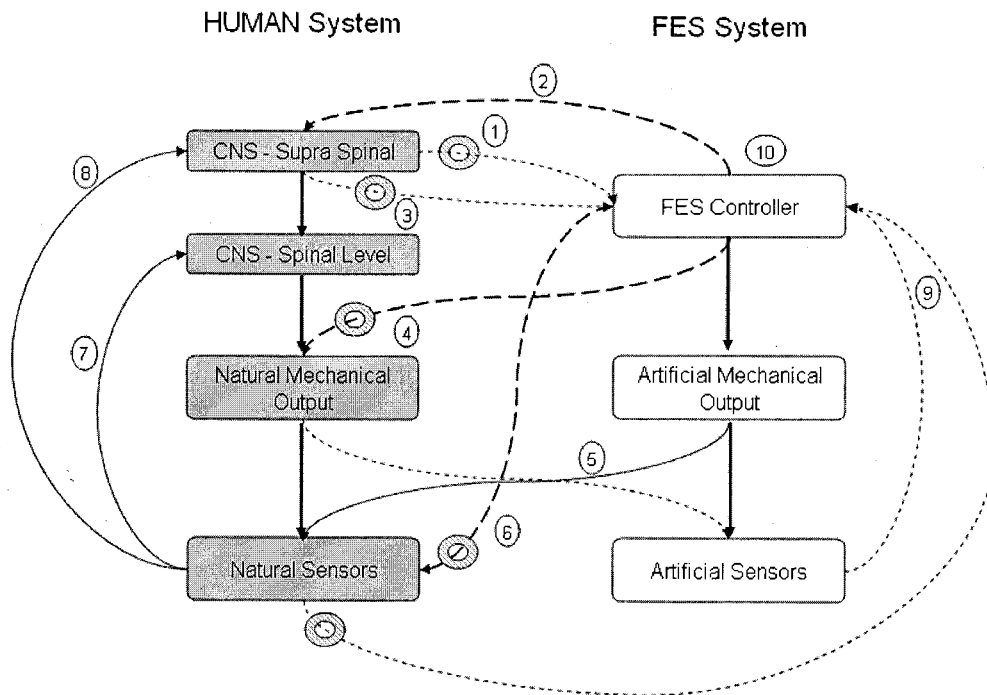
designs include sieve (Mensinger *et al.* 2000), multi array (Branner and Normann, 2000), and intraneural wire electrodes (Yoshida and Horch, 1996). These electrode types were developed with both stimulation and recording in mind and have been used with limited success, but have not gained acceptance for clinical uses, remaining confined to the laboratory. There are a number of common flaws in the general concept of intraneural electrodes: they are prone to migration, nerve damage may be caused by movement, and consequently the electrodes require regular calibration.

An alternative approach is to stimulate and record extraneurally, using nerve cuff electrodes placed circumferentially around peripheral nerves. The primary advantage of cuffs is that they are not required to pierce the epineural sheath in order to stimulate the nerve or record neural activity which reduces the likelihood of nerve damage. In addition, nerve cuffs have been found to record stable signals for over 3 years in animal models (Popovic *et al.* 1993) and pilot studies in humans also produced consistent signals over several years (Haugland *et al.* 1995). Within days of the implant, the nerve cuff becomes encased in connective tissue, which anchors the cuff in place and ensures that signals remain stable (Hoffer and Kallesøe, 2000). The major disadvantages of nerve cuffs, when compared with the previously mentioned intraneural electrodes, are the small signal amplitudes (in the μV range) and low selectivity for both stimulation and recording. Since nerve cuffs encompass an entire nerve, they record the sum of the neural activity throughout the nerve as a whole. However, it has been shown that using multiple channels within a nerve cuff it is possible to selectively stimulate smaller nerve branches within a larger nerve trunk (Grill and Mortimer, 1998). Similarly, it is possible to selectively record from nerve regions using this multiple channel method to improve selectivity (Rozman *et al.* 2000).

In addition to problems with developing suitable electrodes for stimulating and recording, acceptance of FES systems for clinical applications has been hindered by the external location of the control units and power supplies. Early devices were entirely external. However, with advances in electrodes, the opportunity arose to develop partially implanted devices, such as the ActiGait® system by Neurodan. The ActiGait® system has an external footswitch, controller and power supply and utilizes radio-frequency (RF) communication to stimulate through an implanted nerve cuff electrode placed around the Common Peroneal nerve of hemiplegic subjects. The next logical progression is toward

fully implantable systems, which other than occasional interrogation or reprogramming with an external RF communication device, are controlled and powered entirely within an implanted unit. Such systems currently in use include heart pacemakers that monitor cardiac rhythms and stimulate when abnormal heart rhythm occurs. An example is the Vitatron® C-series of pacemakers (Vitatron, 2004) that uses digital processing to monitor heart rhythms and influence the heart rate if required. The tasks that these systems perform, due to the magnitude and periodicity of electrocardiograph signals, are less complex than those required for recording ENG from peripheral nerves and cardiac stimulators also have a comparatively simple stimulation output. The area of heart pacemaker development is very important for battery, communicator, implant casing and connector technology that will also be required for FES implantable devices.

An ultimate goal for FES is a fully implantable system that is externally programmable using RF communication and has an RF-powered, externally rechargeable battery to power a fully implanted system that stimulates and senses in a truly closed-loop manner, to monitor and influence ongoing function. This system would generally need to incorporate multi channel stimulation and recording. To be a truly complete system there would also be a measure of cognitive control by the user and feedback of sensation. This 'complete' system will involve progress in many areas of the field of research. Figure 1 indicates the complexity of the necessary integration of the physiological and artificial systems for the perfect device:



The short dashed lines on the diagram indicate inputs to the FES system. Heavy long dash lines indicate outputs from the FES controller. The grey circles indicate electrode/tissue interfaces. 1) Individual can initiate the action of implanted controller. 2) Cortical stimulation may be utilized to deliver signals elicited by the system. 3) The individual can influence ongoing output of FES system via cortical control. 4) The output from the control system (FES) generates a mechanical output. 5) Artificial prostheses may influence the output of natural sensors and artificial sensors may generate output signals due to both artificial and mechanical outputs. 6) Stimulation of natural sensors can provide sensation relating to the system output. 7) Spinal level reflexes can occur as a consequence of mechanical output. 8) Sensory information is relayed to the supra-spinal centres, for sensation and to influence outputs. 9) Sensory information from natural and artificial sensors is sent back to the FES control system recorded. 10) Controller acts as a comparator and replaces the role of the CNS to provide appropriate descending commands.

Figure 1 – FES System Flowchart

In order to achieve the goal of a fully implantable closed-loop system, research remains crucial across the board. There is still much work into selective and controlled stimulation of nerve and muscle, particularly in terms of cortical and spinal stimulation and recording, which is in the early stage of development, in terms of functional use. Sensors are essential, natural or artificial, since as mentioned previously, open-loop FES systems have many drawbacks. There is also a continual quest to miniaturize anything that is to be implanted within the body. Major concerns include battery size and longevity. To reduce power consumption, simple schemes for monitoring sensory signals

and detecting events are required (Upshaw and Sinkjær, 1998). For recording neural signals, the development of suitable low-noise amplifiers is crucial.

In principle, there are several choices regarding the location to place electrodes for stimulating and/or recording, including the cortex, deep brain structures, spinal cord, intradural or extradural regions of the spinal roots, cranial nerves and peripheral nerves. Cellular/tissue engineering, signal processing, and micro-/nanofabrication are some of the areas of research that are advancing with a goal of interfacing with the neural system (Rutten, 2002). However, even though researchers are working tirelessly to develop electrode interfaces with spinal neurones and brain, there have been many problems. As with other invasive electrodes, migration and damage are important issues. If suitable long-term electrode interfaces with the cortex or spinal neurons are to be achieved, the mechanical impedance between the tissue and electrode must be reduced (Barbeau *et al.* 1999), developing safe implant procedures is also crucial, something that becomes more difficult when accessing deeper and smaller sites (Rutten, 2002). In the review by Barbeau *et al.* (1999), it is noted that finding the exact location of target neurons is difficult. Non-invasive imaging techniques may be adequate in the future, but are presently insufficiently accurate. One way of reducing the need for such accurate electrode placement is to increase the number of electrode channels, but this brings along the associated problems of the number of wires required and subsequent lead wire routing, and increased damage. All of these problems are in addition to the complex signal processing that will be necessary (Rutten, 2002). Surgical procedures in the spinal cord or brain also increase the likelihood of leakage of cerebro-spinal fluid (Stieglitz, 2002). In future applications, these sites may become viable, but to this date the locations that have proven to be safest and remain functional for recording neural signals over the long-term are the peripheral nerves, and nerve cuffs are currently the most stable electrodes available (reviewed by Hoffer and kallesøe, 2000).

The focus of FES is moving towards replicating the fully functioning human system. The progression through system development to try and emulate the intact human includes the goal of restoring complete closed-loop control. In terms of a device to control balance in paraplegics, for this to become reality requires a decision of what the best source of sensory information is. As will be detailed in a later section, it is important to understand that there are many possible sources of afferent information. The

maintenance of upright bipedal stance involves the integration of multi-modal sensory inputs: the visual (Bronstein and Buckwell, 1997), vestibular (Horak *et al.* 1994), and proprioceptive systems (Maurer *et al.* 2000) have all been shown to play significant roles. For control of an FES system for paraplegic standing, the sensory modalities (visual and vestibular) that are still 'connected' to the cortex are likely to play an important role in the upper body to assist in postural control, but cannot replace afferent feedback for controlling a stimulation device, due to the location of the sensors. This leaves only the proprioceptive system, which can be further subdivided by the receptors providing afferent information: muscle spindles, joint receptors, Golgi tendon organs and cutaneous receptors. This particular study focussed on the afferent flow of information from cutaneous receptors of the soles of the feet. It has been shown previously that recording from cutaneous receptors in the tibial nerve of the feline hindlimb, using cuff electrodes, is a viable possibility to provide information regarding foot contact force (Haugland *et al.* 1994).

Recording Afferent Nerve Signals in the Periphery

In the intact system, feedback for the control of limb position is provided by specialized sensors in the skin, joints, muscles, and tendons. It is possible to record afferent ENG signals primarily generated by muscle receptors and cutaneous receptors. Joint receptors are not considered a good source of feedback, since they tend to fire mainly at the limits of the range of motion of a joint, the mobile location and small size of the innervating branches makes recording difficult (Riso *et al.* 2000), and there is some debate as to their actual function (Johnson *et al.* 1995). ENG signals arising from the Golgi tendon organs provide information primarily on the force of muscle contraction as opposed to muscle length. Muscle stretch receptors, more specifically spindles, have been used to provide muscle length and velocity feedback in laboratory settings (Jensen *et al.* 2001, Yoshida and Horch, 1996).

Muscle spindles respond to the stretch/lengthening of muscle, are located within the muscle belly and lie in parallel with skeletal muscle fibres. Muscle spindles have three main components: specialized muscle fibres, sensory axons that terminate on the central region of the sensory organ, and motor axons that regulate spindle sensitivity. The human leg contains approximately 7000 muscle spindles. Recording from spindle afferents has been attempted to provide a control signal for FES systems with some

success. Yoshida *et al* (1996) showed it is possible to control cat ankle position using afferent feedback from muscle stretch receptors to within 4-7°. Micera *et al.* (2001) found that when recording signals from the Common Peroneal and Tibial nerves separately (using nerve cuffs) they could monitor ankle plantarflexion and dorsiflexion. However, a number of problems have surfaced. The Yoshida study used intrafascicular electrodes, which have not yet performed to a level that is practical for long-term use, and in the Micera study the Sural nerve was cut to reduce the cutaneous afferent activity. In addition, it was found that large afferent bursts occur at the initial onset of movement due to thixotropic properties of muscle (Wise *et al.* 1999). Trying to continuously monitor muscle length is problematic when muscle history becomes a factor.

Another issue is the effect of the initial joint position (Jensen *et al.* 2001), since muscle spindles are only responsive over a certain section of their physiological range unless their sensitivity is reset by fusimotor activity. This could have profound effects, particularly when monitoring the stretch of muscles on the anterior portion of the shank, which are not significantly stretched at 90° (neutral standing position). Jensen *et al.* (2001) also confirmed that during ramp and hold movements, the duration of the hold period greatly affected the recorded signals; subsequent spindle afferent firing can be greatly increased when stretch occurs again after a period of rest. This uncertainty problem is likely to occur when attempting to control balance. Another important concern when monitoring muscle spindles is that inevitably there will be significant firing from other large-diameter proprioceptor afferents, such as cutaneous receptors, which may make analyzing data extremely difficult. It is likely that the signals recorded from spindle afferents will be of use in future FES devices; however, to date there has been greater success, in terms of functional use, recording from cutaneous receptors to provide feedback.

Animal research on the use of afferent signals produced by cutaneous receptors has provided an excellent foundation from which to proceed to human studies. The most abundant data has been recorded using the feline model. It is possible to record from peripheral nerves during treadmill walking to extract information regarding foot contact (Strange and Hoffer, 1999). Paw afferent signals were acquired using cuff electrodes placed on two nerves (either Median and Radial or Ulnar and Radial). Electromyographic

(EMG) timing relating to paw contact and lift-off was detected with a high degree of accuracy (average error = 7.8%, standard deviation = 3.0%).

Figure 2 shows an example of ENG signals acquired during treadmill walking from the sciatic nerve of another cat, 605 days post implant. Sciatic nerve activity increases during the stance phase and decreases during the swing phase of walking. From Figure 2 it is easy to see the points at which contact with the ground starts (box 1 on Figure 2) and ends (box 2 on Figure 2).

In addition, ENG signals recorded using cuff electrodes around the sciatic nerve of the cat can provide information about the forces applied to the footpad (Haugland *et al.* 1994). These studies, in particular, found that ENG signals recorded from the cat Tibial nerve with cuff electrodes provide reliable information about perpendicularly applied forces in the 0-10 Newton range. Responses to various force inputs were monitored including: how rate of force increase and decrease affects the ENG signal response, the adaptation in the ENG response during maintained application of force and how ENG signal response relates to the amount of skin indentation. It was found that both static and dynamic information relating to force application could be extracted and that the amount of skin indentation (more significant at the onset of force application) played an important role in the ENG signal response. In addition, ENG signal responses to increases in force were significantly greater than during equivalent decreases in force.

During walking, significantly different data may be provided in each nerve branch. Signals have been recorded from the Sural, Superficial Peroneal, Tibial, Ulnar, Radial, and Median nerves of the cat. Figure 3 shows an example of simultaneous recording from the Tibial and Sural nerves of a cat during treadmill walking. It can be seen that different information is provided, depending on the location of the receptors in each nerve branch. If recordings are taken simultaneously from two or more nerves during the same event, different features can be extracted (Strange and Hoffer, 1999). This suggests that it may be possible to selectively record from separate branches of the same nerve to glean information regarding pressure information from the different regions of the human foot sole.

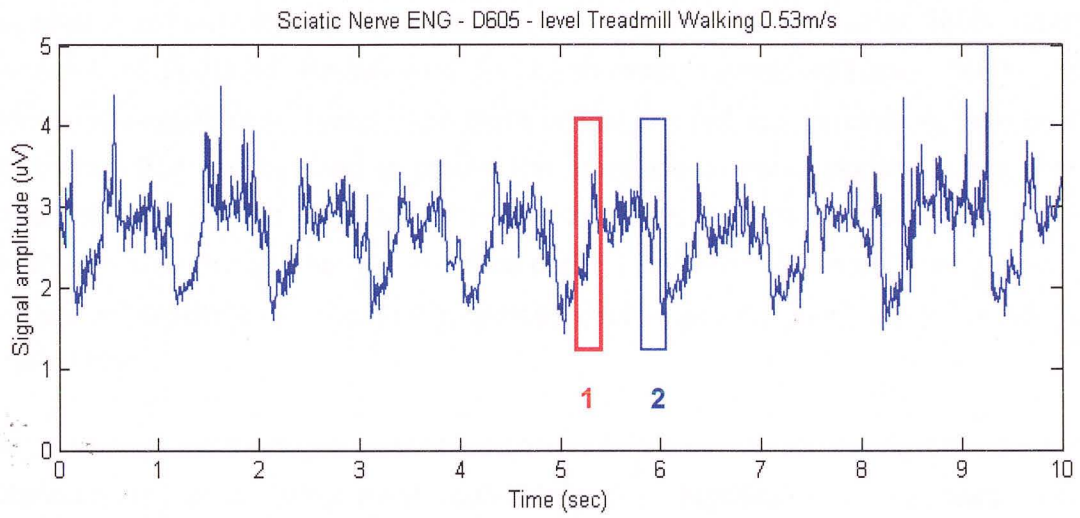


Figure 2 – Feline Treadmill Walking, Event Detection

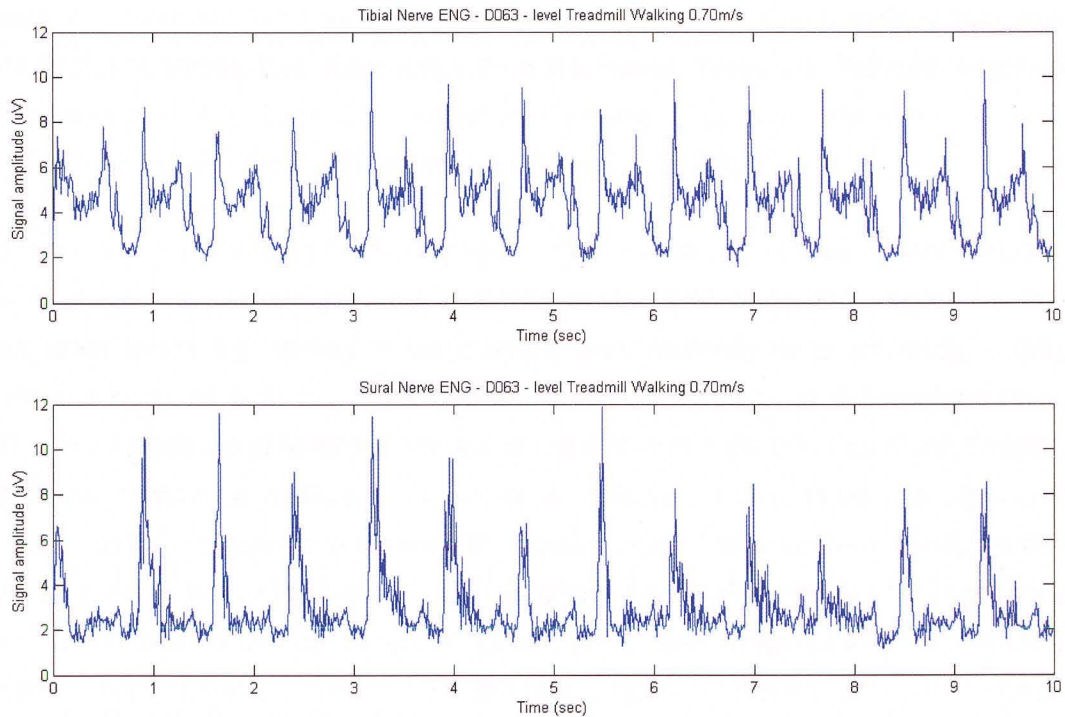


Figure 3 – Feline Treadmill Walking, Nerve Signal Differences

Cutaneous signals have been recorded from the peripheral nerves of various mammalian subjects in addition to the cat, including dog (Rozman *et al.* 2000), rabbit (Jensen *et al.* 2001), rat (Komine *et al.* 2003), primates (Yajima and Larson, 1993), and humans (Haugland *et al.* 1995). From these different recordings, parameters have been established that can be used to predict the amplitude of nerve signals. It has been shown that the general properties of nerves are the same across species but signal amplitudes recorded by a nerve cuff can be determined from fibre types, nerve diameter, conduction velocity and nerve cuff properties (Hoffer and Kallesøe, 2000), as will be detailed later.

As previously mentioned, it is possible to record nerve signals arising from human cutaneous receptors using nerve cuff electrodes. Significant studies have been performed by collecting data from a digital nerve during cat paw slip (Haugland and Hoffer, 1994a) or human finger slip, as a means of controlling grip (Sinkjær *et al.* 1994), and during hemiplegic's gait to correct for dropped foot (Haugland *et al.* 1995). The data collected during gait has shown, as predicted from the cat model, that it is possible to extract perpendicular force as well as shear force information from various receptive fields from the human foot. Recordings from the human Sural and Common Peroneal nerves during walking both provided information regarding foot contact but showed significantly different shapes of ENG bursts (Hansen *et al.* 2003).

The challenges in recording from cutaneous receptors will be covered in later sections. These include the sometimes problematically similar 'ON' and 'OFF' responses that occur when forces are applied to the glabrous skin; relatively large amplitude activity bursts can occur at both the onset and termination of force contact (Haugland *et al.* 1994). The magnitude of recorded signals, in the region of 1 μ V (Haugland and Sinkjær, 1995) also provides a challenge. To further complicate matters, there is a significant amount of noise contamination to deal with, including local EMG, amplifier noise, thermal noise and noise from external sources (Haugland and Hoffer, 1994a). These issues combine to further complicate the challenge of gaining useful information from peripheral nerve signals. However, due to the different frequency ranges of neural signals (approximately between 1-10 KHz) and EMG (below 500 Hz), using appropriate filtering the ENG signal can be successfully recorded in awake subjects, even during stimulation of nearby muscles if special-purpose blanking methods are used (Haugland and Hoffer, 1994b).

Spinal Cord Injury

In the US alone, there are approximately 11,000 new cases of spinal cord injury (SCI) every year, resulting in some form of complete or incomplete paralysis. In December 2003, it was estimated that approximately 243,000 persons with SCI were alive in the US. Of these individuals, the most frequent neurological category is incomplete quadriplegia (30.8%), followed by complete paraplegia (26.6%), incomplete paraplegia (19.7%), and complete quadriplegia (18.6%). Primarily due to advances in emergency medical care, drugs to reduce inflammation of the spinal tissue and motor vehicle safety, recent trends indicate an increasing proportion of persons who survive the accident and are left with incomplete paraplegia and a decreasing proportion of persons with complete quadriplegia (Spinal Cord Injury Information Network, 2004).

In relation to FES, it has been well documented that uninjured peripheral nerves are still viable in terms of stimulation and recording after SCI (Lyons *et al.* 2002, Sinkjær *et al.* 2003, Yoshida and Horch, 1996) and indeed, many studies have shown that the peripheral nerves and muscles below the level of the lesion have been stimulated or recorded from in the research, development and use of FES systems.

The most likely candidates for a FES device to maintain posture are SCI individuals with thoracic or lumbar level lesions, particularly those with injuries between T4 and T12 (Gorman, 2000). These subjects will have a significant amount of upper body control and strength that may be required. In some studies (Triolo *et al.* 1996) higher level patients, up to C5, have been shown to be possible candidates, but the complexity of the stimulation required and surgical implant of electrodes is significantly increased. SCI subjects are also generally of sound mental state and are likely to have the cognitive requirements that will enable them to operate and maintain the system. Usual contraindications for skeletal FES systems include significant joint contractures, dysesthetic pain syndromes, uncontrollable spasticity, osteopenia, lack of cardiopulmonary reserve and lack of motivation (Gorman, 2000). The demographics of SCI show that the modal average age at the occurrence of injury is 19 years with a mean of 32.6 and approximately 81% of those with SCI are male (Spinal Cord Injury Information Network, 2004). This suggests that typical candidates for such a system are likely to be young males, a group that tends to be highly motivated with good upper body strength and generally of reasonably good health.

Not surprisingly, a published study that analyzed the results of an FES prosthesis user forum held at the IFESS 2001 conference (Kilgore *et al.* 2001) found that the ability to stand and balance was of great importance to SCI subjects. The users agreed that standing had been achieved using FES to 50-60%, but balance is the big issue. Standing is not useful unless you can do something once upright! The great advantages of standing have been well documented, including physiological benefits such as reduced decubiti, reduced vascular problems, increased muscle tone, reduction in muscle spasms, and importantly, a statistical increase in physiological self-concept and reduction in the indicators of depression (Agarwal *et al.* 2003, Graupe and Kohn, 1997). There are also significant social and economic implications. The cost benefit due to reduced dependence on caregivers is significant, and there is also likely to be a reduction in lifting injuries that commonly occur when assisting during patient transfers. In the study by Agarwal *et al.* (2003), 73% of subjects that used a Case Western Reserve University system for stand and transfer no longer required assistance to stand or walk, thus reducing both the physical effort and the time required of caregivers.

It is clear that SCI subjects have much to gain from the use of FES systems and in particular from standing and maintaining a stable posture, a goal that is realistic. For this to be accomplished it will be essential to develop sensors that can monitor changes in the centre of pressure of the individual and provide suitable signals to control the delivery of FES. A clear understanding of how the intact human maintains posture is also required.

Biomechanics/Control of Posture

Bipedal stance is intrinsically difficult; supporting a large, top-heavy weight over a small base of support is by no means simple. To make this possible, there must be an element of stiffness in the system and sensory feedback is necessary to monitor position. In the intact human, this feedback is accomplished by the integration of a huge flow of afferent information. It has been shown that part of the sensory contribution to erect posture regulation is provided by the cutaneous receptors on the soles of the feet (Kavounoudias *et al.* 2001). Maurer *et al.* (2000) suggested that somatosensory cues in the feet enable subjects to maintain equilibrium during low-frequency platform tilts. This was shown by mechanically stimulating the soles of the feet to evoke postural sway that is highly correlated with the cutaneous stimuli. It has also been shown that if input from

cutaneous receptors is reduced through ischemic block above the ankles (Diener *et al.* 1984) or by anesthetizing the plantar soles (Thoumie and Do, 1996), the area within which the centre of pressure sways is increased. This body of research suggests that there is information regarding changing posture provided by the cutaneous receptors in the soles; but to what level of accuracy would a system need to monitor the movement of the COP?

A current explanation for the maintenance of posture is the stiffness model. In order to stand, it is vitally important that sufficient stiffness is produced at the ankle joint. It has been an ongoing debate as to the role that ankle stiffness plays in postural control and the level of stiffness that is sufficient to maintain upright posture. One argument is that it is not possible that balance is reflex-driven, due to the long latencies involved in responding to a perturbation. By the time the response has occurred, movement is such that the particular response may no longer be required (Winter *et al.* 2001).

A question often asked is: what is the ideal stiffness level to produce so as the 'pendulum' remains upright but muscle fatigue is not too rapid? Varied results have been found, regarding the amount of stiffness required for maintaining stance. Winter *et al.* (2001) found through biomechanical analysis, that ankle stiffness of approximately 13 Nm/° was normal in intact subjects. However, Matjacic *et al.* (1998), showed that it was possible to remain upright with an ankle stiffness of less than 8 Nm/° if the upper body was used to balance. Given the level of stiffness that is necessary to maintain upright posture, a major factor in the design of FES systems will be the reduction of fatigue. Since a certain level of stiffness will be required, it seems important to try and reduce fatigue other than by simply decreasing the level of stiffness. One possible method to control standing may be to have a system that responds differently according to the amplitude of sway, as may be the case in intact humans. It seems more realistic that balance is maintained by a combination of background stiffness and brief corrections. Within a predetermined range, stance is maintained by varying the level of joint stiffness. Only if a sway limit is exceeded, the system will instigate a correction.

