DEVELOPMENT AND ASSESSMENT OF NOVEL METHODS OF EXERCISE TESTING DURING TREADMILL GAIT IN INCOMPLETE SPINAL CORD INJURY

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Abstract

Approximately 50% of spinal cord injuries result in incomplete paralysis or a complex fracture of the spine with no associated paralysis. Due to the sedentary lifestyle led by the majority of individuals with a spinal cord injury (SCI), those with an incomplete SCI are at increased risk of cardiovascular disease and display muscle atrophy and reduced bone mineral density (BMD) in the paralysed limbs.

Body weight supported (BWS) treadmill exercise, with and without robot-assistance, is an ideal mode of exercise for those with an incomplete SCI. The varying levels of motor control which exist within this population can be accommodated to enable the individual to actively participate in the exercise. To determine if these modes of exercise can improve cardiopulmonary fitness and reverse the muscle atrophy and reduction in BMD associated with an SCI, methods to assess the changes which may occur are necessary. This thesis focuses on the development and assessment of incremental and constant load (step) exercise test (IET and SET) protocols, utilising non-robot- and robot-assisted treadmill exercise, to identify the key indices of cardiopulmonary fitness: peak oxygen uptake ($\dot{V}O_{2peak}$), lactate threshold (LT), slope of $\dot{V}O_2$ as a function of work rate ($\Delta\dot{V}O_2/\Delta WR$) and $\dot{V}O_2$ kinetics ($\tau\dot{V}O_2$). The assessment of adapted dynamometry protocols, utilising functional electrical stimulation (FES), to identify peak voluntary force and the central activation ratio (CAR) is also performed. The main study of this thesis monitors changes in cardiopulmonary fitness, peak voluntary force and CAR of the quadriceps and hamstring muscles, and lower limb BMD in two incomplete SCI subjects who participated in a 20 week BWS treadmill training (BWSTT) programme.

The main outcomes of the BWSTT study were: a substantial improvement in performance parameters (training work rate, peak work rate (WR_{peak}) and the distance walked in 15 minutes), an overall increase in $\dot{V}O_{2peak}$ and peak heart rate (HR_{peak}), a substantial decrease in $\Delta\dot{V}O_2/\Delta WR$ and a decrease in the $\dot{V}O_2$ and HR associated with a step increase in work rate. Accurate identification of an LT, $\tau\dot{V}O_2$ and the voluntary peak force and CAR was not established. An increase in lower limb BMD was not identified in the subject who was 2 years post injury. However, encouragingly an increase was shown in the trabecular BMD of

the right and left tibia of the subject who was 14.5 years post injury.

A novel non-robot-assisted treadmill IET which incorporated nonlinear, equally smooth increases in both speed and gradient was also developed and assessed. The novel protocol produced an average initial metabolic rate, $\dot{V}O_2$ response linearity and $\Delta\dot{V}O_2/\Delta WR$ comparable to a previously verified IET protocol which incorporated a linear increase in speed and a nonlinear, initially rapid, increase in gradient. The novel protocol was also shown to perform better than a constant speed, linear increase in gradient IET. It was concluded that the novel protocol may be more appropriate to those with an impaired gait pattern due to the smooth and gradual changes which occur in both speed and gradient during the test.

Active participation in robot-assisted walking has been shown to elicit a substantial metabolic response. An algorithm to estimate the work rate of a subject actively walking in the Lokomat system was developed in order to utilise their metabolic response for incremental and constant load (step) exercise testing. These novel protocols were assessed in 3 incomplete SCI subjects. The results suggested that the subjects could successfully follow a linear and step increase in target work rate. Therefore, there is the potential for the substantial cardiopulmonary response elicited during active participation in robot-assisted walking to be utilised for exercise testing in those with an incomplete SCI.

The benefits of BWSTT in those with an incomplete SCI have been highlighted in this thesis. It has also been shown that cardiopulmonary exercise testing can potentially be utilised in this population. Whether or not the IETs assessed throughout this thesis provide a true indication of the subjects' actual cardiopulmonary capacity is debatable due to limitations in their gait pattern and lower limb muscle fatigue. Therefore, the accurate detection of an LT and $\tau\dot{V}O_2$ may be key to determining improvements in cardiopulmonary fitness in this population. It is therefore suggested that further study in a larger subject group be carried out to determine the repeatability and reliability of the outcome measures obtained.

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Thesis Outline

- **Chapter 1**: A detailed description of a spinal cord injury (SCI) and its consequences is provided in this chapter. Reduced physical activity levels are implicated in the development of secondary complications: increased risk of cardiovascular disease, muscle atrophy and reduced bone mineral density (BMD). The effects of physical activity on able-bodied individuals are outlined and the methods used to determine cardiopulmonary fitness, muscle strength and BMD are described to identify if they are applicable to those with an SCI.

- **Chapter 2**: The effectiveness of exercise training interventions in those with an SCI are examined with regard to cardiopulmonary fitness, and muscle and bone strength. In particular, the outcomes of gait training in those with an incomplete SCI are discussed. The methods used to evaluate the effectiveness of these interventions are discussed in order to determine their efficacy.

- **Chapter 3**: This chapter describes the 5 month body weight supported treadmill training (BWSTT) programme carried out by 2 incomplete SCI subjects. Also described are the experimental protocols and equipment used to assess the subjects' key indices of cardiopulmonary fitness, voluntary muscle strength and central activation ratio (CAR), lower limb BMD, and 15 minute distance test performance. The methods used to analyse the data obtained are also discussed in detail.

- **Chapter 4 and 5**: The responses of 4 key indices of cardiopulmonary fitness (peak oxygen uptake ($\dot{V}O_{2peak}$), lactate threshold (LT), slope of $\dot{V}O_2$ as a function of work rate ($\Delta\dot{V}O_2/\Delta WR$) and $\dot{V}O_2$ kinetics ($\tau\dot{V}O_2$)) to a period of BWSTT in 2 incomplete SCI subjects are reported separately in Chapters 4 and 5. Also reported is the effect of the BWSTT on training performance, peak work rate (WR_{peak}), peak heart rate (HR_{peak}) and the $\dot{V}O_2$ and HR associated with a step increase in work rate. The effect of the training on the distance the subjects could walk in 15 minutes as well as on their lower limb muscle and bone strength is also reported.

- **Chapter 6**: The theoretical development of a novel incremental exercise test (IET) protocol is outlined in this chapter. Determination of $\dot{V}O_2$ linearity, initial metabolic

cost and cardiopulmonary response parameters ($\dot{V}O_{2peak}$, LT and $\Delta\dot{V}O_2/\Delta WR$) utilising the novel protocol is investigated in one incomplete SCI subject. A comparison of the outcome measures to two previously verified IET protocols is also performed.

- **Chapter 7**: An algorithm to estimate the work rate of a subject walking in a robot-assisted BWS treadmill has been developed. This chapter describes the assessment of novel incremental and step exercise test protocols, utilising real-time visual feedback of this work rate, in 3 subjects with incomplete SCI.

- **Chapter 8**: This chapter brings together the main outcomes of all the studies which comprise this thesis to discuss the potential of BWSTT for improving the cardiopulmonary fitness, muscle strength and lower limb bone mineral density (BMD) of those with an incomplete SCI. The effectiveness of the methods used to identify these improvements is also discussed.

- **Chapter 9**: The main conclusions of the thesis are summarised in this chapter and future areas of research are identified.

Contributions

The main contributions of this PhD thesis are outlined below:

- The results of this thesis have shown that long term body weight supported treadmill training (BWSTT) has the potential for use with those with an incomplete spinal cord injury (SCI).
- Standard able-bodied (AB) incremental and constant load (step) exercise tests (IET and SET) were adapted for use with incomplete SCI subjects during body weight supported (BWS) treadmill walking. The feasibility of their implementation has been established as has the identification of the key indices of cardiopulmonary fitness.
- Dynamometry tests, incorporating the application of functional electrical stimulation (FES), were used to determine the peak voluntary force and central activation ratio (CAR) of the quadriceps and hamstring muscles. The feasibility of this method in those with an incomplete SCI has been established.
- A novel treadmill IET incorporating nonlinear, equally smooth, increases in both speed and gradient was developed. Feasibility and determination of cardiopulmonary response parameters were explored in one incomplete SCI subject. A comparison of the outcome measures to those obtained during two previously verified IET protocols was carried out.
- An algorithm to determine the work rate of a subject walking in a robot-assisted BWS treadmill was developed. This work rate was used to develop novel IET and SET protocols. The feasibility and assessment of these protocols was established in three incomplete SCI subjects.
- The limitations of the cardiopulmonary exercise test and dynamometry test protocols are identified. Suggestions for future investigation to improve the repeatability and reliability of the outcome measures are provided.
- The potential of BWSTT to improve the risk of cardiovascular disease and reverse the muscular atrophy and reduced bone mineral density (BMD) of those with an incomplete

SCI has established it as a clinically relevant intervention for the long-term care of this population.

Publications

1. S. Coupaud, L. Jamieson, H. Berry, A.N. McLean, D.B. Allan, K.J. Hunt, "Musculoskeletal responses to physical interventions in spinal cord injury" in *UK Biomedical Features. Musculo-skeletal Mechanics*, Durham, September 2006

2. K. J. Hunt, L. P. Jamieson, A. Pennycott, T. H. Kakebeeke, C. Perret, and M. Baumberger, "Cardiopulmonary assessment protocols for robot-assisted gait in incomplete spinal cord injury," in *Robotics in Rehabilitation Symposium*, Zürich, Switzerland, 2006.

3. A. Pennycott, K. Hunt, L. Jamieson, C. Perret, and T.H. Kakebeeke, "Estimation and volitional feedback control of the active work rate during robot-assisted gait," *Medical Engineering in Physics (under review).*

4. K. J. Hunt, L. P. Jamieson, A. Pennycott, C. Perret, M. Baumberger, and T. H. Kakebeeke, "Control of work-rate-driven exercise for cardiopulmonary training and assessment during robot-assisted gait in incomplete spinal cord injury," *IEEE Transactions on Neural Systems and Rehabilitation Engineering (under review).*

5. L. P. Jamieson and K. J. Hunt and D. B. Allan, "A treadmill control protocol combining nonlinear, equally smooth increases in speed and gradient: exercise testing for subjects with gait impairment," *Medical Engineering and Physics (submitted).*

Abbreviations

- AB = Able-bodied
- ACSM = American College of Sports Medicine
- ADLs = Activities of daily living
- AFO = Ankle-foot orthosis
- ASIA = American Spinal Injuries Association
- ATP = Adenosine triphosphate
- a-v = Arteriovenous difference
- BMD = Bone mineral density
- BMUs = Basic multicellular units
- BP = Blood pressure
- BPV = Blood pressure variability
- BTPS = Body temperature and pressure, saturated
- BWS = Body weight support
- BWSTT = Body weight supported treadmill training
- CAF = Central activation failure
- CAR = Central activation ratio
- CNS = Central nervous system
- CO = Cardiac output
- CP = Critical power
- CSA = Cross-sectional area

- CSF = Cerebral spinal fluid
- DEXA = Dual energy x-ray absorptiometry
- EDL = Extensor digitorum longus
- EMG = Electromyograph
- ESCS = Epidural spinal cord stimulation
- FES = Functional electrical stimulation
- $F_{ET}O_2$ = Fraction of end-tidal oxygen
- $F_{ET}CO_2$ = Fraction of end-tidal carbon dioxide
- FHS = Functional health status
- H^+ = Hydrogen ions
- HA = Hydroxyapatite
- HCO_3^- = Bicarbonate ions
- HDL-C = High density lipoprotein cholesterol
- HR = Heart rate
- HR_{max} = Maximum heart rate
- HRV = Heart rate variability
- IET = Incremental exercise test
- La^- = Lactate ions
- LDL-C = Low density lipoprotein cholesterol
- LT = Lactate threshold
- LV = Left ventricular
- MC = Maximal contraction
- MESm = Minimum threshold for modeling
- MESr = Minimum threshold for remodeling
- MHC = Myosin heavy chain
- MMT = Manual muscle testing

- MRT = Mean response time
- MS = Multiple sclerosis
- MVC = Maximum voluntary contraction
- OGWS = Overground walking speed
- PCI = Physiological cost index
- PCO_2 = Partial pressure of carbon dioxide
- $P_{ET}CO_2$ = Partial pressure of end-tidal carbon dioxide
- $P_{ET}O_2$ = Partial pressure of end-tidal oxygen
- PO_2 = Partial pressure of oxygen
- $\dot{Q}O_2$ = Rate of intramuscular oxygen uptake
- QoL = Quality of life
- RCP = Respiratory compensation point
- RER = Respiratory exchange ratio
- ROM = Range of motion
- SCI = Spinal cord injury
- SOL = Soleus
- SSIpol = Polar stress-strain index
- STPD = Standard temperature and pressure, dry
- SV = Stroke volume
- TM = Transverse myelitis
- TP = Test point
- $\dot{V}CO_2$ = Rate of carbon dioxide output
- $\dot{V}_E$ = Minute ventilation
- $\dot{V}_E/\dot{V}CO_2$ = Ventilatory equivalent of carbon dioxide
- $\dot{V}_E/\dot{V}O_2$ = Ventilatory equivalent of oxygen
- $\dot{V}O_2$ = Rate of oxygen uptake

- $\dot{V}O_{2max}$ = Maximum oxygen uptake
- $\dot{V}O_{2peak}$ = Peak oxygen uptake
- $\Delta\dot{V}O_2/\Delta WR$ = Slope of oxygen uptake as a function of work rate

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Chapter 1

Introduction

1.1 Chapter Summary

A detailed description of the intact spinal cord and nerves is provided in this chapter. From this, the voluntary functions which remain following a spinal cord injury (SCI) are identified. The secondary medical complications associated with SCI (increased risk of cardiovascular disease, muscle atrophy and reduced bone mineral density) are discussed, and reduced physical activity following injury is implicated in the development of these conditions. Therefore, the final part of this chapter describes the effect of physical activity on the able-bodied (AB) population and the methods used to detect changes in cardiopulmonary fitness, voluntary muscle strength, and bone mineral density in order to identify whether or not the training effects are similar, and the testing methods useful, in the SCI population.

1.2 The Spinal Cord and Nerves

1.2.1 The Spinal Cord

The spinal cord is contained within the spinal canal of the vertebral column. The vertebral foramina of all the vertebrae stack on top of one another to form the canal. There are 8 cervical, 12 thoracic, 5 lumbar, 5 sacral segments and a coccyx through which spinal nerves enter and leave. This provides a protective shield for the cord. Vertebral ligaments, meninges and cerebrospinal fluid provide extra protection.

In adults, the spinal cord extends from the medulla oblongata to the superior border of the lower margin of the L1 vertebral body. Below this point the spinal canal contains only the lumbar, sacral and coccygeal nerves which are collectively termed the cauda equina. The cord itself is roughly cylindrical but flattened slightly in its anterior-posterior dimension, and is 42-45cm long and approximately 2cm in diameter. It is slightly larger in diameter in the

lower cervical and midlumbar regions, and smaller at the inferior tip [1].

1.2.2 Grey and White Matter

The spinal cord is composed entirely of two substances, grey and white matter. The grey matter lies in the centre of the spinal cord and in cross section takes the shape of a butterfly (Figure 1.1). It contains the cell bodies of the motor neurons and neuroglia, as well as the unmyelinated axons and dendrites of association and motor neurones. The commissure of the grey matter contains the central canal that extends the entire length of the spinal cord (Figure 1.1(4)). The grey matter is composed of two large anterior horns (Figure 1.1(2)) which contain the cell bodies of those motor neurones supplying the skeletal muscles. The lateral horn, only present in the thoracic, upper lumbar and sacral segments, contains the cell bodies of those motor neurones that supply smooth and cardiac muscles, or a gland through the autonomic nervous system. There are also two posterior horns (Figure 1.1(1)), which contain neurones of the afferent system on which sensory fibres from the dorsal root ganglion terminate [2].

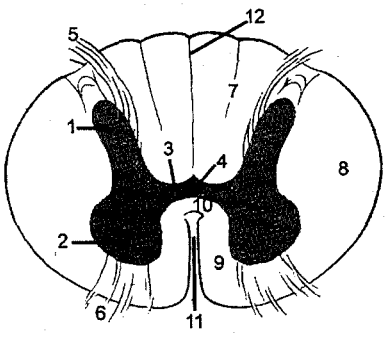


Figure 1.1: The grey and white matter of the spinal cord [2].

The rest of the spinal cord is composed of white matter which carries bundles of myelinated axons of motor and sensory neurones, as well as some interconnecting neurones. It is composed of a posterior column (Figure 1.1(7)) from the posterior septum to the posterior horn (funiculus posterior), a lateral column (Figure 1.1(8)) from the posterior to the anterior horn (funiculus lateralis), and an anterior column (Figure 1.1(9)) from the anterior horn to the anterior fissure [2]. The two halves of the white matter are joined ventrally by the commissural alba (Figure 1.1(10)).

1.2.3 Sensory and Motor Fibres

When sensory neurones reach the posterior horn they send sensory information to the brain via the posterior horn cells [2]. They can also run directly to the anterior horn cells and transmit impulses either directly (simple reflex arc) or via interposed intermediate neurones (multisynaptic reflex arc). There are three different types of afferent neurones which carry different sensations and travel in different areas of the posterior horn. The exteroceptive fibres (Figure 1.2(1)) carry cutaneous sensory impulses such as primary touch, temperature, pain and pressure sensations in the most posterior part of the posterior horn. Impulses from muscles, bones and joints (pain, pressure and the status of the muscle) are carried in the proprioceptive fibres which lie anterior to the exteroceptive fibres (Figure 1.2(2)). The third set of sensory fibres, the interoceptive fibres, carry impulses regarding the sensation of the viscera (Figure 1.2(3)).

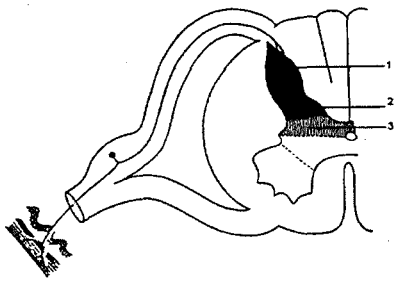


Figure 1.2: Afferent neurones enter the posterior horn [2].

The motor nerves, which carry information to the muscles in response to the information provided by the sensory fibres, lie in two main areas of the anterior horn (Figure 1.3). Motoneurones of the vegetative system lie in the visceromotor area (Figure 1.3(1)), and those which supply striated muscle can be found in the somatomotor area (Figure 1.3(2)). The anterior horn is subdivided somatotopically. The most medial groups of cells supply the axial muscles, and the lateral groups of cells supply the limbs. The more lateral the cells, the more distal the muscles they supply in each limb [2].

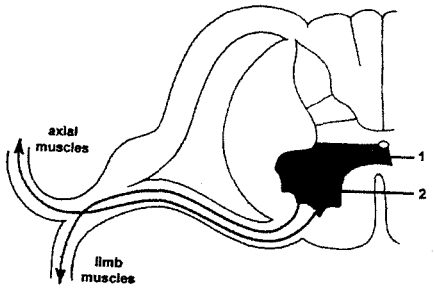


Figure 1.3: Efferent neurones leave the anterior horn [2].

1.2.4 Ascending and Descending Tracts

The various types of motor and sensory tracts are grouped into descending and ascending tracts respectively. Sensory information travels from receptors to the brain via a variety of routes. The anterolateral column contains both the lateral and anterior spinothalamic tract that convey impulses for sensing temperature and pain sensations, and gross pressure and touch sensations respectively. Another sensory tract can be found in the posterior column. This tract carries impulses regarding epicritic sensibility. The nerve fibres from this tract do not synapse and cross in the cord as the other sensory fibres do, instead they ascend directly to the medulla oblongata where they synapse and cross. The lateral column carries principally proprioceptive (and some exteroceptive) impulses [2].

The motor output is conveyed to the muscle by two descending pathways [2]. The pyramidal or corticospinal tract is composed of the lateral corticospinal, anterior corticospinal and the corticobulbar tracts, and conveys nerve impulses originating in the cerebral cortex to cause precise, voluntary movements of skeletal muscle. More than half of these nerves terminate in the cervical cord for upper limb movement, and a quarter terminate in the lumbosacral cord for the lower limbs. The nerve fibres are arranged somatotopically within the tract; lower limb fibres are found peripherally and upper limb fibres medially. The second tract, the extrapyramidal tract, carries semi-voluntary fibres which influence and control the motor system. These fibres arise from the cortex and travel through at least six individualised tracts; the vestibulospinal, ventrolateral and lateral reticulospinal, tegmentospinal, rubrospinal, tectospinal and medial longitudinal tracts.

1.2.5 Blood Supply of the Spinal Cord

The blood supply of the spinal cord is provided by both vertebral and segmental arteries. There are 3 vertebral arteries, two posterior arteries that run longitudinally along the posterior aspect of the cord, and an anterior artery. The anterior artery is largest at the cervical and lumbar enlargements. It gives off branches which penetrate into the commissura alba and the sulcocommissural arteries, and branches that anastomose with the posterior spinal arteries to form a vascular ring around the spinal cord. Vessels penetrate from this ring into the white matter. The segmental arteries give off 31 pairs of spinal rami which pass through the intervertebral foramina and divide into an anterior and posterior radicular branch to supply the spinal roots and meninges.

1.2.6 Spinal Nerves

There are 31 pairs of spinal nerves that connect the central nervous system to receptors, muscles and glands; 8 pairs of cervical, 12 pairs of thoracic, 5 pairs of lumbar, 5 pairs of sacral and 1 pair of coccygeal nerves. Each nerve has two separate points of attachment to the cord, the posterior root which contains the sensory fibres and the anterior root that contains the motor fibres.

Spinal nerves divide into several branches (rami) after they pass through the internal foramen. The posterior, or dorsal, ramus innervates deep muscles and the skin of the posterior surface of the trunk. The anterior, or ventral, ramus innervates the muscles and structures of the upper and lower limbs, and the lateral and anterior trunk. The rami also communicate with components of the autonomic nervous system.

By joining with various numbers of nerve fibres from anterior rami of adjacent nerves, the anterior rami of spinal nerves form networks on both the left and right side of the body. This network is called a plexus (Figure 1.4).

The cervical plexus contains the cervical nerves 1–4. Its nerves innervate the skin at the front of the neck down to the sternum as well as the sternoceidomastoid and trapezius muscles of the neck. It contains the phrenic nerve (C3, 4, 5) which innervates the diaphragm.

The cervical nerves 5, 6, 7, and 8 and the first thoracic nerve form the brachial plexus. This plexus innervates the skin and muscles of the upper limbs and some of the chest muscles. It includes the circumflex nerve (C5, 6) which innervates the deltoid muscles, the shoulder joint and the skin. The radial nerve (C5, 6, 7, 8, T1) which innervates the triceps, wrist extensors and the finger joints is also included in this plexus, as is the musculocutaneous nerve (C5,

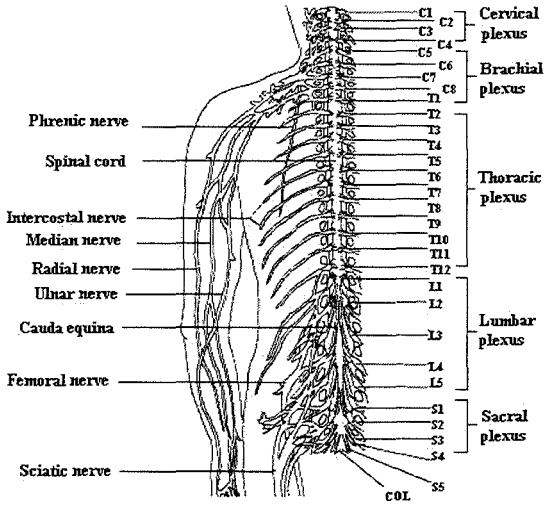


Figure 1.4: Somatic motor system and muscle innervation (adapted from http://fourteen.apptechnc.net/ windelspecht/nervous/index.htm).

6, 7) which innervates the biceps and the skin of the forearm. The median nerve (C5, 6, 7, 8, T1), which is also included in this plexus, innervates the wrist flexors and the small muscles and skin of the thumb and first two fingers. Also included with the other nerves in the brachial plexus is the ulnar nerve (C7, 8, T1) which innervates the muscles of the ulnar aspect of the forearm and the palm of the hand.

Thoracic nerves T1–6, known as the intercostal nerves, innervate the intercostal muscles and the overlying skin. The muscles and skin of the posterior and anterior abdominal wall are innervated by T7–12. The leg muscles are innervated by the lumbar nerves, and the bowel and bladder by the sacral nerves.

Both cranial and spinal nerves form the parasympathetic nervous system, with the spinal nerves exiting the spinal cord between S2 and S4. Sympathetic nervous system fibres exit between C7 and L1.

1.3 Spinal Cord Injury

1.3.1 General Information

Between 1992 and 2006 970 new neurologically complete spinal cord injuries occurred in Scotland. Of these new injuries, ~50% resulted in an injury to the cervical region of the cord while the remaining injuries occurred in the thoracic, lumbar or sacral regions. A further

1204 injuries resulted in either incomplete paralysis or a complex fracture of the spine with no associated paralysis [3]. Regardless of the injury the most common causes were falls, followed by road traffic accidents, a secondary complication to a medical diagnosis, and sporting injuries. The vast majority of these injuries occurred in males, with the most common age at time of injury in 2005–2006 being 40–59 [3]. The resulting syndrome depends on the extent of the direct injury to the cord or compression of the cord by displaced vertebrae or blood clots.

Complete spinal cord lesions can be classified as either anatomical or clinical. A patient is classified as having an anatomically complete spinal cord lesion if the spinal cord is completely severed. If the lesion is classified as clinically complete, the spinal cord is not completely severed, but there is no useful function below the level of the lesion. Complete injuries, regardless of their classification, are most often the result of dislocation of the vertebrae or from injuries sustained by a knife or bullet wound. They may also result from an inflammatory condition (transverse myelitis) or from compression due to a tumour. If an individual has a complete spinal cord injury they are completely paralysed, lose all sensation and have disruption of the autonomic nervous system below the level of the lesion.

When an injury is classified at a specific neurological level, muscles that are innervated by nerves which leave the spinal cord down to and including the neurological level are fully functional. However below this, nerve impulses from the brain cannot pass through the lesion and therefore muscles innervated below the lesion are paralysed. The muscles innervated by the nerves from each spinal cord segment are shown in Figure 1.5.

Those with lesions at C3 and above require a ventilator for breathing as lesions at C1 and C2 result in a loss of all motor function below the head, and at C3 in all motor functions below the neck [4]. All the muscles required for breathing are therefore paralysed. Although the accessory muscles of respiration are paralysed in those with an injury at C4 or below, the innervated diaphragm enables them to have independent inspiration. The diaphragm is solely responsible for breathing in these patients, and as a result, they have markedly limited chest expansion. These patients do not however have any motor control of their upper extremities.

Lesions at C5 enable people to have some upper arm mobility through the use of their shoulder and biceps muscles. As the lesions progress down the cervical segments, patients have more mobility of the upper extremities. Wrist extension and flexion are possible with lesions at C6 and C7 respectively, although finger dexterity will be markedly impaired. More activities are possible at C8 due to the innervation of the finger flexors. However, intrinsic hand movements are not possible until the lesion level is T1 [5]. All tetraplegic patients have some

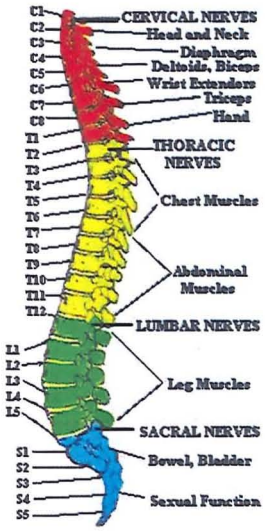


Figure 1.5: Map of the spinal column (taken from www.spinalinjury.net).

impairment of the trunk, legs and bladder, bowel and sexual organs, regardless of their level of injury [4]. Those with a complete injury have complete voluntary impairment of these functions however some autonomic nervous system control may remain.

Those with lesions between T1–T6 have paralysis of the intercostal, trunk and abdominal muscles. The extent of the paralysis of the intercostal and trunk muscles is reduced as the level of the lesion moves down the spinal cord. As a result of this paralysis these patients have markedly limited chest expansion and rely solely on the diaphragm, which is innervated mainly at C4, for breathing. Balance and trunk stability is a potential problem in these patients [4].

Although the chest and trunk muscles are innervated in those with an injury between T7 and L1, the abdominal muscles essentially are not, although the extent of the paralysis is dependent on the lesion level. Breathing may therefore still be slightly compromised, although not to the same extent as in those with a lesion at T6 and above. As with tetraplegic patients, all paraplegics have some impairment of the legs, and bowel, bladder and sexual organs, depending on the severity of their injury [4].

The American Spinal Injuries Association (ASIA) grading system is internationally recognised as an impairment scale, and is used to determine the degree of 'completeness' of an injury by assessing motor and sensory function below the level of injury. It is based on a five-point scale (A–E). A clinically complete spinal cord injury ('A-complete') is defined as

the absence of all motor and sensory function below the level of injury. Being classified 'B-incomplete' indicates that there is some sensation but no motor function below the injury level. Classifications C and D have increasing preservation of motor function. If all motor and sensory function is normal the classification E would be assigned.

Incomplete lesions of the spinal cord are common. Between 2005–2006 60 of the 153 spinal cord injuries which occurred in Scotland resulted in incomplete paralysis, the majority of which resulted in incomplete tetraplegia [3]. Such injuries can result in various syndromes depending on the extent and exact site of the lesion. Central (Cord) Syndrome occurs as a consequence of a hyperextension injury in a rigid, often osteoarthritic spine. The lesion predominates in the grey matter and extends variably into the white matter. This syndrome results in flaccid paralysis of the upper limbs usually involving two segments. The lower limbs often become spastic and have moderate paralysis. Dissociated sensory loss predominates in the thorax and upper limbs, with a retained epicritic sensibility and loss of pain and temperature sensations. Control of urination and defecation is also retained [2].

Anterior Syndrome, another form of incomplete lesion, can occur from all types of injury, although there is a slight predominance of flexion induced fracture-dislocations of the spine and protrusion of the vertebral disc. Due to the causes of the injury, the lesion occurs in the anterior region of the cord; anterior horns, anterolateral tracts, and possibly the anterior spinal artery. Motor loss is profound below the level of injury. Flaccid paralysis of the upper limbs results, covering several segments. The initial flaccid paralysis that occurs in the lower limbs has a rapid return of motor reflexes. As with Central Cord Syndrome there is dissociated sensory loss, however it is disproportionate to the motor loss that occurs. Sensitivity to pain and temperature occur but epicritic and deep sensibilities are retained [2].

Brown-Sequard Syndrome, another form of incomplete lesion, occurs as a consequence of a hemisection of the spinal cord the result either of a fracture and/or dislocation in hyperflexion [2]. The injury often results in an unusual pattern of sensorimotor function [6]; motor function, proprioception, fine touch and vibration discrimination are affected on the same side as the injury and loss of pain, temperature, crude touch and deep pressure on the opposite side. It is the most favourable prognosis as most patients recover the ability to walk, and have satisfactory bowel and bladder control.

Conus Medullaris syndrome occurs following an injury to the sacral cord and lumbar nerve roots. This results in an areflexic bladder, bowel and lower limbs. Sacral reflexes may occasionally show preserved reflexes [6]. Cauda Equina Syndrome involves 'injury to the lumbosacral nerve roots within the neural canal resulting in arefelxic bladder, bowel and

lower limbs [7].

1.3.2 Problems associated with an SCI

Following an SCI the majority of people would be forgiven for thinking that the biggest problem faced by these patients is being unable to walk. However, in conjunction with this, those with an SCI also have a variety of potentially serious medical issues which for many are more problematic than being unable to walk.

Patients with a lesion at T6 and above are at risk of a condition known as autonomic dysreflexia which occurs due to an imbalance in the body systems that control blood pressure [8]. If untreated, blood pressure can rise so high that it can result in a stroke and possibly even death.

Pressure sores are also a major worry for those with an SCI at any level due to their inability to sense pressure and shift position. Unrelieved pressure causes the blood supply to an area to be cut off and as a consequence the area is starved of oxygen and vital nutrients. The area therefore becomes ischaemic and dies. If left untreated the area can become blistered and ulcerous. Not only can the skin be affected but also subcutaneous fat, muscle, and deeper structures. Pressure sores are extremely dangerous and can be life threatening as the infection present in the wound can spread to the blood, heart and bone [5].

Spasticity, another common problem faced by SCI patients, is an exaggeration of the normal reflexes that occur when the body is stimulated in certain ways. It occurs in patients with upper motor neurone damage whose intact spinal reflex arcs below the level of the lesion are isolated from higher centres. Their response to a stimulus therefore becomes exaggerated. It interferes with the patient's ability to carry out activities of daily living (ADLs) and can, in some cases, be so strong that it can throw them out of their wheelchair [5]. It is therefore not surprising that it can be extremely painful and fatiguing.

The bowel and bladder are controlled by both voluntary and autonomic control. Sacral spinal nerves supply the voluntary sphincter muscles, and the autonomic control is via sympathetic pathways from the upper lumbar region, and parasympathetic pathways from the sacral region. Therefore, any patient with an SCI will experience difficulty in emptying their bowel and bladder.

Respiratory disease, in particular pneumonia, is a problem for those with an injury above C3 consequent to the lack of innervation of any of the respiratory muscles and therefore the

inability to clear the lungs. In able-bodied (AB) individuals the diaphragm, which is innervated at C3/4/5, is responsible for most of the inspiratory work during quiet breathing, and the intercostal muscles are involved during deep breathing and coughing. The abdominal muscles are also involved in coughing. However, in those with a lesion at T6 or above the intercostal muscles are fully or partially paralysed depending on the lesion level, and the abdominal muscles are totally paralysed. As mentioned previously, although the chest and trunk muscles are innervated in those with a lesion between T7 and L1, the abdominal muscles are not. Therefore, although not to the same extent as in those with a higher lesion, breathing is still compromised. Due to the lack of innervation of the various muscles involved in breathing, SCI patients, particularly those with a lesion at T6 and above, have a markedly limited chest expansion during breathing and an inability to cough adequately or remove secretions from the lungs. This results in a high risk of lung infection, which is one of the most common complications of acute SCI.

1.3.3 Effect of Spinal Cord Injury on Bone

Osteoporosis below the level of injury is one of the major secondary complications of spinal cord injury. Osteoporosis is diagnosed from bone mineral density (BMD) measurements that are significantly lower than reference values from the healthy general population. However, what is unique about the condition in those with an SCI is that it is exclusively sub-lesional [9, 10, 11, 12]. In paraplegics the pelvis and lower extremities are affected and in tetraplegics bone loss is also found in the upper extremities.

Following an SCI, bone loss in the paralysed limbs is characterised by a decrease in the BMD at the epiphyses, and by a thinning of the cortical thickness (mainly by endocortical resorption) in the diaphyses of the bones (tibia and femur). This decrease in bone mass and BMD is exponential in the epiphyses of the femur and tibia [10], the most common sites for fractures in SCI. Bone mass appears to reach a new steady-state 3 years post injury in the femoral epiphysis and 5 years post injury in the tibial epiphysis. At this point bone mass has been reduced by ~48% in the femoral epiphysis and ~58% in the tibial epiphysis [10]. Although not as severely as in the epiphysis of the femur and tibia, bone mass in the diaphysis also decreases. The diaphysis is another common site for fractures in SCI. A new steady state bone mass has been shown to occur 5 years post injury in the femoral diaphysis and 7 years post injury in the tibial diaphysis with ~34% and ~25% of bone mass lost respectively [10].

The underlying mechanism of such dramatic bone loss is poorly understood. Mechanical stress is believed to have an important role in the determination of BMD, bone morphology and bone strength thus the disuse which follows an SCI must have an important role to play. Many

non-mechanical factors have also been suggested as contributing factors; poor nutritional status, disordered vasoregulation, hypercortisolism (therapeutic or stress-related), alterations in gonadal function and other endocrine disorders [13, 14]. Although the mechanism of bone loss may not be fully understood, it is clear that the dramatic reduction in sub-lesional BMD of people with an SCI at least doubles their lifetime risk of sustaining a fracture compared to an AB person [15]. These fractures commonly occur as a result of a minor trauma such as falling from a wheelchair or during transfers, and have a detrimental effect on the quality of life of those with an SCI.

1.3.4 Effect of Spinal Cord Injury on Muscle

Following an SCI the paralysed muscles exhibit dramatic muscle atrophy which begins almost immediately after injury [16, 17, 18, 19, 20, 21]. In 1999 Castro et al [17] found that only 6 weeks after injury the average paralysed muscle CSAs were 18–46% lower than in AB controls. A further decline of 12–24% was shown 6 months post injury [16]. The atrophy which occurs in the paralysed limbs following an incomplete injury is not as dramatic as that following a complete injury, but is still significant. In a recent case controlled study by Shah et al. [20] a significant decrease of 24–31% was demonstrated in the affected lower extremity muscles compared with control subjects. This atrophy of the lower limb muscles was independent of ambulatory status, and no significant difference was found between the more- and less-involved limbs.

Human muscles are heterogenous with regard to their muscle fibre composition. The function of the muscle determines whether it is composed predominantly of the small diameter, slow fatiguing, highly oxidative type I muscle fibres or the larger diameter, faster fatiguing, higher force producing, glycolytic type IIx fibres. Type IIa muscle fibres are also present in some muscles and have intermediate properties of the two main muscle fibre types.

In addition to the atrophy of the paralysed muscles the composition of the muscle fibres has also been shown to change. Evidence exists which suggest a shift to a predominance of type II muscle fibres following paralysis.

In 1976, Grimby et al. [18] demonstrated, through histochemical analysis of muscle biopsies, that the paralysed vastus lateralis, gastrocnemius and soleus (SOL) muscle of 7 complete SCI subjects were composed mainly (sometimes exclusively) of type II fibres and that all (or nearly all) were type IIb. In comparison, the non-paralysed deltoid muscle fibres were more oxidative and smaller in diameter, suggesting that the muscle fibre conversion is by some means a direct result of paralysis.

These results have also been demonstrated in rat skeletal muscle by Lieber et al. [19]. One year post transection, a dramatic conversion from type I to type II muscle fibres was demonstrated in the SOL muscle: initially 86.8% of muscle fibres were type I, while following transection 97.5% were type II. In the extensor digitorum longus (EDL) muscle the limited number of type I fibres present in the control rats were found to be absent following the transection. Despite the increase in type II fibres in both muscles the manner in which it occurred was different. In the transected EDL muscle the increase was the result of atrophied type I fibres and in the transected SOL muscle the increase was due to the conversion of type I fibres. This may be a consequence of the initial percentage of each fibre type present prior to transection.

As a consequence of the fibre type conversion Lieber et al. [22] demonstrated an increase in the muscle force produced, which was less fused, when the SOL muscle was stimulated at 10Hz one year post transection. This implied that the muscle fibres had a faster contraction and/or relaxation time. The SOL muscle was also found to have a 100% increase in fusion frequency, further indicating an increase in twitch contraction and/or relaxation speed. These properties are characteristic of type II fibres which were found to be in predominance in this muscle following transection [19]. The fact that there were no significant differences in these parameters between the normal and transected EDL muscle provides further evidence that the SOL muscle fibres had converted to type II fibres. This is reinforced by the finding that the contractile properties of the two muscles became more similar.

The timescale of the muscle fibre conversion and atrophy is important for rehabilitation. Knowledge of this would allow appropriate interventions to be implemented which may reduce this trend. In the early 1980s and 1990s Scelsi et al. [23] and Lotta et al. [24] highlighted the preferential atrophy of type II muscle fibres 1-4 months after an SCI. A period of approximately 4 months followed where there was atrophy of both type I and type II fibres. Long term paralysis (approximately 9 months) was shown to result in a reduction in type I fibres and their atrophy. The increase in type II fibres shown to occur at this time was attributed either to the decline in the percentage of type I fibres or the conversion of type I to type II fibres.

In 1997 Burnham et al. [25] used immunofluorescence techniques to determine the rate of change of muscle fibre composition in the vastus lateralis of 12 traumatic SCI patients. Biopsies were also taken from 46 control subjects. The vast majority (98%) of fibres in the control subjects expressed only one myosin heavy chain (MHC) isoform with a slight predominance (60%) of fibres having only the fast MHC (MHCx). Only 2% of fibres were found to co-express both MHC isoforms. The biopsies taken within 1 month of injury demonstrated that during this early phase the MHC isoform remains stable. Between 1 and 20 months post injury an

increase in the proportion of fibres co-expressing both MHC isoforms was found. During this transitional phase the expression of the MHC was altered, possibly by the downregulation of the slow isoform and upregulation of the fast MHC isoform. By 73 months post injury a new steady state was reached. The vast majority of fibres in those with an SCI for longer than 70 months expressed the MHCx isoform (85-100%).

The kinetics of this process were modeled by the authors [25]. They found that if 66% of the fibres were assumed to be slow, then there is a transition of 4.7 months to the co-expressing state and a further time constant of 17 months to the fast state.

Muscle atrophy and fibre type conversion appear to commence approximately 1 month post injury. However, the cause of these changes remains unclear. The atrophy which occurs has been attributed to either denervation or disuse [26]. Denervation atrophy occurs as a result of primary injury to motoneurones in the spinal cord. The ventral and dorsal roots may also be damaged even when the cell bodies are not directly affected. Therefore there is substantial denervation of the muscles supplied by the motoneurones in the spinal cord and the motor nerves that exit the spinal cord through the ventral roots at the level damaged. When muscles lose all innervation, drastic and rapid wasting of the muscle occurs. However, as only a small proportion of the muscles undergo complete denervation it is believed that it cannot be solely responsible for the atrophy of the paralysed muscles.

Although complete denervation of the muscles is uncommon and is therefore not thought to be completely responsible for the muscle atrophy, the level of neural inputs to the muscle must have a significant effect. A recent study investigating muscle atrophy in the affected muscles of those with an incomplete SCI found that the fractional presence of neural inputs to the affected muscles, which results in variable activation of the muscles, reduced the extent of muscle atrophy following paralysis [20].

Disuse would appear to be an obvious explanation for the atrophy of paralysed muscles. It is attributed to concurrent changes in muscle length or loading conditions, and is more pronounced in paralysed muscles that normally bear weight, especially those across single joints. These muscles are composed of slow, fatigue resistant muscle fibres. Scelsi et al. [23] have however disputed the influence which disuse has on the atrophy of paralysed muscles. Their own results, and those of Lotta et al. [24], highlighted the preferential atrophy of type II muscle fibres 1-4 months post injury. Depending on the composition of the muscle fibres, this may or may not dramatically affect the size and/or the number of muscle fibres available to produce force. It is possible however, that even if disuse is not thought to be

the primary cause of atrophy in paralysed muscles post injury, it is still a contributing factor. Shah et al. [20] highlighted in a recent study that there is significant atrophy in the lower extremity muscles in those with an incomplete injury who do not require the use of a wheelchair. Despite having more functional neural inputs than those who require the use of a wheelchair there was no significant difference in the muscle atrophy found. This has been attributed to the fact that those who use assistive aids (e.g. cane, crutches) for ambulation heavily weight bear through their upper extremities. Therefore, weight bearing through the lower limbs is reduced. The resulting disuse and reduced activation of the lower extremities further increases the muscle atrophy.

The mechanism of fibre type transformation is completely unknown. However, a number of hypothesis have been discussed [19]. It was thought that cordotomy may result in high frequency input into the muscle via the peripheral nerve. However, this was deemed unlikely as electromyograph (EMG) profiling has been shown to demonstrate a decreased electrical activity following cordotomy in cats. It has always been suggested that prolonged immobilisation, secondary to the cordotomy, may be the cause of the fibre type conversion, independent of the status of the CNS. Again, this was thought to be unlikely as there is significant data available which shows that immobilisation causes muscle fibre atrophy with little or no change in the relative percentages of the various fibre types.

One feasible explanation for the fibre type conversion is that there may be selective degeneration of the slow alpha motoneurones. However, the results obtained by Lieber et al. [19] deem this to be unlikely as the slow fibres present were randomly scattered throughout the muscle. If there had been selective degeneration, fibre type groupings would be expected.

It has also been suggested that spasticity, a problem experienced by most SCI patients, particularly in the early stages of post injury, may induce the changes observed [24]. In order to determine this, a study comparing the muscle fibre composition post injury of those with and without spasticity is required.

Despite the fact that the mechanism for muscle atrophy and fibre type conversion following an SCI is poorly understood what is certain is that it does occur. Consequently, patients are left with a reduced muscle mass which is highly fatiguable. In complete SCI patients this reduces their ability to participate in prolonged assisted exercise (e.g. functional electrical stimulation (FES) cycling). Although there have been no studies investigating the presence of fibre type conversion in incomplete SCI patients, significant muscle atrophy has been demonstrated. It is likely that a similar conversion to type II muscle fibres occurs in these patients also. Therefore, despite having more voluntary control of the lower limbs the

forces produced cannot be sustained for a long period of time therefore limiting their ADLs as well as reducing their ability to participate in prolonged assisted or voluntary exercise.

1.3.5 Effect of Spinal Cord Injury on the Risk of Cardiovascular Disease

Since the end of World War Two the acute and long term medical treatment of SCI patients has dramatically improved, increasing their life expectancy to near-normal [27]. Consequently, the leading cause of death in SCI has changed. Prior to improvements in medical care, renal failure and urinary tract complications were the leading cause of death post injury. Now, in line with the AB population, the leading causes of death in the SCI population have become respiratory and cardiovascular disease.

In recent reviews by Jacobs and Nash [6] and Nash [28] the risk factors associated with cardiovascular disease were discussed; visceral obesity, elevated body mass indices, reduced lean body mass, diabetes, insulin resistance with obesity and dyslipidemia, and advanced ageing were all cited as contributing factors. In addition to these, those with an SCI also have an atherogenic lipid profile with a decrease in the pulmonary plasma concentration of the high-density lipoprotein cholesterol (HDL-C) which protects against vascular disease.

Physical inactivity is yet another risk factor for the development of cardiovascular disease [6, 28]. As a result of the atrophy and fatigue which occurs in paralysed muscles, those with an SCI have a reduced function for everyday tasks and consequently tend to live a sedentary lifestyle: a quarter of healthy, young people with SCI are not fit enough to perform many ADLs [29]. This lack of exercise further exacerbates the mobility impairment, muscle atrophy and bone demineralisation mentioned previously as well as increasing myocardial atrophy. Changes in lean body mass, body water content and blood volume and an increase in percentage body fat also occur [30].

The cardiac system is also impaired in those with an SCI. In all SCI patients venous pooling occurs in the lower body due to the inactivity of the skeletal muscle pump. This decreases the circulating blood volume, and consequently, venous return to the heart. Via the Frank-Starling mechanism, stroke volume is reduced and cardiac output is impaired [31].

A further complication in tetraplegics is a reduced heart rate, which further contributes to an impaired cardiac output. It has been suggested by Van Loan et al. [32] and Claus-Walker and Halstead [33] that this may be due to sympathetic 'decentralisation'. The central command of sympathetic effector organs such as the myocardium is thought to be abolished due to the interruption of efferent sympathetic outflow. This is believed to result in separation of the

peripheral sympathetic nervous system from the control of the cardiovascular centres of the brain [30]. As a consequence of this, the heart rate of tetraplegics does not typically exceed 130 bpm.

The function of the pulmonary system is also impaired in SCI patients. They have been shown to have significantly lower static and dynamic tidal volume, vital capacity, forced expiratory volume in 1 second and maximum breathing capacity than able-bodied subjects [32].

Peak oxygen uptake ($\dot{V}O_{2peak}$) has previously been used to determine the physical fitness of SCI subjects compared to AB subjects [32, 34, 35, 36]. It was found to be lower in tetraplegics than paraplegics and AB subjects [32, 34, 35], and lower in paraplegics than AB subjects. Controversy exists as to whether the limitation in $\dot{V}O_{2peak}$ is due to the oxygen transport capacity or the ability of the tissues to utilise oxygen. The decrease in stroke volume, heart rate and consequently cardiac output which occurs in tetraplegics, limits the oxygen transport system. It is also affected by the lack of sympathetically induced vasoconstriction of the smooth muscles of the arterioles and venules [30]. In contrast to tetraplegics, paraplegics have been shown to display higher heart rate values at rest and during exercise [36]. However, this increase in heart rate appears unable to compensate for the decrease in stroke volume; therefore the decreased cardiac output also limits the oxygen transport system in paraplegics. The extensive muscle paralysis, which occurs after an SCI, reduces the amount of muscle available for exercise. Consequently, oxygen demand and consumption are limited. This decrease in the ability to utilise oxygen may be fully responsible for limiting $\dot{V}O_{2peak}$. The limitation was shown to be peripheral by Hopman et al. [35]. However, central limitations could not be ruled out as the cardiac output was not measured. Further research is still required in this field.

Due to the problems associated with the inactivity of the skeletal muscle pump, extensive muscle paralysis, impairment of the sympathetic nervous system (lesions above T6) and consequent reduced efficiency of the cardiovascular and pulmonary systems, it is extremely difficult for SCI patients to remain active and physically fit. As a result, these patients do not regularly stress their cardiovascular system and are therefore at high risk of developing cardiopulmonary disease. It would therefore be expected that any form of exercise which these patients could undertake would be beneficial in lowering their cardiovascular risk factors.

1.4 Transverse Myelitis

As mentioned in Section 1.3.1 an SCI can result from inflammatory diseases such as transverse myelitis (TM). One of the subjects who participated in the body weight supported

treadmill training (BWSTT) study has incomplete paraplegia as a consequence of TM. TM is a focal inflammatory disorder of the spinal cord which results in varying degrees of muscle weakness, sensory alterations and autonomic dysfunction [37]. It affects between 1 and 4 people per million per year with the most common age range at onset being 10–19 and 30–39 [37, 38, 39, 40, 41]. There is no sex or familial predisposition to the condition.

In a study by Jeffery and colleagues [41] 45% of TM cases were characterised as parainfectious, 21% were associated with multiple sclerosis (MS), 12% were associated with spinal cord ischaemia, and 21% were idiopathic. Inflammatory diseases other than MS are also known to cause TM [37]. Necrosis of the spinal cord, oedema, and demyelination are essential pathological features of the syndrome [42]. However, Jeffery et al. [41] found that these features were influenced by the underlying cause of the syndrome: spinal cord swelling was more evident in those with parainfectious TM while spinal cord plaques were more common in those with associated MS. The white matter of the spinal cord is more affected resulting in slowing of conduction in the sensory and motor pathways.

On presentation a clearly defined rostral border of sensory dysfunction is often present as is acute inflammation of the spinal cord. When patients reach their maximum level of deficit approximately 50% have lost all movement in their legs, almost all have bladder dysfunction and approximately 80–95% have numbness, paresthesias, or band like dysesthesias [37, 38, 39, 40, 42, 43]. As mentioned previously, autonomic dysfunction also occurs following the onset of TM. As a consequence of this, variable symptoms are present including increased urinary urgency, bowel or bladder incontinence, difficulty or inability to void, incomplete evacuation, or bowel constipation and sexual dysfunction [44].

Poor recovery from TM is predicted by rapid progression of symptoms, back pain and spinal shock, as well as absent central conduction on evoked potential testing and the presence of 14-3-3 protein (a marker of neuronal injury) in the cerebral spinal fluid (CSF) [37]. However, the long-term prognosis is variable. Approximately one third of patients recover with little or no sequelae, one third are left with a moderate degree of permanent disability, and one third have severe disabilities [38, 39, 42]. Consequently, a significant percentage of patients with TM find themselves in a similar condition to those with an SCI at high risk of cardiovascular disease and in need of increased physical activity (see Section 1.3).

1.5 Exercise Training in Able Bodied Individuals

In order to increase cardiorespiratory fitness, the American College of Sports Medicine (ACSM) set the following recommendations [45].

- **Frequency of training**. It is recommended that training takes place 3–5 days a week.
- **Intensity of training**. Training should be carried out at 55–90% of the individuals maximum heart rate (HR_{max}) or 40–85% of their maximum oxygen uptake ($\dot{V}O_{2max}$) reserve or HR_{max} reserve. Those with a low level of fitness should train at the lower levels of these recommended ranges.
- **Duration of training**. Training should be composed of 20–60 minutes of continuous or intermittent (minimum of 10-minute bouts accumulated throughout the day) aerobic activity. The duration of the exercise is intensity dependent, i.e. lower-intensity activity should be conducted over a longer period of time (30 minutes or more) and vice versa. For adults not training for athletic competition, moderate intensity exercise of longer duration is recommended.
- **Mode of activity**. Any activity that uses large muscle groups which can be maintained continuously, and is rhythmical and aerobic in nature is recommended, i.e. walking, hiking, running, rowing, swimming etc.

The improvement in $\dot{V}O_{2max}$with training is determined by an individual's genetic response to the frequency, intensity and duration of training [45].

As can be seen in Figure 1.6, the $\dot{V}O_{2max}$ of world class endurance athletes can exceed 80 $ml.kg^{-1}.min^{-1}$ while that of a sedentary individual is significantly lower at 30 $ml.kg^{-1}.min^{-1}$. During the first 2–3 months of training, $\dot{V}O_{2max}$ can increase in sedentary subjects by 15–30% [46]. Further increases of up to 40–50% can occur over the next 9–24 months of training. After this point $\dot{V}O_{2max}$ plateaus.

As a consequence of endurance training, heart rate (HR) is reduced at a given absolute level of submaximal power output, and stroke volume (SV) is increased [31]. The reduction in HR is partly due to a decrease in sympathetic stimulation. However, the decline in plasma catecholamines is completed by the end of the third week of training, and the reduction in resting and submaximal heart rates continues over a longer period of time. This suggests the involvement of another mechanism. Other mechanisms, such as a decrease in the sensitivity of beta1-receptors on the heart [48], increased vagal control of the heart [49], and an increase in diastolic filling at any given HR as a result of training-induced increases in blood flow [50], have been shown to be involved in the reduction of HR with training.

The mechanisms which result in an increase in $\dot{V}O_{2max}$ following a period of endurance training remain equivocal. However, they may be associated with the training induced increase in

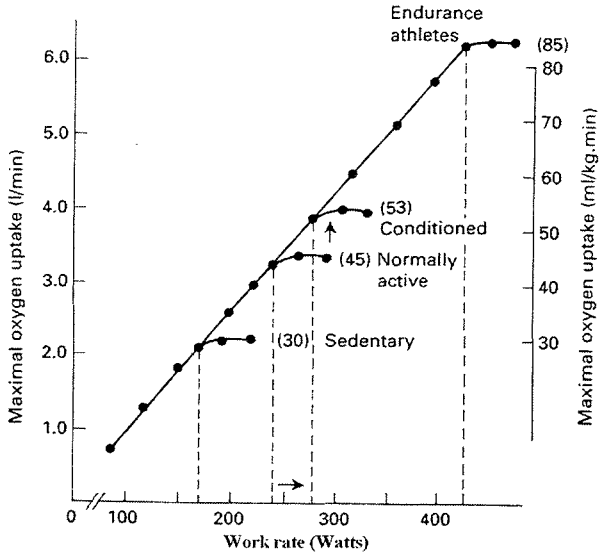


Figure 1.6: The range of $\dot{V}O_{2max}$ that exists within a normal healthy adult population (adapted from [47]).

maximal cardiac output (CO) and maximal arteriovenous (a-v) O_2 difference which increases O_2 delivery to the exercising muscles. This increase in maximal CO is the result, not of an increase in maximal HR, but of an increase in maximal SV which occurs due to an increase in cardiac filling pressure. The greater preload and cardiac filling pressure of an endurance trained athlete is probably due to a higher cardiopulmonary capillary wedge pressure, an increase in diastolic reserve as a result of an increase in peripheral venous compliance, as well as an increase in left ventricular chamber size [51].

Endurance training decreases maximal diastolic blood pressure, without affecting maximal systolic blood pressure. Snell et al. [52] suggested the mechanism for this to be an increased capacity for muscular vasodilation, which lowers the total peripheral resistance, and therefore enables trained individuals to utilise a larger fraction of maximum vascular conductance than sedentary subjects. Ventricular after-load is consequently reduced. This, in combination with adaptations to muscle fibres (to be outlined), increases the capacity for muscle oxygen extraction.

As a response to an increased demand for CO_2 elimination, endurance trained athletes have been shown to have a higher maximal pulmonary ventilation and breathing rate but with a retained maximal tidal volume [53]. As a consequence, these athletes can compensate for

higher levels of lactic acid and tolerate a lower pH, i.e greater metabolic acidosis. The toleration of a lower pH is aided also by the increase in 2,3-diphosphoglycerate, which occurs with endurance training. This results in a shift in the oxy-haemoglobin dissociation curve such that at a given level of PO_2, O_2 is released more readily from haemoglobin.

The total haemoglobin content of blood increases with endurance training, without an increase in concentration, due to an increase in the total number of red blood cells and an increase in blood volume [46]. As a consequence more O_2 is available for oxidative metabolism.

Changes in cardiac structure are also prominent as a result of endurance training as this form of exercise increases cardiac mass and volume. Left-atrial and ventricular dimensions, and intraventricular septal and posterior wall thickness are consistently larger in endurance trained athletes. Absolute left ventricular (LV) mass and LV end-diastolic volume are also increased, even when normalised for lean body mass [46]. Shapiro [54] demonstrated that LV volume is increased by 33% and LV mass increased by 10–20% in endurance athletes when compared to sedentary controls. These parallel increases in LV mass and volume occur in order to maintain a constant relation between systolic blood pressure and the ratio of LV wall thickness to wall radius.

As mentioned previously, adaptations to muscle fibres also occur with endurance training. An increase in oxidative enzyme concentration (i.e. enzymes of fatty acid oxidation, the citric acid cycle, and the respiratory chain) of approximately threefold occurs in the trained leg muscles compared to untrained muscles [55]. Henriksson and Reitman [55] illustrated that in initially untrained individuals an increase of approximately 40–50% in the content of oxidative enzymes in trained muscles occurs, with the most rapid change occurring during the first 3 weeks. Although some increase in the oxidative content of muscle can be obtained with fairly light work, a much more marked increase occurs with a training intensity of 70–80% of $\dot{V}O_{2max}$.

Skeletal muscle capillarisation is also rapidly enhanced with endurance training [55] as is the mitochondrial content. An increase of 50% in the total number of muscle capillaries occurs after 2 months of training at high submaximal exercise intensities. This increases the maximal blood flow capacity and the surface area available for exchange of gases, substrates and metabolites between the blood and muscle [56]. As a consequence, the O_2 diffusion capacity from the blood vessels to respiratory chain enzymes is increased, which may contribute to the increased $\dot{V}O_{2max}$ which occurs with endurance training.

Endurance training has been shown to completely transform type IIx fibres to type IIa [57]

by increasing their oxidative capacity. It is believed that this, and the increase in oxidative complement of type I fibres, may delay the point at which type II muscle fibres are recruited during exercise. As a consequence of the increased oxidative content of the muscle, exercise tolerance is increased.

1.6 Exercise Testing in Able Bodied Individuals

Adaptations to the pulmonary, cardiovascular, and neuromuscular systems which result from endurance training improve O_2 delivery from the atmospheric air to the mitochondria and hence improve the body's ability to carry out oxidative metabolism. The ability to sustain high level exercise can be evaluated by four key aerobic parameters: $\dot{V}O_{2max}$, lactate threshold (LT), work efficiency and the time constant for $\dot{V}O_2$ kinetics ($\tau\dot{V}O_2$), all of which can be accurately measured from a single short-duration ramp exercise test [58].

1.6.1 Maximum Oxygen Uptake

$\dot{V}O_{2max}$ is the body's upper limit for O_2 utilisation. However, the cause of its limitation, whether it be the rate at which O_2 can be delivered to the muscles, the muscle's ability to extract O_2 from the blood it receives or its ability to carry out oxidative metabolism, remains equivocal [59]. Its increase with training may be a consequence of an increase in maximal CO resulting from an increase in SV. This occurs due to increases in left ventricular size, myocardial contractility, and end-diastolic volume. Another contributing factor to the increase in $\dot{V}O_{2max}$ with training is the increase in the a-v O_2 difference. In addition, the O_2 carrying capacity of the blood is increased due to an increased total haemoglobin content.

The magnitude of the increase in $\dot{V}O_{2max}$ with training is dependent on a number of factors [60]: the initial fitness status of the individual, the duration of the training programme, and the duration, intensity and frequency of the individual training sessions. As most training studies have shown an increase in $\dot{V}O_{2max}$ with time, the optimal exercise volume and intensity is unknown [56]. However, there is evidence to suggest that training at 80–100% $\dot{V}O_{2max}$ may be required to induce changes depending on the initial fitness level [60].

In a review by Billat [61] high intensity interval training was shown to be an effective method for increasing $\dot{V}O_{2max}$. By utilising this form of training, individuals are able to train for longer at $\dot{V}O_{2max}$ and have a lower blood lactate concentration than during continuous training. Recently high-intensity interval training has been shown to result in greater improvements in $\dot{V}O_{2max}$ than continuous training [62, 63]. However, due to the strenuous nature

of this form of training high levels of motivation are required in those who participate. It may therefore not be suitable for sedentary individuals and those beginning an exercise programme. These individuals may find the lower intensity of continuous training more comfortable.

As $\dot{V}O_{2max}$ is an accurate gauge of aerobic function, its direct measurement is used to determine the fitness of a subject and to determine if any increases in fitness occur as a result of a training programme. In order to determine $\dot{V}O_{2max}$ an incremental test to volitional exhaustion, such as that described by Whipp and colleagues [58], must be carried out. The $\dot{V}O_{2max}$ is calculated by averaging the $\dot{V}O_2$ of each breath in the last 20 seconds of the incremental phase of the test [64].

The criterion for the attainment of $\dot{V}O_{2max}$, i.e. no further increase in $\dot{V}O_2$ with a further increase in work rate, has been applied to maximal exercise tests since 1923 [65]. However, it has become apparent in recent years that during ramp incremental exercise tests a plateau in $\dot{V}O_2$ is not always achieved, despite maximal subject effort. In a study by Day and colleagues [66] only 17% of subjects demonstrated a plateau in $\dot{V}O_2$ during maximal ramp incremental testing. In those who did not achieve a plateau, whose $\dot{V}O_{2peak}$ was either higher or did not differ from that extrapolated from the linear phase of the response, the $\dot{V}O_{2peak}$ achieved did not differ from that obtained during maximal step exercise tests. Similar results were also obtained in a recent study by Rossiter and colleagues: a plateau in $\dot{V}O_2$ was not demonstrated during a maximal ramp incremental test in any of their subjects [64]. Despite this the $\dot{V}O_{2peak}$ achieved did not differ from that obtained during step exercise at work rates representative of 105% and 95% of the maximum work rate achieved during the preceding ramp incremental test. While studies have shown that 'a plateau in the $\dot{V}O_2$ response is not an obligatory consequence of incremental exercise' [66] it is clear that further tests must be carried out to be certain that the $\dot{V}O_{2peak}$ achieved is indeed representative of the subject's $\dot{V}O_{2max}$.

Although $\dot{V}O_{2max}$ is a key parameter when determining aerobic fitness [58] there is some evidence to suggest that during long-term training programmes $\dot{V}O_{2max}$ will stabilise and further improvements in endurance capacity will be due to improvements in exercise efficiency and the LT [67, 68, 69, 70].

1.6.2 Lactate Threshold

The LT can be described as the highest $\dot{V}O_2$ that can be achieved without a sustained increase in blood and muscle lactate concentration [71]. It has been shown to occur at approximately

50–60% of $\dot{V}O_{2max}$ in healthy, sedentary individuals [72]. In order to elicit significant improvements in the LT individuals must train close to or slightly above the threshold [73]. A higher stimulus may however be needed for conditioned subjects. Following a successful endurance training programme the LT has been shown to shift to a higher absolute work rate and $\%\dot{V}O_{2max}$ [74]. Therefore, a higher relative (% $\dot{V}O_{2max}$) or absolute (running speed or power output) exercise intensity can be sustained without the accumulation of lactate. In elite athletes the LT occurs at approximately 70–80% of $\dot{V}O_{2max}$ [75]. Above this threshold, exercise results in nonlinear increases in metabolic, respiratory and perceptual stress [76, 77], and individuals fatigue rapidly. Therefore, an increase in the LT is a clear indicator of increased endurance capacity [56].

The LT can be determined both invasively and non-invasively during an incremental test [58]. When detecting the LT invasively, blood is withdrawn at set intervals and analysed for blood lactate concentration. The concentrations can be plotted against work rate or $\dot{V}O_2$. The LT is identified as the work rate of $\dot{V}O_2$ at which an inflection in the blood lactate concentration occurs. Above this point there is a sustained increase in blood lactate concentration. However, the exact point at which the LT occurs can be difficult to determine. As blood is not withdrawn continuously, the LT may occur between samples. This invasive method is also expensive to carry out and can cause discomfort for the exercising subject. Consequently, many exercise testing laboratories use the non-invasive pulmonary gas exchange criteria [78, 79]. Using this method, described in Section 3.5.1, the LT is shown to occur at the point at which $\dot{V}CO_2$ increases disproportionately in relation to the increase in $\dot{V}O_2$. This disproportionate increase is due to the production of 'non-metabolic' CO_2 as a result of bicarbonate (HCO_3^-) buffering of the H^+ production by lactate dissociation (Equation (1.1)).

$$H^+ + HCO_3^- \leftrightarrow H_2CO_3 \leftrightarrow CO_2 + H_2O \tag{1.1}$$

The thresholds identified invasively and non-invasively are systematically related and interchangeable in their concept. However, a slight delay exists (~30 seconds) between the point of lactate increase and HCO_3^- decrease: lactate has been shown to increase by ~0.5–1 mmol/L before a decrease in HCO_3^- occurs. Therefore, the two thresholds are quantitatively not identical [72]. There is evidence of non-invasive identification of an LT in McArdle syndrome patients who cannot produce lactate [80]. It is thought in these patients that the K^+ concentration of the plasma may be the principle cause of the disproportionate increase in ventilation [81]. Investigators should therefore be cautious when directly comparing the non-invasive threshold to that found invasively without the supporting evidence from blood lactate measurements.

1.6.3 Efficiency

Efficiency, another key aerobic parameter [58] relates external work achieved to energy expenditure (usually based on $\dot{V}O_2$). There are 3 main kinds of efficiency used: gross, net and work efficiency. Work efficiency accounts for the work done at 0 watts and therefore the actual cost of moving the legs. It is therefore considered to be the best estimate of the actual efficiency of the exercise carried out. It can be measured during an incremental test such as that described by Whipp et al. [58] and requires that the caloric equivalent of the steady-state $\dot{V}O_2$ and external power are known for at least two measured work rates [72] (1 L/min $\dot{V}O_2$ $\doteqdot$ 20 kJ/min). Work efficiency varies only slightly between individuals regardless of their age, sex, and whether they are trained or untrained [72]. For lower extremity cycle ergometer work, normal subjects have an efficiency of ~30% [82].

In healthy, AB individuals, the linear relationship which exists between work rate and $\dot{V}O_2$ during a ramp incremental exercise test (IET) [83] also enables the slope of $\dot{V}O_2$ as a function of work rate ($\Delta\dot{V}O_2/\Delta WR$) of the exercise to be determined by relating the external work carried out to the $\dot{V}O_2$ necessary to achieve that work. It requires that the $\dot{V}O_2$ at two measured work rates be known. The $\Delta\dot{V}O_2/\Delta WR$ calculated during cycle ergometer testing has repeatedly been shown in healthy, able-bodied individuals to be ~10 $ml.min^{-1}.W^{-1}$ [84, 85, 86]. This value has been shown to increase slightly (~11.5 $ml.min^{-1}.W^{-1}$) during treadmill exercise due to the unmeasured work caused by swinging the arms and legs, and the inherent work against friction as the speed increases [86].

1.6.4 Kinetics

An immediate increase in adenosine tri-phosphate (ATP) turnover, in the active muscle cells, is required at the onset of exercise to meet the increased energy demand. However, at exercise onset the production of ATP by oxidative phosphorylation increases relatively slowly. Consequently, an oxygen deficit (the difference between the $\dot{V}O_2$ required for the exercise and the actual $\dot{V}O_2$ measured) exists (Figure 1.7) and the remaining energy demand must be met by 'credit oxidation' [87], by depletion of O_2 stores and 'high-energy' phosphate compounds (predominantly creatine phosphate), and if required by an increased rate of glycolysis [88]. A larger O_2 deficit reflects a higher contribution from these non-oxidative mechanisms of ATP resynthesis. The proportion of total energy derived from atmospheric O_2 increases with time until a steady state is reached where all energy is met from this source.

As demonstrated in Figure 1.7, in response to a constant increase in work rate, intramuscular O_2 uptake ($\dot{Q}O_2$) has been shown to increase as a single exponential function with no discernible delay [89, 90] (Equation (1.2)).

$$\Delta\dot{Q}O_2(t) = \Delta\dot{Q}O_2(ss) \cdot (1 - e^{t/\tau}) \tag{1.2}$$

where

- $\Delta\dot{Q}O_2(t)$ = $\dot{Q}O_2$ increment at time t
- $\Delta\dot{Q}O_2(ss)$ = steady state increment above baseline
- τ = time constant describing the rate at which $\dot{Q}O_2$ rises towards the steady state

The time constant, τ, is a measure of the time required for $\dot{Q}O_2$ to reach 63% of its steady-state in response to a step increase in work rate. $\dot{Q}O_2$ reaches more than 98% of its final amplitude when four time constants have elapsed. At this point the response is functionally complete [90]. The lower the value of τ the faster the $\dot{Q}O_2$ response kinetics and the smaller the O_2 deficit. The higher the value of τ the slower the $\dot{Q}O_2$ response kinetics and the larger the O_2 deficit.

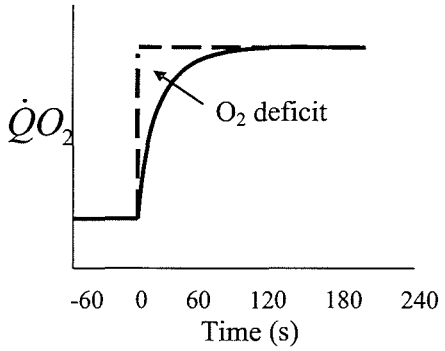


Figure 1.7: Typical response of intramuscular O_2 consumption ($\dot{Q}O_2$) to a step increase in work rate of moderate intensity.

Pulmonary oxygen uptake ($\dot{V}O_2$) kinetics at the lung have been shown to accurately reflect $\dot{Q}O_2$ kinetics in the active muscles and their measurement is non-invasive [91, 92, 93, 94]. As can be seen in Figure 1.8 the dynamic profile of the $\dot{V}O_2$ response in the lungs to a step increase in work rate does differ in one respect from that of muscle. An additional component that has been termed the 'phase I' response is present in the first 15–20s after exercise onset [95]. The alterations in mixed venous composition in the muscles does not influence

pulmonary gas exchange for a period of time which reflects the vascular transit delay between the exercising muscle and pulmonary capillaries. Therefore, the increase in pulmonary $\dot{V}O_2$ evident during the phase I response is 'cardiodynamic' i.e. it is caused by an increase in blood flow.

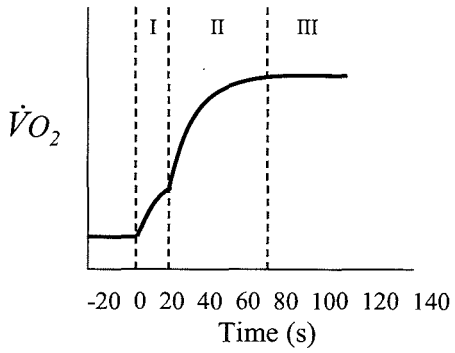


Figure 1.8: Typical response of pulmonary oxygen uptake ($\dot{V}O_2$) to a step increase in work rate of moderate intensity.

Phase II of the response begins when the reduced mixed venous O_2 levels reach the lungs (15–20s after exercise onset). $\dot{V}O_2$ increases exponentially towards a steady state (Equation (1.3)) reflecting the changes in the mixed venous blood caused by the increased extraction of O_2 and production of CO_2.

$$\Delta\dot{V}O_2(t) = \Delta\dot{V}O_2(ss) \cdot (1 - e^{-(t-\delta/\tau)}) \tag{1.3}$$

where

- $\Delta\dot{V}O_2(t)$ = $\dot{V}O_2$ increment at time t
- $\Delta\dot{V}O_2(ss)$ = steady state increment or asymptotic response at the lung
- δ = delay term, preceding the increase in $\dot{V}O_2$
- τ = time constant describing the rate at which $\dot{V}O_2$ rises towards the steady state

As the phase I response is not present in the $\dot{Q}O_2$ response in the muscle the $\dot{V}O_2$ response measured at the lungs lags that of the muscle by 15–20s. Despite this the τ describing the rate at which $\dot{V}O_2$ rises accurately reflects the rise in $\dot{Q}O_2$ in the active muscle to within

±10% [92, 96].

During moderate intensity exercise $\dot{V}O_2$ reaches a steady-state within 3 minutes of exercise onset [97]. This phase III response indicates that the increased metabolic demand is being met by oxidative phosphorylation.

During heavy exercise above the LT, but below the critical power (CP), the $\dot{V}O_2$ response does not reach a steady-state within 3 minutes of exercise onset. As can be seen in Figure 1.9 the response continues to increase until it reaches a delayed steady-state $\dot{V}O_2$ above that which would be predicted for the work rate [97]. This increase above the expected steady state value has been termed the 'slow component' and can delay the attainment of a steady-state by as much as 10–15 minutes [94].

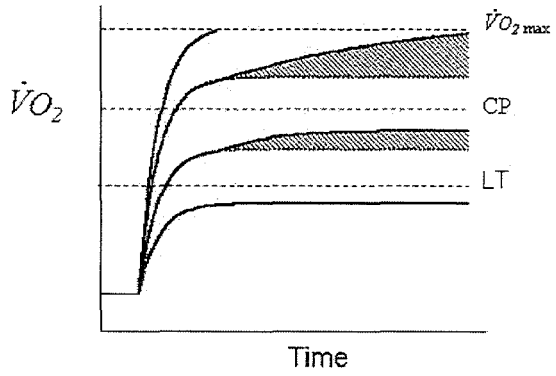


Figure 1.9: Schematic representation of the temporal profile of $\dot{V}O_2$ at the onset of moderate-, heavy-, very heavy- and severe-intensity exercise where the shaded area represents the $\dot{V}O_2$ slow component. LT: lactate threshold. CP: critical power. $\dot{V}O_{2max}$: maximum oxygen uptake [98].