Duarte and Zatsiorsky (1999) suggest that there are two fundamental postural strategies: multi-region and single region. Within these two strategies there are three further sub-divisions: shifting, fidgeting and drifting. In a long trial, all three patterns as a rule will occur. It is suggested that shifts and drifts are likely to be related to the

redistribution of body weight from one foot (region) to another, or even a step, or both. This finding fits well with the hierarchical two-level system for controlling stance, where the upper level provides a reference frame and the lower level maintains equilibrium around a predetermined reference point. The purpose behind drifting is less obvious; perhaps it shows that the CNS is not 'worried' or sensitive to small slow movements until they accumulate to a certain level. Fidgeting was also found to occur during drifting, which reinforces the fact that perhaps drifts are not controlled. Since the COP eventually returns to its original position during fidgets, it is likely that they occur simply to redistribute pressure.

Popovic *et al* 2000 refer to Collins and DeLuca (1995 a,b) suggesting that any postural movement lasting less than 1 second is controlled using open-loop control and displacements with longer time intervals are corrected with closed-loop control of the postural system. The experiments were designed to determine the comfortable regions during standing. Four zones were defined for each subject: unstable, undesirable, low preference and high preference. In addition, Matjacic *et al* (2001) found that two methods were employed to maintain anterior-posterior posture; one strategy used predominantly ankle stiffness to control against small perturbations, and the second strategy used hip and trunk musculature, which is the reactive mechanism employed in response to larger disturbances. It was determined that medio-lateral responses are primarily foot loading and unloading, controlled by hip adductors and abductors.

The strategies that are understood to maintain upright posture primarily involve one of two joints: ankle or hip. It was demonstrated by Horak and Nashner (1986) that anterior-posterior postural adjustments are made using the ankle joint musculature and then radiating sequentially to thigh and then trunk muscles. However, if the support surface is smaller, to maintain upright posture after a disturbance, subjects activated leg and trunk muscles but organized the activity differently. Trunk and thigh muscles antagonistic to those used in the ankle strategy were activated in the opposite sequence, and ankle muscles were generally unresponsive. This activation pattern produced horizontal shear force against the support surface but very little ankle torque. As mentioned previously, it is thought that future FES devices to maintain posture in paraplegic subjects would largely depend on the ankle strategy but may also incorporate considerable input from the subject through movement of the trunk.

In summary, it seems that cutaneous signals may provide adequate signals to control posture if sufficient background ankle stiffness is also produced with FES. The question remains, will these cutaneous signals be sufficient. There is evidence to suggest that it is not necessary to detect small perturbations/oscillations when the subject's COP stays within a "high preference" zone, but stability is only threatened in the "low preference" and "undesirable" regions.

BACKGROUND

This section describes the progress made in the development of FES systems for standing and focuses on the physiology of the sensory receptors of the human and swine. In addition there is a detailed summary of the biomechanics and control of posture, along with the principles of nerve cuff electrodes and their use.

Standing with FES

The development of FES systems that incorporate the use of closed-loop control using natural sensors, in particular the signals arising from the cutaneous receptors is an active area of current research. Although this goal has not been fully achieved yet, there have been important advances. Various systems that have been developed to date and their advantages and disadvantages are outlined below:

Present Systems and their Problems

Over 21 centres worldwide have clinically implemented systems for standing in paraplegic subjects (Gorman, 2000). This section will focus on several complete systems that have been developed and problems that have prevented their full acceptance.

There have been a number of attempts to facilitate standing in paraplegics. In contrast, to date only one FES system for standing and walking has received FDA approval (1994), the Parastep® system by Sigmedics (Graupe and Kohn, 1998). Parastep is described as a non-invasive, microcomputer controlled, neuromuscular stimulation unit. It is battery activated, and uses surface electrodes for stimulation. The user controls the stimulation with finger-activated switches placed on the walker handles. Gait is facilitated using 6 stimulation channels, 3 for each leg, that stimulate the quadriceps (for knee extension), Peroneal nerve (for reflexly-evoked multi joint limb flexion) and gluteal muscles (for hip extension). In order to balance, Parastep® users must use the walker. The system has been relatively well accepted but it is entirely external, which causes serious inconvenience. Due to the open-loop nature of the stimulation, fatigue is a

common problem and many users have found that it has become something they use primarily for exercise.

A number of external devices have used mechanics to maintain upright posture, of which one of the most successful and widely accepted is the Louisiana State University Reciprocal Gait Orthosis (LSU-RGO; Dall *et al.* 1999), essentially a hip-knee-ankle-foot orthosis which was originally designed for patients suffering from severe musculoskeletal disabilities of the lower extremities, such as Spina Bifida and muscular Dystrophy. Initial results with SCI subjects showed that upright posture and ambulation was possible, but indicated very high energy expenditure. To reduce energy cost, a simple FES device incorporating surface electrodes was also incorporated. Stimulation is used to assist during walking and to raise the subject from sit to stand (Solomonow *et al.* 1997). For standing, the LSU-RGO essentially works as leg braces and is thus not particularly high in energy expenditure. However, it cannot be considered a functional device, as it simply locks the legs in place.

Both the LSU-RGO and the Parastep® systems, although they can successfully provide a means of standing and ambulating for paraplegics, have a number of limitations, particularly the use of surface electrodes. Surface electrodes have a number of advantages: they are relatively inexpensive, non-invasive, commercially available, easy to apply, and can be removed without damage to the patient (Gorman 2000). However, they also have major disadvantages for use in FES. They are only suitable for stimulating superficial muscles and this drastically reduces the number of muscles available for stimulation and hence the controllability of the system. Surface electrodes are also prone to movement, which has an effect on stimulation, makes designing control algorithms much more difficult, and increases the need for recalibration. Surface electrodes must be donned and doffed, which takes time and often requires assistance, and external wires are cosmetically poor (Gorman, 2000). As mentioned previously, there are many physical and psychological benefits as a result of stimulating the large muscles of the lower limbs, but with external stimulation the muscles tend to fatigue rapidly, the lack of feedback results in essentially rigid stance and the user must keep hands on the walker essentially at all times.

Due to the fact that both previously mentioned systems utilize surface stimulation, by necessity they also have external controllers and cables, adding to the bulk that the

patients must carry. The cosmetics of a system can be extremely important to SCI subjects who are already conscious of people looking at them funnily, and thus the more 'normal' they can look, the better. A further problem with external stimulation devices is the limited number of available stimulation sites. With only a few stimulation channels, it is only possible to achieve crude control strategies and rigid stance. Extra surface electrodes merely increase the severity of a number of the associated problems such as donning and doffing, and cosmetics. Additionally, it is worth noting that both systems mentioned employ open-loop control with a complete absence of sensory feedback.

A considerable amount of research in the general field of FES has been conducted at the Cleveland FES Center. The Center was created as a consortium of the Cleveland Veterans Association (VA) Medical Center, Case Western Reserve University (CWRU), the MetroHealth Medical Center, and the Edison BioTechnology Center. One of the main research goals of the group was to develop a fully implantable system for exercise, standing and ambulation. The project's principal investigator is Dr Ron Triolo. The first CWRU-implanted devices to provide standing and transfer targeted cervical level SCI patients. Standing was achieved by stimulation of three muscle groups: vastus lateralis or medialis to provide knee extension without hip flexion, lumbar paraspinal muscles (erector spinae), and two hip extensor muscles, including the gluteus maximus and either the posterior portion of adductor magnus or one of the hamstrings (Kobetic *et al.* 1999, Triolo *et al.* 1996). The stimulating electrodes were implanted 'closed helix' electrodes (Triolo *et al.* 2001). A three-stage implementation strategy was used to insure correct stimulation patterns were achieved, which involved initial exercise and stimulation pattern development using a percutaneous setup with 'open helix' electrodes and an external controller. The next stage is still percutaneous but with 'closed helix' electrodes (the 'closed helix' electrodes are enclosed in an elastomer sheath, more suitable for permanent implant). If the electrodes are reliable, the implant of the controller takes place and the percutaneous leads are removed. The use of implanted stimulation electrodes offers many advantages over surface electrodes or percutaneous intramuscular electrodes, especially in relation to the long-term use by patients. Implantable devices offer the advantages of avoiding many of the problems associated with surface electrodes, including complications of lead breakage and care of skin exit points of lead wires (a possible site for infection), which can occur with percutaneous connections. The CWRU system includes two implantable 8-channel Freehand®

(Johnson *et al.* 1999) stimulators/controllers (one for each lower limb). Once the electrodes and controllers are implanted, the standing and walking is accomplished by transmitting specific stimulation patterns to the internal controller by means of a radio frequency transmitter. Using such implanted electrodes, it is possible to recruit muscles more selectively and to recruit deeper muscles than is possible with surface stimulation. The CWRU system has successfully produced standing and gait in SCI subjects (Agarwal *et al* 2003). However, as this system also operates without sensory feedback, premature fatigue is still a problem and the system works in a completely open-loop manner, producing only crude gait movements.

A system under development which includes closed-loop control is Praxis™ (Davis *et al.* 2000), by Neopraxis Pty Ltd. in Australia. This system, as well as having feedback, is also unique in that it is multi-modal: it incorporates both FES for standing and gait, and additional electrodes placed at the Sacral roots (S2, S3 and S4) for bladder (and possibly bowel and erection) control. The components include an implantable stimulator with 22 stimulation channels, "button" electrodes for peripheral nerve stimulation and "linear para-radicular" (LPR) electrodes for stimulation of the sacral roots. Other components include the external controller, which stores up to 9 stimulation patterns, a radio frequency data link, and 5 external sensor packs. The sensor packs are externally attached to each thigh, shank and the trunk and each contains two accelerometers and a rate gyroscope. Follow-up reports of the Nucleus FES22, a precursor to the current Praxis™ system (Nucleus FES24), showed that using this particular stimulator it was possible to produce prolonged, safe, closed-loop controlled standing for 30 to 60 minutes. The improvements from the Nucleus FES22 system to the current model are primarily in reducing the bulk of the sensor packs and the addition of the sacral root electrodes. Although this system has been somewhat successful, it is still largely external and involves a great deal of implant surgery.

Research in this field is ongoing at numerous other locations including Ljubljana, Slovenia by Kralj, Bajd and coworkers, who developed the first continuous FES standing exercise program for paraplegics in 1979. They developed a device that showed that standing for therapeutic purposes can be achieved with two channels of FES delivered to both knee extensors (Bajd *et al* 1999). For this system, considerable arm support is also required.

The systems previously mentioned outline some of the advances and limitations in the devices that have been used to date, but where is this research heading?

Research Directions for FES Standing

It seems that systems developed to date have enabled paraplegics to stand, but only in an abnormal manner. A collaboration in Europe between Donaldson (University College London), Hunt and Gollee (University of Glasgow) and Matjacic and Sinkjær (University of Aalborg) used the approach that if ankle stiffness is high enough, then it is possible to maintain stance through the use of the still viable upper body (Matjacic *et al.* 2003). The main problem that arises with this method is that the stimulation levels needed to maintain a sufficient amount of ankle stiffness in an open-loop setup are so large that they can rapidly produce fatigue. Their study concluded that the duration of standing is directly correlated to muscle strength and the rate of fatigue, and in order to achieve long periods of standing using FES, the subject was locked in a brace that insured the only movement that occurred was about the ankle joints. These researchers felt that the focus of attempting to integrate voluntary motor skills of the upper body will push towards more controlled standing (Hunt *et al.* 2001). The main flaw is that subjects are forced to stand rigidly with strongly contracted muscles and consequently, muscles fatigue rapidly, as was outlined above. This problem may be eradicated if afferent signals are monitored to create a closed-loop system, thus allowing for lower levels of background stimulation interspersed with ongoing postural corrections, a strategy that is expected to reduce fatigue.

The issue of fatigue is extremely important when attempting to develop a standing and balancing system. One approach mentioned by Matjacic *et al.* (1998) is to provide a number of different 'safe' standing positions. These positions are all within the same safe area, when the COP falls within the base of support, but they employ different combinations of muscle activation to maintain stance. Feedback may be used to control switches in posture, much like the method employed by intact humans to facilitate prolonged stance. A control strategy that incorporates the use of sensory feedback from cutaneous receptors may be useful to cause postural changes according to the shifts in COP, when they reach certain limits in terms of distance and/or velocity. As Winter (1998) stated, the center of mass (COM) is assumed to be what is regulated in the gravitational environment as a means to monitor "body sway". However, due to the

complexity involved in establishing the position of the COM as a means of feedback, a simpler approach to monitoring "body sway" is to estimate the change in COM from the change in the COP within the base of support. The COP trace was shown to map the movement of the COM with virtually no time lag. However, this scenario requires sufficient levels of stiffness in the ankles as well as the knees. If the ankles were modelled to behave as pure springs to support the body like an "inverted pendulum", the COP and COM would oscillate perfectly in phase. Winter *et al.* (1998), found that a lag (within 6ms) was consistently measured, suggesting that during the control of stance, intact humans rely heavily on stiffness control. On this basis, if sufficient ankle stiffness is created, the position of the COM can reasonably be predicted from the COP.

In general terms, it is clear that any advanced FES system developed to maintain posture in paraplegics will need to include some form of feedback, and if such feedback is to predict COM from COP, sufficient stiffness will also be required. Methods to overcome premature muscle fatigue have to involve feedback, and a reasonable method to provide this feedback may be to monitor the afferent activity from cutaneous receptors on the soles of the feet.

Anatomy of the Human

To understand the development of systems to control balance in the paraplegic subject, it is important to fully appreciate the complexities of the human system to control posture and in particular the biomechanics and anatomy of the system with an emphasis on the sensory receptors that provide signals that monitor the state of the system.

First we must understand the neural anatomy of the lower limbs, in particular, the feet and ankles.

Neural Anatomy of the Foot and Ankle

The neural anatomy of the human foot includes muscular, arterial and cutaneous elements. For the purpose of simplification, the primary focus in this section is to understand the cutaneous innervation of the glabrous skin on the foot sole. The *Anatomy of the Human Body* (Bartleby, 2000) was used for reference in this section.

The Tibial nerve (Figure 4), the larger of the two terminal branches of the Sciatic (the other being the Common Peroneal), arises from the anterior branches of the fourth and fifth lumbar and first, second, and third sacral nerves. The Tibial nerve descends the leg, covered by the muscles of the calf. The branches of the Tibial nerve are the Articular, Muscular, Medial Sural, Medial Calcaneal, and Medial and Lateral Plantar nerves.

Of concern for this study are the cutaneous branches that supply the soles of the feet. Figure 5 is a simplified display of how the separate branches innervate the soles of the feet. The Medial Calcaneal branch of the Tibial nerve supplies the skin of the heel and medial side of the sole of the foot. The medial plantar nerve, the larger of the two terminal divisions of the Tibial nerve, has a cutaneous branch that pierces the plantar aponeurosis between the Abductor hallucis and the Flexor digitorum brevis. The Lateral Plantar Nerve supplies the skin of the fifth toe and lateral half of the fourth. This can be seen in Figure 4, which shows the many bifurcations.

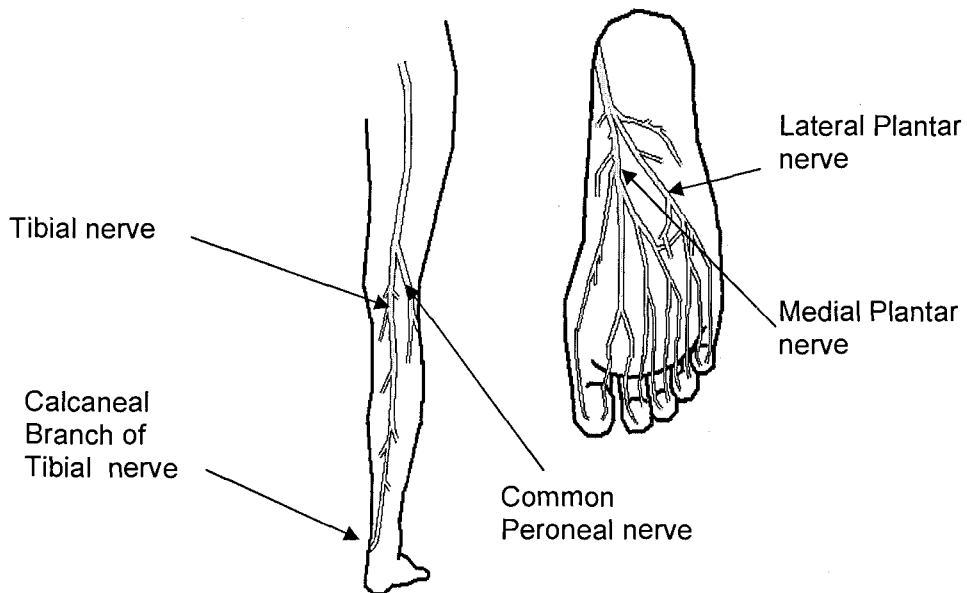


Figure 4 – Tibial Nerve. Bartleby, 2000. (Adapted by permission of S.van Leeuwen)

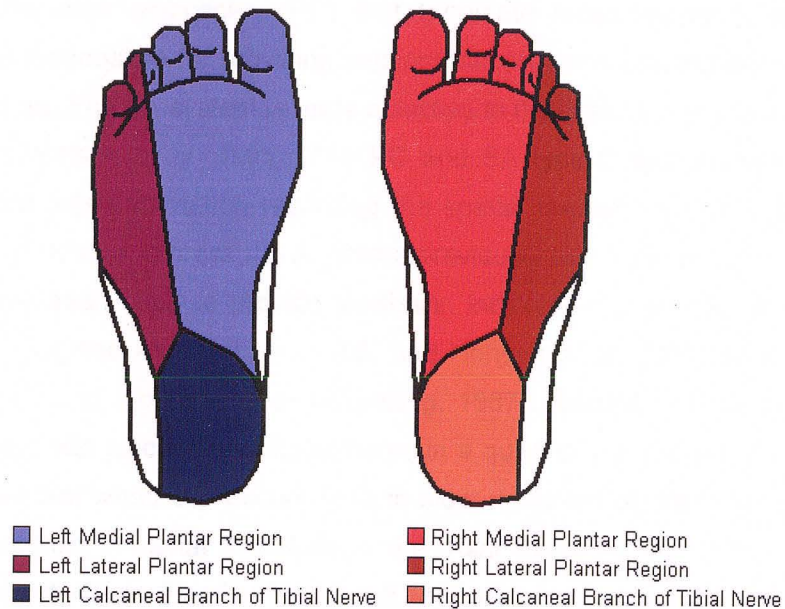


Figure 5 – Simplified Diagram of the Segmental Distribution of the Cutaneous Nerves of the Sole of the Foot. Bartleby, 2000. (Used by permission of S.V.Luewen)

In addition to the neural innervation, it is important to understand the properties of the neural receptors and skin on the feet soles. This will be covered in the next section.

Sensory Receptors/Innervation

The focus of this study is to examine the feasibility of using nerve cuff electrodes to record from peripheral nerves in humans and in particular, to monitor signals arising from mechanoreceptors in the soles of human feet. This section will look closely at the types and distribution of sensory receptors in the human feet, specifically the cutaneous pressure receptors.

Cutaneous Receptors

Cutaneous sensory mechanoreceptors in glabrous skin are known to provide information on pressure and stress. These cutaneous receptors have afferent axons in the A- β range and can be divided into four groups. There are two slowly adapting (SA) types: SA type 1, which terminate just under the epidermis in Merkel cells, and SA type 2 which terminate more deeply in Ruffini corpuscles. There are also two types of rapidly adapting

(FA) sensory endings: FA type 1 Meissner's corpuscles just under the skin surface, and FA type 2 Pacinian corpuscles (PC) that terminate more deeply. The SA type 1 receptors are responsible for providing sensory information regarding perception of fine form and texture. The FA system is more selective in the detection of slip and very small movements (Johnson *et al.* 1995). The PC and SA type 2 systems are deeper and hence, provide less information regarding the spatial makeup of stimuli but are more receptive to vibration and pressure. As stated previously signals from cutaneous sensory receptors have been used to provide feedback, including human heel strike detection during gait (Haugland and Sinkjær, 1995. and Hansen *et al.* 2001) and to detect slip during human grasp (Johansson and Westling, 1987). Recording ENG signals from a nerve cuff electrode placed on a digital nerve in a quadriplegic subject (Haugland *et al.* 1999) showed that when slip occurs (due to slow reduction of grasp force), there is a significant increase in signal amplitude in the Volar digital nerve. These signals were recorded using a single channel nerve cuff (discussed on page 32). When the signal amplitude crosses a chosen threshold level, stimulation is produced and the grip force is increased to prevent further slip. This example clearly demonstrates that by recording signals, which relate to mechanical changes at the skin surface, useful feedback for neural prosthetic devices is available.

Haugland *et al* (1994) also showed the relationship between skin contact force and recorded ENG. They found that it was possible to extract information from the ENG arising from cutaneous receptors of the feline footpad that related to perpendicularly applied force. A model was produced that reliably predicted ENG output from force input; however, the converse relationship did not have a unique solution. In this study a number of problems were highlighted, in terms of extracting contact force information from cutaneous afferent firing. One issue is the "OFF" response. The problem is that an increase in ENG can also be seen when the force declines rapidly, or the application of force is ceased. This may make it difficult to distinguish between rising and falling events. Partly because of this issue, it was found that ENG could be predicted from the force but it was not possible to accurately predict force from the ENG. It is expected that this issue will not arise if the changes in pressure are less rapid, such as during postural shifts while standing.

It seems possible that an application of closed-loop FES could be developed that incorporates the use of cutaneous signals to monitor the foot sole pressure distribution

of a paraplegic subject as the means of providing feedback to maintain upright stance. As the body centre of pressure shifts, the relative pressures on different areas of the soles of the feet change. As the pressure increases there are associated increases in afferent discharge. Kennedy and Inglis (2002), and Kavounoudias *et al.* (1998) have shown that the soles of the feet may, to some extent, provide a map of contact.

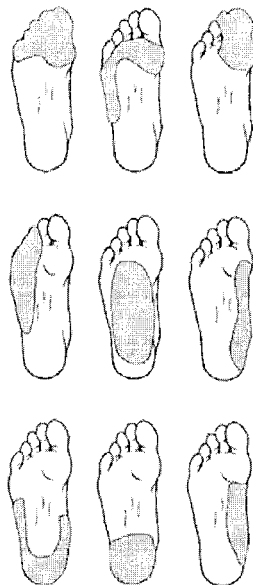


Figure 6 – Distinct Regions of the Foot Sole Based on Multi Unit Activity. Kennedy and Inglis, 2002. (Used by permission of Dr T.Inglis)

Shown in Figure 6 are the nine distinct regions outlined on the foot sole based on the multi-unit activity observed in their subjects by Kennedy and Inglis (2002). If it were possible to selectively record from afferents from two or more separate regions of the foot sole, it may be feasible to monitor the sway of an individual based on relative differences between the selected regions, to give an indication of the amount of body weight shifting among various regions of the feet. Using larger sensory fields such as those shown on Figure 6, which indicate the sensory fields for entire nerve branches, it is apparent that one would only need to record from two nerve branches to get a reasonable impression of the distribution of afferent firing.

It is important to note that it was found that although multi-unit territories varied in size between subjects, the locations of fascicular fields were similar. Thus, it may be assumed that similar control mechanisms will be usable for different subjects. Kennedy

and Inglis (2002) also found that activation thresholds for skin receptors in the foot sole were quite variable. However, importantly, based on their sample, the thresholds of receptors did not appear to be dependent upon location. Unlike the hand, where there is an increased type 1 receptor density in the finger tips (Johansson, 1979), there did not appear to be an accumulation of type 1 receptors in the toes, nor was there any preferred spatial distribution for receptors in the foot. However, while cutaneous information from the plantar skin is important, the entire sole of the foot is primarily involved in weight-bearing actions and thus no specific area is sensitive to specific stimulus. There was a large variability in threshold for activation of individual receptors (FA as low as 0.5 mN to SA as high as 3000 mN). In contrast, the mean threshold for activation of receptors of each type was not found to be significantly different in the separate regions of the foot. Across the sole of the feet there is an even distribution of slowly and rapidly adapting fibres. Kennedy and Inglis (2002), found the following distribution of receptors on the soles of the feet: SA type 1s = 14%, SA type 2s = 15%, FA type 1s = 57%, and FA type 2s = 14%. These findings suggest that signals produced for a given weight distribution should be similar when recorded in different areas of the sole. These results suggest that it may be considered that the foot sole provides a 'map' of the weight distribution were supported by data from Kavounoudias *et al.* (1998), they suggested that the CNS extracts spatially relevant cues from the cutaneous receptors on the soles of the feet that indicate the direction and the amplitude of whole-body inclination. It is also noteworthy that Kennedy and Inglis found that when the foot was off the ground, there was no background firing, i.e. when no loads were applied on the foot sole. It was suggested by Kavounoudias *et al.* (1998) that this is because of the role that the receptors play in signalling ground contact.

The skin on the sole of the foot is entirely glabrous. Properties of glabrous skin differ from hairy skin. It is thought that "glabrous skin has tight connections to subcutaneous tissues that are absent in hairy skin" (Kennedy and Inglis, 2002) and as a consequence, the hairy skin is able to stretch more easily and thus it is thought that hairy skin plays a larger role in joint motion detection. In contrast, the receptors in the glabrous skin may provide more information regarding foot contact. Trulsson (2001) found that glabrous skin is more densely innervated by cutaneous receptors than non-glabrous skin, and it is mentioned that the spatial acuity of the sole tends to be higher than that of the non-glabrous skin on the dorsal side. It is important to note that Trulsson also found that the

mechanoreceptive units found in the human Sural nerve show similar properties to units identified in other mammalian (rabbit, cat and rat) studies of the Sural nerve. There were some differences, though, the most significant of which was the difference in the receptor types when the non-glabrous area of the innervation territory is covered by hair. This, of course, is not the case in the swine foot sole model.

Another concern regarding monitoring cutaneous signals is receptor adaptation. As can be seen in work by Haugland *et al.* (1994), receptor adaptation results in a changing relationship between constant force and ENG. If the force stays constant, the ENG will gradually decline. However, for purposes of maintaining postural control, the primary concern is to be able to detect fairly large changes in forces, not steady state forces.

Anatomy of the Swine

The nature of the swine anatomy makes it a useful model for comparing the signals recorded from the glabrous skin as a comparison with the human. This section will establish similarities and differences between swine and human, in terms of biomechanics, limb anatomy and the sensory receptor location and types.

Neural Anatomy of the swine hind limb

The anatomy of swine is very similar to that of humans in many ways. This has meant that swine have been used as a model for a number of studies, including but not limited to: heart research, dermatological testing, and research into artificial organs. The swine model has also notably been used for testing in FNS research, particularly in the areas of bladder and bowel control (Jezernik *et al.* 2000).

In this study, nerve cuff electrodes were placed around the Tibial nerves of swine. The circumference of the Tibial nerve is approximately 15 mm in mature swine, and the peak nerve conduction velocity is almost identical to that of the human, in the region of 50-60m/s. This is very important for the study, since nerve circumference and velocity are key factors in determining the amplitude of acquired ENG signals. The electrical properties of nerves are similar across mammalian species, but signal amplitudes recorded by a cuff are determined by the fibre types, nerve diameter, conduction velocity and nerve cuff geometrical properties (Hoffer and Kallesøe, 2000).

The Tibial nerve of the swine, similarly to humans, bifurcates into the Medial and Lateral Plantar nerves. Figure 7 shows how each of the branches supplies one of the two digits. During the study, nerve cuff electrodes were placed above the ankle, proximal to the bifurcation and thus encompassed both branches.

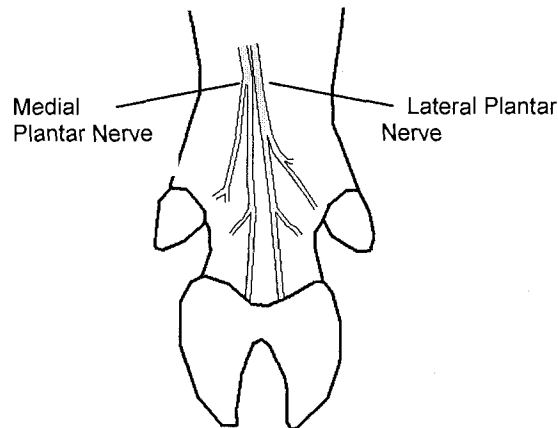


Figure 7 – Plantar View of the Swine Right Hind Limb

Sensory Receptors/Innervation

An essential similarity between humans and swine, in terms of posture, is that the weight bearing is over glabrous skin. Although the swine has a small hoof, the weight is mainly borne on the plantar pads of two central digits. As previously mentioned, studies have shown that upon analysis, like nerves have shown uniform properties across mammalian species (Trulsson, 2000). The only significant differences were found when the nerve innervated regions of skin that were covered with hair.

Biomechanics/Control of Posture

Posture of the swine differs from humans in two fundamental ways: swine are quadrupedal in comparison to bipedal humans, and as can be seen in Figure 8, the swine is digitigrade, essentially the equivalent of standing on two big toes.

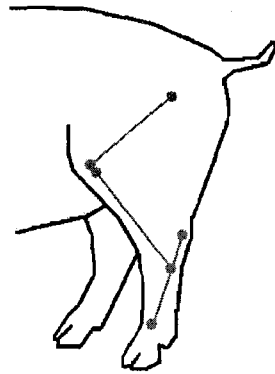


Figure 8 – Hindquarters of the Swine with Schematic Representation of Bones

Due to the fact that swine are quadrupedal, they have a significantly more stable posture than humans. However, for the purpose of this study, the main concern during signal acquisition was not the movement of the body, but rather the relative pressure changes and resultant nerve signals that are evoked. The analysis was performed in such a way that events were matched to similar relative pressure changes observed during the human protocol.

Due to the large weight of the pigs used in the study and the considerably smaller support surface, average pressure on the plantar region is far greater than for humans. For the purpose of this study, the assumption was made that average receptor loading is comparable in the two species, since it may be assumed that skin thickness and toughness increase proportionally with bodyweight. This issue will be addressed again in a later section.

However, studies have shown that postural corrections (and sway) in quadrupedal stance, tend to be primarily performed with hindlimbs, while forelimbs are used as supportive struts (Dunbar *et al.* 1986). This was evident during signal acquisition in the present study.

Summary of Assumptions

In order to compare results between the swine and human, of the following reasonable assumptions were made:

1. Cutaneous receptor density and types are similar in the glabrous skin of swine and the soles of human feet.
2. Receptor density and type do not vary significantly across selected regions of the human foot sole.
3. Maximum ground contact area during stance of any given region of the foot is a reasonable approximation of the contact area for that region throughout the trial, for purposes of calculating regional pressure distribution.
4. Pressure provides a better indication of receptor loading than force.
5. The mechanics of the skin is a function of the weight supported by any given skin area. Thus thicker, tougher skin develops to support greater weight, and therefore deforms proportionally less with the same pressure. This is true across species with glabrous skin.

These assumptions are addressed again in the Methods section.

Nerve Cuff Electrodes

The design of nerve cuff electrodes has evolved over the past 30 years (Hoffer and Kallesøe, 2000). Many changes have been made, particularly to the cuff walls, closure methods, electrode position/type and the number of electrodes placed within the cuff. This section will outline the development history of cuffs, the state of the art and evidence of the safety and efficacy of nerve cuff electrodes in long-term implant studies.

Principles of Design

The design of nerve cuffs is such that they can resolve extra-cellular potentials that propagate along the axons of a nerve. The reasoning behind the recording capabilities of nerve cuffs is well explained by Hoffer and Kallesøe (2000) where the comparison was made between the effect of using hook electrodes to lift a section of nerve and the effect of encompassing a section of nerve with a silicone cuff containing electrodes, as follows:

“When a section of nerve is lifted in to air, it is possible to record a signal whenever an action potential propagates along the nerve; similarly this is possible in the nerve cuff. The amplitude (V) of the action potential recorded is a function of the current amplitude; its wavelength (λ) and the length (2d) of the lifted nerve portion. The signal recorded in the nerve cuff is related non-linearly to the length of the cuff. To obtain the maximal

signal amplitude possible the length of the cuff should approximate λ as closely as possible." (Hoffer and Kallesøe, 2000)

A tripolar configuration of electrodes and a differential input recording amplifier are necessary to exclude extrinsic signals (EMG). To maximize common-mode rejection, the indifferent electrode placement must be equidistant from the central recording electrode. In addition, the electrical impedance of the recording and indifferent contacts should be similar to aid in noise reduction. Some of the problems that have been mentioned previously for other electrodes also apply to the use of implanted electrodes used in an attempt to record nerve signals. These include nerve selectivity, reproducibility of signals, ease of implant, functional longevity, nerve damage, and connective tissue encapsulation (Hoffer and Haugland, 1992). The effect of the long-term application of, and the damage caused by nerve cuffs, has been documented more closely than for any other neural electrodes. As nerve cuffs are not required to puncture the epineural sheath or to make contact with nerve fascicles, the damage caused can be considerably less than by many other electrodes. There is, however, the potential for causing damage if the cuff is ill-fitting. If the cuff internal circumference is too small, compression of the nerve may be caused. On the other hand, if the cuff is too large, it cannot record good signals and may be liable to move; such movement could cause damage. Within a few days of the implant of a nerve cuff, the connective tissue growth that occurs around the outside and in the extra space inside the cuff has two effects: it helps secure the cuff in place, thus reducing the likelihood of damage through movement; and the growth of tissue inside the cuff increases the longitudinal impedance.

The design and implant of the cuff are very important when attempting to minimize damage. During implant, a location for the cuff is chosen that is away from joints, so as to reduce cuff/nerve movement. The section of nerve on which the cuff is placed must be freed sufficiently and be away from blood vessels. An advantage with nerve cuffs is the relatively simple implant method (see Appendix B – Surgical Procedures). Once the nerve has been located and sufficiently freed, the actual placement of the cuff takes only a few minutes. During the implant it is important to carefully route the lead wires to allow for movement, to ensure they are not under excessive stress.

The first clinical prototype use of nerve cuff electrodes to record afferent signals in humans was by Sinkjær and colleagues in Denmark (Haugland and Sinkjær, 1995). As

mentioned previously, this was intended for a system to correct for drop foot in a hemiplegic patient. This system successfully showed that nerve cuffs are a viable option for recording ENG in human limb nerves.

A practical disadvantage of nerve cuffs is the lack of selectivity. A nerve cuff with electrodes that encompass the whole nerve hence records from the entire nerve trunk. It is possible to implant numerous small cuffs, to record from separate nerve branches innervating different muscles, but this requires more surgery and the associated problems of an increased number of electrodes placed on more fragile, smaller nerves. The ideal solution is to somehow record from different nerve fascicles at one location along a main nerve trunk. This can be achieved by using multi-channel, multi-chambered nerve cuffs (MCC's) (Hoffer *et al.* 1998).

The idea behind the development of MCC's is for both stimulation and recording purposes. As can be seen in Figure 9, the inside of the cuff has longitudinal ridges that separate sets of tripolar electrodes, in a sense constraining the space around the nerve into chambers, or channels'. The ridges that form the chambers have the effect of isolating the signals recorded or the stimulation pulse delivered. This design allows for more selective recording.

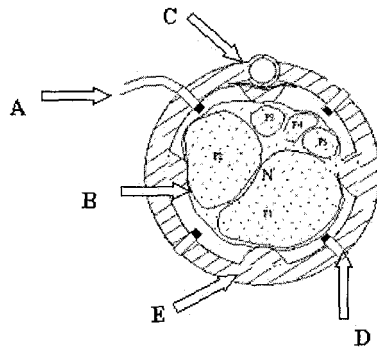
Of all the available options, nerve cuffs are the most reliable electrodes available, and have been implanted long-term for many years (See Figure 2).

Neurocuff™

The general design of the nerve cuffs used in the study is detailed in this section and follows a design patented by Hoffer *et al* (1998). The MCC has a number of unique design properties. An example of an MCC can be seen in A = One piece lead out wire and electrode. B = Nerve bundle. C = Piano-hinge closure system. D = Separate Chamber. E = Chamber Partitions

Figure 9 and Figure 10. A = One piece lead out wire and electrode. B = Nerve bundle. C = Piano-hinge closure system. D = Separate Chamber. E = Chamber Partitions

Figure 9 shows an end on view of the cuff, which shows the chambers and ridges (made of silicone tubing in this example) that separate the sets of recording and indifferent electrodes, creating actual channels.



A = One piece lead out wire and electrode. B = Nerve bundle. C = Piano-hinge closure system. D = Separate Chamber. E = Chamber Partitions

Figure 9 – Multi Channel Nerve Cuff Electrode – End on view (closed).

The figure also shows a nerve naturally comprising several large fascicles. Due to this property, electrodes in a given chamber may become particularly selective to certain fascicles when compared with recording capabilities of electrodes in the other chambers (or channels). For example, the chamber marked “D” in A = One piece lead out wire and electrode. B = Nerve bundle. C = Piano-hinge closure system. D = Separate Chamber. E = Chamber Partitions

Figure 9 is likely to be more sensitive to activity in the large nerve bundle (in this case the Tibial nerve within the Sciatic nerve) when compared with the recording capabilities of the other channels.

Figure 10 shows a schematic drawing of a cuff placed around a nerve just prior to closure. A piano-hinge closure mechanism can be seen. Once the nerve has been freed and the cuff has been carefully placed around the nerve, the two sides are hinged and closed together using the method developed by Kallesøe *et al.* (1996). To hold the hinge elements in place, a suture is fed through the complete tube that is created by the closed hinge. A ground wire is also placed in the cuff. Two different proprietary Neurocuff™ prototypes, provided by Neurostream Technologies, were used in this study: single channel cuffs (SCN), and four-channel cuffs (4CN). For the purpose of this study

comparisons are not made between the recording capabilities of the single and multi-channel cuffs.

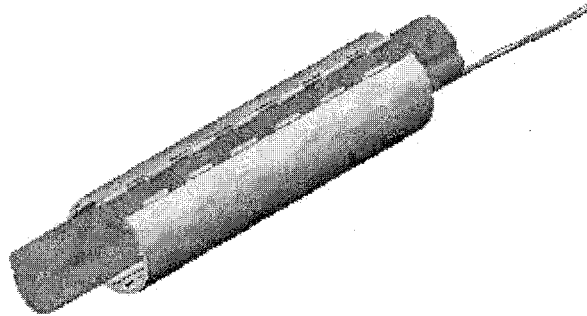


Figure 10 – Multi Channel Nerve Cuff Electrode – Around the nerve.

Safety and Efficacy

A large body of data demonstrates the long-term safety and efficacy of nerve cuff electrodes for recording. This includes nerve cuffs used for several years for heel strike detection in individual human subjects (Hansen *et al.* 2004) and Phrenic nerve pacing using implanted stimulating cuffs for as long as 20 years in some subjects (Glenn *et al.* 1976).

The particular design of cuff used for the study has been used in the Neurokinesiology Laboratory at Simon Fraser University; Canada, for numerous studies. The data shown in Figure 2 was acquired from the sciatic nerve of a cat walking on a treadmill, 605 days post implant.

The nerve cuff materials are of implantable grade and commonly used in the manufacturing of medical devices.

METHODS

General Experimental Design

The objective of this study was to use a swine model to assess the feasibility of using ENG signals arising from cutaneous receptors to determine the movement of the COP during stance. Tibial nerve afferent signals generated by hind foot mechanoreceptors in the swine were monitored in real-time with a prototype version of Neurostep™, a fully implanted, closed-loop, battery operated FES control system. Neurocuff™ electrodes were placed around the Tibial nerves of three swine (two of which were bilaterally implanted). Since the cuffs were placed distal to the exit points of the majority of muscle nerve branches (except for intrinsic foot muscles supplied by the tibial nerve) and due to the biomechanics of quadrupedal posture, the source of the data was considered to be largely cutaneous in origin (see section: Neural Anatomy of the swine hind limb). The ENG signals were rectified, integrated, sampled and telemetered out of the body by the Neurostep™ device.

During recording sessions, the F-Scan® system (A bipedal plantar pressure and force measurement device employing resistive ink technology) was used for simultaneous monitoring of pressure under both hind feet. The sampled ENG data files were stored in a computer together with the F-Scan® pressure data files and these files were later merged. Comparisons were then made with published human data regarding receptive fields of cutaneous receptors, how these fields relate to forces on the foot soles during intentional sway in controlled postural experiments, and whether pressures produced on the human foot soles are comparable to the pressures that evoked Tibial nerve ENG signals in the swine model.

In terms of data collection, the study was composed of two separate protocols. Protocol One involved the acquisition of pressure data during human standing using F-Scan® insole force sensors. Protocol Two involved the simultaneous acquisition of ENG signals arising in the Tibial nerve of swine and F-Scan® pressure recorded under the hind feet during experimentally induced postural shifts.

After data collection was complete, analysis was first performed on the human data, in order to establish the pressure changes that occur in selected regions of the feet during postural sway. Pressure values were converted into relative changes in pressure. These relative values were subsequently converted to equivalent pressure changes for each swine recording. The final part of the analysis was to test whether there were significant changes in ENG signal amplitude during pressure changes representative of human data in the standing swine subjects.

The following sections provide a detailed look at the experimental setup for each protocol and all aspects of the data analysis.

Protocol One – Methods

The purpose of Protocol One was to study the typical changes in pressure on the soles of the human feet during intentional postural adjustments and to investigate the relationship between pressure distribution and the typical innervation areas of the foot soles.

The F-Scan® system (Tekscan) was used to acquire data regarding loading of different areas of the feet during standing. F-Scan® sensors consist of flexible shoe insoles that are 0.15mm thick and weigh only 10g. Due to the 960 Sensels™ in the F-Scan® sensors, they provide detailed moment-to-moment ‘pictures’ of pressure distribution. The F-Scan® sensors work using resistive technology whereby a thin semi-conductive coating (ink) is applied as an intermediate layer between electrical contacts. This ink, unique to Tekscan sensors, provides electrical resistance changes that are proportional to the changes in pressure (Tekscan, 2004).

Experimental Design

F-Scan® movies were recorded from 6 healthy subjects (5 males, 1 female, ages 26 – 39 years), who gave informed consent. Subjects wore comfortable footwear with a heel height of less than 2.5 cm, and were asked to stand quietly with their hands down by their sides and eyes focused towards a location on the wall. After standing quietly for 30 seconds, the subjects were asked to slowly sway close to their postural limit and back to their resting position in 8 different directions (see Figure 11), each time resting at a comfortable location for quiet stance. This protocol was repeated twice. Before the start

of each trial, the subjects were asked to place their feet in a comfortable position. The distance between the heels and the angle θ (Figure 11) were measured. The complete method for acquiring F-Scan® data was as follows:

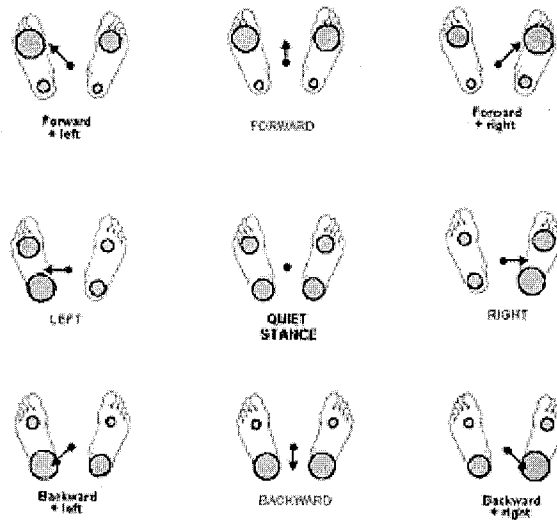


Figure 11 – Eight Directions of Postural Sway and Related Force Changes

- Measure subject's feet and trim insoles to fit as per the F-Scan® manual 5.22. Insoles were used for numerous subjects up to 10 recording sessions in total. For each new subject the insole was trimmed to fit.
- Set up equipment listed below:
 - 2 x Sensor Insoles
 - 2 x Data Acquisition Ankle Cuffs
 - F-Scan® Mobile Unit
 - Laptop Computer with Power Supply
 - F-Scan® External Trigger
 - F-Scan® Battery Pack
- Weigh subject wearing all equipment for calibration purposes.
- Break in sensors. Prior to calibration, the subject was instructed to walk for 10 m and allow the sensors to adjust to the temperature inside the shoe. Walking was not required if sensors were being reused.
- Calibrate sensors. The subject was asked to stand on one limb to calibrate each sensor under the subject's full weight. This calibration was performed again prior to each recording session.
- Set up acquisition parameters. External triggering was enabled and the sampling rate was set to 40 or 50 Hz (depending on Neurostep™ sampling).
- Recording. USB cable connecting the mobile unit with the laptop was disconnected and recordings were completed.

- Download Data. USB cable connecting the mobile unit with the laptop was reconnected to download data.

Initial Data Analysis

The first stage of the data analysis was to export two sets of force files from the F-Scan software: one set to create a COP plot (Figure 14) and one set to create a Force vs. Time plot for each of the six receptor regions to be analyzed (Figure 12). The six receptor regions were selected based on anatomical data of the typical segmental distribution of cutaneous nerves in the foot (see Figure 5). Figure 13 shows the F-Scan® software set up to produce the force files. On the left hand panel the preferences are set to export force data (in Newtons) and the panel on the right displays contact area (in mm²).

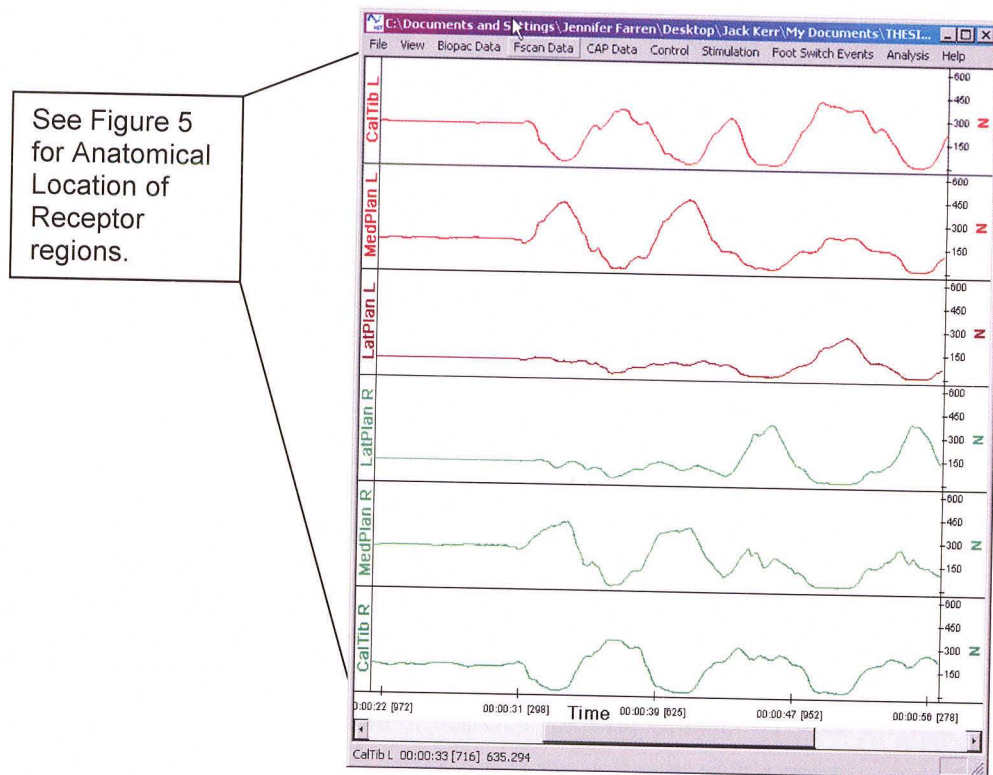


Figure 12 – Force vs. Time Plot for Six Receptor Regions of the Human Foot (Subject 02)

Prior to exporting the data, the values for the maximum contact areas were noted and the maximum contact areas were used to calculate pressure values.

The method used to create the COP plot first involved splitting the recording from each foot into two areas (Figure 15). The COP of each area was then calculated for every frame of data and the resultant of the four vectors was resolved. The size of the toe and heel areas was determined using the F-Scan® software. During the initial 30 seconds of the trial, when the subject was asked to stand upright without shifting weight, the size of the areas that best approximated 50-50 weight distribution on the front and back of the feet was determined. This was done using a Force vs. Time plot showing both areas simultaneously.

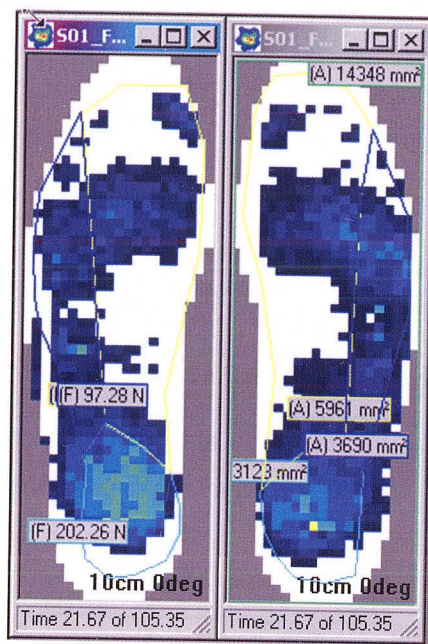


Figure 13 – Setup for Exporting Regionalized Contact Area and Force Data

After the COP file was created, it was possible to monitor the COP movement during sway. Figure 15 shows an example of the COP plot for Subject 01, trial 01. The values for heel separation and angle were entered into the software at this point.

Once the plot was created, time values were exported for the period of sway in each of the eight directions, when the COP moved from quiet standing to 75% of the directional “sway limit”. The 75% value was determined as described by Popovic *et al.* (2000). This value approximates the postural sway at which subjects reach their “undesirable” zone.

Using the exported time values, the pressure changes were then determined in the second F-Scan® file that was created. This provided information regarding the pressure change experienced in each of the selected regions during postural changes.

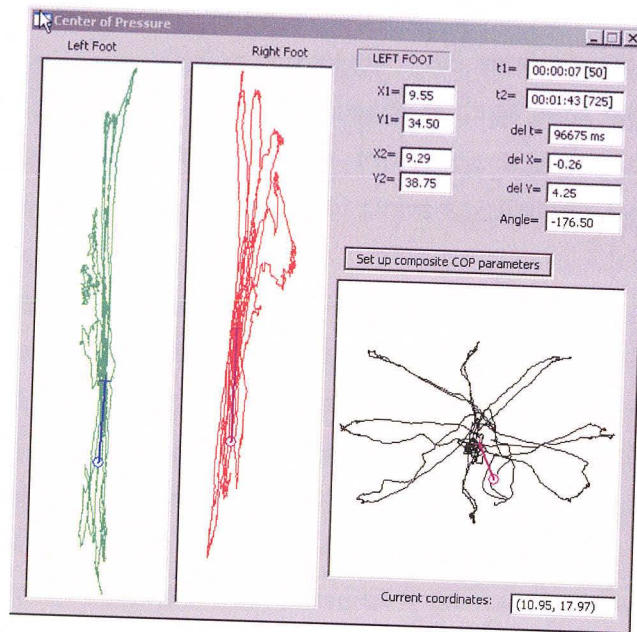


Figure 14 – COP Plot from F-Scan Data (Human Subject #02)

The initial analysis of the human standing data was completed when values had been converted to % change of force for each of the regions.

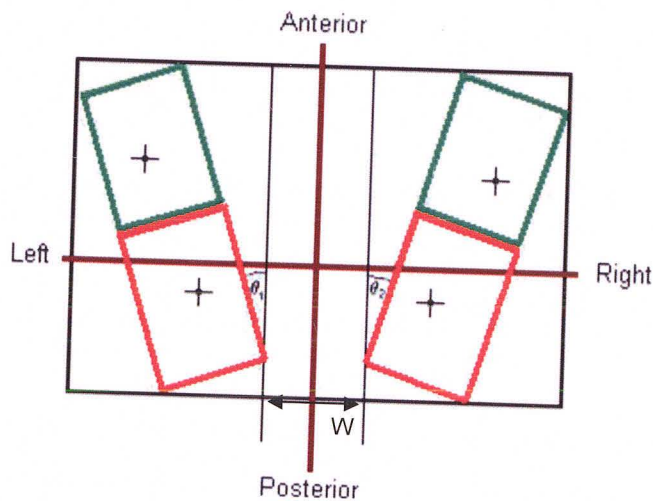


Figure 15 – COP Calculation from F-Scan® Pressure Data

Protocol Two – Methods

Protocol Two involved the simultaneous acquisition of ENG signals and pressure changes under the hind feet of swine subjects. To collect the ENG data for this particular study, a proprietary, fully implantable, prototype FNS device with state-of-the-art amplifiers (Barú, 2003, 2004) was implanted in each of three adult female swine. The implantation procedure was performed with the subject under gas anesthesia. Procedures were approved by the Simon Fraser University Animal Care Committee. A total of five devices were implanted (two subjects received bilateral implants; See Table 1). When a subject received bilateral implants, this was done in two surgical procedures at least two weeks apart, to provide time for recovery. Tripolar Neurocuff™ electrodes (cuff length 30mm, see Table 1 for details regarding cuff circumference) were installed around the Tibial nerve in a location 5-10 cm proximal to the ankle joint and the control unit was placed in a subcutaneous pocket in the ipsilateral thigh area (For complete surgical procedures see Appendix). The recovery period after surgery was found to be short: subjects were able to stand and walk comfortably the day following surgery.