CP is, theoretically, the maximum work rate that can be sustained "for a very long time without fatigue" [99]. However, in practice exhaustion occurs approximately 30–60 minutes after exercise onset [100]. It provides a measure of aerobic fitness and is closely correlated with the highest metabolic rate associated with $\dot{V}O_2$, acid blood status and blood lactate concentration attaining a steady state [101, 102]. Training a critical power or the maximum lactate steady-state has been shown to result in small increases in the associated running velocity and substantial increases in the time to exhaustion at that intensity [103]. To determine CP a ramp test is performed to identify the subject's maximum work rate (WR_{max}). At least 3 high intensity constant load (step) exercise tests (SETs) are performed at work rates chosen to ensure that the subject fatigues in ~4–10 minutes [104]. A hyperbolic relationship

exists between the work rate and the duration for which it can be sustained [99, 101, 105]. Consequently, by linear regression and extrapolation of the time^{-1} vs. work relationship, CP can be identified as the work rate corresponding to the intercept on the x-axis [104].

For work rates above CP, very-heavy intensity exercise, the $\dot{V}O_2$ slow component results in $\dot{V}O_2$ continuing to increase to or towards $\dot{V}O_{2max}$ (Figure 1.9). Consequently the subject fatigues as or immediately after $\dot{V}O_{2max}$ is achieved [106].

The determinants of the slow component remain highly contentious. However, there is evidence that the response profiles of $\dot{V}O_2$ and phosphocreatine concentration to moderate- and high-intensity exercise are the same [96, 107]. This suggests therefore, that the slow component may be linked to the high phosphate cost of force production in the exercising muscle.

The response profile of $\dot{V}CO_2$ and $\dot{V}_E$ to a step increase in work rate have been shown to replicate that of $\dot{V}O_2$. However, the phase II kinetics are slowed in $\dot{V}CO_2$ and $\dot{V}_E$ compared to $\dot{V}O_2$, with $\dot{V}_E$ slightly slower than $\dot{V}CO_2$ [95]. $\dot{V}_E$ has been shown to change in closer proportion to $\dot{V}CO_2$ than $\dot{V}O_2$ in order to maintain arterial PCO_2 and prevent a fall in pH.

The τ of $\dot{V}O_2$ in the moderate intensity domain is in the region of 30–40s in healthy young individuals [108]. Following endurance training this has been shown to decrease [108]. This reduction in τ results in a faster attainment of a steady-state and, consequently, a reduced O_2 deficit. In sedentary individuals and patients with pulmonary and cardiopulmonary disease τ has been shown to increase, increasing the magnitude of the O_2 deficit present [109, 110]. The kinetics of $\dot{V}CO_2$ and $\dot{V}_E$ have been shown to respond in a similar manner [108].

The majority of studies investigating the kinetic profile of $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}_E$ during constant load exercise have used cycle ergometry as their chosen exercise mode. Therefore, it is unknown whether or not the response profiles were consistent between exercise modes. In 1998 Billat and colleagues [111] compared the $\dot{V}O_2$ slow component present in the $\dot{V}O_2$ response profiles of 10 triathletes during a constant load treadmill running and cycling test at 90% of the work rate corresponding to $\dot{V}O_{2max}$. The slow component was calculated as the difference between $\dot{V}O_2$ at the last minute and minute 3 of exercise. They found that the slow component was significantly lower during running compared with cycling (20.90 ± 2.00 vs 268.80 ± 24.00 ml.min^{-1}) and consequently, that there was no relationship between the magnitude of the slow component and the time to fatigue. A study by Jones and McConnell [112] has also shown that during heavy exercise the $\dot{V}O_2$ slow component was significantly smaller in running than in cycling. However, the slow component for running obtained was 10 times greater than that demonstrated by Billat and colleagues [111].

In 2000 Carter and her associates [113] investigated the differences in $\dot{V}O_2$ kinetics across a range of constant load work intensities corresponding to 80% LT and 25%, 50%, 75% $\triangle$ ($\triangle$ being the difference between LT and $\dot{V}O_{2max}$) in treadmill running and cycling. They found that the kinetic responses were similar between exercise modes but that the $\dot{V}O_2$ slow component was significantly greater for cycling than for running at 50% $\triangle$ (334 $\pm$ 183 vs 205 $\pm$ 84 ml.min^{-1}) and 75% $\triangle$ (430 $\pm$ 159 vs 302 $\pm$ 154 ml.min^{-1}).

The differences in the amplitude of the slow component between treadmill and cycling is thought to be related to the differences in muscle contraction regimens. As discussed by Carter and colleagues [113] these differences may include: increased isometric contraction of the upper body musculature in cycling; a higher muscle tension development during the concentric phase of the cycle action leading to rhythmic ischaemia; a greater storage and return of elastic energy during the stretch-shortening activity of running. There may therefore be a greater recruitment of type II muscle fibres in cycling than running at the same relative intensity suggesting that this may be responsible for the development of the slow component.

1.7 Muscle Testing in Able-bodied Individuals

During maximal voluntary contractions (MVC) in healthy AB subjects it is assumed that there is complete activation of the muscle. However this is not always the case. Often the force produced during an MVC is less than the force which the muscle is capable of producing (maximal contraction (MC)). This often occurs as a consequence of central activation failure (CAF) i.e. there is failure of the central motor drive and as a result less than the maximum activation of the muscle occurs. It can result from either a failure to recruit all motor units, or a reduction in the maximal discharge rate [114].

In order to quantify the extent of the CAF, the central activation ratio (CAR) can be calculated as follows:

$$CAR = \frac{MVC\,force}{total\,force} \tag{1.4}$$

where

- CAR = central activation ratio
- $MVC\ force$ = force produced during a maximum voluntary contraction
- $total\ force$ = the summation of the force produced during the MVC and the additional force produced when stimulation is applied

The CAR is defined as the proportion of muscle force obtained that was due to voluntary force production [115]. Therefore, a CAR of one indicates complete voluntary activation of the muscle [114].

A number of methods have been used to determine CAF. In 1954 Merton [116] developed what has become known as the 'twitch interpolation' technique. By superimposing a supramaximal single or double stimulus during an MVC all motor units are recruited. Therefore, any increment in force produced is an indication of incomplete voluntary activation of the muscle.

The voluntary force produced by a muscle is dependent on motor unit recruitment and their discharge rate. Although the 'twitch interpolation' technique does result in motor unit recruitment, due to its single stimulation pulse it does not allow for the summation of force which occurs with repeated stimuli [114]. This may be the reason why various studies have demonstrated the presence of CAF by using superimposed high frequency trains of stimuli where the 'twitch interpolation' technique has not shown or has underestimated its presence [114, 117]. By imposing a high frequency train of stimulation over an MVC, not only are all motor units recruited, but the summation of force which occurs with high frequency stimulation can also occur [114]. Therefore, it is more sensitive when determining CAF to calculate the CAR.

Complete motor unit recruitment during an MVC is uncommon, therefore a CAR of one has rarely been demonstrated. In healthy, young adults the CAR of the knee extensors has been shown to be ~0.98–0.99 [118, 119] and slightly lower in the ankle dorsiflexors, ~0.96 [114, 115]. The CAR ratio is reduced in the knee extensors of the elderly, ~0.94–0.96 [119, 120]. Interestingly Kent-Braun and Alexander [115] demonstrated a higher CAR in the ankle dorsiflexors of the elderly than young adults: ~0.99 and ~0.96 respectively. The difference however was not significant suggesting that the CAR of the ankle dorsiflexors is unaffected by ageing.

1.8 Bone Responses to Training and De-training, and Bone Density Testing in Able-bodied Individuals

Bone strength is determined by the ultimate strength of bone tissue, the spatial distribution of bone material (structure geometry), and the ability of bone to repair microdamage to avoid crack propagation and organ failure [121]. Peripheral Quantitative Computed Tomography (pQCT) can be used to determine the structure and geometry of bone as well as the cross sectional area of the bone and the fat and muscle present. It can therefore measure true volumetric bone density ($g.cm^{-3}$). Other methods used to measure BMD such as Dual Energy

X-ray Absorptiometry (DEXA) measure areal (or projected) BMD in g.cm^{-2}, inaccurately predicting bone strength. DEXA measurements of bone density have also been shown to be affected by body height and bone depth as well as sex, race, and age [122]. pQCT is not affected by these artefacts. It also has the advantage of being able to separate BMD measurement in the trabecular and cortical bone. This is of particular importance in pharmaceutical studies due to the different responses of the two types of bone to such interventions [122]. The fact that BMD in the periphery can be measured with pQCT is an additional benefit. A recent study by Groll and colleagues [123] demonstrated that due to skeletal heterogeneity, particularly in the trabecular bone, there is a need to carry out densitometric measurements at the actual site of interest. These peripheral measures were also shown to be highly reproducible. Due to its ability to measure true volumetric BMD in the periphery and separate trabecular and cortical measurements, pQCT is the most appropriate non-invasive method available in predicting bone strength.

The ability of pQCT to accurately measure muscle cross sectional area is also of great importance, particularly in training and detraining studies, as according to Frost's Mechanostat Theory bone strength is determined by peak muscle forces [124]. This theory was supported in a study by Schiessl and Willnecker [121] who demonstrated a high correlation between muscle cross sectional area and bone strength. The basis of Frost's Mechanostat Theory centres around two distinct thresholds: the minimum threshold for remodelling (MESr) and the minimum threshold for modelling (MESm). If peak strains applied by the muscle do not exceed the MESr, which occurs around 50–100 microstrain [125], basic multicellular units (BMUs) increase, removing bone and decreasing its strength. Strains applied to bone which exceed the MESm at ~1000 microstrain [125] result in the addition of bone and therefore an increase in its strength. This continues until the MESm is no longer exceeded.

Between the two thresholds, strains applied by the muscles in every day activities keep bone in 'conservation mode', reducing bone turnover, preserving existing bone mass and strength, and preventing osteopenia [125]. The bones of the majority of the population remain in this region. The BMD of healthy able-bodied men has been recorded in the epiphyses of the femur and the tibia as 267.6 $\pm$ 32.9 mg.cm^{-3} and 312.7 $\pm$ 49.1 mg.cm^{-3} respectively [10]. In the diaphyses of the bones which are composed predominantly of cortical bone the BMDcort was reported to be 1111.7 $\pm$ 21.0 mg.cm^{-3} and 1156.4 $\pm$25.5 mg.cm^{-3} in the femur and tibia respectively [10].

It has however been shown that below this bone conservation region, below the MESr, bone remodelling can occur rapidly. In a study by Baecker and colleagues [126] during which subjects completed 6 days of complete bed rest, calcium excretion increased during day 1 and

bone resorption markers were shown to have increased significantly by day 2. This study demonstrated just how rapidly bone adapts to unloading with only 24 hours' bed rest sufficient to induce a significant increase in osteoclast activity in healthy subjects.

As unloading of bones rapidly increases bone remodelling, increased loading through physical activity would be expected to increase bone modelling. However, not all physical activity increases the loads applied on bones to the extent that the resulting strains are above the MESm; consequently not all physical activity increases BMD. Although the type, intensity, frequency and duration of activity that produces the best increase in mass and bone strength is unknown, it is necessary that high peak forces with high impact are placed on the target bones and that weight-bearing is involved [127]. As mentioned previously the size of the muscles which apply loads on the bones is highly correlated with bone strength. In relation to this a comparison often discussed in the literature is that between long distance runners and weight lifters [125]. Long distance runners have leaner, lighter, smaller, weaker muscles than weight lifters. Endurance activities do not rely on, nor are they accompanied by, an increase in muscle strength. Therefore, the loading on the bones is not significant enough to increase BMD. In contrast, weight lifters have large, strong muscles which cause large loads on bone. As their muscle strength continues to rise so does the load applied to the bones and consequently the bone strength. It is important therefore when introducing physical activity to increase bone strength, that it is an activity that increases muscular strength. In order to maintain BMD at a higher level the higher level of activity must be maintained. If the activity level is not maintained 'disuse' will occur and bone remodelling will increase, leading to bone loss.

1.9 Conclusion

As discussed in this chapter, the sedentary lifestyle of the majority of individuals with an SCI results in reduced cardiopulmonary fitness, muscular atrophy and bone demineralisation. The implications of these outcomes are serious: increased risk of cardiopulmonary disease, bone fractures and reduced ability to carry out ADLs among many. Increased physical activity has been shown to positively influence cardiopulmonary fitness and muscle and bone strength in AB individuals. Whether or not similar changes occur with training in the SCI population, and what intensity, duration and mode of training may be required to cause these changes, remains equivocal.

As discussed in a review by Jacobs and Beekhuizen [128] it is essential that the primary

outcomes of a training intervention can be accurately and appropriately measured. The established methods used to evaluate the success of a training intervention in the AB population have been discussed in detail in this chapter. However, whether these methods are applicable to the SCI population is uncertain.

The following chapter will therefore examine the effectiveness of exercise training interventions in SCI individuals with regards to cardiopulmonary fitness, and muscle and bone strength. In particular the outcomes of assisted gait training will be discussed. The methods used to evaluate the effectiveness of the interventions will also be discussed in order to determine their efficacy.

Chapter 2

Literature Review

2.1 Chapter Summary

The need for those with a spinal cord injury (SCI) to adopt physical activity as part of their lifestyle has been established. This chapter highlights the discrepancy in the literature in determining appropriate exercise interventions to reverse the secondary complications of an SCI in the complete and incomplete SCI populations. The effect of exercise training on cardiopulmonary fitness, bone demineralisation, and muscle atrophy and fibre type composition has been widely investigated in those with a complete SCI. However, the primary focus of exercise training in those with an incomplete SCI remains the recovery of functional walking: despite the potential of ambulation training to reverse the secondary complications of their injury. The gap in the literature regarding whether ambulation training can improve the cardiopulmonary fitness of these individuals is evident, and is further enhanced by the fact that no exercise testing protocols to accurately determine their fitness have been developed while utilising this mode of exercise. This chapter highlights the need for accurate testing methods to determine if such changes do occur. The unsuitability of the methods presently used to determine muscle strength in those with an incomplete SCI is also discussed. This chapter provides evidence to support the hypothesis that assisted gait training has the potential to increase cardiopulmonary fitness, reverse muscular atrophy and reverse/limit bone demineralisation in incomplete SCI subjects.

2.2 Exercise Training in Spinal Cord Injury

As discussed in Chapter 1, the need for those with a spinal cord injury (SCI) to adopt physical activity as part of their lifestyle is essential in order to prevent the secondary complications of an SCI: cardiovascular disease, muscular atrophy and bone loss. The advice given to those with an SCI regarding exercise training is not particularly different from that given to the able-bodied (AB) population by the American College of Sports Medicine (ASCM) [129]:

- **Frequency of training.** Exercise training should be carried out 3–5 times per week.
- **Duration of training.** The duration of each training session should be 20–60 minutes.
- **Intensity of training.** Training should be carried out at 50–80% of an individual's $\dot{V}O_{2peak}$ or HR_{peak}.
- **Mode of activity.** The following modes of exercise are applicable to this population: arm cranking, wheelchair propulsion, swimming, wheelchair sports, circuit resistance training, electrically stimulated cycling, electrically stimulated walking.

It was recommended in a recent review of exercise in SCI individuals [6] that such individuals should err on the conservative side of the above mentioned exercise durations and intensities to help ensure long-term compliance and injury prevention.

There are a number of special considerations which must be taken into account when training persons with an SCI [6]. Symptoms of overuse such as muscle and joint pain are more exaggerated and compromise activities of daily living (ADLs) more than in the AB population. Consequently, great care must be taken to ensure that overuse injuries do not occur. As mentioned in Section 1.3.2, those with a lesion at T6 and above are at risk of autonomic dysreflexia. Exercise can be a stimulus for this condition therefore great care must also be taken to monitor those exercising for any symptoms of autonomic dysreflexia and to remove the stimulus immediately should any be present. Another special consideration is that those with an SCI can have thermal dysregulation. It is therefore recommended that all exercise sessions should take place in a temperature and humidity controlled environment to reduce the risk of dehydration and over heating. Furthermore, as a consequence of the reduced bone mineral density (BMD) and deconditioning of the muscles discussed in Section 1.3, the risk of musculoskeletal injury in the lower extremities is also higher in this population during lower limb exercise. Care must therefore be taken to ensure the forces applied during exercise are not too large. Following a period of exercise, post-exercise hypotension can also occur in these individuals. Again, care must be taken to identify any symptoms which result.

If these special considerations are accounted for when training individuals with an SCI there is no reason why they cannot fulfill the exercise recommendations outlined above. As will be discussed throughout Section 2.2, when carried out safely, exercise training in this population can positively influence the cardiopulmonary fitness, muscle strength and functional ability of those with an SCI.

2.2.1 Arm Cranking and FES Cycling

Arm cranking is the most common and accessible method of exercise for paraplegics, utilising the voluntary control of the muscle mass in the upper extremities. This form of training has been shown to have a positive effect on the cardiopulmonary fitness of these individuals. There is substantial evidence that both long and short periods of arm crank ergometry training can significantly increase $\dot{V}O_{2peak}$ [130, 131, 132, 133]. Furthermore, a 5 week training study by Sedlock and colleagues [134] demonstrated that this form of training in AB subjects resulted in a significant increase in stroke volume (SV) and decrease in heart rate (HR) at a given submaximal work rate during wheelchair exercise. This suggests that arm crank ergometer training may also help to reduce the physical stress of wheelchair use in paraplegics. A further benefit from this form of training which may ease the physical stress of ADLs is an increase in upper arm strength [132, 133, 135, 136] which has been shown to occur even in the post-acute phase of injury without any detrimental effects of overtraining [136].

Although arm ergometer training has been shown to increase aerobic capacity and muscular strength, its capacity to do so is limited by peripheral fatigue. In order to maximise the effect of aerobic training it is necessary to train using the large muscles of the lower limbs [45]. This is particularly important for those with an SCI who are at increased risk of cardiovascular disease. They require a mode of exercise which will enable them to train for longer periods of time and at higher intensities than arm ergometry in order to maximise the improvement in their cardiopulmonary fitness and thus reduce their risk of developing cardiovascular disease. Consequently, a system of functional electrical stimulation (FES) leg cycling exercise (FES-LCE) was developed which uses the sequential electrical stimulation of the paralysed gluteal, hamstring and quadriceps muscles to enable the cyclical motion of cycling to be achieved. A number of studies have consequently used this mode of exercise in training interventions to determine its effects on the secondary complications of an SCI; cardiopulmonary deconditioning, muscle atrophy and bone demineralisation.

The aerobic capacity of those with an SCI has been shown to increase following a period of FES-LCE training. Short term studies have demonstrated increases in $\dot{V}O_{2peak}$ of between 10–23% depending on the frequency of the training sessions and duration of the training period [137, 138, 139, 140]. A 1 year training study by Mohr and colleagues [141], during which subjects trained for 30 minutes 3 times per week, demonstrated a significant increase of 18% in the subjects' $\dot{V}O_{2peak}$ during the first 6 months of training. Interestingly however, no further increase was shown to occur in the final 6 months of training. The range of improvements in $\dot{V}O_{2peak}$ recorded in these studies may also have been affected by the level of habituation to the exercise carried out prior to the baseline tests. This varied between studies with those who recorded smaller increases in $\dot{V}O_{2peak}$ with a lower training frequency also

allowing greater habituation to the exercise which may have resulted in unrecorded increases in cardiopulmonary fitness [138, 139, 140].

Improvements in aerobic fitness with FES-LCE training were also demonstrated following a 12 week intervention by Faghri and colleagues [142]: during submaximal exercise a significant increase in SV and decrease in HR occurred. Barstow and colleagues [139] also demonstrated an increase in aerobic fitness following an 8 week period of FES-LCE training. Post-training, the mean response time on (MRT_{on}) and off (MRT_{off}) for the same absolute work rate were significantly reduced. The faster MRTs are due to an increase in the aerobic capacity of the muscle: whether this may be due to an increase in the proportion of type I fibres, increased capillarity or increased mitochondrion content is unknown. What is certain however is that peripheral adaptations to the training have occurred.

During the short-term FES-LCE training studies the increase in aerobic fitness is also believed to be due to peripheral adaptations [137, 138, 140]. In addition to a peak FES-LCE test each study carried out a peak arm crank ergometry test pre- and post-training. No significant differences in the peak values obtained from the arm ergometer tests were found. This suggests that the improvements in aerobic capacity demonstrated during FES-LCE were as a consequence of the subjects reaching a previously unattainable cardiopulmonary reserve, unattainable due to poor muscular strength and endurance.

The increase in muscular strength is highlighted in these studies by the increased peak power achieved. In conjunction with this, an increase in the cross sectional area of the lower extremity muscles has also been shown to occur with training [143]. An increase in the oxidative, and thus endurance capacity, of the muscle was demonstrated during the year long training study by Mohr and colleagues [141]. As discussed in Section 1.3.4 the sublesional muscles of those with an SCI are composed of predominantly type IIb muscle fibres: the pre-training muscle biopsies of the vastus lateralis muscle in subjects demonstrated such characteristics. Following 1 year FES-LCE training there was a shift to a predominance of type IIa fibres and a doubling of citrate synthase activity thus indicating an increase in the oxidative capacity of the muscle.

As well as increasing aerobic fitness and reversing muscular atrophy it is also important to determine if physical activity can reverse or slow the decline in BMD which occurs following an SCI. Due to the large muscle forces which are placed on the lower limbs during FES-LCE, a number of studies have investigated whether this form of exercise could have such an effect. In those with an acute SCI, FES-LCE has been shown not to significantly slow the decline in BMD of the tibia when compared to a control group [144]. However, in those with chronic

SCI the effects appear to be determined by the intensity of training (i.e. the peak strains applied to the bone by the muscles) and the bone investigated. Training interventions of 6–12 months have not been able to elicit an increase in the BMD of the femur [145, 146, 147, 148]. However, in a subset of subjects in the 9 month intervention by Bloomfield and colleagues [146] who trained at $\geq$18W for at least 3 months a significant increase in the BMD of the femur was demonstrated suggesting that it may not be the duration, but the intensity, of the training which is important in increasing BMD. A significant increase in the BMD of the proximal tibia has been demonstrated following 1 year FES-LCE training 3 times per week [148]. The occurrence of an increase in the BMD of the proximal tibia but not the femur is thought to be a consequence of the fact that the proximal tibia is the site of insertion of the stimulated muscles and is the site of direct transfer of the pedalling force. Interestingly, this study also found that when the frequency of training was reduced to 1 session per week, the BMD reduced to pre-training values. Therefore, it appears that the frequency of training is important not only in increasing BMD of the lower limb bones, but in maintaining any increases which may have occurred with training.

It is possible that the equipment used to measure BMD in the above mentioned studies [145, 146, 147, 148] may account, to some extent, for the lack of change demonstrated in the femur. As discussed in Section 1.8, DEXA [146, 147, 148] inaccurately predicts bone strength as it is affected by many factors including hypertrophy of the muscle. It is possible in a 6–12 month study that changes in the muscle cross sectional area of the lower limbs will occur thus affecting the measurement of BMD, as changes in soft tissue composition cause artefacts in BMD values derived from DEXA scans

Although the effect of FES-LCE training on lower limb BMD remains equivocal it has been shown to increase the aerobic capacity, and muscular strength and endurance of those with an SCI. A training intervention utilising this mode of exercise would therefore be expected to help reduce the risk of cardiopulmonary disease and reverse the muscular atrophy associated with this condition. It is possible that the effects of FES-LCE on those with an incomplete SCI may not be as pronounced as on those with a complete injury. Due to the pain they may experience as a consequence of retained sensation, those with an incomplete injury may not be able to obtain the work rates necessary to elicit improvements in aerobic capacity, and muscular strength and endurance. Although FES is the only manner in which the paralysed lower limb muscles of those with complete SCI can be activated for exercise, those with an incomplete injury may have some remaining voluntary function which can be utilised for exercise. Consequently, exercise modes such as FES-assisted walking and body weight supported treadmill training (BWSTT) may be optimal for these individuals as it enables them to undergo gait training, the outcomes of which may aid any assisted/unassisted ambulation

that they undertake as well reverse the secondary complications of their injury.

2.2.2 Overground FES-assisted Walking

Overground FES-assisted walking is usually carried out in combination with a walking aid such as a cane or walker to help the individual with upright balance and, although discouraged, to enable them to support some of their body weight through their arms. The muscles that are stimulated during walking vary according to the subject's impairment; most commonly however, the quadriceps muscles are stimulated for support during the stance phase and the common peroneal nerve is stimulated during the swing phase to elicit the withdrawal reflex. The main advantage of FES-assisted walking is that it is task specific: subjects train in overground walking therefore their training directly relates to the function that they are trying to improve.

The effect of overground FES-assisted walking in improving the gait of those with an incomplete SCI is equivocal. In a study by Granat and colleagues [149], during which 6 subjects with incomplete SCI participated in 2 months FES-walking at home, no significant difference was found between the walking speeds obtained while using FES and while using an orthosis. The details of the training programme were not provided therefore it is unknown whether the subjects walked using the system frequently enough, or for long enough, to result in an improvement in their walking speed. Although this study did not provide any evidence that FES-assisted walking can increase the walking speed of those with an incomplete SCI, encouragingly it did show that FES-assisted ambulation is possible outside the laboratory setting and that people will use the system at home. It is therefore possible that with enhanced training an improvement may occur.

In 1993 Granat and colleagues [150] further investigated the effect of FES-assisted walking in the rehabilitation of those with an incomplete SCI. 6 subjects with incomplete lesions at C3/4–L1 participated. As with the previous study, subjects carried out an individualised muscle conditioning programme to strengthen the quadriceps. When the subjects had acquired a functional gait using the FES they were allowed to use the stimulators at home. Each subject had to train for at least 30 minutes, 5 days a week, for a minimum of 3 months. Following this period of training there was found to be no significant increase in walking speed (pre-training 0.06 ($\pm$0.01) – 0.69 ($\pm$0.03) $m.s^{-1}$ and post-training 0.07 ($\pm$0.00) – 0.79 ($\pm$0.02) $m.s^{-1}$). This may have been a consequence of the long latency of the flexion withdrawal response to the stimulation. Although no improvement in walking speed was demonstrated there was found to be a significant increase in the strength of the hip flexors and knee extensors (manual muscle testing (MMT)) and in the force produced during a MVC of the

quadriceps (dynamometry). Although the changes reported in muscle strength are encouraging, they cannot be fully attributed to the FES-assisted walking training carried out by the subjects. As mentioned previously, all subjects underwent a period of muscle conditioning prior to the walking phase of the study which lasted up to 6 months. Consequently, it cannot be excluded that the muscle strengthening period may have had a significant effect on the strength of the muscles, in particular the quadriceps. Regardless of the cause of the increase in muscle strength, its occurrence improved the efficiency of the subjects' walking in orthoses, as highlighted by an overall decrease in the physiological cost index (PCI) (see Equation (2.1)). This is extremely important as not all patients may wish to continue using FES and may wish to continue using their original orthosis.

$$PCI = \frac{HR_w - HR_r}{velocity} \tag{2.1}$$

where

- PCI = physiological cost index
- HR_w = heart rate during walking
- HR_r = heart rate during rest
- $velocity$ = walking speed

The results of a multi-centre evaluation on the long term benefits of FES-assisted walking and acceptance of the system were more encouraging in terms of gait performance [151]. 40 subjects, 31 of whom had an incomplete SCI, participated. Following on average 1 year of FES-assisted walking, walking speed increased by 55% in the SCI group with a significant increase being due solely to the use of the system. The largest relative gains were seen in the slowest walkers. Acceptance of the device was good with 23 subjects continuing to use the FES system on a regular basis following the end of a test period: over 90% agreed that they could walk better using FES.

In 2000, Ladouceur and Barbeau [152] investigated the change in the kinematics and physiological cost of walking that occurs as a consequence of training in FES-assisted walking. 14 subjects with incomplete SCI trained in FES-assisted walking for 43 weeks. The main effect of FES-assisted walking was to change the hip excursion and ankle dorsiflexion during swing and at foot contact. Although this did not change the spatio-temporal parameters of walking (walking speed, cycle length and frequency, as well as time in stance), training in FES-assisted walking did. Both the stride length and frequency were factors in increasing the walking speed, and changes in frequency are due to changes in the duration of the stance.

Also investigated by Ladouceur and Barbeau [152] was the effect that FES had on the physiological cost of walking, measured as the PCI. FES-assisted walking did not change the physiological cost of walking. However, following training it did improve in the majority of subjects. This study concluded that although FES-assisted walking changes the joint angular kinematic pattern of walking, training is necessary to integrate these changes into functional gains.

In 2003 Johnston et al. [153] investigated whether using percutaneous FES to increase pelvic stability as well as to augment stance phase stability and limb advancement during swing would improve the gait of 3 adolescent, incomplete SCI subjects. The stimulation was adapted to address the specific weakness of each subject and the subject then carried out 4 weeks of endurance and strengthening exercises of the implanted muscles. Following training on walking and use of the stimulator, subjects were instructed to use the stimulator, as desired, for a year.

Following one year's use of the FES system, significant improvements occurred in functional outcomes with the FES on and off. The oxygen cost of walking without FES decreased from 0.79 ($\pm$0.13) ml.kg^{-1}.m^{-1} at baseline to 0.44 ($\pm$0.02) ml.kg^{-1}.m^{-1} at 12 months, a greater improvement than that seen for walking with FES. This improvement could possibly be attributed to the increase in the voluntary strength of the implanted muscles which occurred. As well as affecting the oxygen cost of walking, the increase in muscle function may also have contributed to the changes in gait parameters with FES on and off: increased maximum walking distance and speed, increased step length and improved joint kinematics.

A further determinant of the success of FES-assisted walking is whether or not it improves walking ability significantly more than the use of an orthosis. This was investigated by Kim and associates [154] in 19 subjects with incomplete SCI and was found not to be the case. While the use of FES did significantly increase walking speed it did not result in a significantly improved performance compared to the use of an ankle-foot orthosis (AFO). FES was only found to be superior to the AFO in terms of foot clearance. However, when combined, FES and AFO gave the most significant results in terms of gait speed and duration compared to no orthosis.

A recent study by Thrasher and colleagues [155] further investigated the effect of FES-assisted walking training on gait parameters. 5 subjects with incomplete spinal cord injury trained for 15–30 minutes, 2–3 sessions a week, for 12–18 weeks in FES-assisted walking. 3 subjects trained overground and 2 subjects trained on a treadmill. Following the training intervention 4 subjects significantly increased their walking speed and 1 subject experienced a significant reduction in their preferred assistive devices. This increase in speed was maintained in 3/3

subjects who returned for a follow-up test 10 weeks later. The results of this study may however be affected by the fact that, although all subjects used FES to assist their walking during training, the method of training used differed: one group of subjects trained overground and one group trained on a treadmill. As will be discussed in Section 2.2.3 treadmill training has additional influences on walking training in these subjects which may have biased the results. It is possible therefore that the results of this study may not accurately represent the effects of FES-assisted walking on the gait parameters of incomplete SCI subjects.

The main advantages of FES-assisted walking are that it is task specific and, as demonstrated by Granat and colleagues [149], it can be integrated into home use. However, the non-physiological recruitment of muscle fibres by FES results in fast fatigue in the muscles and consequently could limit the duration of the exercise period. Although it does appear that improvements in gait speed and endurance do not occur just from the use of FES [152, 154], there is conflicting evidence as to whether or not training with the device may elicit such improvements [149, 150, 151, 152, 153, 155]. However, it does appear, in terms of gait speed, that more promising results are obtained by subjects who have a low initial speed. This may be because those who can walk faster already have better control over their muscle groups therefore the addition of FES to try and improve the function of that muscle will not have as great an effect as it would in those with poor control. Encouragingly, FES-assisted walking has been shown to result in an increase in voluntary muscle strength [150, 153]. To what extent this increase is due to the period of muscle strengthening which occurs prior to any period of FES-assisted walking is unknown but would be of considerable interest. This increase in muscle strength may also contribute to the decrease in the physiological cost of walking demonstrated following FES-assisted walking training [150, 152, 153]. The reduction in the physiological cost of walking results in reduced exertion and may therefore enable subjects to walk for longer prior to fatigue. This reduction, as well as being influenced by an increase in muscle strength, may also be the result of subjects adopting a more efficient gait pattern as a consequence of training. Although encouraging results have been obtained from this form of exercise training in terms of muscle strength and the physiological cost of walking, no investigations appear to have been undertaken to identify any affects on BMD which may occur as a consequence of the increased loading of the lower limbs during training, nor have any studies investigated the effects which an increased training load may have on cardiopulmonary fitness.

2.2.3 Body Weight Supported Treadmill Walking

Work carried out on primates indicate that "relearning of walking can only be done by intensive exercise of upright walking" [156]. A number of methods exist to offer this form of training to humans with locomotor impairment: walking in water, training in parallel bars,

or as mentioned previously with canes or a rollator with or without the use of FES. However, none of these allow the "rules of spinal locomotion" to be optimally applied. It is important during training to load (i.e. put body weight onto) the fully extended limb during the stance phase and to unload and shift the body weight onto the contralateral limb shortly before swinging the ipsilateral limb [157]. Walking in water makes it impossible to properly load the limbs, and when training in parallel bars or with canes or a rollator patients have a tendency to maintain an upright body position by supporting their body with their arms and mechanical devices. Consequently, insufficient loading may occur. Treadmill training combined with body weight support (BWS) does however provide an ideal method for implementing the "rules of spinal locomotion" by allowing individuals to properly load their limbs and removing the need for weight bearing through their arms. It is therefore an ideal means by which incomplete SCI patients can train to improve their gait as well as to help prevent/reduce the secondary complications of their injury.

In 1995 Wernig and colleagues [157] investigated to what extent treadmill therapy would improve the gait of incomplete SCI patients compared to conventional therapy. 44 chronic incomplete SCI subjects participated, with 12 subjects acting as a temporal control group by carrying out 5.5–11.1 months of conventional post acute therapy before beginning the treadmill therapy. The effect of treadmill therapy in acute incomplete SCI subjects was also investigated: 45 acute SCI subjects who participated in the treadmill therapy were compared to 40 acute SCI subjects treated conventionally. Those who participated in the treadmill therapy programme trained on the treadmill for 30 minutes, once (sometimes twice) a day, 5 days per week with the duration of the intervention dependent on the extent of the initial paralysis. During the training programme BWS was gradually reduced to increase the training intensity and overground walking, stair climbing and walking outdoors were attempted as soon as possible. The success of the intervention and its superiority over conventional therapy for both the acute and chronic SCI subjects was evident. Locomotion improved in almost all chronic SCI subjects. In the temporal control group 9/12 subjects who were wheelchair bound following conventional therapy learned to walk with no help following the period of treadmill training. In a subgroup of 18 chronic subjects who had been matched in terms of level, severity, and time post injury, and in the duration and onset of training periods to a group of 14 chronic SCI subjects who had only participated in conventional therapy, the results further supported the superiority of treadmill therapy over conventional therapy in terms of gait rehabilitation: 14/18 subjects who had carried out treadmill therapy became independent walkers compared to 1/14 who had participated in conventional therapy. Similar results were obtained for the acute SCI group with 92% becoming independent walkers following treadmill therapy compared to 50% following conventional therapy. During both treadmill and conventional therapy no changes in voluntary muscle function were noted.

These improvements in walking ability achieved as a consequence of the treadmill therapy appeared to be maintained. 6 months to 6 years post study 15 subjects had further improved and none had reduced their walking capability [156].

The results obtained by Wernig and colleagues demonstrated encouraging improvements in walking ability following treadmill training which can be maintained [156, 157]. However, the varying lengths of the intervention and follow-up periods makes it difficult to assess the duration of training required for such improvements to occur or to determine how long they can be maintained. A number of studies have been carried out which address these issues.

In 2001 Protas and colleagues [158] carried out a standardised treadmill training study to determine the effect of treadmill training on walking speed, endurance, energy expenditure and muscle strength. A small convenience sample of 3 incomplete SCI subjects participated. Training was scheduled for 1 hour a day, 5 days per week for 12 weeks. During each session the subject walked until fatigued then rested before continuing. Each subject was given a target of 20 minutes walking in each session. The BWS and therapist assistance was reduced, and the speed increased as required to increase the intensity of the training. Following the 12 week training period overground walking speed significantly increased (0.118 – 0.318 $m.s^{-1}$) as did endurance (20.3 – 63.5 m/5min). Despite no significant increase in muscle strength a significant decrease in energy expenditure occurred (1.96 – 1.35 $ml.kg^{-1}.m^{-1}$) suggesting an improved walking economy.

In order to determine if long term treadmill training could further enhance gait improvement and positively enhance the psychological well being of incomplete SCI subjects, Hicks and colleagues [159] carried out a year-long treadmill training study with 14 incomplete SCI subjects. Subjects trained on the treadmill 3 days per week for a year. Throughout the training period BWS was reduced and treadmill speed was increased to increase the training intensity. Following 1 year training, treadmill walking speed significantly increased by 180% (0.5 ($\pm$0.3) – 1.4 ($\pm$0.8) $km.h^{-1}$), the amount of BWS provided during training sessions was significantly reduced (71.3 ($\pm$10.3) – 19.5 ($\pm$12.2) %), and the distance walked per session significantly increased 335% (221.4 ($\pm$186.8) – 961.7 ($\pm$463.8) m). 6 subjects also improved their capacity to walk overground. Although a significant improvement in life satisfaction and satisfaction with physical function did occur there was no significant change in levels of depression, perceived health or ability to perform independent ADLs.

In the 8 months following the cessation of the training study subjects were invited to participate in once weekly BWSTT or once weekly BWSTT in combination with 2 sessions per

week of fitness training. At the end of this 8 month period there was a slight decline in treadmill walking performance although overground walking scores remained relatively stable. A slight decrease in satisfaction with physical function occurred also. The study highlighted the fact that not only can treadmill training positively affect treadmill walking ability but it can also have a positive effect on indices of subjective well-being. It was also concluded by the authors that these improvements are mostly maintained for 8 months following cessation of training. However, although adherence rates were low for the 8-month training period (~30% for BWSTT and ~25% for BWSTT plus fitness training) post study, it was still not a period of complete cessation of exercise. Therefore, it cannot provide an accurate account of how well improvements in treadmill walking ability and subjective well-being can be maintained following the cessation of a period of treadmill training.

Another study which investigated the effects of BWSTT on the psychological well-being of incomplete SCI subjects was carried out by Effing and colleagues [160]. They determined the effect of 12 weeks BWSTT on the functional health status (FHS) and quality of life (QoL) in 3 incomplete SCI subjects. The subjects trained for 30 minutes, 5 days per week, for 12 weeks with the BWS, therapist assistance and speed altered as appropriate to increase the training intensity. As has been discussed previously the walking speed and distance walked during each session increased with training, and less assistance was required by the therapists. Following the 12 week training period positive changes in QoL and FHS were present although small and diverse. This study does suggest that BWSTT can positively influence the QoL and FHS of those with an incomplete SCI, however the sample size was very small. Therefore, a randomised control trial is required to determine, with certainty, if BWSTT can positively influence these outcomes.

As discussed in this section, BWSTT has been shown to positively influence the walking ability in those with an incomplete SCI and has the potential to positively affect their psychological well-being. However, as BWSTT provides mechanical loading of the lower limbs, a further area of interest in this field is the effect that this form of training may have on reducing/preventing bone loss and muscle atrophy following an SCI. In 2005, Giangregorio and colleagues [161] investigated the effect of such an intervention in acute SCI subjects. 5 acute SCI subjects (4 complete and 1 incomplete injury) carried out BWSTT twice a week for 24 weeks. Throughout the training period the duration of the session and speed of walking were increased, and BWS decreased to alter the intensity of the training as required. Following 24 weeks of BWSTT the BMD (measured by DEXA) decreased in all measured lower limb sites: proximal femur, distal femur and proximal tibia. It is possible given that the subjects were in the rapid phase of BMD decline post-injury (see Section 1.3.3) that the training intensity

may not have been high and/or frequent enough to prevent this decline. An interesting observation was however made in this study: the subject with the most ambulatory capacity (i.e. the incomplete SCI subject) demonstrated the smallest reduction in lower limb BMD. It is possible therefore that by including both incomplete and complete SCI subjects in the same subject group, that an accurate account of the effect of BWSTT on BMD post-injury was not given. The rate and severity of the decline in BMD may not be as high in incomplete subjects as it is in complete subjects and the training intensities required to modify this decline may differ between groups. In order to determine this, a study with distinct complete and incomplete SCI groups, and corresponding control groups must be carried out.

Although 24 weeks of BWSTT did not positively affect BMD in these subjects it is encouraging to note that following a period of BWSTT the muscular atrophy which occurs following an SCI can be prevented and/or partially reversed in the thigh and calf. This positive outcome may aid subjects with their ADLs and in any overground walking that they may carry out.

Prior to Giangregorio et al. [161], de Bruin and colleagues [162] also investigated the effectiveness of an early intervention BWSTT programme in attenuating BMD loss after acute SCI. 13 subjects with incomplete or complete acute SCI participated in the study. They were allocated to either a combined standing and walking programme which involved subjects carrying out 0.5 hours of walking and 0.5 hours of standing 5 days per week for 6 months, or to a standing only programme where subjects were instructed to stand for 1 hour per day, 5 days per week, for 6 months. During BWSTT therapists provided assistance in the gait pattern if required. The BMD of the tibia was determined pre- and post-study by pQCT. Subjects who, for unforseen circumstances, were unable to participate in their allocated intervention formed an immobilisation group. Following the 6 month training period there was a significant difference in the trabecular BMD of the immobilisation and intervention groups. The BMD in the epiphysis of the tibia in those who had been immobilised was markedly reduced compared to the intervention groups. There was however no significant difference in the trabecular BMD between the two intervention groups. No significant difference was found in the BMD of the cortical bone in any of the groups.

This study has demonstrated that treadmill training does reduce bone loss following an SCI in conjunction with standing, but so does standing in isolation. This is an interesting observation as it is thought, as was discussed in Section 1.8, that it is the strains applied by the muscles on the bone which maintains BMD. It is possible, as in the study by Giangregorio et al. [161], that the inclusion of both incomplete and complete SCI subjects in the same group may have affected the results. It may be the case that the strains placed on the bones by

the muscles during BWSTT in the complete subjects were not that much higher than during standing as the therapists moved their legs for them. On the other hand, the incomplete subjects may have been able to achieve training intensities which placed significantly higher strains on the bones from the muscles than during standing. Therefore, had a group of solely incomplete subjects been studied, a difference in the BMD between the two groups may have been demonstrated. Regardless of the differences which may or may not exist between incomplete and complete SCI subjects and the lack of significant difference in the results of the two interventions, this study highlights the importance of an intervention in the acute phase of injury to try and prevent the decline in BMD. The differences between the results of this study and that of Giangregorio et al. [161] may be due to apparatus used to measure the BMD. de Bruin et al. [162] used pQCT which can accurately measure BMD in the periphery and can separate the BMD measurement of cortical and trabecular bone. Giangregorio and colleagues [161] on the other hand used DEXA, known to be affected by changes in muscle bulk which were demonstrated in their study, and unable to separate BMD of cortical and trabecular bone. In the study by de Bruin et al. [162] no significant differences were found in the BMD of the cortical bone. It is possible therefore that any changes which may have occurred in the trabecular bone of subjects in the Giangregorio study may have been masked by the lack of change in the cortical bone.

As discussed in Section 1.3.5, a further secondary complication of SCI is an increased risk of cardiovascular disease resulting predominantly from the sedentary lifestyle that the majority of these individuals lead. A number of studies have investigated the effect of BWSTT on the risk factors for cardiovascular disease. In 2004 Stewart and colleagues [163] investigated whether 6 months of BWSTT would alter the blood lipid profile of 9 incomplete SCI subjects. As mentioned in Section 1.3.5, those with an SCI have been shown to have dyslipidemia and reduced HDL-C plasma concentration which helps protect against vascular disease. The subjects performed BWSTT 3 times per week for 6 months with the velocity, duration and amount of BWS altered according to the individual's rate of improvement. Therapist assistance was provided when required. As has been seen in previous studies, the subjects' walking velocity and duration significantly increased and the amount of BWS provided decreased following training. Encouragingly, the period of treadmill training resulted in beneficial alterations in the blood lipid profile: an 11% decrease in plasma total cholesterol and a 13% decrease in plasma low density lipoprotein cholesterol (LDL-C). This study provided some evidence that BWSTT can be an effective stimulus to induce anti-atherogenic benefits in those with an incomplete SCI.

This study also provided evidence of the beneficial effects of BWSTT in terms of muscle fibre atrophy, composition and oxidative capacity. Following the period of 6 months BWSTT the

muscle fibre area (vastus lateralis) of type I and IIa fibres increased suggesting a reversal of the muscular atrophy which occurs following an SCI. This reversal of atrophy was described by the authors as "relative hypertrophy" as it appears to have restored the muscle fibre sizes to within the range of normal values. Changes were also observed in the fibre type composition of the muscle: a reduction in type IIax/IIx fibres, a decrease in IIx MHC and an increase in type IIa fibres. The activity of the oxidative enzymes citrate synthase and 3-hydroxy-acy-CoA dehydrogenase was also shown to have increased following training. The shift in muscle fibre type from IIax/IIx to predominantly type IIa and the increase in the activity of the oxidative enzymes is important in terms of fatigue resistance. The adaptations in the skeletal muscle which occurred as a consequence of this training intervention have positive implications in terms of ambulatory capacity and the ability to perform ADLs.

The effects of BWSTT on the risk factors for cardiovascular disease was further investigated by Phillips et al. [164] who determined its effect on blood glucose regulation which, if poor, is a risk factor for type 2 diabetes and/or metabolic syndromes associated with the progression of type 2 diabetes. Type 2 diabetes is a known risk factor for the development of cardiovascular disease. 9 subjects with incomplete SCI participated in the study and carried out 3 sessions of BWSTT per week for 6 months. The training duration and velocity were increased, and the therapist assistance and BWS decreased as required to increase training intensity. Again treadmill training velocity and duration were significantly increased following the training period. More importantly however, in terms of the risk of cardiovascular disease, the training intervention improved glycemic regulation, and increased glucose oxidation and storage. Consequently, the associated risk of type 2 diabetes is reduced.

The improvements in overground and treadmill walking as a consequence of BWSTT are evident. There is also evidence to suggest that the muscular atrophy which occurs post-SCI can be reversed and that some of the risk factors of cardiovascular disease can be reduced. However, the evidence for whether or not it can affect the sub-lesional loss in BMD is equivocal, possibly affected by the methods used for measuring the BMD and the inclusion of both incomplete and complete SCI in the same study group. The effect which this form of training may have on the BMD of those with chronic SCI does not appear to have been investigated thus far. A further area of interest which has not been addressed is the improvements in cardiopulmonary fitness which may occur with training. Low levels of cardiopulmonary fitness are also associated with increased risk of cardiovascular disease and therefore need to be investigated.

2.2.4 FES-assisted Body Weight Supported Treadmill Walking

Helping to guide, and in some cases move, the legs of a paralysed individual for the duration of a training session places an enormous physical work load on the therapist. The main advantage of FES-assisted BWS treadmill walking therefore, is that it removes this work load from the therapist. Despite this, there have been surprisingly few studies which have investigated the effects of this combined technique.

The main advantage of FES-assisted walking training compared with BWSTT is that it is task specific. Consequently, those who have studied the effects of FES-assisted BWSTT have focussed strongly on whether any improvements in treadmill walking transfer to overground walking. In 2001 Field-Fote [165] investigated whether this cross-over effect took place. 19 subjects with incomplete SCI participated in the study. They trained 3 times a week for 12 weeks. The duration of each session was 1.5 hours and subjects were allowed to determine their own walk and rest bouts. Electrical stimulation was applied to the subject's peroneal nerve and the BWS (up to 30%) and speed were adjusted to allow subjects to walk optimally. Following the period of training there was a significant increase in treadmill walking speed (0.23 ($\pm$0.12) – 0.49 ($\pm$0.20) m.s^{-1}) and distance (93 ($\pm$84) – 243 ($\pm$139) m). When walking overground subjects were allowed to use their preferred assistive device but no FES or BWS was provided. Regardless of this a cross-over effect was shown to occur with overground walking speed (OGWS) significantly increasing from 0.12 ($\pm$0.8) to 0.21 ($\pm$0.15) m.s^{-1}. Significant increases in lower extremity motor scores were also demonstrated post training in both the stimulated and non-stimulated leg.

It is important in order to maintain an effective gait pattern that there is good intralimb co-ordination. Whether this intralimb co-ordination could be improved with training was investigated by Field-Fote and Tepavoc [166]. 14 subjects with incomplete SCI participated in a 12 week FES-assisted BWSTT programme during which they trained 3 times per week. The duration of each session was 1.5 hours and as with the previous study [165] subjects were allowed to determine their own walking and rest bouts. During each session electrical stimulation was applied to the subject's peroneal nerve, and the BWS and speed were adjusted to alter the intensity of the training session. Following 12 weeks of training 9/14 subjects demonstrated greater intercycle agreement. This increase in the consistency of the walking pattern occurred despite highly significant increases in both treadmill walking speed and OGWS of 158% and 84% respectively.

FES-assisted BWSTT has been shown to improve both treadmill and overground walking ability in those with chronic SCI [165, 166]. Whether such improvements can occur in those with acute SCI was investigated by Postans and colleagues [167]. 14 acute incomplete SCI

subjects participated in the study. All subjects took part in a control period (A) involving a standard physiotherapy regimen 5 days per week for 4 weeks, and an intervention period (B) involving gait training on a treadmill 5 days per week for 4 weeks. Subjects were randomly assigned to either AB or BA. During the intervention period subjects carried out a maximum of 25 minutes walking with rest periods as appropriate. Stimulation was applied to the quadriceps during stance and the peroneal nerve to elicit flexion withdrawal during the swing phase, and speed and BWS were modified as required to optimise gait. Subjects were assessed before the first randomly assigned period and in the final week of each period.

Following completion of the 8 week study it was evident that a greater increase in OGWS and endurance was achieved after the FES-assisted BWSTT period compared with after the period of standard physiotherapy. Although volitional muscle strength did increase throughout the 8 week period the fact that no pattern in the increase was evident suggests that it was not due to the intervention. It is also possible given the fact that the subjects were in the acute phase of injury that some spontaneous recovery may have occurred. If this had affected the results in any way one would have expected to have seen similar increases regardless of the intervention. Therefore, this study highlights the fact that FES-assisted BWSTT could potentially accelerate gait training in those with acute incomplete SCI.

Although FES is normally applied via surface stimulation other methods are available for clinical trials with the aim of reducing the long term inconvenience to the subject of donning and doffing the system. In a study by Carhart and colleagues [168] the effectiveness of one such device in a BWSTT programme was investigated. 1 incomplete SCI subject was recruited for the study. He participated in a BWSTT (no FES) programme for 2 hours per day (rest intervals as required), 5 days per week during which therapist assistance and BWS decreased, and speed increased as required. An epidural spinal cord stimulation (ESCS) device was implanted into the subject when he could walk independently at a minimum speed of 0.65 m/s with BWS $\leq$20% while maintaining gait temporal symmetry of $\leq$50%. The ESCS device was an externally powered system with an implanted receiver and electrodes. Following recovery, the subject was retrained to pre-surgical levels before introducing ESCS. Training then continued until the subject could support 80% of his body weight and stepping demonstrated consistent inter- and intralimb co-ordination at the established treadmill rate. The ESCS was then applied in alternating treadmill and overground training sessions until the performance plateaued, at which point the training focussed solely on overground training with ESCS.

Following the initial 12 weeks of BWSTT there was a significant improvement in treadmill

performance: an increase in walking speed and weight bearing; an improvement in hip extension during stance; an increase in knee and hip ROM; and bilateral improvements in step lengths, and cycle, swing and stance times. These improvements did not however cross-over to overground walking. Walker-assisted overground walking remained limited by heavy reliance on the walker for BSW, slow speeds, poor endurance and a marked sense of effort. Following the introduction of ESCS to the BWSTT the improvements in treadmill walking increased further and a cross-over effect was seen in overground walking. OGWS doubled and the subject's sense of effort was reduced suggesting that ESCS facilitated learning of a functional overground walking pattern as speed improved both with and without application of stimulation.

The evidence presented in Sections 2.2.2 – 2.2.4 demonstrates the varying positive outcomes of overground FES-assisted walking, BWSTT and FES-assisted BWSTT. But is one form of training more beneficial to individuals with an incomplete SCI than another? In 2005, Field-Fote and colleagues investigated this. They compared the effects of 4 types of locomotor training in incomplete SCI subjects:

1. BWS treadmill training with manual assistance (TM)
2. BWS treadmill training with peroneal nerve stimulation (TS)
3. BWS overground training with peroneal nerve stimulation (OG)
4. treadmill training with robotic assistance (LR) (See Chapter 7)

27 subjects were randomly assigned to one of the 4 training groups. Subjects then trained for 45 minutes, 5 days per week, for 12 weeks with the BWS maintained at $\leq$30%. Following the training period there was a significant increase in OGWS and step length in all groups with no significant differences between the groups. There was great variability within the groups, with those who had a slower initial speed increasing their walking speed far more than those who had a faster initial walking speed. The sample size was small, therefore a larger study is required to confirm these results. Despite this, this study does suggest that all forms of locomotor training are associated with improved walking performance with no one form of training being superior.

The methods available for exercise training in those with an SCI have been outlined in Section 2.2. It is clear from the evidence presented that research into the effects of exercise on the secondary complications of an SCI (increased risk of cardiovascular disease, muscular atrophy and bone demineralisation) is more advanced for those with a complete injury. This may be because studies with incomplete SCI individuals are difficult to design satisfactorily. There is great variability in function between individuals at a given lesion level or ASIA

grade, and consequently, there may also be great variability in their response to exercise. However, it is essential to determine if exercise can reverse the secondary complications of their injury. Despite the ability of some individuals with an incomplete SCI to use their remaining voluntary function to participate in exercise, this area of research is relatively unexplored. Understandably a lot of research has been carried out into whether or not different forms of gait training can improve an individual's gait performance. Yet the evidence as to whether this form of training could also increase their cardiopulmonary fitness, reverse their muscular atrophy and bone demineralisation, and increase their voluntary control of their partially paralysed muscles is either absent or minimal. As described in Sections 2.2.2 – 2.2.4 gait training does appear, overall, to improve the walking ability of those with an incomplete SCI but it is important also to determine whether this form of training can reverse the secondary complications of their injury.

2.3 Exercise Testing in Spinal Cord Injury

Cardiopulmonary exercise testing is important as it provides information regarding the capacity and efficiency of the cardiovascular, respiratory and muscular systems during exercise activities [128]. During maximal exercise it gives an indication of the maximal capacity of these systems. This is particularly important in those with an SCI whose physiological responses to exercise differ from AB individuals. Exercise testing, therefore, is a useful tool in understanding the kind of exercise training that those with an SCI will respond to and the adaptations to training which take place.

2.3.1 Arm Cranking and FES Cycling

As discussed in Section 2.2, ACE is the most common method for exercise training in paraplegia and is therefore also the most common method used to assess their cardiopulmonary fitness. In 1988, Davies and Shephard [169] assessed the physical fitness of highly active and inactive paraplegics via a continuous multistage peak ACE test during which the power increased 8.5W/min until volitional fatigue. The CO and SV of the active group were found to be 34–45% higher than the inactive group possibly due to upper body hypertrophy allowing a larger blood flow to the working tissues. The average $\dot{V}O_{2peak}$ obtained for the active group (2.24 l.min^{-1}) was significantly higher than that of the inactive group (1.56 l.min^{-1}). As can be seen in Figure 1.6 (Section 1.5) the $\dot{V}O_{2peak}$ obtained for the inactive paraplegics is lower than that associated with sedentary AB individuals. Despite physical training the cardiopulmonary fitness of the active paraplegics in this study is similar to that of sedentary AB persons.

A number of studies have directly compared the cardiopulmonary fitness of SCI and AB subjects. Zwiren and Bar-Or [170] compared the cardiopulmonary functions during rest, submaximal and maximal exercise in wheelchair bound athletes, wheelchair bound sedentary individuals, AB athletes and AB sedentary individuals. As was found by Davies and Shephard [169] the $\dot{V}O_{2peak}$ of wheelchair athletes was significantly higher than that of sedentary wheelchair individuals (35 ($\pm$7.6) vs 19 ($\pm$5.5) ml.kg^{-1}.min^{-1}). The $\dot{V}O_{2peak}$ of wheelchair athletes was also found to be higher than that of AB sedentary individuals (25.8 ($\pm$4) ml.kg^{-1}.min^{-1}) suggesting that with training SCI individuals can increase their physical fitness above that of the sedentary AB population. Surprisingly, no significant difference was found between the $\dot{V}O_{2peak}$ of wheelchair and AB athletes. The $\dot{V}O_{2peak}$ obtained for the AB athletes (38.1 ($\pm$6.3) ml.kg^{-1}.min^{-1}) is lower than would be expected for this population (see Section 1.5, Figure 1.6). It is possible that the sports which the athletes participated in (basketball, swimming, discus and wrestling) may have affected the results. Discus and wrestling are not endurance sports. However, it is more likely that the lower than expected $\dot{V}O_{2peak}$ obtained for the AB athletes is a consequence of the testing method. It would be expected had the maximal exercise test been performed on a treadmill or cycle ergometer rather than an arm crank ergometer, that the AB athletes would have achieved a higher $\dot{V}O_{2peak}$. No significant difference was found in the cardiopulmonary fitness of the sedentary AB and SCI individuals.

Although lower than that of sedentary AB subjects, the $\dot{V}O_{2peak}$ of paraplegics obtained during a continuous ACE IET was found, by Van Loan and colleagues [32], not to be significantly different (28.2 ($\pm$6.8) vs 25.3 ($\pm$7.4) ml.kg^{-1}.min^{-1}). Despite no significant difference in HR_{max} between the 2 groups, the SV and CO of the paraplegics were found to be significantly lower than the AB subjects. It is possible that the lack of significance in the $\dot{V}O_{2peak}$ between the 2 groups may be a consequence of the inclusion of paraplegic subjects who considered themselves to be wheelchair athletes. Therefore, the paraplegic subject group may not be truly representative of the sedentary paraplegic population.

In a study by Jacobs and colleagues [36] the $\dot{V}O_{2peak}$ measured during an ACE IET was found to be significantly lower in 20 sedentary complete SCI subjects than 20 sedentary AB subjects (19.6 ($\pm$3.2) vs 26 ($\pm$4.4) ml.kg^{-1}.min^{-1}). At rest and across all matched submaximal work rates which elicited a similar $\dot{V}O_2$, HR was significantly higher and, as shown in previous studies [32, 169], SV and CO were significantly lower for the SCI subjects.

The results of these studies have shown that the cardiopulmonary fitness of sedentary SCI individuals is lower than that of sedentary AB individuals [32, 36, 169]. However, with training this can be reversed [169, 170]. The fact that there is no significant difference in the HR_{max} between SCI and AB individuals [32] is to be expected as those with an injury below T4 have

been shown not to be affected by sympathetic decentralisation which limits cardioacceleration [171, 172, 173]. However, the significantly greater HR at rest and submaximal work rates in SCI than AB individuals occurs to compensate for the significant reduction shown in SV and CO. This reduction in SV and CO is a consequence of the absent activation of the lower limb skeletal muscle pump which in turn reduces venous return.

ACE in both AB and SCI individuals is limited by local muscular fatigue. Therefore, physiological parameters obtained from an IET are referred to as peak responses rather than maximal responses. In AB individuals the $\dot{V}O_{2peak}$ from an ACE IET has been shown to be ~70% of that produced during maximal treadmill testing [174]. Assuming that a similar situation occurs in SCI individuals there is therefore a need for a mode of exercise which activates the paralysed large lower limb muscles in order to determine their true maximal aerobic capacity.

As discussed in Section 2.2, sequential stimulation of the quadriceps, hamstrings and gluteal muscles with FES can successfully elicit a cycling motion. Training with FES-LCE has been shown to increase the cardiopulmonary fitness of those with an SCI [137, 138, 139, 140, 141, 142]. However, whether the $\dot{V}O_{2peak}$ obtained in these studies [137, 138, 139, 140, 141] is representative of the maximum aerobic capacity of the individuals is debatable.

In 2002, Raymond and colleagues [175] demonstrated that activation of the paralysed skeletal muscle pump during FES-LCE does improve venous return, increasing ventricular filling pressures and consequently augmenting SV and CO. At an equivalent submaximal $\dot{V}O_2$, HR and SV were shown not to differ between a group of 6 AB subjects and a group of 6 complete paraplegic subjects. CO was shown to be higher in the SCI group. This mode of exercise does therefore appear to augment the reduced SV and CO which occurs during ACE and may therefore elicit true maximum values.

Despite improvements in SV and CO with activation of the skeletal muscle pump, FES-LCE has been shown to be very inefficient. At a given work rate $\dot{V}O_2$, $\dot{V}_E$ and HR responses were significantly higher for SCI individuals than AB individuals performing voluntary leg cycling [176]. When quantified, the efficiency of the exercise was shown to be substantially lower than voluntary cycling (2–14% vs 4–34%) [177]. The reduced efficiency was suggested by the authors to be due to a variety of factors: nonphysiologic (peripheral) activation of the paralysed muscles, histochemical changes which occur in the muscles with disuse (see Section 1.3.4), inappropriate muscle fibre type recruitment, FES-induced muscle spasms and inappropriate biomechanics for specific movements. Although this inefficiency may be advantageous for cardiopulmonary training due to the high metabolic rate associated with a given

work rate, it may not be good for exercise testing as the tests may be limited by peripheral fatigue prior to central fatigue.

This was implied in the results obtained by Barstow and colleagues [178]. They demonstrated very long $MRT_{on}\dot{V}O_2$, $MRT_{on}\dot{V}CO_2$ and $MRT_{on}\dot{V}_E$ values (165 (±62) s, 173 (±58) s, 202 (±61) s respectively) and $MRT_{off}\dot{V}O_2$, $MRT_{off}\dot{V}CO_2$ and $MRT_{off}\dot{V}_E$ values (103 (±28) s, 136 (±20) s, 144 (±34) s respectively) during FES-LCE unassisted, unloaded cycling at 50 rpm in 6 complete SCI subjects. It was suggested by the authors that these longer than normal values were due to the recruitment of type IIb muscle fibres, a pattern of recruitment not identical to that of voluntary recruitment of muscles, due to the selective recruitment of type IIb fibres by FES and because the majority of fibres in the paralysed muscles are type IIb (see Section 1.3.4). The slowed kinetics may therefore be the result of the reduced aerobic capacity of the stimulated muscle. However, it is possible, due to the inclusion of subjects with a lesion at or above T4, that an impaired cardiovascular response to the exercise stimulus may have affected the results.

A number of FES-LCE training studies have carried out ACE pre- and post-training to determine if the training adaptations are peripheral or central. Consequently, they provide a direct comparison of the $\dot{V}O_{2peak}$ values obtained from an ACE IET and FES-LCE IET. In a study by Hooker and colleagues [137] the peak work rate both pre- and post-training was shown to be substantially higher in the ACE test. Both HR_{peak} and $\dot{V}O_{2peak}$ were also shown to be higher during the ACE test. However, the significance of the differences was not provided. Mutton and colleagues [140] did not find a significant difference in the $\dot{V}O_{2peak}$ obtained during an ACE IET and a FES-LCE IET. However the peak work rate and HR_{peak} were found to be significantly higher in the ACE test. Similar results were demonstrated by Barstow and colleagues [179]. They also found similar $\dot{V}O_{2peak}$ for ACE and FES-LCE but with ACE producing a significantly higher peak work rate and HR_{peak}. ACE was also shown to have significantly faster MRT_{on} and MRT_{off} than FES-LCE during a submaximal test at work rates which yielded an equivalent $\dot{V}O_2$. It is possible that the differences in MRT could be due to differences in the conditioning levels of the muscles used.

Although FES-LCE has been shown to augment the reduced SV and consequently CO associated with ACE [175] it has not been shown to elicit $\dot{V}O_{2peak}$ values that are significantly higher than those obtained during an ACE IET. ACE is limited by peripheral fatigue yet it is possible, due to the muscle fibre composition of the paralysed lower limbs and the non-physiological recruitment of muscle fibres, that FES-LCE may be also. In a quest to determine the true maximum aerobic capacity of SCI individuals, a number of research groups have investigated the combined effect of ACE and FES induced contractions of the paralysed

lower limb muscles in eliciting peak physiological parameters.

During submaximal exercise Davis and colleagues [180] demonstrated that the addition of FES-induced isometric contractions of the paralysed leg muscles during ACE increased SV and/or CO due to the activation of the skeletal muscle pump which augmented venous return. However, no significant difference in $\dot{V}O_2$ or HR were found at a given submaximal work rate. Similar results were also obtained by Hopman and colleagues [35] who found no significant difference in the $\dot{V}O_{2peak}$ obtained by 5 tetraplegic and 4 paraplegic subjects when FES-induced isometric contractions were carried out in conjunction with ACE. It is possible that this may however be a consequence of rapid muscle fatigue. The authors did not increase the strength of FES as the muscles fatigued to maintain a strong contraction and thus augment the venous return. Static FES contractions of the paralysed lower limb musculature do not appear to augment aerobic metabolism.

The effect of dynamic FES muscle contractions on peak and submaximal ACE has also been investigated. Contrary to the previous results, the addition of FES-LCE at OW to ACE significantly increased $\dot{V}O_{2peak}$ and submaximal steady state $\dot{V}O_2$ at a given work rate. No significant differences were found for HR, CO or work rate, although SV was increased. The results of this study support those of Mutton and colleagues [140] who found, both pre- and post-training, that ACE and FES-LCE produced a significantly higher $\dot{V}O_{2peak}$ than ACE alone. These studies therefore suggest that the addition of FES-LCE to ACE elicits greater levels of metabolic demand than without it. It has been suggested [181] that the higher frequencies of contraction during cycling augment venous return and increase muscle metabolism to a greater extent than static FES induced contractions.

2.3.2 Assisted Walking

Improvements in aerobic fitness in incomplete SCI individuals following gait training does not appear to have been investigated in the literature. Therefore, there are no examples of exercise tests to determine whether improvements in the key indicators of aerobic fitness discussed in Section 1.6 ($\dot{V}O_{2max}$, LT, efficiency and the time constant for $\dot{V}O_2$ kinetics) occur with this form of training.

$\dot{V}O_{2peak}$ has however been studied, to a limited extent, in complete SCI subjects. In a study carried out by Brissot and colleagues [182] subjects performed a walking test, using the Parastep FES ambulation system and walker, to determine their $\dot{V}O_{2peak}$. During the gait assessment, subjects walked at a constant speed of 0.1 $m.s^{-1}$ for 6 minutes, and $\dot{V}O_2$ was measured during the last minute of the test. Although the average $\dot{V}O_{2peak}$ obtained during

the walking test was very close to that obtained during an arm ergometry test (20.8 and 21.9 $ml.kg^{-1}.min^{-1}$ respectively) the test itself was not a true peak test. The subjects exercised for a specified period of time at a specified pace, not until exhaustion or until they could no longer increase their walking speed.

The walking test implemented by Jacobs and Mahoney [183] was an improvement compared to the protocol implemented by Brissot et al. [182]. Subjects were asked to negotiate a 10 m passageway in a series of walking bouts of 2 minutes duration or longer, with increasing speed. This was continued to the point of volitional exhaustion or to the point where the subject could no longer increase the speed of the FES gait. Although the duration of discontinuous exercise tests are prolonged in comparison to ramp exercise tests and an LT cannot be accurately identified by the v-slope method [78] and standard gas exchange criteria [79], $\dot{V}O_{2peak}$ can still be accurately determined. During this protocol however, subjects were required to turn at the end of the walkway which would place stress on their upper extremities and cardiorespiratory system. This may have affected the results obtained. However, considering that the Parastep system is used for overground ambulation the method used for determining $\dot{V}O_{2peak}$ was satisfactory.

In agreement with the results obtained by Brissot and colleagues [182], Jacobs and Mahoney [183] also found there to be no difference in the $\dot{V}O_{2peak}$ values recorded during peak ambulation and arm ergometry tests (22.7 ($\pm$3.9) and 22.9 ($\pm$3.8) $ml.kg^{-1}.min^{-1}$ respectively). This may be due to the fact that FES gait is essentially arm exercise due to the use of the walker which is lifted and lowered with each step. As the speed of walking increases it has been suggested [183] that there is greater reliance on the arms for support and that an increasingly inefficient technique occurs. Consequently, peak velocity and $\dot{V}O_{2peak}$ may be limited by the strategy associated with the technology rather than total muscle force or cardiorespiratory functioning.

One study has investigated cardiopulmonary responses to FES-assisted BWS treadmill walking in those with an incomplete SCI [184]. During 10 minutes of treadmill walking at 0.5 $km.h^{-1}$ the average $\dot{V}O_{2peak}$ obtained was 11.41 ($\pm$3.11) $ml.kg^{-1}.min^{-1}$. The authors stated that this was a $\dot{V}O_{2peak}$. However, as in the study by Brissot and colleagues [182], this test was not a peak exercise test. The subjects exercised for a pre-specified speed and duration, and despite exercising on a treadmill, no attempts were made to increase the work rate during the test. What was carried out, essentially, was a constant load exercise test the main outcome of which is the $\dot{V}O_2$ kinetics not $\dot{V}O_{2peak}$. No attempt was made by the authors to determine the $\dot{V}O_2$ kinetics. However, this study did show that in incomplete tetraplegics FES-assisted BWS treadmill walking can increase $\dot{V}O_2$ by 251.72% from rest and therefore

has the potential to increase the cardiopulmonary fitness of these individuals.

As outlined in this chapter the primary focus of ambulation training is to maximise the functional walking ability of those with an incomplete SCI. The consequent gap in the literature as to whether ambulation training (overground, FES-assisted BWSTT, BWSTT) can be used to increase the cardiopulmonary fitness of those with an incomplete SCI is further emphasised by the lack of studies which have focussed on developing testing protocols to monitor such changes. In order to accurately determine the cardiopulmonary fitness of incomplete SCI individuals and to determine if a training programme can improve their fitness, exercise tests, superior to those described above, must be developed to measure the required physiological variables.

2.4 Muscle Testing in Spinal Cord Injury

Accurate assessment of muscle strength is important in order to aid diagnosis, to detect any improvement or deterioration of neurological status and to help plan a patient's rehabilitation [185]. Measures of upper arm isokinetic strength have been shown, in those with paraplegia, to correlate significantly with $\dot{V}O_{2peak}$, blood lactate accumulation during submaximal exercise and cardiorespiratory endurance performance time [186]. Therefore, accurate assessment of muscular strength could help to predict whether a subject should participate in a cardiopulmonary training programme and at which level.

Lower extremity muscle strength scores have previously been shown to be significantly associated with functional walking in people with incomplete SCI [154]. Therefore, as a consequence of gait training it is possible that the maximal voluntary strength of lower extremity muscles may increase in those with an incomplete SCI thus further improving their walking ability and helping to improve their ability to carry out ADLs. This increase in voluntary muscle strength may be the result of hypertrophy of the muscle or the recruitment of motor units which were previously not firing, or were firing suboptimally.

The most widely used method for measuring muscle strength is MMT. It grades strength on a 5 point scale (10 intervals) according to the muscle's ability to act against gravity or against a resistance applied by an examiner. MMT is a very subjective method for a variety of reasons: the examiner's subjective judgement of the amount of resistance applied during the test, what is normal muscle strength for an individual given the person's age and size, and the relative strengths of the tester and patient [187]. It is also possible that training between therapists may have differed and that they develop their own techniques and standards for grading muscle strength [187]. MMT has been shown in those with SCI to be insufficiently

sensitive to assess muscle strength, at least for grade 4 and higher, and to detect small or moderate increases in muscle strength [188]. It was therefore recommended in a recent review by Ellaway and colleagues [189] that changes in voluntary strength in those with an incomplete SCI should be measured using dynamometry. Despite this recommendation it appears that lower extremity muscle strength testing with dynamometry has not been investigated in this subject group.

It is unlikely given the subject group that a true maximum contraction will voluntarily be achieved. This could however be achieved using FES. As discussed in Section 1.7 it has been demonstrated that applying electrical stimulation to a muscle in the form of twitches during an MVC results in the actual muscle force of the muscle being produced. This is due to the activation of motor units which cannot be voluntarily recruited, or were previously firing suboptimally.

This test should provide information with regard to how the training is affecting muscle fibre recruitment. Whether it allows better recruitment of available muscle fibres (increased force with a corresponding increase in the muscle activation ratio) or whether it results in hypertrophy solely of the muscle fibres which the FES is recruiting (increased force without a corresponding increase in muscle activation ratio).

2.5 Analysis of Open Research Areas

Treadmill therapy has the potential to improve the cardiopulmonary conditioning, voluntary function and lower limb BMD of those with an incomplete SCI. However, if it is to be offered clinically as a rehabilitation strategy, evidence must be gathered to support its effectiveness.

As discussed in Sections 2.2.2 – 2.2.4 the efficacy of FES-assisted gait with incomplete SCI subjects, both overground and on a treadmill, has previously been assessed by monitoring walking speed, stride length, endurance, the physiological and oxygen cost, % body weight (treadmill), and by performing observational gait analysis and MMT. However, these methods do not provide a means of measuring changes in cardiopulmonary conditioning or for accurately monitoring improvements in voluntary muscle function.

No protocols for accurately measuring cardiopulmonary fitness during treadmill walking have been developed for those with an incomplete SCI, nor has dynamometry been utilised to monitor changes in voluntary muscle strength. There is therefore a need to develop and evaluate the suitability of testing protocols to measure these outcomes in the incomplete

SCI population. Consequently, the following chapters will describe the development and evaluation of novel methods of exercise testing and muscle strength testing. Additionally, the effects of 5 months treadmill training on the cardiopulmonary fitness, voluntary muscle strength and BMD of 2 incomplete SCI subjects will be described and discussed.

Chapter 3

Methods

3.1 Chapter Summary

The aim of this study is to describe the development and evaluation of novel methods of exercise testing during body weight supported (BWS) treadmill walking in those with an incomplete spinal cord injury (SCI). Novel methods of muscle strength testing are also developed and evaluated. These novel assessment methods were used in this study to monitor changes in cardiopulmonary fitness and voluntary muscle strength during 5 months of BWS treadmill training (BWSTT).

2 subjects with an incomplete SCI were recruited for the study. Both subjects carried out a period of ~2 months BWSTT prior to the baseline tests to increase the duration that they could walk for to 15 minutes. Following baseline tests the subjects completed 5 months of formal BWSTT. Every 4 weeks throughout this training period the subjects' key indices of cardiopulmonary fitness (peak oxygen uptake ($\dot{V}O_{2peak}$), lactate threshold (LT), slope of $\dot{V}O_2$ as a function of work rate ($\Delta\dot{V}O_2/\Delta WR$) and the time constant for oxygen uptake kinetics ($\tau\dot{V}O_2$)) were determined via an incremental exercise test (IET) and a constant load (step) exercise test (SET). The subjects' walking performance was also evaluated every 4 weeks by the 15 minute distance test. Changes in voluntary muscle strength and central activation ratio (CAR) were evaluated by the twitch test prior to any walking training, at baseline and following 2.5 and 5 months of formal BWSTT. The bone mineral density (BMD) of the distal and proximal epiphyses and diaphyses of the tibia and the distal epiphyses and diaphyses of the femur was measured by peripheral Quantitative Computed Tomography (pQCT) prior to recruitment to the study and following completion of the 5 months of formal BWSTT.

This chapter describes the experimental protocols and equipment used to assess the above mentioned outcome measures. The methods used to analyse the data obtained are also discussed in detail.

3.2 Subjects

Prior to recruitment of subjects, this study was reviewed and approved by the Research Ethics Committee of the Southern General Hospital. Following ethical approval two subjects with an incomplete spinal cord injury (SCI) were recruited (Table 3.1).

Subject	Sex	Level of injury	ASIA Grade	Age (years)	Time Post Injury (years)	Gait Assistance Required
A	Female	T9	D	41	2	BWS
B	Male	T6	C	40.5	14.5	BWS plus FES on left peroneal nerve

Table 3.1: Details of the SCI subjects. ASIA: American Spinal Injuries Association. BWS: body weight support. FES: functional electrical stimulation.

Subject A's SCI was caused by transverse myelitis, subject B sustained a spinal cord lesion as a result of a traumatic injury. Both subjects met the following inclusion criteria which was set for admission to the study;

1. Incomplete paraplegia or tetraplegia secondary to a spinal cord lesion.
2. Subjects will previously have been discharged from hospital following primary rehabilitation.
3. Subjects will be capable of independent ambulation, where necessary with orthotic support.
4. Female subjects should not be pregnant.
5. No significant history of autonomic dysreflexia.
6. No history of significant osteoporosis, or associated previous history of spontaneous lower limb fracture. Bone density will be measured in the epiphyses of the tibia and femur of both legs using peripheral Quantitative Computed Tomography (pQCT). Trabecular BMD values of above 110 $mg.cm^{-3}$ and 70 $mg.cm^{-3}$ for the femoral and tibial distal epiphyses respectively are required for admission to the study.
7. No history of coronary heart disease.
8. No clinical features of significant cardio-respiratory impairment.
9. Absence of hypertension.

3.3 Apparatus

3.3.1 Treadmill

A treadmill (Woodway LOKO S70 system, Germany) with an integral static partial body weight support (BWS) system was used for all exercise testing and gait training sessions (Figure 3.1). The treadmill could be controlled manually via a hand-rail keypad situated on the treadmill bars or by a programme (Metasoft 2.7, CORTEX Biophysik GmbH, Germany) on a PC linked to the treadmill. In order to accommodate the slow walking pace of SCI subjects the increments in treadmill speed and gradient were specifically adapted. When controlled manually the treadmill gradient increased in 0.1% increments from 0–20% and the speed in 0.01 $m.s^{-1}$ increments. When computer-controlled, the increments in treadmill gradient remained the same and the speed increased in 0.05 $m.s^{-1}$ increments.

Figure 3.1: A subject walking on the treadmill during a training session. The harness was attached to the static unloading system and ~30% of the subject's body weight was supported.

A ramp was attached to the front of the treadmill for wheelchair access, and the treadmill belt was wide enough to accommodate the wheelchair. During all gait training and exercise testing sessions, subjects were attached to the partial BWS system which could support a percentage, or all, of the subject's body weight. A harness, which was fastened around the subject's waist and under their legs, was attached to the system. With the static unloading system, weights counterbalanced the body equally as the subject walked through the swing and stance phase. This ensured the support remained constant throughout the session. Adjustable bars were also placed on either side, and in front of the subject. Subjects were discouraged from using these bars for weight bearing but were permitted to use them to aid with balance. A large mirror was placed in front of the subject and on their right hand side

to encourage them to maintain an upright posture while walking.

3.3.2 Breath-by-breath Gas Exchange

During cardiopulmonary exercise testing the O_2, CO_2 and N_2 concentrations, and the volume of each breath were continuously monitored using a breath-by-breath system (Msx ErgoSpirometer System, Morgan Medical Ltd, UK) in order to measure and record the following pulmonary gas exchange and ventilatory variables: rate of oxygen uptake ($\dot{V}O_2$), rate of carbon dioxide production ($\dot{V}CO_2$), minute ventilation ($\dot{V}_E$), respiratory exchange ratio (RER), end-tidal fraction of O_2 ($F_{ET}O_2$) and CO_2 ($F_{ET}CO_2$). The subject breathed though a mouthpiece with a sample line which was connected to the Msx, and wore a noseclip to prevent any gas escaping.

Gas Analysis

Respired gas concentrations were measured every 20 ms by a quadrupole mass spectrometer. Using this system, the respired gas is continuously sampled at $\sim$30 ml.min^{-1} and is drawn along the capillary sample line into the mass spectrometer. The pressure drop along the sample line allows a very small flow of the gas sample to be drawn into the high vacuum chamber of the analyser. Inside the high vacuum chamber the gas sample molecules are subjected to electron bombardment ionisation. The ions which form are injected down the axis of the quadrupole and separated by the electrostatic fields of the quadrupole lens. This ion separation is based on the mass-to-charge ratio of the individual ion so that at any given point only one mass-to-charge ratio can pass through the analyser. This process has the effect of "electrically filtering" the component species of the inflowing gas i.e. only one species at a time can pass through the analyser to the electron multiplier and the ion detector. Each constituent of the sampled gas emerges, one at a time, from the ion detector as a small voltage proportional to the fractional concentration of that gas species in the original sample. The voltage is then amplified and undergoes analogue-to-digital conversion.

Flow Measurement

Respiratory flow rate was measured using a bi-directional turbine volume transducer (Interface Associates, Laguna Niguel, USA). The turbine volume transducer is composed of a turbine flow sensor and an impeller. The impeller is driven in opposite directions by the inspired and expired gas flow. The turbine flow sensor transmits 4 infra-red beams across the bore of the impeller which are broken when the impeller spins. These interruptions in

the light beam are detected by the 4 phototransistors contained in the turbine flow sensor, the rate of which provides a measure of instantaneous impeller velocity. Gas flow is therefore directly proportional to the impeller velocity.

The output signal from the turbine volume transducer is linear between the ranges of 0.1–12 $l.s^{-1}$ with an accuracy of $\pm 2\%$. In order to prevent any external factors such as saliva from influencing the movement of the impeller, and thus affecting the accuracy of the measurements, a screen and saliva trap were placed between the impeller and mouthpiece assembly.

Gas Exchange Algorithms

Online calculation of ventilatory and pulmonary gas exchange variables was performed breath-by-breath using the algorithms of Beaver and colleagues [190]. These algorithms operate on the same mass-balance principles as classical gas collection methods (i.e. Douglas bags). The continuously measured expired flow is divided into consecutive temporal samples at the same frequency as the gas concentrations are being analysed. Summation of these samples provides a measure of the volume of the expired gas (V_E (l)) in a given period of time. To determine $\dot{V}_E$ ($l.min^{-1}$) for each breath V_E is summed across the expired duration of the breath and divided by the expired duration.

The same principles are applied for the calculation of $\dot{V}O_2$ ($l.min^{-1}$) and $\dot{V}CO_2$ ($l.min^{-1}$): the same process is applied to the product of the gas concentration and the expired flow for each sampling period. Therefore, calculation of $\dot{V}O_2$ and $\dot{V}CO_2$ is the sum of VO_2 (l) and VCO_2 (l) respectively, across the expired duration of the breath, divided by the expired duration.

Calibration

Prior to calibration of the mass spectrometer and turbine volume transducer, the current environmental conditions (i.e. barometric pressure, ambient temperature and relative humidity) were entered into the computer. This allowed the appropriate correction factor to be applied, taking account of the atmospheric conditions throughout the experiment. All values were corrected to STPD (standard temperature and pressure, dry), except $\dot{V}_E$ which was corrected to BTPS (body temperature and pressure, saturated).

The temperature of the laboratory was set to $\sim 20^oC$ which is the standard laboratory temperature for able-bodied (AB) exercise testing. Due to the increased risk of disturbed heat balance which has been demonstrated in SCI subjects whilst exercising in the cold and heat

[191], 20°C was also deemed an appropriate testing temperature for the SCI subjects who participated in this study.

Calibration of the mass spectrometer was performed using a precision-analysed gas of known concentration and ambient air. Following completion of each exercise test the precision-analysed gas and ambient air were sampled again to ensure the consistency of the calibration. On the rare occasion that the pre- and post-experimental measurements differed by more than 1%, the data were discarded.

Calibration of the turbine volume transducer was also performed prior to each exercise test. A known volume of air (3 l) was passed through the impeller housed within the turbine volume transducer. "Inspired" and "expired" gas flow, across a range of flow rates, was simulated using a precision syringe (Hans Rudolph, Kansas City, USA) and the measured volume was accepted if between 2.99–3.01 l. Following completion of each test the volume calibration was also checked to ensure there were no pre- to post-experimental discrepancies.

Temporal alignment of the gas concentration and volume signals is required to obtain an accurate measure of the breath-by-breath pulmonary gas exchange variables. The delay between the gas concentration and volume signals is calculated using algorithms specified by the manufacturer (Morgan Medical Ltd, UK). The algorithms are based on the principle that when the volume signal breaks a given threshold, representing a given % change (which occurs with a time delay of $\leq$10 ms), this represents the onset of the breath. This is phase-aligned with the onset of changes in the gas concentration signals for O_2, CO_2 and N_2 (which occurs with the same rapid response kinetics), allowing accurate calculation of the pulmonary gas exchange variables.

3.3.3 Heart Rate

Heart Rate (HR) was continuously monitored and recorded throughout all exercise tests and training sessions using a short range telemetry HR monitor (Polar S410, Polar Electro Oy, Finland).

3.3.4 Stimulators

A two-channel stimulator (Odstock O2CHS), controlled via a finger switch by the investigator, was used for subject B, to apply surface stimulation to the left peroneal nerve to elicit the withdrawal reflex during gait. This was to correct for drop foot, and to achieve foot clearance during the swing phase. Round surface electrodes (50mm PALS Ultraflex, Axelgaard,

Denmark) were applied on the skin surface over the popliteal fossa and the head of the fibula. The parameters of stimulation delivered were 40 Hz, 40 mA and 115-350 μs depending on the strength of the reflex response.

During the twitch tests (see Section 3.4.4) an eight-channel surface stimulator (Stanmore [192]), controlled via Simulink software on a PC, was used to deliver the stimulation train to the quadriceps and hamstring muscles. The stimulator delivered current controlled, monophasic, charge balanced stimulation pulses via round surface electrodes (70mm PALS Platinum, Axelgaard, Denmark).

3.3.5 Dynamometer

A Biodex System 3 Dynamometer (Biodex Medical Systems, Inc., UK) was used to measure the voluntary and total muscle force produced by the quadriceps and hamstring muscles of both subjects (Figure 3.2).

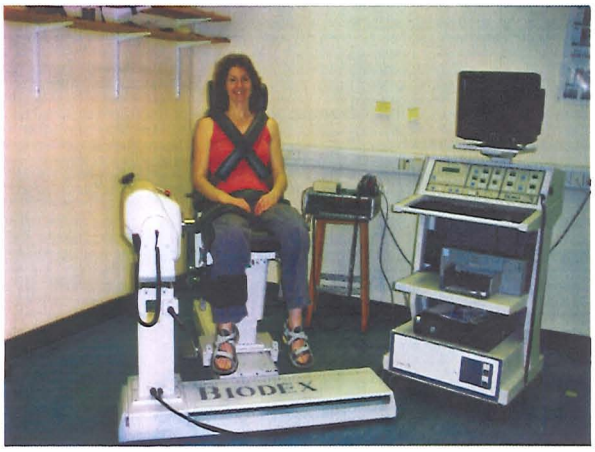


Figure 3.2: A subject seated in the dynamometer. Stabilisation straps are secured over the subject's shoulders, pelvis and thigh. The testing limb is secured to the dynamometer attachment.

The dynamometer and dynamometer chair could be moved in a variety of directions to allow the optimal position for testing the muscles of the knee joint to be achieved. The dynamometer attachment, to which the lower limb was attached, was secured onto the dynamometer shaft in the centre of the dynamometer. The dynamometer attachment could be modified to fit any length of limb. Once secured, this provided an index for proper alignment of the anatomical angle of rotation. In order to isolate the muscle being tested a number of stabilisation straps (thigh strap, pelvic strap and two shoulder straps) attached to the dynamometer chair, were wrapped around the subject and secured tightly into buckles.

The dynamometer was attached to a controller which transferred signals from the dynamometer to a PC and vice versa. Biodex Advantage Software was the Windows based software package used to produce and implement the required protocol, and to record and analyse the resulting data.

Prior to each test the dynamometer was calibrated with a known weight to ensure validity of the results. The required testing protocol was then defined by entering the mode of exercise (e.g. isometric), the joint angle, the direction of contraction (towards/away), the test pattern (e.g. extension/flexion) and the contraction and relaxation time. Once saved this protocol was implemented when the test was started. Prior to this however, the subject's range of motion (ROM) was set by recording the subject's limit in each direction. This ensured that the dynamometer did not try to move the subject's knee outwith this range.

The subject's limb weight was also recorded by positioning it at an angle less than 45 degrees from horizontal. The subject was then asked to relax the limb and the weight was recorded. This was an important measurement, as for various joints in the body (e.g. knee), the weight of the limb can be a significant factor in measuring the torque produced by the corresponding muscles. Therefore, the software performs gravity correction on the torque data. This involves measuring the weight of the limb and applying the correction based on the direction of the shaft rotation; if the limb is contracting away (e.g. quadriceps muscle) the correction factor is added to the measured torque, if it is contracting towards (e.g. hamstrings muscle) it is subtracted. The torque is corrected as in Equation (3.1):

$$T^{limb} = \frac{T_2^{limb}}{\cos(A)} \tag{3.1}$$

The torque of the limb is then used to calculate the correction factor (Equation 3.2).

$$T_c^{limb} = T^{limb} \cdot \cos(B) \tag{3.2}$$

where

- T^{limb} = torque of the limb at the position of maximum gravity effect (horizontal)
- T_2^{limb} = torque produced when the limb is weighed prior to the test
- T_c^{limb} = correction factor
- A = angle from the horizontal at which the limb is weighed prior to the test
- B = testing angle from the horizontal

The actual torque produced by the subject during a muscle contraction is measured by strain gauges in the dynamometer shaft. These strain gauges are attached to an H bridge configuration. When torque is applied to the shaft during a muscle contraction the H bridge becomes unbalanced and a voltage output, proportional to the applied torque, is produced. The voltage produced is then converted back into torque and displayed on the PC.

3.3.6 Peripheral Quantitative Computed Tomography Scanner

A pQCT scanner (Stratec XCT 3000, Stratec Medizintechnik, Pforzheim, Germany) was used to measure the BMD of the lower limbs [193]. This system measures the attenuation of X-rays, which are linearly transformed into hydroxyapatite (HA) densities. It is calibrated with respect to fat which is set at 0 mgHA. Consequently water results in 60 mgHA. Quality assurance scans were performed prior to each scanning session using the manufacturer's phantom.

3.4 Protocols

3.4.1 Treadmill Training Protocol

Pre-baseline Treadmill Training

In order to increase the duration of walking to a level which would allow cardiopulmonary baseline tests to be carried out, each subject participated in a period of pre-baseline treadmill training. A target of 15 minutes continuous walking at a speed of 0.1 $m.s^{-1}$ and a gradient of 0% was set. Each subject attended the laboratory for training sessions twice a week. Both subjects required the use of the BWS system during walking with ~30% of their body weight being supported during each training session. To enable subject B to lift his left foot clear of the treadmill belt during walking FES was used on his left peroneal nerve as described in Section 3.3.4.

Subjects were permitted to carry out intermittent training (i.e. walk for as long as possible and then rest for 10 minutes before carrying out another walking bout) in order to achieve the target duration for each session. This continued until an overall continuous duration of 15 minutes was achieved 3 sessions in a row. At this point the baseline cardiopulmonary and muscle twitch tests were carried out. The number of training sessions carried out by each subject prior to the baseline tests are shown in Table 3.2.

When the subjects were ready to perform the baseline tests additional sessions were used to determine the range of speeds and gradients at which they could walk.

Subject	Number of training sessions
A	19
B	15

Table 3.2: Number of training sessions prior to baseline tests.

Treadmill Training Programme

Following the baseline tests the subjects participated in a five month training programme. The frequency of the training sessions was increased to three times per week.

During the first week of post-baseline test training each subject was asked to walk at 0.1 m.s $^{-1}$ (or 0.15 m.s^{-1} if they completed their 15 minute distance test at this speed (see Section 3.4.3)), 0% gradient for as long as possible (up to 30 minutes) during all sessions. The longest duration achieved was used as a reference point for the starting duration for the subsequent training sessions. The duration achieved was rounded up to the nearest 5 minutes as shown in Table 3.3.

Longest duration achieved during the first week of walking training (min)	Duration of subsequent training sessions (min)
15-20	20
20-25	25
25-30	30

Table 3.3: Duration of treadmill walking training sessions.

The target duration of each training session was increased by 5 minutes every 3 weeks, with the maximum duration being 30 minutes. During all training sessions subjects carried out intermittent training to ensure that they achieved the target duration. This continued until the subject's overall exercise time equalled that of the target duration.

During the training period subjects had to increase the speed and gradient at which they could walk. During speed training the gradient of the treadmill was kept to 0% and during gradient training the treadmill speed was kept to 0.15 m.s^{-1}. These training sessions took place on alternate sessions.

Once the subject could complete 15 minutes of continuous walking at a treadmill speed of 0.1 m.s^{-1} (or 0.15 m.s^{-1}), 0% gradient the speed or gradient was increased for the next session. During the training period an increase in speed or gradient was made when the subject could achieve 3 consecutive sessions at a particular speed or gradient (phase 1). The higher speed was that of phase 1 plus 0.05 m.s^{-1}, or 0.10 m.s^{-1} if the subject was able. The gradient

was increased in 0.5% or 1% increments. During training sessions the subjects could drop down to the phase 1 speed or gradient if they felt that they could complete the session in one continuous walking bout. However, an increase was not made until the entire training session was completed at the higher speed or gradient. Throughout all training sessions ~30% of the subjects' body weight was supported.

3.4.2 Cardiopulmonary Exercise Test Protocols

On arrival to the laboratory for cardiopulmonary exercise testing the subject's health was determined by completion of a health questionnaire and by monitoring their blood pressure. If their blood pressure exceeded 160/95 they were allowed to rest for 5 minutes before it was re-taken. Only if the subject's blood pressure was below 160/95 and they were deemed to be in good health were they allowed to participate in the exercise test.

In order to minimise the effect of extraneous factors on the data recorded, subjects were asked to refrain from the following prior to any cardiopulmonary exercise test:

- Participating in strenuous exercise for 24 hours
- Alcohol consumption for 24 hours
- Caffeine ingestion for 4 hours
- Food ingestion for 2 hours

Subjects were also asked to consume similar meals on test days. It was also essential that subjects had 100% compliance with the prescribed gait training programme for 14 days prior to testing.

Once the subject was deemed suitable for participation in the test they put on the HR monitor. They were then helped into the harness and attached to the static partial BWS system. As with the training sessions ~30% of the subject's body weight was supported during all cardiopulmonary exercise tests.

The cardiopulmonary exercise tests were carried out every 4 weeks throughout the 5 month training programme. Prior to each set of tests the subject's weight was measured using wheelchair scales (Marsden, DP2400).

Familiarisation

Prior to the baseline cardiopulmonary exercise tests, the subjects had been attending the laboratory for ~2 months for treadmill training. They were therefore already familiar with the environment, treadmill, BWS system and the research team. A formal familiarisation period was however necessary to familiarise the subjects with the breath-by-breath system and testing protocols. Their reaction to new equipment and testing protocols could influence the reliability of the variables under investigation giving an inaccurate characterisation of the response. It was therefore essential that the subjects were comfortable in the environment in which the exercise tests were carried out and with the equipment and protocols used. It was also essential that the testing conditions remained constant for each testing session.

In preparation for the tests, the following procedures were carried out prior to commencement of the familiarisation test:

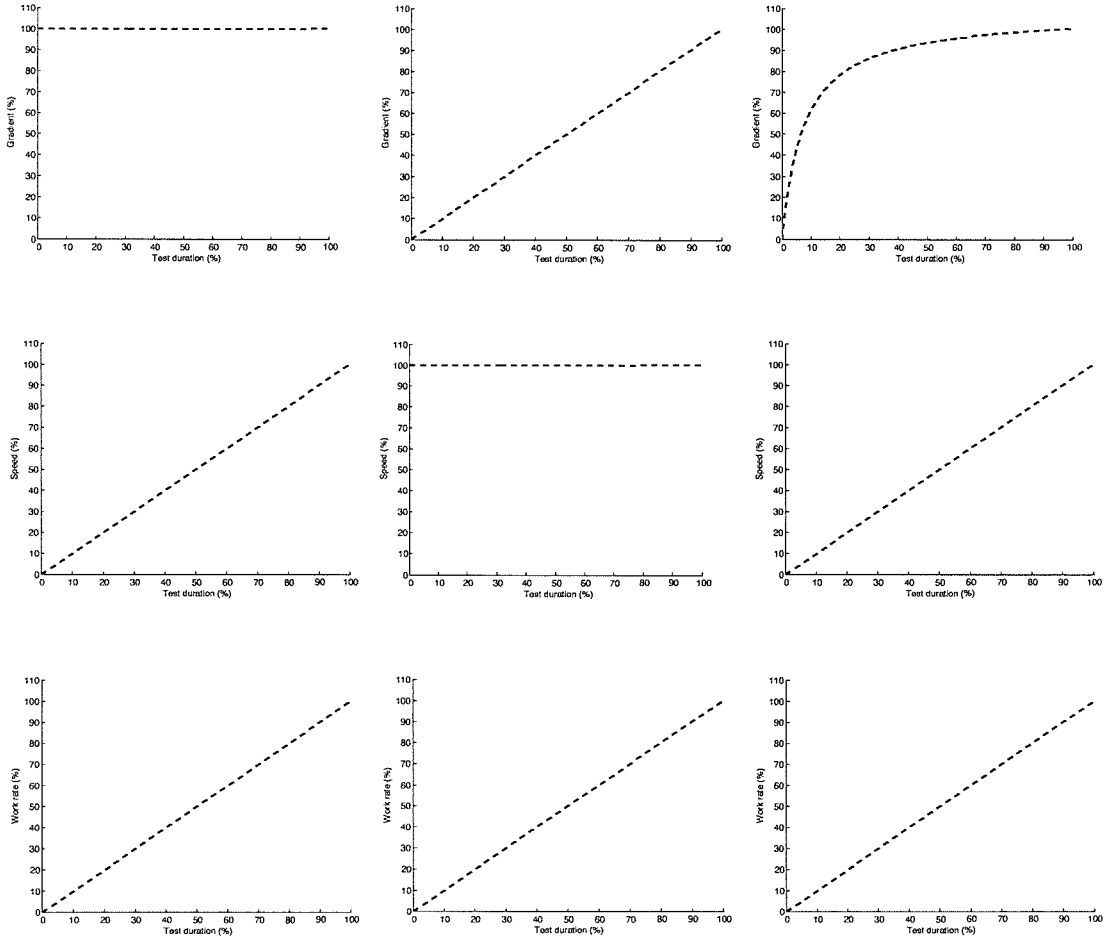
- The maximal incremental exercise test (IET) and constant load (step) exercise test (SET) protocols were described to the subject in layman's terms, as was the purpose of each test.
- The subject was then asked to put on the various pieces of equipment to be worn during the experimental procedure (e.g. mouthpiece, noseclip, heart rate monitor) and the purpose of each piece was explained briefly.
- The headset which held the mouthpiece was adjusted to fit the subject comfortably.
- The communication signals for during the experimental procedure were explained to the subject: thumbs up if they were comfortable with everything, thumbs down if they were not.

If the subject was content they then went on to perform either a maximal IET or an SET.

Maximal Incremental Exercise Test

During a maximal IET to the limit of tolerance a progressive, linear increase in work rate is imposed on the subject and consequently a progressive increase in physiological stress. As discussed in Section 1.6 it has been recommended [58] that a single short duration ramp test is appropriate to accurately measure maximum oxygen uptake ($\dot{V}O_{2max}$), lactate threshold (LT) and O_2 cost/efficiency. This exercise test can therefore provide an indication of the cardiopulmonary fitness of an individual and monitor changes in cardiopulmonary fitness which may result as a consequence of an exercise training programme.

When using a treadmill to perform an IET there are two standard protocols used which provide a linear increase in work rate. The first, as can be seen in Figure 3.3(a), incorporates a constant gradient and linear increase in speed (see Equation (3.3)).



(a) Constant gradient, linear speed (b) Linear gradient, constant speed(c) Curvilinear gradient, linear speed

Figure 3.3: Treadmill gradient and speed profiles which result in a linear increase in work rate.

$$WR = m \cdot g \cdot v \cdot \sin\Theta \tag{3.3}$$

where

- WR = work rate
- m = subject's body weight in kilograms
- g = gravitational acceleration, 9.81 m.s^{-2}

- v = speed
- $\sin\Theta$ = sine of the angle of inclination

However, if the speed is increased at too fast a pace the test becomes a measure of the subject's ability to move their legs quickly and/or efficiently enough, rather than metabolic factors. Furthermore, if too steep a grade is chosen as the constant inclination then a high initial metabolic cost will result which, in subjects who have very poor cardiopulmonary fitness, may mask key indices of cardiopulmonary fitness i.e. LT. The second method available for maximal incremental exercise testing on a treadmill is to maintain a constant speed and increase the sine of the angle of inclination (see Figure 3.3(b), Equation (3.3)). This method, although an improvement on the previous, also has problems associated with it: if too low a speed is selected then a very steep gradient results before the level of tolerance is reached.

The issues associated with performing maximal IETs on a treadmill were recently addressed by Porszasz and colleagues [86]. They demonstrated that by increasing the subject's walking speed linearly and the treadmill gradient curvilinearly a linear increase in work rate would result (see Figure 3.3(c)) with the subject fatiguing at a moderate speed in approximately 10 minutes. By stating the subject's initial and final treadmill speeds, and predicting their maximum work rate, the inclination profile which will force a linear increase in work rate can be determined as in Equation (3.4).

$$grade(t) = \frac{[[(WR_{max}/m \cdot g \cdot V_o) - grade_o] \cdot t + 10 \cdot grade_o]}{[[(V_{max}/V_o) - 1] \cdot t + 10]} \tag{3.4}$$

where

- $grade$ = tangent of the angle of inclination
- WR_{max} = maximum work rate
- m = subject's body weight in kilograms
- g = gravitational acceleration, 9.81 $m.s^{-2}$
- V_0 = initial speed
- $grade_o$ = tangent of the initial angle of inclination
- t = time
- V_{max} = maximum speed

It was suggested by Porszasz and colleagues [86] that this protocol may be useful for those with severely limited exercise tolerance. Consequently, it may be a useful method for testing

those with an SCI.

In order to determine if this new method is appropriate for those with an SCI and whether it is superior to methods which have been established in the able-bodied (AB) population but not yet utilised in the SCI population, both subjects performed 2 IETs at each test point: the Porszasz protocol and a test which maintained a constant speed while increasing the sine of the angle of inclination. The format of each testing session was identical (Figure 3.4).

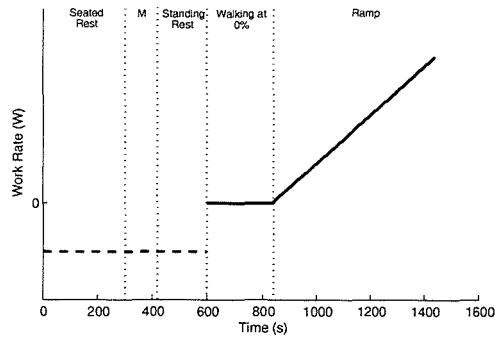


Figure 3.4: Schematic representation of the incremental exercise test profile. The duration of the resting and walking at 0% phases were altered to ensure the subject's breathing was stabilised. The duration of the ramp phase was subject-dependent although the incrementation rate was set for the subject to reach their limit of tolerance in 8–12 minutes. M: moving. There was no set duration for this phase.

Prior to the exercise test the subject carried out a 5 minute warm up at a speed of 0.15 $m.s^{-1}$, 0% gradient. After completion of the warm up they were removed from the partial BWS system and seated on a chair placed on the stationary treadmill belt. They were then attached to the breath-by-breath system described in Section 3.3.2. The subject also wore a nose clip.

A period of quiet breathing followed which was closely monitored for signs of hyperventilation by the investigator. This period of rest lasted for 5 minutes. However, it was extended should the subject require longer to recover from the warm up. Once it was apparent that the subject had recovered from the warm up (RER 0.75-0.90, $F_{ET}CO_2$ ~6%, $\dot{V}_E$ 5-10 $l.min^{-1}$) they were asked to stand and were once again attached to the BWS system. This movement caused fluctuations in the subject's breathing pattern. Therefore, they were asked to carry out a period of standing rest for 3 minutes, or until it was evident that their breathing was stable and within the previously described range. This stabilisation is important before beginning an exercise phase in order to obtain valid results and for accurate, non-invasive estimation of

the LT during an IET.

During hyperventilation CO_2 is "blown off" and hence the body's CO_2 stores are depleted. If a subject was allowed to begin exercising whilst hyperventilating a proportion of the metabolically produced CO_2 would replace these depleted stores. Once the stores were replaced most of the CO_2 produced at the muscles would be exchanged at the lungs. This would be shown on the V-slope plot as an accelerated rise in $\dot{V}CO_2$ relative to $\dot{V}O_2$, and the cause may be mistaken as the production of non-metabolic CO_2. This underestimation of the LT has been termed a pseudo-threshold [194, 195, 196].

Following the period of standing rest, the subject carried out a period of 4 minutes walking at a treadmill gradient of 0% and speed of 0.15 $m.s^{-1}$ (unless otherwise stated in Chapters 4 and 5). This phase was extended if the subject's breathing had not stabilised. Following this period of walking the subject immediately began the ramp phase of the test. The desired incrementation rate in speed and/or gradient was pre-programmed into the treadmill computer controller to provide a linear increase in work rate as a function of time. The incrementation rate was determined by the investigator and was dependent on the speeds and gradients at which the investigator felt the subject could walk safely. The specifics of the incrementation rates for each subject are provided in Chapters 4 and 5. The rates were chosen with the aim of ensuring that the subject reached their limit of tolerance in 8–12 minutes [197]. It is important that the rate of incrementation is not too slow as this can result in an underestimation of $\dot{V}O_{2max}$ as a consequence of poor subject motivation. It is also evident that no additional information is achieved from prolonged tests [58]. On the other hand, if the incrementation rate is too fast it can result in inaccuracies in determining the LT as a large proportion of metabolically produced CO_2 is washed into the body stores [194]. This results in a shallow lower slope and consequently makes it more difficult to detect the real LT. $\dot{V}O_{2max}$ can also be underestimated as subjects cannot produce the muscular forces required at high work rates which have been attained with rapid rates of change.

The increase in speed and/or gradient continued until the subject reached volitional exhaustion. On attainment of the limit of tolerance, treadmill speed and gradient were reduced to 0 $m.s^{-1}$, 0% respectively. It was noted during the familiarisation tests that further walking in the recovery phase resulted in further physiological stress for the subject. Therefore, during the recovery phase the breath-by-breath and BWS system were removed from the subject and they were seated on a chair on the stationary treadmill belt. The subject's HR was then monitored closely for $\sim$5 minutes to ensure they had recovered from the exercise.

Constant Load Exercise Test Protocol

At each test point both subjects also carried out an SET (Figure 3.5). Prior to the test the subject performed a warm up at a treadmill gradient of 0% and speed of 0.15 $m.s^{-1}$. The duration of the rest phases and indices of recovery were identical to that of the IET. Following the period of standing rest the subject walked at a treadmill gradient of 0% and speed of 0.15 $m.s^{-1}$ for 15 minutes. The increase in speed was pre-programmed into the treadmill computer controller to provide a seamless increase in speed at the desired time. On completion of the 15 minute walking phase the treadmill was stopped and the subject stood on the stationary treadmill belt for a period of quiet breathing. This period of recovery continued until the investigator determined that the physiological variables ($\dot{V}O_2$, $\dot{V}_E$, HR) had returned to pre-exercise levels.

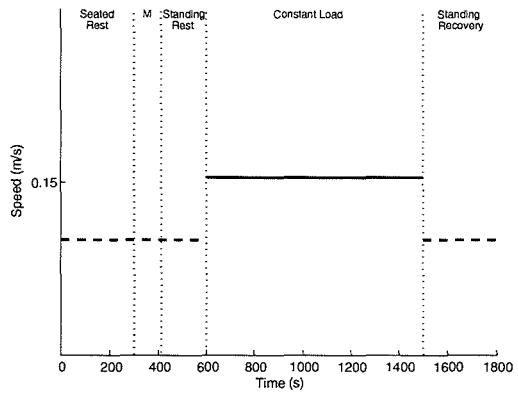


Figure 3.5: Treadmill speed profile during the constant load exercise test. Treadmill gradient remained at 0% throughout. The duration of the resting and recovery periods could be extended to ensure the subject's breathing had stabilised. M: moving. There was not a set duration for this period.

The treadmill speed and gradient of this test were chosen as both subjects were able to walk for 15 minutes at 0.15$m.s^{-1}$, 0% at the point of baseline testing. The speed and duration of the test were kept constant throughout the duration of the study to allow a comparison of the kinetic response at the various test points.

3.4.3 15 Minute Distance Test Protocol

Both subjects also performed a 15 minute distance test every 4 weeks during the 5 month training period. They were prepared for the 15 minute distance test as described in Section 3.4.2. Cardiopulmonary monitoring equipment was not used during this test but the subject's HR was continually monitored. Following a 5 minute warm up at a treadmill gradient of 0%

and speed of 0.15 $m.s^{-1}$ the subject was removed from the BWS system and seated on a chair on the stationary treadmill belt. They then rested for 10 minutes to ensure they had recovered from the warm up. Following this they were asked to stand and were reattached to the BWS system. Prior to commencement of the test the subject chose what speed they would like to begin walking. They were then instructed to walk at a gradient of 0% for 15 minutes with ~30% of their body weight supported by the static BWS system. Subjects were not permitted to talk during the test in order to ensure that the heart rate response was reflective only of the exercise being carried out. However, if they wanted the speed of the treadmill to be increased or decreased during the 15 minute test they could ask the investigator. The speed of the treadmill was only altered if instructed to do so by the subject.

3.4.4 Twitch Test Protocol

As discussed in Section 1.7, in order to quantify the extent of central activation failure (CAF) the central activation ratio (CAR) of the muscle must be calculated. Not only is this important for those with an SCI in terms of accurately measuring the extent of their muscle weakness, it can also, as discussed in Section 2.4, provide information as to how training is affecting muscle fibre force production: better recruitment of available muscle fibres or hypertrophy of the muscle fibres recruited by the FES. Both subjects who participated in the 5 month treadmill training study performed such tests at 4 test points: prior to commencing pre-baseline training to provide an accurate measure of the CAR before any walking training had taken place; at baseline to determine if the pre-baseline walking training had produced any effect on muscle force and also to provide a baseline measurement prior to the more intensive training programme; and following 2.5 and 5 months training.

On arrival for a testing session the skin of the subject's lower limbs was checked for any damage which may be a contraindication to FES use i.e. cuts, burns, abrasions. If the subject's skin was found to be intact, round surface electrodes were placed over the subject's hamstring and quadriceps muscles on both legs. The subject then transferred from their wheelchair onto the dynamometer chair. The settings of the dynamometer and dynamometer chair were then altered to the pre-determined settings for the individual subject. The pelvic strap, two shoulder straps and thigh strap of the leg to be tested were then attached.

At each test point the quadriceps muscles were tested with the knee at 90^o of flexion with the subject sitting in an upright position. The hamstrings were also tested in this position and with the subject in a supine position with the knee at 30^o of flexion. In order to maximize the period of rest between testing the hamstring muscles in the two positions, the tests were carried out in the following order: right hamstring at 90^o, right quadriceps at 90^o, left hamstring at 90^o, left quadriceps at 90^o, right hamstring at 30^o, left hamstring at 30^o.

The subject performed 3 maximum voluntary contractions (MVCs) with each muscle in each position. Each contraction lasted 5 seconds and there was 240 seconds rest between each one to allow the muscle to recover. During each MVC the subject was asked to sit with their arms folded to eliminate any upper body movement which may contribute to the force being produced by the muscle. The subject was verbally encouraged to produce as much force as possible during the voluntary contraction and to maintain that force for the whole 5 seconds. ~3 seconds after the onset of the MVC, when the investigator determined a plateau in the force being produced [198, 199], a 10 pulse stimulation train was applied to the muscle with the following parameters: 140 mA, 600 μs, 100 Hz. This was the maximum output from the stimulator used and was well tolerated by both subjects. The subject was encouraged to maintain their MVC throughout the stimulation train and to the end of the test. The force produced throughout each MVC was monitored and recorded by the Biodex.

3.4.5 Bone Scan Protocol

As mentioned in Section 3.2, BMD in the distal and proximal epiphyses and diaphyses of the tibia and in the distal epiphyses and diaphyses of the femur of both legs was determined prior to a subject's inclusion into the study. This test was then repeated at the end of the 5 month training study, therefore ~7 months after the first test, to determine if any changes had occurred as a consequence of the walking training.

The subjects attended the Nuclear Medicine Department at the Southern General Hospital, Glasgow where a Clinical Scientist performed the scans and analysed the data obtained. The length of their tibia in each leg was measured from the distal end of the medial malleolus to the medial joint cleft. The femur length was recorded as approximately equal to the tibia length. The subject then transferred from their wheelchair onto a height-adjustable patient couch. Throughout the testing period the subject lay supine.

A scout view of the tibia was carried out in order to locate the joint cleft and a reference line placed on the distal endplate. Tibial scans were then performed at 4%, 14%, 38% and 66% of the total bone length from the distal end of the bone. Scout views were then performed for the proximal tibia and femur and reference lines set. The tibia was then scanned at 4% from the proximal end of the bone. Femur scans were performed at 4% and 25% of the total bone length from the distal end. A more proximal scan of the femur would have been desirable. However, due to insufficient abduction of the hip, this was not possible. Slice thickness was set at 2 mm. Voxel size was 0.5 mm in the tibia and 0.3 mm in the femur.

3.5 Analysis

3.5.1 Incremental Exercise Test

Editing

The underlying physiological response to exercise is masked in breath-by-breath data by inter-breath fluctuations commonly referred to as "noise" [200]. This "noise" is often a consequence of irregularities in the subject's breathing pattern which may be caused by coughing, swallowing, sighing etc. These events can cause the breath-by-breath equipment to mis-trigger. Mis-triggered breaths are usually evident in the breath-by-breath data as markedly larger or smaller breaths than the mean response. They are unlikely to be real breaths and should therefore be removed [200, 201].

It has been recommended that points outwith ± 4 standard deviations of the mean response be removed during the editing process [200, 201]. By removing the points outwith these prediction intervals, there is less than 0.0001 probability that they were representative of the actual physiological response.

However, inter-breath fluctuations in the breath-by-breath data of SCI subjects does appear to be greater than in AB subjects. Therefore, we cannot be as confident that removing points outwith 4 standard deviations of the mean response would remove all points which are not part of the underlying physiological response. Therefore, during editing of the cardiopulmonary data obtained in this study points outwith 2 standard deviations of the mean response were removed. There is therefore less than 0.05 probability that they are representative of the true physiological response to the exercise.

The editing process for the IET breath-by-breath data was performed using Origin 7.5 (OriginLab Corporation, USA) software as outlined below:

- **Step 1.** The responses of all breath-by-breath variables throughout the test were plotted against time; B_f, V_T, T_I, T_E, $F_{ET}O_2$, $F_{ET}CO_2$, $\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}_E$ and RER.
- **Step 2: Rest Phase (Seated).** A linear line of gradient zero was fitted to B_f, V_T, T_I, T_E, $F_{ET}O_2$ and $F_{ET}CO_2$. 95% prediction bands were set around the mean response and outliers removed. This process was repeated for $\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}_E$ and RER.
- **Step 3: Moving Phase.** The data in this phase was not edited as it was not of physiological relevance and no standard response could be fitted to it.
- **Step 4: Rest Phase (Standing).** See step 2.

- **Step 5: Walking at a given speed on 0% gradient.** A linear line of best fit, the gradient set by the software, was fitted to B_f, T_I, T_E, $F_{ET}O_2$ and $F_{ET}CO_2$. An exponential line of best fit was fitted to the V_T response if the profile allowed. If an exponential could not be fitted a linear line with the gradient set by the software was. 95% prediction bands were then set around the mean response of these variables and the outliers removed. An exponential was then fitted to $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}_E$. If this was not possible a linear line, gradient set by software, was fitted. A linear line was also fitted to the RER response. 95% prediction bands were then set around the mean response and outliers removed.

- **Step 6: Ramp Phase.** A linear line of best fit, gradient set by software, was fitted to B_f, V_T, T_I, T_E, $F_{ET}O_2$ and $F_{ET}CO_2$. 95% prediction bands were set around the mean response and outliers removed. This process was then repeated for $\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}_E$ and RER.

During the editing process points were removed from B_f, V_T, T_I, T_E, $F_{ET}O_2$ and $F_{ET}CO_2$ first as they are the raw variables used to compute $\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}_E$ and RER. Consequently, only points which were missed during the initial editing process would be seen as outliers in $\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}_E$ and RER. Substantially fewer points are removed from these variables.

The edited data were used in the calculation of all outcome variables.

Peak Oxygen Uptake

As discussed in Section 1.6.1, a plateau in $\dot{V}O_2$ is not always achieved during an IET despite maximal subject effort. It has been recommended [64, 66] that additional tests be performed to ensure that the $\dot{V}O_{2peak}$ achieved during an IET is indeed representative of the subject's $\dot{V}O_{2max}$. However, given the amount of subject participation in this study and the already intense testing period at each test point, it was deemed inappropriate to ask the two subjects involved to perform another maximal exercise test. Therefore, the maximum $\dot{V}O_2$ achieved by a subject during an IET in this study is referred to as $\dot{V}O_{2peak}$.

$\dot{V}O_{2peak}$ was calculated by averaging all the data points in the final 20 seconds of the incremental phase of the test [64]. This period was believed to be sufficient so as to ensure that sufficient data was included to remove the influence of inter-breath fluctuations on the mean value obtained and short enough to exclude data which was part of the transient response preceding $\dot{V}O_{2peak}$ [64].

Lactate Threshold

The LT was estimated using standard gas exchange criteria [79] and the V-slope method [78]. During the ramp phase of an IET $\dot{V}O_2$ increases linearly with respect to work rate following a short delay equal in duration to the MRT. $\dot{V}CO_2$ also increases linearly until a disproportionate increase occurs with respect to $\dot{V}O_2$ at the point of LT. Above the LT all the lactic acid produced is dissociated to lactate (La^-) and hydrogen (H^+) ions. The H^+ produced are buffered by bicarbonate ions (HCO_3^-) resulting in the production of non-metabolic CO_2:

$$H^+ + HCO_3^- \leftrightarrow H_2CO_3 \leftrightarrow CO_2 + H_2O \tag{3.5}$$

The non-metabolic, or "excess", CO_2 produced when lactate accumulates during exercise above the LT is evolved rapidly. At this point a deflection point can be seen on the $\dot{V}CO_2$-$\dot{V}O_2$ plot which indicates that CO_2 is being cleared in excess of that produced aerobically. As can be seen in Figure 3.6, the $\dot{V}O_2$ at which the LT occurs can therefore be determined.

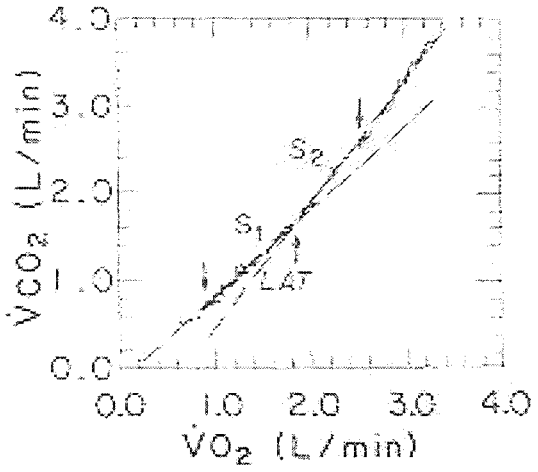


Figure 3.6: Representation of the disproportionate increase in carbon dioxide production with respect to oxygen uptake which occurs at the lactate threshold. $\dot{V}CO_2$: carbon dioxide production. $\dot{V}O_2$: oxygen uptake. S_1: lower slope. S_2: upper slope. [78].

When using the V-slope method to identify the LT it is important to use only the region of interest when fitting the lower (S1) and upper (S2) slopes to the V-slope plot [78]. Therefore the initial kinetic data and the data which followed the respiratory compensation point (RCP) were excluded from the analysis. The kinetic data were excluded by removing all data points before the linear increase in $\dot{V}CO_2$ occurs. Data following the RCP were excluded by removing all data points which followed further changes in the gas exchange variables, a

consequence of the falling pH providing a further ventilatory stimulus and hyperventilation, the details of which are provided below. The intercept of the S1 and S2 slopes is the point of LT.

To support the findings of the V-slope method and reliably estimate the LT it is recommended that the responses of a range of ventilatory based variables to incremental exercise also be considered [79] (Figure 3.7).

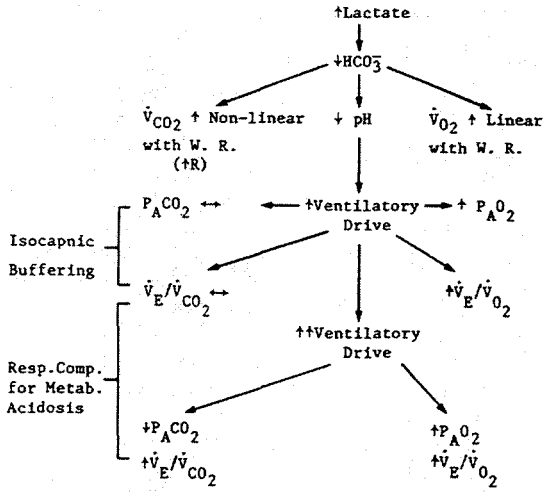


Figure 3.7: The effect of increasing lactate concentration on gas exchange. [83].

The increase in $\dot{V}CO_2$ relative to $\dot{V}O_2$ at the LT results in an increase in the ventilatory drive, and consequently $\dot{V}_E$. During a period of isocapnic buffering which follows the LT $\dot{V}_E$ increases proportionately to $\dot{V}CO_2$ but disproportionately to $\dot{V}O_2$. Therefore, at the point of the LT the ventilatory equivalent of oxygen ($\dot{V}_E/\dot{V}O_2$) increases and the ventilatory equivalent of carbon dioxide ($\dot{V}_E/\dot{V}CO_2$) remains stable. Corresponding to this, an increase in the end-tidal partial pressure of oxygen ($P_{ET}O_2$) also occurs. During hyperventilation the length of the breath becomes shorter and therefore at the termination of the breath $P_{ET}O_2$ is higher. At the LT the end-tidal partial pressure of carbon dioxide ($P_{ET}CO_2$) does not change because although the breaths become shorter the CO_2 gradient is higher due to the presence of non-metabolic CO_2. Following this period of isocapnic buffering there is a further alteration in gas exchange termed the RCP. At this point hyperventilation occurs with respect to $\dot{V}CO_2$ and therefore $\dot{V}_E$ increases disproportionately to $\dot{V}CO_2$. Consequently, at this point $\dot{V}_E/\dot{V}CO_2$ increases and $P_{ET}CO_2$ decreases. The non-invasive methods of detecting LT are summarised in Figure 3.8.

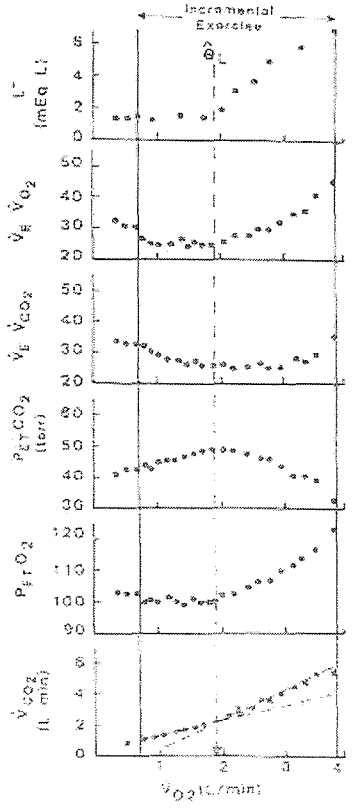
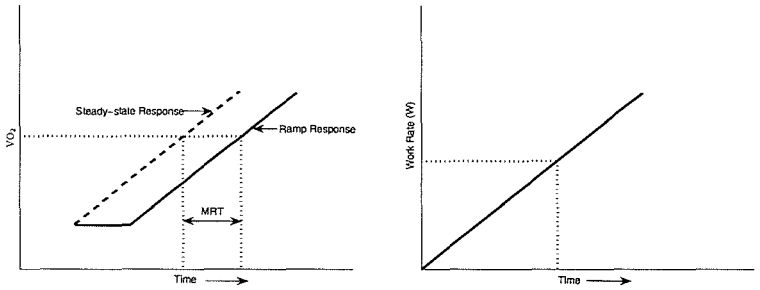


Figure 3.8: At the point of the lactate threshold a disproportionate increase in carbon dioxide production with respect to oxygen uptake occurs (bottom plot). This is confirmed by a corresponding increase in the ventilatory equivalent of oxygen (second plot) and the end-tidal partial pressure of oxygen (fifth plot): the ventilatory equivalent of carbon dioxide (third plot) and the end-tidal partial pressure of carbon dioxide (fourth plot) remain stable. The oxygen uptake at which the lactate threshold is determined non-invasively also corresponds to the point at which it is determined invasively by blood lactate concentration (top plot). L^-: blood lactate concentration. $\dot{V}_E/\dot{V}O_2$: ventilatory equivalent of oxygen. $\dot{V}_E/\dot{V}CO_2$: ventilatory equivalent of carbon dioxide. $P_{ET}CO_2$: end-tidal partial pressure of carbon dioxide. $P_{ET}O_2$: end-tidal partial pressure of oxygen. $\dot{V}CO_2$: carbon dioxide production. $\dot{V}O_2$: oxygen uptake. [202].

Once the $\dot{V}O_2$ at which the LT occurred had been estimated for each test, the work rate at which it occurred was determined. The work rate estimate obtained at this $\dot{V}O_2$ is a non steady-state measure because the ramp $\dot{V}O_2$ lags behind the steady-state $\dot{V}O_2$ value by a time equal to the mean response time (MRT). This difference can be estimated as it stabilises due to the constant rate of change that the subject is exposed to.

The steady-state work rate at which the LT occurred was determined by firstly plotting time against $\dot{V}O_2$. As can be seen in Figure 3.9(a), by duplicating the slope of the response and

fitting it to the start of the ramp phase the time corresponding to the MRT could be established. Consequently, the time at which the steady-state work rate corresponding to the LT occurs could be determined. By plotting time-work rate, the actual work rate could be determined (Figure 3.9(b)).



(a) Time-$\dot{V}O_2$ plot (b) Time-WR plot

Figure 3.9: Determination of the steady-state work rate at the lactate threshold. (a) The time corresponding to the mean response time and consequently the time at which the steady-state work rate corresponding to the lactate threshold are determined. (b) The actual steady-state work rate at the lactate threshold is determined.

Slope of Oxygen Uptake as a function of Work Rate

When determining the slope of $\dot{V}O_2$ as a function of work rate ($\Delta\dot{V}O_2/\Delta WR$) of the exercise only the linear phase of the $\dot{V}O_2$ response was considered. From the time-$\dot{V}O_2$ plot the time at which the kinetic phase ended and, if present, the plateau phase began was determined. The corresponding work rates were then calculated. $\dot{V}O_2$ was plotted against work rate and a linear line of best fit was fitted to the data excluding the kinetic and plateau phases. The slope of the line provided the $\Delta\dot{V}O_2/\Delta WR$ of the exercise ($ml.min^{-1}.W^{-1}$).

Peak Heart Rate

The Polar Precision Software used for analysis provided a 15 or 30 second average of the HR response if the duration of the exercise session was less than 30 minutes or 30–60 minutes respectively. HR_{peak} was recorded as the highest HR prior to achievement of the limit of tolerance.

3.5.2 Constant Load Exercise Test

Editing

The editing procedure performed on the breath-by-breath data of the SETs was identical to that outlined in Section 3.5.1 with the following exception:

- **Step 6: Recovery Phase.** A linear line of best fit, gradient set by software, was fitted to B_f, T_I, T_E, $F_{ET}O_2$, $F_{ET}CO_2$. If the profile of the response allowed, an exponential line of best fit was fitted to V_T. If an exponential line could not be fitted a linear line of best fit was fitted to the data. 95% prediction bands were set around the mean response of these variables and outliers were removed. An exponential line of best fit was then fitted to $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}_E$. If this was not possible a linear line, gradient set by software, was fitted. A linear line was also fitted to the RER response. 95% prediction bands were set around the mean response and outliers removed.

Kinetics

In order to determine a subject's $\tau\dot{V}O_2$ response from rest to exercise at a treadmill speed and gradient of 0.15 $m.s^{-1}$, 0% gradient respectively, the phase II response was isolated. This was done by excluding the phase I response, taken to be the first 20 seconds of the response, from the fitting window [95]. As discussed in Section 1.6.4, the increasing $\dot{V}O_2$ which occurs during phase I is a consequence of increased blood flow. Including phase I data in the analysis will therefore distort the fit of the actual response to the exercise.

When fitting the exponential line to the response, the fitting window was set from 20 seconds post exercise onset to the end of the constant load phase of the test. The equation used for the exponential fit was:

$$y = P1 + dss \cdot (1 - exp(-(x - d)/\tau)) \tag{3.6}$$

where

- $P1$ = starting value (mean response of previous phase)
- dss = difference between the start and end value
- d = delay (20 seconds from phase onset)
- τ = time constant

The τ value obtained represents the time taken for $\dot{V}O_2$ to reach 63% of its steady state value.

The same process was used to determine $\tau\dot{V}O_2$ for the recovery phase of the test.

Increase in Oxygen Uptake from Rest to Steady-state Exercise

To determine the increase in oxygen uptake from rest to steady-state exercise ($\Delta\dot{V}O_2$) for each test, the average of all the breaths in the final 60 seconds of the rest phase was subtracted from the average of all the breaths in the final 60 seconds of the exercise phase.

3.5.3 15 Minute Distance Test

During the 15 minute distance test the distance walked by the subject was displayed on the treadmill data monitor. Following completion of the test this distance was recorded.

3.5.4 Twitch Test

Following completion of each test the force trace produced during each contraction was plotted using Matlab (version 7.0.4, The MathWorks Inc) and the maximum voluntary and total force produced were determined. From the three contractions performed for each muscle at each test point, the contraction which produced the highest voluntary force was used for analysis. The CAR was calculated as shown in Equation (3.7).

$$CAR = \frac{MVC\ force}{total\ force} \tag{3.7}$$

where

- CAR = central activation ratio
- $MVC\ force$ = force produced during a maximum voluntary contraction
- $total\ force$ = summation of the force produced during a maximum voluntary contraction plus the additional force produced when the stimulation was applied.

3.5.5 Bone Mineral Density

The manufacturer's software (XCT 550, Stratec Medizintechnik, Pforzheim, Germany) was used to analyse the pQCT scans. From the epiphyseal slices (4% scan sites) bone cross-sectional area (CSA), bone mass, trabecular BMD and total BMD were obtained. A contour algorithm with thresholds of 180 mg/cm^3 in the distal tibia, 150 mg/cm^3 in the proximal tibia and 130 mg/cm^3 in the distal femur was used to find the periosteal surface of each bone's epiphysis [10] and thus determine total bone mass, CSA and BMD. In order to calculate trabecular BMD, concentric pixel layers were peeled off the bone's perimeter until the central 45% area of the total bone CSA was left. The bone parameters obtained from the diaphyseal slices (14%, 25% and 38% sites) were: bone CSA, cortical bone CSA, cortical BMD and polar strength-strain index (SSIpol). A contour algorithm with a threshold of 280 mg/cm^3 identified the periosteal surface of the diaphysis and the bone mass, total CSA and SSIpol

were calculated. Cortical bone was identified using the standard manufacturer's threshold of 710 mg/cm^3 and the cortical BMD and cortical CSA were calculated.

Chapter 4

Case Study - Subject A

4.1 Chapter Summary

The response of 4 key indices of cardiopulmonary fitness (peak oxygen uptake ($\dot{V}O_{2peak}$), lactate threshold (LT), slope of $\dot{V}O_2$ as a function of work rate ($\Delta\dot{V}O_2/\Delta WR$) and $\dot{V}O_2$ kinetics ($\tau\dot{V}O_2$)) to 16 weeks body weight supported treadmill training (BWSTT) in 1 incomplete spinal cord injured (SCI) subject are reported and discussed in this chapter. Also reported is the effect of the BWSTT on training performance, peak work rate (WR_{peak}), peak heart rate (HR_{peak}) and the oxygen uptake ($\dot{V}O_2$) and heart rate (HR) associated with a step increase in work rate. The effect of the training on the distance subject A could walk in 15 minutes as well as on lower limb muscle and bone strength is also reported.

Throughout the training period the duration and work rate of the training increased substantially: duration and treadmill speed doubled and treadmill gradient increased 100%. The WR_{peak} achieved during the incremental exercise test (IET) continued to increase at each test point (TP) (1.41–9.37 W). $\dot{V}O_{2peak}$ did increase substantially (8.23–10.19 $ml.kg^{-1}.min^{-1}$) although not continually, as did HR_{peak} (89–119 bpm). A large decrease in the $\Delta\dot{V}O_2/\Delta WR$ during the IET (115–29.03 $ml.min^{-1}.W^{-1}$) occurred with training. At no TP was an LT detected from the IET. During the constant load (step) exercise test (SET) a τ value could either not be obtained or the value obtained indicated that the subject's $\dot{V}O_2$ did not reach a steady-state. However, the average $\dot{V}O_2$ in the final 20 seconds of the test did decrease substantially (10.07–6.89 $ml.kg^{-1}.min^{-1}$). The peak voluntary force obtained by subject A with her right quadriceps muscles consistently increased at each TP. For the left quadriceps muscles and the left and right hamstring muscles such a response was not found for either the peak voluntary force or the central activation ratio (CAR). The BMD of the epiphyses and the cortical cross sectional area (CSA) of the diaphysis of the tibia and femur consistently decreased throughout the training period. By completion of the study the distance that subject A could walk in 15 minutes increased by ~100%.

The results obtained from the IETs suggest that a true indication of subject A's peak cardiopulmonary capacity was not obtained. It is likely that the tests were limited peripherally, by subject A's ability to maintain a functional gait pattern, rather than centrally by the cardiopulmonary system. Alterations in gait pattern and highly fatiguable lower limb muscles may also have been responsible for the fact that $\dot{V}O_2$ did not stabilise during the SET. This may have also affected her performance in the 15 minute distance test. Although the results obtained were positive, the distance subject A could walk on a particular day would be dependent on her ability to maintain a functional gait pattern. Variable subject performance is also likely to have affected the measurement of the peak voluntary muscle force and CAR. The testing method used to measure bone strength in the lower limbs is unaffected by subject performance. The intensity of training was not sufficient to reverse the natural decline associated with someone in the early stages post-injury (2 years).

The results of this study suggest that standard methods of exercise testing can be adapted for use with an incomplete SCI subject. Although unable to provide a true indication of cardiopulmonary capacity, the tests were able to detect major performance improvements and training effects. Further investigation is however required to determine the repeatability and reliability of the outcome measures obtained.

4.2 Method Deviations

The testing protocols and analysis of the data obtained for subject A were carried out as outlined in Chapter 3 with the following exceptions:

- Subject A was unable to walk at the range of speeds and gradients required to perform the Porszasz IET protocol. Therefore, at each TP only one IET was carried out: constant speed and linear increase in gradient.

- Subject A was unable to stand stationary for the duration of the standing rest phase. Her legs appeared to be too weak to support her for that period of time: she would repeatedly lift herself up on the parallel bars. Therefore, during this phase subject A relaxed into the harness, allowing it to support her whole body weight. The cardiopulmonary data obtained during this phase is therefore not reflective of the physiological stress placed on the subject during upright standing.

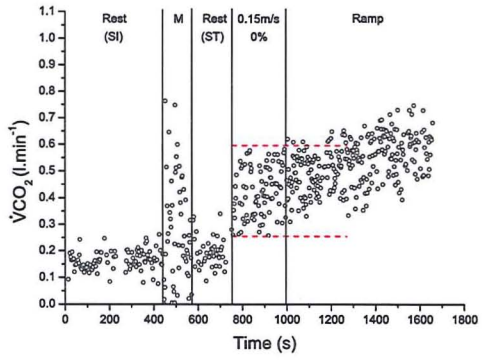
- As discussed in Section 3.5.1, it is important to remove the kinetic phase of the ramp data when determining the point of deflection on the V-slope. This is carried out by removing the data points which occurred prior to the point at which $\dot{V}CO_2$ increased

above the previous phase response. However, accurate and consistent determination of this phase from subject A's IETs was difficult (see Table 4.1).

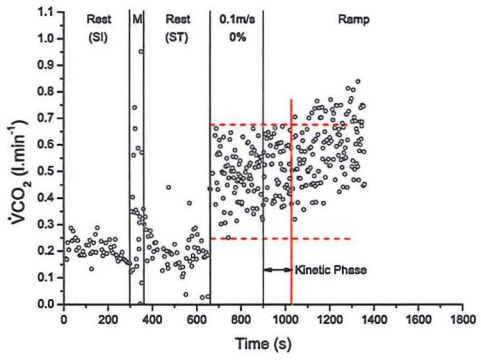
IET	TP1 (week 0)	TP2 (week 5)	TP3 (week 9)	TP4 (week 13)	TP5 (week 17)
Kinetic phase duration (s)	134	NA	132	90	170

Table 4.1: Duration of the kinetic phase during subject A's incremental exercise test at each test point. IET: incremental exercise test. TP: test point. NA: no value was obtained.

In some instances the kinetic phase could not be determined (see Figure 4.1(a)) and in other cases it appeared to last for a significant percentage of the total ramp phase duration (see Figure 4.1(b)). The kinetic phase was therefore not excluded from the V-slope analysis. This also applied when determining the slope of $\dot{V}O_2$ as a function of work rate ($\Delta\dot{V}O_2/\Delta WR$): a linear line of best fit was fitted through all the data points in the WR-$\dot{V}O_2$ plot.



(a) Kinetic phase could not be determined. The $\dot{V}CO_2$ data begins to increase immediately at the start of the ramp phase.



(b) Kinetic phase comprises a significant percentage of the total duration of the ramp phase.

Figure 4.1: An example of a long and short duration kinetic phase. The duration of the kinetic phase is the time between the start of the ramp phase and the point at which $\dot{V}CO_2$ increases above the previous phase response (indicated by a solid red line). SI: sitting. M: moving. ST: standing. Edited plots.

- When determining $\dot{V}O_2$ at rest during both the IETs and SETs, the first 90s of data were excluded from the analysis to include only data which had attained a steady-state. At the start of each rest phase the $\dot{V}O_2$ fell prior to stabilising, possibly as the subject adjusted to the new conditions.
- During the SET at TP2 and TP5, $\dot{V}O_2$ began to increase prior to the start of the

walking phase. Therefore, the final 20s and 60s respectively of the standing rest phase data was excluded from the analysis.

- As subject A was 2 years post-injury when the study commenced the BMD of her lower limbs was still in the phase of decline [10]. Consequently, an additional bone scan was performed before the start of the formal training period (baseline).

- During week 16 of training, subject A did not complete all of her training sessions due to illness. Therefore, the cardiopulmonary and 15 minute distance tests scheduled for week 17 were not carried out. It took a further 3 weeks for subject A to achieve the previous training intensity and, in accordance with the training protocol, only at that point did counting of the training weeks recommence. Following one full week of training at the previous intensity, subject A completed what was her 16th week of training and therefore the cardiopulmonary and distance testing could be carried out. Although at reduced intensity, subject A did continue to train during this period which may have affected her walking ability, muscle strength and bone parameters. Therefore, for analysis of the 15 minute distance test and the muscle and bone data, subject A effectively performed 20 weeks of treadmill training.

4.3 Results

4.3.1 Training Performance

The speed and gradient at which subject A trained in the two sessions prior to each TP are shown in Table 4.2. Prior to TP1 subject A had achieved the pre-specified target of 15 minutes continuous walking at 0.10 $m.s^{-1}$, 0%. An increase in the training speed and gradient occurred prior to TP2 and again before TP3. Following this, the speed during speed training sessions remained at 0.20 $m.s^{-1}$ and the gradient during the gradient sessions at 1%.

Test Point	TP1 (week 0)	TP2 (week 5)	TP3 (week 9)	TP4 (week 13)	TP5 (week 17)
Speed ($m.s^{-1}$)	0.10	0.15	0.20	0.20	0.20
Gradient (%)	0.00	0.50	1.00	1.00	1.00
Duration (mins)	15	15	25	30	30

Table 4.2: The duration and corresponding training speed and gradient of the final speed and gradient training sessions prior to each test point. The treadmill gradient during speed training sessions remained at 0% throughout the training programme and the treadmill speed during the gradient training sessions remained at 0.15$m.s^{-1}$. TP: test point.

4.3.2 Maximal Incremental Exercise Test

The speed and incrementation rate chosen for each IET are provided in Table 4.3. The speed of the test was increased to 0.15 $m.s^{-1}$ at TP2 as subject A felt confident in her ability to walk at that speed for the duration of the test. Despite an increase in the training speed to 0.2 $m.s^{-1}$ by TP3, subject A did not feel confident walking at this speed with an increasing gradient. Therefore, the treadmill speed remained at 0.15 $m.s^{-1}$ for the remaining tests. The incrementation rate was chosen by the investigator with the aim of ensuring that the subject reached their limit of tolerance in 8-12 minutes [197].

IET	TP1 (week 0)	TP2 (week 5)	TP3 (week 9)	TP4 (week 13)	TP5 (week 17)
Speed ($m.s^{-1}$)	0.10	0.15	0.15	0.15	0.15
Incrementation rate (%/min)	0.4	0.4	0.5	0.8	1.1

Table 4.3: Constant treadmill speed and the gradient incrementation rate during each incremental exercise test. IET: incremental exercise test. TP: test point.

The key outcome measures for each IET are shown in Table 4.4.

IET	TP1 (week 0)	TP2 (week 5)	TP3 (week 9)	TP4 (week 13)	TP5 (week 17)
Ramp duration (s)	465	668	643	740	770
$\dot{V}O_{2peak}$ ($l.min^{-1}$)	0.58	0.63	0.86	0.65	0.71
$\dot{V}O_{2peak}$ ($ml.kg^{-1}.min^{-1}$)	8.23	8.82	12.13	9.17	10.19
$\dot{V}O_2$ at LT ($l.min^{-1}$)	NA	NA	NA	NA	NA
WR at LT (W)	NA	NA	NA	NA	NA
$\Delta\dot{V}O_2/\Delta WR$ ($ml.min^{-1}.W^{-1}$)	115	43.23	88.21	30.76	29.03
HR_{peak} (bpm)	89	105	127	110	119
Peak Gradient (%)	3.1	4.4	5.4	9.8	14.1
WR_{peak}	1.41	3.10	3.69	6.76	9.37
Seated resting $\dot{V}O_2$ ($l.min^{-1}$)	0.17	0.22	0.20	0.18	0.19
Standing resting $\dot{V}O_2$ ($l.min^{-1}$)	0.19	0.24	0.23	0.24	0.19

Table 4.4: Key outcome measures for subject A's incremental exercise test at each test point. IET: incremental exercise test. TP: test point. $\dot{V}O_{2peak}$: peak oxygen uptake. LT: lactate threshold. $\Delta\dot{V}O_2/\Delta WR$: slope of oxygen uptake as a function of work rate. HR_{peak}: peak heart rate. WR_{peak}: peak work rate.

Peak Work Rate

The peak gradient achieved by subject A at each TP increased with training, and consequently, as can be seen in Figure 4.2, so did the WR_{peak} obtained.

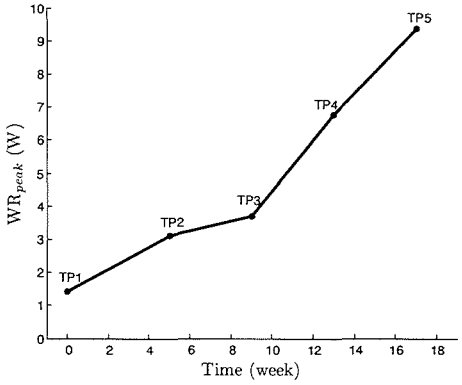


Figure 4.2: WR_{peak} achieved during subject A's incremental exercise test at each test point. TP: test point.

Peak Oxygen Uptake

Despite the increasing WR_{peak} at each TP, a corresponding increase in $\dot{V}O_{2peak}$ did not always occur. As can be seen in Figure 4.3, following a large increase in the $\dot{V}O_{2peak}$ obtained at TP3, the $\dot{V}O_{2peak}$ obtained at TP4 was reduced to almost the same level as at TP2. A further increase was shown to occur at TP5. However, it did not achieve the value obtained at TP3.

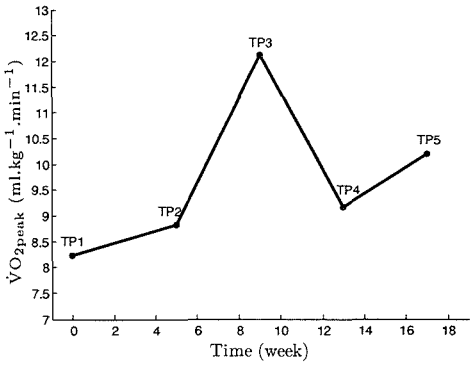


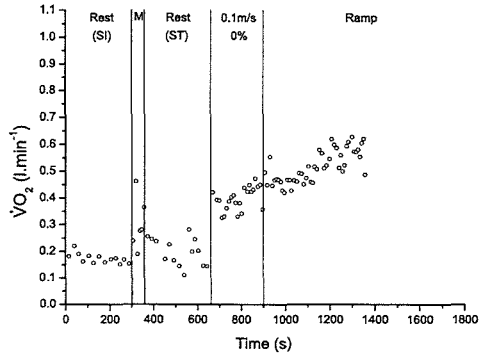
Figure 4.3: $\dot{V}O_{2peak}$ obtained during subject A's incremental exercise test at each test point. TP: test point

The $\dot{V}O_2$ profiles for each of subject A's IETs are shown in Figure 4.4. With the exception

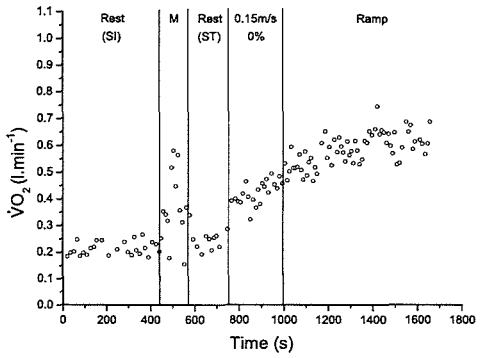
of TP3 and TP5 the $\dot{V}O_2$ responses in the ramp phase of the test do not appear to be particularly linear in response to the linear increase in work rate (see also Table 4.5).

IET	TP1	TP2	TP3	TP4	TP5
R^2	0.44	0.39	0.68	0.59	0.69

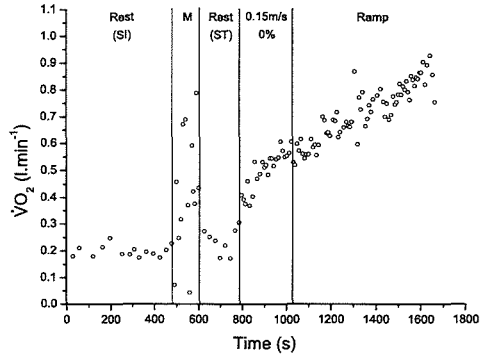
Table 4.5: Linearity of the $\dot{V}O_2$ response during each of Subject A's incremental exercise tests represented by the correlation coefficient (R^2). IET: incremental exercise test. TP: test point.



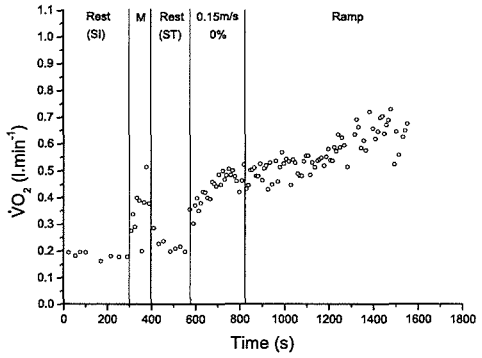
(a) TP1



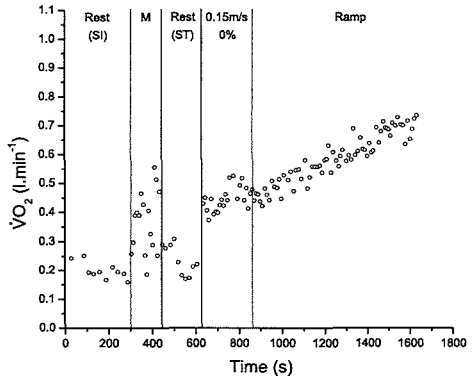
(b) TP2



(c) TP3



(d) TP4



(e) TP5

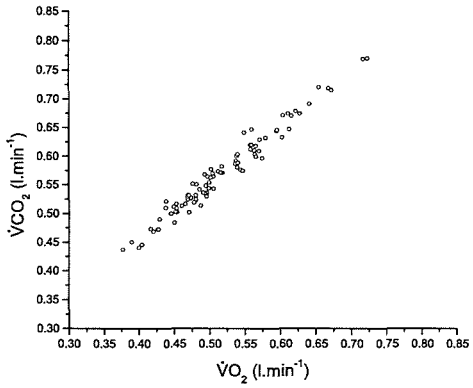
Figure 4.4: $\dot{V}O_2$ profile for subject A's incremental exercise test at each test point. SI: sitting. M: moving. ST: standing. TP: test point. 4 breath average plots.