Subject	Limb	Device Filter	Cuffs on Tibial Nerve	Approx Nerve Circ (mm)
01	Right	850 Hz – 6 KHz	One Single Channel Neurocuff One Four Channel Neurocuff	15
02	Left	850 Hz – 6 KHz	One Single Channel Neurocuff One Four Channel Neurocuff	5.5
	Right	850 Hz – 5 KHz	Two Single Channel Neurocuffs	9.5
03	Left	850 Hz – 5 KHz	One Four Channel Neurocuff	18
	Right	850 Hz – 5 KHz	One Four Channel Neurocuff	18

Table 1 – Swine Subject Details

A limitation of the implanted Neurostep™ device for the purposes of this study was that it provided pre-processed data that was rectified and sampled at a lower frequency before it was telemetered out of the body; therefore, the raw electroneurographic data could not be directly acquired. However, a major benefit was wireless real-time ENG recording that did not require the passage of wires through the skin of the swine. As well, the parameters, particularly the amplifier within the device, were optimised for ENG recording. The amplifiers used in the implanted device had a bandwidth of either 850 Hz to 6 kHz, or 850 Hz to 5 kHz (all values $\pm 5\%$). Figure 16 shows the frequency spectrum of ENG signals collected from a different swine subject in a preliminary acute experiment, where the raw nerve signals were also available. It can be seen that the majority of the power of the nerve signal lies near the centre of the amplifier frequency bandpass region. Filtering the signal in the chosen bandpass region was shown to exclude unwanted EMG activity. For more details of the implanted amplifiers for each subject, see specifications in Appendix A – Device Specifications.

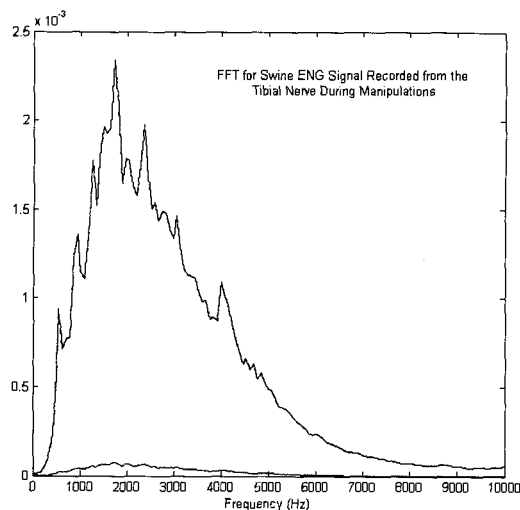


Figure 16 – FFT for Swine ENG Recorded from Tibial Nerve

The ENG data obtained using the Neurostep™ device was internally sampled, rectified and bin integrated before transmission out of the body. The sampling rate and bin integration time for the majority of trials were set at 25 ms and 16 ms, respectively. This output provided a relatively smooth envelope representation of the ENG signal.

The swine posture was gently perturbed using manual shifts of the subjects' hips. Since the objective of the study was to determine the relationship between the recorded pressure and the ENG, it was not necessary to produce exactly repeatable inputs. Video footage was collected for each trial and was used as necessary to monitor the movement of the hindquarters during postural shifts. These data were analyzed in the same way as the relative pressure changes monitored with the F-Scan® system during human standing using Protocol One. (See Protocol One – Methods).

Experimental Design

To simultaneously acquire ENG signals from one or two implanted Neurostep™ systems and reliably merge these data with the monitored F-Scan® force data required a careful setup. This was challenging, since there were either three or four different sets of data to be collected using two separate laptop computers. In order to merge data subsequently for analysis, it was necessary to acquire all these data simultaneously using a synchronization “bookmark”. This procedure was particularly important when recording bilaterally using two independent Neurostep™ devices. The three or four channels that needed to have a time reference were: F-Scan®, video, ENG “left leg” and ENG “right leg” (if bilateral). Bookmarks were simultaneously introduced into each of the two ENG files during recording. The ENG data were then adjusted to align the bookmarks in the two records. In order to align the F-Scan® file with the ENG files, the F-Scan® recording trial was started by a trigger signal generated simultaneously with the bookmarks. This enabled accurate merging of the ENG files with the F-Scan® force. Finally, to also align the simultaneously recorded video footage with the force and ENG data, a beep was recorded into the video sound track when the F-Scan® was triggered.

Each implanted Neurostep™ system could provide up to five channels of data, but only one channel could be monitored at a time. Therefore, to obtain data from other available channels the entire procedure was repeated. To collect useful data, the procedure for recording from the swine subjects was performed in a controlled, sequential manner, detailed below:

1. Start F-Scan® and load calibration files. Calibration of the sensors was performed prior to start of each recording session using a human subject with known weight.
2. Position swine subject on treadmill. The F-Scan® sensors were placed on a flat surface inside a transparent box and the subject was fed in such a position as to

- ensure that the two hind limbs were placed over the sensors. A wooden frame was then temporarily secured between the feet to minimize foot movements.
3. Place radio frequency (RF) header over implanted Neurostep™ device. The RF header was manually held pressed against the skin over the implanted device. (Two RF headers were needed to communicate with two implanted Neurostep™ devices in bilaterally implanted subjects).
 4. Communicate with device(s) and select and program channel(s) for recording.
 5. Prepare F-Scan® for use of external trigger
 6. Program the device(s) 'ready to record'.
 7. Start Video Camera recording. The video camera was aligned behind the hind limbs, in order to capture mediolateral sway.
 8. Start device recording mode(s). Neurostep™ device(s) were started and signals acquired.
 9. Simultaneously add bookmarks in the ENG file(s) and start F-Scan®.
 10. Recording. Once the recording had begun, the subject was allowed to adjust its own posture. If the subject stood "quiet" for more than a few seconds, sway was induced by gently nudging the hips.
 11. Stop F-Scan®
 12. Stop ENG recording(s)
 13. Stop Video Camera

Once recordings were complete, files were transferred to a single laptop computer for analysis.

Definition of Good Trials

Only "good" swine posture trials were fully analyzed in this study. A good trial was one that met the following criteria:

1. Two F-Scan® files, one for each foot, were obtained. If only one file was collected, then unilateral analysis could be completed if all other criteria were met.
2. For bilateral analysis, two ENG files were acquired, each with a simultaneously introduced bookmark (one ENG file was required for unilateral analysis).
3. A complete video recording of the trial was made.
4. Upon watching the F-Scan movies and video recording, only sections of the movies where both feet were on the sensors or when one foot was in the air were included. If at any stage ground contact was made outside the sensor surface, this section was excluded.
5. No files were corrupt. On some occasions, the F-Scan® system skipped some frames of data and if so, these files were excluded.

NOTE: Trials weren't excluded due to poor signal quality, but only when the above criteria were not met.

Collecting good data for the bilateral trials was very challenging. In order to record good data the two RF programming headers were held in place simultaneously while the subject stood in place over the sensors. After significant training the subjects would more reliably stand in place; however, they were easily startled and therefore did not like their feet being held in place. The final solution was to develop a system, by which a "steep sided canyon" (See Figure 17) was built that meant the feet could only stand comfortably when directly over the sensors. This system also had a bar across the front to prevent the feet from moving forward (not shown in Figure 17). Due to the shape of the sensors, and as there was no bar behind the feet, the feet were still not always on the sensors. The amount of time that the subjects remained cooperative was also limited (only during lunch time and as long as the food supply lasted), so data collection time was at a premium.

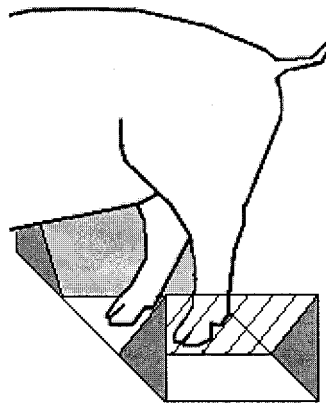


Figure 17 – "Steep Sided Canyon" Setup for Positioning Swine on Sensors

Initial Data Analysis

During initial analysis, the ENG data acquired from the swine was exported using the Neurostep™ software and saved as text files for merging. In addition, the relevant F-Scan® files were opened. Each file was carefully inspected to establish whether the trial was "good". If accepted, the maximum foot contact area was recorded and force files were exported for merging. In contrast to Protocol One, the swine foot surface area was not split into regions; rather the pressure under each entire foot was monitored.

The exported ENG text file was now imported into the Neurostep™ proprietary event detection analysis program. Parameters were set to detect features in the ENG signal, such as a rise and/or fall in nerve activity of certain amplitude and duration. Noise spikes of width within a defined narrow region were excluded. Typical filter values were an ENG signal increase of 3 thresholds with a rise time of between 100 and 800 ms. ENG signals that included spikes of less than 100 ms in duration were excluded. The results of this analysis were exported as a text file.

At this point, using custom-developed Windows-based software, all the files were merged together. The merged file included: left foot force, right foot force, ENG right and or ENG left, and analysis results. An example is shown in Figure 18 below:

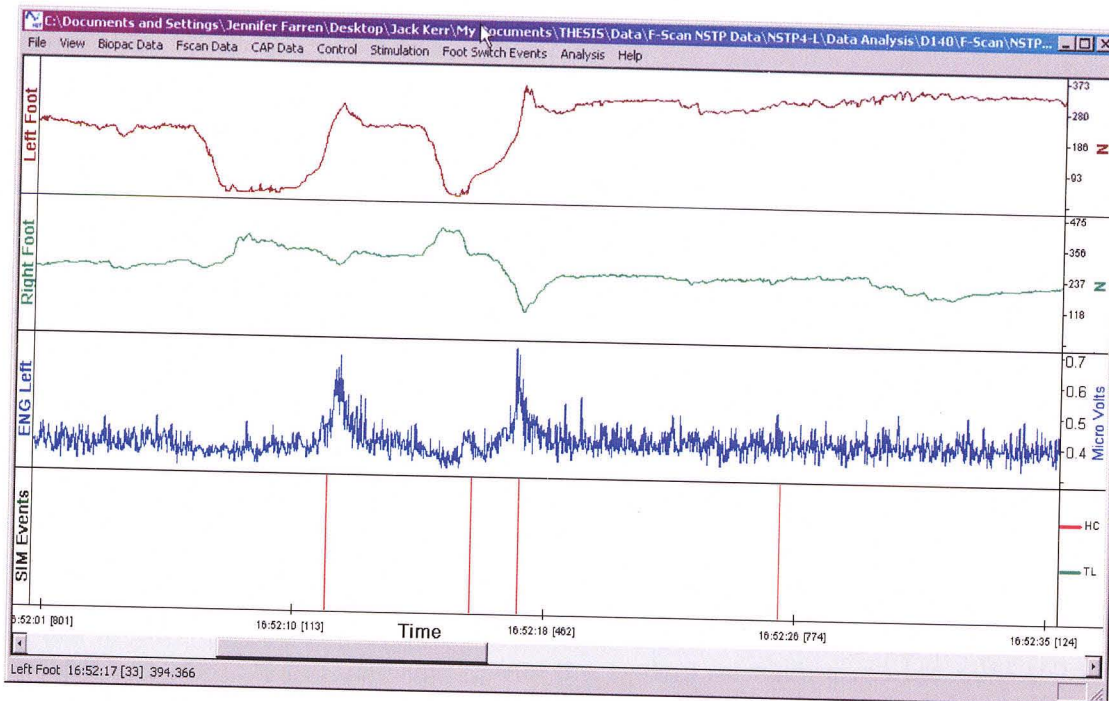


Figure 18 – Plot of Merged Force, ENG and Event Detection Files (Swine subject SW2).

The accuracy of the file merging was limited by two factors: the sampling frequencies of the data acquisition and the timing of the examiner to introduce bookmarks simultaneously. The maximum error due to the sampling was ± 25 ms between the force and marker files. The two marker files were aligned according to the simultaneous introduction of bookmarks. This was thought to be an insignificant error when compared with sampling rates. In addition, there was a delay between the depressing of the key and the bookmark introduction in the file. However, this was tested for and it was found

that the delay was consistently 600 ms for both laptop computers with the same programs running. The bookmark delay was accounted for during the merging by shifting the file timing. The parameters for event detection were adjusted for optimal detection without false acceptances (see Final Data Analysis). Once the simulation files, force files and ENG were exported, the results from the two protocols could be related.

Final Data Analysis Methods

Unilateral Swine Recordings

Analysis was performed to determine whether ENG signal changes were detected when a pressure increase greater than 15% occurred. During analysis, there were three possible outcomes in terms of event detection (see Figure 19):

Missed event – a situation that arose when a pressure change of 15% or greater occurred, but did not result in an event being detected from the ENG signal (e.g., Box 1 in Figure 19)

False acceptance – a situation where no significant change in force was seen but a change in the ENG signal occurred, which was mistakenly interpreted as a detection of a significant pressure change event (e.g., Box 3 in Figure 19)

Detected event – a situation where a pressure change occurred and a resulting change in the ENG signal amplitude met the predetermined detection parameters (e.g., Box 2 and 4 in Figure 19)

For every missed or detected event, both the magnitude of the pressure change and the rate of change of pressure were noted for subsequent analysis. For each trial, it was possible to compute the detection rate of the system for each given pressure change. Using these detection rate figures, it was possible to extrapolate whether a certain postural sway in humans would produce a detectable change in afferent ENG.

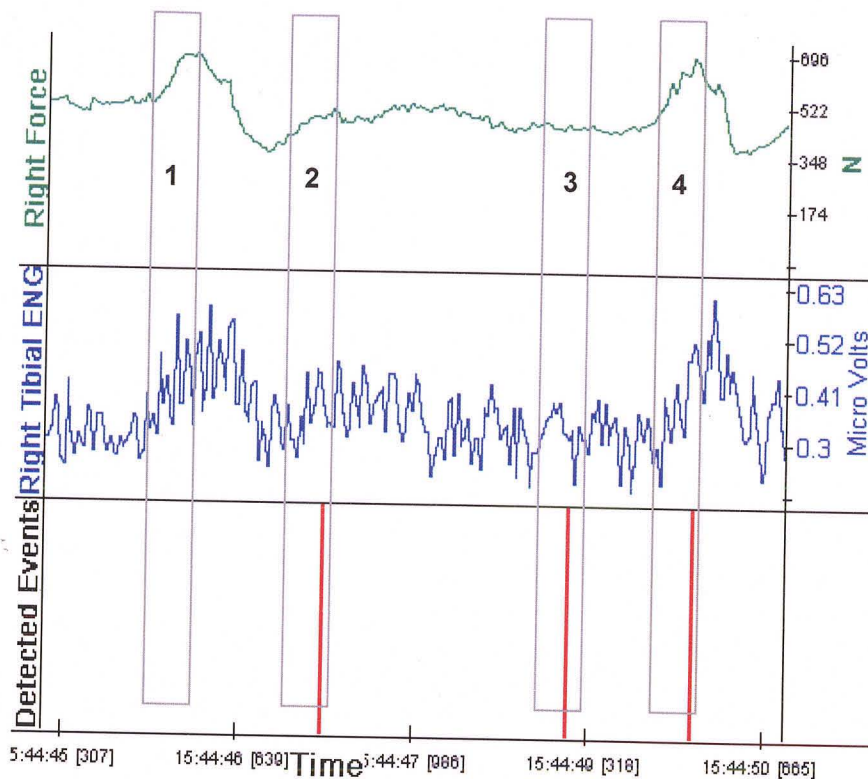


Figure 19 – Examples of Missed, False and Detected Events

Bilateral Swine Recordings

In addition to the event detection analysis described above, testing was done to examine whether there were advantages in comparing processed ENG signals bilaterally for increased sensitivity to sway. It was hypothesized that perhaps sway could be matched to the difference in ENG signals, even in cases when events were not detected in the individual ENG signals.

This analysis was performed by outputting the filtered simulator file for each hind limb with the event detection feature turned off. The values of the left ENG file were then normalized and subtracted from the values of the right ENG file for every sample. The same computation was done with the force files. Statistical analysis was then performed to evaluate the relationship between the difference in the ENG files and the changes in force.

Comparisons were then made with the event detection using unilateral analysis, to determine whether there were any significant improvements.

RESULTS

Protocol One

As may be expected, results from the human standing trials showed increases in force and pressure in each of the six foot sole regions when sway was directed toward that region. The data was analyzed to measure absolute changes in force and the changes in pressure relative to the pressure experienced in a foot sole region during quiet standing. In addition, the rates of change of force and pressure were plotted. For all data analysis of the force and pressure changes, displays in this and following sections will show both positive and negative changes. A positive change indicates that there was an increase in the force, and a negative value conversely shows there was a decline in force. Analysis of Protocol One data primarily involved establishing the range of values that may be required to determine the movement of COP during posture in humans.

Force Change (N)

It was important to first establish whether force measurements provided sufficient information regarding receptor loading, or whether pressure values should be calculated.

The magnitude of the change in force for each of the eight sway directions, in each of the six foot sole regions, is shown below in Figure 20 as the average and S.D. for all 6 subjects. The plots clearly indicate the general weight shifting that may be expected. The greatest weight shift to a single region occurred when the weight shift was towards a corner of the postural sway zone. For example, when the weight shifted towards the back and left, the majority of the weight was shifted onto and supported by the left receptor region of the Calcaneal branch of the Tibial nerve (CT), which had an increase of $260 \pm 117\text{N}$. In comparison, when the weight was shifted forward and right, the weight supported by the left CT region declined by $184 \pm 85\text{N}$.

It is important to note that these force change data do not provide a clear indication of concomitant changes in receptor loading. For example, the force may increase by the same amount in two separate areas, but due to the sizes of the regions, the pressure change on the receptors may be unequal. Also, the standard deviation is quite high for

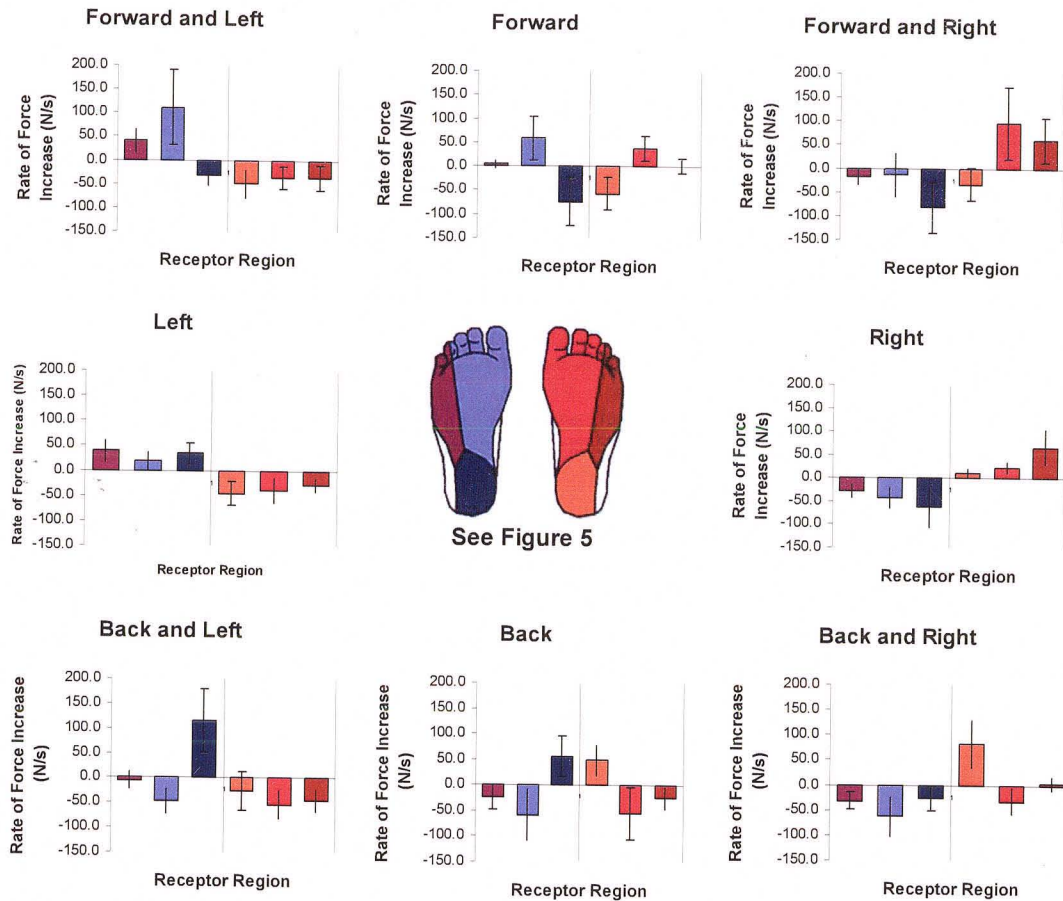


Figure 21 – Rate of Force Increase in Six Selected Regions during Intentional Human Postural Sway in Eight Directions (Average and S.D. of 6 Subjects)

Calculating Pressure from Force

To quantify the percentage changes in pressure during sway, the quiet standing pressure for each region was first calculated. Table 2 shows the average values for force and pressure in each region during quiet standing. On average, forces exerted on the LP regions of the feet were significantly lower than the forces exerted on the MP regions. However, the pressure exerted on the MP regions was lower, on average, due to the larger innervated area. The CT region, in comparison, had the largest forces and pressure measurements.

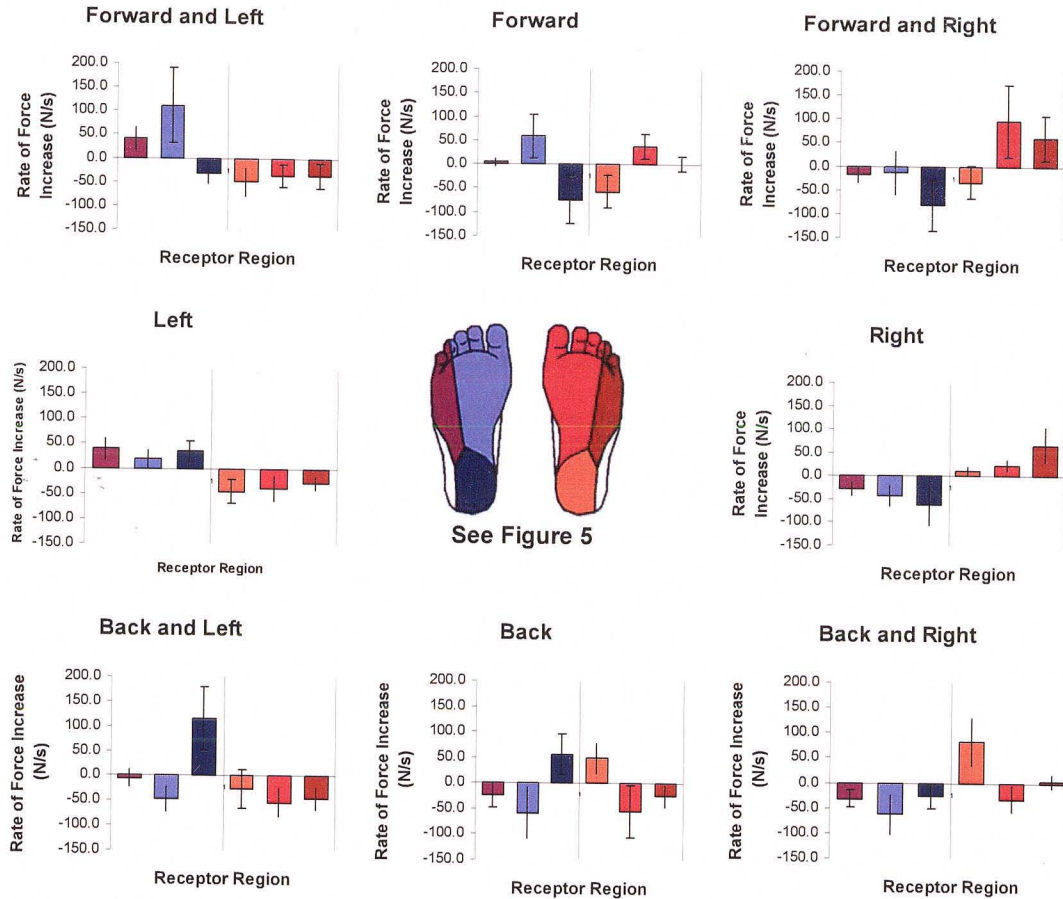


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Region	Quiet Force (N)		Quiet Pressure (Kpa)	
	Mean	S.D.	Mean	S.D.
MP-L	152.5	24.5	20.2	2.5
LP-L	92.5	7.9	22.9	2.3
CT-L	228.7	38.4	65.0	11.0
MP-R	175.5	49.5	24.0	8.3
LP-R	114.5	13.0	30.9	3.0
CT-R	193.7	36.3	55.7	11.3

Table 2 – Mean and S.D. of Force and Pressure Measurements during Quiet Standing in Humans, Monitored in the Six Receptor Regions.

Pressure Increase (%) and Rate of Pressure Increase

In this section the pressure changes during intentional sway were plotted and comparisons were made with the changes in force measured during sway.

Once the values for quiet standing were established for each subject and each trial, the percentage pressure increase was calculated. Figure 22 shows the percentage pressure increase on each region during intentional sway. It may be noted that there was considerable variation in the results between the monitored force changes (see Figure 20) and after converting to pressure using maximum contact area and normalizing (see Figure 22). For example, the average change in force in the right LP region during forward right sway was only 65% of the force change in the right MP region. However, in terms of pressure changes, the increase in the right LP pressure during forward left sway was 140% of the pressure in the right MP region. Figure 23 shows the rate of pressure increase measured for each receptor region during intentional sway in each of the eight sway paths.

Figure 24 shows the inter-trial variability for a representative single subject (Subject 4). Each receptor region is displayed as a separate plot showing the percent pressure increase monitored during sway in the eight directions. Generally, results are reasonably similar with one clear difference: the values for Trial Two show smaller values for the MP and LP regions on both feet (regions loaded during forward movements) and the values for Trial One show smaller values for the CT region of each foot (regions loaded during backward movements). Since the same placement of the regions was used for all trials for each subject, the most obvious explanation is that the subject simply loaded more on

the fore-feet in Trial One than in Trial Two. This assumption is reinforced by the data displayed in Table 3, which shows the forces and pressures monitored during quiet standing were much greater in the fore-foot regions for Trial One then Two.