Lactate Threshold

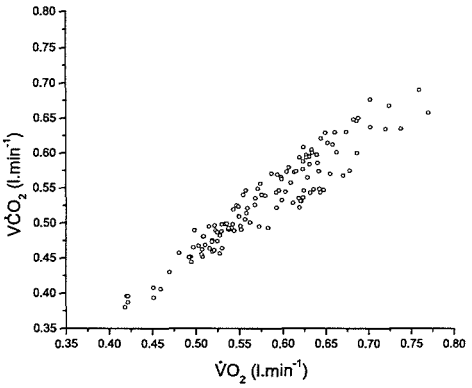
The $\dot{V}O_2$ at which the LT occurred during each test was estimated using the non-invasive V-slope method [78] and supported by the responses of $\dot{V}_E/\dot{V}O_2$, $\dot{V}_E/\dot{V}CO_2$, $F_{ET}O_2$ and $F_{ET}CO_2$ [79]. However, as is stated in Table 4.4 the presence of an LT was not identified during any of subject A's IETs. As can be seen in Figure 4.5, no detectable deflection point is present in any of the V-slope plots.

The responses of the supporting respiratory variables are also not indicative of the presence of an LT (Figures 4.6 and Appendix A). During the ramp phase of an IET $\dot{V}_E/\dot{V}O_2$ is expected to fall gradually and level off before increasing at the point of the LT. Only at TP5 (Figure 4.6(a)) does the response follow such a pattern and thus suggest the presence of an LT. As $\dot{V}_E$ is closely coupled to $\dot{V}CO_2$, an increase in $\dot{V}_E/\dot{V}CO_2$ does not occur at the LT. The $\dot{V}_E/\dot{V}CO_2$ response is expected to fall gradually and have reached a steady-state at the point of the LT before increasing again at the respiratory compensation point (RCP). At TP1, $\dot{V}_E/\dot{V}CO_2$ is falling and does, as expected, begin to reach a steady-state. However, at no other TP does the $\dot{V}_E/\dot{V}CO_2$ profile display the expected response. The $\dot{V}_E/\dot{V}O_2$ and $\dot{V}_E/\dot{V}CO_2$ responses to the ramp increase in work rate are not, with two exceptions, the standard responses expected from an able-bodied (AB) subject. At TP1 and TP5 where the $\dot{V}_E/\dot{V}O_2$ or $\dot{V}_E/\dot{V}CO_2$ responses are as expected, the corresponding variable does not show the standard response and therefore does not support the presence of an LT.

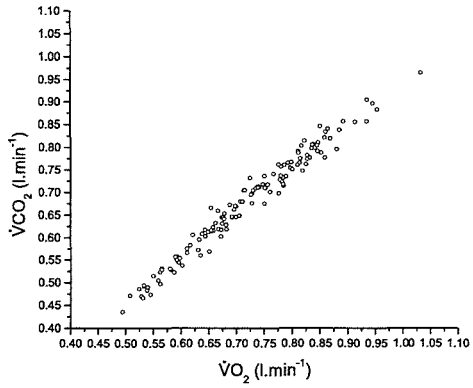
A similar situation is also found with the $F_{ET}O_2$ and $F_{ET}CO_2$ responses to the increasing work rate. $F_{ET}O_2$ is expected to fall and reach a steady-state prior to the LT. At the point of the LT $F_{ET}O_2$ increases as $\dot{V}_E$ increases disproportionately to $\dot{V}O_2$. Only at TP5 (Figure 4.6(c)) does the $F_{ET}O_2$ response suggest the presence of an LT. None of the $F_{ET}CO_2$ responses reflect that which would be expected if an LT was present: increasing prior to and attaining a steady-state at the point of the LT, then decreasing again at the RCP.



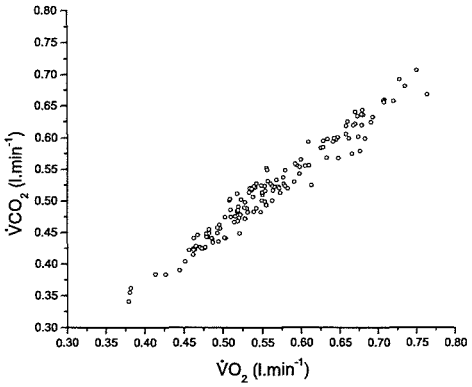
(a) TP1



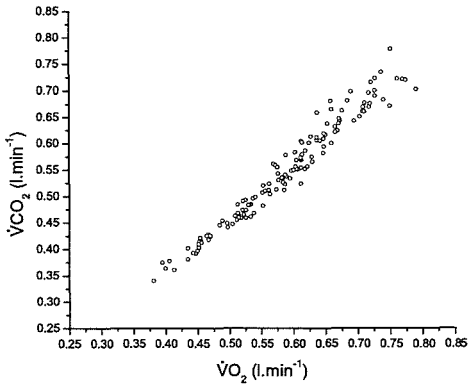
(b) TP2



(c) TP3

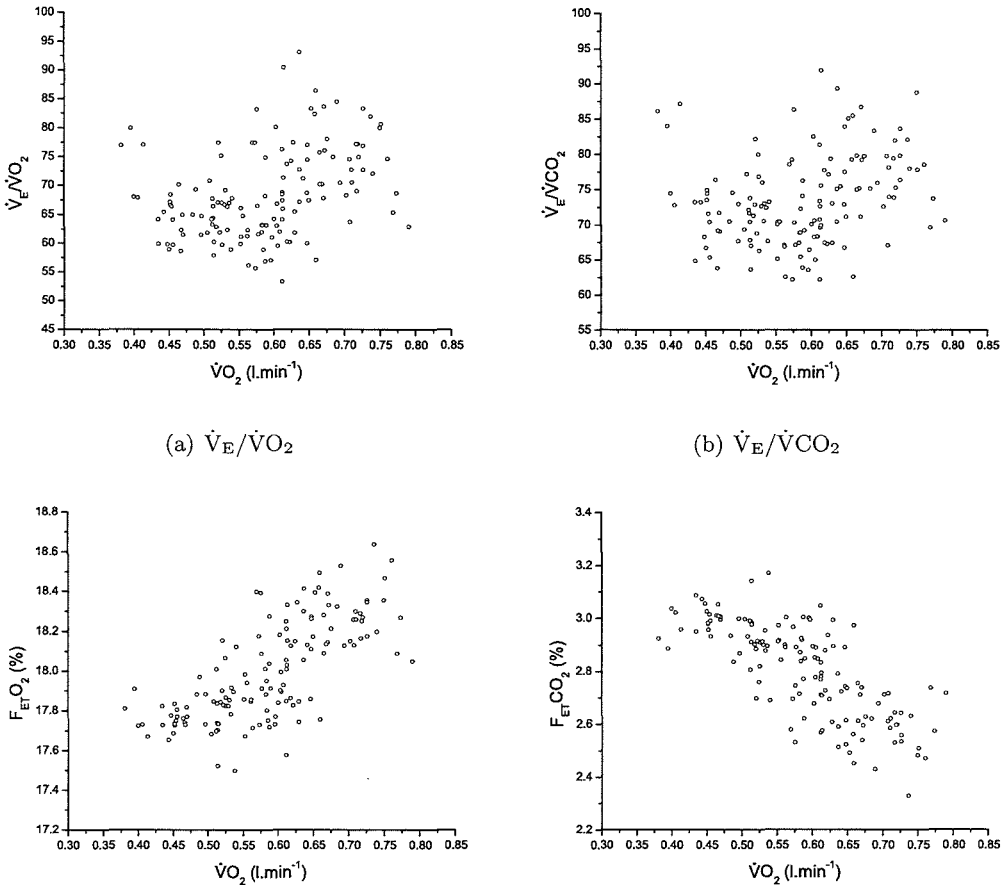


(d) TP4



(e) TP5

Figure 4.5: V-slope plots for each of subject A's incremental exercise tests. Kinetic phase not removed. 2 breath average plots.



(a) $\dot{V}_E/\dot{V}O_2$ (b) $\dot{V}_E/\dot{V}CO_2$

(c) $F_{ET}O_2$ (d) $F_{ET}CO_2$

Figure 4.6: Respiratory variable responses during the ramp phase of the incremental exercise test at test point 5. Kinetic phase not removed. 2 breath averaged plots.

Slope of Oxygen Uptake as a function of Work Rate

With the exception of TP3, the $\Delta\dot{V}O_2/\Delta WR$ of walking during the IET decreased with training. As can be seen in Figure 4.7 there is a quite dramatic decrease in the $\Delta\dot{V}O_2/\Delta WR$ following the first 4 weeks of training. However, at TP3 it increases again before decreasing for the rest of the training period.

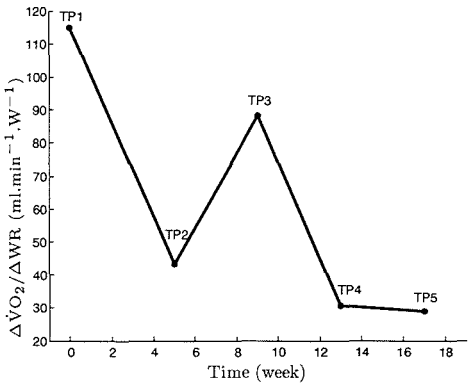
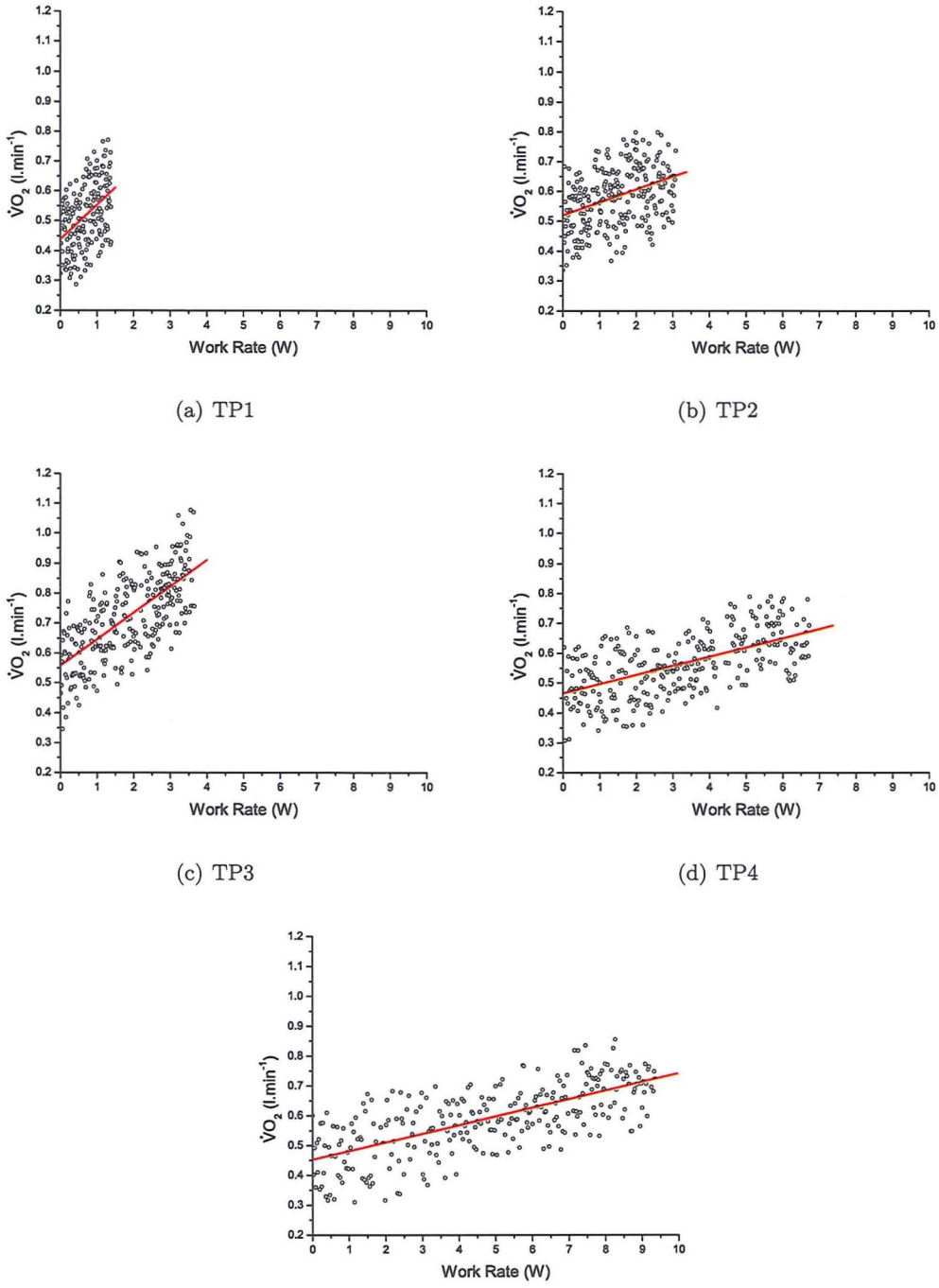


Figure 4.7: The $\Delta\dot{V}O_2/\Delta WR$ obtained during subject A's incremental exercise test at each test point. TP: test point.

As can be seen in Figure 4.8(c) the increase in the $\Delta\dot{V}O_2/\Delta WR$ at TP3 is a consequence of a large increase in the $\dot{V}O_2$ response to the exercise without a large increase in the WR_{peak} achieved.



(a) TP1

(b) TP2

(c) TP3

(d) TP4

(e) TP5

Figure 4.8: The $\Delta\dot{V}O_2/\Delta WR$ for subject A's incremental exercise test at each test point, represented by the slope of the straight line fit.

Peak Heart Rate

As can be seen in Figure 4.9, the increase in HR_{peak} achieved by subject A during her IET did not increase continually from TP1–5: the highest HR_{peak} was achieved at TP3. However, following 16 weeks of BWSTT the HR_{peak} achieved by subject A did increase substantially from 89–119 bpm (31%).

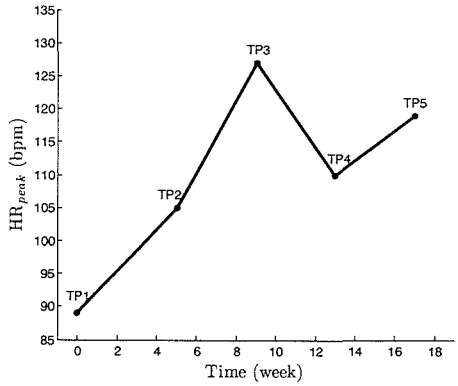


Figure 4.9: Peak heart rate achieved during subject A's incremental exercise test at each test point. HR_{peak}: peak heart rate. TP: test point.

4.3.3 Constant Load Exercise Test

At each TP the speed and gradient of the SET remained at 0.15 $m.s^{-1}$, 0% respectively to allow a direct comparison of the response kinetics and thus determine their adaptation to training. The key outcome variables for each test are provided in Table 4.6 and the $\dot{V}O_2$ response profiles are shown in Figure 4.11.

As can be seen in Figure 4.11, the $\dot{V}O_2$ response to the step increase in work rate did not attain a steady-state, at any TP, by the end of the exercise phase. No τ value was obtained at TP1 and TP3 as there was not an exponential profile to the response. The unexpectedly high τ values obtained at TP2, 4 and 5 are indicative of a response which has not reached steady-state. The τ values obtained do not decrease with training, showing no pattern to their response.

Due to the fact that the $\dot{V}O_2$ response did not reach a steady-state during any of the tests, $\Delta\dot{V}O_2$ could not be determined. The final 20s of the $\dot{V}O_2$ response was averaged for each test to provide an indication of the $\dot{V}O_2$ at the end of each test. As can be seen in Figure

SET	TP1 (week 0)	TP2 (week 5)	TP3 (week 9)	TP4 (week 13)	TP5 (week 17)
Step duration (s)	755	900	900	900	900
Step $\dot{V}O_2$ (final 20s) ($l.min^{-1}$)	0.71	0.62	0.60	0.53	0.48
Step $\dot{V}O_2$ (final 20s) ($ml.kg^{-1}.min^{-1}$)	10.07	8.68	8.46	7.48	6.89
HR_{peak} (bpm)	98	97	106	90	87
$\Delta\dot{V}O_2$ ($l.min^{-1}$)	NA	NA	NA	NA	NA
$\tau\dot{V}O_2$ (s)	NA	572.46	NA	300.58	549.18
Speed ($m.s^{-1}$)	0.15	0.15	0.15	0.15	0.15
Gradient (%)	0	0	0	0	0
Seated resting $\dot{V}O_2$ ($l.min^{-1}$)	0.19	0.20	0.19	0.19	0.17
Standing resting $\dot{V}O_2$ ($l.min^{-1}$)	0.19	0.22	0.21	0.23	0.21

Table 4.6: Key outcome variables for subject A's constant load (step) exercise test at each test point. SET: step exercise test. $\Delta\dot{V}O_2$: increase in oxygen uptake from rest to steady state. $\tau\dot{V}O_2$: time constant for oxygen uptake. NA: no value was obtained.

4.10, this decreased with training.

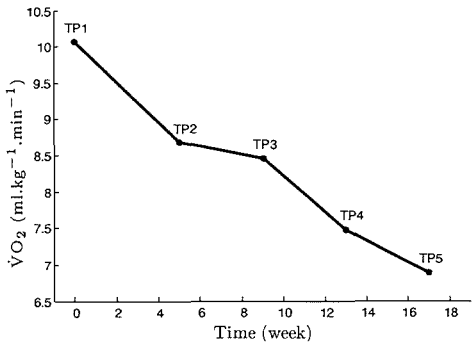
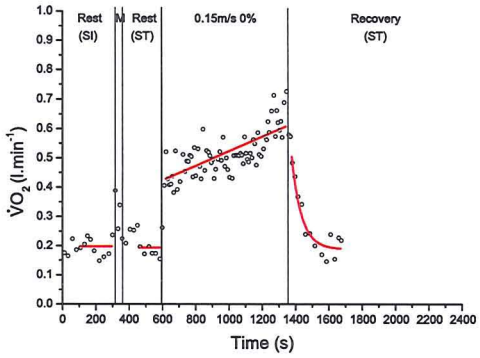
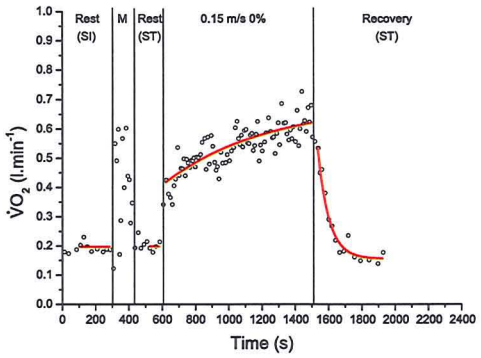


Figure 4.10: $\dot{V}O_2$ during the final 20 seconds of subject A's constant load (step) exercise test at each test point. TP: test point.

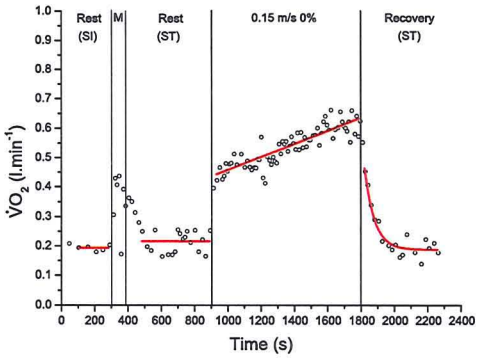
It is evident that the HR response to the step increase in work rate did not stabilise but, like the $\dot{V}O_2$ response, continued to increase throughout (see Figure 4.12). The HR_{peak} during each test is provided in Table 4.6.



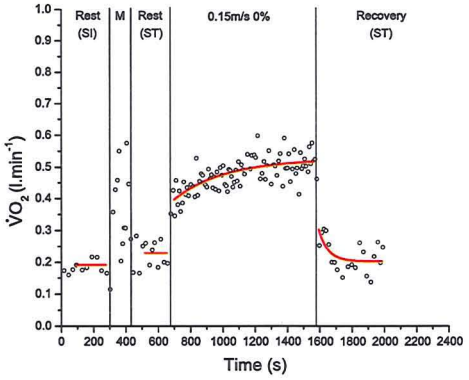
(a) TP1



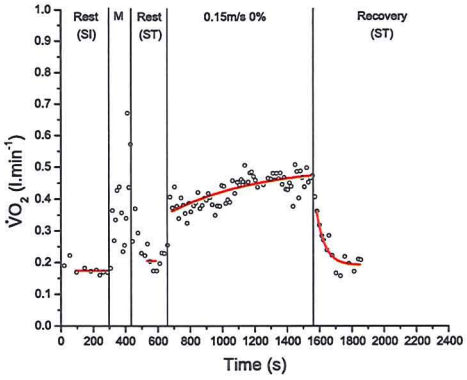
(b) TP2



(c) TP3

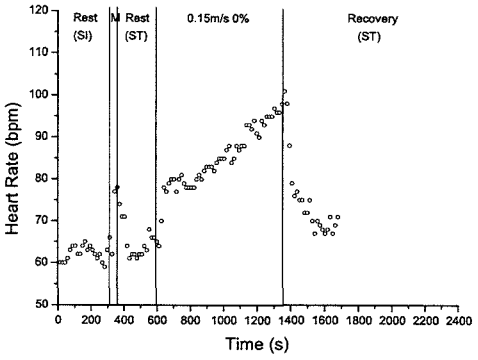


(d) TP4

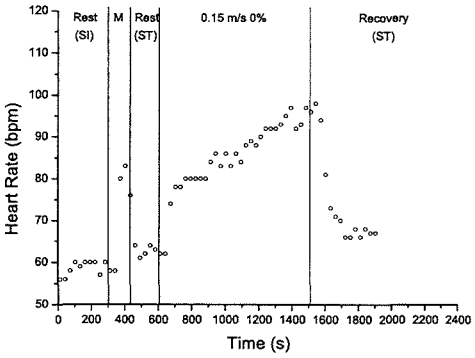


(e) TP5

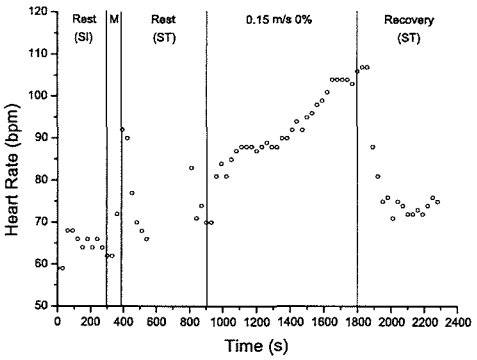
Figure 4.11: $\dot{V}O_2$ profile for subject A's constant load (step) exercise test at each test point. SI: sitting. M: moving. ST: standing. TP: test point. 4 breath average plots.



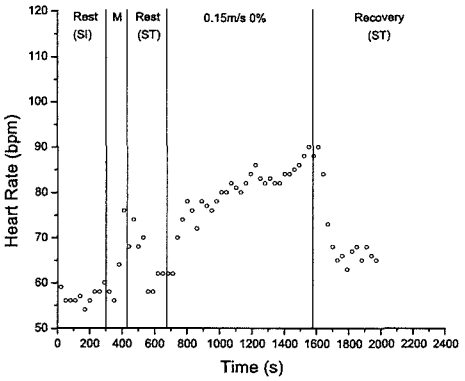
(a) TP1



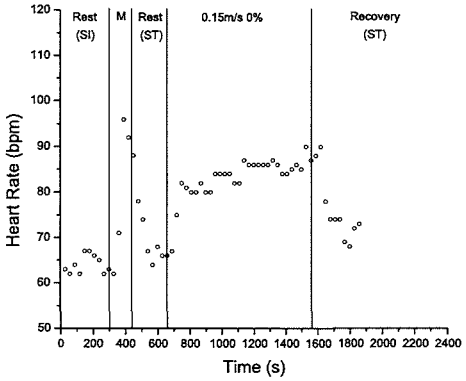
(b) TP2



(c) TP3



(d) TP4



(e) TP5

Figure 4.12: HR profile for subject A's constant load (step) exercise test at each test point. M: moving. TP: test point.

4.3.4 15 Minute Distance Test

As can be seen in Table 4.7, the speeds chosen by subject A for the 15 minute distance test increased at each TP. Consequently, following 5 months of BWSTT, the distance achieved in 15 minutes increased by ~100%.

Distance Test	TP1 (week 0)	TP2 (week 5)	TP3 (week 9)	TP4 (week 13)	TP5 (week 21)
Speed ($m.s^{-1}$)	0.10	0.15	0.15–0.20	0.20	0.20–0.24
Distance (m)	94	135	177	179	191

Table 4.7: Walking speed and distance achieved by subject A during the 15 minute distance test at each test point. TP: test point.

4.3.5 Twitch Test

Right Hamstring Muscle at 90^o flexion

The key outcome measures for the right hamstring muscle test at 90^o of flexion at each TP are provided in Table 4.8. The corresponding force traces are shown in Figure 4.13.

At all TPs the contraction which produced the highest voluntary force also produced the highest total force when the stimulation was applied to the contracting muscle. The peak voluntary force provided in Table 4.8 for each TP represents the maximum force prior to the delivery of the stimulation. However, as can be seen in Figure 4.13 subject A was unable to maintain a steady-state voluntary force and therefore the peak voluntary force reported does not always correspond to the force produced immediately prior to stimulation delivery.

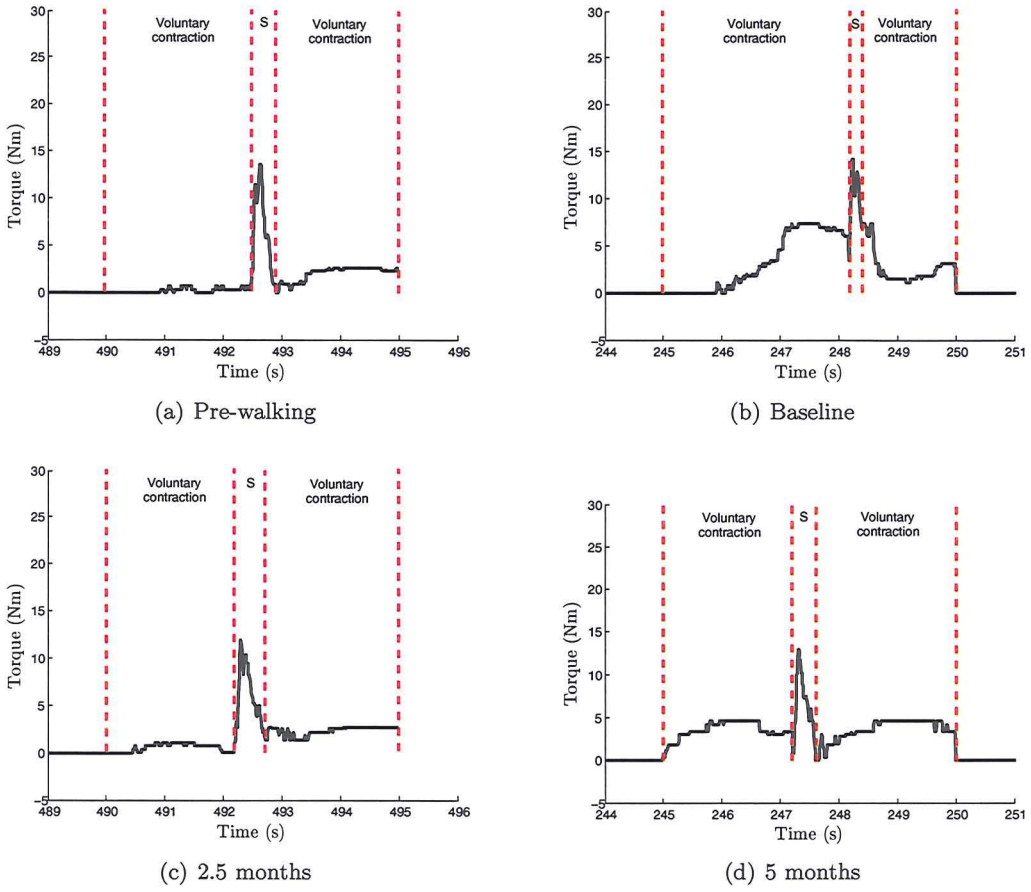
Test	Pre-walking	Baseline	2.5 months	5 months
Peak voluntary force (Nm)	0.70	7.30	1.10	4.60
Peak total force (Nm)	13.60	14.20	11.90	13.00
CAR	0.05	0.51	0.09	0.35

Table 4.8: Key outcome measures for subject A's right hamstring test at 90^o of flexion, at each test point. CAR: central activation ratio.

Throughout the duration of the training period, ~7 months, the peak voluntary force that subject A could produce with her right hamstring positioned at 90^o of flexion appears to have increased. However, the maximum peak voluntary force over the whole training period (7.30 Nm) was produced at baseline prior to the formalised 5 month training period. The maximum peak total force and central activation ratio (CAR) were also produced at this TP.

There is great variation in the CAR between TPs (0.05–0.51), with the CAR at 2.5 months being approximately equal to the CAR produced prior to any walking training.

As can be seen in Figure 4.13, the voluntary force produced following delivery of the stimulation is, at pre-walking and at 2.5 months, higher than that produced prior to its stimulation.



(a) Pre-walking

(b) Baseline

(c) 2.5 months

(d) 5 months

Figure 4.13: Force trace profiles produced by subject A with the right hamstring positioned at 90^o of flexion. As indicated on each of the plots, subject A contracted her right hamstring for 2–3 seconds, a short stimulation burst (S) was then added following which subject A maintained her voluntary contraction for the remainder of the test.

Right Hamstring Muscle at 30^o flexion

The key outcome measures for the right hamstring test at 30^o of flexion at each TP are provided in Table 4.9 and the corresponding force trace profiles in Figure 4.14.

The contraction which produced the highest voluntary force at each test point also produced the highest total force. As can be seen in Figure 4.14, subject A was unable to maintain a steady-state contraction in her right hamstring at 30^o of flexion. Therefore, the peak voluntary force shown in Table 4.9 is not always representative of the force produced immediately prior to the stimulation delivery.

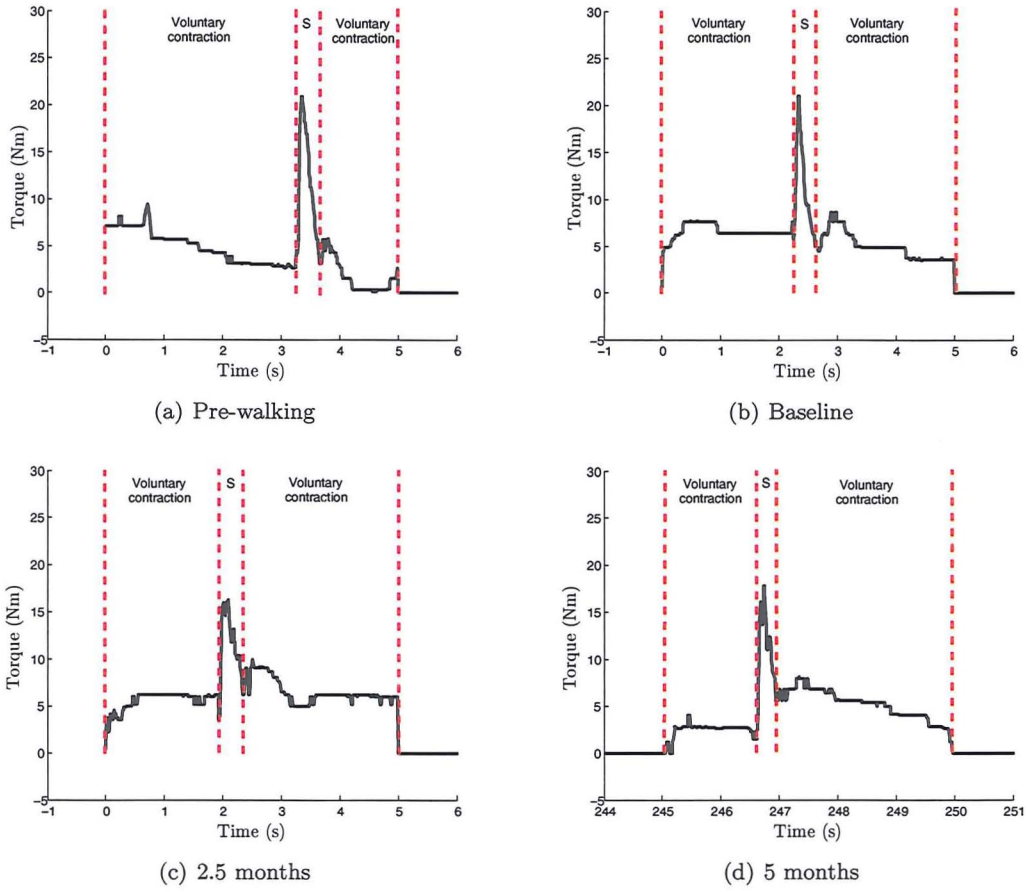
Test	Pre-walking	Baseline	2.5 months	5 months
Peak voluntary force (Nm)	9.50	7.10	6.20	4.10
Peak total force (Nm)	20.90	21.10	16.30	17.90
CAR	0.45	0.37	0.38	0.23

Table 4.9: Key outcome measures for subject A's right hamstring test at 30^o of flexion, at each test point. CAR: central activation ratio.

The peak total force produced by the hamstrings at 30^o of flexion is higher at each TP than when they are positioned at 90^o of flexion. This is not however the case for the peak voluntary force. At the pre-walking and 2.5 month stage the peak voluntary force produced by the hamstrings is significantly higher when positioned at 30^o of flexion compared to 90^o of flexion. However, at the baseline and 5 month test point the peak voluntary force produced is slightly less.

The peak voluntary force produced by subject A with the hamstrings positioned at 30^o of flexion is shown to decrease steadily with training from 9.50–4.10 Nm. With slight fluctuations, the peak total force and CAR have also been shown to decrease overall with training.

As can be seen in Figure 4.14, with the exception of the pre-walking test, the peak voluntary force produced after the delivery of the stimulation is higher than that produced before it.



(a) Pre-walking

(b) Baseline

(c) 2.5 months

(d) 5 months

Figure 4.14: Force trace profiles produced by subject A with the right hamstring positioned at 30^o of flexion. As indicated on each of the plots, subject A contracted her right hamstring for 2–3 seconds, a short stimulation burst (S) was then added following which subject A maintained her voluntary contraction for the remainder of the test.

Right Quadriceps Muscle at 90^o flexion

The key outcome measures for the right quadriceps test at each TP are provided in Table 4.10 and the corresponding force traces in Figure 4.15. No data is provided for the 5 month TP as subject A had skin damage on her thigh that was unrelated to the study. Therefore, the test was not performed. The contraction which produced the highest peak voluntary force also produced the peak total force at each TP.

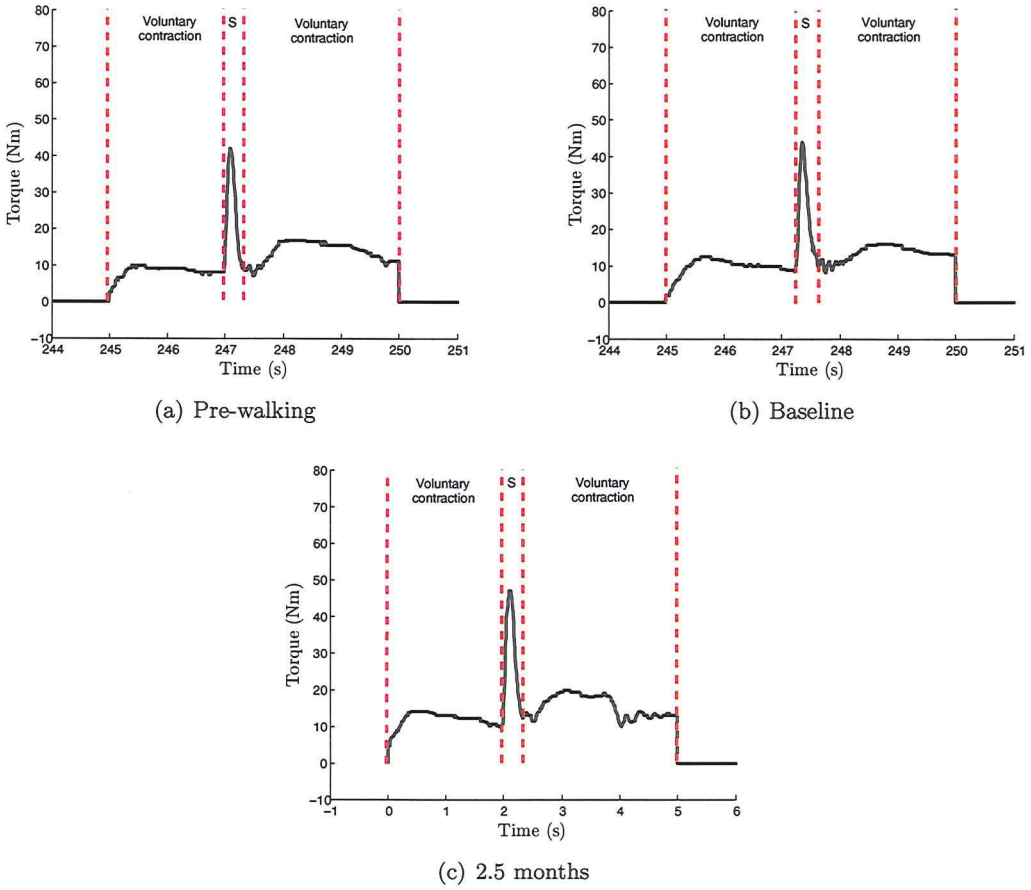
Test	Pre-walking	Baseline	2.5 months	5 months
Peak voluntary force (Nm)	9.90	12.60	14.20	NA
Peak total force (Nm)	42.00	43.70	47.10	NA
CAR	0.24	0.39	0.30	NA

Table 4.10: Key outcome measures for subject A's right quadriceps test at 90^o of flexion, at each test point. CAR: central activation ratio.

Although the voluntary force produced by subject A is more stable than for the hamstring tests, a steady-state contraction is still not maintained. Therefore, the peak voluntary force provided in the table does not always represent the force prior to delivery of the stimulation.

The peak voluntary and peak total force produced at each TP is higher than that produced for the hamstring muscle. From the pre-walking to the 2.5 month test the peak voluntary force and the peak total force that subject A could produce from their right quadriceps positioned at 90^o flexion increased steadily from 9.90–14.20 Nm and 42–47.10 Nm respectively. Despite the higher forces produced the CAR obtained at each TP is not higher than that produced by the hamstrings positioned at 30^o of flexion. An overall increase in the CAR of the right quadriceps did occur. However it peaked at baseline rather than at the 2.5 month TP.

As can be seen in Figure 4.15, the voluntary force produced after the stimulation delivery is consistently higher at all TPs.



(a) Pre-walking

(b) Baseline

(c) 2.5 months

Figure 4.15: Force trace profiles produced by subject A with the right quadriceps positioned at 90^o of flexion. As indicated on each of the plots, subject A contracted her right quadriceps for 2–3 seconds, a short stimulation burst (S) was then added following which subject A maintained her voluntary contraction for the remainder of the test.

Left Hamstring Muscle at 90° flexion

The key outcome measures for the left hamstring test at 90° of flexion at each TP are shown in Table 4.11 and the corresponding force traces in Figure 4.16.

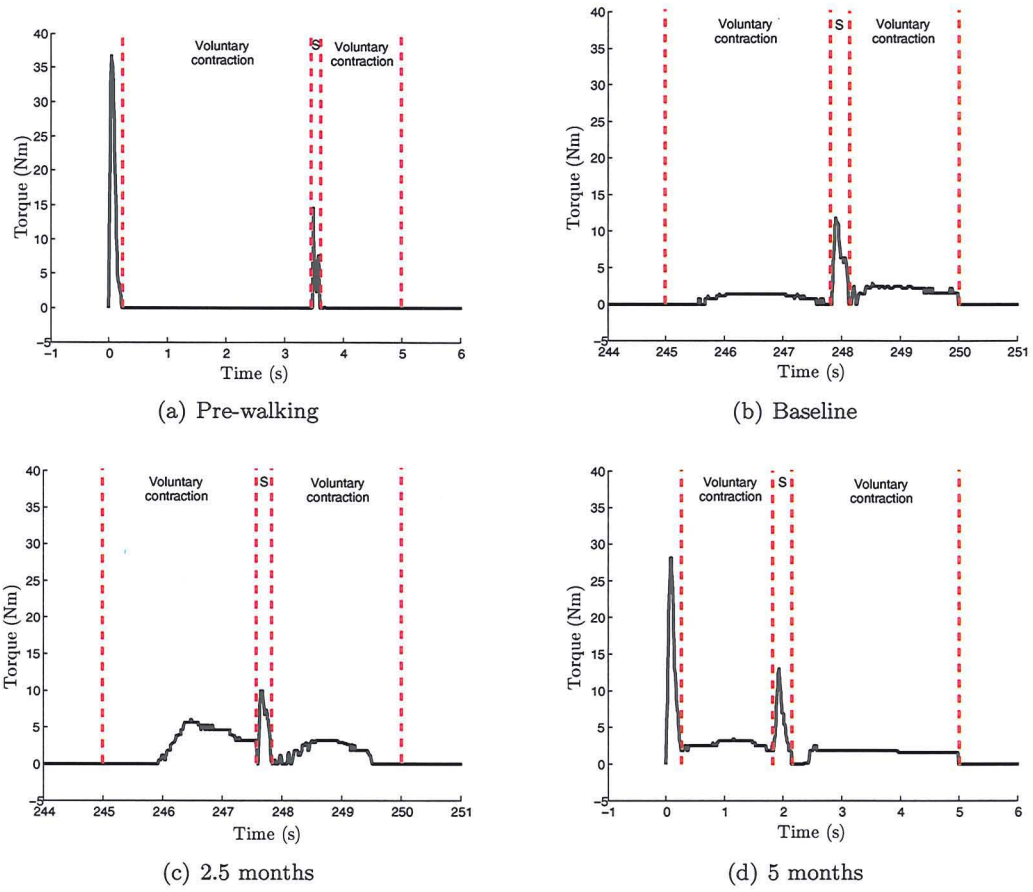
Test	Pre-walking	Baseline	2.5 months	5 months
Peak voluntary force (Nm)	0.00	1.40	6.10	3.30
Peak total force (Nm)	14.60	11.80	10.00	12.90
CAR	0.00	0.12	0.61	0.26

Table 4.11: Key outcome measures for subject A's left hamstring test at 90° of flexion, at each test point. CAR: central activation ratio.

The contraction which produced the highest voluntary force also produced the highest total force at all TPs except baseline (total force was 0.70 Nm lower than the maximum). As can be seen in Figure 4.16, subject A could not maintain a steady-state voluntary contraction. Therefore, the peak voluntary force does not always represent the voluntary force prior to stimulation delivery. The large peak forces at the start of the force trace for the pre-walking and 5 month tests were caused by the investigator moving the dynamometer arm to start the timer.

During the pre-walking test subject A was unable to produce any voluntary force with her left hamstring muscle at 90° of flexion. With training this increased, with the maximum force produced at 2.5 months. The CAR also increased, peaking at 2.5 months. The peak total force fluctuated between TPs.

As can be seen in Figure 4.16, only at baseline was the voluntary force after the stimulation delivery higher than before it.



(a) Pre-walking

(b) Baseline

(c) 2.5 months

(d) 5 months

Figure 4.16: Force trace profiles produced by subject A with the left hamstring positioned at 90^o of flexion. As indicated on each of the plots, subject A contracted her left hamstring for 2–3 seconds, a short stimulation burst (S) was then added following which subject A maintained her voluntary contraction for the remainder of the test. The large increase in force at the start of the pre-walking (a) and the 5 month (d) tests was caused by the investigator moving the dynamometer arm to start the timer.

Left Hamstring Muscle at 30° flexion

The key outcome measures for the left hamstring muscle test at 30° of flexion at each TP are shown in Table 4.12 and the corresponding force traces in Figure 4.17.

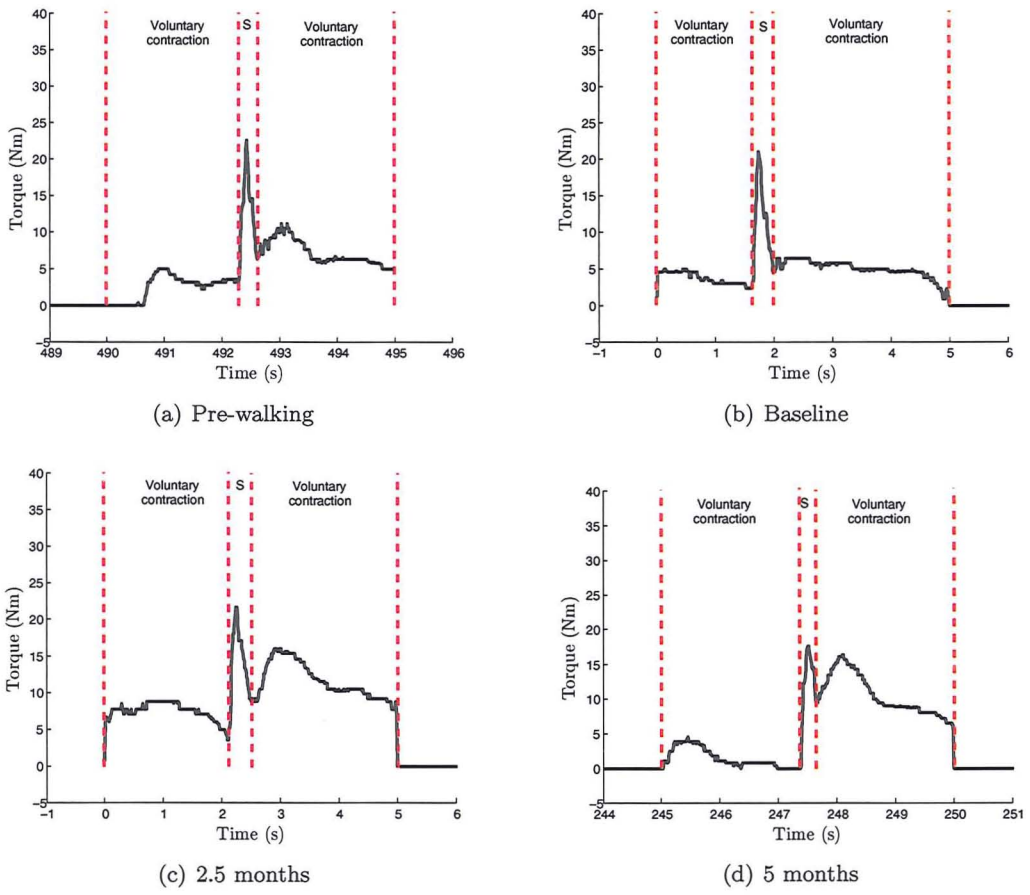
Test	Pre-walking	Baseline	2.5 months	5 months
Peak voluntary force (Nm)	4.90	5.00	8.70	4.50
Peak total force (Nm)	22.50	21.00	21.60	17.60
CAR	0.22	0.24	0.40	0.26

Table 4.12: Key outcome measures for subject A's left hamstring test at 30° of flexion, at each test point. CAR: central activation ratio.

The contraction which produced the highest voluntary force also produced the highest total force at all TPs. As subject A was unable to maintain a steady-state contraction, the peak voluntary force provided in Table 4.12 does not always correspond to the force prior to delivery of the stimulation.

Following ~7 months of treadmill training the voluntary force produced by subject A did not change nor did the CAR. It fluctuated at each TP, peaking at 2.5 months. At each TP the voluntary force produced with the hamstrings at 30° flexion was higher than at 90° flexion.

As can be seen in Figure 4.17, the voluntary force produced following delivery of the stimulation is consistently higher than before it.



(a) Pre-walking

(b) Baseline

(c) 2.5 months

(d) 5 months

Figure 4.17: Force trace profiles produced by subject A with the left hamstring positioned at 30° of flexion. As indicated on each of the plots, subject A contracted her left hamstring for 2–3 seconds, a short stimulation burst (S) was then added following which subject A maintained her voluntary contraction for the remainder of the test.

Left Quadriceps Muscle at 90^o flexion

The key outcome measures for the left quadriceps test at 90^o flexion at each TP are given in Table 4.13 with the corresponding force traces in Figure 4.18.

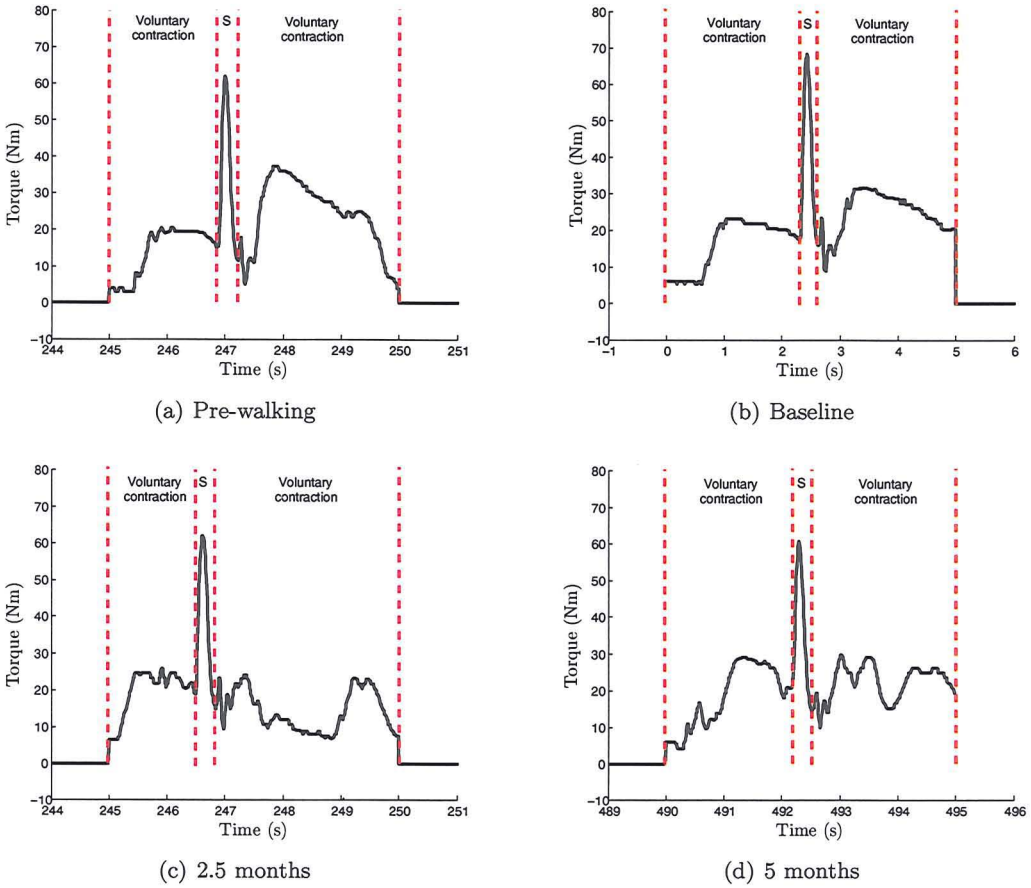
Test	Pre-walking	Baseline	2.5 months	5 months
Peak voluntary force (Nm)	20.50	30.10	25.90	29.20
Peak total force (Nm)	62.00	73.80	62.10	60.70
CAR	0.33	0.41	0.42	0.48

Table 4.13: Key outcome measures for subject A's left quadriceps test at 90^o of flexion, at each test point. CAR: central activation ratio.

The contraction which produced the highest voluntary force during this test also produced the highest total force. As can be seen in Figure 4.18, subject A was unable to maintain a steady-state voluntary contraction. Therefore, the peak voluntary force provided in Table 4.13 is not always representative of the force prior to delivery of the twitch.

The peak voluntary force produced by subject A increased with ~7 months treadmill training from 20.50–29.20 Nm. However, the peak force produced did fluctuate peaking at 30.10 Nm at baseline. The CAR did consistently increase at each TP from 0.33–0.48.

As can be seen in Figure 4.18 the voluntary force produced following delivery of the stimulation is higher than that prior to its delivery at each TP.



(a) Pre-walking

(b) Baseline

(c) 2.5 months

(d) 5 months

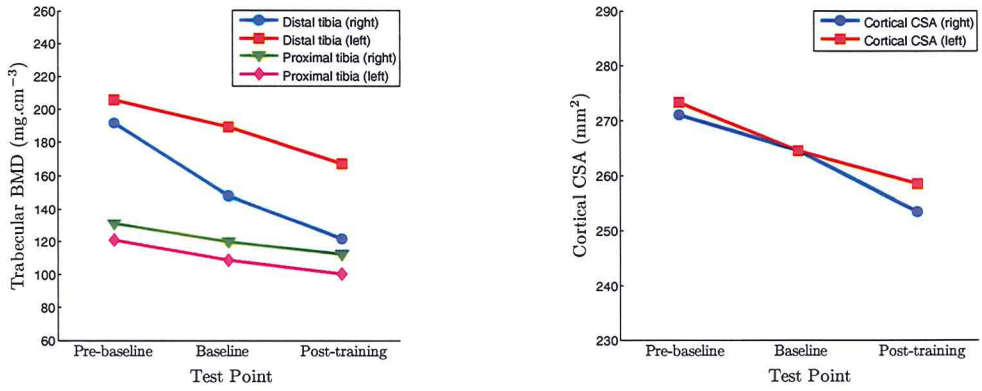
Figure 4.18: Force trace profiles produced by subject A with the left quadriceps positioned at 90^o of flexion. As indicated on each of the plots, subject A contracted her left quadriceps for 2–3 seconds, a short stimulation burst (S) was then added following which subject A maintained her voluntary contraction for the remainder of the test.

4.3.6 Bone Parameters

The BMD, bone CSA and bone mass of subject A's right and left tibia and femur are shown, for each TP, in Table 4.14. As can be seen in Figure 4.19(a), the trabecular BMD of the right and left proximal and distal tibia continued to decrease throughout the training period. At both epiphyses, a larger percentage of BMD was lost from the left tibia with the largest loss being found in the left distal tibia (36.70% Pre- to Post-baseline). Overall, a higher percentage decrease in BMD was found to occur in the distal tibia compared to the proximal tibia.

The cortical CSA measured in the diaphysis of the tibia is also shown to have decreased throughout the training study in both the left and right leg (Figure 4.19(b)). The percentage decline in CSA from Pre- to Post-baseline differed by only 1.1% between the left and right leg.

The results obtained also show that in the tibia, the rate of decline in the BMD of the epiphyses is faster than that of the CSA of the diaphyses.



(a) Trabecular BMD of the left and right distal and proximal tibia.

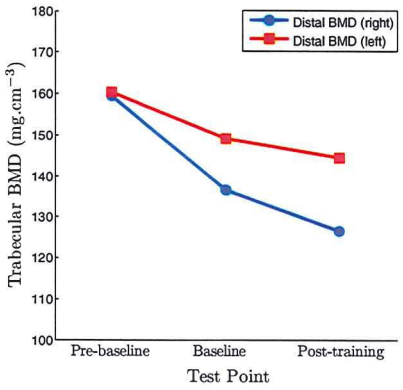
(b) Cortical CSA of the diaphysis of the left and right tibia.

Figure 4.19: Trabecular bone mineral density and cortical cross-sectional area of subject A's left and right tibia at each test point. BMD: bone mineral density. CSA: cross-sectional area.

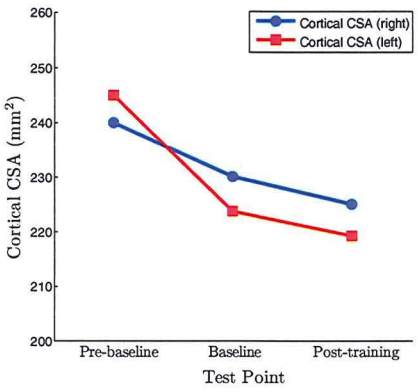
Similar results were also obtained for the femur. As can be seen in Figure 4.20(a), the trabecular BMD of the distal femur also continued to decrease throughout the training period. However, in contrast to the tibia the percentage decline in the right leg was higher than in the left. The CSA of the diaphysis of the femur was also shown to have decreased at each TP, with the percentage decline shown to be higher in the left leg than in the right.

Bone	Region	Scan Site	Parameter	Pre-baseline		Baseline		Post-training		% change (Pre-baseline to Baseline)		% change (Baseline to Post-training)		% change (Pre-baseline to Post-training)	
				Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
Tibia	Epiphysis (distal)	4	BMDtrab (mg/cm^3)	191.43	205.07	147.15	188.73	121.26	166.72	-23.10	-8.0	-17.60	-11.70	-18.70	-36.70
			BMDtot (mg/cm^3)	234.30	246.47	191.24	218.17	171.40	198.53	-18.4	-11.5	-10.40	-9.0	-19.50	-26.80
			Bone mass (g/cm)	2.58	2.79	2.15	2.47	1.88	2.26	-16.70	-11.5	-12.60	-8.50	-19.00	-27.10
	Diaphysis	38	BMDcort (mg/cm^3)	1151.83	1155.14	1149.24	1157.58	1145.82	1156.38	-0.20	0.20	-0.30	-0.10	-0.50	0.10
			CSAcort (mm^2)	270.75	273.00	264.25	264.25	253.25	258.25	-2.40	-3.20	-4.2	-2.3	-6.50	-5.40
			Bone mass (g/cm)	3.38	3.42	3.29	3.34	3.21	3.26	-2.70	-2.30	-2.40	-2.40	-5.00	-4.70
	Epiphysis (proximal)	4	BMDtrab (mg/cm^3)	130.61	120.38	119.18	108.00	111.90	100.07	-8.80	-10.30	-6.10	-7.30	-14.30	-16.90
			BMDtot (mg/cm^3)	172.49	156.77	150.48	141.70	141.68	134.36	-12.80	-9.60	-5.80	-5.20	-17.90	-14.30
			Bone mass (g/cm)	3.96	3.62	3.49	3.29	3.20	3.01	-11.90	-9.10	-8.30	-8.50	-19.20	-16.90
Femur	Epiphysis (distal)	4	BMDtrab (mg/cm^3)	159.32	160.15	136.27	149.08	126.24	144.40	-14.50	-6.90	-7.40	-3.10	-20.80	-9.80
			BMDtot (mg/cm^3)	183.56	196.21	164.94	178.45	155.47	173.43	-10.10	-9.10	-5.70	-2.80	-15.30	-11.60
			Bone mass (g/cm)	6.02	6.37	5.42	5.86	5.07	5.60	-10.10	-8.0	-6.50	-4.40	-15.80	-12.10
	Diaphysis	25	BMDcort (mg/cm^3)	1130.75	1120.62	1120.35	1126.27	1158.60	1118.44	-0.90	0.50	3.40	-0.70	2.50	-0.20
			CSAcort (mm^2)	239.81	244.76	229.89	223.55	224.75	219.06	-4.10	-8.70	-2.20	-2.0	-6.30	-10.50
			Bone mass (g/cm)	3.66	3.70	3.48	3.47	3.40	3.40	-4.90	-6.20	-2.30	-2.0	-7.10	-8.10

Table 4.14: Bone parameters determined from subject A's pQCT scans. BMDtotal: total bone mineral density. BMDcort: cortical bone mineral density. CSAcort: cortical cross-sectional area.



(a) Trabecular BMD of the left and right distal femur.



(b) Cortical CSA of the left and right femur.

Figure 4.20: Trabecular bone mineral density and cortical cross-sectional area of subject A's left and right femur at each test point. BMD: bone mineral density. CSA: cross-sectional area.

4.4 Discussion

4.4.1 Training Performance

Between TP3 and the end of the training programme the speed during the speed training sessions remained at 0.20 m.s^{-1} and the gradient during the gradient training sessions at 1%. Considering the preferred (not the maximum) walking speed of AB individuals is 1.0–1.5 m.s^{-1} [203], a training speed of 0.2 m.s^{-1} is very slow. It has been shown [203, 204] that while AB individuals adapt to an increase in walking speed by increasing their stride length and stride frequency, the maximum walking speed of those with an incomplete SCI is limited, as a consequence of their altered neural drive, by their capacity to increase their stride frequency. In order to adapt to increasing walking speed, those with an incomplete SCI increase their stride length. However, they achieve their maximum stride length at a much lower walking speed than AB individuals.

In a study by Pépin and colleagues [204] the reported preferred treadmill walking speed of 7 incomplete SCI subjects, without any training, was 0.3–0.8 m.s^{-1}. The maximum treadmill speeds obtained were 0.6–1.3 m.s^{-1}, with all subjects able to walk up to 0.5 m.s^{-1}. All subjects included in the study were classified ASIA D the same as subject A, yet following the training study she was unable to achieve the preferred walking speed of the slowest of Pépin and colleagues' subjects. This suggests that subject A's walking ability is limited compared to others with the same ASIA classification.

Prior to participation in BWS treadmill training studies, the treadmill walking speeds of incomplete SCI subjects have been shown to be 0.118–0.318 $m.s^{-1}$ [158], 0.14 ($\pm$0.08) $m.s^{-1}$ [159] and 0.15 ($\pm$0.03) $m.s^{-1}$ [164]. The treadmill speeds were not set by the investigators in these studies but self-selected by the participating subjects. The initial treadmill training speed of 0.1 $m.s^{-1}$ chosen for this study prior to the baseline tests, was pre-determined to allow the subjects to increase the duration of their walking whilst having a minimum effect on cardiovascular fitness. However, it is comparable with the self-selected treadmill speeds demonstrated in previous studies.

Following 12 weeks' treadmill training the mean treadmill speed of 3 incomplete SCI subjects who trained for a maximum of 30 minutes, 5 days per week increased from 0.09–0.16 $m.s^{-1}$ to 0.16–0.32 $m.s^{-1}$ [160]. 6 months of 3 sessions a week treadmill training has been shown to increase treadmill walking speed in incomplete SCI subjects to 0.35 ($\pm$ 0.04) $m.s^{-1}$ [164] whilst 12 months of training increased treadmill walking speed to 0.39 ($\pm$0.22) $m.s^{-1}$ [159]. A direct comparison of the maximum training speed achieved by subject A to the values presented in the literature cannot be made. During treadmill training sessions in the studies discussed above therapist assistance was provided to help aid the subject's walking pattern by placing their foot on the treadmill belt or maintaining trunk stability. The training speed was selected depending on the subject's performance. In this study no therapist assistance was provided to help aid the walking pattern of subject A and therefore possibly increase the speed at which she could walk. Also, the speed at which subject A walked during the training sessions was determined by the investigator according to the protocol outlined in Chapter 3: the subject was only allowed to increased their walking speed if they had completed 3 sessions of required duration. Subject A found it difficult to complete 3, 30 minute sessions at 0.2 $m.s^{-1}$. Therefore, her training speed was not increased. It is possible, had her training speed not been limited by the duration for which she could walk, that she may have self-selected a faster treadmill walking speed. As can be seen in Table 4.7 the self-selected speeds for her 15 minute distance test at TP5 were at some points higher than her training speed.

4.4.2 Maximal Incremental Exercise Test

Peak Work Rate

Following 16 weeks of BWSTT the WR_{peak} achieved by subject A during an IET increased by 565% from 1.41–9.37 W. As the speed of testing did not change after TP2, the increase in WR_{peak} was a consequence of the increase in the peak gradient achieved.

An increase in the WR_{peak} achieved with training was expected. With training the cardiopulmonary fitness of AB individuals increases. They are therefore able to increase the

WR_{peak} which they can achieve as cardiopulmonary fitness is no longer a limiting factor at their previous WR_{peak}. However, whilst the increase in WR_{peak} achieved by subject A may be a consequence of improved cardiopulmonary fitness, it is also possible that it may be a consequence of an improved walking ability. With each period of treadmill training it was noted that subject A's stability whilst walking improved (her legs gave way less), her stride length increased and she appeared less reliant on the side bars for support. It is possible therefore, that the increase in WR_{peak} observed may be due to an improved capacity to walk.

Peak Oxygen Uptake

The $\dot{V}O_{2peak}$ obtained at each TP by subject A is low. No treadmill $\dot{V}O_{2peak}$ data has previously been reported for those with an incomplete SCI. Therefore, the baseline value obtained for subject A can only be compared to those utilising different modes of exercise. When the baseline value obtained is compared to the results of studies investigating the fitness of sedentary paraplegics, the $\dot{V}O_{2peak}$ of subject A is significantly lower than previously reported for that population (Table 4.15).

Study	Subject group	Testing mode	$\dot{V}O_{2peak}$ ($ml.kg^{-1}.min^{-1}$)
Zwiren and Bar-Or 1975 [170]	sedentary paraplegics	ACE	19 ($\pm$ 5.5)
Jacobs et al., 2002 [36]	sedentary paraplegics	ACE	19.6 ($\pm$ 3.2)
Jacobs and Mahoney 2002 [183]	sedentary paraplegics	FES-assisted overground walking	22.7 ($\pm$ 3.9)
Present study	subject A sedentary paraplegic	BWS treadmill walking	8.23

Table 4.15: Comparison of $\dot{V}O_{2peak}$ values obtained for sedentary paraplegics in other investigations to that obtained at baseline for subject A. ACE: arm crank ergometry. FES: functional electrical stimulation. BWS: body weight supported.

As discussed in Section 1.5, $\dot{V}O_{2peak}$ is expected to increase following a period of cardiopulmonary training. However, it is possible that the increase in $\dot{V}O_{2peak}$ achieved by subject A following 16 weeks BWSTT was the consequence of an improved walking ability which enabled her to utilise a previously unattainable cardiopulmonary reserve. The fact that $\dot{V}O_{2peak}$ did not consistently increase at each TP supports the idea that it is likely that the IET did not provide a true indication of subject A's maximum cardiopulmonary capacity. It was noted by the investigator that following an IET subject A did not feel physically exhausted, nor did she look physically exhausted as one would expect of a subject having completed a

maximum IET. Subject A also commented on a number of occasions that she had stopped the test because she felt her legs could no longer maintain a functional gait pattern: prior to this her legs would often collapse. It therefore appears that her IETs may have been limited peripherally rather than centrally due, possibly, to the atrophied muscles and fast fatiguing muscle fibres which have been shown to be present in the paralysed lower extremities of paraplegics [16, 17, 18, 20, 21, 23, 24, 25], as well as limited neural control.

It would have been advantageous for subject A to have performed a peak arm crank ergometry (ACE) test at each TP. Although it has been demonstrated in the AB population that the $\dot{V}O_{2peak}$ obtained from an ACE IET is ~70% of that obtained during maximum treadmill exercise [174], an ACE IET would have provided an indication of the extent to which the $\dot{V}O_{2peak}$ obtained in this study was affected by lower limb peripheral limitations.

It is also possible that the increasing work rate during the IETs is less important in subject A reaching her limit of tolerance than the actual duration she is walking for. As can be seen in Table 4.16, the $\dot{V}O_2$ obtained during the final 20 seconds of the SET where the work rate remains constant is higher than that obtained during the IET at TP1 and is approximately equal to that obtained at TP2.

Test point	IET	SET	% difference
TP1	8.23	10.07	+ 22
TP2	8.82	8.68	- 1.6
TP3	12.13	8.46	- 30
TP4	9.17	7.48	- 18
TP5	10.19	6.89	- 32

Table 4.16: Average of the final 20 seconds of the $\dot{V}O_2$ response ($ml.kg^{-1}.min^{-1}$) during the incremental and constant load (step) exercise test at each test point, as well as the percentage difference in the constant load (step) exercise test result compared to the incremental exercise test result. IET: incremental exercise test. SET: step exercise test. TP: test point.

It is possible that as the walking progressed and subject A's lower limb muscles became more fatigued that she had to work increasingly harder to maintain a functional gait pattern. To do this she may have altered her gait pattern or leaned more heavily on the side bars for support thus increasing the muscle mass involved in the exercise and hence the demand for O_2. Therefore, although the lower limb work rate at which she was exercising remained constant or increased at a constant rate, the total (lower limb and upper body) work rate did not.

This may also explain why the $\dot{V}O_2$ response during the IETs is not well fit by a linear relationship. If subject A altered her gait pattern during a test or began to lean more heavily

on the bars more muscle mass would be engaged in the exercise and therefore the linear work rate profile which had been set, and the subject was expected to follow, would be altered. As no measurement of the forces placed through the arms or feet was recorded an accurate measure of how the total work rate profile changed throughout a test could not be obtained.

Lactate Threshold

An LT could not be estimated during the IET of subject A at any TP. This may be a consequence of a low signal-to-noise ratio. However, as discussed previously it is possible that the WR profile of each test may not have been linear due to the changes in the subject's gait pattern and/or by her leaning on the side bars. Consequently, as shown in Section 4.3.2, the $\dot{V}O_2$ profile would not be linear. In order to accurately estimate the LT by V-slope analysis and gas exchange criteria the work rate profile must be linear. This may explain why one cannot be determined.

It is also possible that an LT could not be determined because subject A was either exercising at work rates above or below it. The respiratory variable plots should help to determine this. Below the LT $\dot{V}_E/\dot{V}O_2$ and $\dot{V}_E/\dot{V}CO_2$ are expected to fall gradually and reach a steady-state. At TP1, TP2 and TP4 this is the response that was produced. Below the LT $F_{ET}O_2$ is also expected to decrease and stabilise but $F_{ET}CO_2$ is expected to be increasing. However, for TP1, TP2, and TP4 the resulting profiles do not support the suggestion that subject A is exercising below the LT. No pattern in either response can be determined at TP1 and TP4 and at TP2 $F_{ET}O_2$ is stable then decreases and $F_{ET}CO_2$ is stable then increases. The response of $F_{ET}O_2$ at TP2 reflects that which would be expected of $F_{ET}CO_2$ at the RCP, and the response of $F_{ET}CO_2$ that which would indicate the presence of an LT in $F_{ET}O_2$. The responses of all the respiratory variables at TP3 and TP5 do not support the suggestion that subject A was exercising below the LT at any point during the ramp.

The profiles of the respiratory variables at TP1, TP2 and TP4 do not support the suggestion that subject A may be exercising above the LT. However, at TP3 this may have been the case; $\dot{V}_E/\dot{V}O_2$ and $F_{ET}O_2$ are increasing, $F_{ET}CO_2$ is decreasing (indicating subject has reached RCP), and $\dot{V}_E/\dot{V}CO_2$ remains stable suggesting that subject A is at or above the LT. The profiles produced at TP5 do indicate that, despite no deflection point in the $\dot{V}O_2$-$\dot{V}CO_2$ relationship, an LT may be present; $\dot{V}_E/\dot{V}O_2$ and $F_{ET}O_2$ both increase following a period of stabilisation and $F_{ET}CO_2$ and $\dot{V}_E/\dot{V}CO_2$ are both stable followed by an increase. Although the actual point of the LT cannot be estimated from the $\dot{V}_E/\dot{V}CO_2$ and $F_{ET}CO_2$ profiles the fact that there is a period of stabilisation suggests that it is present. However, the non-identification of an LT at the other TPs and the inconsistency in the respiratory

variable profiles reduce the certainty that a true LT can be identified.

With the exception of TP5 the respiratory variable profiles obtained at each TP provide contradictory evidence as to the intensity at which subject A is exercising (i.e. above or below the LT). Therefore, they provide no additional information as to why an LT could not be determined using V-slope analysis.

Slope of Oxygen Uptake as a function of Work Rate

The $\Delta\dot{V}O_2/\Delta WR$ was also measured from the IETs as a third parameter of aerobic fitness. Although not particularly important for cardiopulmonary training, this outcome measure provides an indication of performance and endurance capacity. A high $\Delta\dot{V}O_2/\Delta WR$ results from large amounts of O_2 being required for ATP production which is undesirable for endurance performance.

The $\Delta\dot{V}O_2/\Delta WR$ obtained at each TP is high and may be a consequence of the deconditioned muscles and possible predominance of type II muscle fibres which has been shown to occur by 70 months post injury in SCI patients [25]. Consequently, more O_2 is required for a given amount of work.

Despite an increase in the $\Delta\dot{V}O_2/\Delta WR$ at TP3, it did decrease dramatically from baseline to TP5 (75%). Although this may be a consequence of increased cardiopulmonary fitness, indicated by an overall increase in $\dot{V}O_{2peak}$, it is also possible that it is a consequence of an improved and thus more efficient gait pattern. Regardless of its origin this significant decrease in $\Delta\dot{V}O_2/\Delta WR$ is extremely important as it indicates a reduced cardiopulmonary stress whilst walking at a given work rate.

Peak Heart Rate

A 31% increase in the HR_{peak} achieved by subject A during the IET occurred following 16 weeks of BWSTT. This suggests that subject A was able to access a previously unattainable heart rate reserve due, possibly, to an improved walking ability. Therefore, had subject A been able to further improve her walking ability it is likely that she would have achieved a higher HR_{peak}. It is possible that the HR_{peak} achieved at TP3, which is higher than that achieved at all other TPs, may have been a consequence of a good, functional gait pattern on that particular testing day.

4.4.3 Constant Load Exercise Test

For able-bodied (AB) subjects exercising at a steady-state work rate below the LT, $\dot{V}O_2$ is expected to reach a steady-state in ~3 minutes [97] and with training the τ value obtained is expected to decrease [108].

From the SET at each TP a τ value could either not be obtained or the value obtained was extremely large thus supporting the observation (Figure 4.11) that the $\dot{V}O_2$ response did not reach a steady-state.

In order to perform at a given work rate below the LT the body requires a given amount of O_2. However, during each SET subject A required an increasing amount of O_2 as the test progressed. It is possible that although the lower limb work rate remained constant throughout the test the total (lower limb and upper body) work rate increased. As discussed previously, as subject A's lower limb muscles weakened and her limb co-ordination declined she would have had to work harder to maintain an upright posture and functional gait pattern thus increasing the amount of O_2 required for the exercise.

Despite the fact that the $\dot{V}O_2$ response to the step increase in work rate did not stabilise it is encouraging that the $\dot{V}O_2$ in the final 20 seconds of the test decreased at each TP, indicating that the physiological stress was decreasing. This is likely to be due to an improved, more efficient gait pattern possibly as a consequence of improved muscle endurance and co-ordination.

4.4.4 15 Minute Distance Test

Following 20 weeks of BWSTT, the distance which subject A could walk in 15 minutes increased by ~100%. As can be seen in Table 4.7 the speed chosen by the subject increased at each TP. This may be due to improved gait co-ordination and muscle endurance which is also supported by an increase in the WR_{peak} achieved during the IETs and in training performance.

The results of this test are extremely encouraging as it shows that in a given period of time subject A has not only increased the distance at which she can walk but also the work rate at which she can train.

4.4.5 Twitch Tests

From the results of all the twitch tests it is evident that subject A cannot maintain a steady-state maximum contraction for 2-3 seconds. This may be a consequence of fluctuating recruitment of muscle fibres because of fluctuations in the signals to the motor units.

With training, only the peak voluntary force produced by the right quadriceps at 90^o of flexion consistently increased at each TP. This suggests that BWSTT has increased the strength of the right quadriceps muscle. The peak voluntary force produced by the left quadriceps muscles at 90^o of flexion was increased at each TP compared to pre-walking. Although the peak voluntary force did increase following $\sim$7 months BWSTT, the increase was not consistent. An increase in the strength of the quadriceps is encouraging as this may help with activities of daily living (ADLs) such as transfers as well as providing more support during the stance phase of walking.