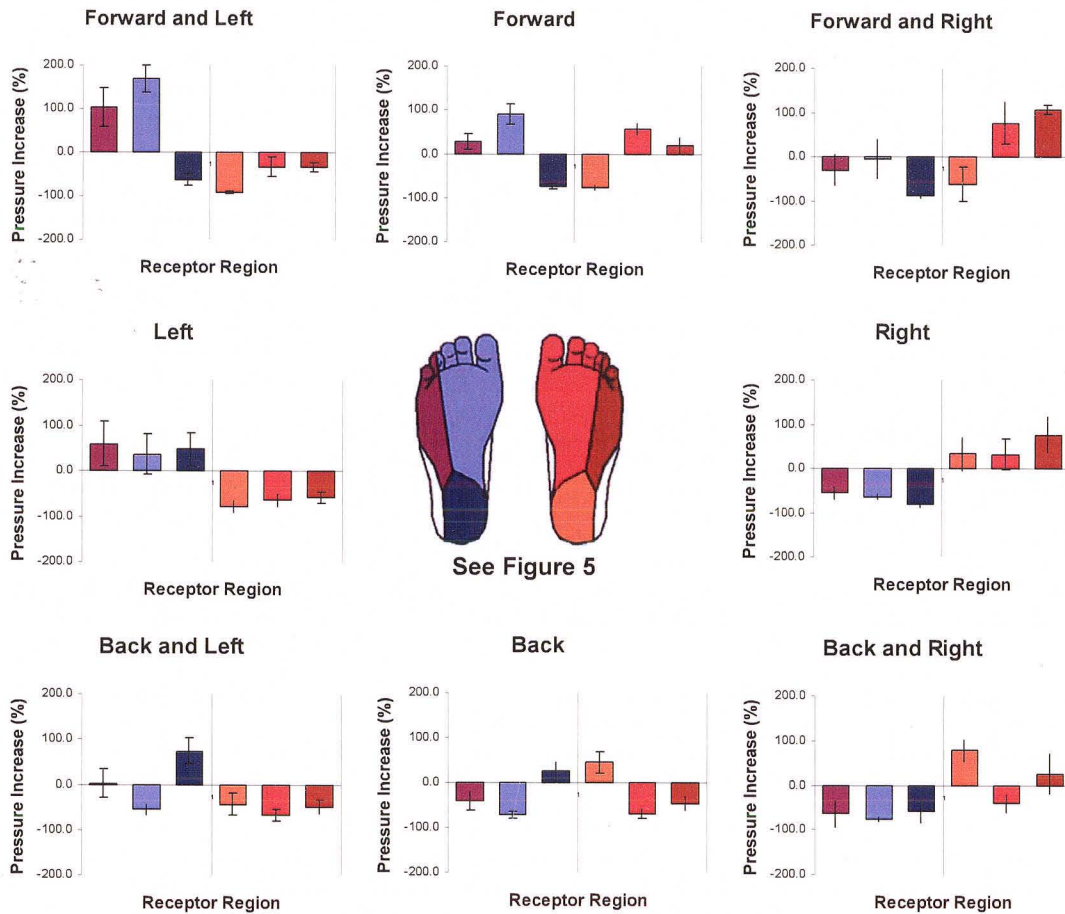


Figure 22 – Pressure Increase over Six Selected Regions during Intentional Human Postural Sway in Eight Directions (Average and S.D. of 6 Subjects)

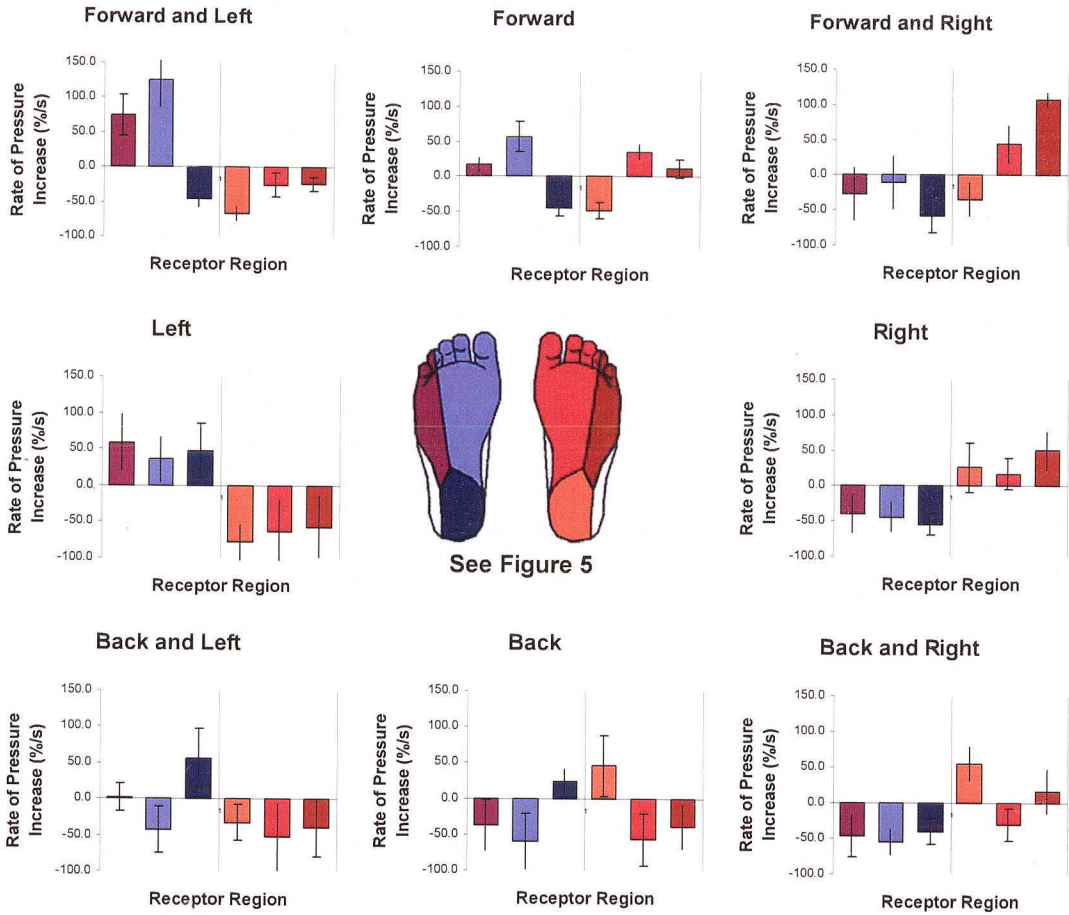


Figure 23 – Rate of Pressure Increase over Six Selected Regions during Intentional Human Postural Sway in Eight Directions (Average and S.D. of 6 Subjects)

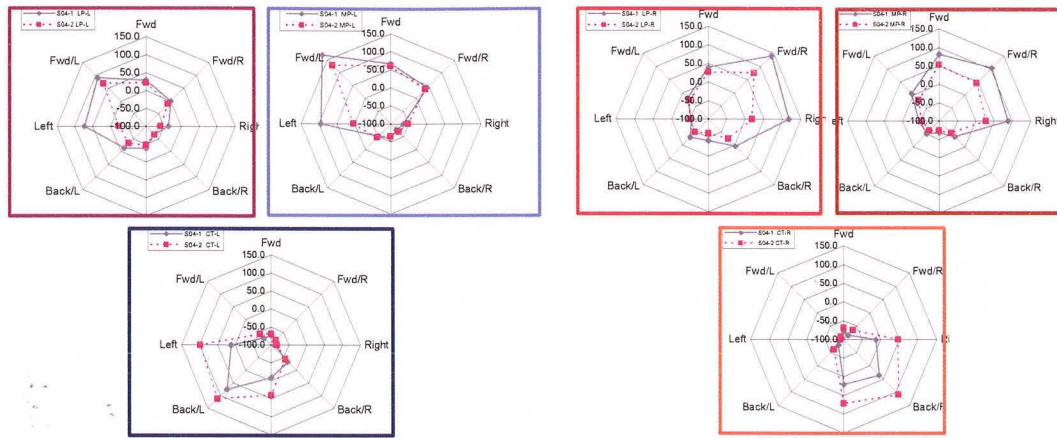


Figure 24 – Inter-trial Variability, Both Trials for Subject Two, Pressure Increase (%) is Plotted for Both Trials in Each of the Six Receptor Regions during Intentional Sway Towards Eight Directions.

S2-1

	Q Force	Cont Area	Q P (Kpa)
MP-L	175	0.0092	19.02
LP-L	99	0.0042	23.57
CT-L	191	0.0035	54.57
MP-R	193	0.0089	21.69
LP-R	136	0.0041	33.17
CT-R	196	0.0037	52.97

S2-2

	Q Force	Cont Area	Q P (Kpa)
MP-L	158	0.0097	16.29
LP-L	87	0.0044	19.77
CT-L	236	0.0035	67.43
MP-R	160	0.0093	17.20
LP-R	100	0.0031	32.26
CT-R	266	0.0034	78.24

Table 3 – Subject Two, Trials One and Two: Quiet Standing Forces and Pressures

Relationship between Pressure Increase and Rate of Increase

The correlation coefficient between pressure increase and rate of pressure increase was found to be 0.99. In one regard this is not surprising, since for each sway the time taken to reach a position was the same for all regions, thus the pressure change was proportional by default. However, there were variations in each trial and subject, which influenced the average. The high correlation suggests that subjects controlled their sway according to how much weight was being shifted. Small weight shifts occurred slowly, whereas larger shifts required more significant movement that must occur at a faster rate (perhaps more difficult to control).

Figure 25 shows a composite plot of pressure increase versus rate of pressure increase for all six individual human subjects. In terms of inter subject variability, the results fall within a relatively tight band with few exceptions, other than perhaps S04 who may have pushed himself to a farther postural limit.

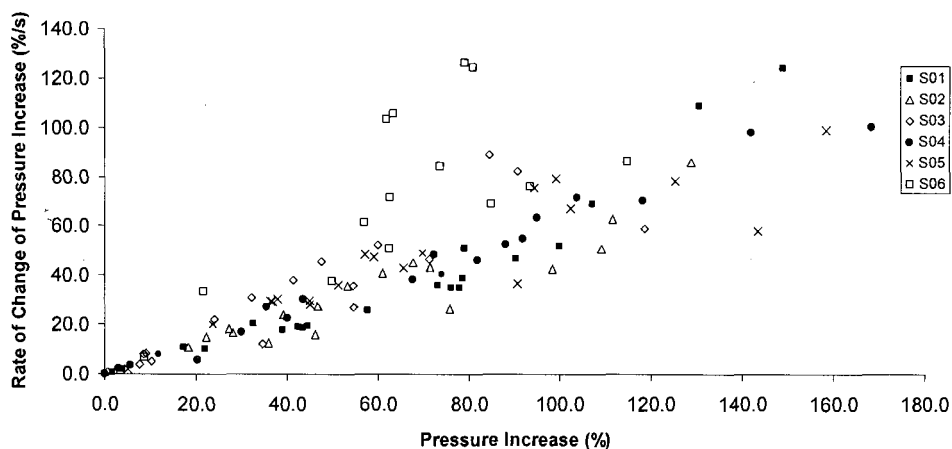


Figure 25 – Pressure Increase vs. Rate of Pressure Increase during Intentional Postural Sway in Humans (6 subjects)

Figure 26 shows in more detail the distribution of pressure changes in each of the six receptor regions. These data show that pressure changes were comparable across regions. The only obvious disparity was between the MP-L and MP-R values. MP-L included the three largest values. A larger subject sample and greater number of trials would be needed to understand the significance of this difference.

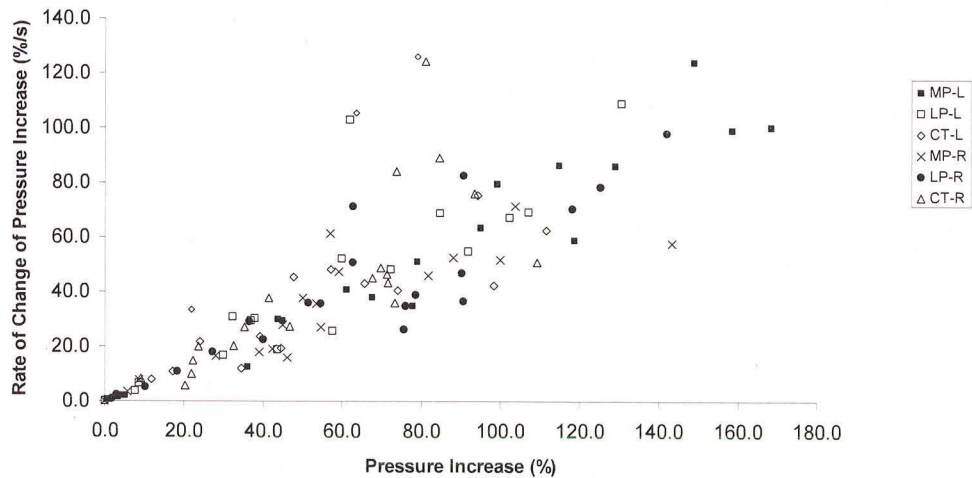


Figure 26 – Pressure Increase vs. Rate of Pressure Increase during Intentional Postural Sway in Humans (6 Sway Regions)

Selecting Values that may be Important for Postural Control using an FES Device

After compiling all the human data, the average and standard deviation for the pressure changes in each receptor region during intentional sway were established. The average data can be seen in the two tables shown below (Table 4 and Table 5).

Sway Direction	Receptor Region					
	MP-L	LP-L	CT-L	MP-R	LP-R	CT-R
Fwd	89.9	27.1	-55.4	56.9	18.5	-77.8
Fwd/R	-4.8	-30.3	-87.5	76.5	107.2	-61.8
Right	-63.8	-55.7	-81.7	31.8	75.8	32.8
Back/R	-76.8	-64.5	-58.6	-41.1	24.8	77.6
Back	-71.5	-41.3	25.1	-69.2	-46.4	45.1
Back/L	-55.8	1.9	73.0	-66.8	-49.7	-43.5
Left	35.8	58.6	47.6	-64.4	-57.2	-78.3
Fwd/L	168.7	102.6	-62.7	-33.3	-33.4	-92.5



Table 4 – Average Pressure Increase (%) during Intentional Postural Sway in Humans

Sway Direction	Receptor Region					
	MP-L	LP-L	CT-L	MP-R	LP-R	CT-R
Fwd	56.4	16.2	-35.2	35.4	12.0	-48.1
Fwd/R	-11.5	-26.8	-57.5	44.4	76.0	-34.4
Right	-44.0	-40.0	-54.4	17.4	50.2	26.4
Back/R	-55.3	-47.1	-40.5	-30.8	15.5	54.7
Back	-60.1	-37.1	22.6	-57.0	-39.4	42.0
Back/L	-42.2	1.6	56.1	-51.8	-39.6	-32.4
Left	22.1	51.4	40.5	-58.3	-51.9	-61.9
Fwd/L	125.2	73.8	-45.7	-25.5	-25.1	-67.7

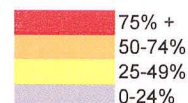


Table 5 – Average Rate of Pressure Increase (%/s) during Intentional Postural Sway in Humans

From these tables, a set of unique values was determined that may be used to detect direction and extent of sway from measured pressure increases. This enabled the creation of a set of mutually exclusive regions or pairs of regions that may be used to detect COP movement using an FES system for controlling posture in paraplegic subjects.

Direction of Sway	Foot Sole Regions of Greatest Pressure Change
Forward	MP-L and MP-R
Forward Right	MP-R and LP-R
Right	LP-R
Back Right	CT-R
Back	CT-L and CT-R
Back Left	CT-L
Left	LP-L
Forward Left	MP-L and LP-L

Table 6 – Key Regions for Detecting Postural Sway in Each of Eight Directions

Due to the outlying values for the MP-L region, these values were not included when determining average and standard deviation values for this data. The average value and standard deviation of pressure increase in these particular regions was $72 \pm 24\%$. This range of pressure increases was used as a target to determine the detection rates of interest in the data obtained from the swine subjects (Protocol Two).

In addition, the influence of the rate of pressure increase (Table 5) was considered for the same set of sway directions and receptor regions outlined in Table 6, the average and standard deviation of the rate of pressure increase was $51 \pm 15\%/s$

Figure 27 shows a plot of the averaged pressure increase data for each of the receptor regions. It is evident that there is a clear relationship between the amount of pressure increase and the rate of increase. The dashed box on Figure 27 indicates how the select range of values that was determined as crucial, falls within all of the averaged pressure increases during intentional sway.

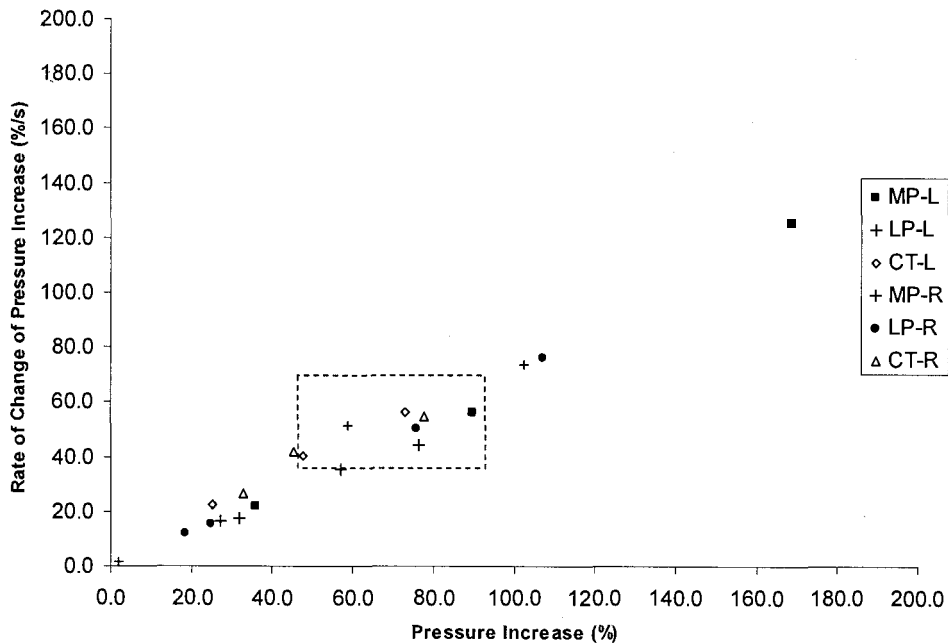


Figure 27 – Pressure Increase vs. Rate of Pressure Increase during Intentional Human Postural Sway, Average Pressure Increases during Intentional Sway in Eight Directions

Figure 28 and Figure 29 indicate how the full range of human data were distributed by pressure increase and rate of pressure increase. The figures indicate a wide range of pressure increases but the majority (90%) of events had rates of pressure increase below 75 %/s.

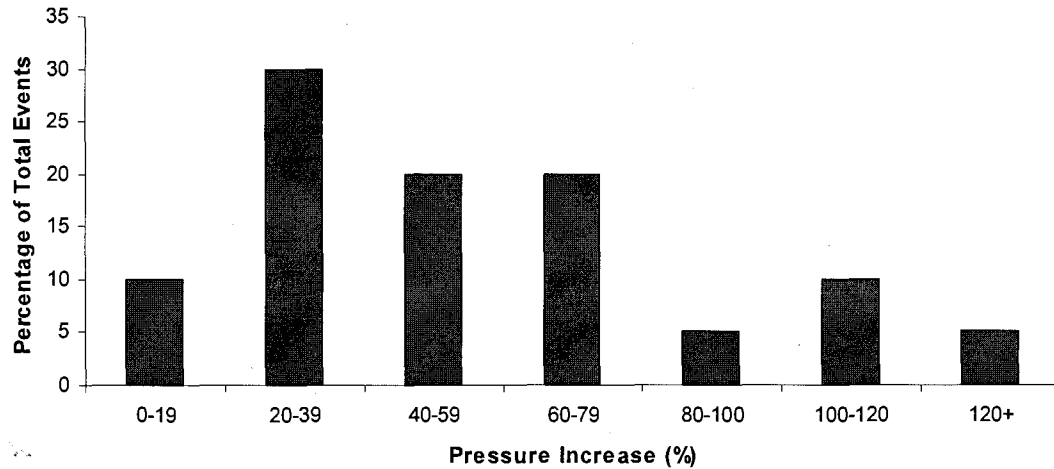


Figure 28 – The Frequency of Sway Events by Pressure Increase for all Six Regions of the Feet during Intentional Postural Sway in 6 Human Subjects

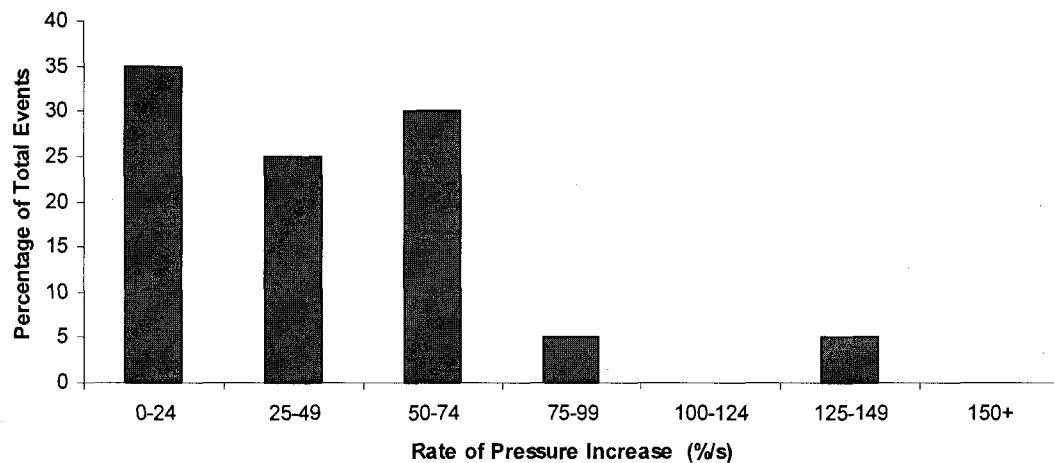


Figure 29 – The Frequency of Sway Events by Rate of Pressure Increase for all Six Regions of the Feet during Intentional Postural Sway in 6 Human Subjects

Protocol Two

Unilateral Analysis

The primary focus of this analysis was to establish the relationship between changes in pressure under the hind feet of swine and whether there was a significant change in the ENG signal recorded from the Tibial nerve cuff in one hind limb. In addition, the swine

was used as a model for comparing pressure increases with those that occurred during intentional postural sway in humans.

Initial analysis was performed by attempting to detect events in the ENG signal that related to significant pressure increases. In order that later comparisons could be made with human data, it was important to use pressure values that were normalized with respect to the average pressure per region during quiet standing, as stated previously. This procedure was performed prior to analysis for each trial, by calculating the pressure from the force during quiet standing and the maximum contact area experienced throughout the trial. Table 7 shows the collated results from all swine trials.

An event was defined as the occurrence of a rise in pressure of at least 15% of the quiet standing pressure. Events were discarded if they included a negative slope during the pressure increase. It can be seen in Table 7 that the overall event detection rate was 83.9%. The average pressure increase for detected events was $58 \pm 30\%$, whereas the average rate of pressure increase was $121 \pm 89\%$. The values for the rate of pressure change are important and will be discussed later. It should also be noted that 23 false events occurred, this will be discussed later.

Total Events	Correctly Detected Events				Missed Events			
	Number	% Total	P inc (%)	P inc %/s	Number	% Total	P inc (%)	P inc %/s
93	78	83.9	58	126	15	16.1	33	79
			30	89			21	50

False Events =	23
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P inc (%) = Pressure Increase as percentage of quiet standing pressure

PR (KPa/s) = Rate of absolute pressure increase

P inc (%/s) = Rate of percentage pressure increase

Table 7 – Collated Results for all Swine Postural Data

Figure 30 provides an indication of the inter-subject variability for the swine trials. The missed and detected events clearly lie within the same regions but considerably more events were observed during trials for swine subject SW2-L, in the lower ranges of both pressure increase and rate of pressure increase. It would appear that in general, values required for detection were similar, but the events were generally of a greater pressure magnitude for Swine Subject SW1-R.

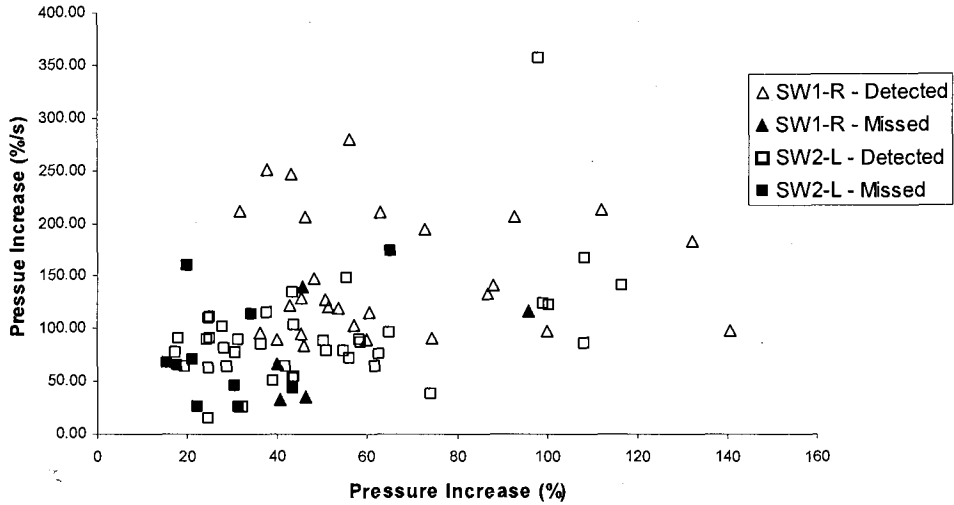


Figure 30 – Inter-subject Variability of Pressure Increase vs. Rate of Pressure Increase during Postural Perturbations for Two Swine Subjects: SW1-R and SW2-L

Figure 31 provides data on inter-trial variability from a single swine subject. No patterns emerged to suggest that some trials were more or less accurate in terms of detection than other trials. The detection rate for Day 119 was 76.5% and the detection rate for Day 123 was 70.6%.

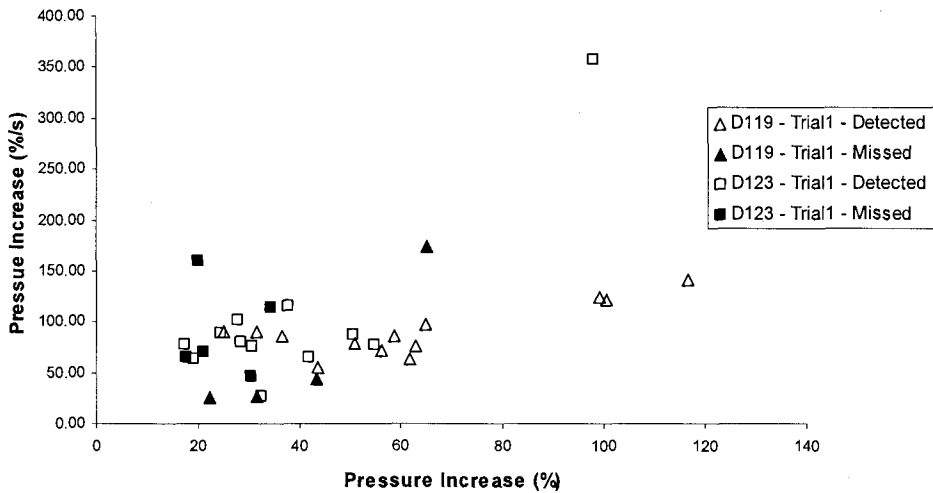


Figure 31 – Inter-trial Variability of Pressure Increase vs. Rate of Pressure Increase during Postural Perturbations for Subject: SW2-L (D119 and D123)

It is important to note that for each swine subject, the same detection parameters were used for all trials, as it was felt that this would be a likely scenario for practical applications in future FES devices.

Bilateral Analysis

A bilateral analysis was also performed to determine whether it was advantageous for monitoring postural sway.

One reason for bilateral analysis is that even if the pressure increase is too small to be detected from the ENG signal arising in one limb alone, the difference between the ENG signals in the two limbs may allow detection. As the weight is transferred onto one limb it is taken off the other. For example, if the force increases under the left limb by 15%, which proves to be undetectable, but also decreases under the right limb by 15%, the total difference of 30% may be represented by a detectable difference in the ENG (since the signal from the left Tibial nerve is likely to increase, while the signal monitored on the right Tibial nerve is likely to decrease). Additionally, by continually monitoring the change in ENG in a minimum of four receptor regions, it may be possible to accurately track the movement of the COP.

Unfortunately, bilateral analysis of the swine data did not provide any further information regarding otherwise undetectable pressure increases in this study. It was found that due to the signal quality, the averaging required to sufficiently smooth the signal effectively erased the signal features, unless they were large enough that they were detected in the unilateral analysis anyway.