Conversely, the peak voluntary force produced by the right hamstrings at 30^o of flexion has decreased with training. If this did occur then a similar pattern of response would be expected at 90^o of flexion. This was not the case. Although the force produced at a given position may be lower than at another position, the overall pattern of the response to the training would be expected to be the same given that it is the same muscle being tested. The discrepancy in the pattern of the results obtained for the same muscle at two different testing positions suggests that the true voluntary peak force of the muscle was not obtained. Testing the hamstring muscles at 30^o of flexion does however, appear to enable the subject to produce more force from the muscle than at 90^o of flexion. This is likely to be because the subject has better leverage with the leg straighter.

In a recent publication [205], the peak knee extensor force of 10 incomplete SCI subjects was accurately measured using dynamometry. It was found to be 36% and 24% of the peak voluntary force produced by non-injured controls in the less- and more-involved limbs respectively. The peak forces reported, 57 ± 18 Nm and 85 ± 20 Nm for the more-involved and less-involved limbs respectively, are significantly higher than that obtained by subject A at any TP. The peak voluntary force produced by subject A with her more-involved limb was 14.20 Nm and with her less-involved limb, 30.10 Nm. From the results obtained it appears unlikely that the tests used are sensitive to changes in the peak voluntary muscle force of the hamstring and quadriceps muscles of incomplete SCI subjects. Fluctuations between TPs and consequently no consistent response to the training suggests variable subject performance. This may be due to subject motivation, variation in the ability to recruit motor units and, as for the walking tests, more muscle fatigue on particular days.

Variability was also present in the determination of the total muscle force produced by the imposition of a stimulation train on a maximally contracting muscle. It would be expected that as the electrodes were placed over the muscles in the same position and the same stimulation parameters were used for each test, the peak total forces obtained would be more consistent. This may have been affected by the fact that subject A was unable to maintain a steady-state contraction. Therefore, the voluntary force produced prior to stimulation delivery was not always the subject's peak.

By calculating the ratio between the torque produced by the superposition of a supra-maximal twitch on a peak isometric contraction and the torque produced by the same stimulus in the potentiated, resting muscle, Jayaraman and colleagues [205] demonstrated that the voluntary activation deficit of those with an SCI was 42±8% and 66±9% for the less- and more-involved limb respectively compared to 5±2% for non-injured controls. In this study we attempted to determine the CAR, another indicator of the extent of central activation failure (CAF). However, given the variability in peak voluntary and total force production it is unlikely that the CARs obtained at each TP accurately reflect this. Further investigation is required to determine the accuracy of these tests.

An interesting observation from the results of the twitch tests is that the peak voluntary force produced after the delivery of the stimulation train is often higher than before it. Further investigation is required to determine if this is a physiological response of the muscle to the stimulation or whether it can be explained by increased subject effort when they see, following delivery of the stimulation train, how much force their muscle is capable of producing.

4.4.6 Bone Parameters

The trabecular BMD and cortical CSA of subject A's right and left tibia and femur continued to decrease from Pre-baseline to Post-training. Therefore, despite the period of Pre-baseline treadmill training and the 5 month treadmill training programme no positive effects have been shown in the lower limb bones of subject A. On recruitment to the study, subject A was only 2 years post injury and therefore, as discussed in Section 1.3.3, still in the fast phase of decline in trabecular BMD and cortical CSA which occurs following an SCI. It appears, therefore, that the treadmill training was of insufficient intensity to halt or reverse this decline.

It is possible that the rate of decline in trabecular BMD and cortical CSA may have been reduced by the training intervention. However, as the expected rate of decline is unknown this cannot be concluded.

4.4.7 Multiple Sclerosis

Subject A has transverse myelitis as a consequence of multiple sclerosis (MS). Although she does not feel that she is affected by her MS it may be possible that this is because her spinal cord lesion is masking the complications of the disease. MS is a degenerative disease which affects the nervous system. Sufferers' motor responses are often slowed and their muscles weakened. They can also have days where they are more affected by their condition than others. It is probable that subject A's MS was affecting her and if so what affect did it have on the tests that she performed? It is possible that her condition may explain the variability in walking performance that was sometimes present existed between training sessions: during some sessions her legs appeared unable to generate the force and co-ordination required to walk for any length of time and the fatigue she felt from walking could vary greatly between sessions. If such variability in training performance was present it is highly probable that variability in testing performance existed also. If on a particular testing day subject A was being affected by her MS then the results obtained cannot be representative of what she is physically capable of achieving. Further investigation is required to determine the extent to which subject A's MS may have affected her training and testing performance.

4.4.8 Repeatability and Reliability of Testing Protocols

It would have been preferable to carry out a period of testing prior to the training study to determine the reliability and repeatability of the testing protocols used. By only carrying out one test at each TP we do not know if the result obtained is truly representative of the subject's response to the exercise. There is evidence in the literature that there can be day to day variation of up to 10% in the exercise responses of AB subjects [66]. It is therefore important, as discussed in the literature [200], to ensure that protocols used are repeatable in measuring the required outcomes and do not produce more variation than would generally be expected.

The response of subject A at TP3 does not follow the expected pattern of response to training. The $\Delta\dot{V}O_2/\Delta WR$ of the exercise increases at this point whilst the overall pattern of response to the training programme is a continued decrease. $\dot{V}O_{2peak}$ has been shown to increase throughout the training programme. However, the dramatic increase in $\dot{V}O_{2peak}$ obtained at TP3 is not in keeping with the response profile and thus at TP4, it decreased. As the reliability of the tests is not known, it is unclear whether this was the actual physiological response to the exercise or an outlying response. It is also not known how indicative of the subject's cardiopulmonary fitness the results obtained are, and how much they are affected by her ability to maintain a functional gait pattern on a given day. If repeat tests had been carried out prior to the training study, the effect of the gait pattern on day to

day variability in performance could have been determined. If the variability between tests was high it would provide evidence that the test were not reliable or repeatable. However, if the variability was low it would indicate that the results obtained at each TP were indeed reflective of the subject's actual cardiopulmonary capacity and not of her ability to maintain functional walking.

It is important to determine the repeatability and reliability of all the tests used in this study, not just the cardiopulmonary tests. If it is possible that the cardiopulmonary exercise tests were affected by subject A's walking ability it is highly likely that the 15 minute distance test will also have been affected. The accuracy of the 15 minute distance test may also have been affected by the fact that subject A chose her own walking speed during the test. As the training speed was limited during the study, subject A did not experience walking over a wide range of speeds and therefore, may not have been aware of the range of speeds at which she could safely walk. Therefore, although her chosen testing speeds did on occasion increase above her training speed it is possible that she may have been able to walk faster, something which may have been determined had repeat tests been performed.

Subject A's variable muscle performance and fatigue is likely to also have affected her twitch test results. The inconsistent response to training of the individual muscle groups supports this. It is also possible that subject A, who is not used to trying to produce high forces from her partially paralysed lower limb muscles, is unaware of the maximum force she is capable of producing and, therefore, may not be achieving her maximum voluntary force with each contraction.

4.5 Conclusion

Standard exercise protocols were adapted for use with an incomplete SCI during BWS treadmill walking. The tests were successfully performed at 4 weekly intervals during a 16 week BWSTT programme. During this BWSTT programme the subjects training performance improved greatly: training duration and treadmill speed doubled and treadmill gradient increased 100%. This was reflected, pre- to post-training, in the large increase in WR_{peak} obtained during the IET as well as an overall increase in $\dot{V}O_{2peak}$ and HR_{peak}. It does however appear that the tests may have been limited by a variable gait pattern and weak lower limb muscles. It is likely that these factors may have affected other outcome measures. However, extremely encouraging results were still obtained: a substantial decrease in the $\Delta\dot{V}O_2/\Delta WR$ of the IET and in the final $\dot{V}O_2$ of the SET. A 100% increase in the distance walked during the 15 minute distance test also occurred. It is clear that an improvement in the subject's

gait occurred with training.

The use of standard dynamometry tests to determine the extent of CAF were also adapted for use with the SCI subject. The determination of an increase in the voluntary peak force in the quadriceps muscles with training is encouraging. However, the repeatability of the outcome measures requires further investigation. No improvement was found in the trabecular BMD of the proximal and distal epiphyses of the tibia and distal epiphyses of the femur. Nor was any improvement found in the CSA of the diaphyses of the tibia and femur. However, this may have been due to subject A still being in the fast phase of decline in BMD which occurs post-injury.

The results of this study are encouraging as they show that standard methods of exercise testing can be adapted for use with an incomplete SCI subject. Further investigation is however required to determine the repeatability and reliability of the outcome measures obtained. Further research must also be carried out to determine the extent to which subject A's MS may have affected her performance and consequently the results obtained.

Chapter 5

Case Study - Subject B

5.1 Chapter Summary

The response of 4 key indices of cardiopulmonary fitness (peak oxygen uptake ($\dot{V}O_{2peak}$), lactate threshold (LT), slope of $\dot{V}O_2$ as a function of work rate ($\Delta\dot{V}O_2/\Delta WR$) and $\dot{V}O_2$ kinetics ($\tau\dot{V}O_2$)) to 20 weeks of body weight supported treadmill training (BWSTT) in 1 incomplete spinal cord injured (SCI) subject are reported and discussed in this chapter. Also reported is the effect of the BWSTT on training performance, peak work rate (WR_{peak}), peak heart rate (HR_{peak}) and the oxygen uptake ($\dot{V}O_2$) and heart rate (HR) associated with a step increase in work rate. The effect of the training on the distance subject B could walk in 15 minutes as well as lower limb muscle and bone strength is also reported.

At all test points (TPs) subject B carried out an incremental exercise test (IET) during which the treadmill speed remained constant and the gradient increased linearly (IET A). At TPs 3, 4 and 6 he also performed an IET which incorporated step increases in treadmill speed and corresponding changes in the gradient incrementation rate (IET B). Throughout the training period the WR_{peak} achieved during the IET A increased at each TP (6.22–43.99 W). At TPs 3, 4 and 6 the WR_{peak} achieved during the IET B was higher than that obtained during IET A. $\dot{V}O_{2peak}$ increased slightly with training (13.84–13.91 $ml.kg^{-1}.min^{-1}$). However, it fluctuated between TPs with the highest $\dot{V}O_{2peak}$ achieved at TP5 (18.15 $ml.kg^{-1}.min^{-1}$). At TP4 and TP6, the $\dot{V}O_{2peak}$ obtained during IET B was slightly higher than obtained during IET A. The $\Delta\dot{V}O_2/\Delta WR$ decreased substantially with training suggesting an improvement in the efficiency of the subject's gait pattern. However, the magnitude of this decrease may have been affected by the increase in testing speed and thus internal work being performed at each TP. During the constant load (step) exercise test (SET) a τ value, which indicated that the subject's $\dot{V}O_2$ reached a steady-state, could only be determined in 50% of the tests performed. Encouragingly however, the $\dot{V}O_2$ and HR associated with the SET decreased with training.

The peak voluntary force obtained by subject B with his left quadriceps group increased up to the 2.5 month TP. At the 5 month TP it had decreased to below the pre-walking value. The peak voluntary force for the right quadriceps muscle group decreased following ~7 months BWSTT. The results for the hamstring muscle groups were affected by spasms in the lower limbs. The trabecular bone mineral density (BMD) of the distal femur and proximal tibia, and the cortical cross-sectional area (CSA) of the femur remained unchanged following ~7 months BWSTT. However, an increase of 4.9% and 19.6% in the trabecular BMD of the right and left distal tibia respectively, did occur. By completion of the study the distance that subject B could walk in 15 minutes increased by 121%.

The results obtained from the IETs suggest that a true indication of subject B's peak cardiopulmonary capacity was not obtained. It is likely that the tests were limited peripherally by subject B's walking capacity, rather than centrally by his cardiopulmonary system. Alterations in gait pattern and highly fatiguable lower limb muscles may explain why $\dot{V}O_2$ did not stabilise during all SETs. Variable subject performance may account for some of the variation shown in the twitch test results, although spasms also had an effect.

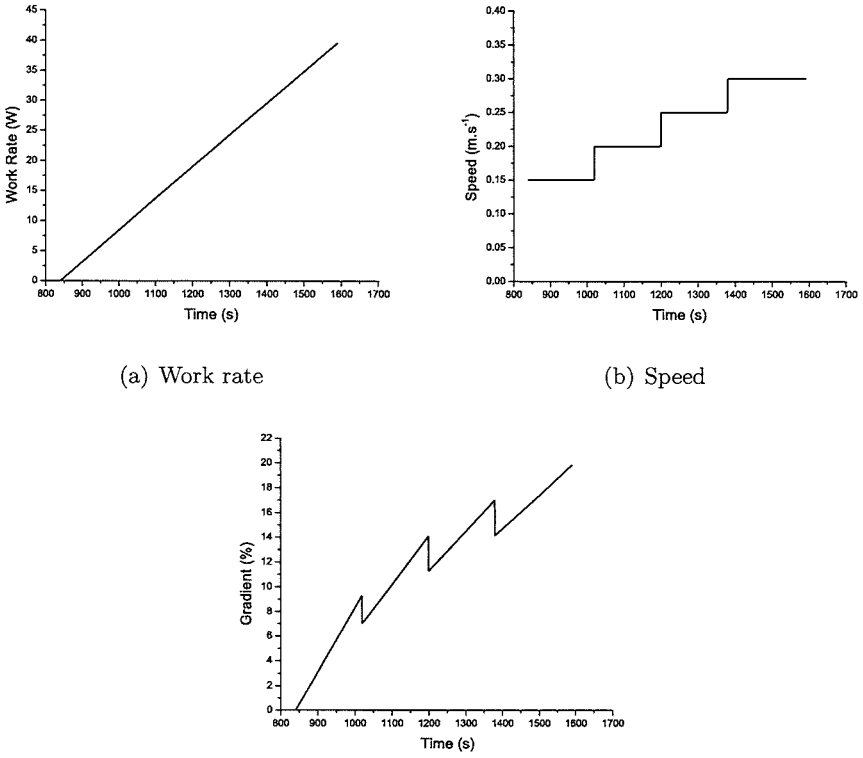
The results obtained for subject B do however suggest that 20 weeks of BWSTT has the potential to substantially increase the walking performance of those with an incomplete SCI. The results also suggest that exercise testing methods used for AB subjects to determine cardiopulmonary fitness and voluntary muscle strength can be adapted for use with incomplete SCI subjects and that they can identify improvements in some key physiological performance parameters. However, further investigation is required to determine the reliability and repeatability of the results obtained.

5.2 Method Deviations

The testing protocols and analysis of the data obtained for subject B were carried out as outlined in Chapter 3 with the following exceptions:

- Subject B was unable to walk at the range of speeds and gradients required to perform the Porszasz IET protocol. Therefore, at each TP he performed an IET during which the speed remained constant and the gradient increased linearly (IET A). At TP3 another IET (IET B) was introduced which incorporated step increases in speed. As for IET A, the end work rate which the subject was expected to achieve was determined by the investigator. At the start of the ramp phase the subject continued to walk at the speed of the previous 0% gradient phase. Following a pre-specified period of time,

the speed of the treadmill was incremented by 0.05 $m.s^{-1}$. In order to maintain a linear increase in work rate, the treadmill gradient was reduced and then increased at an altered incrementation rate. This was done each time the treadmill speed increased until the subject ended the test. An example of a work rate, speed and gradient profile for this test is shown in Figure 5.1.



(a) Work rate

(b) Speed

(c) Gradient

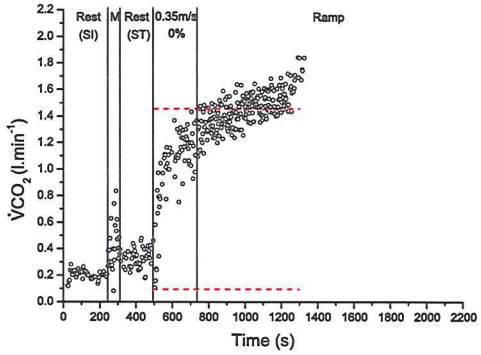
Figure 5.1: An example of the work rate, speed and gradient profile during the alternative treadmill incremental exercise test B.

- As discussed in Section 4.2, accurate and consistent determination of the kinetic phase from subject A's IETs was difficult. This was also found to be the case for subject B (Table 5.1).

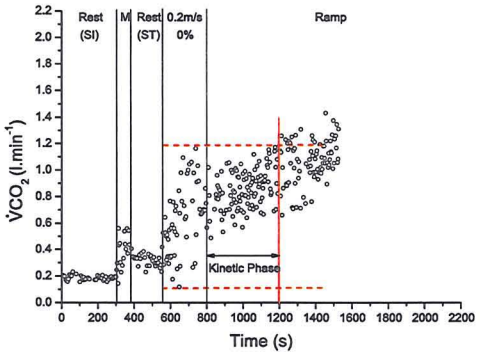
  As can be seen in Figure 5.2, in some instances the kinetic phase could not be determined, whilst in others it appeared to account for a significant proportion of the ramp phase duration. The kinetic phase was therefore not excluded from the V-slope analysis. It was also not excluded in the determination of the slope of $\dot{V}O_2$ as a function of work rate ($\Delta\dot{V}O_2/\Delta WR$): a linear line of best fit was fitted through all the data points in the WR-$\dot{V}O_2$ plot.

IET	TP1 (week 0)	TP2 (week 5)	TP3 (week 9)	TP3B (week 9)	TP4 (week 13)	TP4B (week 13)	TP5 (week 17)	TP6 (week 21)	TP6B (week 21)
Kinetic phase duration (s)	88	277	400	100	585	170	NA	NA	NA

Table 5.1: Duration of the kinetic phase during subject B's incremental exercise test at each test point. IET: incremental exercise test. TP: test point. NA: no value was obtained.



(a) Kinetic phase could not be determined. The $\dot{V}CO_2$ data begins to increase immediately at the start of the ramp phase.



(b) Kinetic phase comprises a significant percentage of the total duration of the ramp phase.

Figure 5.2: An example of a long and short duration kinetic phase. The duration of the kinetic phase is taken as the time between the start of the ramp phase and the point at which $\dot{V}CO_2$ increases above the previous phase response (indicated by a solid red line). SI: sitting. M: moving. ST: standing. Edited plots.

- Subject B's $\dot{V}O_2$ fell at the start of each period of rest as he adjusted to the new conditions. Therefore, the first 90 seconds of the response was excluded when determining $\dot{V}O_2$ at rest during both the IETs and SETs.
- As previously mentioned in Section 3.3.4, stimulation was applied to the left peroneal nerve of subject B to elicit the withdrawal reflex during walking.

5.3 Results

5.3.1 Training Performance

The speed and gradient at which subject B trained in the two sessions prior to each TP are shown in Table 5.2. Prior to TP1 subject B had achieved the pre-specified target of 15 minutes continuous walking at 0.10 m.s^{-1}, 0%. During the first week of post-baseline test training, subject B walked continuously for 30 minutes at 0.15 m.s^{-1}, 0%. Therefore, in accordance with the training protocol (see Section 3.4.1) the duration of his subsequent training sessions was set to 30 minutes. As this was the maximum training duration set for this study it remained constant for the duration of the 20 week training programme. The training speed increased up to and including TP4. Following this it remained at 0.30 m.s^{-1}. The treadmill gradient during training increased at TP2, then again at TP4, reaching 5.00% by TP6.

Test Point	TP1 (week 0)	TP2 (week 5)	TP3 (week 9)	TP4 (week 13)	TP5 (week 17)	TP6 (week 21)
Speed ($m.s^{-1}$)	0.10	0.15	0.20	0.30	0.30	0.30
Gradient (%)	0.00	1.00	1.00	3.00	3.00	5.00
Duration (mins)	15	30	30	30	30	30

Table 5.2: The duration and corresponding training speed and gradient of the final speed and gradient training sessions prior to each test point. The treadmill gradient during speed training sessions remained at 0% throughout the training programme and the treadmill speed during the gradient training sessions remained at 0.15 $m.s^{-1}$. TP: test point.

5.3.2 Maximal Incremental Exercise Test

The speed and incrementation rate chosen for each IET are provided in Table 5.3. From TP3 to TP5 the speed of the test was continually increased. Subject B did not feel comfortable walking faster than 0.35 $m.s^{-1}$ for the duration of the IET. Therefore, at TP6 the speed was not increased. The range of speeds and the incrementation rates chosen for each IET B are provided in Table 5.4. The maximum speed corresponds to the speed of the IET A at each TP. The incrementation rate was chosen by the investigator with the aim of ensuring that the subject reached their limit of tolerance in 8–12 minutes [197].

IET A	TP1 (week 0)	TP2 (week 5)	TP3 (week 9)	TP4 (week 13)	TP5 (week 17)	TP6 (week 21)
Speed ($m.s^{-1}$)	0.15	0.15	0.20	0.30	0.35	0.35
Incrementation rate (%/min)	0.4	1.1	1.5	1.5	1.5	1.6

Table 5.3: Constant treadmill speed and the gradient incrementation rate during each incremental exercise test A. IET: incremental exercise test. TP: test point.

IET B	TP3 (week 9)	TP4 (week 13)	TP6 (week 21)
Speed ($m.s^{-1}$)	0.15, 0.20	0.15, 0.20, 0.25, 0.30	0.15, 0.20, 0.25, 0.30, 0.35
Incrementation rate (%/min)	~2.4, ~1.9	3.1, ~2.4, ~1.9, ~1.7	~3.7, ~2.8, 2.2, 1.9, ~1.6

Table 5.4: Treadmill speed and corresponding gradient incrementation rate during each incremental exercise test B. IET: incremental exercise test. TP: test point.

The key outcome measures for each IET A are shown in Table 5.5, and for IET B in Table 5.6.

IET A	TP1 (week 0)	TP2 (week 5)	TP3 (week 9)	TP4 (week 13)	TP5 (week 17)	TP6 (week 21)
Ramp duration (s)	900	686	730	675	595	705
$\dot{V}O_{2peak}$ ($l.min^{-1}$)	1.42	1.13	1.39	1.70	1.83	1.42
$\dot{V}O_{2peak}$ ($ml.kg^{-1}.min^{-1}$)	13.84	10.88	13.71	16.82	18.15	13.91
$\dot{V}O_2$ at LT ($l.min^{-1}$)	NA	NA	NA	NA	NA	NA
WR at LT (W)	NA	NA	NA	NA	NA	NA
$\Delta\dot{V}O_2/\Delta WR$ ($ml.min^{-1}.W^{-1}$)	66.57	26.00	19.57	14.98	9.40	4.52
HR_{peak} (bpm)	134	132	132	150	151	157
Peak gradient (%)	6.0	12.5	18.1	16.7	14.7	18.6
WR_{peak}	6.22	13.13	24.24	33.48	34.28	43.99
Seated resting $\dot{V}O_2$ ($l.min^{-1}$)	0.24	0.26	0.23	0.25	0.27	0.27
Standing resting $\dot{V}O_2$ ($l.min^{-1}$)	0.38	0.45	0.39	0.44	0.42	0.46

Table 5.5: Key outcome measures for subject B's incremental exercise test A at each test point. IET: incremental exercise test. TP: test point. $\dot{V}O_{2peak}$: peak oxygen uptake. LT: lactate threshold. $\Delta\dot{V}O_2/\Delta WR$: slope of oxygen uptake as a function of work rate. HR_{peak}: peak heart rate. WR_{peak}: peak work rate.

IET B	TP3 (week 9)	TP4 (week 13)	TP5 (week 17)	TP6 (week 21)
Ramp duration (s)	793	750	NA	900
$\dot{V}O_{2peak}$ ($l.min^{-1}$)	1.12	1.77	NA	1.49
$\dot{V}O_{2peak}$ ($ml.kg^{-1}.min^{-1}$)	11.05	17.51	NA	15.59
$\dot{V}O_2$ at LT ($l.min^{-1}$)	NA	NA	NA	NA
WR at LT (W)	NA	NA	NA	NA
$\Delta\dot{V}O_2/\Delta WR$ ($ml.min^{-1}.W^{-1}$)	19.56	24.29	NA	14.91
HR_{peak} (bpm)	135	154	NA	153
Peak gradient (%)	19.70	19.80	NA	20.00
WR_{peak}	26.33	39.54	NA	47.17
Seated resting $\dot{V}O_2$ ($l.min^{-1}$)	0.24	0.28	NA	0.27
Standing resting $\dot{V}O_2$ ($l.min^{-1}$)	0.43	0.43	NA	0.45

Table 5.6: Key outcome measures for subject B's incremental exercise test B at each test point. Subject B did not carry out incremental exercise test B at test points 1 and 2. No data is available at test point 5 as the test was not carried out due to illness. IET: incremental exercise test. TP: test point. $\dot{V}O_{2peak}$: peak oxygen uptake. LT: lactate threshold. $\Delta\dot{V}O_2/\Delta WR$: slope of oxygen uptake as a function of work rate. HR_{peak}: peak heart rate. WR_{peak}: peak work rate.

Peak Work Rate

As can be seen in Figure 5.3 the WR_{peak} achieved by subject B during the IET A at each TP increased consistently with training. Following 20 weeks treadmill training the WR_{peak} achieved by subject B had increased 607% from 6.22–43.99 W.

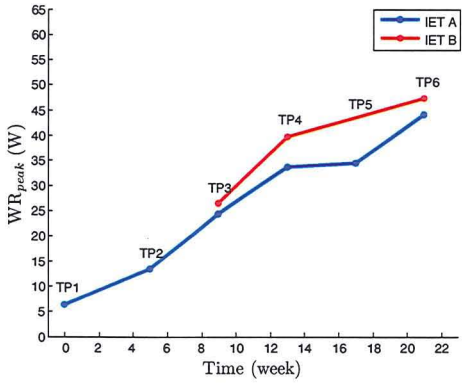


Figure 5.3: WR_{peak} achieved during subject B's incremental exercise test A at each test point and during his incremental exercise test B at test points 3, 4 and 6. TP: test point.

The WR_{peak} achieved during each IET B also consistently increased with training and, as can be seen in Figure 5.3, was higher at each TP than that achieved during the IET A.

Peak Oxygen Uptake

Although an increase in WR_{peak} occurred at each TP, a corresponding increase in $\dot{V}O_{2peak}$ did not always occur. As can be seen in Figure 5.4, despite an increase in the WR_{peak} achieved during the IET A, the $\dot{V}O_{2peak}$ obtained at TP2 was lower than that achieved at TP1. The $\dot{V}O_{2peak}$ achieved at TP3 increased to approximately the same level as at TP1. Following this the $\dot{V}O_{2peak}$ achieved at each TP continued to increase with training until at TP6 it decreased to approximately the same level as TP1 and TP3.

As is shown for the IET A, the $\dot{V}O_{2peak}$ achieved during the IET B at each TP also increased from TP3 to TP4 and decreased at TP6. As can be seen in Figure 5.4, the $\dot{V}O_{2peak}$ achieved at TP3 was lower during the IET B than during the IET A. However, at TP4 and TP6 the $\dot{V}O_{2peak}$ achieved during IET B was higher than that achieved during the IET A.

The $\dot{V}O_2$ profiles for subject B's IET A and IET B at each TP are shown in Figures 5.5 and 5.6 respectively. With the exception of the $\dot{V}O_2$ profile produced during IET B at TP4

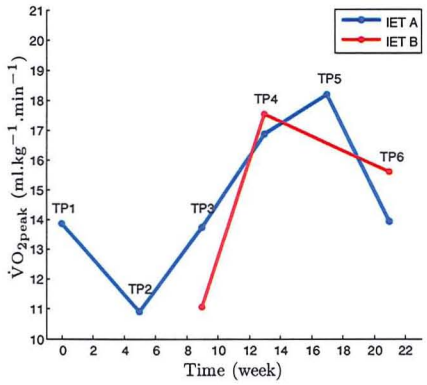


Figure 5.4: $\dot{V}O_{2peak}$ obtained during subject B's incremental exercise test A at each test point and during his incremental exercise test B at test points 3, 4 and 6. TP: test point.

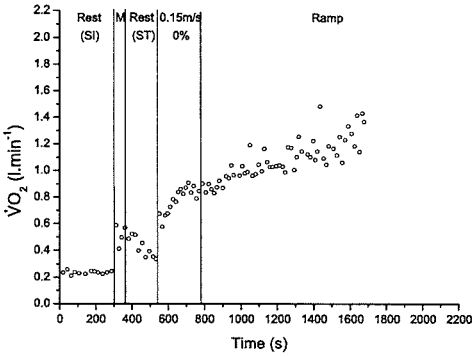
(Figure 5.6 (b)) the $\dot{V}O_2$ response to the linear increase in work rate during the ramp phase of each IET is not well fit by a linear relationship (see also Table 5.7 and 5.8).

IET	R^2 value
TP1	0.55
TP2	0.54
TP3	0.63
TP4	0.75
TP5	0.63
TP6	0.43

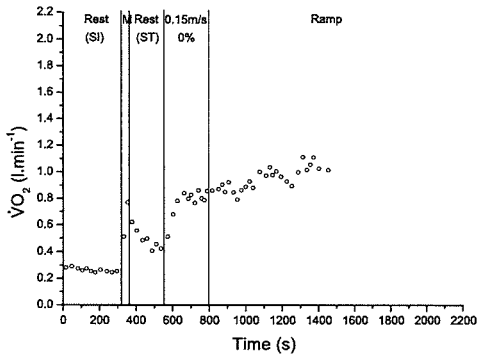
Table 5.7: Linearity of the $\dot{V}O_2$ response during Subject B's incremental exercise test A at each test point, represented by the correlation coefficient (R^2) value. IET: incremental exercise test. TP: test point.

IET	R^2 value
TP3	0.63
TP4	0.95
TP6	0.85

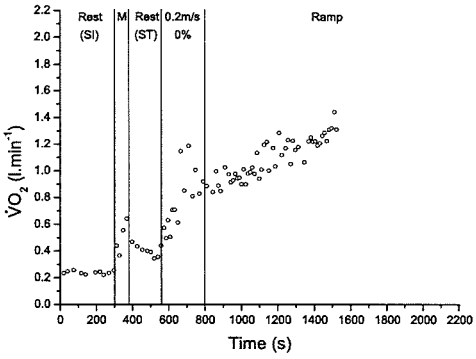
Table 5.8: Linearity of the $\dot{V}O_2$ response during Subject B's incremental exercise tests B at each test point, represented by the correlation coefficient (R^2). IET: incremental exercise test. TP: test point.



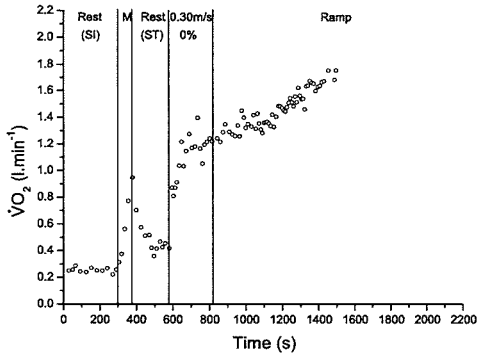
(a) TP1



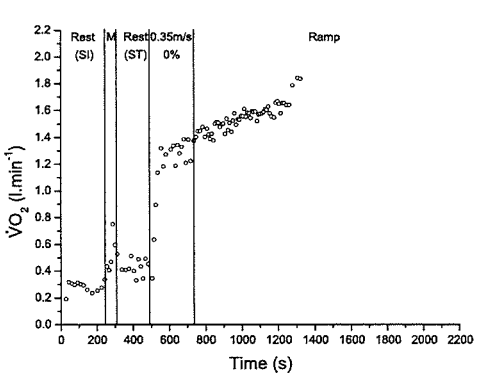
(b) TP2



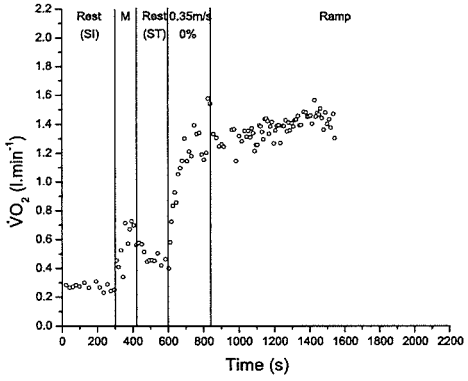
(c) TP3



(d) TP4

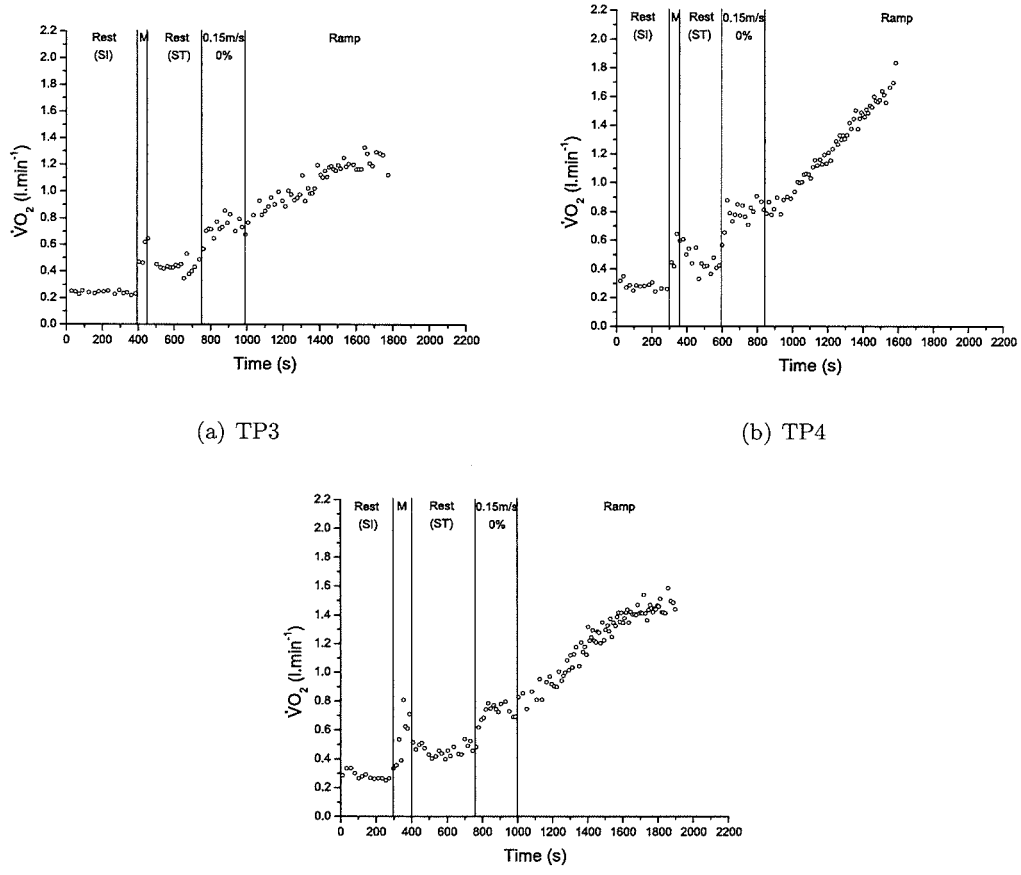


(e) TP5



(f) TP6

Figure 5.5: $\dot{V}O_2$ profile for subject B's incremental exercise test A at each test point. SI: sitting. M: moving. ST: standing. TP: test point. 4 breath average plots.



(a) TP3

(b) TP4

(c) TP6

Figure 5.6: $\dot{V}O_2$ profile for subject B's incremental exercise test B at each test point. SI: sitting. M: moving. ST: standing. TP: test point. 4 breath average plots.

Lactate Threshold

The $\dot{V}O_2$ at which the LT occurred during each test was estimated using the non-invasive V-slope method [78] and supported by the responses of $\dot{V}_E/\dot{V}O_2$, $\dot{V}_E/\dot{V}CO_2$, $F_{ET}O_2$ and $F_{ET}CO_2$ [79]. However, as is stated in Tables 5.5 and 5.6 the presence of an LT was not identified during any of subject B's IET As or IET Bs. As can be seen in Figures 5.7 and 5.9, no detectable deflection point is present in any of the V-slope plots.

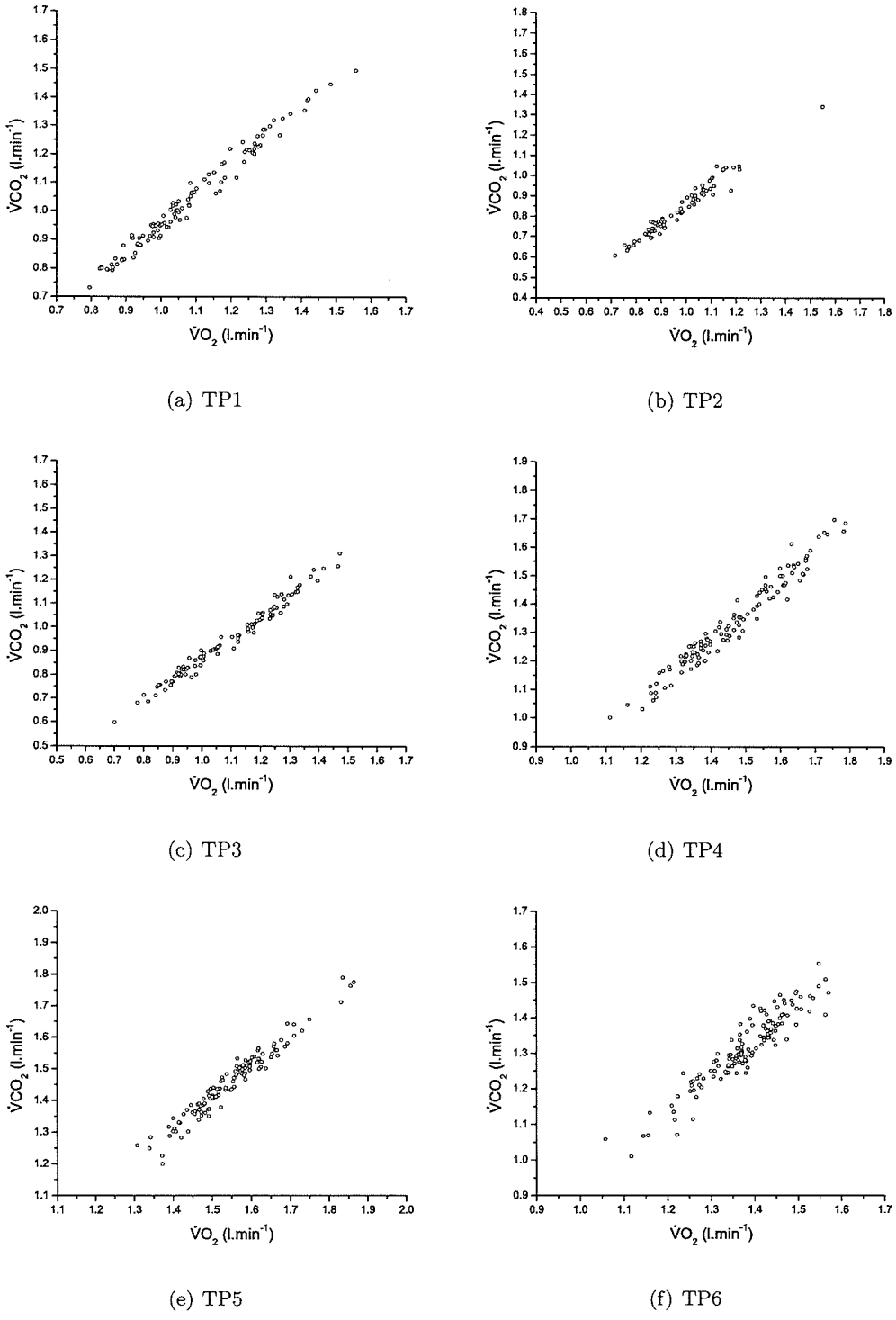
The responses of the supporting respiratory variables during IET A do not suggest the presence of an LT. As can be seen in Figure 5.8 and Appendix B, the noise of the breath-by-breath data makes it difficult to determine the exact pattern of the responses. During the ramp phase of the IET, $\dot{V}_E/\dot{V}O_2$ is expected to fall gradually and reach a steady-state before increasing at the point of the LT. At TP2 and TP6, $\dot{V}_E/\dot{V}O_2$ appears to decrease and then increase again which may suggest the presence of an LT. As $\dot{V}_E/\dot{V}CO_2$ is closely coupled to $\dot{V}_E$, an increase in $\dot{V}_E/\dot{V}CO_2$ does not occur at the LT. The $\dot{V}_E/\dot{V}CO_2$ response is expected to fall gradually and reach a steady-state at the point of the LT before increasing again at the respiratory compensation point (RCP). At no TP does $\dot{V}_E/\dot{V}CO_2$ display the expected response. The $\dot{V}_E/\dot{V}O_2$ and $\dot{V}_E/\dot{V}CO_2$ responses to the ramp increase in work rate do not reflect the standard responses which would be produced by an able-bodied (AB) subject and therefore do not support the presence of an LT.

A similar situation is also found with the $F_{ET}O_2$ and $F_{ET}CO_2$ responses to the increasing work rate. The expected $F_{ET}O_2$ response is identical to that of $\dot{V}_E/\dot{V}O_2$. As for $\dot{V}_E/\dot{V}O_2$, the $F_{ET}O_2$ responses at TP2 and TP6 do suggest the presence of an LT. However, at no other TP does $F_{ET}O_2$ display the expected response. None of the $F_{ET}CO_2$ responses reflect that which would be expected if an LT was present: increasing prior to and attaining a steady-state at the point of the LT, then decreasing at the RCP.

The responses of the respiratory variables during IET B are clearer than those of the IET A (see Figure 5.10 and Appendix B). At TP6B a clear increase in $\dot{V}_E/\dot{V}O_2$ following a period of steady-state can be seen, suggesting the presence of an LT. However, at no other TP is this expected response displayed. At no TP does the $\dot{V}_E/\dot{V}CO_2$ response reflect that which would be expected if an LT was present.

A similar situation is also found with the $F_{ET}O_2$ and $F_{ET}CO_2$ responses to the increasing work rate. A clear increase in $F_{ET}O_2$, following a period of steady-state, is present at TP6B suggesting the presence of an LT. However, at no other TP is the expected $F_{ET}O_2$ response displayed. None of the $F_{ET}CO_2$ responses reflect that which would be expected if an LT was present. As for the IET As, the supporting respiratory variable responses of the IET Bs do

not support the presence of an LT.



(a) TP1

(b) TP2

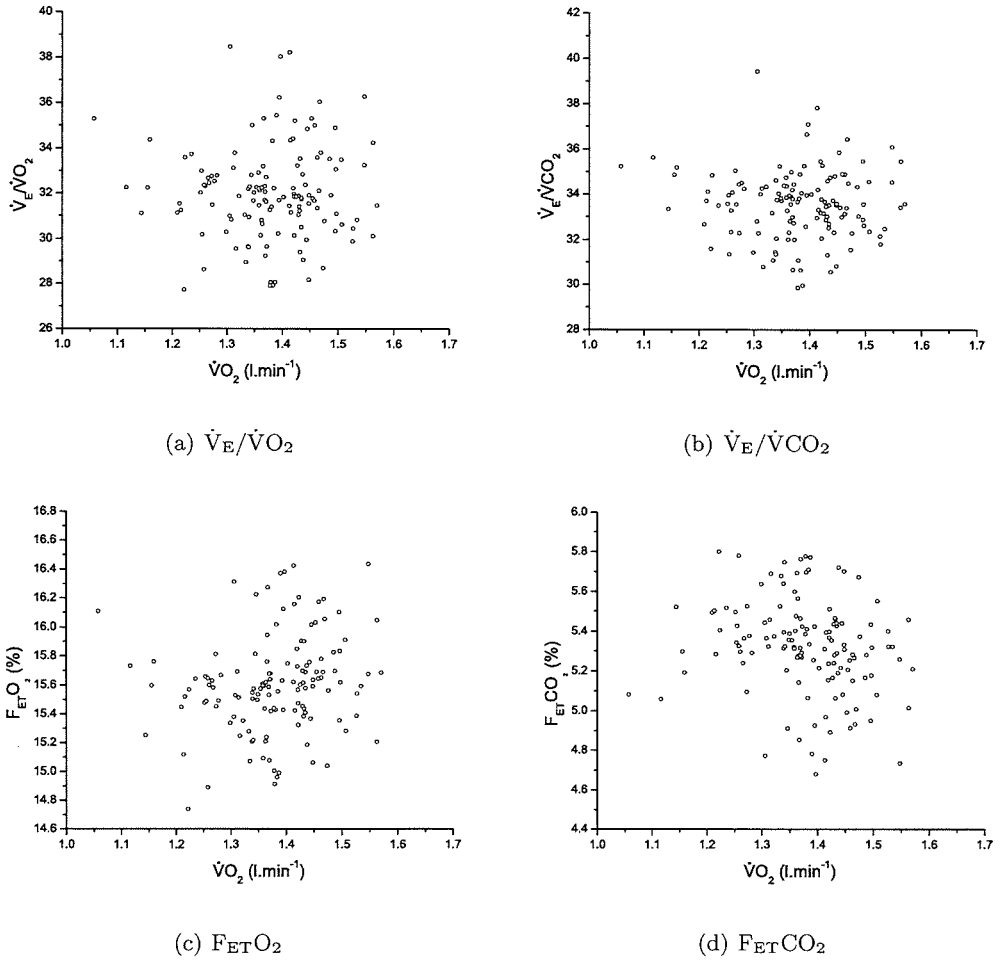
(c) TP3

(d) TP4

(e) TP5

(f) TP6

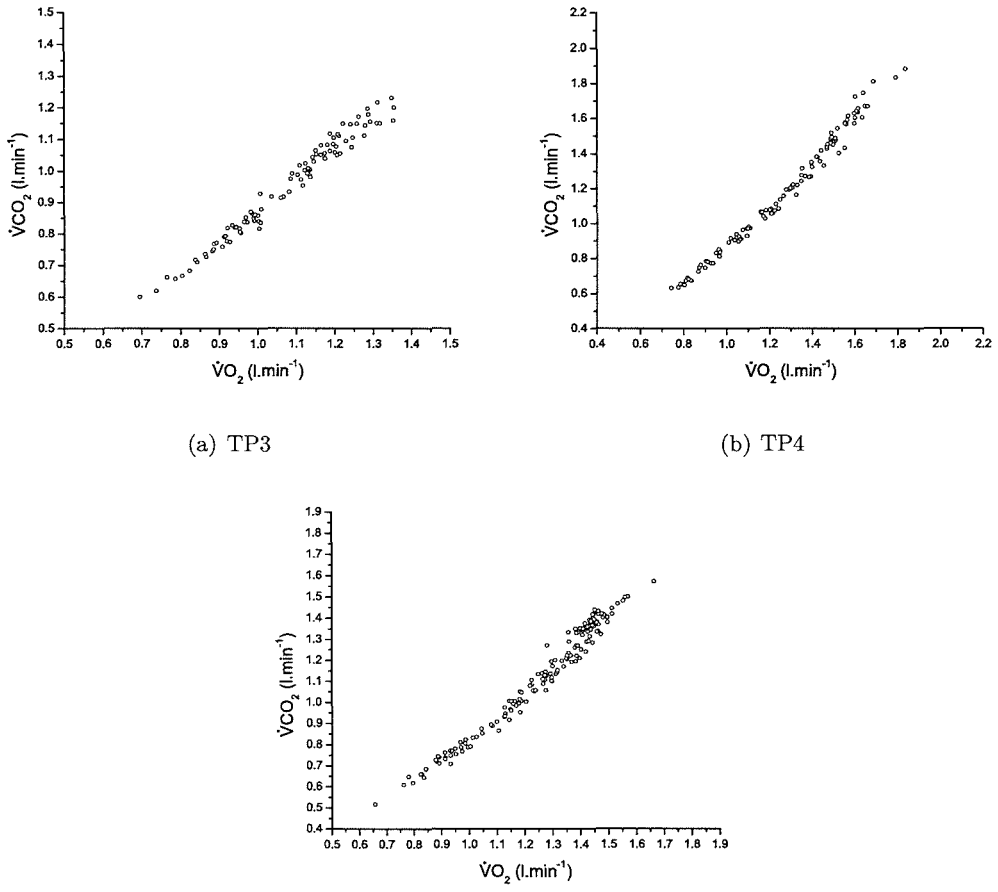
Figure 5.7: V-slope plots for subject B's incremental exercise test A at each test point. Kinetic phase not removed. 2 breath average plots.



(a) $\dot{V}_E/\dot{V}O_2$ (b) $\dot{V}_E/\dot{V}CO_2$

(c) $F_{ET}O_2$ (d) $F_{ET}CO_2$

Figure 5.8: Respiratory variable responses during the ramp phase of the incremental exercise test A at test point 6. Kinetic phase not removed. 2 breath averaged plots.

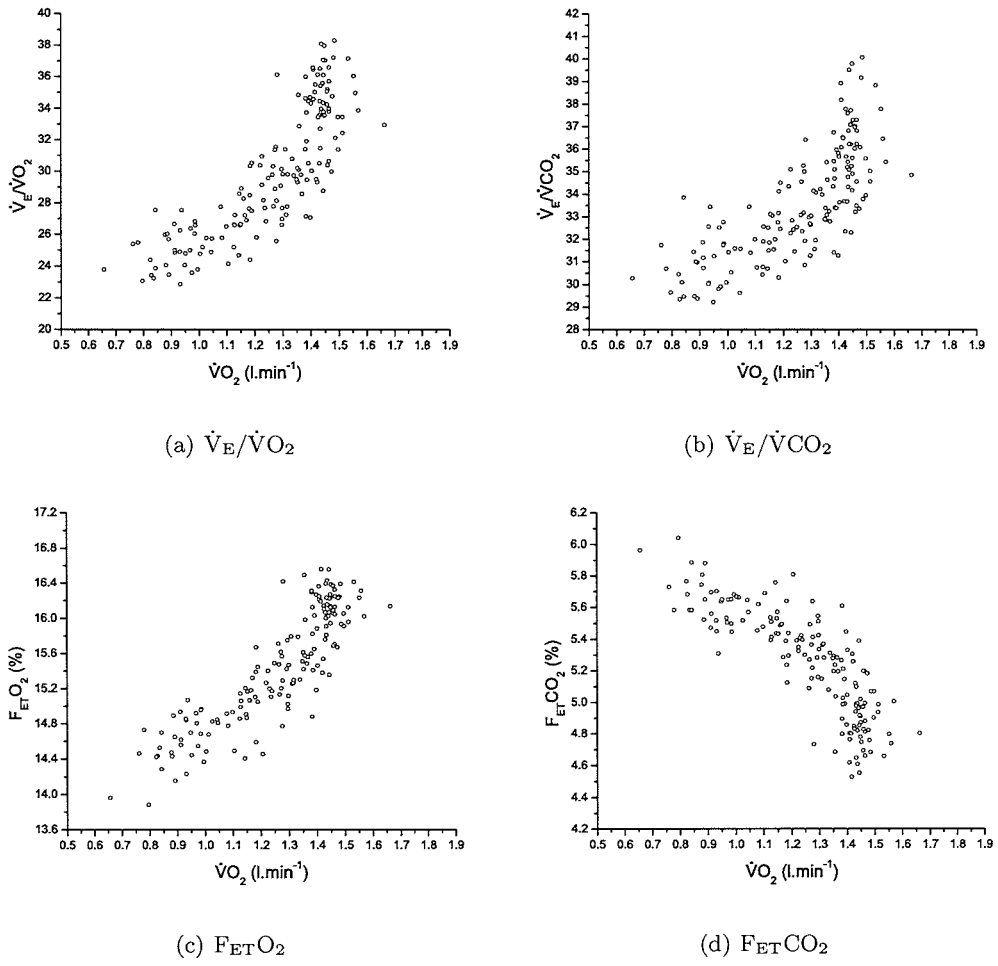


(a) TP3

(b) TP4

(c) TP6

Figure 5.9: V-slope plots for subject B's incremental exercise test B at each test point. Kinetic phase not removed. 2 breath average plots.



(a) $\dot{V}_E/\dot{V}O_2$ (b) $\dot{V}_E/\dot{V}CO_2$

(c) $F_{ET}O_2$ (d) $F_{ET}CO_2$

Figure 5.10: Respiratory variable responses during the ramp phase of the incremental exercise test B at test point 6. Kinetic phase not removed. 2 breath averaged plots.

Slope of Oxygen Uptake as a function of Work Rate

As can be seen in Figure 5.11, the $\Delta\dot{V}O_2/\Delta WR$ of walking during the IET A decreased substantially with training, with the largest decrease occurring during the first four weeks of training. Following 20 weeks of treadmill training $\Delta\dot{V}O_2/\Delta WR$ decreased by 93% from 66.57–4.52 $ml.min^{-1}.W^{-1}$

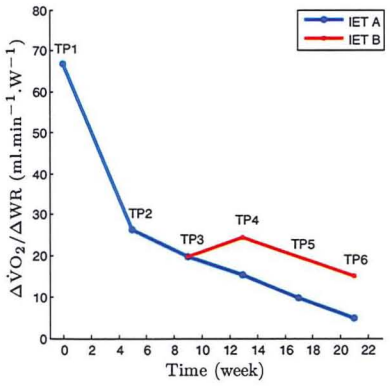
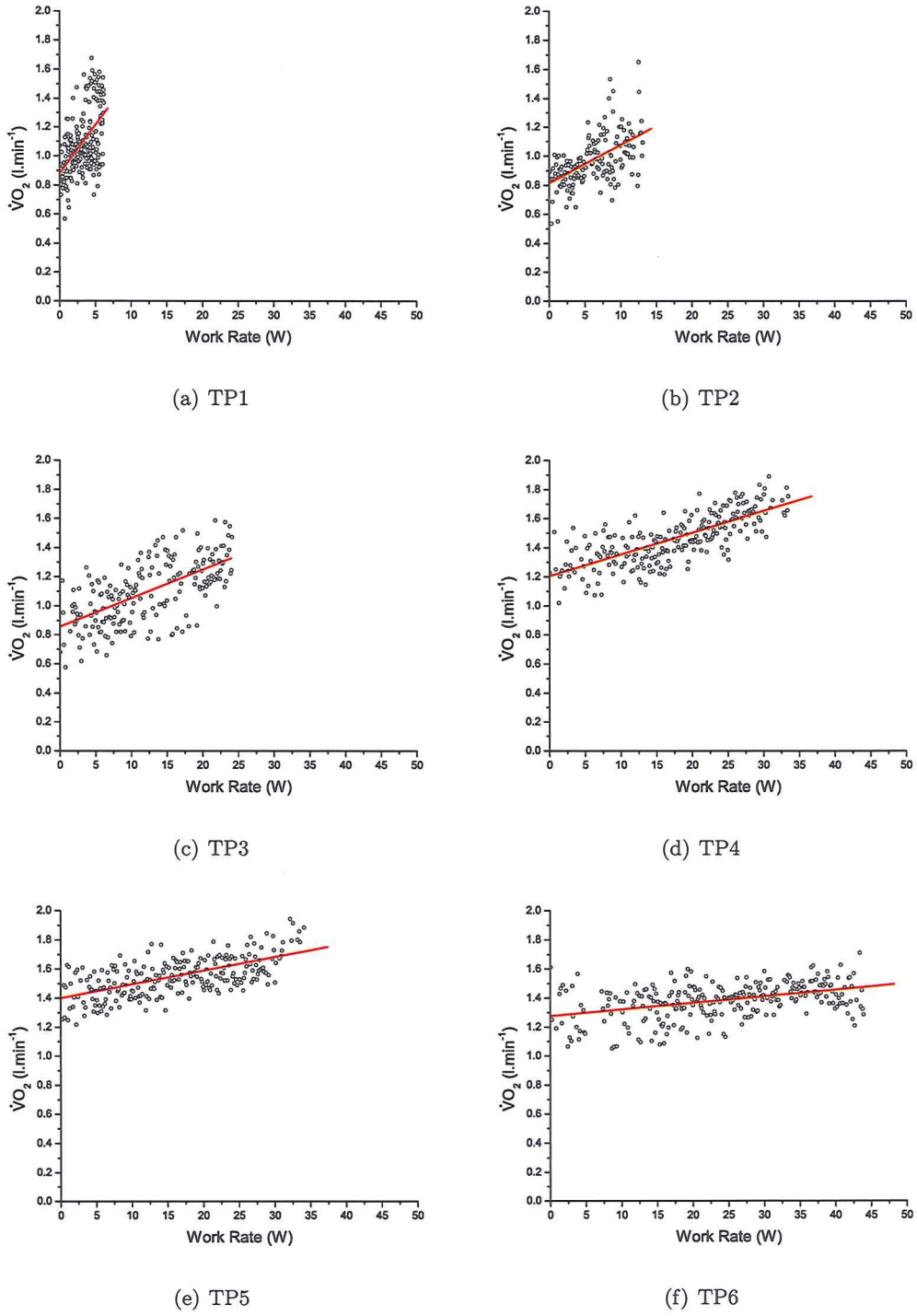


Figure 5.11: The slope of $\dot{V}O_2$ as a function of work rate obtained during subject B's incremental exercise test A at each test point and during his incremental exercise test B at test points 3, 4 and 6. $\Delta\dot{V}O_2/\Delta WR$: slope of oxygen uptake as a function of work rate. TP: test point.

As can be seen in Figure 5.11 the $\Delta\dot{V}O_2/\Delta WR$ obtained during the IET B does decrease with training. However, it is shown to increase from TP3 to TP4 before decreasing at TP6. The $\Delta\dot{V}O_2/\Delta WR$ obtained during the IET B at TP3 is equal to that obtained from the IET A. However, at TP4 and TP6, it is substantially higher during the IET B than during the IET A.

The WR-$\dot{V}O_2$ plots from the IET A and IET B at each TP are shown in Figures 5.12 and 5.13 respectively.



(a) TP1

(b) TP2

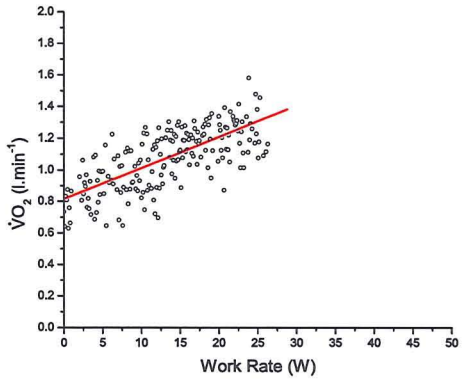
(c) TP3

(d) TP4

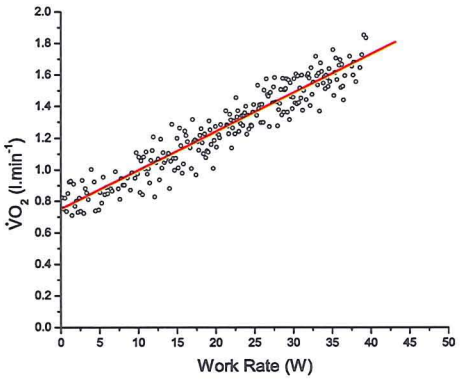
(e) TP5

(f) TP6

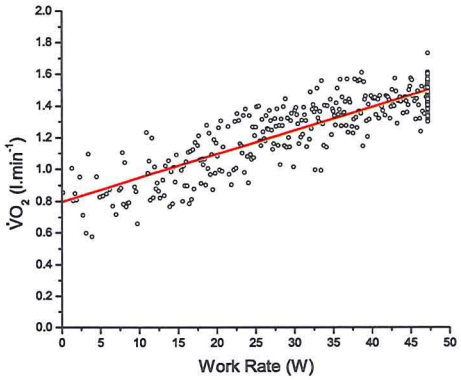
Figure 5.12: The $\Delta\dot{V}O_2/\Delta WR$ for subject B's incremental exercise test A at each test point, represented by the slope of the straight line fit.



(a) TP3



(b) TP5



(c) TP6

Figure 5.13: The $\Delta\dot{V}O_2/\Delta WR$ for subject B's incremental exercise test B at each test point, represented by the slope of the straight line fit.

Peak Heart Rate

As can be seen in Figure 5.14, the HR_{peak} achieved by subject B during his IET A increased substantially between TP1 and TP6. During the first three IETs the HR_{peak} achieved was quite low, ranging from 132–134 bpm. However, at TP4 it increased to 150 bpm and on completion of the 20 weeks BWSTT programme had reached 157 bpm, a 17% increase from baseline.

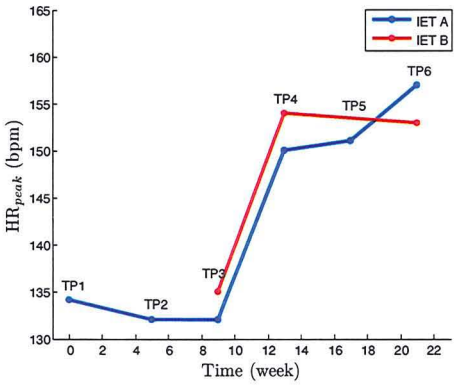


Figure 5.14: HR_{peak} achieved during subject B's incremental exercise test A at each test point and during his incremental exercise test B at test points 3, 4 and 6. TP: test point.

In comparison to the HR_{peak} achieved during the IET A, the HR_{peak} achieved during the IET B was slightly higher at TP3 and TP4 (Figure 5.14). In contrast to the IET A, there was no further increase in HR_{peak} at TP6 during the IET B.

5.3.3 Constant Load Exercise Test

At each TP the speed and gradient of the SET remained at 0.15 $m.s^{-1}$, 0% respectively to allow a direct comparison of the response kinetics and thus determine their adaptation to training. The key outcome variables for each test are provided in Table 5.9 and the $\dot{V}O_2$ response profiles are shown in Figure 5.16.

As can be seen in Figure 5.16 (b and c), the $\dot{V}O_2$ response to the step increase in work rate reached a steady-state at TP2 and TP3. This is confirmed by the detection of corresponding τ values which show that $\dot{V}O_2$ reached a steady-state within the 15 minute duration of the test (Table 5.9). Although the τ value obtained for TP6 was ~3 times higher than that obtained at TP2 and TP3, it still suggests that the $\dot{V}O_2$ response reached a steady-state within the 15 minute test duration. A τ value was not obtained for the $\dot{V}O_2$ response at TP4

SET	TP1 (week 0)	TP2 (week 5)	TP3 (week 9)	TP4 (week 13)	TP5 (week 17)	TP6 (week 21)
Step duration (s)	900	900	900	900	900	900
Step $\dot{V}O_2$ (final 20s) ($l.min^{-1}$)	1.30	0.82	0.83	0.88	0.91	0.82
Step $\dot{V}O_2$ (final 20s) ($ml.kg^{-1}.min^{-1}$)	12.67	7.99	8.09	8.90	9.03	8.23
HR_{peak} (bpm)	130	83	84	93	94	95
$\Delta\dot{V}O_2$ ($l.min^{-1}$)	NA	0.39	0.42	NA	NA	0.40
$\tau\dot{V}O_2$ (s)	579.41	41.43	29.22	NA	491.02	139.42
Speed ($m.s^{-1}$)	0.15	0.15	0.15	0.15	0.15	0.15
Gradient (%)	0	0	0	0	0	0
Seated resting $\dot{V}O_2$ ($l.min^{-1}$)	NA	0.26	0.25	0.26	0.27	0.27
Standing resting $\dot{V}O_2$ ($l.min^{-1}$)	0.37	0.43	0.41	0.44	0.44	0.42

Table 5.9: Key outcome variables for subject B's constant load (step) exercise test at each test point. SET: step exercise test. $\Delta\dot{V}O_2$: increase in oxygen uptake from standing rest to steady state. τ: time constant for oxygen uptake. NA: no value was obtained.

suggesting that it did not reach a steady-state. As can be seen in Figure 5.16 (d), the $\dot{V}O_2$ response continued to increase linearly throughout the test. τ values were obtained at TP1 and TP5. However, they were unexpectedly high indicating that the $\dot{V}O_2$ response did not reach a steady-state within the 15 minute test duration. As can be seen in Figure 5.16 (a and e), the $\dot{V}O_2$ responses did not continually increase linearly as it did at TP4. However, it did not reach a steady-state. Although $\tau\dot{V}O_2$ does appear to decrease with training, there is no pattern to the response with the lowest $\tau\dot{V}O_2$ identified at TP3.

As a steady-state $\dot{V}O_2$ was not reached at TP1, TP4 and TP5, $\Delta\dot{V}O_2$ could not be calculated. However, as can be seen in Table 5.9 the $\Delta\dot{V}O_2$ at TP2, TP3 and TP6 remained approximately equal.

The final 20s of the $\dot{V}O_2$ response was averaged for each test to provide an indication of the $\dot{V}O_2$ at the end of each test. As can be seen in Figure 5.15, the $\dot{V}O_2$ at the end of the test decreased substantially following 5 months BWSTT although this decrease was not continuous.

It is evident that the HR response to the step increase in work rate did not stabilise but

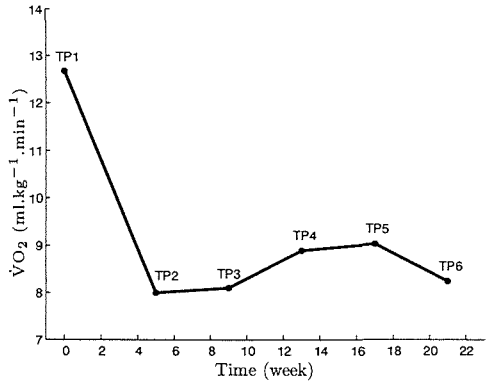
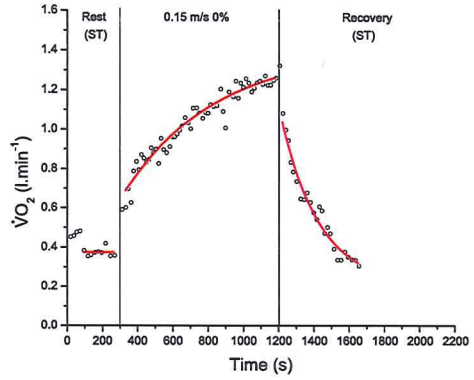
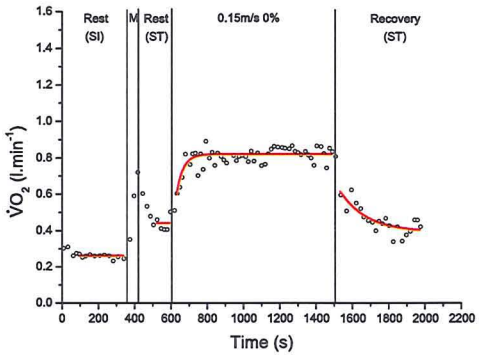


Figure 5.15: $\dot{V}O_2$ during the final 20 seconds of subject B's constant load (step) exercise test at each test point. $\dot{V}O_2$: rate of oxygen uptake. TP: test point.

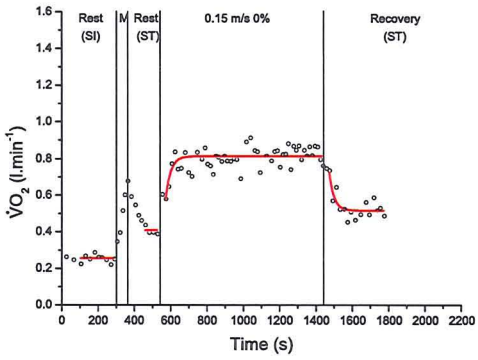
continued to increase throughout the test (Figure 5.17). The HR_{peak} during each test is provided in Table 5.9.



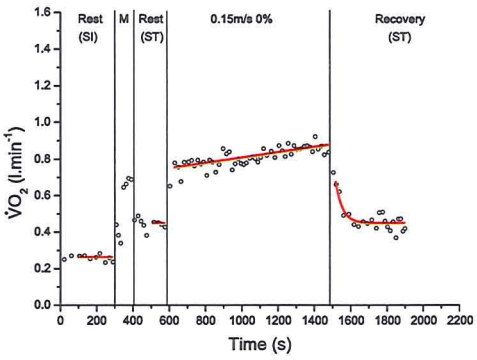
(a) TP1



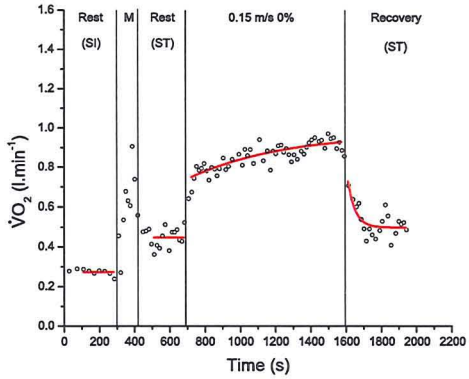
(b) TP2



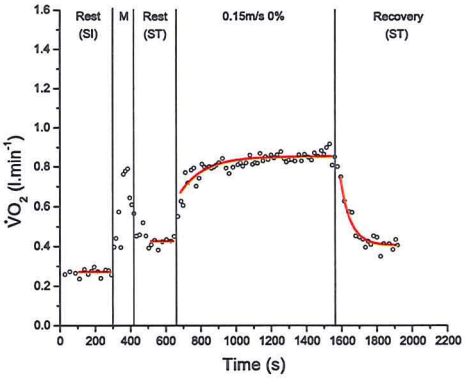
(c) TP3



(d) TP4

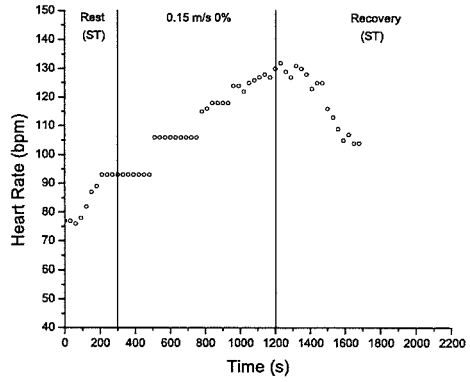


(e) TP5

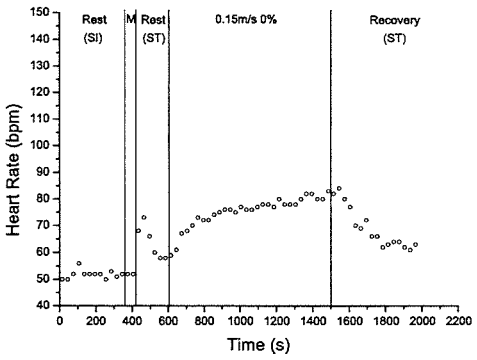


(f) TP6

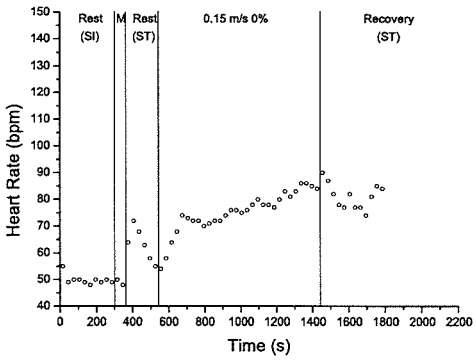
Figure 5.16: $\dot{V}O_2$ profile for subject B's constant load (step) exercise test at each test point. SI: sitting. M: moving. ST: standing. TP: test point. 4 breath average plots.



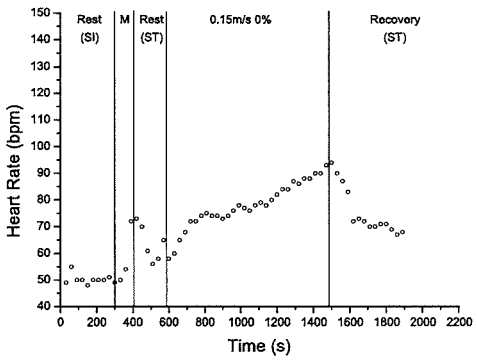
(a) TP1



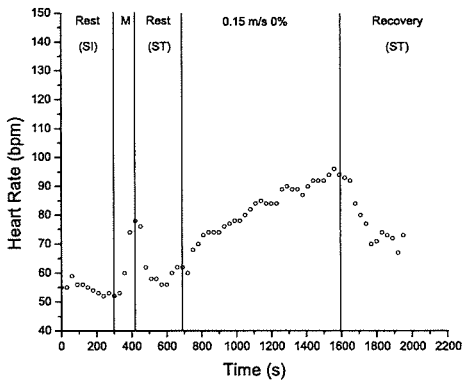
(b) TP2



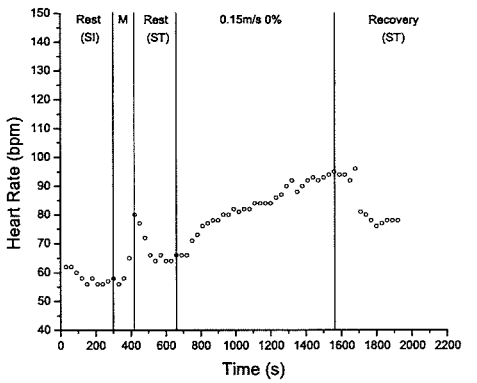
(c) TP3



(d) TP4



(e) TP5



(f) TP6

Figure 5.17: HR profile for subject B's constant load (step) exercise test at each test point. SI: sitting. M: moving. ST: standing. TP: test point.

5.3.4 15 Minute Distance Test

As can be seen in Table 5.10, the speeds chosen by subject B for the 15 minute distance test increased at each TP. Consequently, following 5 months of BWSTT, the distance achieved in 15 minutes increased by 121%.

Distance Test	TP1 (week 0)	TP2 (week 5)	TP3 (week 9)	TP4 (week 13)	TP5 (week 17)	TP6 (week 21)
Speed ($m.s^{-1}$)	0.15	0.15–0.22	0.20–0.25	0.30–0.33	0.25–0.35	0.30–0.40
Distance (m)	142	175	219	279	291	314

Table 5.10: Walking speed and distance achieved by subject B during the 15 minute distance test at each test point. TP: test point.