The four plots below in Figure 32 and Figure 33 provide an example of how features were lost when analysis was performed comparing the force and ENG bilaterally. The top plot in Figure 32 (SW2-R) shows a significant increase in ENG during ground contact and closely matches the force profile during pressure changes, particularly the double spike noticeable in the force. The bottom left plot in Figure 32 (SW2-L) also shows the close correlation between acquired ENG and Force, although quite noisy, there is a clear relationship. The two plots in Figure 33 show the relationship between the difference in the ENG signals arising in, and forces experienced by the left and right limbs. The top plot in Figure 33 was created by subtracting the filtered ENG signal acquired using the left implant from the filtered ENG signal acquired using the right implant. In addition, the

resulting “difference” values were further smoothed using a 4-point moving average. Both signals were acquired simultaneously and processed off-line. Although there is a general relationship between the force and ENG, features were lost.

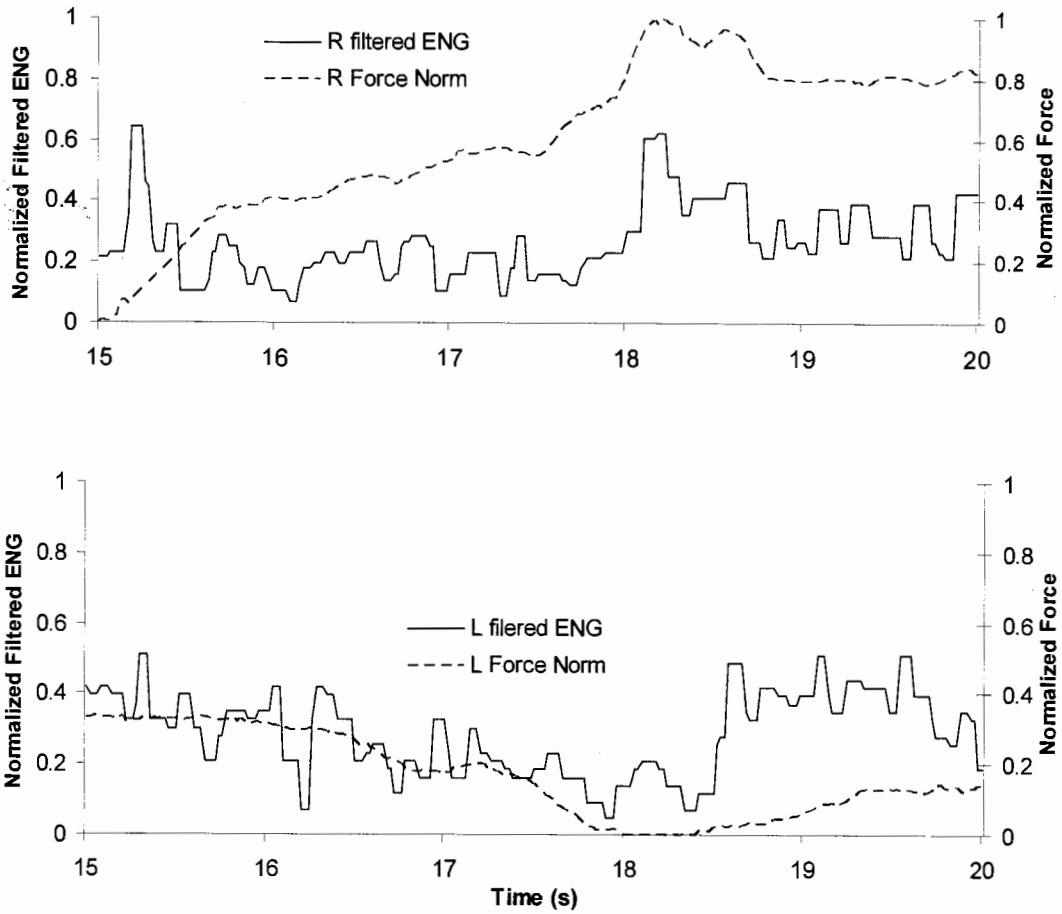


Figure 32 –Top Plot: SW2-R Normalized Filtered ENG and Force during Standing, Bottom Plot: SW2-L Normalized Filtered ENG and Force during Standing

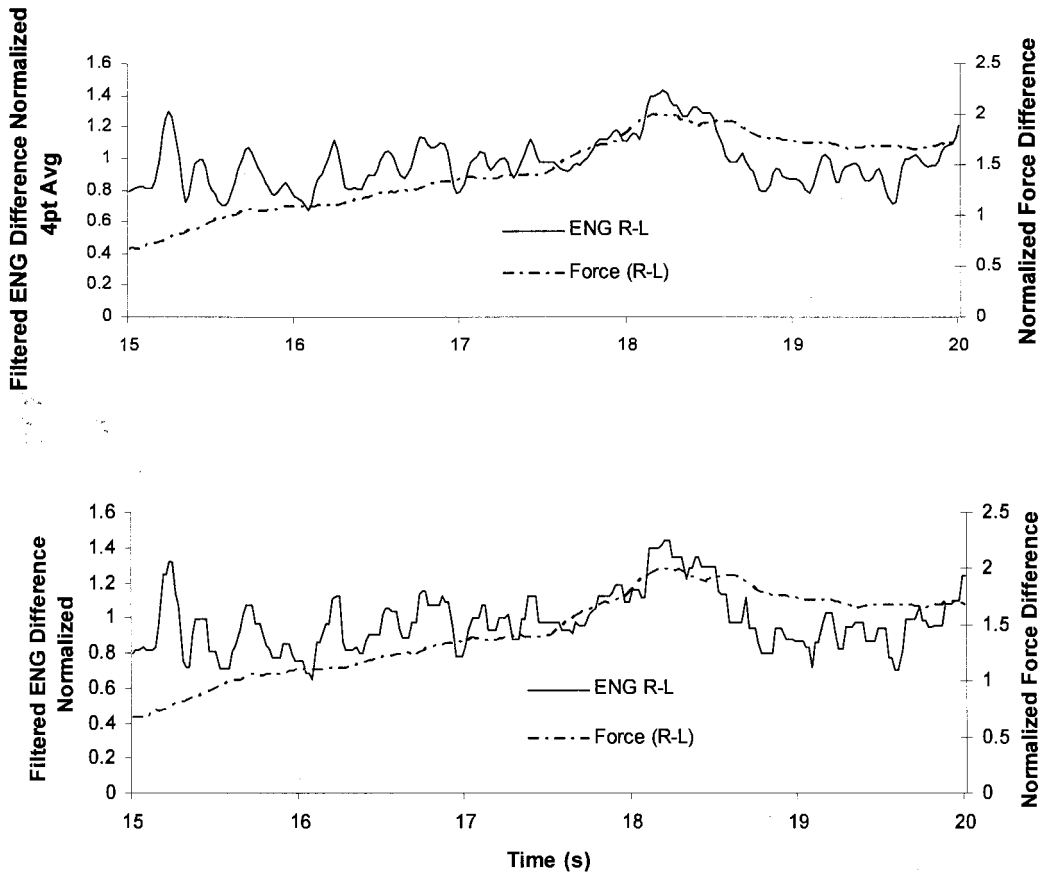


Figure 33 – Top Plot: SW2 Left and Right Filtered, Normalized and Averaged ENG Difference and Left and Right Force Difference during Standing, Bottom Plot: SW2 Left and Right Filtered, Filtered and Normalized ENG Difference and Left and Right Force Difference during Standing

Comparisons between Protocols One and Two

Figure 34 compares the Swine sway event detection rates for various ranges of pressure increase, to the Human data. It can be seen that the swine detection rates were generally improved with increased pressure change; however, a surprisingly high detection rate was also observed in the 0-19% increase range. The majority of human events actually occurred in the band from 20-60%, where swine event detection rates were lowest.

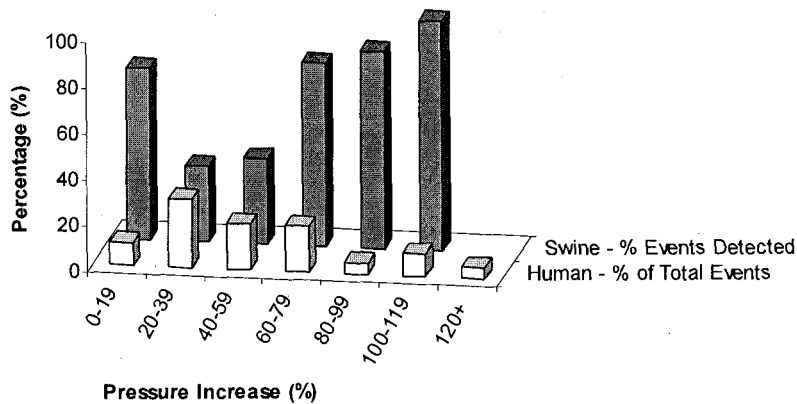


Figure 34 – Comparison between Frequency of Occurrence of Pressure Increase during Human Intentional Sway and Representative Swine Detection Rates

Figure 35 compares the distribution of rates of pressure increase during human trials with the detection rates in swine trials at similar pressure ranges. It is clear that the rate of pressure increase influenced the event detection rate. Only 8% of Swine events that were detected from the ENG signal had a rate of pressure increase less than 50% per second. In contrast, during human trials, 60% of events had a rate of pressure increase of less than 50% per second. However, missed events were widely spread. Half the Swine events with a slow rate of change (less than 50% per second) were detected. The figure clearly indicates that when the rate of pressure increase was below 75 %/s, detection was poor; but this was the range where 90% of all human events occurred. If the rate of pressure changes was above 75%/s, the detection was on average 98%.

Figure 36 shows the relationship between the human data and missed and detected events in the swine, regarding both pressure increase and rate of increase.

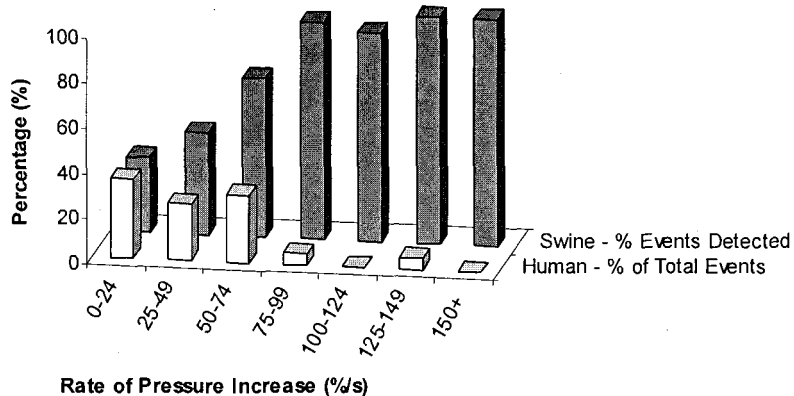


Figure.35 – Comparison between Rate of Pressure Increase during Human Intentional Sway and Representative Swine Detection Rates

Figure 36 shows that the pressure increases produced during intentional postural sway were, in many cases, large enough to have been detected from ENG signals such as were recorded in the swine model. A 94% detection rate was achieved for events within the range specified for pressure increase in the Protocol One results (shown as the large-dashed box in Figure 36). However, the rates of change of pressure in the human data were significantly lower than in the swine data.

The dashed-dot-dot box in Figure 36 shows the complete forest of human data collected and the detection rate for the entire swine set within that region was 87%. However, this detection rate may not be a fair indication of the likely success of detection in humans, since most of the values from Protocol One would not be used to control posture, as indicated in Table 4.

The region of interest may be considered as contained by the box with small dashes on the plot, which indicates the selected range of values from Table 4 and Table 5 of pressure increase and rate of pressure increase observed in Human subject data. This box has outer limits equal to the mean \pm 1 S.D. for the pressure increase and the rate of pressure increase. Within this region, the detection rate was 100%. However, the overlap was very small and thus conclusions can not be made. It should be noted that the swine data had an average rate of pressure increase of 78%/s in comparison to the human data within this region, which had a rate of pressure increase of 57%/s.

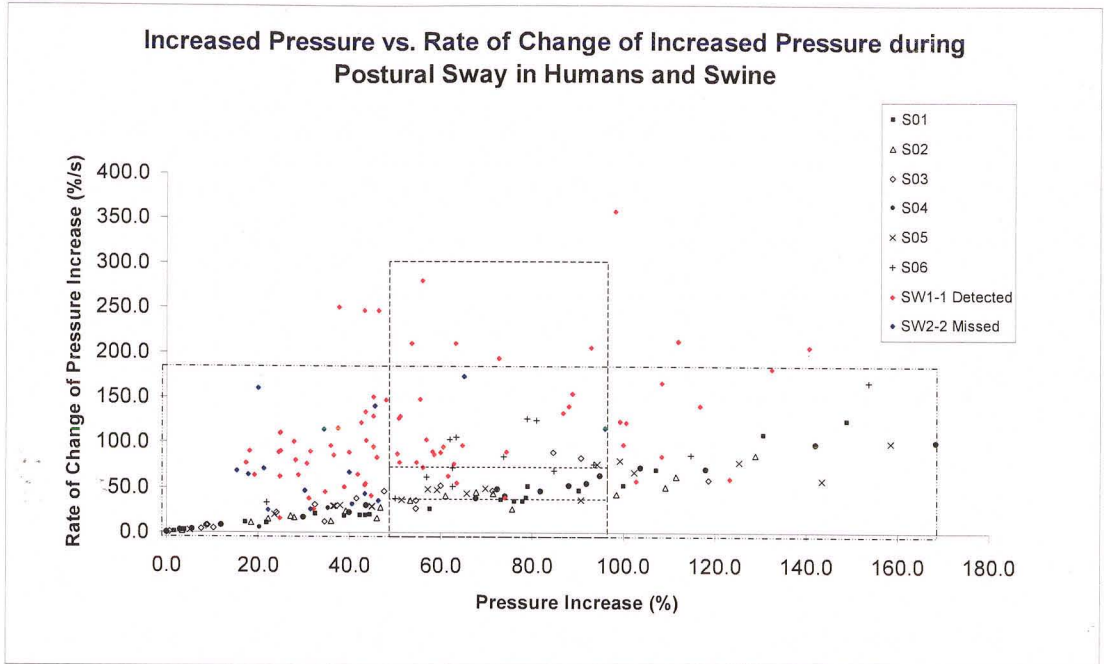


Figure 36 – Pressure Increase vs. Rate of Pressure Increase during Postural Sway for Swine and Human Standing.

DISCUSSION

This study was the first ever to use a fully implanted nerve signal recording system to acquire ENG signals during normal posture in awake animals and to study the relationship between pressure changes on the soles of the feet and changes in recorded ENG signals. This Discussion will focus on the utility of these signals to monitor postural sway, and on whether this method could be used in the future to provide feedback for control of posture in paralyzed people using an implanted FES system, but first the objectives will be reviewed:

Objective One

What is the relationship between the change in pressure on the glabrous skin mechanoreceptors in the hind foot of the swine during postural perturbations and the resultant electroneurographic (ENG) signals recorded using nerve cuff electrodes placed around the Tibial nerve?

Using this swine posture model, it was possible to successfully monitor sway and detect events with 15% greater in pressure than the typical values observed during quiet standing. In a certain range of swine postural perturbation trials, 100% of the events were detected successfully by monitoring changes in ENG signals recorded in the Tibial nerve. The average overall detection rate for all "good" swine trials was 83%.

Figure 37 highlights some properties of the recorded nerve signals. The signal changes within the boxes indicate the importance of the rate of pressure increase. The force change in the left-hand boxes was only 40N (16% increase) and the rate of force increase was 62 N/s (24.6 %/s), yet the result was a large measurable increase in neural activity. In comparison, the force change the right-hand boxes shows a magnitude of force increase of 76 N (30% increase) but only at a rate of 12.7 N/s (5.1 %/s), and for these conditions, little or no increase in ENG signal occurred. This was probably due to the FA type 2 receptor thresholds not being crossed and thus not firing (Johansson and Westling, 1987).

Figure 37 also indicates that the largest ENG signals occurred with the largest and fastest force changes, which are also the force changes that started at very low force levels. This is consistent with the findings of Haugland *et al.* (1994), who determined that the magnitude of the ENG response from skin sensors relates to both absolute skin deformation and relative skin deformation. In other words, relative deformation is greatest at low levels of force, since, once the skin starts to compress, it takes a lot more force to further deform the skin: a nonlinear property. This may partially explain why ENG signals arising during gradual postural sway, when the feet were already loaded, were not always of significant amplitude even though the pressure increases could be relatively large. We consequently may depend importantly on sensory information coming from skin areas that are only lightly loaded; where the pressure changes should be more noticeable in the ENG. In particular, the response to shear forces arising from receptors located at the edges of the skin contact area with the ground may play an important role in detecting increases in pressure in already loaded regions of the foot sole.

Andreasen and Struijk (2003) found in recordings from the Sural nerve in humans (lateral side of foot) that during force application, the best results, in terms of force prediction, occurred when rate of force change was highest. When force changes were "very slow" over a small or large distance, the goodness of fit (GOF) was only 58 and 66% respectively. In comparison, the GOF was 82.2% for dynamic trials. Since, in their study, the applied force was not equivalent to the actual force experienced during stance, Andreasen and Struijk (2003) predict that an increased signal would occur during actual foot loading. In reality, what may happen is that signals get "crowded out" by background firing and important slow shifts may not be detectable. This would also be consistent with the findings of Haugland *et al.* (1994), suggesting the amount of skin indentation is an important factor.

In addition, adaptation could occur in the pressure-sensitive skin mechanoreceptors. The pairs of horizontal dotted lines in Figure 39 highlight the ENG response to a large pressure increase. Each line shows the root mean square value of the ENG signal for that section. The lower (thick dashed black) line indicates the baseline signal level, determined when the foot is off the ground. The large change in pressure was caused by a step taken by the swine subject. This is very obvious in the nerve signal, an initial burst can be seen on contact, but before and after the step there were two periods of

maintained contact. During the second period a larger portion of the subject's weight was supported by the left hind foot. There is also a change in the amplitude of the "DC" component of the ENG. This is similar to the findings of Haugland *et al* (1994), who showed in the cat model that for a force held constant for a prolonged period, the ENG approaches a final value that is dependent on the force step. In the present study, the difference in ENG signal is obscured by the noise present in the alert, active animal. Although a measurable difference in DC level of the ENG signal can be observed, this signal source may be inefficient for detecting changes in force because large samples may be required to determine that the signal has increased above the noise level.

It is apparent that during the rapid force changes shown in Figure 37, that no OFF response is clearly evident. There is a small increase in ENG amplitude prior to the large burst on the second contact but this seems to be the initial contact. OFF responses were apparent during some pressure decreases but were not as usual as in feline data (Haugland *et al.* 1994). This may partially be due to both the noise level acquired signals and the sampling and bin integration, which may have hidden the sharp, narrow signal increases.

An important part of ensuring accurate analysis was to create consistent rules regarding event detection. Figure 38 shows examples of how events were classified. The area in the shaded box provides an example of a detected event, the increase in force is accompanied by an increase in ENG signal amplitude and as a consequence, event detection. On the other hand, the first and second simulator events may be considered as false acceptances. A false acceptance is the situation that arises when an "event" is detected by the simulator but the signal change is not as a consequence of an increase in force. The simulator is essentially detecting noise that "looks" like an increase in signal. There were 23 false acceptances in total during all swine trials and they were not included in the detection percentage. False acceptances generally only just match the minimum parameters for detection. In a closed-loop FES application for paraplegic stance control, a stimulation protocol that simply increased stiffness in response to small signal increases (this would include most false acceptances) could be used, in order to not compromise stance stability. Missed events (not shown in Figure 38) are far simpler to account for. This type of situation arose when the increase in signal was not sufficient to be detected by the simulator, even though the force change was sufficient to constitute an event; 16% of all events were missed during swine trials.

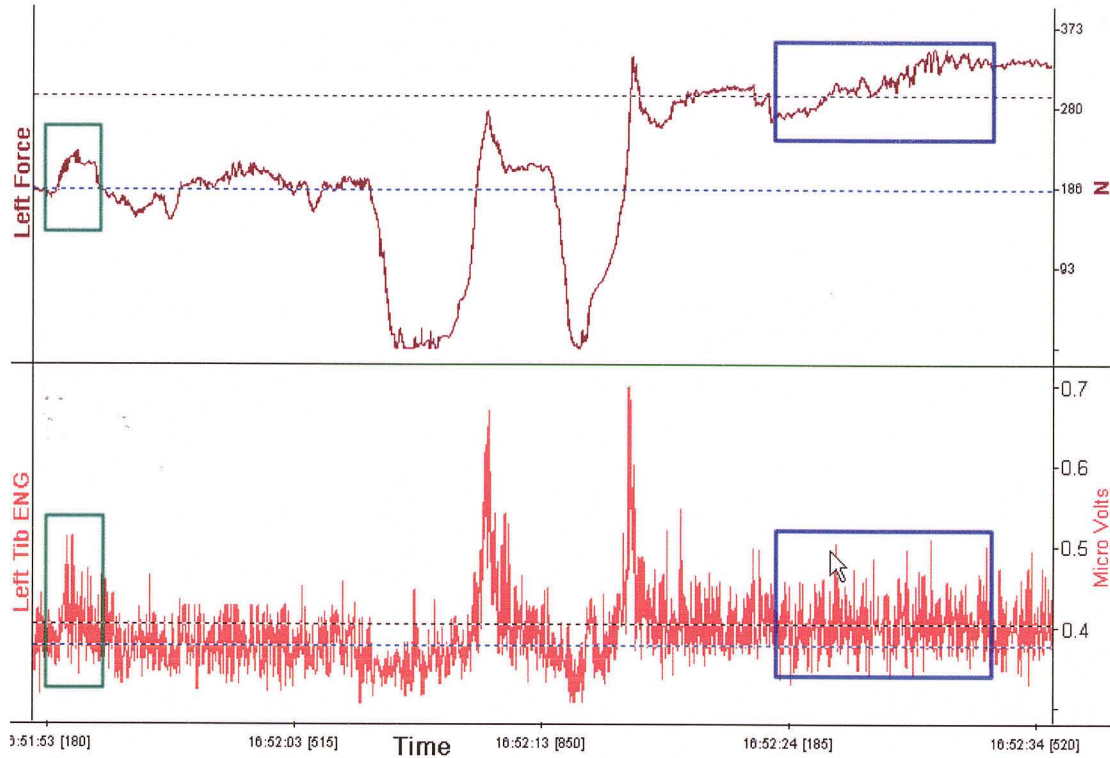


Figure 37 – Examples of Event Detection during Postural Perturbations in Swine Standing

The quality of signals recorded during postural trials was similar to what was observed during walking in the same swine subjects. During walking, ENG signal burst amplitudes were in the range of 0.2 to 0.4 μV , with a baseline around 0.4 μV . However, the noise ripple was significant, in the region of 0.1 μV peak to peak. An example of the signal quality during a standing trial is shown in Figure 39. In Figure 39 it can be seen that although the increase in mean value of the ENG signal is clear to the eye (region between the right-hand dashed lines), it is only about 0.2 μV larger than the mean value of noise (bounded by the left-hand dotted lines). Although the signal quality did vary between subjects, all values were within the 0.2 to 2.0 μV range.

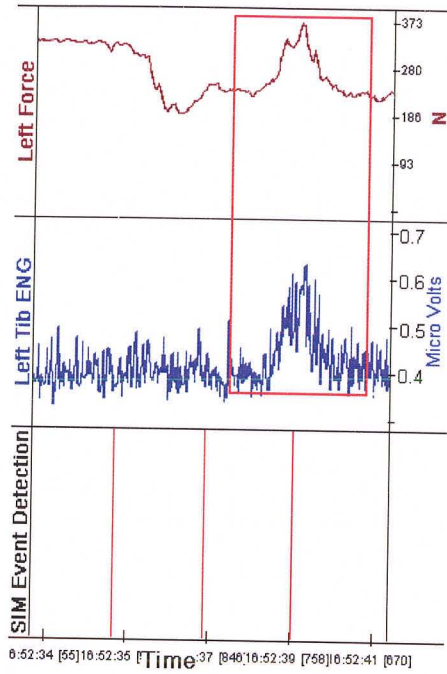


Figure 38 – Detected Events and False Acceptances

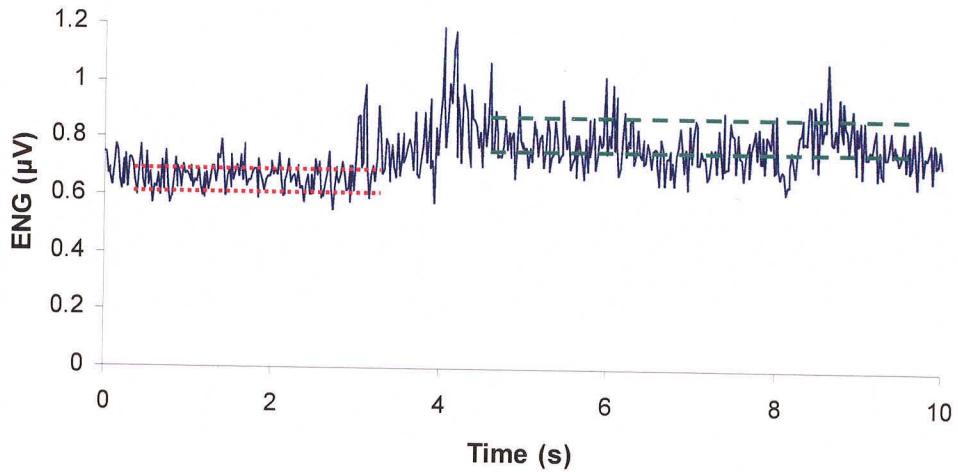


Figure 39 – Signal Quality during Standing, Recorded from the Tibial nerve of Swine, Subject P2-L 260 Days Post Implant.

Objective Two

How does the pressure distribution on the soles of human feet during stance relate to the innervation of sensory nerve receptive fields?

The human results indicate that if ENG data is available from the nerve branches that supply three receptor regions on each foot, it is possible to detect sway in each of eight directions. This is an important finding, since it may be possible in future to acquire signals from these three distal branches of the Tibial nerve. Although force changes vary greatly in the different regions, the relative pressure changes are quite evenly distributed across the regions.

Objective Three

How do typical ground contact pressure changes that occur during standing compare between humans and swine? Are relative differences likely to influence the usefulness of ENG signals?

The swine certainly didn't replicate the range of directions tested for human postural sway. However, the assumptions made in this thesis made it possible to measure changes in pressure across trials. The same technique was used for both humans and swine. The actual directions of sway in the swine were not analyzed, since the majority of movement was mediolateral. A notable disparity between the human and swine trials was in the rate of pressure increase. There was a clear difference between the rates of pressure increase in human and swine subjects, it is difficult to establish from these data the extent to which human sway events would be detectable from ENG signals, given the lower rates of pressure increase in human sway.

The analysis provided in this study suggests that the range of relative pressure changes observed in the human are similar to those occurring in the swine model. However, it is important to note that the rate of pressure increase associated with detectable ENG signals in the swine model was significantly higher than rate of pressure increases seen in self paced human postural sway. Hence, it is difficult to make firm conclusions on whether equivalent changes would have been detected from ENG signals recorded in humans during postural tasks.

The results have shown that sway events were detectable from the percentage change in pressure in swine. However, the rate of change of pressure during human postural sway can be considerably lower. In agreement with the work of Haugland *et al.* (1994) with the cat model, it was found that the amplitude of the ENG signal depended not only on the amplitude of the force increase but also the rate of force increase. Because of the intrinsic mechanics of quadrupedal posture, swine or cat subjects can stably bear their full weight on three limbs, if necessary. Thus, swine often take one of their feet completely off the ground during postural adjustments. Although these events were not included in the analyzed results, some large weight transfer events were included, and in numerous cases the force was approximating zero before it increased again.

Since swine can stay in the same place while moving a foot, they seem to fidget more often than humans. This may go some way to explaining why there were so many large, rapid pressure changes in the swine trials. Humans, on the other hand, tend to more slowly sway or drift (Duarte and Zatsiorky, 1999) to gradually change postural location.

Also, the foot contact area virtually always stays the same for swine, so there is no rolling-like action as with humans when the COP slowly drifts. This means that the weight does not get redistributed across the foot of the swine as it does for humans. Due to the size and structure of the swine foot, there appears to be relatively little shift of pressure across the sole; pressure changes tend to be more of an ON/OFF type. Thus, a small shift of the hips can constitute a rapid, large change in pressure.

It is also possible that when a weight shift was externally imposed, the swine sometimes facilitated a shift, rather than letting the examiner control their weight distribution. A common occurrence was that the subject lifted a limb when the weight was shifted, taking the opportunity to fidget! It would be more equivalent to a human subject picking up a foot. Unfortunately human data of this type were not available for direct comparison.

Objective Four

Are there advantages in using bilateral versus unilateral ENG signal analysis to monitor stance perturbations in swine?

For the swine data collected in this study, bilateral analysis was not found to be beneficial. If the signal quality was sufficient this method may be useful but for slow postural sway combining the signals (by subtraction) requires that the signals are extremely smooth; otherwise the noise may cancel out the signal change. This requires that very large samples are used, which may influence control strategies. It also by necessity means that in averaging the ENG, the subtle changes that one is searching for may be lost. However, if the signal could be improved, this kind of detection may play an important role for future FES devices, in particular, to monitor slow COP shifts that may take place close to the limit of postural sway. The similarity of the ENG signals during the "ON" and "OFF" responses may also be problematic for this type of postural feedback control. With rapid weight transfers such signals arising in unison in the left and right Tibial nerve may cancel each other out. For example, if there is a rapid weight shift to the left, the ENG signal amplitude will increase ("ON" response) due to the rapid pressure increase on the left, but may also increase in the right ENG signal due to the rapid pressure decrease ("OFF" response) on the right side. However, it was also found that if the signals were of a large enough amplitude to be detected, they would have been detected anyway in the unilateral analysis.

In summary, it seems that bilateral analysis could be useful but the signal to noise ratio has to be considerably higher than that observed in this study.

Other Issues

F-Scan® system accuracy

A possible cause for inaccuracy in the results was sensor calibration. Since the weight of the swine, or more specifically the portion of that weight that was applied over the sensors, was unknown, sensor calibration was performed using a standing human subject. The F-Scan system is ideally calibrated using a weight similar to that which it will be monitoring and this was achieved as closely as possible. However, it was felt that by normalizing the pressure changes, a more accurate comparison could be made. The range of swine and human pressures monitored was well within the nominal working range of the F-Scan sensors (1-150 psi or 7-1034 Kpa). The maximum pressure recorded for all trials was 350 Kpa.

Although it was extremely important to get accurate force and pressure measurements, the key aspect of this analysis was to examine the relationship between relative pressure changes. This involved comparing the force and pressure readings as percent increases, a procedure that is likely to have improved the accuracy of observations.

Timing of Event Detection

The sampling rate during acquisition (50 samples/sec) and the timing uncertainty of the complex data file merging procedure limited the accuracy with which the exact timing of ENG activity and postural events could be measured. However, given the nature of slow sway in humans, there would be, by necessity, small delays in detection, consistent with the large sample times that may be required to monitor the ENG changes. However, fairly long reaction times in the order of 200-300 ms are typical for normal postural control in the intact human, so it seems reasonable to suggest that ENG-based corrections could be made in adequate time to control paraplegic posture with FES. The time delay due to the physiological system, and filtering and processing the signal should not be any longer than in the intact human. As well, given the slow nature of the postural forces that were being monitored, it seems that little would have been gained by processing the signal with smaller bin widths and a faster sampling rate. During, brief forward and backward horizontal surface perturbations relatively stereotyped patterns of leg and trunk muscle activation were elicited with 73 to 110 ms latencies (Horak and Nashner, 1986). These more rapid responses are reflex driven and may prove difficult to replicate in an FES device. Ideally, a system would maintain controlled posture and the subject would not experience these more rapid weight shifts.

Signal filtering and Origin

As stated previously, a great deal of research has been performed into acquiring ENG signals from peripheral nerves. Throughout this research it has been important to record only neural energy and exclude external noise and the influence of EMG interference. With this type of application in mind, and through additional signal analysis, the bandpass of the amplifier filters of the devices used were designed to exclude energy outside of the range 500-5000Hz or 500-6000Hz. It was confirmed in an earlier study at the Neurokinesiology Laboratory by recording raw nerve signals in the swine that the majority of the energy in the ENG signal was centred in this range (see Figure 16).

To confirm the cutaneous origin of the recorded ENG signals, a test was performed with the subject under gas anaesthesia, which confirmed that signal amplitude increased when the plantar surfaces of the hind feet were mechanically tapped with a blunt probe. In addition, during some early trials a signal increase was observed when weight was applied to the rear of the subject during otherwise quiet standing. The location of the nerve cuff around the Tibial nerve was sufficiently distal that the nerve was almost entirely cutaneous in origin, other than the small nerve branches that innervate intrinsic muscles of the foot. However, the spindles in the intrinsic muscles of the feet may produce synergistic ENG signals if they fire during posture. It is likely that any activity will be present during moments of weight shift, which may have increased the ENG signal amplitude. In the human this may be more problematic due to the complexity of the musculature of the foot sole. In addition, there may have been some afferent activity due to the sheer forces experienced at the feet, particularly apparent in quadrupedal stance.

Assumptions for Comparisons between Swine and Human Data

1) Receptor density and types are similar in the glabrous skin of swine and human feet. It was not possible from the results of the study to validate this prediction, but previously published data suggests this to be correct. Although the size of multi-unit territories varied between subjects, Kennedy and Inglis (2002) found that the locations of the fascicular fields were generally similar. Thus, it appears likely that similar control mechanisms could be used for different paraplegic subjects. Data from other animal studies, most notably on the receptive fields of the Sural nerve that showed similar receptors in the weight bearing glabrous skin of rabbits, cats and rats (Trullson, 2000) also support the validity of this assumption

2) Receptor density and type does not alter significantly across the human foot sole. This assumption was also made using published data showing that receptors were widely distributed without an accumulation in the toes (Kennedy and Inglis, 2002).

3) The maximum contact area of any given foot region is a reasonable approximation to calculate pressure. This was definitely valid for the swine model as the contact area seemed to stay very similar throughout trials. For the human subjects it was slightly more varied, but analysis showed that using the contact area during quiet standing the approximation undershot the values during high pressure. It should be noted that

maximum contact areas also generally occurred during maximum forces, so using the maximum contact area was a better approximation for analysis, since the primary concern was when weight is shifted and thus force is high in a region.

4) Pressure rather than force in a region provides a better indication of receptor loading. Pressure seems to be a better indicator of receptor loading, particularly as this is a form of normalization, in that the area is taken into consideration in itself. As described in the Results section, the force change in a region may not provide a fair indication of receptor loading. For example, the force may be the same in two separate regions, but if one region is half the size of the other, each receptor in the smaller region will experience double the force.

5) Mechanics of skin can be seen as a function of the weight supported by any given skin area. According to this assumption, thicker skin develops to support greater weight and therefore would deform proportionally less with the same absolute pressure (or would require higher pressure to reach similar deformation as thinner skin). This is likely to be true across species with glabrous skin. The swine Tibial nerve signals, in the range of 0.4 to 2.0 μV , were similar to those recorded in the human (0.1 – 1.0 μV Hansen et al 2003). Since peripheral nerves and glabrous skin receptors have shown similarities across species (Trulsson, 2001), it seems reasonable to assume that skin thickness and compliance contribute to producing similar signal amplitudes. The size of the foot support region should not matter much if receptor densities and sensitivities are comparable in the two regions. The individual receptor signals should be the same for similar net deformations, and the size of the total nerve signal from a skin region is determined by the total number of active receptors, which is proportional to area. Receptor density is a fixed property for each system. The swine has greater weight supported by smaller skin area, but has thicker skin to support the greater weight and therefore, less deformation of skin per unit pressure change. All that matters to each receptor is the amount of local skin deformation it senses. With this in mind, by normalizing pressure, the amount of nerve activity can be predicted for human nerves, based on pig data, since the nerve size and conduction velocity are similar (See Overview for Anatomical Details).

Test Improvements

With hind sight, some improvements could have been made to acquire better data. The first aspect concerns the subjects (swine) for which a more controlled training period may have been useful. It was only towards the end of the study that they really began to relax around the equipment and with the foot placement.

Additionally, a greater emphasis could have been made to create swine force increases that were more comparable with those that occurred during human posture, since a limiting factor in the analysis was the poorly overlapping ranges for the rate of pressure change. This finding was not expected, but could perhaps be avoided in future by carefully influencing the swine postural changes or accepting a smaller subset of trials where pressure changes did not exceed the range of human values. Careful monitoring of the twisting of hips would also help to identify whether there is an increase in ENG signal due to the sheer forces on the feet.

Improvements that could benefit future FES systems

One method for potentially recording larger nerve signals is to use a smaller nerve. This could be the case if cuffs were implanted on the CT, MP and LP for monitoring postural sway. However, the smaller the nerve and the more distal the location more difficult it is to implant electrodes and record good signals (Hoffer and Kallesøe, 2000). This location is also likely to require the passage of lead wires across the ankle joint, which brings the associated problem of lead breakage. In addition, smaller nerves are more delicate and generally require more careful surgical access.

It is clear that the ENG signal provides information about the changes in COP. Even during slow weight shifts, changes can be seen with the naked eye. Unfortunately though, the signal to noise ratio in these swine experiments was not always sufficient for these small changes to be reliably detected. In order to improve the ratio, the signal amplitude needs increasing and/or the noise must be reduced. Is this possible?

The amplifiers in these devices were state-of-the-art, approximating the physical limit of technology, so the emphasis would seem to be on increasing the signal. Modifications to the design of cuff electrodes could bring about small changes, perhaps by improving the electrode-nerve interface.

CONCLUSIONS

The results of this study show that although many challenges remain in developing a control system for paraplegic standing with FES, based on peripheral nerve signal feedback, the proposed approach it may be feasible. Signals were acquired using fully implanted devices in awake subjects and COP displacement events could be detected during normal postural sway. The magnitude of the signals and the noise level make online event detection difficult but with small system improvements it seems that it would be possible to monitor sufficiently large movements of the COP during standing.

Future Control of Stance with FES

For any future FES systems, it is important to maintain sufficient ankle stiffness (Matjacic et al (1998) suggest 8 Nm/°), in which case you may have passive spring-like control. It is important that ankle stiffness remains high enough to relate movements of the COP with the COM as previously discussed. Thus, the standing paraplegic human may be considered as an inverted pendulum with the ankle musculature providing stiffness. Unfortunately, the issue of providing sufficient stiffness is closely related to developing muscle fatigue. In order to reduce fatigue, various strategies would need to be incorporated for postural shifts. With an intelligent control system it may be possible to develop a similar hierarchical setup to the intact human in terms of sway areas for different responses. In essence, it may not be necessary to know the exact force as a consequence of movement, as long as it is known that only a small inconsequential movement has occurred. The simple pre-programmed response would be to increase ankle stiffness. Only when the subject is significantly unstable, approaching an undesirable position, does the system require that a specific, more significant, corrective movement take place. A second kind of pre-programmed response, set for different sway paths, shall be activated. It seems from the data collected in this study that in future such signals may be detected using nerve cuff electrodes. However, it would be naïve to think that a device for the control of paraplegic standing would be entirely in response to feedback acquired from cutaneous receptors. It may be more reasonable to assume that only specific movements are monitored through nerve cuffs and that such signals would play a role in maintaining balanced upright posture. In addition, artificial

sensors are likely to play an important role, specifically the use of accelerometers for switching between states.

Due to the fact that the analysis shows that there are significantly different changes in pressure using the six zone method, it seems possible that this system could work essentially as threshold detection, taking into account the slope of the signal change as well as the amplitude. Monitoring signals but not acting upon them unless a particular threshold or rising event occurs, justifying the necessary response. To further the effectiveness of the system a lower threshold would be set that monitors the activity in other receptor regions; sway direction could be confirmed by testing that a lower threshold was simultaneously crossed in a separate zone that relates to the specific sway path.

A system for postural control should also take into account that it is not always necessary to return to the 'perfect' central point. If the sway takes the body in one direction then the correction will only be made to return the COP to the nearest correction point. Likewise, if a further movement takes place, the subsequent adjustment will only be to the nearest correction point and not to the "centre". Movement back to the 'ideal position' would only occur if the time elapsed at one of the intermediate correction points was longer than a set time period. Thus to reduce muscular fatigue, further stimulation would occur to slowly move the body back to the 'ideal position'. In addition, upper body control and integration (Matjacic *et al.* 2003) seems crucial for postural stability.

It is important to note that the feedback aspect of an FES system is crucial but is only a part of what would be a very complex system. Complex stimulation parameters need to be established and controlled, advances must be made in battery technology, stimulation and recording electrodes can still be further improved for selectivity and the problems of cognitive control and actual sensation should be further examined.

APPENDICES

APPENDIX A – DEVICE SPECIFICATIONS

Prototype Neurostep™ System

Implantable Control Unit

The control unit is a fully implanted device (akin to a heart pacemaker). For this study the device was used to acquire ENG from the Tibial nerve of the swine. The recorded signals were sampled at a rate of 50Hz, collected and integrated in bins of 11ms. The programming software acquired the signals in real-time. Five devices were implanted in 3 subjects (bilaterally in two). The table below shows the amplifier specifications:

Subject	Filter (Hz)	Amplifier Gain (dB)	Integrator gain	Noise (μ Vrms)	CMRR @ 250 Hz (dB)
1-R and 2-L	850 - 6000	90.5 \pm 5%	3.03	< 0.7	> 85 \pm 5%
4-R, 5-L, and 5-R	850 - 5000	86 \pm 5%	4.03	< 0.65	> 85 \pm 5%

Programming Header and Interface

External component of the Neurostep™ programming system that includes the hardware and firmware to communicate with the implanted control unit.

Programming Software

The software that enables the user to program and acquire signals from the implanted device. This software is windows compatible and was used for both the signal acquisition and early stages of analysis.

Neurocuffs™

The implanted system included two Neurocuff™ recording electrodes . However, only one channel was acquired at any time. For details regarding the specifics of the Neurocuff™ design see Nerve Cuff Design section on page 32. The nerve cuffs were linked to the control unit with flexible insulated wire leads.

F-Scan® Force Sensing System

The F-Scan® system provided the opportunity to measure bipedal plantar pressures and forces using 0.15 mm thick sensors. The sensors were placed either inside the shoes or on a flat, firm surface. The system included the following software and hardware:

Software Features

The FScan software allows the user to watch, edit and export recorded data. An essential first step during analysis was to observe the F-Scan data in conjunction with the video footage to confirm that trials were “good”. 2-D and 3-D displays of real-time and recorded data were available for this analysis. In addition, displays of pressure and force curves over time, as well as Viewing data frame by frame were available. Using the software, it is also possible to isolate and analyze specific sensor areas and subsequently export files with COP and/or force data for the entire foot or specific regions. These files were exported for further analysis.

Sensor Description

The F-Scan sensors comprise a matrix of 960 Sensing Elements/Foot, with 4 Sensors/cm² (25 sensors/in²). The technology used to measure the force is resistive Ink technology. As the pressure increases the ink is compressed, which alters the resistivity. In order to calibrate the sensors, a known weight was placed on the sensors. The system is designed to acquire data with a sampling rate from 1-165 Hz; 40 Hz was used during testing. The operating range was 1-150 PSI and the sensors measured 0.15mm in thickness.

APPENDIX B – SURGICAL PROCEDURES

The implant procedure for the prototype device and Neurocuffs™ can be broken into four distinct stages: Tibial nerve exposure, cuff installation, wire routing and creating a subcutaneous pocket for the device. These stages are outlined below.

1) Exposure of Tibial Nerve. With the subject anaesthetised under gas anaesthesia and using sterile technique, an incision was made along the medial surface of the shank and the Tibial nerve was located. A length of nerve between 4 and 7 cm was freed from connective tissue, and the nerve circumference was measured in several locations using a flexible silicone ruler. A nerve cuff of the desired circumference was selected (All cuffs were 30mm in length) and placed around the nerve.

2) Installation of Neurocuff™. The cuff was carefully placed under the nerve with its lead wires exiting distally and then turning proximally. The cuff was positioned around the nerve and closed by interlinking the two halves of the cuff (Figure 10) and passing a suture through the links to provide a tight seal.



Medial View of Tibial Nerve and Cuff

3) Routing of Wires. Once the cuff was positioned around the nerve, the wires and connectors were passed to a subcutaneous pocket in a lateral thigh location for placement of the implantable prototype device. This procedure involved the use of a

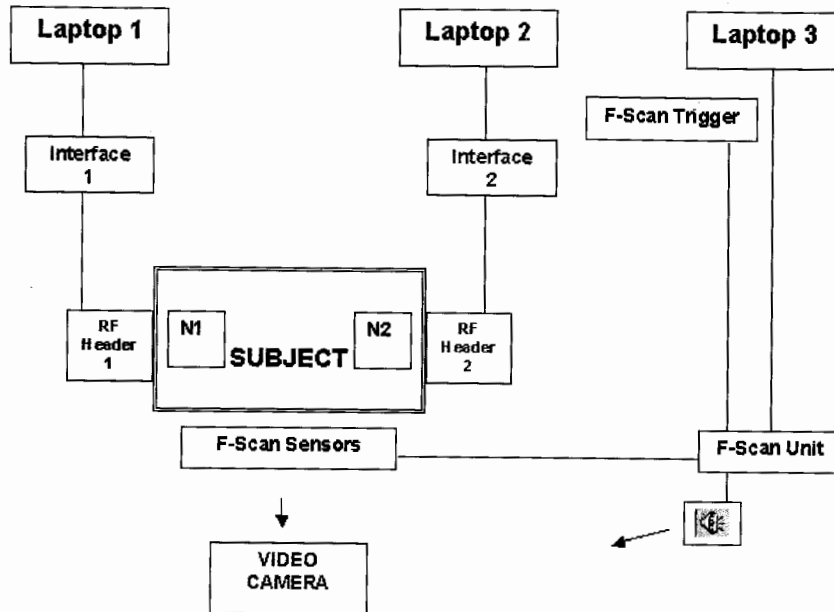
tubular probe to pass the wires and connectors. Once the wires were passed to the pocket location, the first incision was closed in layers.

4) Creating a Subcutaneous Pocket for the Device. The lead wires were connected to the device and a pocket was created in which to locate the device by carefully separating the skin from underlying tissue. Once the device was in place the second incision was closed in layers.

Training of swine subjects

Prior to implant surgery, the subjects were conditioned to stand and walk on a motorized treadmill. In most cases, the subject was walking on the treadmill again one or two days post surgery. However, recording ENG requires contact with the skin over the implanted device. Tests were not performed until any sensitivity or inflammation as a consequence of surgery had subsided.

APPENDIX C – SCHEMATIC OF RECORDING SETUP



APPENDIX D – PROTOCOL ONE DATA

The two tables directly below show the mean and standard deviation of force changes produced in the six receptor regions during Human sway in each of eight directions.

Average and SD of results

LEFT

Direction of Sway	MP-L				LP-L				CT-L			
	FM (N)		FR (N/s)		FM (N)		FR (N/s)		FM (N)		FR (N/s)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Fwd	136.7	74.7	58.7	46.0	11.8	18.8	4.1	7.4	-173.4	82.3	-73.9	50.2
Fwd/R	-22.1	49.1	-13.3	27.2	-39.3	24.8	-18.4	15.6	-183.9	85.0	-82.4	52.3
Right	-116.0	71.8	-43.1	21.4	-72.4	33.7	-27.8	14.5	-157.7	109.0	-62.6	44.0
Back/R	-142.1	70.9	-62.4	40.0	-72.8	34.2	-31.6	17.5	-68.7	56.3	-26.9	23.5
Back	-124.9	89.3	-58.4	49.2	-42.8	28.1	-23.7	24.6	121.1	79.6	55.1	39.8
Back/L	-108.6	51.3	-47.1	24.5	-6.9	30.6	-5.1	17.0	260.3	116.6	115.6	64.6
Left	74.6	75.8	19.6	17.6	130.3	60.0	38.7	21.9	111.9	55.5	34.3	20.9
Fwd/L	251.6	124.3	111.0	78.9	95.5	48.1	40.8	24.8	-88.5	47.4	-30.8	22.9

RIGHT

Direction of Sway	MP-R				LP-R				CT-R			
	FM (N)		FR (N/s)		FM (N)		FR (N/s)		FM (N)		FR (N/s)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Fwd	90.7	55.1	39.0	25.9	9.1	39.6	1.1	15.1	-150.1	71.0	-57.7	33.8
Fwd/R	208.6	114.8	95.7	75.5	137.3	78.8	60.6	46.9	-77.7	62.0	-33.1	33.3
Right	49.8	33.6	21.8	12.0	170.4	95.0	67.5	37.9	31.8	31.5	10.2	9.1
Back/R	-76.5	61.0	-32.3	26.1	5.7	34.7	3.7	13.4	234.7	125.2	83.0	47.4
Back	-94.9	49.9	-55.3	51.0	-44.6	21.9	-24.7	21.9	106.8	55.7	48.6	29.7
Back/L	-119.5	58.1	-52.8	29.0	-108.1	52.7	-44.8	23.9	-46.1	64.5	-26.1	39.0
Left	-101.1	51.4	-39.7	25.0	-83.5	38.1	-27.9	13.4	-155.1	82.7	-45.2	23.8
Fwd/L	-80.2	45.5	-36.4	24.0	-85.2	50.2	-36.7	25.1	-110.5	51.0	-49.1	30.2

MP = Medial Plantar N. Region
 LP = Lateral Plantar N. Region
 CT = Calcaneal Branch of Tibial N. Region
 FM = Force Magnitude
 FR = Force Rate of Change

The following two tables show the mean and standard deviation of pressure changes produced in the six receptor regions during intentional postural sway in each of eight directions.

Average and Stdev of Pressure results

LEFT

Direction of Sway	MP-L				LP-L				CT-L			
	P Inc%		PR %/s		P Inc%		PR %/s		P Inc%		PR %/s	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Fwd	89.9	24.5	56.4	22.2	27.1	18.9	16.2	10.2	-73.5	6.0	-45.4	10.0
Fwd/R	-4.8	44.9	-11.5	37.3	-30.3	35.2	-26.8	36.7	-87.5	5.6	-57.5	25.3
Right	-63.8	7.2	-44.0	19.9	-55.7	14.9	-40.0	26.5	-81.7	5.9	-54.4	14.7
Back/R	-76.8	5.3	-55.3	18.0	-64.5	28.8	-47.1	28.8	-58.6	24.1	-40.5	17.8
Back	-71.5	8.6	-60.1	38.2	-41.3	20.2	-37.1	35.2	25.1	22.2	22.6	17.7
Back/L	-55.8	11.2	-42.2	32.0	1.9	31.5	1.6	18.7	73.0	29.2	56.1	42.1
Left	35.8	43.9	22.1	30.7	58.6	49.0	51.4	38.7	47.6	37.1	40.5	37.6
Fwd/L	168.7	31.5	125.2	37.8	102.6	45.4	73.8	29.7	-62.7	13.6	-45.7	12.1

RIGHT

Direction of Sway	MP-R				LP-R				CT-R			
	P Inc%		PR %/s		P Inc%		PR %/s		P Inc%		PR %/s	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Fwd	56.9	13.5	35.4	10.9	18.5	18.7	12.0	13.1	-77.8	5.2	-48.1	10.7
Fwd/R	76.5	48.3	44.4	28.1	107.2	32.2	76.0	52.0	-61.8	39.4	-34.4	24.0
Right	31.8	35.0	17.4	22.1	75.8	40.4	50.2	27.0	32.8	37.2	26.4	34.7
Back/R	-41.1	19.7	-30.8	23.0	24.8	45.1	15.5	30.6	77.6	25.1	54.7	23.6
Back	-69.2	9.1	-57.0	36.1	-46.4	15.1	-39.4	30.1	45.1	25.4	42.0	42.7
Back/L	-66.8	13.0	-51.8	45.8	-49.7	15.7	-39.6	40.3	-43.5	24.6	-32.4	24.6
Left	-64.4	14.8	-58.3	45.1	-57.2	12.7	-51.9	42.0	-78.3	13.5	-61.9	24.1
Fwd/L	-33.3	22.6	-25.5	16.9	-33.4	10.0	-25.1	9.9	-92.5	3.2	-67.7	9.8

MP = Medial Plantar N. Region

LP = Lateral Plantar N. Region

CT = Calcaneal Branch of Tibial N. Region

P Inc% = Pressure Increase

PR = Rate of Pressure Increase

APPENDIX E – PROTOCOL TWO DATA

The following tables show the data collected during the “good” swine recording sessions for P1-R and P2-L.