5.3.5 Twitch Test

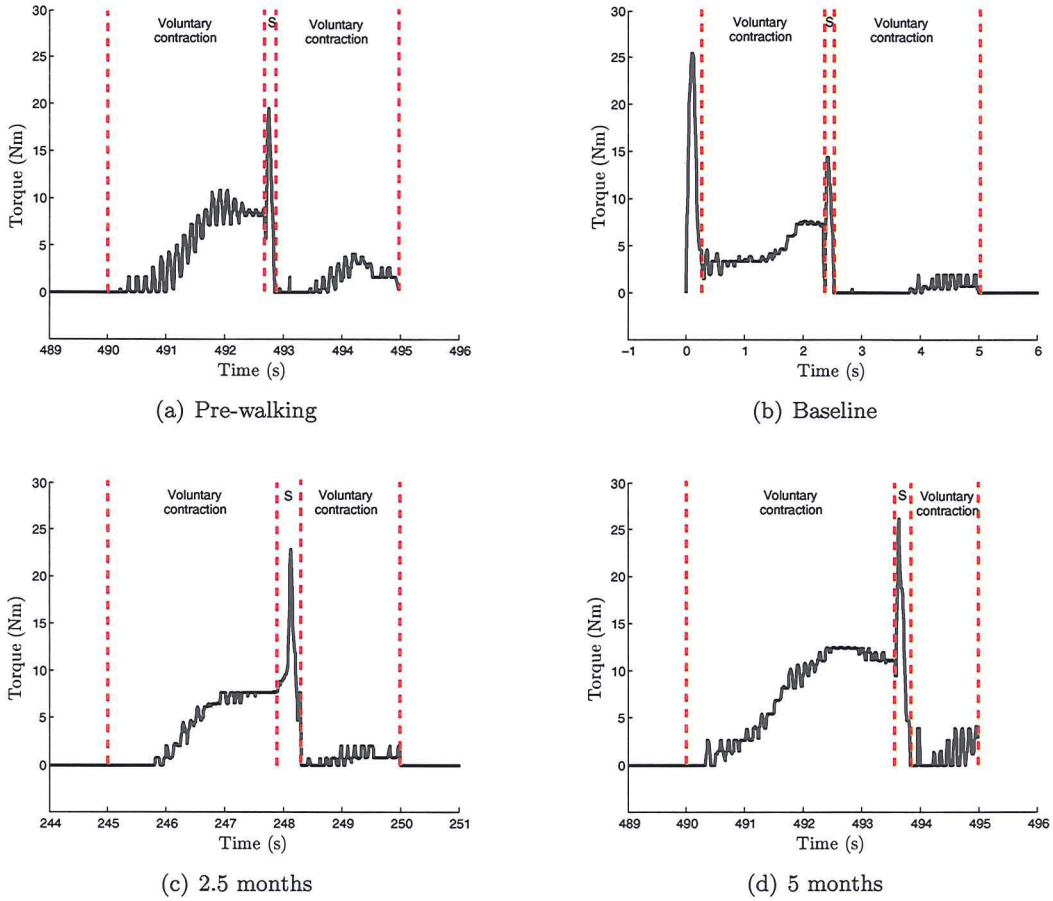
Right Hamstring Muscle at 90^o flexion

The key outcome measures for the right hamstring muscle test at 90^o of flexion at each TP are provided in Table 5.11. The corresponding force traces are shown in Figure 5.18.

Test	Pre-walking	Baseline	2.5 months	5 months
Peak voluntary force (Nm)	10.80	7.60	7.70	12.50
Peak total force (Nm)	19.50	14.40	22.90	26.20
CAR	0.45	0.53	0.34	0.48

Table 5.11: Key outcome measures for subject B's right hamstring test at 90^o of flexion, at each test point. CAR: central activation ratio.

At all TPs, with the exception of the 5 month TP, the contraction which produced the highest voluntary force also produced the highest total force when the stimulation was applied to the contracting muscle. The total force produced at the 5 month TP was 1.3 Nm lower than the maximum total force attained across all 3 contractions. The peak voluntary force provided in Table 5.11 for each TP represents the maximum force produced prior to the delivery of the stimulation. However, as can be seen in Figure 5.18 (a) and (d) subject B was not always able to maintain a steady-state voluntary force. Therefore, the peak voluntary force reported does not always correspond to the force produced immediately prior to stimulation delivery. Following $\sim$7 months of BWSTT, the peak voluntary force that subject B could produce with his right hamstring positioned at 90^o of flexion increased. However, this increase was not continuous throughout the training period, decreasing at the baseline and 2.5 month TPs. The peak total force and CAR also increased following $\sim$7 months of BWSTT, however the increase was not continuous between each TP.



(a) Pre-walking

(b) Baseline

(c) 2.5 months

(d) 5 months

Figure 5.18: Force trace profiles produced by subject B with the right hamstring positioned at 90 degrees of flexion. As indicated on each of the plots, subject B contracted his right hamstring for 2–3 seconds, a short stimulation burst (S) was then added following which subject B maintained his voluntary contraction for the remainder of the test. The large increase in force produced at the start of the baseline test (b) was caused by the investigator moving the dynamometer arm to start the timer.

Right Hamstring Muscle at 30^o flexion

The key outcome measures for the right hamstring test at 30^o of flexion at each TP are provided in Table 5.12 and the corresponding force trace profiles in Figure 5.19.

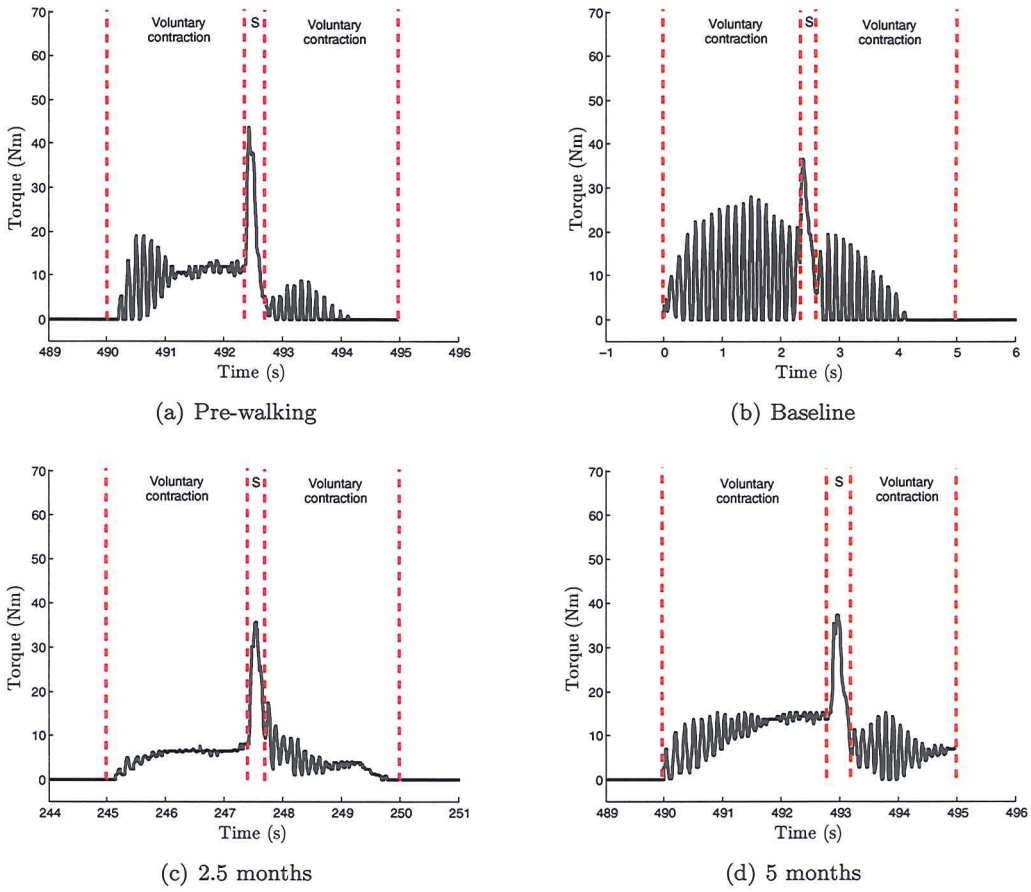
Test	Pre-walking	Baseline	2.5 months	5 months
Peak voluntary force (Nm)	19.00	27.90	10.00	20.10
Peak total force (Nm)	43.70	36.50	37.40	42.80
CAR	0.43	0.76	0.27	0.47

Table 5.12: Key outcome measures for subject B's right hamstring test at 30^o of flexion, at each test point. CAR: central activation ratio.

The contraction which produced the highest voluntary force during the 2.5 and 5 month tests also produced the highest total force. However, during the pre-baseline and baseline tests the total force associated with the peak voluntary force was 2.4 Nm and 0.4 Nm lower, respectively, than the maximum total force. With the exception of the 2.5 month test, subject B was unable to maintain a steady-state voluntary contraction in his right hamstring at 30^o flexion. Therefore, the peak voluntary force shown in Table 5.12 is not always representative of the force produced immediately prior to the stimulation delivery.

The peak voluntary force and peak total force produced by the hamstrings at 30^o of flexion is higher at each TP than when they are positioned at 90^o of flexion.

The peak voluntary force produced by subject B with the hamstrings positioned at 30^o is shown to increase slightly following $\sim$7 months BWSTT. However, this increase was not continuous at each TP with the highest peak voluntary force being produced at baseline. The peak total force decreased slightly over the same period of training. Again the decrease was not continuous with the lowest peak total force obtained at baseline. The fluctuations in the CAR were quite large although it is shown to increase slightly with training.



(a) Pre-walking

(b) Baseline

(c) 2.5 months

(d) 5 months

Figure 5.19: Force trace profiles produced by subject B with the right hamstring positioned at 30 degrees of flexion. As indicated on each of the plots, subject B contracted his right hamstring for 2–3 seconds, a short stimulation burst (S) was then added following which subject B maintained his voluntary contraction for the remainder of the test.

Right Quadriceps Muscle at 90^o flexion

The key outcome measures for the right quadriceps test at each TP are provided in Table 5.13 and the corresponding force traces in Figure 5.20.

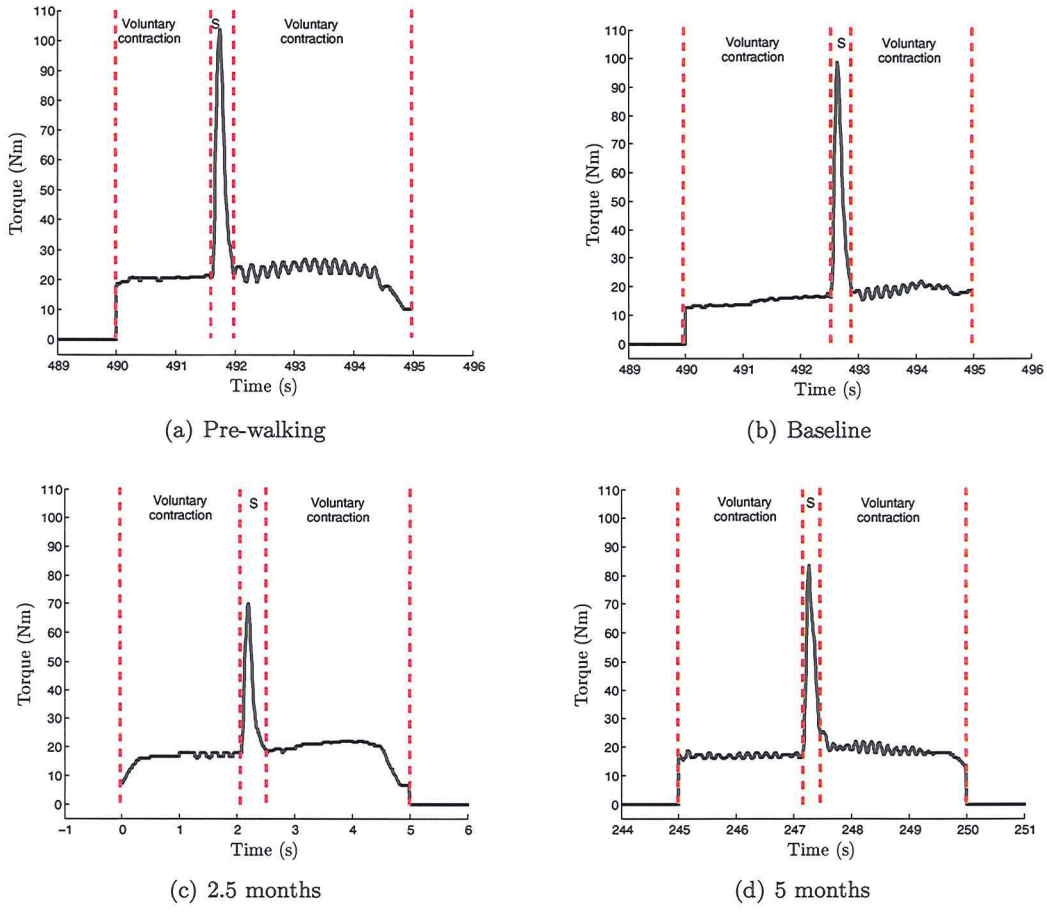
Test	Pre-walking	Baseline	2.5 months	5 months
Peak voluntary force (Nm)	21.60	17.60	18.00	18.80
Peak total force (Nm)	103.70	98.70	70.10	83.50
CAR	0.21	0.18	0.26	0.23

Table 5.13: Key outcome measures for subject B's right quadriceps test at 90^o of flexion, at each test point. CAR: central activation ratio.

Only at pre-baseline and baseline was the highest total force produced during the same contraction as the highest voluntary force. During the 2.5 month test the total force produced was 3.9 Nm lower than the maximum and during the 5 month test it was 2.2 Nm lower than the maximum.

Following ~7 months of BWSTT the peak voluntary force produced by the right quadriceps at 90^o of flexion decreased from 21.60–18.80 Nm. The peak total force, which was higher than that produced by the right hamstrings at each TP, also decreased following ~7 months BWSTT. The decrease in both outcome measures was not continuous at each TP. The CAR remained relatively unchanged.

As can be seen in Figure 5.20, the voluntary force produced after the stimulation delivery is slightly higher at all TPs.



(a) Pre-walking

(b) Baseline

(c) 2.5 months

(d) 5 months

Figure 5.20: Force trace profiles produced by subject B with the right quadriceps positioned at 90 degrees of flexion. As indicated on each of the plots, subject B contracted his right quadriceps for 2–3 seconds, a short stimulation burst (S) was then added following which subject B maintained his voluntary contraction for the remainder of the test.

Left Hamstring Muscle at 90° flexion

The key outcome measures for the left hamstring test at 90° of flexion at each TP are shown in Table 5.14 and the corresponding force traces in Figure 5.21.

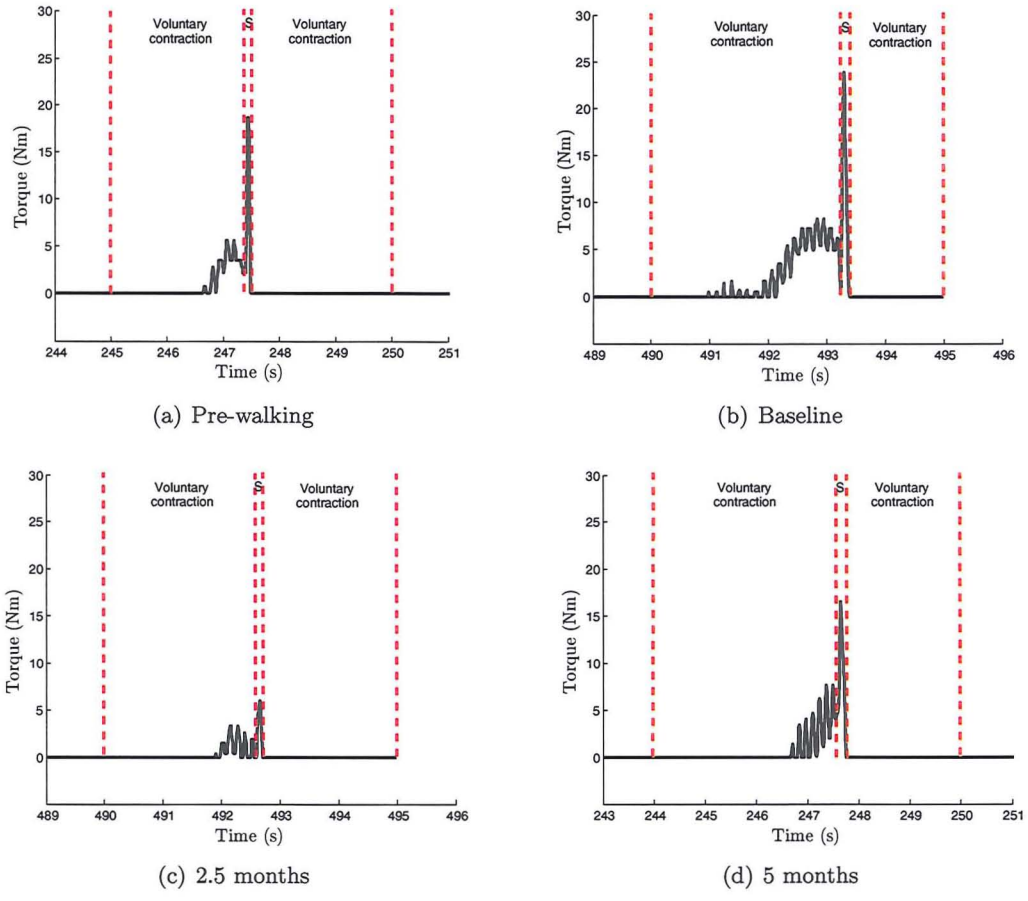
Test	Pre-walking	Baseline	2.5 months	5 months
Peak voluntary force (Nm)	5.60	8.30	3.30	7.60
Peak total force (Nm)	18.70	23.90	6.00	16.50
CAR	0.30	0.35	0.55	0.46

Table 5.14: Key outcome measures for subject B's left hamstring test at 90° of flexion, at each test point. CAR: central activation ratio.

Only at the 5 month TP was the highest total force produced during the same contraction as the highest voluntary force. The total force produced during the contraction which produced the highest voluntary force at the pre-baseline, baseline and 2.5 month TPs was 1.4 Nm, 14.90 Nm and 1.10 Nm lower than the maximum total force respectively. As can be seen in Figure 5.21, subject B could not maintain a steady-state contraction. Therefore, the peak voluntary force does not always represent the voluntary force prior to stimulation delivery.

With training it does appear as though the peak voluntary force which subject B could produce with his left hamstring positioned at 90° of flexion increased. However, the increase was not consistent at each TP with the highest peak voluntary force produced at baseline. The peak total force decreased slightly following ~7 months of BWSTT, with a dramatic reduction found at the 2.5 month TP. The CAR appears to have increased with training.

As can be seen in Figure 5.21, subject B was unable to produce any voluntary force following the stimulation delivery.



(a) Pre-walking

(b) Baseline

(c) 2.5 months

(d) 5 months

Figure 5.21: Force trace profiles produced by subject B with the left hamstring positioned at 90 degrees of flexion. As indicated on each of the plots, subject B contracted his left hamstring for 2–3 seconds, a short stimulation burst (S) was then added following which subject B maintained his voluntary contraction for the remainder of the test.

Left Hamstring Muscle at 30° flexion

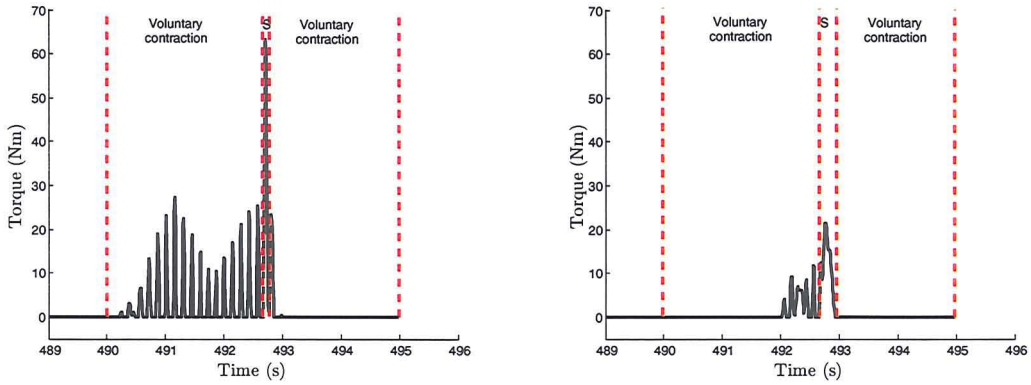
The key outcome measures for the left hamstring muscle test at 30° of flexion at each TP are shown in Table 5.15 and the corresponding force traces in Figure 5.22.

Test	Pre-walking	Baseline	2.5 months	5 months
Peak voluntary force (Nm)	27.40	11.80	16.70	8.00
Peak total force (Nm)	63.30	21.40	27.70	23.20
CAR	0.43	0.55	0.60	0.34

Table 5.15: Key outcome measures for subject B's left hamstring test at 30° of flexion, at each test point. CAR: central activation ratio.

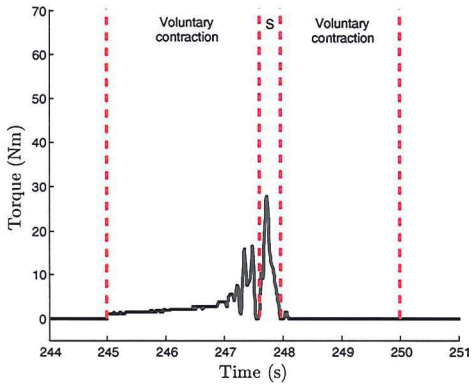
Only at the pre-baseline TP was the highest maximum total force produced during the same contraction as the highest peak voluntary force. The total force produced during the contraction which produced the highest voluntary force was 11.90 Nm lower than the maximum at baseline, 2.8 Nm lower than the maximum at the 2.5 month TP, and 10.40 Nm lower than the maximum at the 5 month TP. As can be seen in Figure 5.22, subject B could not maintain a steady-state voluntary contraction. Therefore, the peak voluntary force provided in Table 5.16 is not always representative of the force prior to delivery of the twitch.

The peak voluntary force produced by subject B with his left hamstring positioned at 30° decreased substantially following ~7 months BWSTT. The decrease was not consistent at each TP, increasing at the 2.5 month TP before decreasing again at 5 months. The peak voluntary force was higher at each TP than that produced with the hamstrings positioned at 90° of flexion. The peak total force produced also decreased substantially following ~7 months BWSTT. An increase was also seen in this outcome measure at the 2.5 month TP. The CAR is also shown to have decreased.

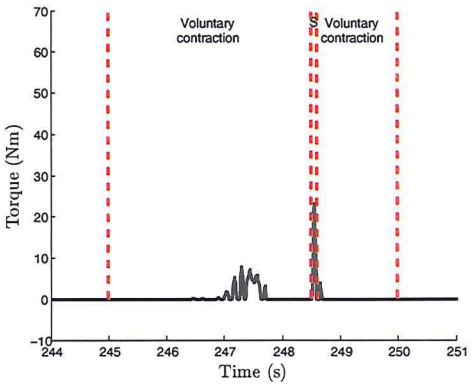


(a) Pre-walking

(b) Baseline



(c) 2.5 months



(d) 5 months

Figure 5.22: Force trace profiles produced by subject B with the left hamstring positioned at 30 degrees of flexion. As indicated on each of the plots, subject B contracted his left hamstring for 2–3 seconds, a short stimulation burst (S) was then added following which subject B maintained his voluntary contraction for the remainder of the test.

Left Quadriceps Muscle at 90^o flexion

The key outcome measures for the left quadriceps test at 90^o of flexion are given in Table 5.16 with the corresponding force traces in Figure 5.23.

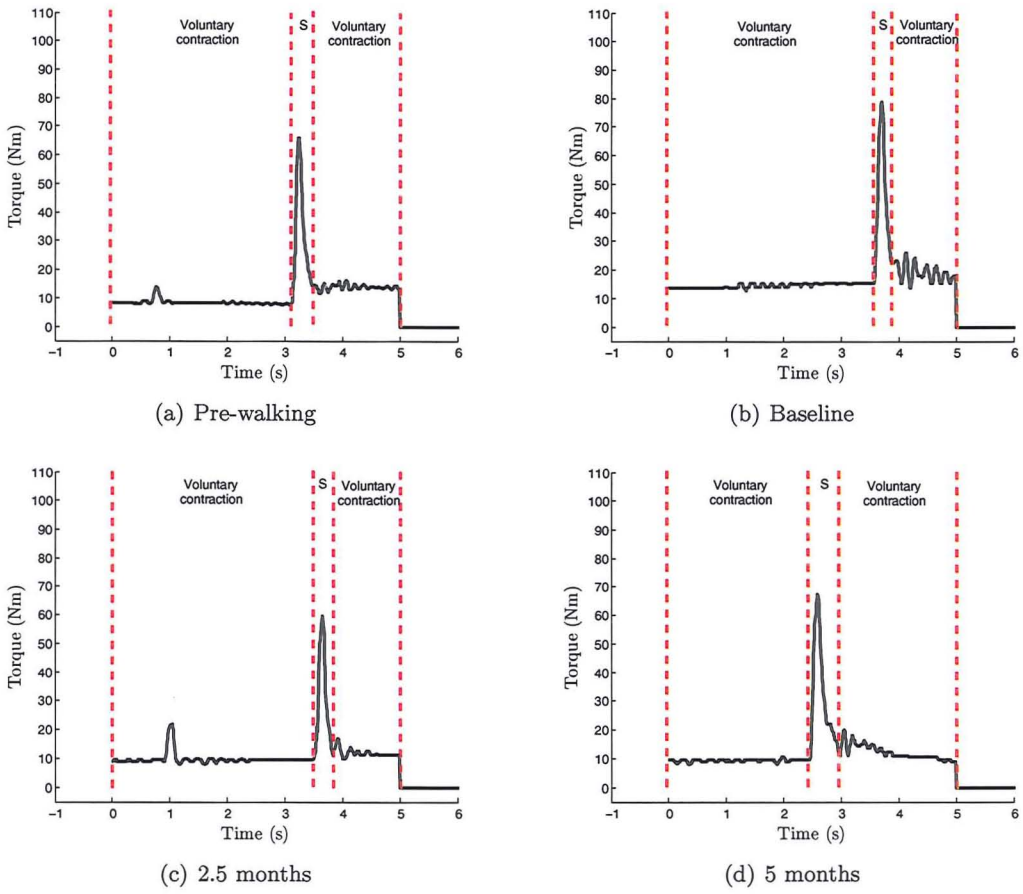
Test	Pre-walking	Baseline	2.5 months	5 months
Peak voluntary force (Nm)	14.10	15.10	22.20	10.80
Peak total force (Nm)	66.20	78.80	59.70	67.50
CAR	0.21	0.19	0.37	0.16

Table 5.16: Key outcome measures for subject B's left quadriceps test at 90^o of flexion, at each test point. CAR: central activation ratio.

At baseline and the 5 month TP the highest total force produced occurred during the same contraction as the highest voluntary force. During the pre-baseline tests the total force produced during the contraction which produced the highest voluntary force was 1.1 Nm lower than the highest total force: during the 2.5 month test is was 0.3 Nm lower. The peak voluntary force presented in Table 5.16 is the highest voluntary force produced during the contraction and may therefore not correspond to the voluntary force prior to the stimulation delivery.

From the pre-baseline to the 2.5 month TP the peak voluntary force produced by subject B increased steadily. However, at the 5 month TP it decreased to below the pre-baseline value. The peak total force produced fluctuated at each TP, increasing slightly following $\sim$7 months of BWSTT. The highest peak total force was produced at baseline. The CAR also fluctuated between TPs showing an overall decrease following $\sim$7 months of BWSTT.

As can be seen in Figure 5.23, the peak voluntary force produced following the stimulation delivery was higher than that prior to its delivery at each TP.



(a) Pre-walking

(b) Baseline

(c) 2.5 months

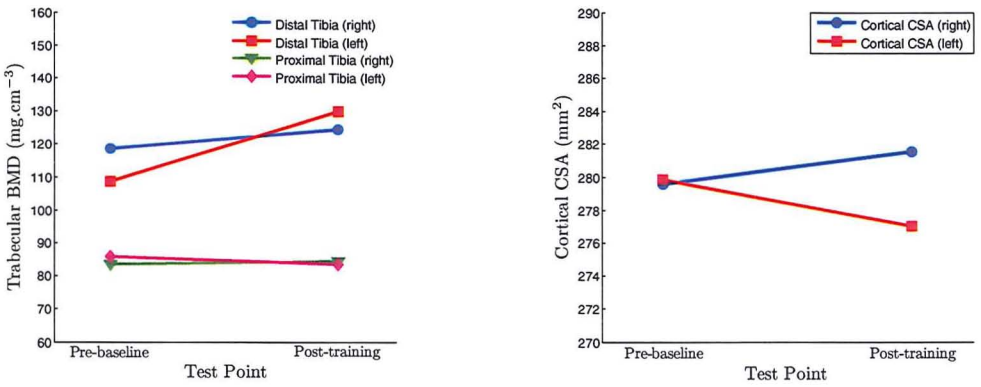
(d) 5 months

Figure 5.23: Force trace profiles produced by subject B with the left hamstring positioned at 90 degrees of flexion. As indicated on each of the plots, subject B contracted his left quadriceps for 2–3 seconds, a short stimulation burst (S) was then added following which subject B maintained his voluntary contraction for the remainder of the test.

5.3.6 Bone Scan

The bone mineral density (BMD), bone cross-sectional area (CSA) and bone mass of subject B's right and left tibia and femur are shown in Table 5.17 prior to any walking training (Pre-baseline) and following the initial pre-baseline and formal 5 month training period (Post-training). As can be seen in Figure 5.24 (a), the trabecular BMD of both the right and left distal tibia increased with training: the largest increase was found in the left distal tibia (19.6% Pre-baseline to Post-training). The trabecular BMD of the right and left proximal tibia remained relatively unchanged throughout training with an increase of only 1.1% in the right proximal tibia and a decrease of only 2.8% in the left proximal tibia.

The cortical CSA, measured in the diaphysis of the tibia, also remained relatively unchanged, following ~7 months of BWSTT, in both the left and right leg (Figure 5.24 (b)). The cortical CSA of the tibia increased by 0.7% in the right leg and decreased by 1.0% in the left leg.



(a) Trabecular BMD of the left and right distal and proximal tibia.

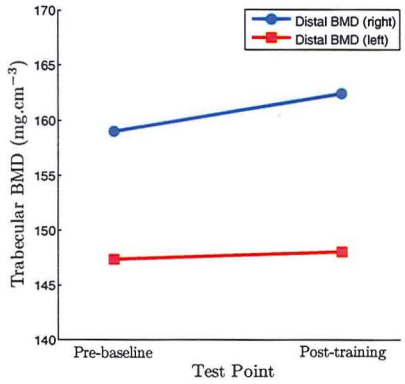
(b) Cortical CSA of the diaphysis of the left and right tibia.

Figure 5.24: Trabecular bone mineral density and cortical cross-sectional area of subject B's left and right tibia at each test point. BMD: bone mineral density. CSA: cross-sectional area.

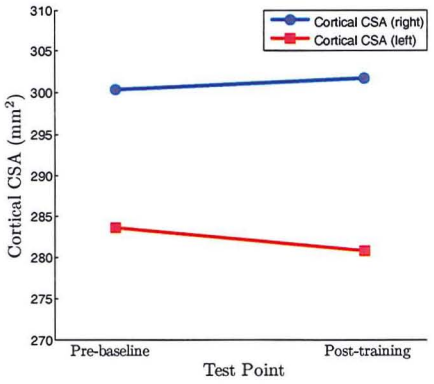
In contrast to the trabecular BMD of the distal tibia, little change was observed in the trabecular BMD of the distal femur with training (Figure 5.25 (a)). The trabecular BMD of the right and left distal femur increased by 2.2% and 0.5% respectively. The differences observed in the cortical CSA of both the right and left femur were also negligible (0.5% increase and 1.0% decrease respectively).

Bone	Region	Scan Site	Parameter	Pre-Baseline		Post-training		% change	
				Right	Left	Right	Left	Right	Left
Tibia	Epiphysis (distal)	4	BMDtrab (mg/cm^3)	118.4	108.3	124.2	129.6	4.9	19.6
			BMDtot (mg/cm^3)	184.2	169.3	188.2	190.6	2.1	12.6
			Bone mass (g/cm)	2.68	2.43	2.75	2.78	2.6	14.4
	Diaphysis	38	BMDcort (mg/cm^3)	1121.9	1119.2	1118.5	1115.6	-0.3	-0.3
			CSAcort (mm^2)	279.5	279.8	281.5	277.0	0.7	-1.0
			Bone mass (g/cm)	3.62	3.62	3.63	3.58	0.3	-1.1
	Epiphysis (proximal)	4	BMDtrab (mg/cm^3)	83.1	85.5	84.0	83.2	1.1	-2.8
			BMDtot (mg/cm^3)	136.1	130.8	136.1	134.1	0.0	2.5
			Bone mass (g/cm)	4.50	4.38	4.45	4.48	-1.1	2.3
Femur	Epiphysis (distal)	4	BMDtrab (mg/cm^3)	158.9	147.2	162.3	147.9	2.2	0.5
			BMDtot (mg/cm^3)	197.8	190.6	200.1	192.6	1.2	1.1
			Bone mass (g/cm)	7.6	7.2	7.7	7.3	0.8	1.7
	Diaphysis	25	BMDcort (mg/cm^3)	1102.7	1107.7	1107.7	1111.0	0.5	0.3
			CSAcort (mm^2)	300.2	283.5	301.6	280.7	0.5	-1.0
			Bone mass (g/cm)	4.33	4.07	4.36	4.06	0.7	-0.3

Table 5.17: Bone parameters determined from subject B's pQCT scans. BMDtrab: trabecular bone mineral density. BMDtotal: total bone mineral density. BMDcort: cortical bone mineral density. CSAcort: cortical cross-sectional area.



(a) Trabecular BMD of the left and right distal femur.



(b) Cortical CSA of the left and right femur.

Figure 5.25: Trabecular bone mineral density and cortical cross-sectional area of subject B's left and right femur at each test point. BMD: bone mineral density. CSA: cross-sectional area.

5.4 Discussion

5.4.1 Training Performance

Following 12 weeks of BWSTT subject B's training speed increased 3-fold, from 0.10–0.30 m.s^{-1}. During the remaining 8 weeks of training the training speed did not increase further. Although the speed at which subject B could walk during his training sessions did increase substantially it is still very slow when compared to that of able-bodied (AB) individuals whose preferred (not maximum) walking speed is 1.5 m.s^{-1} [203]. As discussed in Section 4.4.1, the ability of those with an incomplete SCI to increase their walking speed is limited by their inability to increase their stride frequency. In order to adapt to increases in walking speed they increase their stride length. However, those with an incomplete SCI reach their maximum stride length at a much lower walking speed than AB individuals and therefore, as for subject B, their maximum walking speed can be very limited.

Despite being very low compared to AB individuals, the maximum training speed achieved by subject B is comparable with that of other incomplete SCI subjects following a period of treadmill training. In a study by Effing and colleagues [160], the mean treadmill speed of 3 incomplete SCI subjects following 12 weeks of 30 minutes, 5 days per week treadmill training was 0.16–0.32 m.s^{-1}. Despite the frequency of the training sessions being lower, subject B achieved a comparable training speed following the same number of weeks training. He also achieved a comparable treadmill walking speed to those incomplete SCI subjects who had been training for 6 months (0.35 ($\pm$ 0.04) m.s^{-1}) [164] and 12 months (0.39 ($\pm$ 0.22) m.s^{-1})

[159]. This is despite the fact that therapist assistance with foot placement and trunk stability was provided in these studies, if required, and that the subject's speed was selected depending on their performance. In this study no therapist assistance was provided although FES was applied to the left peroneal nerve to elicit the withdrawal reflex and thus prevent foot drop. Also, the subject's training speed was determined by the investigator according to the protocol outlined in Chapter 3: the subject was only allowed to increase their walking speed if they completed 3 sessions of the required duration. Subject B was unable to complete 3, 30 minute sessions at 0.30 $m.s^{-1}$, therefore, his training speed was not increased. It is possible, had his training speed not been limited by the duration for which he could walk, that subject B would have self-selected a faster treadmill walking speed. As can be seen in Table 5.10 the self-selected walking speeds for the 15 minute distance tests were higher at each TP than the corresponding training speed.

On completion of the 20 week training programme the gradient at which subject B walked during his training sessions increased substantially from 0–5%. Subject B commented that he felt walking on a gradient easier than walking on the flat as it helped with his foot placement.

During the first week of training, following the baseline tests, subject B completed 3, 30 minute training sessions. Therefore, in accordance with the training protocol outlined in Chapter 3 the training duration was set to 30 minutes. This was the maximum training duration set for the study and consequently the duration of the training sessions for the remainder of the study could not be increased.

The improvements in training performance following 20 weeks of BWSTT were substantial and may indicate an improved walking ability and/or an increased cardiopulmonary fitness.

5.4.2 Maximal Incremental Exercise Test

Peak Work Rate

Following 20 weeks of BWSTT the WR_{peak} achieved by subject B during an IET A increased by 607% from 6.22–43.99 W. As can be seen in Table 5.5 this increase in work rate was a consequence of an increase in the testing speed and in the peak gradient achieved.

The WR_{peak} achieved during the IET B was higher than during the IET A at each TP. It is possible that this was because subject B performed the IET B second and therefore may have been more aware of what he could achieve at that TP. The gradual increase in speed which occurred during the IET B may also have attributed to the slightly higher WR_{peak} at

each TP. As subject B did not walk at a continually faster speed throughout the test it is possible that his legs began to fatigue slightly later and that he could therefore maintain a co-ordinated gait pattern for longer.

Considering the maximum gradient that could be achieved on the treadmill was 20%, the peak gradients achieved from TP3 onwards are exceptionally high (14.7–20%), especially during the IET B. This suggests that the tests may have been limited by how fast subject B could walk. During IET 6B subject B reached the maximum treadmill gradient. Had he been able to walk faster the gradient would have decreased again with the next increase in speed, and he may have achieved a higher WR_{peak}.

An increase in the WR_{peak} achieved with training was expected. As mentioned previously, with training the cardiopulmonary fitness of AB individuals increases. They are therefore able to increase the WR_{peak} which they can achieve as cardiopulmonary fitness is no longer a limiting factor at their previous WR_{peak}. Whilst it is possible that the improvements in WR_{peak} achieved by subject B may be a consequence of increased cardiopulmonary fitness it is also probable that it is a consequence of an improved walking ability.

Peak Oxygen Uptake

The $\dot{V}O_{2peak}$ obtained by subject B at each TP are exceptionally low. No data is available on the $\dot{V}O_{2peak}$ obtained during BWS treadmill walking for incomplete SCI subjects. Therefore, the baseline value obtained for subject B can only be compared to those obtained for the SCI population using different modes of exercise. As can be seen in Table 5.18, the baseline $\dot{V}O_{2peak}$ obtained for subject B is significantly lower than that previously reported for those with an SCI who have a sedentary lifestyle, although it does lie in the lower range of the values reported by Zwiren and Bar-Or [170]. The $\dot{V}O_{2peak}$ obtained peaks at TP5, following 16 weeks BWSTT. At 18.15 $ml.kg^{-1}.min^{-1}$, it lies within the range of values reported for the sedentary SCI population [36, 170, 183].

As discussed in Section 1.5.1, $\dot{V}O_{2peak}$ is expected to increase following a period of cardiopulmonary training. However, it is possible that the increases in $\dot{V}O_{2peak}$ demonstrated were a consequence of an improved walking ability which allowed subject B to utilise a previously unattainable cardiopulmonary reserve. $\dot{V}O_{2peak}$ has, however, not been shown to increase continuously with training. Following the first four weeks of training $\dot{V}O_{2peak}$ decreased from 13.84 $ml.kg^{-1}.min^{-1}$ to 10.88 $ml.kg.min^{-1}$ despite an increase of ~100% in the WR_{peak} achieved. This may be a consequence of subject B leaning on the side bars more during the baseline test, consequently increasing the muscle mass involved in the exercise and hence the

Study	Subject group	Testing mode	$\dot{V}O_{2peak}$ ($ml.kg^{-1}.min^{-1}$)
Zwiren and Bar-Or 1975 [170]	sedentary paraplegics	ACE	19 ($\pm$ 5.5)
Jacobs et al., 2002 [36]	sedentary paraplegics	ACE	19.6 ($\pm$ 3.2)
Jacobs and Mahoney 2002 [183]	sedentary paraplegics	FES-assisted overground walking	22.7 ($\pm$ 3.9)
Present study	subject B sedentary paraplegic	BWS treadmill walking	13.84

Table 5.18: Comparison of $\dot{V}O_{2peak}$ values obtained for sedentary paraplegics in other investigations to that obtained at baseline for subject B. ACE: arm crank ergometry. FES: functional electrical stimulation. BWS: body weight supported.

O_2 requirement. By TP2 subject B was more comfortable walking on the treadmill and may therefore not have felt it necessary to support himself further on the parallel bars. Therefore, at this TP he would not be performing any work in addition to what was pre-determined and thus increasing his demand for O_2.

As discussed previously, it is possible from TP3 onwards that subject B's tests were limited by the speed at which he could walk. This is especially the case during the IET B at each TP where subject B achieved a peak gradient close to or at the maximum treadmill gradient. Had he been able to walk faster he would have been able to reach further into his cardiopulmonary reserve which was closed to him because of his walking capacity.

The $\dot{V}O_{2peak}$ values achieved during the IET B at TP4 and TP6 were slightly higher than during the IET A. This is to be expected as the WR_{peak} achieved is also higher. However, despite the slightly higher WR_{peak} achieved, the $\dot{V}O_{2peak}$ achieved during the IET B test at TP3 is slightly lower than during the IET A test. It is possible, due to the increase in the testing speed to 0.20 $m.s^{-1}$ at TP3, that subject B may have gripped the parallel bars of the treadmill to help steady himself during the IET A. As mentioned previously, this would increase the O_2 requirement due to the inclusion of more muscle mass in the exercise. As the speed of the IET B began at 0.15 $m.s^{-1}$ it is possible that subject B was more at ease during this test and therefore did not feel the need for as much additional support, reducing slightly the O_2 demand for the exercise.

It is also important to mention that following an IET, subject B did not appear nor feel physically exhausted as one would expect of a subject who had just completed a maximum IET. He commented on a number of occasions that he had stopped the test because he could

no longer maintain a functional gait pattern. It appears therefore, that subject B's IETs were limited peripherally rather than centrally due, possibly, to the atrophied and fast fatiguing muscle fibres which have been shown to be present in the paralysed extremities of paraplegics [16, 17, 18, 20, 21, 23, 24, 25], as well as limited neural control which limited the speed at which he could walk. As mentioned in Section 4.4.2, a peak arm ergometery test would have provided an indication of the extent of this peripheral limitation.

With the exception of the IET B at TP4, the $\dot{V}O_2$ response to the pre-specified linear increase in work rate is not well fit by a linear relationship. By altering his gait pattern or leaning more heavily on the bars the amount of muscle mass engaged in the exercise would change and therefore the linear increase in work rate would be altered. During tests in which high peak gradients were achieved subject B was pushed back into the harness and consequently had to use the bars to maintain an upright posture. This would increase the muscle mass involved and the pre-defined linear increase in work rate would be altered. As no measurement of forces through the arms or feet were taken, there is no accurate measurement of the total work rate profile. The alteration in the work rate profile during the test may account for the apparent lack of linearity in the $\dot{V}O_2$ response.

Lactate Threshold

An LT could not be estimated during the IET of subject B at any TP. It is possible that this is because the work rate profile may not have been linear due to changes in the subject's gait pattern and/or by him leaning on the bars. Consequently, as can be seen in Section 5.3.2 the $\dot{V}O_2$ profile would not be linear. It is necessary, in order to accurately estimate the LT using V-slope analysis and gas exchange criteria, that the work rate profile is linear. This may therefore explain why one cannot be determined.

It is also possible that an LT cannot be determined because subject B is exercising above or below it. The supporting respiratory variable plots should help to determine this. However, the noise of the data during the IET A at each TP makes it difficult to determine the pattern of the responses. Below the LT $\dot{V}_E/\dot{V}O_2$ and $\dot{V}_E/\dot{V}CO_2$ are expected to fall gradually and attain a steady-state. Only at TP3 was this response produced. $F_{ET}O_2$ is also expected to decrease and reach a steady-state below the LT. At TP3 this response was also produced. Only the $F_{ET}CO_2$ response was not indicative of the subject exercising below the LT: increasing and then reaching a steady-state. Above the LT, $\dot{V}_E/\dot{V}O_2$ and $F_{ET}O_2$ are expected to be increasing. $\dot{V}_E/\dot{V}CO_2$ and $F_{ET}CO_2$ remain in steady-state and at the respiratory compensation point increase and decrease respectively. It does appear that subject B may have been exercising above the LT during the IET A at TP1: $F_{ET}O_2$ is increasing and $F_{ET}CO_2$ decreasing. However, the responses of $\dot{V}_E/\dot{V}O_2$ and $\dot{V}_E/\dot{V}CO_2$ are hard to distinguish and

therefore cannot support this observation. At TP4 and TP5, all respiratory variables support the fact that subject B is exercising above his LT. This is possible as the testing speed at these TPs was increased to 0.30 $m.s^{-1}$ and 0.35 $m.s^{-1}$ and consequently, as can be seen in Figure 5.5, the steady-state $\dot{V}O_2$ prior to the start of the ramp accounted for a significant proportion of the $\dot{V}O_{2peak}$. As mentioned previously, the respiratory variable responses at TP3 and TP6 do suggest the presence of an LT, however as all variables are not in agreement and an LT has not been determined at any other TP there is less confidence in these findings. The noise of the breath-by-breath data also makes it difficult, in some cases, to establish the exact response profile of the respiratory variables.

As mentioned previously, the response profiles of the respiratory variables during the IET B at each TP are much clearer. At TP4 it appears as though subject B is exercising above the LT; $\dot{V}_E/\dot{V}O_2$, $\dot{V}_E/\dot{V}CO_2$ and $F_{ET}O_2$ are increasing and $F_{ET}CO_2$ decreasing. This may also have been the case at TP3, although this cannot be concluded for certain as the response of $\dot{V}_E/\dot{V}CO_2$ is unclear. The response profiles at TP6 suggest the possible presence of an LT: $\dot{V}_E/\dot{V}O_2$ and $F_{ET}O_2$ are in steady-state and then increase. Although there is also a period of stabilisation followed by an increase in $\dot{V}_E/\dot{V}CO_2$, the increase appears to occur at the same point as in $\dot{V}_E/\dot{V}O_2$. The $F_{ET}CO_2$ response is decreasing which suggests, not the presence of an LT, but of the RCP.

The determination of an LT, or whether the subject was exercising above or below it, is affected by the low signal-to-noise ratio of the breath-by-breath data and a lack of full agreement in the supporting respiratory variable responses. At TP3 the respiratory variable responses suggested that during IET A when the treadmill speed was 0.2 $m.s^{-1}$, subject B was exercising below the LT. Yet during IET B when the initial treadmill speed was 0.15 $m.s^{-1}$ the responses suggested he was exercising above it. There is also uncertainty regarding the results obtained at TP4. During the IET A the treadmill speed was 0.30 $m.s^{-1}$ and the respiratory variable responses suggested that subject B was exercising above the LT. This was also the case during the IET B despite the fact that the starting treadmill speed was 0.15 $m.s^{-1}$ and that at TP3 there is the suggestion that subject B was exercising below the LT at a faster speed. There is great uncertainty regarding the determination of the LT in this subject.

Slope of Oxygen Uptake as a function of Work Rate

The results of IET A show that the $\Delta\dot{V}O_2/\Delta WR$ substantially decreased following 20 weeks of BWSTT. However, from TP3 onwards the treadmill speed of the test increased which may have affected the results obtained. Changing the testing speed alters the amount of internal work performed and thus the O_2 requirement (see Figure 5.5). Therefore, the amount of

external work that the subject performs to achieve the same total work decreases.

As the equation used to identify the slope of $\dot{V}O_2$ as a function of work rate (Equation (5.1)) only measures the amount of external work performed by the subject (work against gravity), it is biased by the $\dot{V}O_2$ associated with the internal work being performed.

$$\text{Slope of } \dot{V}O_2 \text{ as a function of work rate} = \frac{\Delta \dot{V}O_2}{\Delta WR} \tag{5.1}$$

- $\Delta \dot{V}O_2$ = increase in oxygen uptake from baseline
- ΔWR = increase in work rate from baseline

For example, if at a given TP subject B performed 2 IETs, one at 0.15 $m.s^{-1}$ and one at 0.35 $m.s^{-1}$ with a $\dot{V}O_{2peak}$ of 1.7 $l.min^{-1}$ and a Δ work rate of 30 W, the $\Delta \dot{V}O_2/\Delta$WR would be biased by the $\dot{V}O_2$ associated with walking at 0 W (0% gradient). If for 0.15 $m.s^{-1}$ the associated $\dot{V}O_2$ was 0.8 $l.min^{-1}$ and for 0.35 $m.s^{-1}$ it was 1.3 $l.min^{-1}$, the $\Delta \dot{V}O_2/\Delta$WR of the tests would be 30 $ml.min^{-1}.W^{-1}$ and 13 $ml.min^{-1}.W^{-1}$ respectively. Therefore, tests of different speeds cannot be directly compared as increasing the treadmill speed decreases $\Delta \dot{V}O_2/\Delta$WR regardless of a training effect. Consequently, the decrease shown in this study may be due to the different testing speeds.

However, the decrease in $\Delta \dot{V}O_2/\Delta$WR is substantial. Therefore, it is probable that the decrease is not solely due to the different gait efficiencies at different speeds. At TP1 and TP2 the test speed was 0.15 $m.s^{-1}$ and the $\Delta \dot{V}O_2/\Delta$WR was shown to decrease between TPs by 61%. At TP5 and TP6 the test speed was also the same (0.35 $m.s^{-1}$) and $\Delta \dot{V}O_2/\Delta$WR decreased between TPs by 52%. This suggests that a training effect was present. Although the extent of the training effect cannot be quantified because of changes in the initial $\dot{V}O_2$ with different testing speeds, the results do suggest that subject B's gait pattern did become more efficient.

Unfortunately, a direct comparison of the $\Delta \dot{V}O_2/\Delta$WR of IET A and IET B at each TP cannot be made as the initial treadmill speed and thus internal work and associated $\dot{V}O_2$ differed. The internal work did not remain constant during the IET B as the treadmill speed changed at specified time points during the test. This would affect the $\Delta \dot{V}O_2/\Delta$WR obtained. As the internal work differed between IET Bs, the $\Delta \dot{V}O_2/\Delta$WR cannot be compared between tests.

Peak Heart Rate

A 17% increase in the HR_{peak} achieved during the IET A occurred following 20 weeks of BWSTT. This suggests that subject B was able to access a previously unattainable heart rate reserve because of an increased walking ability. It is likely, had subject B been able to further increase the speed at which he could walk, that he would have been able to achieve a higher HR_{peak}.

As can be seen in Figure 5.14, the HR_{peak} obtained during the IET A and IET B at each TP are comparable. This is extremely positive as it shows that both tests pushed subject B to approximately the same limit of tolerance and therefore the peak values obtained can be compared.

5.4.3 Constant Load Exercise Test

For AB subjects exercising at steady-state work rates below the LT, $\dot{V}O_2$ is expected to reach a steady-state in ~3 minutes [97] and with training the τ value obtained is expected to decrease [108].

At TP2, TP3 and TP6 a τ was established which indicated that $\dot{V}O_2$ reached a steady-state within 15 minutes. However, at TP6 the τ obtained was ~5 times higher than that obtained at TP3 suggesting a decrease in fitness. This is highly unlikely as subject B had carried out a further 12 weeks of BWSTT.

At the remaining TPs, a τ could either not be determined or the value obtained was extremely high. At TP1 a τ of 579.41s was obtained, and as can be seen in Figure 5.16 the $\dot{V}O_2$ continued to increase throughout the test. It is possible that this may have been a consequence of subject B leaning on the bars more for support and to help aid stepping during the swing phase as the test progressed. Consequently, more muscle would be engaged in the exercise and thus the demand for O_2 increased. If this was the case then the actual or perceived work rate would continue to rise despite the reference work rate remaining constant.

The τ obtained at TP2 and TP3 suggests that subject B was comfortable at the testing speed and did not appear to rely on the support of the bars, thus increasing the actual or perceived work rate. The decrease in τ suggests that there may have been an increase in fitness between TPs. However, without repeat tests this cannot be concluded for certain.

At TP4–6 a τ could either not be obtained or the value obtained was substantially higher

than at TP2–3. This again suggests possible alterations in the work rate which may, once again, have been caused by subject B leaning on the bars more. By TP4 the 0.15 $m.s^{-1}$ testing speed was too slow. At this point it was half his training speed. Therefore, it is possible that while subject B used the bars to aid his gait when he found the test hard, he may also have used them to help adjust his gait pattern when the speed was uncomfortably slow.

$\Delta\dot{V}O_2$ was calculated for the SETs in which $\dot{V}O_2$ reached a steady-state. As mentioned previously, the body requires a given amount of O_2 for a given amount of work. Therefore, as expected the $\Delta\dot{V}O_2$ did not change between TPs. Despite the longer τ at TP6 $\dot{V}O_2$ still reached approximately the same end value.

As can be seen in Figure 5.15, the $\dot{V}O_2$ in the final 20 seconds of the SET decreased dramatically between TP1 and TP2 suggesting a decrease in the physiological stress of the exercise. Between TP3 and TP6 the $\dot{V}O_2$ in the final 20 seconds of the test fluctuated, increasing slightly at TP4 and TP5 where the τ value could either not be obtained or was extremely large. It is likely that the decrease in the physiological cost of the exercise between TP1 and TP2 was caused by an improved gait efficiency. This may have been a consequence of improved muscle endurance. However, as the $\dot{V}O_2$ did not continue to decrease between TP2 and TP6 it is more likely that the improved gait efficiency may have been caused by improved co-ordination of the gait pattern which possibly did not alter significantly following the first 4 weeks of training.

Performing another SET at a speed equal to the IET A speed would have allowed us to determine if $\dot{V}O_2$ did not reach a steady-state because of an uncomfortably slow testing speed. If a steady-state $\dot{V}O_2$ was reached at a faster testing speed it would imply that $\dot{V}O_2$ did not reach a steady-state during the 0.15 $m.s^{-1}$ test because of increasing reliance on the bars for assistance and alterations in gait. Although increasing the step size would not allow analysis of the effects of training, it would enable us to determine if a lower signal to noise ratio would be achieved and therefore a τ value be more easily identified.

5.4.4 15 Minute Distance Test

Following 20 weeks of BWSTT, the distance subject B could walk in 15 minutes increased 121%. As can be seen in Table 5.10, the speeds at which he chose to walk during the test increased at each TP.

The results obtained are extremely encouraging as they show that in a given period of time

subject B has increased the distance he can walk and also the work rate at which he can train. This may have been due to improved muscle endurance and/or gait co-ordination which is also supported by a large increase in the WR_{peak} achieved during the IETs and in training performance.

The speeds chosen for the 15 minute distance tests from TP4–6 are 2–3.5 times higher than the speed of the SET. This highlights just how much slower the SET speed was than subject B's chosen walking speed. It therefore suggests that the SET was uncomfortable for subject B and consequently it is possible that he would have made alterations to his gait pattern to try and improve his comfort during the tests. Alterations to his gait pattern would have affected the work rate profile.

5.4.5 Twitch Tests

The results of subject B's twitch tests have been badly affected by spasms in his lower limbs. As can be seen in Figures 5.21 and 5.22, any voluntary force produced by the left hamstrings is masked by the force produced by spasms. Therefore, we cannot get a true indication of the voluntary force generating capacity of the muscle. The peak voluntary force provided in Tables 5.14 and 5.15, therefore, represent the peak force produced whilst the muscle was in spasm. Subject B's left leg is his more-affected limb and he often has spasms in it. It is perhaps unsurprising therefore that a true indication of the voluntary force production could not be obtained.

The right hamstring tests were also affected by spasms, although not to the same extent. The voluntary force produced by the hamstrings positioned at 90^o of flexion increased from baseline to the 5 month TP, following 20 weeks of formalised BWSTT. A decrease occurred from the pre-walking to baseline TP, but as can be seen in Figure 5.18, spasms were present prior to delivery of the stimulation pulse. Therefore, the peak voluntary force provided in Table 5.11 does not represent the actual voluntary force which subject B was capable of producing at that TP. It is possible, therefore, that the peak voluntary force may have increased throughout the entire training period. The same pattern of response is present for the peak total force. No pattern is present for the CAR.

At each TP the voluntary force produced is higher with the hamstrings positioned at 30^o of flexion compared to 90^o of flexion. This is likely to be because the subject has more leverage on the muscle and can therefore generate more force. The exception to this is during the 2.5 month test with the right leg positioned at 30^o of flexion. Following an increase in the peak voluntary force from pre-walking to baseline, it decreased by more than 50% during the 2.5

month test. However, the 2.5 month test is the only TP not to have been affected by spasms prior to stimulation delivery. Therefore, it may be the only one to accurately represent the true voluntary force.

Prior to delivery of the stimulation pulse neither the left or right quadriceps appear to have been affected by spasms. Unsurprisingly, given that it is his less-involved limb, subject B produced a higher peak voluntary force with his right quadriceps muscles than his left. The only exception to this was at the 2.5 month TP where the voluntary force produced by the left quadriceps muscles was higher. However, this peak force was not maintained. The peak voluntary force produced by the right quadriceps positioned at 90^o of flexion appears to have decreased with training. The largest decrease was found between the pre-walking and baseline TPs (4 Nm). Over the following 20 weeks BWSTT the voluntary force increased slightly. Although the decrease between pre-walking and baseline does not appear to be significant, it accounts for a decrease of 18.5%. The peak total force produced by the right quadriceps at 90^o of flexion also decreased from pre- to post-training, although a slight increase occurred between the 2.5 and 5 month TPs. No pattern is present for the CAR.

The peak voluntary force produced by the left quadriceps at 90^o of flexion also decreased from pre-walking to the 5 month TP. However, this decrease was not continuous, occurring only at the 5 month TP. The peak total force produced fluctuated between TPs but from pre-baseline to the 5 month TP it remained approximately the same. No pattern is present in the response of the CAR.

As discussed in Section 4.4.5, the peak voluntary forces produced by the quadriceps muscles has recently been investigated in those with an incomplete SCI [205]. The peak voluntary forces were found to be 57 ($\pm$ 18) Nm and 85 ($\pm$ 20) Nm for the more- and less-involved limbs respectively. The results obtained by subject B were significantly lower than this: 21.60 Nm for the less-involved limb and 22.20 Nm for the more-involved limb, although this force was not maintained.

The results suggest that the improvements shown in the training and 15 minute distance test performance, and in the WR_{peak}, may not be due to improvements in voluntary muscle strength. It is possible therefore that the improvements in these performance parameters are due to improved gait co-ordination and lower limb muscle endurance.

The variability present in the peak voluntary force between TPs may have been due to variable subject performance and differing levels of muscular fatigue. Variability was also present in the total force produced by the muscle. This was not expected to the same extent as the

voluntary muscle force as the electrodes were placed in the same position and the same stimulation parameters were used for each test. This may have been affected by the fact that the subject's peak voluntary force did not always occur prior to delivery of the stimulation pulse.

Due to the variability present in the peak voluntary and peak total forces it is unlikely that the CAR calculated at each TP accurately reflects the extent of central activation failure during the contraction. Further investigation is required to determine the accuracy of these tests.

As was found for subject A, the voluntary force produced by subject B following delivery of the stimulation was higher, during the quadriceps tests, than before it. Whether this is a physiological response of the muscle to the stimulation or is due to increased subject effort, requires further investigation.

5.4.6 Bone Parameters

At the start of the BWSTT study, subject B was 14.5 years post-injury and so his bones were therefore in a steady-state phase [10]. Consequently, any changes in trabecular BMD or cortical CSA would be expected to be as a consequence of training. The results of this study show that training intensity was not high enough to have any significant impact on the cortical CSA of the tibia and femur nor on the trabecular BMD of the distal femur and proximal tibia. However, it did result in a 4.9% increase in the trabecular BMD of the right distal tibia and a substantial increase of 19.6% in the left distal tibia.

It should be mentioned that subject B was prescribed anti-resorptive osteoporosis medication (once weekly 35 mg Risedronate (bisphosphonate) tablets with calcium and vitamin D supplement tablets three times daily) by his physician at the same time as commencement of the study. The prescription of these drugs was unrelated to the study. Risedronate is an anti-resorptive drug and is therefore only used in the phase of bone loss. As subject B was in the steady-state phase of bone loss the drug should not have had an effect on his results. It can be postulated that any changes observed were due to the intervention as the drugs are not expected to have had an effect. However, as the medication was maintained throughout the duration of the study, the fact that they may have had some positive effect cannot be ruled out.

Prior to participation in the study the BMD of the right tibia and femur was higher than the left. The left limb is subject B's more-involved limb, therefore the weaker voluntary control of the muscles on the left is likely to be responsible for this. It is interesting to note the large difference in the improvement in trabecular BMD of the distal tibia between limbs: the

increase in the left is substantially higher than in the right. One explanation for this may be the use of FES on the left peroneal nerve to elicit the withdrawal reflex. External stimulation of the nerve resulted in a strong withdrawal reflex caused by activation of the tibialis anterior muscle. This may have resulted in a larger muscular load on the bone than could voluntarily be achieved on the right side.

5.4.7 Repeatability and Reliability of Testing Protocols

The importance of determining the repeatability and reliability of the testing protocols has been discussed in Section 4.4.8. As was highlighted by the results presented in this chapter, the cardiopulmonary tests were affected by limitations in the subject's gait. Therefore, it is essential to assess how constant these limitations are, and what affect they have on the outcome parameters.

The twitch test results were also variable and in some instances badly affected by lower limb spasms. The variability in the outcome measures of these tests must also be assessed to determine their accuracy.

5.5 Conclusion

Standard cardiopulmonary exercise testing protocols for AB subjects were adapted for use with an incomplete SCI subject during BWS treadmill walking. The tests were successfully performed at 4 weekly intervals during a 20 week BWSTT programme. The results obtained provided information regarding cardiopulmonary status and how it was altered with training. It does however appear that the tests may have been limited by the subject's walking ability. Further investigation is required to determine the extent of this peripheral limitation.

Standard dynamometry tests to determine the extent of CAF were also adapted for use with the SCI subject. Spasms hindered the identification of the true voluntary peak force in the hamstring muscle. In the quadriceps muscles the results were more encouraging. However, the repeatability of the outcome measures requires further investigation.

Subject B's training performance increased substantially during the 20 week training period both in terms of training speed and gradient. A highly encouraging result was obtained during the 15 minute distance test. A 121% increase in the distance walked highlights the improvement in the subject's gait which occurred during the 20 week training period. Another highly significant result was the large increase in the trabecular BMD of the left distal tibia.

Although the cardiopulmonary exercise tests may have been limited by the subject's walking ability they still produced encouraging results. Following 20 weeks of BWSTT the WR_{peak} achieved by subject B during the IET increased substantially by 607%. A large increase in HR_{peak} was also shown to occur as was an increasing trend in $\dot{V}O_{2peak}$. A large decrease in the $\Delta\dot{V}O_2/\Delta WR$ of the IET also occurred. The $\dot{V}O_2$ and HR associated with the SET were also shown to decrease with training.

The results of this study are encouraging as they show that standard exercise testing methods for AB subjects can be adapted for use with an SCI subject. Further investigation is however required to determine the repeatability and reliability of the tests used in this study and to determine how applicable they are to the wider incomplete SCI population.

Chapter 6

A Treadmill Protocol Combining Nonlinear, Equally Smooth Increases in Speed and Gradient: exercise testing for subjects with gait impairment

6.1 Chapter Summary

Incremental exercise testing with a linear increase in work rate is the recommended method for clinical exercise testing. A recent incremental exercise test (IET) protocol (A), incorporating a linear increase in speed and a nonlinear, initially rapid increase in gradient, has been developed which addresses some limitations of traditional testing methods. Although developed for subjects with cardiovascular impairment, it does not account for those who may also have an impaired gait pattern. Here we propose a novel protocol (B) which incorporates nonlinear, equally smooth, increases in both speed and gradient and we experimentally assess its oxygen uptake response linearity and initial metabolic cost.

The following procedures were carried out: (i) Theoretical development of new test protocol; (ii) determination of oxygen uptake response linearity, initial metabolic cost and cardiopulmonary response parameters (peak oxygen uptake ($\dot{V}O_{2peak}$), lactate threshold (LT), slope of $\dot{V}O_2$ as a function of work rate ($\Delta\dot{V}O_2/\Delta P$)); (iii) comparison of the outcome measures with two previously-verified IET protocols (A and C (constant speed, linear increase in gradient)). Feasibility and outcomes were explored in a single-subject case study (incomplete spinal cord injury). Respiratory variables were recorded breath-by-breath.

The average initial metabolic rate ($\dot{V}O_2$) was substantially lower during protocol A (0.49 ($\pm$ 0.12) l.min^{-1}) and protocol B (0.52 ($\pm$ 0.05) l.min^{-1}) than during protocol C (1.35 ($\pm$ 0.04) l.min^{-1}). The average linearity of the $\dot{V}O_2$ response during protocols A and B (0.97 ($\pm$ 0.00 and 0.95 ($\pm$ 0.02)), respectively) were higher than during protocol C (0.91 ($\pm$ 0.02)). The average $\Delta\dot{V}O_2/\Delta P$ of protocol C (6.53 ($\pm$ 0.46) ml.min^{-1}.W^{-1}) was lower than that of protocol A (10.02 ($\pm$ 1.16) ml.min^{-1}.W^{-1}) and protocol B (10.03 ($\pm$ 0.91) ml.min^{-1}.W^{-1}). No differences were found in these key parameters of clinical exercise testing between protocols A and B.

The new protocol B performs better than protocol C and is comparable with the previously-verified protocol A. When testing subjects with an impaired gait pattern, it may be advantageous to use the new protocol B due to the gradual increases in both speed and gradient throughout the test.

The work in this chapter has been submitted for publication:

- L. P. Jamieson, K. J. Hunt, and D. B. Allan, "A treadmill control protocol combining nonlinear, equally smooth increases in speed and gradient: exercise testing for subjects with gait impairment," *Medical Engineering in Physics (submitted).* [206].

6.2 Introduction

An incremental exercise test (IET), with a linear increase in work rate to the limit of tolerance, is the recommended procedure for assessment in clinical exercise testing [207, 208]. Following a short delay, oxygen uptake ($\dot{V}O_2$) normally increases linearly during a cycle IET at a rate of $\sim$10 ml.min^{-1}.W^{-1} [84, 85, 86] and at a rate of $\sim$11 ml.min^{-1}.W^{-1} during a treadmill IET [86]. It is this rate of increase in $\dot{V}O_2$ with respect to work rate, or the O_2 cost of the exercise, which has been shown to deviate in impaired subjects. A reduction in O_2 cost is indicative of cardiovascular dysfunction and has been shown to occur in those with peripheral or pulmonary vascular disease (8.29 $\pm$ 1.17 ml.min^{-1}.W^{-1}) [84] and hypertrophic cardiomyopathy (9.2 $\pm$ 1.3 ml.min^{-1}.W^{-1}) [85]. Using peak values obtained from IETs to determine disease is not recommended as they can be decreased with detraining and can be symptom limited [85]. Therefore, the linearity of the $\dot{V}O_2$ response is a discriminating factor in the assessment of disease. For accurate diagnosis it is therefore essential that the linearity of the work rate profile during an IET be guaranteed.

A low initial metabolic rate is also important when designing an IET, particularly for impaired subjects, to ensure that key parameters of aerobic fitness, such as the lactate threshold

(LT), are captured in the data obtained. A high initial metabolic rate reduces the duration of the test and thus data available for analysis. Standard treadmill exercise testing protocols do not account for this. When the angle of inclination of the treadmill remains constant and the speed increases linearly a high initial metabolic rate occurs if a steep grade is chosen. However, if a low initial grade is chosen to ensure a low initial metabolic rate then the speed is increased so quickly that the limit of tolerance may be determined by the subject's ability to move their legs quickly and/or efficiently enough. If the speed of the treadmill remains constant and the angle of inclination is increased, a low speed will result in a low initial metabolic rate. However, the treadmill inclination may increase to a very steep grade before the limit of tolerance is reached. If a high speed is chosen a large initial metabolic cost will result.

These limitations of standard clinical exercise tests have been investigated [86]. A new treadmill exercise test was developed which produced a low initial metabolic rate and, through a linear increase in speed and a nonlinear increase in gradient, resulted in a linear increase in work rate with the subject fatiguing at a comfortable walking speed. We refer to this here as protocol A. This test was designed for subjects with cardiovascular impairment and did appear to address the problems associated with clinical exercise testing. However, it does not take into account those with an impaired gait pattern who may be required to perform such a test. In patients with an impaired gait, such as those with an incomplete spinal cord injury (SCI), the ability to cope with the sharp initial increase in gradient during this test may be limited. They may be more able to adapt their gait to more gradual changes in speed and gradient.

The aim of this work was therefore to propose a new treadmill IET protocol (B) which incorporates nonlinear, equally smooth increases in both speed and gradient and to experimentally assess its associated oxygen uptake response linearity and initial metabolic cost. The results obtained using the new protocol with an incomplete SCI subject were compared to those achieved when performing protocol A [86] and a standard, constant-speed IET treadmill protocol (C).

6.3 Methods

6.3.1 Theory

In protocol A [86] the algorithm for the incremental phase guarantees a linear increase over time in the rate of work done to overcome gravity by combining a linear increase in treadmill speed with a nonlinear increase in slope. In addition, a low initial metabolic rate is achieved,

using low initial values of speed and slope. A limitation of protocol A is that, since the increase in speed is constrained to be linear, the rate of change of speed is constant, which in turn results in a relatively high rate of change in slope near the start of the incremental phase and a low rate of change in slope towards the end of the test (see example in Figure 6.1). Here a new protocol (B) is derived which guarantees a linear increase in work rate while speed and slope are constrained to increase in the same relative proportion, i.e. equally smoothly, to achieve the desired linear increase in work rate.

The exercise work rate P, above the "unloaded" walking condition at zero slope, is given by

$$P(t) = mgv(t)\sin\theta(t) \tag{6.1}$$

where m is net mass (i.e. the unsupported component of body mass), g is the gravitational field strength, v is speed, and θ is the inclination angle. For an IET, where a linear increase in work rate is required, we have

$$P(t) = k^P t + P_0, \tag{6.2}$$

where P_0 is the initial work rate and k^P is the rate of change of work rate. Given a pre-specified final work rate P_f and test duration t_f, the work rate slope is $k^P = (P_f - P_0)/t_f$.

Taken together, equations (6.1) and (6.2) imply that, to achieve a linear increase in work rate, speed and inclination angle are constrained in general to satisfy

$$v(t)\sin\theta(t) = \frac{k^P t + P_0}{mg} \tag{6.3}$$

The algorithm for protocol A [86] considers the special case where treadmill speed is constrained to increase linearly, i.e. $v(t) = k^v t + v_0$, where the rate of change of speed is $k^v = (v_f - v_0)/t_f$, with v_0 and v_f the initial and final speeds, respectively. With this algorithm, therefore, the appropriate treadmill angle at any time t is obtained exactly as

$$\theta(t) = \arcsin\frac{k^P t + P_0}{mg(k^v t + v_0)} \tag{6.4}$$

(Porszasz and colleagues [86] derive an approximation to this exact solution.) The exact solution is used in the example shown in Figure 6.1, confirming that the rate of change of slope is relatively high in the initial phases of the work rate ramp, and relatively low in the late stages.

The alternative algorithm proposed here is designed to ensure that v and θ both change in the same relative proportion in response to the demanded increase in P throughout the incremental test. To achieve this, we specify that the profiles for both speed and the sine of the angle are to be constrained to follow a common basic nonlinear functional form, denoted $f(t)$. Speed, which increases from v_0 to v_f, takes the following nonlinear form:

$$v(t) = f(t) + v_0 \tag{6.5}$$

Clearly, $f(t)$ must be constrained to satisfy $f(0) = 0$ and $f(t_f) = v_f - v_0$. The sine of the angle is then required to follow a scaled version of f, starting at the initial value $\sin\theta_0$ and ending at the final value $\sin\theta_f$, thus

$$\sin\theta(t) = kf(t) + \sin\theta_0 \ (\Rightarrow\ \theta(t) = \arcsin(kf(t) + \sin\theta_0)) \tag{6.6}$$

where k is a scaling factor whose value is seen to be

$$k = \frac{\sin\theta_f - \sin\theta_0}{v_f - v_0} \tag{6.7}$$

With these definitions of v and θ, the constraint equation (6.3), which guarantees a linear increase in work rate, implies that

$$(f(t) + v_0)(kf(t) + \sin\theta_0) = \frac{k^P t + P_0}{mg} \tag{6.8}$$

Expansion and rearrangement of this expression leads to the following quadratic equation in $f(t)$:

$$kf^2(t) + (kv_0 + \sin\theta_0)f(t) + \left(v_0\sin\theta_0 - \frac{k^P t + P_0}{mg}\right) = 0 \tag{6.9}$$

We are interested in the positive solution $f(t)$ of this equation, which is

$$f(t) = \frac{-b + \sqrt{b^2 - 4ac(t)}}{2a} \tag{6.10}$$

where the constants a and b and the time-dependent variable $c(t)$ can be identified from (6.9) as

$$a = k \tag{6.11}$$

$$b = kv_0 + \sin\theta_0 \tag{6.12}$$

$$c(t) = v_0\sin\theta_0 - \frac{k^P t + P_0}{mg} \tag{6.13}$$

The above solution can be summarised in the following algorithmic procedure:

step 1 Choose initial conditions for speed, angle and work rate (ensuring that the choices conform with the basic constraint (6.3)).

step 2 Calculate the work rate slope using $k^P = (P_f - P_0)/t_f$.

step 3 Calculate the scaling factor k using equation (6.7).

step 4 Calculate the constants a and b using equations (6.11)–(6.12).

For each time of interest, t, perform the following steps:

step 5 Calculate the value of $c(t)$ using equation (6.13).

step 6 Calculate $f(t)$ as the solution (6.10).

step 7 Calculate the required speed $v(t)$ and angle $\theta(t)$ using equations (6.5) and (6.6), respectively.

Figure 6.1 shows the speed and slope solutions, for the subject who participated in this study, obtained using the algorithm for protocol A and the new algorithm proposed above (protocol B), for a given linear increase in workrate. In this solution, $m = 117.2$ kg, while the initial and final speeds and angles are chosen as follows: $v_0 = 0.1$ m·s^{-1}, $v_f = 1.2$ m·s^{-1}, $\theta_0 = 0.0$ rad (grade 0%), $\theta_f = 0.2091$ rad (grade 21.2%). This gives minimum and maximum work rates $P_0 = 0$ W and $P_f = 286.13$ W. The test duration was chosen as $t_f = 900$ s.

For protocol A, the speed increases linearly according to the dashed line, while the angle increases nonlinearly as shown in the dash-dot line. Clearly, the angle increases rapidly during the initial phase of the test (reaching ~70% of its final value within 1/6 of the test duration), but very little during the latter part of the test (increasing only less than 10% during the final 1/2 of the test duration). For the new algorithm, speed and angle increase equally smoothly according to the solid line.