FM (N) = Magnitude of the Force Change

P inc (%) = Pressure Increase

ED (ms) = Event Duration

FR(N/s) = Rate of Force Increase

P inc (%/s) = Rate of Pressure Increase

SW1: Right Limb - D52

Trial 1 - F06 Single Channel Cuff, Impedance = TBC

Contact Area 0.0015

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Total Events	Correctly Detected Events								Missed Events							False Events	
	Number	% Total	FM (N)	P inc (%)	ED (ms)	FR(N/s)	PR (Kpa)	P inc %/s	Number	% Total	FM (N)	P inc (%)	ED (ms)	FR(N/s)	PR (Kpa)		P inc %/s
7	6	85.7	132	54	450	293.3	195.56	119.24	1	14.3	100.0	41	1275.0	78.4	52.29	31.88	2
			149	61	525	283.8	189.21	115.37									
			346	141	1450	238.6	159.08	97.00									
			126	51	425	296.5	197.65	120.52									
			114	46	225	506.7	337.78	205.98									
			78	32	150	520.0	346.67	211.38									
Average =			158	64	538	356.5	237.7	144.9			100.0	40.7	1275.0	78.4	52.3	31.9	
Stdev =			95	39	469	123.3	82.2	50.1									

Trial 2 - F03 Single Channel Cuff, Impedance = TBC

Total Events	Correctly Detected Events								Missed Events							False Events	
	Number	% Total	FM (N)	P inc (%)	ED (ms)	FR(N/s)	PR (Kpa)	P inc %/s	Number	% Total	FM (N)	P inc (%)	ED (ms)	FR(N/s)	PR (Kpa)		P inc %/s
4	4	100.0	179	73	375	477.3	318.22	194.04	0	0.0							2
			105	43	350	300.0	200.00	121.95									
			140	57	550	254.5	169.70	103.47									
			250	102	150	1666.7	1111.11	677.51									
Average =			169	68	356	674.6	449.8	274.2									
Stdev =			62	25	164	668.3	445.5	271.7									

SW1: Right Limb - D87

Trial 1 - F4 Single Channel Cuff, Impedance = TBC Contact Area 0.0015 QF 250

Total Events	Correctly Detected Events							Missed Events							False Events		
	Number	% Total	FM (N)	P inc (%)	ED (ms)	FR (N/s)	PR (Kpa)	P inc %/s	Number	% Total	FM (N)	P inc (%)	ED (ms)	FR (N/s)		PR (Kpa)	P inc %/s
7	5	71.4	158	63	300	526.7	351.11	210.67	2	28.6	114.0	46	325.0	350.8	233.85	140.31	
			113	45	475	237.9	158.60	95.16			240.0	96	825.0	290.9	193.94	116.36	
			232	93	450	515.6	343.70	206.22									
			113	45	350	322.9	215.24	129.14									
			108	43	175	617.1	411.43	246.86									
Average =			145	58	350	444.0	296.0	177.6			177.0	70.8	575.0	320.8	213.9	128.3	
SD =			53	21	121	157.4	104.9	63.0			89.1	35.6	353.6	42.3	28.2	16.9	

Trial 2 - F6 Ch3, Impedance = TBC

Total Events	Correctly Detected Events							Missed Events							False Events						
	Number	% Total	FM (N)	P inc (%)	ED (ms)	FR (N/s)	PR (Kpa)	P inc %/s	Number	% Total	FM (N)	P inc (%)	ED (ms)	FR (N/s)		PR (Kpa)	P inc %/s				
17	15	88.2	331	132	725	456.6	304.37	182.62	2	11.8	116.0	46	1300.0	89.2	59.49	35.69					
			280	112	525	533.3	355.56	213.33			100.0	40	600.0	166.7	111.11	66.67					
			232	93	450	515.6	343.70	206.22													
			250	100	1025	243.6	162.60	97.56													
			90	36	375	240.0	160.00	96.00													
			217	87	650	333.8	222.56	133.54													
			94	38	150	626.7	417.78	250.67													
			120	48	325	369.2	246.15	147.69													
			150	60	675	222.2	148.15	88.89													
			186	74	825	225.5	150.30	90.18													
			140	56	200	700.0	466.67	280.00													
			115	46	550	209.1	139.39	83.64													
			220	88	625	352.0	234.67	140.80													
			127	51	400	317.6	211.67	127.00													
			100	40	450	222.2	148.15	88.89													
			Average =			177	71	530			371.2	247.4	148.5			108.0	43.2	950.0	127.9	85.3	51.2
			SD =			75	30	234			159.9	106.6	63.9			11.3	4.5	495.0	54.8	36.5	21.9

Totals

Total Events	Correctly Detected Events							Missed Events							False Events	
	Number	% Total	FM (N)	P inc (%)	ED (ms)	FR (N/s)	PR (Kpa)	P inc %/s	Number	% Total	FM (N)	P inc (%)	ED (ms)	FR (N/s)		PR (Kpa)
35	30	85.7	162	65	443	462	307.72	186.31	5	14.3	128	52	933	176	117.16	70.47
			72	29	276	275	183.41	111.66			50	20	424	49	32.36	19.42

SW2: Left Limb - D110

Trial 1 - F11 Ch3, Impedance = 3.95 KΩ QF 540.0 Contact Area 0.0023
QP 234.8 1034.3

Total Events	Correctly Detected Events							Missed Events							False Events						
	Number	% Total	FM (N)	P inc (%)	ED (ms)	FR (N/s)	PR (KPa)	P inc %/s	Number	% Total	FM (N)	P inc (%)	ED (ms)	FR (N/s)		PR (KPa)	P inc %/s				
16	15	93.8	234	43	825	283.6	123.32	52.53	1	6.3	83.0	15	225.0	368.9	160.39	68.31					
			135	25	225	600.0	260.87	111.11													
			134	25	1600	83.8	36.41	15.51													
			585	108	1275	458.8	199.49	84.97													
			134	25	400	335.0	145.65	62.04													
			236	44	425	555.3	241.43	102.83													
			585	108	650	900.0	391.30	166.67													
			210	39	775	271.0	117.81	50.18													
			156	29	450	346.7	150.72	64.20													
			235	44	325	723.1	314.38	133.90													
			134	25	225	595.6	258.94	110.29													
			400	74	1925	207.8	90.34	38.48													
			98	18	200	490.0	213.04	90.74													
			300	56	375	800.0	347.83	148.15													
			315	58	650	484.6	210.70	89.74													
			Average =			259	48	888			475.7	206.8	88.1			83.0	15.4	225.0	368.9		
			SD =			156	29	524			227.4	98.9	42.1								

SW2: Left Limb - D119

Trial 1 - F07 Ch3, Impedance = 3.43 KΩ QF 353.0

Total Events	Number	% Total	Correctly Detected Events							Missed Events							False Events
			FM (N)	P inc (%)	ED (ms)	FR (N/s)	PR (KPa)	P inc %/s	Number	% Total	FM (N)	P inc (%)	ED (ms)	FR (N/s)	PR (KPa)	P inc %/s	
17	13	76.5	199	56	775	255.5	111.08	72.38	4	23.5	230.0	65	375.0	613.3	266.67	173.75	4
			355	101	825	430.3	187.09	121.90			163.0	43	1000.0	153.0	66.52	43.34	
			154	44	800	192.5	83.70	54.53			111.0	31	1200.0	92.5	40.22	26.20	
			222	63	825	269.1	117.00	76.23			78.0	22	875.0	89.1	38.76	25.25	
			229	65	670	341.8	148.80	96.82									
			88	25	275	320.0	139.13	90.65									
			111	31	350	317.1	137.89	89.84									
			218	62	975	223.6	97.21	63.34									
			180	51	650	276.9	120.40	78.45									
			412	117	825	489.4	217.13	141.47									
			207	59	675	306.7	133.33	86.87									
			129	37	425	303.5	131.97	85.99									
			350	99	800	437.5	190.22	123.94									
Average =			219	62	682	321.1	139.6	91.0			143	41	863	237.0	103.0		
SD =			98	28	210	88.1	38.3	25.0			66	19	351	252.6	109.8		

SW2: Left Limb - D123

Trial 1 - F04 Ch3, Impedance = 3.48 KΩ QF 495.0

Total Events	Number	% Total	Correctly Detected Events							Missed Events							False Events
			FM (N)	P inc (%)	ED (ms)	FR (N/s)	PR (KPa)	P inc %/s	Number	% Total	FM (N)	P inc (%)	ED (ms)	FR (N/s)	PR (KPa)	P inc %/s	
17	12	70.6	271	55	700	387.1	168.32	78.21	5	29.4	170.0	34	300.0	566.7	246.38	114.48	3
			207	42	650	318.5	138.46	64.34			88.0	18	275.0	320.0	139.13	64.85	
			250	51	575	434.8	189.04	87.83			105.0	21	300.0	350.0	152.17	70.71	
			180	32	1225	130.6	56.79	26.38			150.0	30	650.0	230.8	100.33	46.62	
			488	98	275	1767.3	768.38	357.02			99.0	20	125.0	782.0	344.35	160.00	
			138	28	275	501.8	218.18	101.38									
			86	17	225	382.2	166.18	77.22									
			186	38	325	572.3	248.83	115.62									
			95	19	300	318.7	137.68	63.97									
			140	28	350	400.0	173.91	80.81									
			121	24	275	440.0	191.30	88.89									
			152	31	400	380.0	165.22	76.77									
Average =			191	39	465	502.6	218.5	101.5			122	25	330	451.9	195.5	81.3	
SD =			109	22	288	412.6	179.4	83.4			36	7	193	226.7	98.6	45.8	

SW2: Left Limb - D140

Trial 1 - F02 Ch3, Impedance = 3.12 KΩ QF 250.0 0.160

Total Events	Number	% Total	Correctly Detected Events							Missed Events							False Events
			FM (N)	P inc (%)	ED (ms)	FR (N/s)	PR (KPa)	P inc %/s	Number	% Total	FM (N)	P inc (%)	ED (ms)	FR (N/s)	PR (KPa)	P inc %/s	
8	8	100.0	257	103	1775	144.8	62.95	57.82	0	0.0							2
			308	123	2057	149.7	65.10	59.89									
			112	45	1100	101.8	44.27	40.73									
			87	35	775	112.3	48.81	44.90									
			78	31	825	94.5	41.11	37.82									
			222	89	575	386.1	167.86	154.43									
			113	45	300	376.7	163.77	150.67									
			159	64	1150	138.3	60.11	55.30									
Average =			187	67	1070	188.0	81.7	75.2									
SD =			86	34	593	121.0	52.6	48.4									

Total Events	Number	% Total	Correctly Detected Events							Missed Events							False Events
			FM (N)	P inc (%)	ED (ms)	FR (N/s)	PR (KPa)	P inc %/s	Number	% Total	FM (N)	P inc (%)	ED (ms)	FR (N/s)	PR (KPa)	P inc %/s	
58	48	82.8	209	54	726	372	161.67	88.95	10	17.2	116	27	473	353	149.76	91.29	15
			31	5	404	212	92.30	49.71			48	15	373	236	102.45	52.90	

BIBLIOGRAPHY

- Agarwal S, Triolo RJ, Kobetic R, Miller M, Bieri C, Kukke S, Rohde L, Davis JA Jr. Long-term user perceptions of an implanted neuroprosthesis for exercise, standing, and transfers after spinal cord injury. *J Rehabil Res Dev.* 2003 May-Jun;40(3):241-52.
- Andreasen LN, Struijk JJ. Skin contact forces extracted from human nerve signals--a possible feedback signal for FES-aided control of standing. *IEEE Trans Biomed Eng.* 2003 Dec;50(12):1320-5.
- Bajd T, Kralj A, Stefancic M, Lavrac N. Use of functional electrical stimulation in the lower extremities of incomplete spinal cord injured patients. *Artif Organs.* 1999 May;23(5):403-9.
- Bajd T, Munih M, Kralj A. Problems associated with FES-standing in paraplegia. *Technol Health Care.* 1999;7(4):301-8.
- Barbeau H, McCrear DA, O'Donovan MJ, Rossignol S, Grill WM, Lemay MA. Tapping into spinal circuits to restore motor function. *Brain Res Rev.* 1999 Jul;30(1):27-51. Review.
- Bartleby (2000). *Gray's Anatomy of the Human Body: The Sacral and Coccygeal Nerves.* Retrieved, October 20th 2004. <http://www.bartleby.com/107/213.html>
- Barú M. Custom ASIC for Electroneurographic Recording using Nerve Cuff electrodes, M.A.Sc. thesis, Simon Fraser University, 2003.
- Branner A, Normann RA. A multielectrode array for intrafascicular recording and stimulation in sciatic nerve of cats. *Brain Res Bull.* 2000 Mar 1;51(4):293-306.
- Bronstein AM, Buckwell D. Automatic control of postural sway by visual motion parallax. *Exp Brain Res.* 1997 Feb;113(2):243-8.
- Collins JJ, De Luca CJ. The effects of visual input on open-loop and closed-loop postural control mechanisms. *Exp Brain Res.* 1995;103(1):151-63.
- Collins JJ, De Luca CJ. Upright, correlated random walks: A statistical-biomechanics approach to the human postural control system. *Chaos.* 1995(b)Mar;5(1):57-63.
- Creasey GH. Electrical stimulation of sacral roots for micturition after spinal cord injury. *Spinal Cord Injury.* 1993 Aug; 20 (3): 505-15

- Dall PM, Muller B, Stallard I, Edwards J, Granat MH. The functional use of the reciprocal hip mechanism during gait for paraplegic patients walking in the Louisiana State University reciprocating gait orthosis. *Prosthet Orthot Int.* 1999 Aug;23(2):152-62.
- Davis R, Houdayer T, Andrews B, and Barriskill A. (2000, Jan 15). Multi-functional implantable Praxis stimulator for paraplegia. Presentation #59, 6th Internet world congress for biomedical sciences. Retrieved Oct 23rd 2003 from (<http://www.uclm.es/inabis2000/symposia/files/059/index.htm>)
- DeLisa JA, Lee HJ, Baran EM and Lai K. *Manual of Nerve Conduction Velocity and Clinical Neurophysiology.* Lippincott Williams and Wilkins (1994)
- Diener HC, Dichgans J, Guschlbauer B, Mau H. The significance of proprioception on postural stabilization as assessed by ischemia. *Brain Res.* 1984 Mar 26;296(1):103-9.
- Duarte M, Zatsiorsky VM. Patterns of center of pressure migration during prolonged unconstrained standing. *Motor Control.* 1999 Jan;3(1):12-27.
- Dunbar DC, Horak FB, Macpherson JM, Rushmer DS. Neural control of quadrupedal and bipedal stance: implications for the evolution of erect posture. *Am J Phys Anthropol.* 1986 Jan;69(1):93-105.
- Glenn WW, Phelps ML. Diaphragm pacing by electrical stimulation of the phrenic nerve. *Neurosurgery.* 1985 Dec;17(6):974-84. Review.
- Gorman PH. An update on functional electrical stimulation after spinal cord injury. *Neurorehabil Neural Repair.* 2000;14(4):251-63. Review.
- Graupe D, and Kohn KH. Functional neuromuscular stimulator for short-distance ambulation by certain thoracic-level spinal-cord-injured paraplegics. *Surg Neurol.* 1998 Sep;50(3):202-7.
- Grill WM, Mortimer JT. Stability of the input-output properties of chronically implanted multiple contact nerve cuff stimulating electrodes. *IEEE Trans Rehabil Eng.* 1998 Dec;6(4):364-73.
- Hansen M, Haugland M, and Sinkjaer T. Case study in generalization performance of real time foot-drop correction using natural sensors and machine learning. *IFESS 2001. Conference proceedings.*
- Hansen M, Haugland M, Sepulveda F. Feasibility of using Peroneal nerve recordings for deriving stimulation timing in a foot drop correction system. *Neuromodulation.* 2003;6(1):68-77.
- Hansen M, Haugland MK, Sinkjaer T. Evaluating robustness of gait event detection based on machine learning and natural sensors. *IEEE Trans Neural Syst Rehabil Eng.* 2004 Mar;12(1):81-8.

- Haugland MK, and Sinkjaeær T. Cutaneous whole nerve recordings used for correction of footdrop in hemiplegic man. *IEEE Trans Rehab Eng.* 1995 Dec; 3(4):307-17.
- Haugland MK, and Sinkjaeær T. Interfacing the body's own sensing receptors into neural prosthesis devices. *Technol Health Care.* 1999;7(6):393-9. Review.
- Haugland, M. and Hoffer, J.A. Slip information provided by nerve cuff signals: application in closed-loop control of functional electrical stimulation. *IEEE trans. Rehab. Eng.* 2:29-36, 1994a.
- Haugland, M. and Hoffer, J.A. Artifact-free sensory nerve signals obtained from cuff electrodes during functional electrical stimulation of nearby muscles. *IEEE trans. Rehab. Eng.* 2:37-40, 1994b.
- Haugland, M., Hoffer, J.A. and Sinkjaeær, T. Skin contact force information in sensory nerve signals recorded by implanted cuff electrodes. *IEEE Trans. Rehab. Eng.* 2:18-28, 1994.
- Hoffer JA, Stein RB, Haugland MK, Sinkjaeær T, Durfee WK, Schwartz AB, Loeb GE, Kantor C. Neural signals for command control and feedback in functional neuromuscular stimulation: a review. *J Rehabil Res Dev.* 1996 Apr;33(2):145-57. Review.
- Hoffer, J.A. and Haugland, M. Signals from tactile sensors in glabrous skin suitable for restoring motor functions in paralyzed humans. In: *NEURAL PROSTHESES: Replacing Motor Function after Disease or Disability*, R.B. Stein, P.H. Peckham and D. Popovic, editors. Oxford Univ. Press, pp. 99-125, 1992.
- Hoffer, J.A. and K. Kallesøe. How to use nerve cuffs to stimulate, record or modulate neural activity. Chapter 5 in *Neural Prostheses for Restoration of Sensory and Motor Function*, K.A. Moxon and J.K. Chapin, Eds., CRC Press, pp. 139-175, 2000.
- Hoffer, J.A. Chen, Y. Strange, K. and Christensen, P. Nerve Cuff having One or More Isolated Chambers. United States Patent 5,824,027, October 20, 1998.
- Horak FB, Nashner LM. Central programming of postural movements: adaptation to altered support-surface configurations. *J Neurophysiol.* 1986 Jun;55(6):1369-81.
- Horak FB, Shupert CL, Dietz V, Horstmann G. Vestibular and somatosensory contributions to responses to head and body displacements in stance. *Exp Brain Res.* 1994;100(1):93-106.
- Hunt KJ, Gollee H, Jaime RP. Control of paraplegic ankle joint stiffness using FES while standing. *Med Eng Phys.* 2001 Oct;23(8):541-55.
- Jensen W, Lawrence SM, Riso RR, Sinkjaeær T. Effect of initial joint position on nerve-cuff recordings of muscle afferents in rabbits. *IEEE Trans Neural Syst Rehabil Eng.* 2001 Sep;9(3):265-73.

- Jezernik S, Wen JG, Rijkhoff NJ, Djurhuus JC, Sinkjaeær T. Analysis of bladder related nerve cuff electrode recordings from preganglionic pelvic nerve and sacral roots in pigs. *J Urol*. 2000 Apr;163(4):1309-14.
- Johansson RS, and Westling G. Signals in tactile afferents from the fingers eliciting adaptive motor responses during precision grip. *Exp Brain Res*. 1987;66(1):141-54.
- Johansson RS, Vallbo AB. Tactile sensibility in the human hand: relative and absolute densities of four types of mechanoreceptive units in glabrous skin. *J Physiol*. 1979 Jan;286:283-300.
- Johnson KO, Popovic D, Riso RR, Koris M, Van Doren C, Kantor C. Perspectives on the role of afferent signals in control of motor neuroprostheses. *Med Eng Phys*. 1995 Oct;17(7):481-96. Review.
- Johnson MW, Peckham PH, Bhadra N, Kilgore KL, Gazdik MM, Keith MW, Strojnik P. Implantable transducer for two-degree of freedom joint angle sensing. *IEEE Trans Rehabil Eng*. 1999 Sep;7(3):349-59.
- Kallesøe, K. Hoffer, J.A. Strange, K. and Valenzuela, I. Implantable Cuff having Improved Closure. United States Patent 5,487,756, January 30, 1996.
- Kavounoudias A, Roll R, Roll JP. The plantar sole is a 'dynamometric map' for human balance control. *Neuroreport*. 1998 Oct 5;9(14):3247-52.
- Kavounoudias A, Roll R, Roll JP. Foot sole and ankle muscle inputs contribute jointly to human erect posture regulation. *J Physiol*. 2001 May 1;532(Pt 3):869-78.
- Kennedy P, and Inglis T. Distribution and behaviour of glabrous cutaneous receptors in the human foot sole. *J Physiol*. 2002 538(3): 995-1002.
- Kilgore KL, Scherer M, Bobblitt R, Dettloff J, Dombrowski DM, Godbold N, Jatich JW, Morris R, Penko JS, Schremp ES, Cash LA. Neuroprosthesis consumers' forum: consumer priorities for research directions. *J Rehabil Res Dev*. 2001 Nov-Dec;38(6):655-60.
- Kobetic R, Triolo RJ, Uhlir JP, Bieri C, Wibowo M, Polando G, Marsolais EB, Davis JA Jr, Ferguson KA. Implanted functional electrical stimulation system for mobility in paraplegia: a follow-up case report. *IEEE Trans Rehabil Eng*. 1999 Dec;7(4):390-8.
- Liberson WT, Holmquest HJ, Scot D, Dow M. Functional electrotherapy: stimulation of the peroneal nerve synchronized with the swing phase of the gait of hemiplegic patients. *Arch Phys Med Rehabil*. 1961 Feb;42:101-5.
- Lyons GM, Sinkjaeær T, Burrige JH, Wilcox DJ. A review of portable FES-based neural orthoses for the correction of drop foot. *IEEE Trans Neural Syst Rehabil Eng*. 2002 Dec;10(4):260-79. Review.

- Matjacic Z, Bajd T. Arm-free paraplegic standing--Part I: Control model synthesis and simulation. *IEEE Trans Rehabil Eng.* 1998 Jun;6(2):125-38.
- Matjacic Z, Hunt K, Gollee H, Sinkjaer T. Control of posture with FES systems. *Med Eng Phys.* 2003 Jan;25(1):51-62. Review.
- Matsukawa K, Komine H, Tsuchimochi H, Murata J, Yonezawa Y, Kondo K, Seki Y. Implantable microelectrodes with new electro-conductive materials for recording sympathetic neural discharge. *Jpn J Physiol.* 2003 Feb;53(1):61-4.
- Maurer C, Mergner T, Bolha B, Hlavacka F. Vestibular, visual, and somatosensory contributions to human control of upright stance. *Neurosci Lett.* 2000 Mar 10;281(2-3):99-102.
- Mensing AF, Anderson DJ, Buchko CJ, Johnson MA, Martin DC, Tresco PA, Silver RB, Highstein SM. Chronic recording of regenerating VIIIth nerve axons with a sieve electrode. *J Neurophysiol.* 2000 Jan;83(1):611-5.
- Micera S, Jensen W, Sepulveda F, Riso RR, Sinkjaer T. Neuro-fuzzy extraction of angular information from muscle afferents for ankle control during standing in paraplegic subjects: an animal model. *IEEE Trans Biomed Eng.* 2001 Jul;48(7):787-94.
- Peckham PH, Keith MW, Kilgore KL, Grill JH, Wuolle KS, Thrope GB, Gorman P, Hobby J, Mulcahey MJ, Carroll S, Hentz VR, Wiegner A; Implantable Neuroprosthesis Research Group. Efficacy of an implanted neuroprosthesis for restoring hand grasp in tetraplegia: a multicenter study. *Arch Phys Med Rehabil.* 2001 Oct;82(10):1380-8.
- Peterson DK, Nochomovitz ML, Stellato TA, Mortimer JT. Long-term intramuscular electrical activation of the phrenic nerve: efficacy as a ventilatory prosthesis. *IEEE Trans Biomed Eng.* 1994 Dec;41(12):1127-35.
- Popovic DB, Stein RB, Jovanovic KL, Dai R, Kostov A, Armstrong WW. Sensory nerve recording for closed-loop control to restore motor functions. *IEEE Trans Biomed Eng.* 1993 Oct;40(10):1024-31.
- Popovic M, Pappas IP, Nakazawa K, Keller T, Morari M, Dietz V. Stability criterion for controlling standing in able-bodied subjects. *J Biomech.* 2000 Nov;33(11):1359-68.
- Riso RR, Mosallaie FK, Jensen W, Sinkjaer T. Nerve cuff recordings of muscle afferent activity from tibial and peroneal nerves in rabbit during passive ankle motion. *IEEE Trans Rehabil Eng.* 2000 Jun;8(2):244-58.
- Rozman J, Zorko B, Bunc M. Selective recording of electroneurograms from the sciatic nerve of a dog with multi-electrode spiral cuffs. *Jpn J Physiol.* 2000 Oct;50(5):509-14.

- Rutten WL. Selective electrical interfaces with the nervous system. *Annu Rev Biomed Eng.* 2002;4:407-52.
- Sinkjaeær T, Haugland M, Haase J. Natural neural sensing and artificial muscle control in man. *Exp Brain Res.* 1994;98(3):542-5.
- Sinkjaeær T, Haugland M, Inmann A, Hansen M, Nielsen KD. Biopotentials as command and feedback signals in functional electrical stimulation systems. *Med Eng Phys.* 2003 Jan;25(1):29-40. Review.
- Solomonow M, Reisin E, Aguilar E, Baratta RV, Best R, D'Ambrosia R. Reciprocating gait orthosis powered with electrical muscle stimulation (RGO II). Part II: Medical evaluation of 70 paraplegic patients. *Orthopedics.* 1997 May;20(5):411-8.
- Spinal Cord Injury Information Network (2004, Aug). Facts and Figures at a Glance. Retrieved Nov 23rd 2004, from <http://images.main.uab.edu/spinalcord/pdf/files/factsfig.pdf>
- Stieglitz T. Implantable Microsystems for Monitoring and Neural Rehabilitation, Part II. *Med Dev Technol.* 2002 Jan-Feb; 13(1):24-7
- Strange KD, Hoffer JA. Gait phase information provided by sensory nerve activity during walking: applicability as state controller feedback for FES. *IEEE Trans Biomed Eng.* 1999 Jul;46(7):797-809.
- Tekscan (2004, Sep 14). F-Scan Mobile Specifications: Retrieved Nov 11th 2004. http://www.tekscan.com/medical/specs_mobile.html
- Thoumie P, and Do MC. Changes in motor activity and biomechanics during balance recovery following cutaneous and muscular deafferentation. *Exp Brain Res.* 1996 Jul;110(2):289-97.
- Triolo RJ, Bieri C, Uhlir J, Kobetic R, Scheiner A, Marsolais EB. Implanted Functional Neuromuscular Stimulation systems for individuals with cervical spinal cord injuries: clinical case reports. *Arch Phys Med Rehabil.* 1996 Nov;77(11):1119-28.
- Triolo RJ, Liu MQ, Kobetic R, Uhlir JP. Selectivity of intramuscular stimulating electrodes in the lower limbs. *J Rehabil Res Dev.* 2001 Sep-Oct;38(5):533-44.
- Trulsson M. Mechanoreceptive afferents in the human sural nerve. *Exp Brain Res.* 2001 Mar;137(1):111-6.
- Upshaw B, Sinkjaeær T. Digital signal processing algorithms for the detection of afferent nerve activity recorded from cuff electrodes. *IEEE Trans Rehabil Eng.* 1998 Jun;6(2):172-81.
- Vallbo AB, and Johansson RS. Properties of cutaneous mechanoreceptors in the human hand related to touch sensation. *Hum Neurobiol.* 1984;3(1):3-14.

- Vitatron (2004, May 28). Heart Pacemaker, Physicians information: Vitatron C-series. Retrieved Oct 20th 2003 from:
http://www.vitatron.com/physicians/?us/3_3_pacemakers/3_3_5_cseries.htm
- Winter DA, Patla AE, Prince F, Ishac M, Gielo-Perczak K. Stiffness control of balance in quiet standing. *J Neurophysiol.* 1998 Sep;80(3):1211-21.
- Winter DA, Patla AE, Rietdyk S, Ishac MG. Ankle muscle stiffness in the control of balance during quiet standing. *J Neurophysiol.* 2001 Jun;85(6):2630-3.
- Wise AK, Gregory JE, Proske U. The responses of muscle spindles to small, slow movements in passive muscle and during fusimotor activity. *Brain Res.* 1999 Mar 6;821(1):87-94.
- Yajima Y, Larson CR. Multifunctional properties of ambiguous neurons identified electrophysiologically during vocalization in the awake monkey. *J Neurophysiol.* 1993 Aug;70(2):529-40.
- Yoshida K, and Horch K. Closed-loop control of ankle position using muscle afferent feedback with functional neuromuscular stimulation. *IEEE Trans Biomed Eng.* 1996 Feb;43(2):167-76.