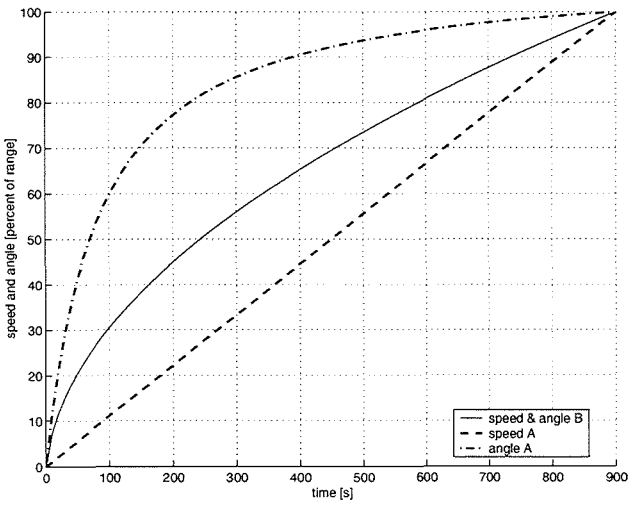


Figure 6.1: Speed and angle profiles obtained using the protocol A (speed - dashed line; angle - dash-dot line) and the new method, protocol B, proposed here (both speed and angle given by the solid line). Speed and angle are scaled to represent a percentage of their respective min–max ranges.

6.3.2 Subjects

This study was approved by the Southern General Hospital Research Ethics Committee. 1 male subject aged 54 with an incomplete SCI (neurological level C5/6, American Spinal Injuries Association (ASIA) grade D) was recruited for this study following completion of a medical examination. The subject was 12 years post-injury and required a walking stick for community ambulation. Prior to participation the subject provided written, informed consent.

6.3.3 Experimental Design

Prior to formal exercise tests, a test to determine the range of speeds and gradients over which the subject could comfortably walk on the treadmill (Woodway LOKO S70 system, Germany) was carried out. This was deemed necessary due to the subject's incomplete SCI and consequent unsteady gait pattern. The subject was attached to an overhead body weight support (BWS) system, via a harness, during all treadmill exercise tests. This was a safety precaution in case his gait became unstable as the treadmill speed increased. None of the subject's body weight was supported.

A treadmill speed of 1.0 $m.s^{-1}$ was chosen as the speed at which the constant speed, linear increase in gradient tests (protocol C) could be performed safely and comfortably. The treadmill gradient was increased at 1.5 $\%.min^{-1}$. The subject was unable to walk significantly faster than 1.0 $m.s^{-1}$, therefore the speed profile during protocols A and B did not increase substantially beyond this point. The corresponding gradient profiles were designed to enable the subject to reach his predicted limit of tolerance. The work rate profile of each test was designed with the aim of ensuring that the subject reached his limit of tolerance in the recommended 8–12 minutes [197]. For protocols A and B, the actual speed and angle profiles are those computed in the above example and plotted in Figure 6.1. The subject carried out one familiarisation and 3 repeat tests for each protocol.

6.3.4 Measurements

Throughout each IET, the subject's O_2, CO_2 and N_2 concentrations, as well as the volume of each breath were continuously monitored using a breath-by-breath system (Msx ErgoSpirometer System, Morgan Medical Ltd, UK) in order to measure and record the following pulmonary gas exchange and ventilatory variables: rate of oxygen uptake ($\dot{V}O_2$), rate of carbon dioxide output ($\dot{V}CO_2$), minute ventilation ($\dot{V}_E$), respiratory exchange ratio (RER), fraction of end-tidal O_2 ($F_{ET}O_2$) and CO_2 ($F_{ET}CO_2$). The subject wore a mouthpiece with

a sample line which was connected to the Msx and a wore a noseclip to prevent any gas escaping. The turbine was calibrated prior to each exercise test using a 3 litre volumetric syringe. Calibration of the mass spectrometer was performed using ambient air and a certified precision-analysed gas mixture (5.65% CO_2, 14.543% O_2) prior to and following each test.

The subject's heart rate (HR) was continuously measured and recorded during each test by a short range telemetry HR monitor (Polar S410, Polar Electro Oy, Finland).

6.3.5 Analysis

The raw, breath-by-breath data points were processed to remove outliers before data analysis was performed (Origin Version 7.5, OriginLab Corporation, Northampton, USA) [200, 201]. Outlier removal was done by performing a least-squares fit to each phase of each test, and then removing data points outwith the corresponding 95% confidence intervals. Line fitting and estimation of cardiopulmonary performance parameters was then carried out using the edited data.

Estimation of the cardiopulmonary parameters was carried out as follows:

- Initial metabolic rate: The final 60 seconds of the $\dot{V}O_2$ data before the start of the ramp phase was averaged to give an indication of the initial metabolic rate.
- Peak work rate (P_{peak}): The peak speed v_{peak} and peak angle θ_{peak} achieved during an IET were used to determine P_{peak} as

$$P_{\text{peak}} = mgv_{\text{peak}} \sin\theta_{\text{peak}} \tag{6.14}$$

- $\dot{V}O_{2\text{peak}}$: The $\dot{V}O_{2\text{peak}}$ was calculated by averaging the $\dot{V}O_2$ of each breath in the final 20 seconds of the ramp phase [64].
- HR_{peak}: A 15 second average of the HR response throughout the test was provided for analysis. HR_{peak} was recorded as the highest HR prior to attainment of the limit of tolerance.
- Slope of $\dot{V}O_2$ as a function of work rate: The $\Delta\dot{V}O_2/\Delta P$ was taken as the slope of the linear line fitted through the $\dot{V}O_2$-workrate plot, excluding the kinetic and plateau phases of the response:

$$\text{Slope of } \dot{V}O_2 \text{ as a function of work rate} = \frac{\Delta\dot{V}O_2}{\Delta P} \tag{6.15}$$

- Linearity of $\dot{V}O_2$ response: The correlation coefficient (represented by the R^2 value) associated with the linear line through the $\dot{V}O_2$-workrate plot provided an indication of the linearity of the $\dot{V}O_2$ response.
- Lactate threshold: The LT was estimated using the V-slope method [78] and standard gas exchange criteria [79].

The results obtained from the 3 repeat tests of each protocol were averaged to provide a mean response for each key parameter. The edited breath-by-breath responses from the three repeat tests of each protocol were interpolated, phase aligned and averaged. A 5 point average was used for graphical displays.

6.4 Results

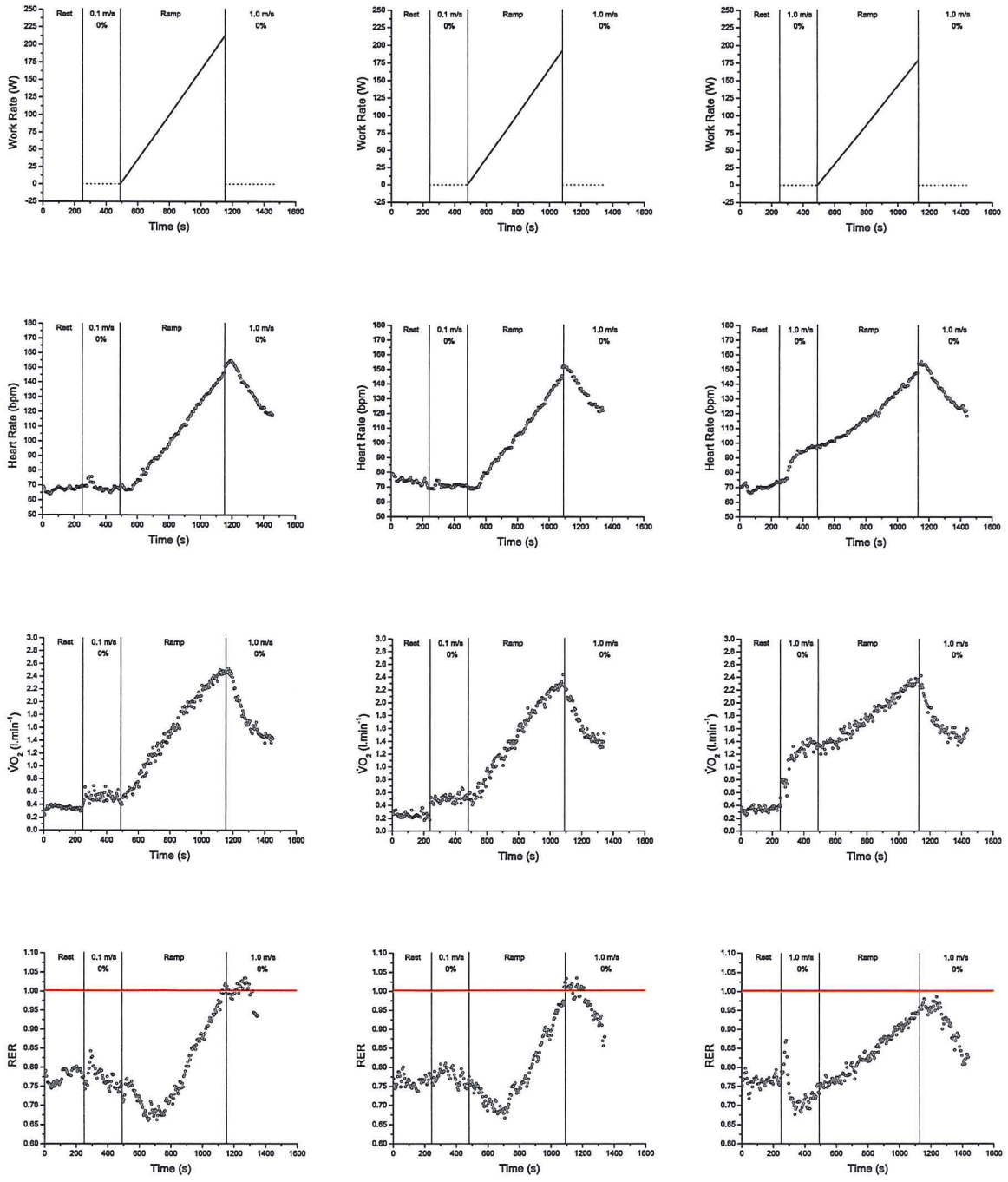
The average response plots for each protocol are shown in Figure 6.2. The mean value for each key parameter is shown in Table 6.1.

Test	IET A	IET B	IET C
Test duration (s)	670.33 (± 6.43)	642.33 (± 37.23)	662.00 (± 19.97)
Peak gradient (%)	17.20 (± 0.00)	17.70 (± 0.60)	16.40 (± 0.50)
Peak speed ($m.s^{-1}$)	1.11 (± 0.01)	1.03 (± 0.03)	1.00 (± 0.00)
P_{peak} (W)	215.23 (± 2.04)	205.81 (± 12.12)	185.61 (± 5.60)
$\dot{V}O_{2peak}$ ($l.min^{-1}$)	2.45 (± 0.25)	2.38 (± 0.07)	2.37 (± 0.06)
$\dot{V}O_{2peak}$ ($ml.kg^{-1}.min^{-1}$)	20.91 (± 2.15)	20.28 (± 0.62)	20.25 (± 0.49)
HR_{peak} (bpm)	147 (± 3.61)	151 (± 3.00)	151 (± 5.57)
Linearity of $\dot{V}O_2$ response (correlation co-efficient R^2)	0.97 (± 0.00)	0.95 (± 0.02)	0.91 (± 0.02)
$\Delta\dot{V}O_2/\Delta P$ ($ml.min^{-1}.W^{-1}$)	10.02 (± 1.16)	10.03 (± 0.91)	6.53 (± 0.46)
$\dot{V}O_2$ at LT ($l.min^{-1}$)	1.61 (± 0.05)	1.60 (± 0.19)	NA
Non SS WR at LT (W)	111.74 (± 15.07)	109.42 (± 24.70)	NA
Initial metabolic rate ($\dot{V}O_2$ $l.min^{-1}$)	0.49 (± 0.12)	0.52 (± 0.05)	1.35 (± 0.04)

Table 6.1: Mean response of each key parameter for each incremental exercise test protocol performed. Protocol A: Porszasz and colleagues [86]. Protocol B: Section 6.3. Protocol C: constant speed, linear gradient. P_{peak}: peak work rate. $\dot{V}O_{2peak}$: peak oxygen uptake. HR_{peak}: peak heart rate. $\Delta\dot{V}O_2/\Delta P$: slope of oxygen uptake as a function of work rate. LT: lactate threshold. SS: steady-state.

6.4.1 Peak Work Rate

The average work rate profile achieved by the subject during each IET protocol is shown in Figure 6.2, top row. The P_{peak} achieved during protocols A and B are similar (215.23 (±



(a) Protocol A (b) Protocol B (c) Protocol C

Figure 6.2: The average work rate, heart rate, oxygen uptake and respiratory exchange ratio profiles for each incremental exercise test protocol. Protocol A: Porszasz and colleagues [86]. Protocol B: Section 6.3. Protocol C: constant speed, linear gradient. HR: heart rate. $\dot{V}O_2$: oxygen uptake. RER: respiratory exchange ratio.

2.04) W and 205.81 (± 12.12) W respectively) and are both higher than that achieved during protocol C (185.61 (± 5.60) W).

6.4.2 Peak Oxygen Uptake

The average $\dot{V}O_2$ profile produced during each IET protocol is shown in Figure 6.2, third row. There was no substantial difference in the average $\dot{V}O_{2peak}$ achieved during each protocol (A: 2.45 (± 0.25) l.min^{-1}; B: 2.38 (± 0.07) l.min^{-1}; C: 2.37 (± 0.06) l.min^{-1}).

6.4.3 Initial Metabolic Rate

As can be seen in Figure 6.2, third row, the initial metabolic rate ($\dot{V}O_2$ prior to the ramp phase) is substantially higher during protocol C (1.35 (± 0.04) l.min^{-1}) than during protocols A and B (0.49 (± 0.12) l.min^{-1} and 0.52 (± 0.05) l.min^{-1} respectively).

6.4.4 Linearity of Oxygen Uptake Response

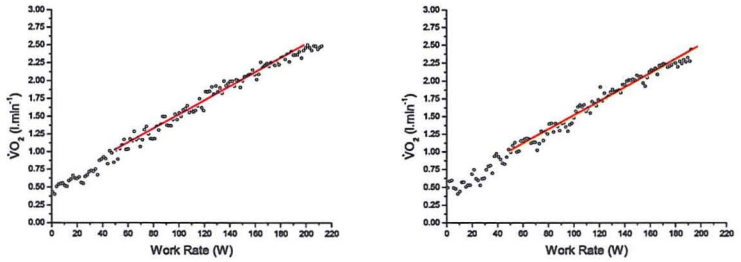
The average linearity of the $\dot{V}O_2$ response during protocol C (0.91 (± 0.02)) was found to be lower than during the protocol A (0.97 (± 0.00)) and protocol B (0.95 (± 0.02)).

6.4.5 Slope of Oxygen Uptake as a function of Work Rate

The $\dot{V}O_2$-workrate plots for the IETs of Figure 6.2 are shown in Figure 6.3 where the slope of $\dot{V}O_2$ as a function of work rate is the slope of the linear fit, $\Delta\dot{V}O_2/\Delta P$. The average $\Delta\dot{V}O_2/\Delta P$ for protocol C (6.53 (± 0.46) ml.min^{-1}.W^{-1}) was found to be substantially lower than both protocol A (10.02 (± 1.16) ml.min^{-1}.W^{-1}) and protocol B (10.03 (± 0.91) ml.min^{-1}.W^{-1}). The average slope of $\dot{V}O_2$ as a function of work rate for protocols A and B was similar.

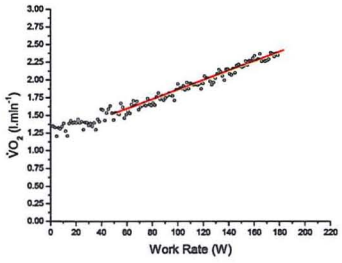
6.4.6 Lactate Threshold

The average V-slope and respiratory gas exchange plots from each IET protocol are provided in Figure 6.4. No LT was found during protocol C: as can be seen in Figure 6.4(c), top graph, there is no detectable deflection point in the $\dot{V}O_2$-$\dot{V}CO_2$ relationship. The supporting respiratory variable profiles for protocol C provide evidence that the subject is exercising above his LT: $\dot{V}_E/\dot{V}O_2$ and $F_{ET}O_2$ are increasing and $F_{ET}CO_2$ is in a steady-state. An LT was however determined during protocols A and B. As can be seen in Figure 6.4(a), top graph, a



(a) Protocol A

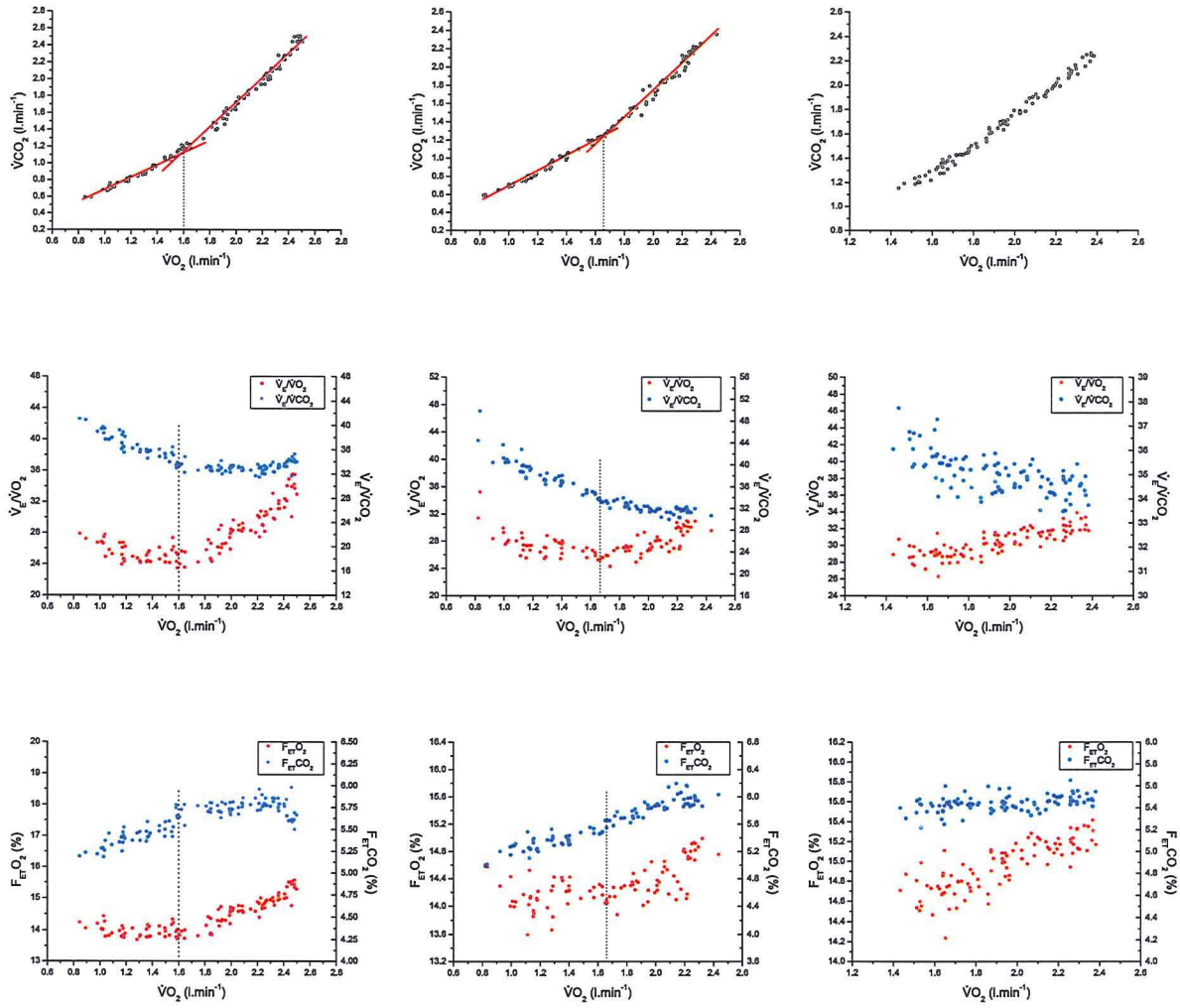
(b) Protocol B



(c) Protocol C

Figure 6.3: The average $\dot{V}O_2$-workrate relationship for each incremental exercise test protocol. Protocol A: Porszasz and colleagues [86]. Protocol B: Section 6.3. Protocol C: constant speed, linear gradient. $\dot{V}O_2$: oxygen uptake.

clear deflection point can be identified in the $\dot{V}O_2$-$\dot{V}CO_2$ relationship during protocol A. The presence of the LT at that point is supported by the response of $\dot{V}_E/\dot{V}O_2$ and $F_{ET}O_2$, both of which increase. Further support is provided by $\dot{V}_E/\dot{V}CO_2$ and $F_{ET}CO_2$, both of which are in steady-state at the $\dot{V}O_2$ corresponding to the LT. An example of the LT plots from protocol B is shown in Figure 6.4(b). As can be seen in Figure 6.4(b), top graph, a clear deflection point can be identified in the $\dot{V}O_2$-$\dot{V}CO_2$ relationship. As in protocol A, the presence of the LT is supported by an increase in $\dot{V}_E/\dot{V}O_2$ and $F_{ET}O_2$ at the same $\dot{V}O_2$ as the deflection occurs in the V-slope plot. No substantial difference was found in the average $\dot{V}O_2$ at which the LT occurred between protocol A (1.61 ($\pm$ 0.05) l.min^{-1}) and protocol B (1.60 ($\pm$ 0.19) l.min^{-1}). There was also little difference in the average non-steady-state work rate at which the LT occurred (111.74 ($\pm$ 15.07) W and 109.42 ($\pm$ 24.70) W, respectively).



(a) Protocol A (b) Protocol B (c) Protocol C

Figure 6.4: The average V-slope and respiratory gas exchange responses during the ramp phase of each incremental exercise test protocol. Protocol A: Porszasz and colleagues [86]. Protocol B: section 6.3. Protocol C: constant speed, linear gradient. $\dot{V}CO_2$: rate of carbon dioxide output. $\dot{V}O_2$: rate of oxygen uptake. $\dot{V}_E/\dot{V}O_2$: ventilatory equivalent of oxygen. $\dot{V}_E/\dot{V}CO_2$: ventilatory equivalent of carbon dioxide. $F_{ET}O_2$: fraction of end-tidal oxygen. $F_{ET}CO_2$: fraction of end-tidal carbon dioxide.

6.5 Discussion

The results of the case study show that initial metabolic rate, oxygen uptake linearity and $\Delta\dot{V}O_2/\Delta P$ of the treadmill exercise are similar for the new protocol (B) and the Porszasz protocol (A). When compared with a constant-speed protocol (C), initial metabolic rate with

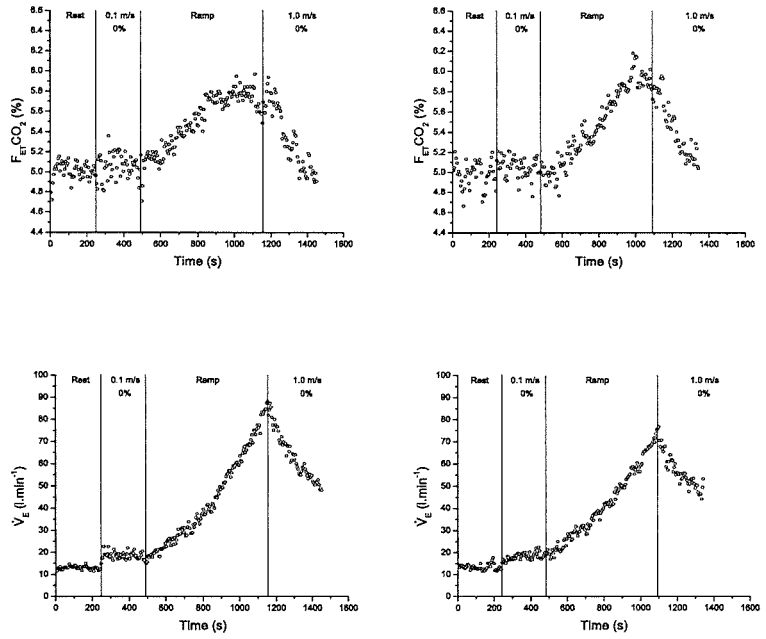
A and B is substantially lower and oxygen uptake linearity is higher. In these regards, protocols A and B are clearly superior to C.

The lower linearity of the $\dot{V}O_2$ response during protocol C may be a consequence of increased upper body movement due to the fast speed at which the subject walked throughout the test. Increased upper body movement increases the demand for O_2 at a given work rate thus distorting the linear relationship between the two variables. As the linearity of the $\dot{V}O_2$ response is higher with protocols A and B, confidence is raised in clinical exercise testing that any deviation from the expected $\dot{V}O_2$ profile would be a consequence of a disease process.

The results indicate that the $\Delta\dot{V}O_2/\Delta P$ for protocol C is significantly lower than that of protocols A and B, and that the $\Delta\dot{V}O_2/\Delta P$ obtained during protocols A and B is approximately equal to that expected of an able-bodied individual [84, 85]. The difference in cost between A/B and C may be an artefact, related to the difference in the progression of internal work rate during the IETs. With protocol C, internal work rate, which is the work rate associated with walking on the flat at a given speed, is constant throughout the test. Thus, in this case the slope of $\dot{V}O_2$ as a function of work rate, $\Delta\dot{V}O_2/\Delta P$ (Equation 6.15), is a true definition of the oxygen requirement of increasing work done against gravity. For protocols A and B, however, speed increases throughout the test, resulting in a progressive increase in the internal work rate required to walk at equivalent speeds on the flat and in an increasing O_2 requirement for this added internal work. The slope of $\dot{V}O_2$ as a function of work rate equation, $\Delta\dot{V}O_2/\Delta P$, therefore has an increasing and neglected component of oxygen uptake in the numerator: this will tend to result in overestimation of O_2 cost during these protocols. This phenomenon was previously predicted by Porszasz and colleagues [86], but it was also noted there that interpretations of deviations from linearity in the $\dot{V}O_2$ response are not compromised.

Although an LT was determined at a similar $\dot{V}O_2$ during protocols A and B, it is possible that neither of these thresholds accurately reflect the start of non-metabolic $\dot{V}CO_2$ production. As can be seen in Figure 6.2, the RER profile produced during these two tests decreases at the start of the ramp phase. This suggests that the subject was hyper-ventilating prior to the start of the ramp. As can be seen in Figure 6.5, $F_{ET}CO_2$ is below 6% and V_E is above 10 $l.min^{-1}$ during rest and prior to the ramp. This further supports the suggestion that the subject was hyper-ventilating.

By hyper-ventilating prior to exercise the subject empties his CO_2 stores. The CO_2 produced during exercise refills these stores. When they are full, more CO_2 is produced at the mouth resulting in a pseudo-threshold [196]. It is therefore possible that the threshold identified



(a) Protocol A (b) Protocol B

Figure 6.5: The average $F_{ET}CO_2$ and $\dot{V}_E$ profile for each incremental exercise test protocol. Protocol A: Porszasz and colleagues [86]. Protocol B: Section 6.3. Protocol C: constant speed, linear gradient. $F_{ET}CO_2$: fraction of end-tidal carbon dioxide. $\dot{V}_E$: minute ventilation.

during these IETs is in fact a pseudo-threshold. It is important to note also that an LT could not be determined during protocol C. The results suggest that the subject was exercising above his LT thus emphasising the importance of a low initial metabolic rate to ensure that all key indices of cardiopulmonary fitness can in principle be determined.

The theoretical contribution of this work is the derivation of a new treadmill protocol (B) with nonlinear, equally-smooth increases in speed and angle (but still with a guaranteed linear increase in work rate). These speed/angle properties may be more desirable than alternative proposals (A), and may be especially beneficial for subjects with gait impairment because the specified increases in speed and angle over their respective min-max ranges are evenly spread over the whole work range. Protocols A and B have both been shown to provide a low initial metabolic rate and have comparable $\dot{V}O_2$ linearity and $\Delta\dot{V}O_2/\Delta P$. The choice of which protocol to use during clinical exercise testing must therefore be determined by the walking capability of the subject being tested. Subjects such as those with an incomplete SCI or those who have suffered a stroke may have an unsteady and limited gait. The large

increase in gradient which occurs at the start of protocol A may be problematic to these subjects. The more gradual increase in gradient which occurs during the new protocol B may be more suited to subjects with an impaired gait pattern as the adaptations to their gait which they must make will, at each stage of the IET, be smaller.

The experimental results provide confirmation of the feasibility of straightforward implementation of the new protocol B, and evidence that the outcome measures are at least comparable with those from protocol A.

To conclude with certainty that the new protocol (B) is at least comparable to previously verified protocols, the significance of the differences between the results obtained from the three protocols must be determined. As this was a single subject case study, this could not be carried out. However, the results obtained are encouraging and do suggest that further investigation with a larger subject group is therefore warranted.

6.6 Conclusions

A novel IET protocol has been developed which provides a low initial metabolic rate and $\Delta\dot{V}O_2/\Delta P$ and $\dot{V}O_2$ linearity comparable to a previously verified protocol. The gradual increase in speed and gradient which occurs during the new protocol may be more appropriate for testing those with an impaired gait pattern.

Chapter 7

Assessment of Novel Methods of Exercise Testing during Robot-assisted Treadmill Walking in Incomplete Spinal Cord Injury

7.1 Chapter Summary

Robot-assisted methods of body weight supported treadmill training (BWSTT) have previously been developed to remove the physical strain on therapists which is associated with manual BWSTT. Robot-assisted treadmill walking has been shown to elicit a metabolic response in those with a spinal cord injury (SCI) during both "passive" and active walking. In order to utilise this response for cardiopulmonary training and exercise testing, we developed an algorithm to estimate the work rate of a subject actively walking in the Lokomat system. Through real-time visual feedback of this work rate, incremental exercise test (IET) and step exercise test (SET) protocols were developed. This chapter describes the assessment of these novel cardiopulmonary assessment protocols in 3 subjects with incomplete SCI.

Each subject performed 2 IETs and 2 SETs. A target work rate profile was displayed during each test on a head height screen in front of the subjects. The subjects were instructed to keep their actual work rate as close to this target profile as possible. Throughout each test the subject's respiratory variables were continuously monitored by a breath-by-breath system and were later analysed for the key indices of cardiopulmonary fitness (peak oxygen uptake ($\dot{V}O_{2peak}$), lactate threshold (LT), slope of $\dot{V}O_2$ as a function of work rate ($\Delta\dot{V}O_2/\Delta WR$) and oxygen uptake kinetics ($\tau\dot{V}O_2$)).

The results obtained suggest that the subjects could successfully follow a linear and step increase in target work rate. "Passive" walking elicited a substantial metabolic response compared to rest (40–130% increase in $\dot{V}O_2$). Encouragingly, during active walking all subjects increased their metabolic response further with $\dot{V}O_{2peak}$ 100–200% higher than the $\dot{V}O_2$ associated with "passive" walking.

Further investigation is required into the repeatability and reliability of the testing protocols used and the key indices of cardiopulmonary fitness obtained. However, this study has shown that active participation during robot-assisted walking can elicit a substantial cardiopulmonary response and that there is the potential for this response, via real time work rate feedback, to be utilised for exercise testing and guided exercise training sessions in those with an incomplete SCI.

The following publications have resulted from this work:

- K. J. Hunt, L. P. Jamieson, A. Pennycott, T. H. Kakebeeke, C. Perret, and M. Baumberger, "Cardiopulmonary assessment protocols for robot-assisted gait in incomplete spinal cord injury," in *Robotics in Rehabilitation Symposium*, Zürich, Switzerland, 2006. [209].
- A. Pennycott, K. Hunt, L. Jamieson, C. Perret, and T.H. Kakebeeke, "Estimation and volitional feedback control of the active work rate during robot-assisted gait," *Medical Engineering in Physics (under review).* [210]
- K. J. Hunt, L. P. Jamieson, A. Pennycott, C. Perret, M. Baumberger, and T. H. Kakebeeke, "Control of work-rate-driven exercise for cardiopulmonary training and assessment during robot-assisted gait in incomplete spinal cord injury," *IEEE Transactions on Neural Systems and Rehabilitation Engineering (under review).* [211].

7.2 Introduction

As discussed in Sections 2.2.3–2.2.4, the effect of BWSTT on the walking capacity of those with an incomplete SCI has been widely studied and its effects have been shown to be superior to conventional therapy [156, 157]. Despite the positive effect that this form of training has on the walking capacity of those with an incomplete SCI and on other factors such as muscle hypertrophy [163] and the risk factors for cardiovascular disease [163, 164], its use within the clinical setting is limited. BWSTT can require up to 3 therapists per patient depending on the support and guidance required. It is labour intensive for the therapists involved and consequently the duration of the session is often reduced.

The number of therapists required to perform each session as well as the physical stress involved, has limited the applicability of BWSTT within the clinic. As a consequence of this, robot-assisted methods for BWSTT have been developed [212, 213] which remove the need for therapist assistance. One such system is the Lokomat driven-gait orthosis (Hocoma AG, Volketswil, Switzerland [212]). Used in combination with a treadmill, this system moves the patients legs in a physiological gait pattern thus removing the physical strain on therapists, prolonging the duration of the training and allowing training to begin at an earlier stage post injury.

Research carried out with this system has shown that it can help improve overground walking for those with an incomplete SCI by improving gait velocity and endurance [214]. It has also been shown to elicit a metabolic response when the patient is walking passively within the system i.e. the driven-gait orthoses are moving the legs with no voluntary contribution from the patient. In 2004, Nash and colleagues [215] reported a 57% increase in $\dot{V}O_2$ and a 20% increase in heart rate from standing rest to passive walking in one SCI subject with a complete C4 lesion. A similar result was reported recently by Israel and colleagues [216] in 12 incomplete SCI subjects. Interestingly, they also demonstrated a significantly higher steady-state $\dot{V}O_2$ when the subjects actively participated in the walking, providing maximum voluntary effort whilst walking with the driven-gait orthosis.

The elicitation of a metabolic response during passive and active walking in the Lokomat suggests that it could be used for cardiopulmonary training for those with an SCI, particularly those with an incomplete injury who can actively participate in the exercise. As discussed in Section 2.5, in order to monitor the effects of cardiopulmonary training, reliable methods of exercise testing are necessary to determine the key indices of cardiopulmonary fitness; peak oxygen uptake ($\dot{V}O_{2peak}$), lactate threshold (LT), slope of $\dot{V}O_2$ as a function of work rate ($\Delta\dot{V}O_2/\Delta WR$) and oxygen uptake kinetics ($\tau\dot{V}O_2$). We developed an algorithm to estimate the work rate of a subject actively walking in the Lokomat. Through real-time visual feedback of this work rate we developed IET and SET protocols. The aim of this study was therefore to assess these novel cardiopulmonary assessment protocols for robot-assisted gait in a convenience sample of 3 subjects with incomplete SCI.

7.3 Methods

7.3.1 Subjects

Prior to recruitment of subjects, this study was reviewed and approved by the Ethics Committee of Luzern Canton, Switzerland. Following ethical approval, three subjects were recruited

for the study the details of whom are provided in Table 7.1. Prior to participation in the study all subjects provided written and informed consent.

Subject	Sex	Age (years)	Level of Injury	ASIA Grade	Time Post Injury	Body Mass (kg)	BWS (kg)
A	M	41	T6	C	14.5	102	40
B	M	32	T11/12	C	3	112	45
C	F	42	T9	D	2	70	35

Table 7.1: Details of the SCI subjects. ASIA: American Spinal Injuries Association. BWS: body weight support.

Subject A and B sustained a spinal cord lesion as a result of a traumatic injury, while subject C's lesion was caused by transverse myelitis.

7.3.2 Apparatus

Robotic Treadmill

A driven-gait orthosis (Lokomat, Hocoma AG, Volketswil, Switzerland), integrated with a treadmill (Woodway GmbH, Weil am Rhein, Germany) and a motor-driven body weight support (BWS) system with real time feedback control for precise body weight unloading (Lokolift, Hocoma AG) was utilised for the cardiopulmonary assessment (see Figure 7.1). The driven-gait orthosis is composed of two exoskeletal leg orthoses which are secured at the subject's hip, above the knee and above the ankle. To prevent drop foot, elastic bands are fixed and secured around the subject's toes. The subject is also secured around the trunk and pelvis by straps attached to the back plate.

The stepping pattern of the driven-gait orthosis is computer controlled and synchronized with the treadmill belt speed. The orthoses contain position sensors at the hip and knee joints which monitor the positioning of the joints and allow knee and hip extension and flexion at the appropriate point in the gait cycle.

Breath-by-breath Gas Exchange

During cardiopulmonary exercise testing the O_2, CO_2 and N_2 concentrations, as well as the volume of each breath were continuously monitored using a breath-by-breath system (Oxycon Alpha, Jaeger GmbH, Höchberg, Germany) in order to measure and record the following

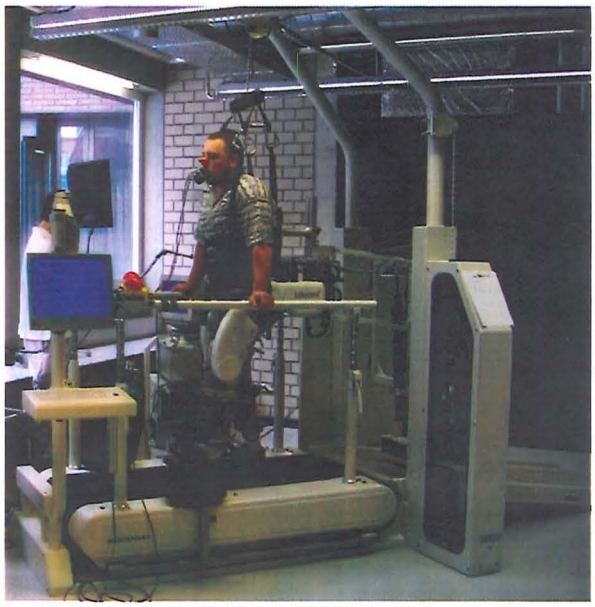


Figure 7.1: A subject performing a cardiopulmonary exercise test. The subject is secured in the driven-gait orthosis. The harness around their trunk is attached to the body weight unloading system and a percentage of their body weight supported. The target work rate for the subject to follow is displayed on the head height screen as well as the actual work rate that the subject is producing in real time.

pulmonary gas exchange and ventilatory variables: rate of oxygen uptake ($\dot{V}O_2$), rate of carbon dioxide production ($\dot{V}CO_2$), minute ventilation ($\dot{V}_E$), respiratory exchange ratio (RER), partial pressure O_2 ($P_{ET}O_2$) and CO_2 ($P_{ET}CO_2$) (see Section 3.3.2 for further information). The subject breathed through a mouthpiece which contained a turbine for measurement of gas flow and a sample line which was connected to the gas analyser. A nose clip was also worn to prevent any gas from escaping.

The breath-by-breath system was calibrated prior to each test: the turbine by a 3-litre volumetric syringe and the gas analyser using ambient air and a certified calibration gas mixture.

Heart Rate

HR was continuously monitored and recorded using a short range telemetry HR monitor (Polar S610, Polar Electro Oy, Kempele, Finland).

7.3.3 Protocols

Estimation of Active Work Rate

The robotic orthoses of the Lokomat are feedback-controlled to keep a subject's gait pattern within a pre-determined gait trajectory which is defined by desired joint angles and angular velocities. When a subject walks "passively" in the Lokomat, the robotic orthoses pull their legs through the appropriate gait cycle. If the subject tries to assist with the walking, the orthoses brake the movement to ensure that the target gait trajectory is not altered.

Force sensors at the orthoses' joints (hip and knee) measure the forces applied by the subject when assisting with walking. The positioning of the joints throughout the gait cycle are also continuously measured. Using this information an algorithm was developed which can estimate the work rate of a subject actively walking with the Lokomat [210].

The orthoses of the Lokomat are moved by a motor which applies a force to the thigh or shank. As the force is applied around an angle of rotation (i.e. the hip or knee joint) a measure of the torque produced is obtained (Equation (7.1)).

$$T = FL \tag{7.1}$$

where

- T = torque (Nm)
- F = force (N)
- L = moment arm (m)

Consequently, the work rate produced at a given time point can be determined (Equation (7.2)).

$$WR = T\omega \tag{7.2}$$

where

- WR = work rate (W)
- ω = angular velocity (rad.s^{-1})

Over a complete gait cycle, the work rate produced at each joint fluctuates depending on the angle of the joint. An average work rate is therefore taken as the work rate at that joint for a given gait cycle. In order to determine the total work rate produced during a gait cycle the

work rates produced at all 4 joints are summed as shown in Equation (7.3).

$$WR^t = \sum_{i=1}^{4} T_i \omega_i \tag{7.3}$$

where

- WR^t = total work rate (W)
- T_i = torque produced at a given joint (Nm)
- ω_i = angular velocity of a given joint

Prior to each exercise test a period of "passive" walking was carried out during which subjects were instructed to exert enough force vertically to maintain an upright posture but not to contribute to the horizontal walking motion. Consequently, the associated work rate could be identified. The actual work rate produced when the subject was actively assisting walking was therefore taken as the work rate produced in addition to that during passive walking (Equation 7.4).

$$WR_i^{net} = WR_i^{active} - WR_i^{passive} \tag{7.4}$$

where

- $WR_i{}^{net}$ = actual work rate produced during subject assisted walking at a given joint
- $WR_i{}^{active}$ = measured work rate during subject assisted walking at a given joint
- $WR_i{}^{passive}$ = measured work rate during passive walking at a given joint

Volitional Work Rate Control via Visual Feedback

The actual work rate produced by a subject during an exercise test was filtered and displayed to the subject in real time using a screen positioned at head height in front of the treadmill. The target work rate was also displayed and the subject was instructed to apply force to the robot limbs in order that the actual work rate performed by the subject matched the target work rate profile (Figure 7.2).

Cardiopulmonary Exercise Test Protocols

Familiarisation

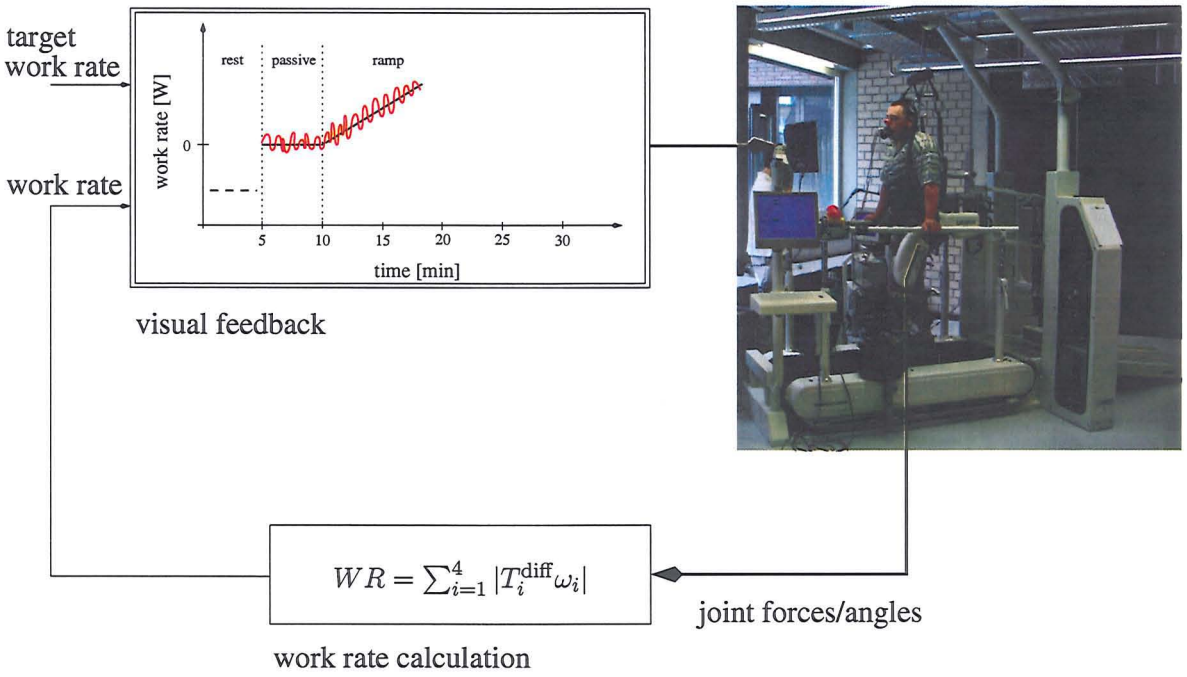


Figure 7.2: Structure for manual, volitional control of work rate, including work rate estimation and visual feedback to subject. The forces and angles at the orthoses' knee and hip joints are continuously measured and processed by an algorithm which estimates active exercise work rate (see equations (7.3)–(7.4)). The block labelled "visual feedback" is a schematic representation of the graphic displayed in real time to the subject via the flat-panel display at the front of the treadmill: the subject sees a target work rate (straight lines) and the current, estimated work rate (wavy line), and is instructed to provide sufficient voluntary force such that the actual work rate follows the target as closely as possible. The example shown is an incremental exercise test work rate profile. Adapted from [211].

Prior to performing any cardiopulmonary exercise tests the subject was invited to the laboratory for two familiarisation sessions. As discussed in Section 3.4.2, a subject's response to a new environment can influence the reliability of the variables under investigation and thus provide an inaccurate characterisation of the response. Therefore, it was essential during the familiarisation period that subjects became comfortable with the investigation team, testing protocols and equipment.

During the first familiarisation session subjects were introduced to the research team. As described in [212], the Lokomat exoskeleton can be adjusted to fit each individual subject. Therefore, measurements were taken of the subject's lower limb to ensure the exoskeleton was set to the subject's requirements. The Lokomat settings which provided the most physiological gait pattern (i.e. hip and knee flexion and extension when appropriate and an absence of drop foot) were established and the subject walked passively in the system in order to

become accustomed to it.

During the next session the subject was encouraged to walk actively in the system and to produce a maximum voluntary contribution. The maximal incremental exercise test (IET) and the constant load (step) exercise test (SET) protocols were then explained in layman's terms to the subject. Following this the subject performed a short IET allowing them to practice linearly increasing the force which they applied to the orthoses during walking, whilst following a target work rate profile. They also performed a short SET to become accustomed to maintaining a constant level of voluntary force required for a steady-state target work rate. Subjects were then asked to put on the various pieces of equipment to be used during the experimental procedures and the purpose of each piece was explained fully.

Incremental Exercise Test

Each subject performed 2 IETs to the limit of tolerance, during which a target linear increase in work rate was displayed on the screen for the subject to follow. As discussed in Section 1.6 it has been recommended, for able-bodied (AB) subjects [58], that a single short duration ramp test is appropriate to accurately measure maximum oxygen uptake ($\dot{V}O_{2max}$), lactate threshold (LT) and O_2 cost/efficiency. This exercise test can therefore provide an indication of the cardiopulmonary fitness of an individual and monitor changes in cardiopulmonary fitness which may result as a consequence of an exercise training programme. A schematic representation of the phases of the IET performed by each subject is shown in Figure 7.3.

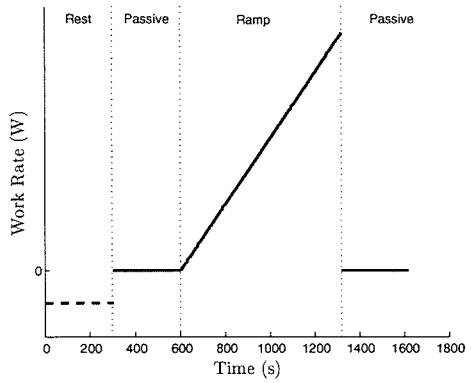


Figure 7.3: A schematic representation of the incremental exercise test profile. The resting and passive walking phases could be extended to ensure that the subject's breathing was stabilised. The duration of the ramp phase was subject-dependent although the incrementation rate was set with the aim of the subject reaching their limit of tolerance in 8–12 minutes.

Once the subject was positioned in the Lokomat they performed a short warm up to ensure that the system was correctly positioned and the gait pattern optimal. Following recovery from this the subject was connected to the breath-by-breath system and carried out a period of rest, during which the cardiopulmonary variables were monitored. Throughout the resting phase the subject stood on the treadmill attached to the Lokomat. A percentage of their body weight, which remained constant throughout the test, was supported (see Table 7.1). If the respiratory variables had not stabilised after 5 minutes the phase was extended.

A 5 minute period of "passive" walking followed. The speed was set to that which resulted in a functional gait pattern for the subject (Table 7.2) and remained constant for the duration of the test. The phase was extended if the respiratory variables had not stabilised.

Subject	Testing speed ($m.s^{-1}$)
A	0.44
B	0.47
C	0.42

Table 7.2: Treadmill speed during the incremental exercise test performed by each subject.

Following the period of passive walking the subject immediately began the incremental phase of the test. The incrementation rate was chosen by the investigators with the aim of ensuring that the subject reached their limit of tolerance within the recommended 8–12 minutes [197]. The reasons why the incrementation rate is not increased too quickly or too slowly have been discussed previously (see Section 3.4.2). During the incremental phase of the test, the target work rate displayed on the screen increased linearly with time. The subject was instructed to increase their active contribution to keep the actual work rate close to the target. The target work rate continued to increase until the subject could no longer match it i.e. when the actual work rate remained below the target for 15 seconds despite verbal encouragement from the investigators to increase active participation.

On attainment of the limit of tolerance the subject was instructed not to actively participate in the walking and to let the robotic-orthoses move their legs passively. This period of passive walking lasted for 5 minutes during which the subject's respiratory variables and HR were monitored to ensure they had recovered from the exercise. This phase was extended if required.

Constant Load Exercise Test

Prior to commencement of the SET the subject carried out a warm up to ensure correct positioning of the Lokomat and a functional gait pattern. The periods of rest and "passive"

walking which followed are identical to that described for the IET. The walking speed for each subject during the SET is shown in Table 7.3.

Subject	Testing speed ($m.s^{-1}$)
A	0.44
B	0.47
C	0.42

Table 7.3: Treadmill speed during the constant load (step) exercise test performed by each subject.

Following the period of "passive" walking the subject immediately began a 15 minute period of active walking. The target work rate displayed on the screen represented 40% of the estimated peak work rate obtained during the familiarisation session. The subject was encouraged to actively push against the orthoses while walking in order to keep their actual work rate as close as possible to the target work rate. On completion of the 15 minute period of active walking the subject carried out 5 minutes of passive walking as described for the IET. A schematic representation of the SET performed by each subject is shown in Figure 7.4.

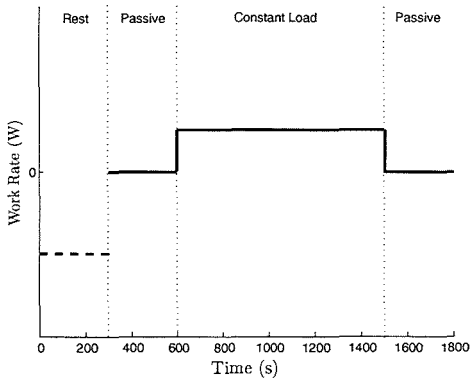


Figure 7.4: A schematic representation of the constant load (step) exercise test profile. The resting and passive walking phases could be extended to ensure that the subject's breathing was stabilised.

7.3.4 Analysis

Incremental Exercise Test

Prior to analysis, the breath-by-breath data obtained from the IETs was edited, as described in Section 3.5.1, to remove the inter-breath fluctuations commonly referred to as "noise".

Following this, the key outcome measures were determined from the edited data as outlined below.

- WR_{peak}: A "rolling" average was calculated for the incremental phase of each IET. All the data points in the 10 seconds prior to and following each work rate reading were averaged to smooth the data. The WR_{peak} was taken as the highest value prior to the end of each incremental phase.

- $\dot{V}O_{2peak}$: $\dot{V}O_{2peak}$ was calculated by averaging all the data points in the final 20 seconds of the incremental phase of the test [64] (for full details see Section 3.6.1).

- HR_{peak}: A HR reading was provided every 5 seconds throughout the test. HR_{peak} was recorded as the highest HR prior to attainment of the limit of tolerance.

- Lactate threshold: The LT was estimated using standard gas exchange criteria [79] and the V-slope method [78] (for full details see Section 3.5.1). Due to the difficulties in identifying the kinetic phase for a number of data sets, all the data in the incremental phase was used for analysis.

- $\Delta\dot{V}O_2/\Delta WR$: To determine $\Delta\dot{V}O_2/\Delta WR$ for the exercise, the edited $\dot{V}O_2$ was plotted against the filtered work rate data. As the work rate was recorded every 0.2 seconds there was not a $\dot{V}O_2$ which corresponded to every work rate reading. Therefore, in order to align the data, each time a $\dot{V}O_2$ was recorded the work rate which occurred at the time nearest (greater) to that $\dot{V}O_2$ was noted i.e. if a breath was recorded at 0.37 seconds the closest work rate reading would be at 0.4 seconds. An average of this and the 4 preceding work rates was recorded as the corresponding work rate to an individual $\dot{V}O_2$ measurement. $\dot{V}O_2$ was plotted against work rate and a linear line of best fit was fitted to the data. The slope of the linear line provided the $\Delta\dot{V}O_2/\Delta WR$ ($ml.min^{-1}.W^{-1}$). Due to the difficulties in identifying the kinetic phase for a number of data sets, all data in the incremental phase was included in the analysis.

- Linearity of $\dot{V}O_2$ response. An indication of the linearity of the $\dot{V}O_2$ response was provided by the correlation coefficient (R^2) associated with the linear line of best fit through the $\dot{V}O_2$-WR plot.

- Resting $\dot{V}O_2$: To ensure that the subject had adjusted to the testing conditions and consequently that their breathing had stabilised, the first 90 seconds of the resting phase response were excluded from analysis. An average of all the remaining data points in the resting phase was calculated to determine the resting $\dot{V}O_2$.

- Passive $\dot{V}O_2$: An average of all the data points in the final 60 seconds of the passive phase was calculated to determine the passive $\dot{V}O_2$.

Constant Load Exercise Test

As for the IET, the breath-by-breath data obtained during each SET was edited as outlined in Sections 3.5.1 and 3.5.2. Following this, the key outcome measures were determined from the edited data as outlined below.

- $\Delta\dot{V}O_2$: To determine the $\Delta\dot{V}O_2$ for each test, the average of all the breaths in the final 60 seconds of the passive phase was subtracted from the average of all the breaths in the final 60 seconds of the step phase.
- $\tau\dot{V}O_2$: In order to determine the $\tau\dot{V}O_2$ response from the passive to the step phase, the phase I response was isolated and an monoexponential line of best fit was fitted to the remaining data [95]. $\tau\dot{V}O_2$ was calculated as the time taken for $\dot{V}O_2$ to reach 63% of its steady-state value (for full details see Section 3.5.2).
- O_2 cost: The O_2 cost was calculated by dividing $\Delta\dot{V}O_2$ by ΔWR. ΔWR was calculated as the average work rate during the step phase minus the work rate during the passive phase (0W).
- Resting $\dot{V}O_2$: As for the IET.
- Passive $\dot{V}O_2$: As for the IET.

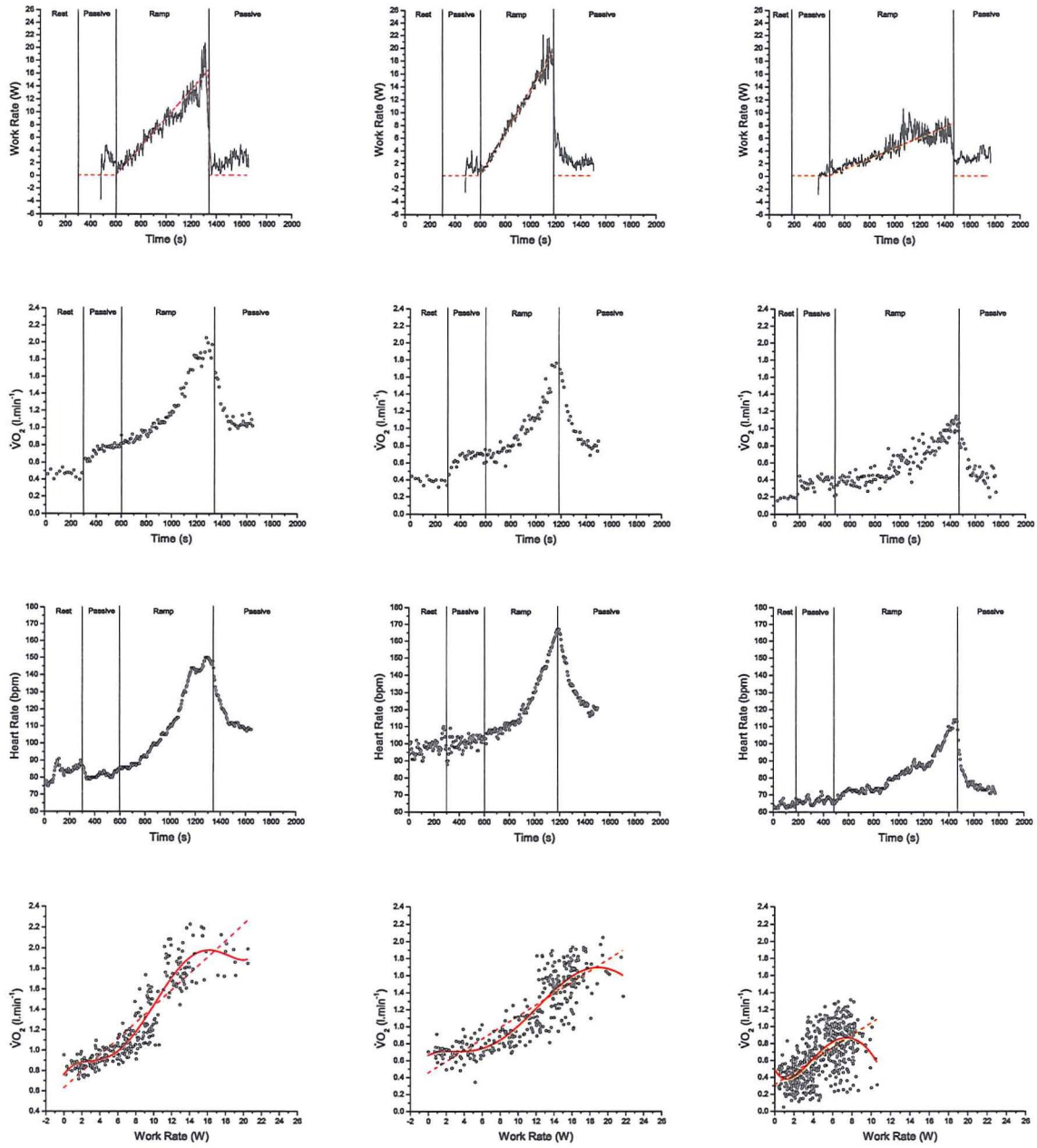
7.4 Results

7.4.1 Maximal Incremental Exercise Test

The work rate, $\dot{V}O_2$ and HR profiles, as well as the WR-$\dot{V}O_2$ relationship, during one IET for each subject are shown in Figure 7.5. The key outcome measures are provided in Table 7.4.

The LT was estimated using the non-invasive V-slope method [78] and supported by the responses of $\dot{V}_E/\dot{V}O_2$, $\dot{V}_E/\dot{V}CO_2$, $P_{ET}O_2$ and $P_{ET}CO_2$ [79]. However, as is stated in Table 7.4 the presence of an LT was not identified during the IET performed by any of the subjects. As can be seen in Figure 7.6, no detectable deflection point is present in any of the V-slope plots.

However, the supporting respiratory variable responses of subject B (Figure 7.7(b)) do suggest that an LT may be present. As expected $\dot{V}_E/\dot{V}O_2$ and $P_{ET}O_2$ are shown to increase after declining and reaching a steady-state. Following a slight delay from the point of change in $\dot{V}_E/\dot{V}O_2$ and $P_{ET}O_2$, $\dot{V}_E/\dot{V}CO_2$ and $P_{ET}CO_2$ increase and decrease respectively. The supporting respiratory variable responses of subjects A and C, however, do not support the presence of an LT. As can be seen in Figure 7.7 (a and c), $\dot{V}_E/\dot{V}O_2$ and $P_{ET}O_2$ appear to

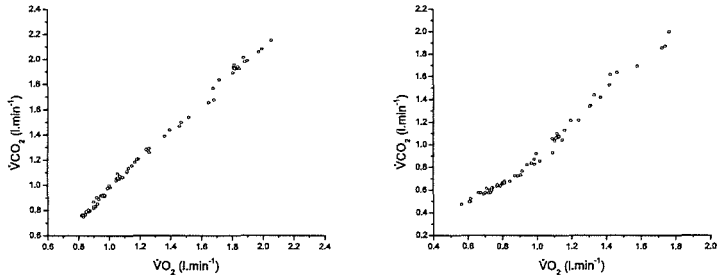


(a) Subject A (b) Subject B (c) Subject C

Figure 7.5: Work rate (top row), oxygen uptake (second row) and heart rate (third row) profiles during an incremental exercise test performed by each subject. The work rate - oxygen uptake relationship is shown in the bottom row for each test. The slope of $\dot{V}O_2$ as a function of work rate was calculated as the slope of the linear line though the data (red dashed line). A line of best fit (red solid line) was also fitted to the data to indicate how the work rate - oxygen uptake relationship changed throughout the test. $\dot{V}O_{2peak}$: peak oxygen uptake. 4 breath averaged data.

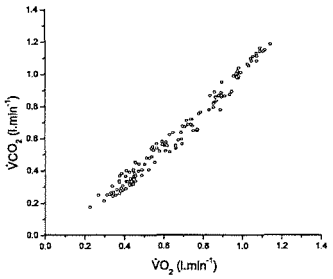
Subject	A	B	C
WR_{peak} (W)	18.9	19.6	7.6
$\dot{V}O_{2peak}$ ($l.min^{-1}$)	1.92	1.71	1.04
$\dot{V}O_{2peak}$ ($ml.kg^{-1}.min^{-1}$)	18.82	15.27	14.86
HR_{peak} (bpm)	150	167	114
$\dot{V}O_2$ at the LT ($l.min^{-1}$)	NA	NA	NA
non-SS WR at LT (W)	NA	NA	NA
$\Delta\dot{V}O_2/\Delta WR$ ($ml.min^{-1}.W^{-1}$)	80	66	73
Linearity of $\dot{V}O_2$ response (correlation coefficient R^2)	0.89	0.84	0.58
Resting $\dot{V}O_2$ ($l.min^{-1}$)	0.47	0.38	0.20
"Passive" $\dot{V}O_2$ ($l.min^{-1}$)	0.80	0.69	0.35

Table 7.4: Key outcome measures for an incremental exercise test performed by each subject. WR_{peak}: peak work rate. $\dot{V}O_{2peak}$: peak oxygen uptake. HR_{peak}: peak heart rate. LT: lactate threshold. SS: steady-state. $\Delta\dot{V}O_2/\Delta WR$: slope of oxygen uptake as a function of work rate. NA: no value was obtained.



(a) Subject A

(b) Subject B

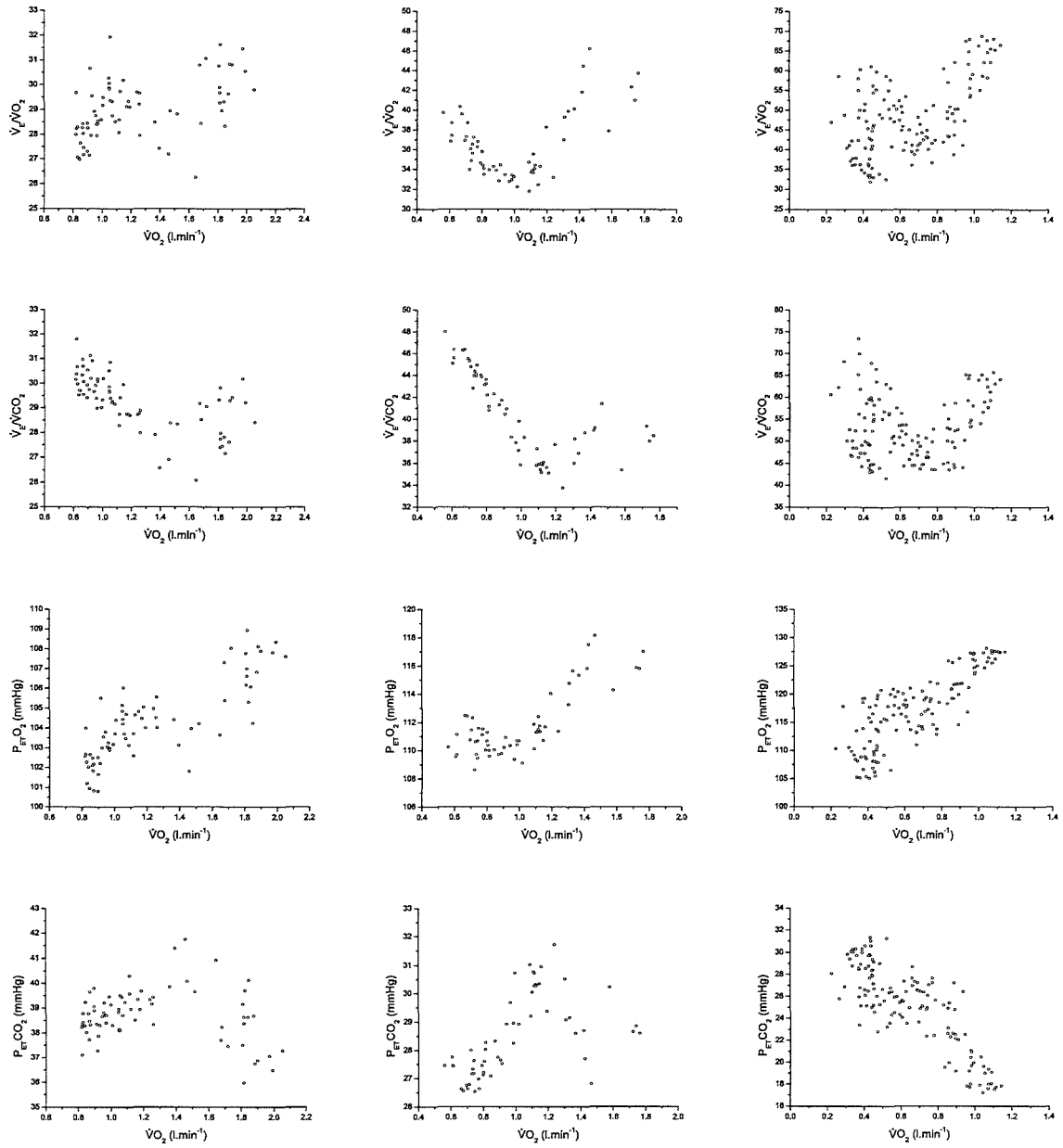


(c) Subject C

Figure 7.6: The V-slope plot for an incremental exercise test performed by each subject. $\dot{V}O_2$: oxygen uptake. $\dot{V}CO_2$: carbon dioxide production. 4 breath averaged data.

increase, decrease slightly and then increase sharply. The $\dot{V}_E/\dot{V}CO_2$ and $P_{ET}CO_2$ responses of subject A suggest that an LT may be present. However, for subject A $P_{ET}CO_2$ is continually decreasing suggesting that the subject has reached her respiratory compensation point (RCP). Due to the inconsistency in the respiratory variable response profiles of subjects A

and C, they do not provide evidence to support the presence of an LT.



(a) Subject A (b) Subject B (c) Subject C

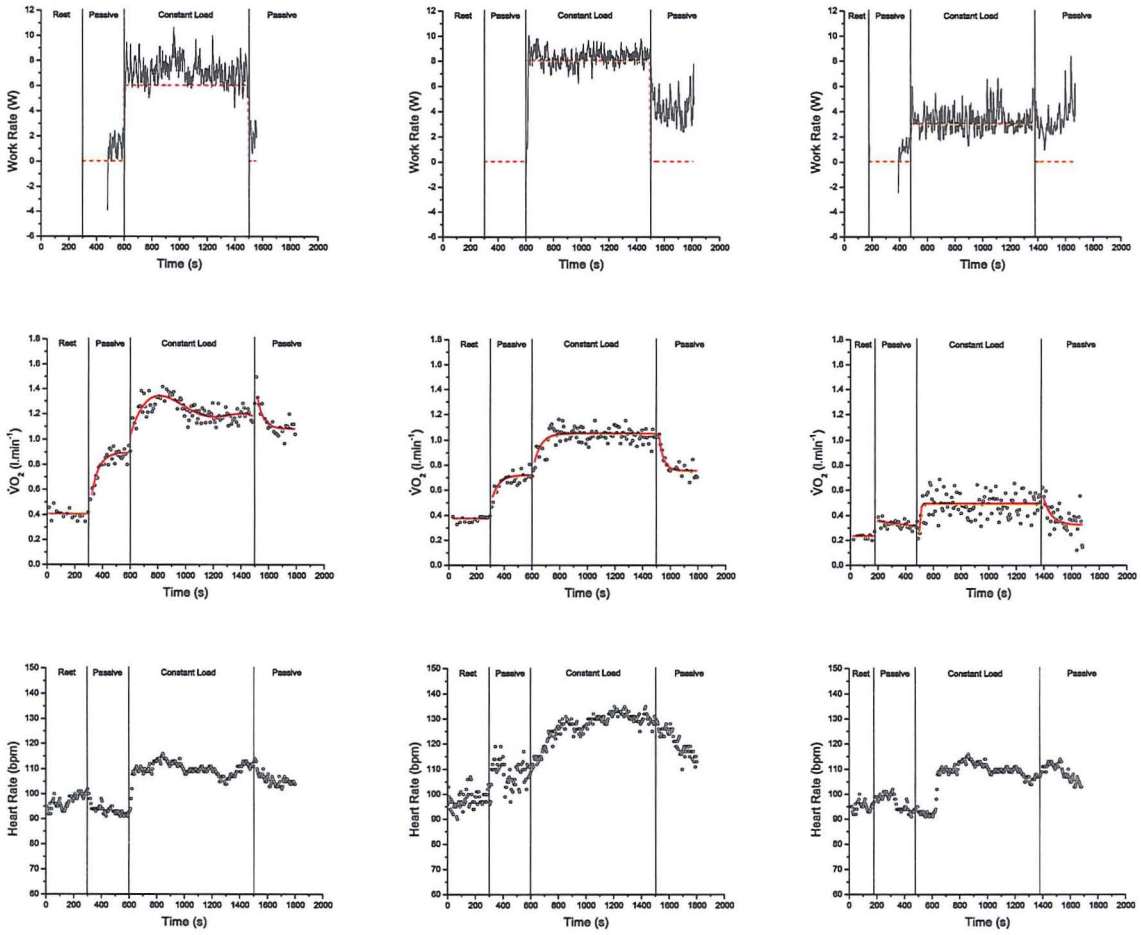
Figure 7.7: Respiratory variable responses during an incremental exercise test performed by each subject. $\dot{V}_E/\dot{V}O_2$: ventilatory equivalent of oxygen. $\dot{V}_E/\dot{V}CO_2$: ventilatory equivalent of carbon dioxide. $P_{ET}O_2$: partial pressure of oxygen. $P_{ET}CO_2$: partial pressure of carbon dioxide. 4 breath averaged data.

7.4.2 Constant Load Exercise Test

The work rate, $\dot{V}O_2$, and HR profiles for one SET for each subject are shown in Figure 7.8. The key outcome measures are listed in Table 7.5.

Subject	A	B	C
Reference WR (W)	6	8	3
Actual WR (W)	7.1	8.2	3.3
$\Delta\dot{V}O_2$ ($l.min^{-1}$)	0.32	0.29	0.20
$\tau\dot{V}O_2$ (s)	NA	53	15
O_2 cost ($ml.min^{-1}.W^{-1}$)	45.07	35.37	60.61
Resting $\dot{V}O_2$ ($l.min^{-1}$)	0.39	0.37	0.22
"Passive" $\dot{V}O_2$ ($l.min^{-1}$)	0.89	0.72	0.31

Table 7.5: The key outcome measures for a constant load (step) exercise test performed by each subject. WR: work rate. $\Delta\dot{V}O_2$: increase in oxygen uptake from "passive" to active walking. $\tau\dot{V}O_2$: time constant for oxygen uptake. NA: no value was obtained.



(a) Subject A (b) Subject B (c) Subject C

Figure 7.8: The work rate (top row), oxygen uptake (middle row) and heart rate (bottom row) profiles for a constant load (step) exercise test performed by each subject. The reference (red dashed line) and the actual (black solid line) work rate during each test are shown on the time-work rate plot. $\dot{V}O_2$: oxygen uptake. 4 breath averaged data.

7.5 Discussion

7.5.1 Passive Walking

A metabolic response has been shown to occur during "passive" walking in the Lokomat (Figures 7.5 (second row) and 7.8 (middle row)). The percentage increase in $\dot{V}O_2$ between standing rest and "passive" walking during the IET and SET is shown in Table 7.6.

As can be seen in Table 7.6, the percentage increase in $\dot{V}O_2$ from rest to "passive" walking

Subject	Test	Resting $\dot{V}O_2$ ($l.min^{-1}$)	"Passive" $\dot{V}O_2$ ($l.min^{-1}$)	Percentage increase (%)
A	IET	0.47	0.80	70
A	SET	0.39	0.89	128
B	IET	0.38	0.69	81
B	SET	0.37	0.72	95
C	IET	0.20	0.35	75
C	SET	0.22	0.31	41

Table 7.6: The percentage increase in oxygen uptake from rest to "passive" walking during an incremental and constant load (step) exercise test performed by each subject. IET: incremental exercise test. SET: constant load (step) exercise test. $\dot{V}O_2$: oxygen uptake.

does differ between tests for each subject. It is possible that this may be due to the subject altering the amount of weight that they are supporting through their arms. Consequently, their demand for oxygen will differ.

Despite the large increase in $\dot{V}O_2$ with "passive" walking, whether or not a training effect would take place at that intensity is debatable. According to the American College of Sports Medicine (ACSM) guidelines [45], AB individuals must train at 40–85% of their $\dot{V}O_{2max}$ reserve which is calculated as in Equation (7.5).

$$\dot{V}O_{2max}\,\text{reserve} = \dot{V}O_{2max} - \dot{V}O_2\,\text{at rest} \tag{7.5}$$

The percentage of $\dot{V}O_{2peak}$ reserve achieved by each subject during their IET and SET is shown in Table 7.7.

Subject	Test	Percentage of $\dot{V}O_{2peak}$ reserve (%)
A	IET	55
A	SET	58
B	IET	52
B	SET	54
C	IET	42
C	SET	38

Table 7.7: The percentage of peak oxygen uptake reserve achieved during the "passive" walking phase of an incremental and constant load (step) exercise test performed by each subject. IET: incremental exercise test. SET: constant load exercise test. $\dot{V}O_{2peak}$: peak oxygen uptake.

With the exception of subject C's SET, each subject achieved the recommended training intensity during "passive" walking. This indicates that although the subjects did not actively participate in the walking, the metabolic cost of maintaining an upright gait posture

whilst their legs were moved passively may be sufficient to provide enough cardiopulmonary stress to improve their cardiopulmonary fitness. However, as will be discussed in Section 7.5.2, it is likely that the $\dot{V}O_{2peak}$ obtained during the IETs does not represent the subject's true maximum cardiopulmonary capacity. Consequently, the percentage of $\dot{V}O_{2peak}$ reserve shown in Table 7.7 which was achieved during "passive" walking may be overestimated. The percentages of $\dot{V}O_{2peak}$ reserve shown in Table 7.7 are also affected by changes in the $\dot{V}O_2$ associated with "passive" walking. It is therefore essential, to accurately gauge the intensity of "passive" walking, that the subject's effort and support be kept constant.

The metabolic cost of "passive" walking is likely to be affected by the amount of BWS provided. It is possible therefore that by altering the amount of BWS, without compromising the subject's gait pattern, that the metabolic challenge of "passive" walking may be increased to the extent that training adaptations may occur. Whether the metabolic response of maintaining an upright posture during "passive" walking is significant enough for cardiopulmonary training requires further investigation.

7.5.2 Maximal Incremental Exercise Test

Peak Work Rate

As can be seen in Figure 7.5 (top row), all subjects were able to maintain a linear increase in work rate by increasing their voluntary effort in response to the visual feedback display on the screen. This is a skill which must be learned, and subjects were given time during the familiarisation period to do so. Once learned, it can be used for incremental exercise testing and also for cardiopulmonary exercise training, during which subjects would follow a pre-defined work rate protocol.

Peak Oxygen Uptake

Measures of $\dot{V}O_{2peak}$ have not previously been reported for those with an incomplete SCI using the Lokomat as the mode of testing. Consequently, there is no reference data with which to compare our results. Table 7.8 provides reference $\dot{V}O_{2peak}$ data for sedentary SCI subjects using different modes of exercise for testing: data from the 3 subjects in this study is inserted for comparison.

A direct comparison of the $\dot{V}O_{2peak}$ of subjects A and C to those of previous studies cited in Table 7.8 cannot be made as both subjects had previously taken part in the 5 month BWSTT

Study	Subject group	Testing mode	$\dot{V}O_{2peak}$ ($ml.kg^{-1}.min^{-1}$)
Zwiren and Bar-Or 1975 [170]	sedentary paraplegics	ACE	19 ($\pm$ 5.5)
Jacobs et al., 2002 [36]	sedentary paraplegics	ACE	19.6 ($\pm$ 3.2)
Jacobs and Mahoney 2002 [183]	sedentary paraplegics	FES-assisted overground walking	22.7 ($\pm$ 3.9)
Present study	subject A treadmill trained paraplegic	Lokomat	18.82
Present study	subject B sedentary paraplegic	Lokomat	15.27
Present study	subject C treadmill trained paraplegic	Lokomat	14.86

Table 7.8: Comparison of $\dot{V}O_{2peak}$ values obtained for sedentary paraplegics in other investigations to that obtained during a Lokomat incremental exercise test for subject A, B and C. $\dot{V}O_{2peak}$: peak oxygen uptake. ACE: arm crank ergometry. FES: functional electrical stimulation.

study discussed in Chapters 4 and 5. Consequently, neither subject could be deemed sedentary. Having continued with their treadmill training following completion of the BWSTT study, subjects A and B had, at the point of Lokomat testing, been training for approximately 10 and 12 months respectively. It is interesting to note however, that despite this training the $\dot{V}O_{2peak}$ obtained by subject A is comparable to that obtained by sedentary paraplegics during arm crank ergometry (ACE) [36, 170] and FES-assisted overground walking [183]. The $\dot{V}O_{2peak}$ obtained by subject C is at the lower end of the range of values obtained by Zwiren and Bar-Or [170] and is actually lower than those obtained by Jacobs and colleagues [36] and Jacobs and Mahoney [183]. Despite being regarded as a sedentary paraplegic who had previously not participated in any form of cardiopulmonary training, the $\dot{V}O_{2peak}$ obtained by subject B during the IET is higher than that obtained by subject C. His $\dot{V}O_{2peak}$ is within the range of values obtained by Zwiren and Bar-Or [170] for sedentary paraplegics performing ACE yet lower than those obtained by Jacobs and colleagues [36, 183].

The robotic orthoses of the Lokomat maintain the subject's gait pattern regardless of the amount of voluntary input from the subject. Therefore, unlike the IETs discussed in Chapters 4 and 5 it is unlikely that the Lokomat IETs are limited by the subject's ability to maintain a functional gait pattern. However, it is possible that the tests may still be limited peripherally rather than centrally by the voluntary effort required by the subjects to follow the target work rate profile. As the test proceeds the subject is required to exert an

increasing amount of force on the orthoses. Given the atrophied muscles and fast fatiguing muscle fibres shown to be present in the paralysed lower extremities of those with an SCI [16, 17, 18, 20, 21, 23, 24, 25], it is probable that the amount of force that the subjects could exert during the IET was limited. Consequently, the $\dot{V}O_{2peak}$ obtained during the Lokomat IET may not truly reflect the maximum cardiopulmonary capacity of the subject, but the cardiopulmonary capacity available to them when utilising their partially paralysed lower limbs for exercise.

An ACE IET would provide an indication of the extent of this peripheral limitation. The $\dot{V}O_{2peak}$ obtained during an ACE IET with able-bodied (AB) subjects has been shown to be ~70% of that obtained during maximum treadmill exercise [174]. Therefore, although the ACE IET would not provide a true indication of the maximum cardiopulmonary capacity of the subject it would provide an indication as to whether the $\dot{V}O_{2peak}$ obtained during the Lokomat IET is limited even further because of a more substantial peripheral limitation.

Despite the possibility that the $\dot{V}O_{2peak}$ may be limited peripherally by atrophied and fast fatiguing lower limb muscles, it is encouraging to note that all subjects were able to elicit a high metabolic rate during the ramp phase of the IET. As can be see in Table 7.9, the $\dot{V}O_{2peak}$ obtained was, in all subjects, substantially higher than the $\dot{V}O_2$ during rest. It is also encouraging to note that the $\dot{V}O_{2peak}$ achieved by each subject was also substantially higher than that obtained during "passive" walking. This emphasises the importance of active walking in the Lokomat for increasing the demand on the cardiopulmonary system and consequently for increasing the training stimulus.

Subject	Resting $\dot{V}O_2$ ($l.min^{-1}$)	"Passive" $\dot{V}O_2$ ($l.min^{-1}$)	$\dot{V}O_{2peak}$ ($l.min^{-1}$)	Percentage increase from rest (%)	Percentage increase from "passive" (%)
A	0.47	0.80	1.92	309	140
B	0.38	0.69	1.71	350	102
C	0.20	0.35	1.04	420	197

Table 7.9: The percentage increase from resting and "passive" walking to peak oxygen uptake during an incremental exercise test performed by each subject. $\dot{V}O_2$: oxygen uptake. $\dot{V}O_{2peak}$: peak oxygen uptake.

This substantial increase in $\dot{V}O_2$ during active walking could be utilised for cardiopulmonary training by providing guided training programmes for SCI patients with the aim of improving their cardiopulmonary fitness and reducing their risk of cardiovascular disease.

Linearity of Oxygen Uptake Response

As can be seen in Figure 7.5 (second row) and Table 7.4, the $\dot{V}O_2$ response during the incremental phase of the IET is not well fit by a linear relationship. This may be a consequence of unmeasured work being performed through the arms: as the test progressed the subjects may have increasingly relied on the side bars for support and to aid in their production of force against the orthoses. Consequently, more muscle mass is involved in the exercise and the demand for oxygen increased. As no force sensors were present on the treadmill bars, no indication of the work being done through the arms can be provided. It is also possible that difficult interactions between the subject and the treadmill belt and robotic orthoses resulted in unmeasured work being performed.

The possibility that unmeasured work was being performed may explain why the $\dot{V}O_2$ response is not continually linear despite an apparent linear increase in work rate throughout the incremental phase. It is likely that as the test progressed and the task of increasing the amount of voluntary force against the orthoses became more difficult, the work rate may have been underestimated ($\dot{V}O_2$ appears to increase faster as the end of the test approaches).

A further explanation for the lack of linearity in the $\dot{V}O_2$ response may be that the work rate associated with passive walking may differ as the test progresses, thus altering the identification of the actual work rate produced by the subject. Further investigation is required to investigate whether this is the case or whether unmeasured work can account for the observations discussed.

Slope of Oxygen Uptake as a function of Work Rate

The $\Delta\dot{V}O_2/\Delta WR$ for the exercise is also affected by the non-linearity of the $\dot{V}O_2$ response. As can be seen in Figure 7.5 (bottom row, red solid line), the relationship between $\dot{V}O_2$ and work rate changes throughout the test. The $\dot{V}O_2$ profile suggests that the $\Delta\dot{V}O_2/\Delta WR$ of the exercise is higher at the end of the test compared to the start. This may be a consequence of increased and unmeasured work. The $\Delta\dot{V}O_2/\Delta WR$ for each test presented in Table 7.4 is therefore the average $\Delta\dot{V}O_2/\Delta WR$ for the test. Before the $\Delta\dot{V}O_2/\Delta WR$ for walking in the Lokomat during an IET can be established, the work rate estimation must be further investigated.

Lactate Threshold

As stated in Table 7.4, an LT was not identified for any subject during their IET. As can be seen in Figure 7.6, no detectable deflection point is present in the $\dot{V}O_2$-$\dot{V}CO_2$ relationship for

subjects A and C. For subject B however, the relationship does not remain linear throughout the test. The profile appears to be an extended S-shape. It is possible that an LT was not identified during any of the tests because the work rate profile was not linear throughout the incremental phase. As discussed previously this may have been a consequence of unmeasured work performed by the subject. In order to accurately estimate an LT using V-slope analysis and gas exchange criteria the work rate profile must be linear. This may explain why one could not be determined.

It is also possible that an LT could not be detected because the subject was exercising either above or below the threshold. Below the LT, $\dot{V}_E/\dot{V}O_2$ is expected to fall and attain a steady-state before increasing again at the point of the LT. An identical response is also expected for $P_{ET}O_2$. $\dot{V}_E/\dot{V}CO_2$ also decreases and reaches a steady-state below the LT. However, at the LT it remains in a steady-state, only increasing again at the respiratory compensation point (RCP). Below the LT $P_{ET}CO_2$ increases and is in a steady-state at the point of the LT. At the RCP $P_{ET}CO_2$ decreases again. As can be seen in Figure 7.7 (a), the $\dot{V}_E/\dot{V}O_2$ (top row) and $P_{ET}O_2$ (third row) responses for subject A do not appear to follow the expected pattern of an AB subject exercising either above or below the LT: both responses appear to increase, decrease slightly and then increase again sharply. The response profiles of $\dot{V}_E/\dot{V}CO_2$ and $P_{ET}CO_2$ are suggestive of a subject who started the incremental phase below the LT and by the end had reached their RCP. As there is no consistency between the V-slope and respiratory variable plots the intensity at which the subject was exercising during the incremental phase of the IET cannot be concluded.

Although the supporting respiratory variable data for subject C (Figure 7.7(c)) is noisier than for subject A, the overall response profiles for all the respiratory variables are similar with the exception of $P_{ET}CO_2$ which appears to be decreasing from the start of the exercise suggesting that the subject was exercising above the LT. It is therefore also difficult to determine at which intensity subject C is exercising during the incremental phase of the test.

The supporting respiratory variable profiles of subject B (Figure 7.7(b)) all suggest the presence of an LT. An increase in $\dot{V}_E/\dot{V}O_2$ and $P_{ET}O_2$ appears to occur at the same point, with a slight delay before an increase in $\dot{V}_E/\dot{V}CO_2$ occurs. The decrease in $P_{ET}CO_2$, which suggests the subject has reached RCP, occurs at approximately the same point as the increase in $\dot{V}_E/\dot{V}CO_2$. Although the respiratory variable responses do suggest the presence of an LT the absence of a clear deflection point in the V-slope plot and the absence of repeat tests casts uncertainty over this finding.

Peak Heart Rate

As can be seen in Figure 7.5 (third row), the HR_{peak} obtained by each subject during their IET is substantially higher than the HR at rest and during "passive" walking, indicating a large stress on the cardiovascular system. As for the $\dot{V}O_2$ response, this indicates that by increasing the amount of voluntary effort whilst walking in the Lokomat, subjects with an SCI would be able to train, using this system, to improve their cardiopulmonary fitness.

7.5.3 Constant Load Exercise Test

As can be seen in Figure 7.8 (top row), all three subjects were able to maintain a steady-state work rate whilst actively walking in the Lokomat. This is encouraging as it suggests that those with an incomplete SCI can follow a target steady-state work rate which can be utilised for both exercise training and testing sessions.

During steady-state exercise below the LT $\dot{V}O_2$ is expected, in AB individuals, to reach a steady-state in less than 3 minutes [97]. $\dot{V}O_2$ did reach a steady-state during the 15 minute SET for subjects B and C. However, this was not the case for subject A. An "overshoot" in the $\dot{V}O_2$ response occurred at the onset of exercise which was not mirrored in the work rate profile. It is possible that the apparent "overshoot" in $\dot{V}O_2$ may reflect unmeasured work that is being performed.

Due to the "overshoot" in $\dot{V}O_2$ a τ could not be determined for subject A. A τ of 53 seconds was obtained for subject B confirming that the $\dot{V}O_2$ response did reach steady-state within the duration of the test. A τ of 15 seconds was obtained for subject C which suggests an almost immediate increase in $\dot{V}O_2$. Further investigation is required into the determination of τ to support the findings of this study.

7.5.4 Repeatability and Reliability Testing

As discussed in Section 7.5.2, the $\dot{V}O_2$ response during the IET is not well fit by a linear relationship. Whether this is the consequence of unmeasured work, or an underlying physiological response of incomplete SCI to this form of exercise requires further investigation. Performing IETs on the Lokomat with AB subjects would enable us to investigate this. If their $\dot{V}O_2$ response to a linear increase in work rate is linear, it would suggest that there is not an issue with the work rate determination. However, if their response is not linear it would imply that there is a significant amount of unmeasured work which is not being accounted for.

Once the issue of linearity is resolved it is essential that the repeatability and reliability of both the IET and SET protocols be determined. This will enable the consistency of the outcome measures to be determined as well as whether the outcome measures are truly reflective of the subject's capacity. The repeatability of key outcome measures should be determined firstly in AB subjects. The key outcome measures could then be compared to those obtained during lower limb cycling. Comparing the results of the two modes of exercise would provide necessary information such as whether the peak values obtained during the IET are truly reflective of the subject's maximum cardiopulmonary capacity. A comparison of the peak and steady-state work rates achieved would also provide an indication as to the extent of any unmeasured work being performed. Only once we are confident in the reliability and repeatability of the testing protocols should an investigation as to how this is affected by incomplete SCI be carried out.

7.6 Conclusion

The results of this study are encouraging as they show that active participation during robot-assisted walking can elicit a substantial cardiopulmonary response. Consequently, it appears that exercise testing via real time work rate feedback is possible with incomplete SCI subjects. It has been demonstrated that subjects can follow a pre-defined work rate profile which could not only be used to obtain standard outcome variables during exercise testing, but also for guided exercise training sessions. Further investigation is however required to determine the repeatability and reliability of the testing protocols.

Chapter 8

Discussion

8.1 Chapter Summary

This chapter brings together the main outcomes of all the studies which comprise this thesis to analyse the potential of body weight supported treadmill training (BWSTT) for improving the cardiopulmonary fitness, muscle atrophy and reduced lower limb bone mineral density (BMD) of those with an incomplete SCI. The methods used to identify these improvements are also analysed. The substantial effect that this form of training has on performance parameters (peak work rate (WR_{peak}), 15 minute distance test and training performance) is identified. The potential for adapted able-bodied and novel incremental and constant load (step) exercise test (IET and SET) protocols to identify the key indices of cardiopulmonary fitness (peak oxygen uptake ($\dot{V}O_{2peak}$), lactate threshold (LT), slope of $\dot{V}O_2$ as a function of work rate ($\Delta\dot{V}O_2/\Delta WR$) and $\dot{V}O_2$ kinetics ($\tau\dot{V}O_2$)) during robot- and non-robot-assisted treadmill exercise in those with an incomplete SCI is highlighted. Also discussed in this chapter is the use of standard dynamometry tests to determine the peak force and central activation ratio (CAR) of the quadriceps and hamstring muscles of incomplete SCI individuals. Limitations associated with the protocols developed throughout this thesis are identified and possible explanations offered.

8.2 Potential Benefits of Robot- and Non-robot-assisted Body Weight Supported Treadmill Exercise in Incomplete Spinal Cord Injury

Body weight supported treadmill training (BWSTT) whether with robot assistance or without, has the potential to positively influence the reduced cardiopulmonary fitness, muscle atrophy and reduced lower limb bone mineral density (BMD) associated with a spinal cord injury (SCI). As discussed throughout this thesis, the sedentary lifestyle led by the majority

of individuals with an SCI increases their risk of cardiovascular disease. Consequently, in line with the able-bodied (AB) population, the leading cause of death for those with an SCI has become respiratory and cardiovascular disease [27]. Physical activity can help to reduce this risk. Body weight supported (BWS) treadmill exercise is an ideal method of exercise for those with an incomplete SCI. Those with more lower limb control can walk safely and securely attached to the BWS system. If part of their gait cycle requires assistance, this can be provided by a therapist or by the use of functional electrical stimulation (FES). Robot-assisted treadmill exercise can be utilised for all individuals with an incomplete SCI. However, it is likely to be of most benefit to those with weaker lower limb muscles and less voluntary control as the robot orthoses will maintain their gait pattern. The intensity of robot-assisted treadmill training can be modified by varying the amount of active participation provided by the individual.

By actively participating in the exercise and consequently increasing the strain provided by the muscles on the lower limb bones, BWS treadmill exercise has the potential to reverse the decline in BMD which occurs in the paralysed lower limbs following an SCI [9, 10, 11, 12]. Therefore, it has the potential to reduce their risk of osteoporosis and incidence of lower limb fractures which are often a secondary complication of an SCI.

The potential also exists for this form of exercise to increase the strength and endurance of the lower limb muscles which are greatly atrophied following an SCI [16, 17, 18, 19, 20, 21]. This would in turn result in an improvement in many functional outcomes such as an increased ability to perform activities of daily living (ADLs). Improvements in gait performance through increased muscular endurance and improved technique is also a potential benefit.

The main study of this thesis investigated the effects of BWSTT on these secondary complications of an SCI. The potential for various methods of exercise testing to determine the key indices of cardiopulmonary fitness (peak oxygen uptake ($\dot{V}O_{2peak}$), lactate threshold (LT), slope of $\dot{V}O_2$ as a function of work rate ($\Delta\dot{V}O_2/\Delta WR$), and $\dot{V}O_2$ kinetics) were highlighted, as was the use of standard dynamometry tests to determine peak voluntary force and the central activation ratio (CAR) of the hamstring and quadriceps muscles. Potential issues with implementing such protocols with incomplete SCI subjects were identified.

8.3 Functional Outcomes

During the BWSTT study (Chapters 4 and 5) the 15 minute distance test was utilised to monitor improvements in the subjects' gait performance. Following 20 weeks of BWSTT

subjects A and B increased the distance they could walk in 15 minutes by ~100% and 121% respectively. This is an extremely significant result as it indicates a substantial improvement in gait performance for both subjects. This was also highlighted by considerable improvements in training performance and in the peak work rate (WR_{peak}) achieved during the incremental exercise test (IET).

The substantial increases in the above mentioned outcomes are very encouraging as it suggests that BWSTT has the potential to improve the walking ability of those with an incomplete SCI. Whether this increase can be transferred to overground walking would require further investigation. Although the effect of the training on ADLs was not measured, both subjects did report that with training their transfers became easier as did walking on parallel bars or with a zimmer frame. This is an important observation as it suggests that for the subjects everyday tasks required less effort.

As was shown in this study, improvements in gait performance enabled both subjects to train for longer at a higher work rate. Consequently, there is an enhanced potential to increase cardiopulmonary fitness. In order to determine the key indices of cardiopulmonary fitness and monitor how they change with training, cardiopulmonary exercise testing must be performed. The studies which comprise this thesis investigated the feasibility of implementing standard AB treadmill IET and SET protocols as well as novel IET and SET protocols during robot-assisted and non-robot-assisted BWS treadmill exercise in those with an incomplete SCI.

8.4 Cardiopulmonary Exercise Testing

8.4.1 Incremental Exercise Testing

During treadmill incremental exercise testing we would expect to be able to determine a subject's $\dot{V}O_{2max}$, LT and $\Delta\dot{V}O_2/\Delta WR$. A measure of maximum heart rate (HR_{max}) would also be obtained.

Maximum Oxygen Uptake

During a maximum IET with an AB subject $\dot{V}O_{2max}$ is identified as a plateau in $\dot{V}O_2$ despite a further increase in work rate [65]. Recent research has however shown that this plateau does not occur in the majority of individuals [64, 66]. Maximal constant load (step) exercise tests (SETs) must also be carried out to ascertain whether or not the maximum $\dot{V}O_2$ achieved during a maximal IET is indeed representative of the subject's $\dot{V}O_{2max}$. It is now recommended that in the absence of additional testing, the maximum $\dot{V}O_2$ achieved during an IET must be referred to as $\dot{V}O_{2peak}$. $\dot{V}O_{2peak}$ is also the preferred term if there is a

peripheral limitation which prevents the subject from giving a maximum cardiopulmonary effort. For these reasons the maximum $\dot{V}O_2$ achieved by the incomplete SCI subjects who performed IETs in all of the studies which comprise this thesis is referred to as $\dot{V}O_{2peak}$.

Following a period of endurance training the $\dot{V}O_{2max}$ of AB individuals is expected to increase. As discussed in Section 1.5 the reasons for this increase remain equivocal but are likely to be associated with central and peripheral adaptations which result in an increase in the maximum cardiac output (CO) and maximum arteriovenous (a-v) O_2 difference. During the BWSTT study outlined in Chapters 4 and 5, $\dot{V}O_{2peak}$ did increase following 16 and 20 weeks training in subjects A and B respectively. However, in contrast to the expected result, this increase was not continuous at each test point (TP).

A possible explanation for this is that the tests were not limited centrally, as for healthy AB subjects, but peripherally by the subjects' ability to maintain a functional gait pattern. Neither subject felt or looked physically exhausted following an IET and often commented that they had ended the test because their legs were tired and they could not continue walking. The reasons for this varied between the two subjects. For subject A the atrophied muscles and fast fatiguing fibres likely to be present in her lower limbs [16, 17, 18, 20, 21, 23, 24, 25], in conjunction with the limited neural control, resulted in her legs becoming progressively weaker as the test progressed. Consequently, she reached a point where her gait pattern was no longer functional. How quickly this happened did appear to vary from day to day (possibly due to her multiple sclerosis (MS)) and consequently reduced the certainty that the $\dot{V}O_{2peak}$ achieved was at all reflective of her true cardiopulmonary capacity. From TP3 onwards, the IETs performed by subject B were limited by the speed at which he could walk rather than his cardiopulmonary capacity. He achieved exceptionally high peak gradients during his tests but his limited neural control meant that he could not increase his walking speed further.

The limitations in the gait pattern of both subjects suggests that the standard AB treadmill IETs adapted for use with incomplete SCI subjects did not provide a true indication of their maximum cardiopulmonary capacity. This is also supported by the fact that during subject A's initial SETs the $\dot{V}O_2$ achieved in the final 20 seconds of the tests were higher or approximately equal to that achieved during the IETs.

The fact that $\dot{V}O_{2peak}$ did not increase at each TP despite an increase in work rate may have been due to alterations in gait pattern or the subjects leaning more heavily on the bars. This alters the demand for O_2 as the muscle mass involved in the exercise is changed.

Although the increase in $\dot{V}O_{2peak}$ was not continuous throughout the training study, the fact

that it did increase overall is encouraging as it suggests that both subjects were able to utilise a previously unattainable cardiopulmonary reserve and consequently increase the intensity at which they could train.

The IETs developed for robot-assisted treadmill exercise (Chapter 7) were not limited by the subjects' ability to maintain a functional gait pattern as the robot orthoses maintained this for them. However, it is likely that they were still limited peripherally by the subjects' atrophied and fast fatiguing lower limb muscles which limited their ability to increase the force required to follow the increasing work rate. Consequently, it is possible that this novel method of incremental exercise testing is also unable to provide a true indication of the cardiopulmonary capacity of those with an incomplete SCI.

It would be of interest to perform an arm crank ergometery (ACE) IET at the same point as either the standard treadmill IET or the novel robot-assisted IET to determine the extent to which the $\dot{V}O_{2peak}$ obtained is affected by the peripheral limitations discussed. In AB subjects the $\dot{V}O_{2peak}$ achieved during an ACE IET is ~70% of that obtained during maximal treadmill exercise [174]. Therefore, although in our subjects the ACE IET would not provide an indication of maximum cardiopulmonary capacity, it would provide an indication as to how much the treadmill tests are limited by the lower limbs. By monitoring the extent to which the difference in $\dot{V}O_{2peak}$ between the ACE and treadmill is reduced with training we would be able to monitor the extent to which the lower limb peripheral limitation is being removed.

Linearity of Oxygen Uptake Response

It is important to note at this point that the $\dot{V}O_2$ response to the linear increase in work rate during both the robot-assisted and non-robot assisted IETs is not well fit by a linear relationship. This is likely to be a consequence of unmeasured work being performed. It is possible that as the tests progressed the subjects increased the use of their upper body by leaning more heavily or pulling on the side bars to help maintain a functional gait pattern. As mentioned previously, this would increase the muscle mass involved in the exercise and thus the O_2 demand. This may also have resulted from the subject altering their gait pattern during the non-robot assisted IETs. Additional unmeasured work may have resulted during the robot-assisted IETs from difficult interactions between the subject and treadmill belt. As the test progressed, the task of producing force against the orthoses became more difficult. Therefore, it is likely that the work rate may have been underestimated.

Although the lower limb work rate remained linear throughout the tests the total work rate

(upper body plus lower limbs) performed by the subject may not have. This may have affected the determination of a number of key indices of cardiopulmonary fitness.

Lactate Threshold

An LT can be estimated non-invasively during an AB IET using V-slope and gas exchange analysis [78, 79]. At the point of LT a disproportionate increase in carbon dioxide output ($\dot{V}CO_2$) with respect to $\dot{V}O_2$ occurs. Corresponding changes in the respiratory variable profiles can also be identified: $\dot{V}_E/\dot{V}O_2$ and $F_{ET}O_2$ increase while $\dot{V}_E/\dot{V}CO_2$ and $F_{ET}CO_2$ remain stable. With cardiopulmonary training the work rate at which the LT occurs is expected to increase.

The identification of an LT during the IET with the incomplete SCI subjects is of additional importance due to the issues raised regarding the determination of peak cardiopulmonary capacity. As the identification of an LT is not influenced by the subject reaching peak cardiopulmonary capacity it may be the only accurate marker of cardiopulmonary fitness obtained from an IET in this population.

Unfortunately, an LT was not detected at any TP during the non-robot-assisted or robot-assisted IETs. This may have been a consequence of the non linear increase in $\dot{V}O_2$ discussed previously which suggests a nonlinear increase in work rate during the tests. In order to accurately estimate an LT using V-slope analysis and gas exchange criteria, a linear increase in work rate is necessary.

It is also possible that the subjects may have been exercising above or below the LT. However, the low signal-to-noise ratio makes the exact response profiles of the respiratory variables difficult to determine.

Slope of Oxygen Uptake as a Function of Work Rate

The $\Delta\dot{V}O_2/\Delta WR$ for AB individuals is 10 $ml.min^{-1}.W^{-1}$ during a cycle ergometry IET [84, 85, 86] and $\sim$11 $ml.min^{-1}.W^{-1}$ during a treadmill IET [86]. This does not change as a consequence of cardiopulmonary training: subjects are able to exercise further up the slope but the gradient of the slope does not change. The gradient of the slope can however change if there is improved skill and better technique in exercise performance. It can also change if an initial limitation in the muscle or in the delivery of O_2 to the muscle, which prevented it from working effectively, is addressed through training.

The $\Delta\dot{V}O_2/\Delta WR$ for subject A was higher at each TP than that obtained for AB subjects, as were the initial values obtained for subject B. This may have been a consequence of an inefficient gait pattern and/or a predominance of type IIb fibres in the paralysed lower limbs [17, 18, 19, 22, 23, 24, 25]. Following 16 and 20 weeks of BWSTT respectively, subjects A and B substantially reduced their $\Delta\dot{V}O_2/\Delta WR$. This is an extremely significant result as it indicates a reduced cardiopulmonary stress whilst walking.

The reduction in $\Delta\dot{V}O_2/\Delta WR$ shown by subject A is likely to be the consequence of an improved gait pattern. Following 16 weeks of BWSTT, her stride length had increased and her gait was more stable. It is also possible that there may have been a shift in the fibre type composition of her lower limb muscles from type IIb to type IIa fibres as a result of the endurance training performed. An increase in the endurance capacity of the muscle is also indicated by the large increases in performance outcomes discussed previously. It is therefore possible that O_2 delivery to the lower limbs may also have been improved and O_2 more effectively utilised.

The results of subject B are more difficult to interpret because of the necessary increase in the testing speed as the study progressed. This biased $\Delta\dot{V}O_2/\Delta WR$ by the $\dot{V}O_2$ associated with walking at 0W (0% gradient) [217]. However, a decrease in $\Delta\dot{V}O_2/\Delta WR$ did occur between TPs where the testing speed remained constant. Consequently, although we cannot quantify the overall training effect it does appear to be present. It is likely that this may also have been due to an improved gait pattern and possible muscle adaptations.

Although a training effect has occurred for both subjects it is likely that the values obtained have been affected by the non-linearity of the $\dot{V}O_2$ response and therefore represent an average $\Delta\dot{V}O_2/\Delta WR$ for the test. This was certainly the case for the robot-assisted treadmill IET during which the $\dot{V}O_2$ - work rate relationship changed throughout. The results obtained were substantially higher than that of an AB subject. However, before an accurate indication of $\Delta\dot{V}O_2/\Delta WR$ and how it may change with training can be obtained for treadmill exercise in incomplete SCI subjects, the linearity of the work rate profile must be guaranteed.

Maximum Heart Rate

In AB individuals, one of the criteria for establishing if a maximal effort has been given during an IET is the attainment of the subject's maximum heart rate (HR_{max}) (220-age (years) $\pm$10%) [218], although this has been shown to be affected by age, resting heart rate, body weight and smoking status [219]. With training an individuals HR_{max} does not change but does occur at a higher maximum work rate (WR_{max}).

Following 16 and 20 weeks of BWSTT respectively, both subject A and B increased the HR_{peak} achieved during the IET. This suggests that both subjects were able to utilise a previously unattainable heart rate reserve, due possibly to an improved gait pattern. If they had been able to further improve their gait pattern and walking speed it is likely that both subjects would have been able to achieve a higher HR_{peak}.

The HR_{peaks} achieved during the robot-assisted IET were also limited peripherally by the subjects' ability to produce force in their lower limbs. Whether a true HR_{max} can ever be achieved by those with an incomplete SCI is debatable as the large lower limb muscles can never, voluntarily, be completely utilised. As the cardiovascular system cannot be used to its true maximum potential we cannot determine improvements in cardiopulmonary fitness through changes in the peak values obtained from an IET. However, it is encouraging to note that we can identify if subjects are able to utilise a previously unattainable heart rate reserve. This would suggest that they would therefore be able to train at a higher intensity.

The results of the BWSTT and robot-assisted treadmill study suggest that IETs may not provide a true indication of maximum cardiopulmonary capacity of wheelchair bound SCI individuals. All tests are limited peripherally by atrophied and fast fatiguing lower limb muscles and an inability to maintain a functional voluntary gait pattern. The accurate estimation of an LT and the $\Delta\dot{V}O_2/\Delta WR$ is affected by the non-linearity of the $\dot{V}O_2$ response and the low signal-to-noise ratio. It is also clear that subject performance can vary on a day to day basis. It may be preferable therefore, prior to training, that subjects train their gait until their performance has stabilised, i.e. the stability of their walking is constant, reliance on side bars is removed and no further improvements in the gait pattern can be identified. This would hopefully remove the day to day variation in their gait pattern which may affect the outcome measures and reduce the effect that improvements in gait may have on the indices of cardiopulmonary fitness. Further investigation is required to determine the repeatability and reliability of the key outcome measures discussed.

Incremental Exercise Testing with Ambulatory Incomplete Spinal Cord Injured Individuals

There may be more potential for incremental exercise testing in incomplete SCI individuals whose gait pattern is limited but do not require the use of a wheelchair. In Chapter 6, a feasibility study to determine the most appropriate method of testing such individuals was evaluated.

Due to the low cardiopulmonary fitness of this population it is important that a low initial metabolic rate occurs during an IET to ensure that all key indices of cardiopulmonary fitness (i.e. the LT) are captured in the data. The results of the study support this: an LT could not be determined during the constant speed, linear increase in gradient IET which elicited a substantially higher initial metabolic rate than the novel and previously verified [86] protocols tested. The results obtained for the key indices of cardiopulmonary fitness: $\dot{V}O_{2peak}$, LT, $\Delta\dot{V}O_2/\Delta WR$ were similar for the proposed novel protocol and the previously verified protocol [86]. As it is important to ensure subject comfort during testing, the novel protocol may be more appropriate for this population due to the gradual increase in speed and gradient which gives subjects more time to adapt their gait to the changes presented to them. Although it appears that the principles of AB exercise testing may be appropriate for this subject group, there is a need to develop protocols which account for the physical limitations of the subjects.

Although the subject involved in this study could walk, the results do suggest possible variation in performance between repeat tests. Further work is required with a larger sample size to determine the repeatability and reliability of outcome measures and to determine if a significant difference exists in any of the outcomes between protocols. It would also be interesting to perform an ACE IET to determine if the subject's gait pattern, although far superior to that of the wheelchair bound subjects, still limits the peak cardiopulmonary capacity more than the peripheral limitations associated with arm exercise.

8.4.2 Constant Load (Step) Exercise Tests

In AB individuals $\dot{V}O_2$ is expected to reach a steady-state within 3 minutes in response to a step increase in work rate below the LT [97]. With cardiopulmonary exercise training the response kinetics are expected to quicken as indicated by a decrease in $\tau\dot{V}O_2$ [108]. Given the low cardiopulmonary fitness of those with an SCI, it was expected that the response kinetics obtained from our subjects during an SET would be slowed compared to those of AB subjects [178]. As the BWSTT study progressed $\tau\dot{V}O_2$ was expected to decrease.

The identification of $\tau\dot{V}O_2$ during the SETs of both subjects who participated in the BWSTT study was difficult. $\tau\dot{V}O_2$ could not be determined at any TP for subject A and although a value could be obtained for subject B at all TPs except TP4, only at TP2, 3 and 6 did it suggest that $\dot{V}O_2$ reached a steady-state within the 15 minute test duration. The difficulty in determining $\tau\dot{V}O_2$ may have been a consequence of a low signal-to-noise ratio and/or alterations in the work rate profile. In the majority of SETs $\dot{V}O_2$ did not reach a steady-state. This may have been a consequence of the subjects increasing the amount of upper body work they performed as the test progressed. As discussed previously this would increase the O_2

demand of the exercise.

We also had difficulty in accurately determining $\tau\dot{V}O_2$ during the robot-assisted SETs. It is possible that the unmeasured work at the start of subject A's SET and a low signal-to-noise ratio during subject C's test may be the cause of this. Only during subject B's test did the $\dot{V}O_2$ response reflect the expected exponential profile.

In order to accurately determine $\tau\dot{V}O_2$ during an SET a step increase in work rate must be guaranteed. Repeat tests are also necessary to determine the repeatability and reliability of the outcome measure.

Another outcome measure of an SET is the O_2 cost. As $\dot{V}O_2$ reached a steady-state during the robot-assisted SETs the O_2 cost could be determined. However, in order to accurately obtain this outcome the actual work rate being performed by the subject must be identified.

As $\dot{V}O_2$ did not reach a steady-state during all of subject A's and half of subject B's non-robot-assisted SETs, $\Delta\dot{V}O_2$ could not be obtained. Therefore, changes in the $\dot{V}O_2$ at the end of the test were monitored. Encouragingly, this was shown in both subjects to substantially decrease with training indicating a substantial reduction in the metabolic stress associated with a given work rate.

The SET has the potential to be adapted for use with incomplete SCI subjects. However, the work rate profile must be guaranteed to ensure that unmeasured upper body work does not increase and thus distort the $\dot{V}O_2$ response. Due to the issues raised regarding the identification of true peak cardiopulmonary capacity the attainment of accurate $\dot{V}O_2$ kinetics during an SET may be the key to identifying improvements in cardiopulmonary fitness in this population.

8.5 Twitch Tests

Standard dynamometry tests [114, 115, 118, 119, 120] were used in the BWSTT study to determine changes in the peak voluntary force and central activation ratio (CAR) of the quadriceps and hamstring muscles of both subjects. Although the peak voluntary force of the muscles may not have increased as the subjects were training for endurance, it was hoped that this test would establish if the training had increased the number of motor units that subjects could voluntarily recruit (increased peak force with a corresponding increase in CAR) or if muscle fibre hypertrophy had occurred (increase in peak force with no corresponding

increase in CAR).

However, the tests were relatively unsuccessful. Lower limb muscle spasms occurred during each of subject B's hamstring tests. Consequently, a true indication of his peak voluntary force production could not be obtained. This was also the case for subject A. Although not affected by spasms, she appeared unable to maintain a steady-state voluntary contraction during both the hamstring and quadriceps muscle tests. It is possible that this may be a consequence of fluctuations in the signal getting through the lesion in the spinal cord to contract the muscle. The variation which was present in the response between TPs may also have be due to subject motivation and more muscle fatigue on particular days.

It is clear that the peak total force produced by the subjects was affected by the peak voluntary force which they produced. As the electrodes were positioned in exactly the same place we expected the results to be more consistent. However, this was not the case.

As we were unable to accurately determine the peak voluntary force or peak force of the hamstring and quadriceps muscles of both subjects we could not accurately identify or monitor changes in the CAR. In principle the concept of identifying the CAR in those with an SCI is very relevant to both research and the clinic. It is important to determine if BWSTT can result in hypertrophy of the lower limb muscles or increase the number of motor units the individual can voluntarily recruit. Both are clinically relevant outcome measures; hypertrophy of the muscle may help with transfers and other ADLs while increasing the voluntary recruitment of motor units may, for some individuals, reduce the level of assistance they require for ambulation. However, this study has raised issues as to the accuracy and consistency of the outcome measures. The importance of the outcome measures suggests that further investigation into their reliability and repeatability in a larger subject group is warranted.

8.6 Bone Parameters

Peripheral Quantitative Computed Tomography (pQCT) is the recommended method of measuring the bone mineral density (BMD) and lower limb cross-sectional area (CSA) of the tibia and femur [10]. We utilised this method to determine if BWSTT would increase the BMD and CSA of the tibia and femur in our two subjects.

The results obtained differed between subjects and appeared to be dependent on their time post-injury. At two years post-injury, subject A was still in the rapid phase of bone loss [10]. Throughout the training period the BMD and CSA of her tibia and femur continued

to decrease, suggesting that the intensity of the training was insufficient to halt the natural decline. It is possible that the training may have slowed the rate of decline. However, without reference data we cannot conclude this for certain.

In our chronic subject (B) who was in the steady-state phase of bone loss [10] the BWSTT had no significant impact on the cortical CSA of the tibia and femur or on the trabecular BMD of the distal femur and proximal tibia. Encouragingly however, an increase in the trabecular BMD of the right distal tibia and a substantial increase in the left distal tibia were shown to occur. As discussed in Section 5.4.6, this asymmetry may have been a consequence of the use of FES on the left peroneal nerve which may have resulted in a stronger contraction and thus a larger strain on the bone than could voluntarily be achieved. It is possible, but highly unlikely given his time post-injury, that anti-resorptive osteoporosis medication taken by the subject during the study may have affected the results obtained.

The use of BWSTT to increase the BMD and CSA of the partially paralysed lower limbs of those with an incomplete SCI is clinically relevant as it may help to reduce the high incidence of lower limb fractures prevalent in this population. Previous studies which have investigated the effect of BWSTT on BMD have had a mixed subject group of incomplete and complete SCI subjects [161, 162]. The results of these studies are immediately affected by the variation in muscular strain which can be applied to the muscles by the two groups. It can be hypothesised that, as those with an incomplete SCI can voluntarily produce higher muscular forces, BWSTT may have more potential to positively influence the BMD of their lower limbs.

The results of our study suggest that BWSTT could potentially improve the BMD of those with an incomplete SCI who are in the steady-state phase of bone loss. Therefore, further investigation with a larger subject group is warranted. Although the BMD and CSA of subject A's tibia and femur continued to decrease with training we do not know if the rate of bone loss was reduced. A larger study investigating the effect of BWSTT on the BMD and CSA of SCI individuals in the rapid phase of bone loss should also be carried out. It would however be difficult to perform a case-controlled study in those with an incomplete SCI due to the functional variation which exists at each lesion level and ASIA grading. However, it would be necessary to have reference data with which to compare the decline to determine if it was reduced.

It is also important that any studies monitoring the effect of BWSTT on the BMD and CSA of the lower limb bones be a long term intervention. Initially, it is likely that subjects would be unable to train at a high enough intensity to have an impact on their bone integrity. However, as their walking ability increases and thus the intensity of their training increases

also, they may be able to do so.

Chapter 9

Conclusions and Future Work

9.1 Conclusions

The studies which comprise this thesis have demonstrated that robot-assisted and non-robot-assisted body weight supported (BWS) treadmill exercise can be utilised for those with an incomplete spinal cord injury (SCI). Two subjects with incomplete SCI successfully completed a 5 month BWS treadmill training (BWSTT) programme which resulted in substantial improvements in training performance and in the distance achieved during the 15 minute distance test.

Standard able-bodied (AB) incremental and constant load (step) exercise testing protocols were adapted for use with a BWS treadmill to monitor improvements in cardiopulmonary fitness with training. The incremental exercise test (IET) successfully detected improvements in peak work rate (WR_{peak}) and in the slope of oxygen uptake as a function of work rate ($\Delta\dot{V}O_2/\Delta WR$) highlighting further the substantial improvement in gait performance which occurred with training. It appears, however, that the estimation of peak oxygen uptake ($\dot{V}O_{2peak}$), lactate threshold (LT), peak heart rate (HR_{peak}) and $\dot{V}O_2$ kinetics ($\tau\dot{V}O_2$), as indicators of cardiopulmonary fitness were affected by variations in the quality of the subjects' gait pattern both during and between tests, by alterations in the work rate profile and by the low signal-to-noise of the breath-by-breath data.

Active participation in the robot-assisted treadmill exercise has been shown to result in an increased metabolic rate above that associated with passive walking. This increase in metabolic rate has the potential to be utilised for exercise training and, as shown in this thesis, for cardiopulmonary exercise testing. Subjects were able to successfully follow a ramp and step increase in work rate by altering the amount of force they exerted against the robot orthoses. Similar issues to those raised for the non-robot-assisted exercise tests were however identified regarding the attainment of a true peak cardiopulmonary capacity due to the fast

fatiguability of the lower limb muscles. The accuracy of the work rate profiles during the IETs and SETs also requires further investigation due to its effect on the estimation of LT, $\Delta\dot{V}O_2/\Delta WR$ and $\tau\dot{V}O_2$.

The key indices of cardiopulmonary fitness were obtained during a novel IET protocol with one ambulatory incomplete SCI subject. The results were comparable to a previously verified protocol. However, the novel protocol may be more appropriate for this population due to the gradual, equally smooth increases in speed and gradient which occur throughout.

BWSTT has also been shown to have the potential to increase the lower limb BMD of those with chronic incomplete SCI. Whether it can reduce the rate of bone loss in those with an SCI who are in the rapid phase of bone loss remains equivocal. There is also the possibility that BWSTT may result in muscle fibre hypertrophy or increase the number of motor units the subject can voluntarily recruit. However, dynamometry tests used to detect this during the BWSTT study were affected by spasms and variation in the peak voluntary force during each contraction.

The studies which comprise this thesis have shown that robot- and non-robot-assisted treadmill exercise can be utilised for those with an incomplete SCI. These modes of exercise have the potential to improve the risk of cardiovascular disease, muscle atrophy and reduced lower limb BMD associated with an incomplete SCI.

9.2 Future Work

BWSTT both with and without robot-assistance could potentially increase the cardiopulmonary fitness of those with an incomplete SCI. It would therefore be of interest to investigate further the effectiveness of the IETs and SETs in determining the key indices of cardiopulmonary fitness. In order to determine the repeatability and reliability of the testing protocols and the outcome measure obtained, a larger sample size is required with subjects performing 3–4 repeat tests. Large inter-subject variation would be expected due to the wide variation in the motor ability within the population. However, low intra-subject variation would provide the evidence that between test variation in walking performance does not affect the outcome measures obtained. By performing repeat tests and averaging the intra-subject responses, we would hope to reduce the breath-by-breath noise. This would increase the reliability of the outcome measures obtained and may also enable identification of previously unattainable indices of cardiopulmonary fitness.

It would also be beneficial to investigate further the issue of work rate linearity during the robot-assisted treadmill IET which was highlighted. A study with AB would enable us to determine if the non-linear $\dot{V}O_2$ profile observed is an actual physiological response of incomplete SCI subjects to a linear increase in work rate or whether it was actually a consequence of a nonlinear increase in work rate. If this was the case a non-linear $\dot{V}O_2$ profile would also be observed in the AB subjects.

It would also be of interest to investigate the repeatability and reliability of the outcome measures in AB subjects performing robot-assisted treadmill IETs to determine if a true indication of maximal cardiopulmonary capacity and the key indices of cardiopulmonary fitness can be identified. By comparing these results to those obtained from standard cycle ergometry IETs, their accuracy could be obtained.

The evaluation of a novel IET protocol in Chapter 6 produced encouraging results in one incomplete SCI subject. It would be of significant interest to perform a larger scale study with AB subjects to determine the comparability of the key outcome measures obtained to those obtained from previously verified treadmill IET protocols. This would hopefully provide the evidence that the novel protocol can be used accurately as an alternative IET. It would then be beneficial to determine the repeatability and reliability of the outcome measures in those with an incomplete SCI who do not require the use of a wheelchair and to determine the most appropriate protocol for incremental exercise testing in this population.

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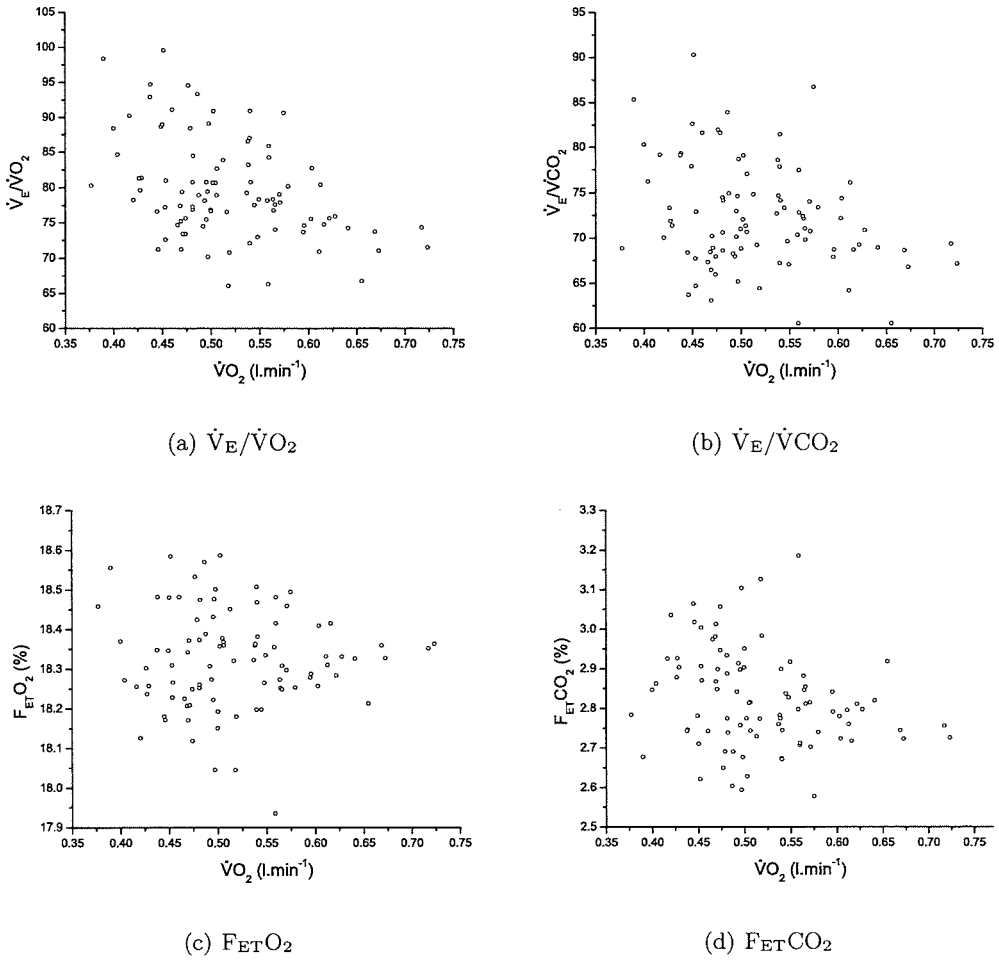
Appendices

Appendix A

Respiratory Variable Profiles, Subject A

A.1 Test Point 1

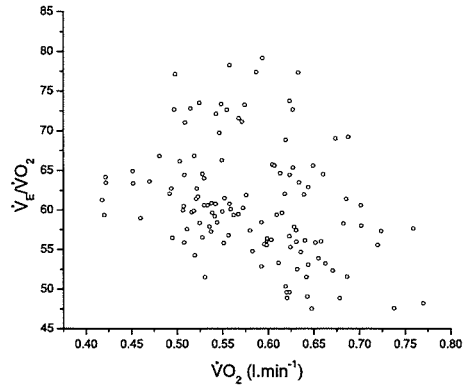


(a) $\dot{V}_E/\dot{V}O_2$ (b) $\dot{V}_E/\dot{V}CO_2$

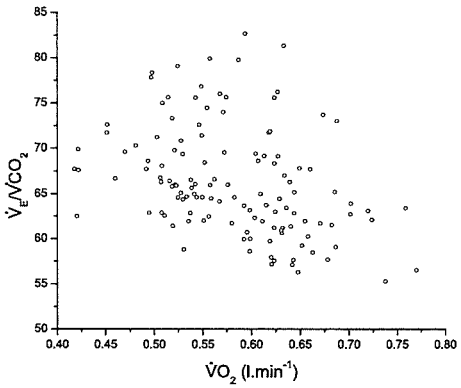
(c) $F_{ET}O_2$ (d) $F_{ET}CO_2$

Figure A.1: Respiratory variable responses during the ramp phase of subject A's incremental exercise test at test point 1. Kinetic phase not removed. 2 breath averaged plots.

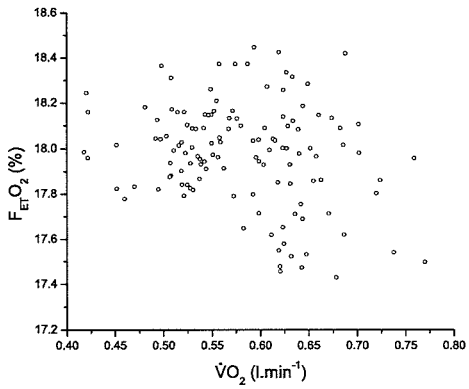
A.2 Test Point 2



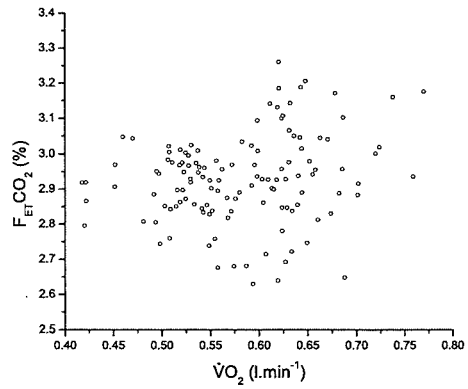
(a) $\dot{V}_E/\dot{V}O_2$



(b) $\dot{V}_E/\dot{V}CO_2$



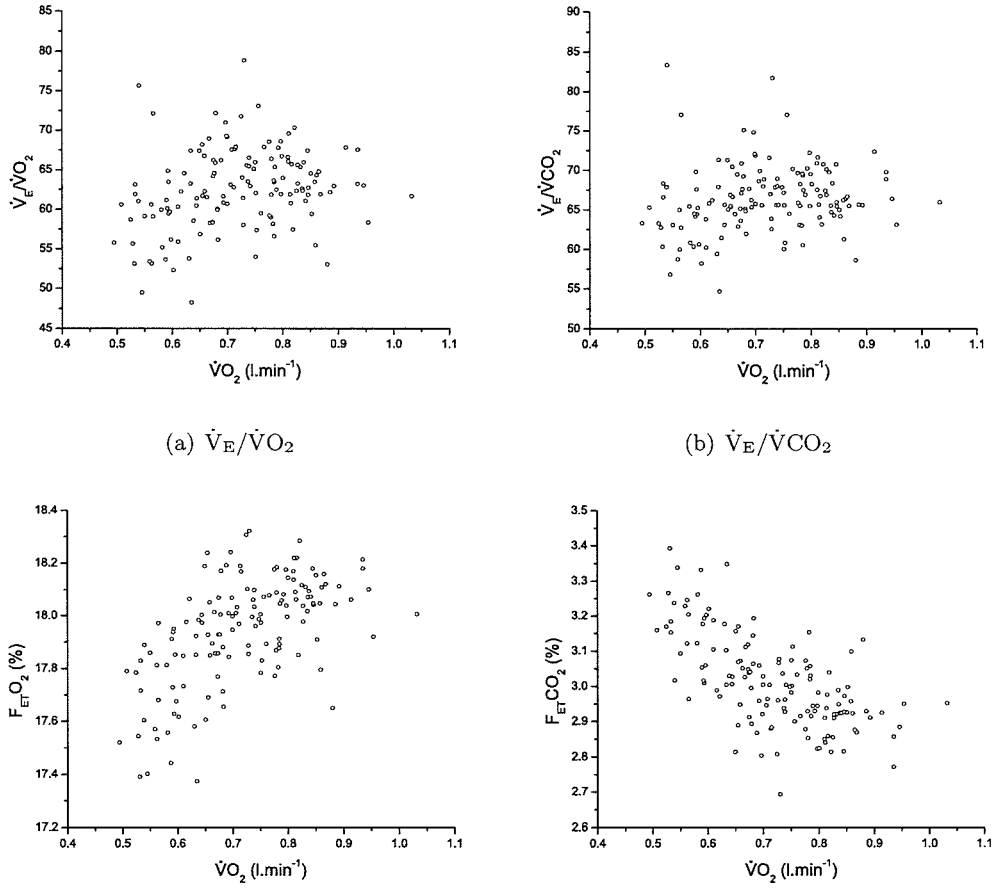
(c) $F_{ET}O_2$



(d) $F_{ET}CO_2$

Figure A.2: Respiratory variable responses during the ramp phase of subject A's incremental exercise test at test point 2. Kinetic phase not removed. 2 breath averaged plots.

A.3 Test Point 3

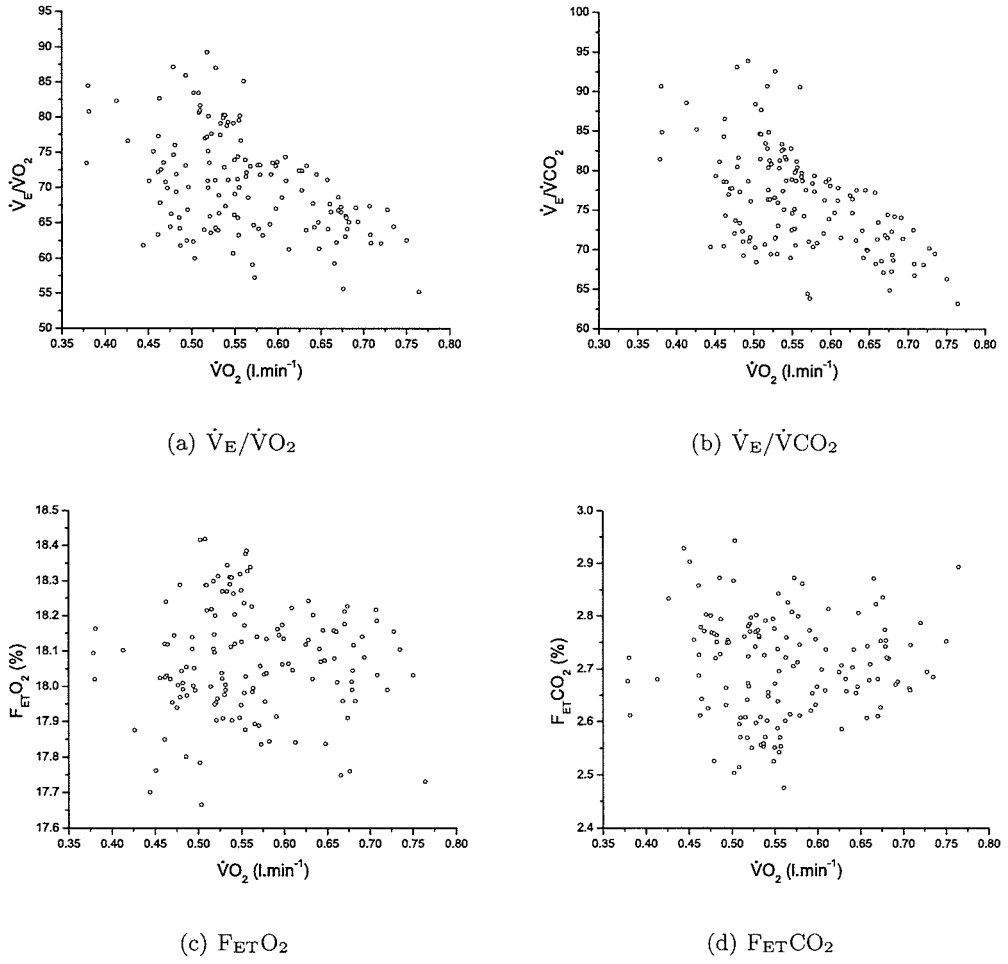


(a) $\dot{V}_E/\dot{V}O_2$ (b) $\dot{V}_E/\dot{V}CO_2$

(c) $F_{ET}O_2$ (d) $F_{ET}CO_2$

Figure A.3: Respiratory variable responses during the ramp phase of subject A's incremental exercise test at test point 3. Kinetic phase not removed. 2 breath averaged plots.

A.4 Test Point 4



(a) $\dot{V}_E/\dot{V}O_2$ (b) $\dot{V}_E/\dot{V}CO_2$

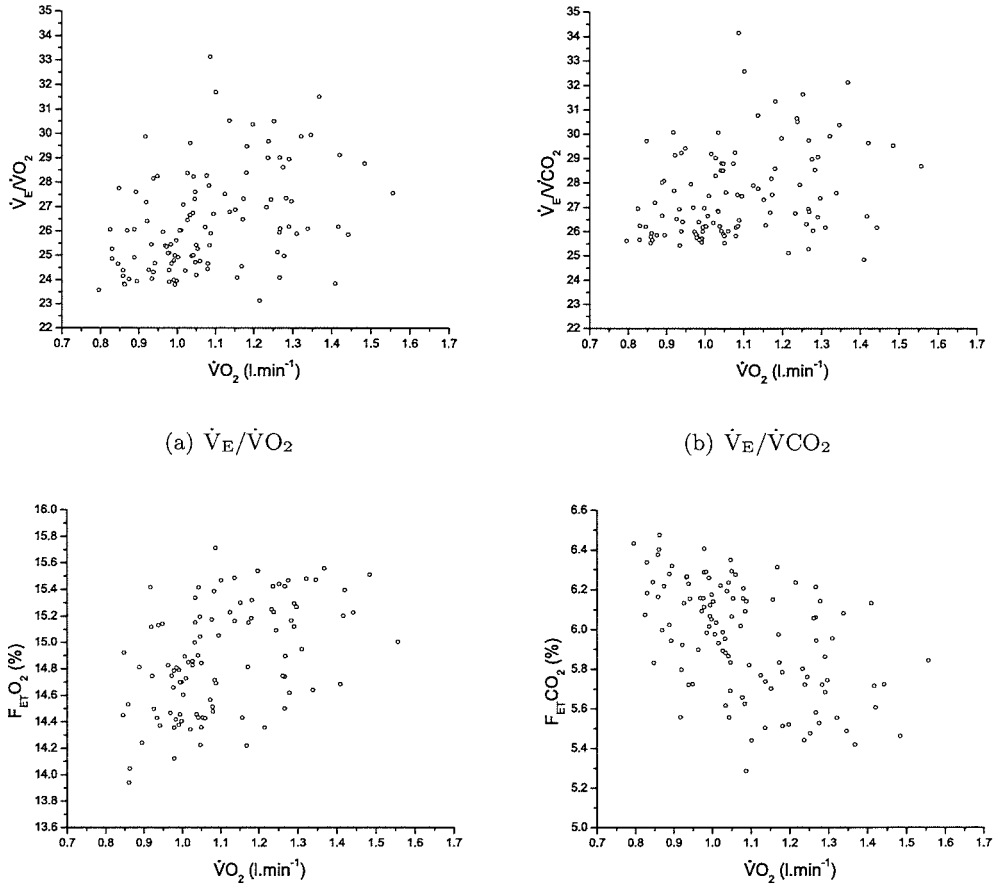
(c) $F_{ET}O_2$ (d) $F_{ET}CO_2$

Figure A.4: Respiratory variable responses during the ramp phase of subject A's incremental exercise test at test point 4. Kinetic phase not removed. 2 breath averaged plots.

Appendix B

Respiratory Variable Profiles, Subject B

B.1 Test Point 1

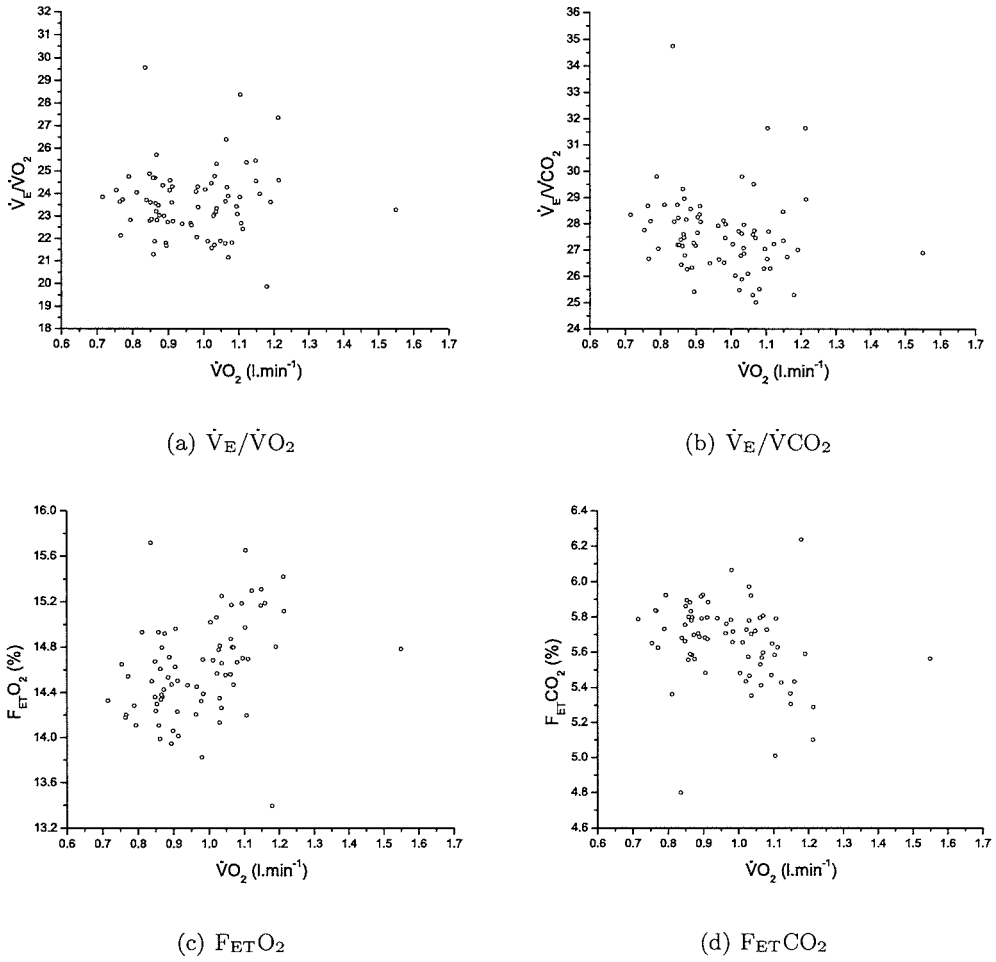


(a) $\dot{V}_E/\dot{V}O_2$ (b) $\dot{V}_E/\dot{V}CO_2$

(c) $F_{ET}O_2$ (d) $F_{ET}CO_2$

Figure B.1: Respiratory variable responses during the ramp phase of subject B's incremental exercise test at test point 1. Kinetic phase not removed. 2 breath averaged plots.

B.2 Test Point 2

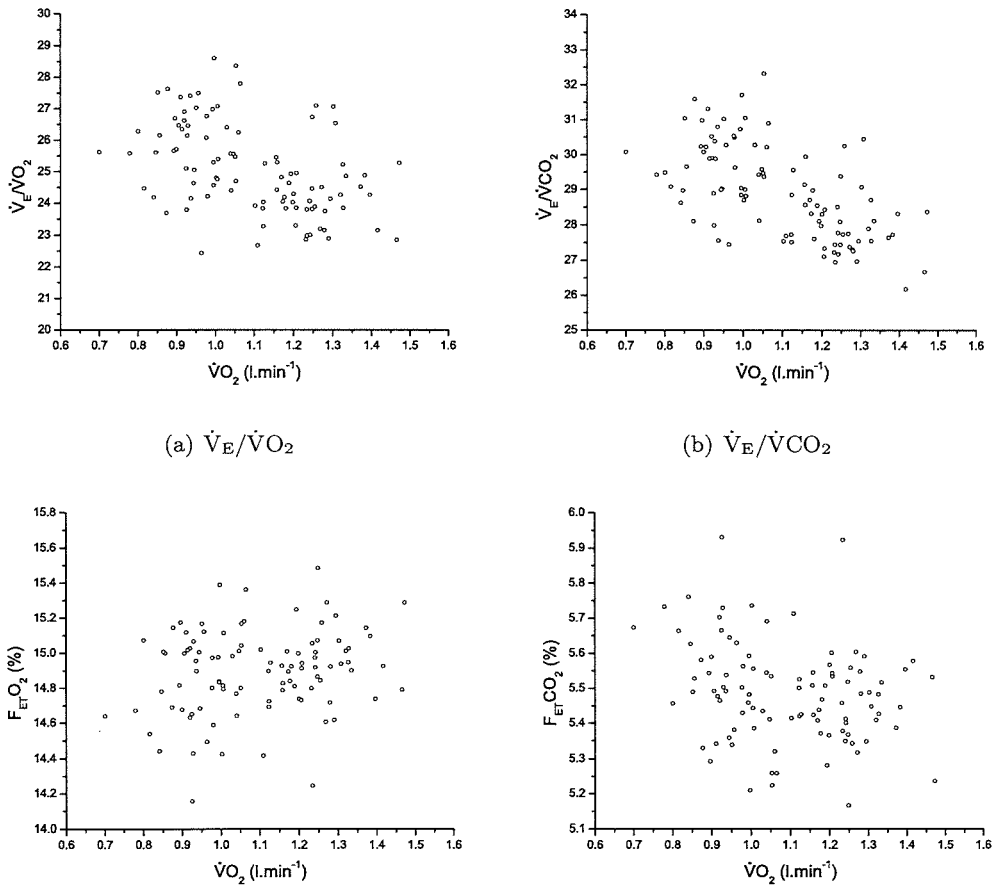


(a) $\dot{V}_E/\dot{V}O_2$ (b) $\dot{V}_E/\dot{V}CO_2$

(c) $F_{ET}O_2$ (d) $F_{ET}CO_2$

Figure B.2: Respiratory variable responses during the ramp phase of subject B's incremental exercise test at test point 2. Kinetic phase not removed. 2 breath averaged plots.

B.3 Test Point 3

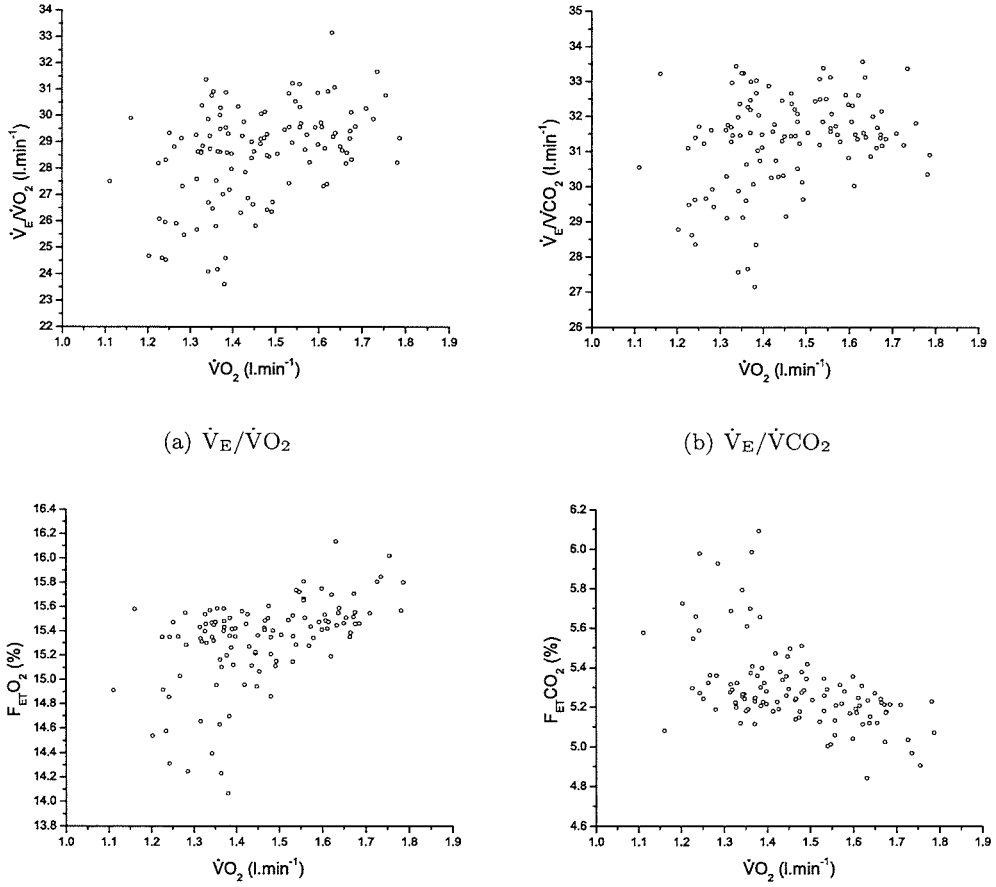


(a) $\dot{V}_E/\dot{V}O_2$ (b) $\dot{V}_E/\dot{V}CO_2$

(c) $F_{ET}O_2$ (d) $F_{ET}CO_2$

Figure B.3: Respiratory variable responses during the ramp phase of subject B's incremental exercise test at test point 3. Kinetic phase not removed. 2 breath averaged plots.

B.4 Test Point 4

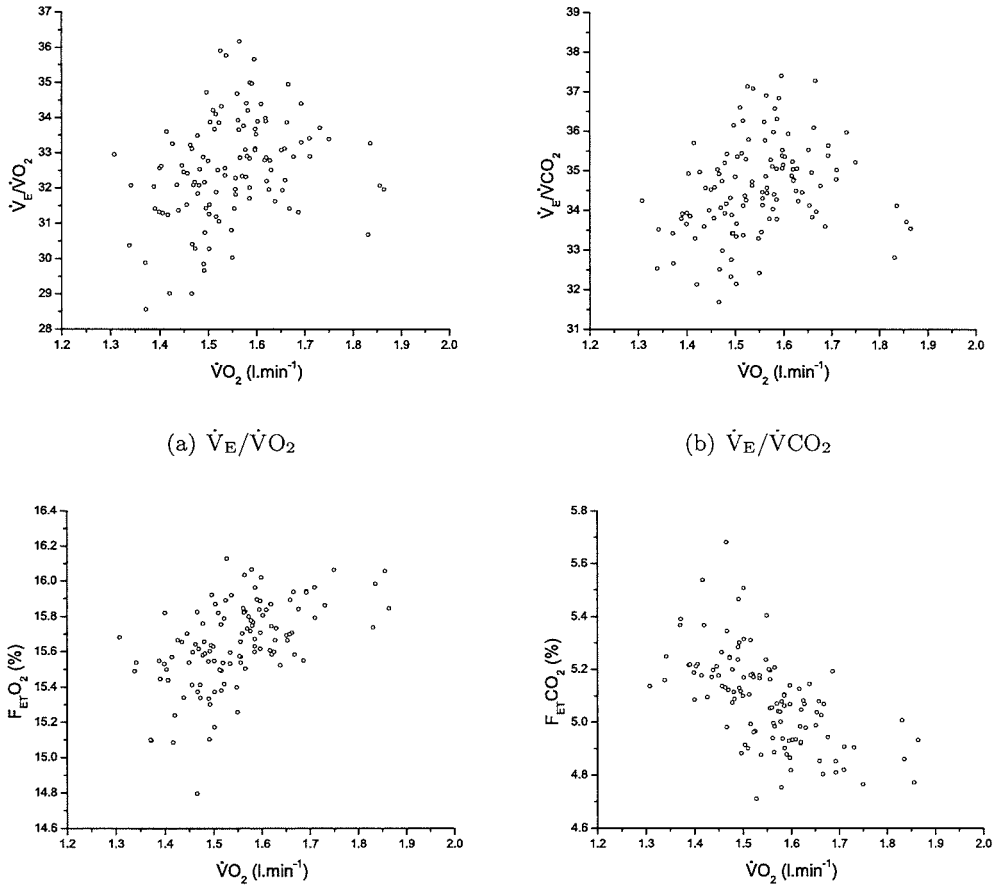


(a) $\dot{V}_E/\dot{V}O_2$ (b) $\dot{V}_E/\dot{V}CO_2$

(c) $F_{ET}O_2$ (d) $F_{ET}CO_2$

Figure B.4: Respiratory variable responses during the ramp phase of subject B's incremental exercise test at test point 4. Kinetic phase not removed. 2 breath averaged plots.

B.5 Test Point 5

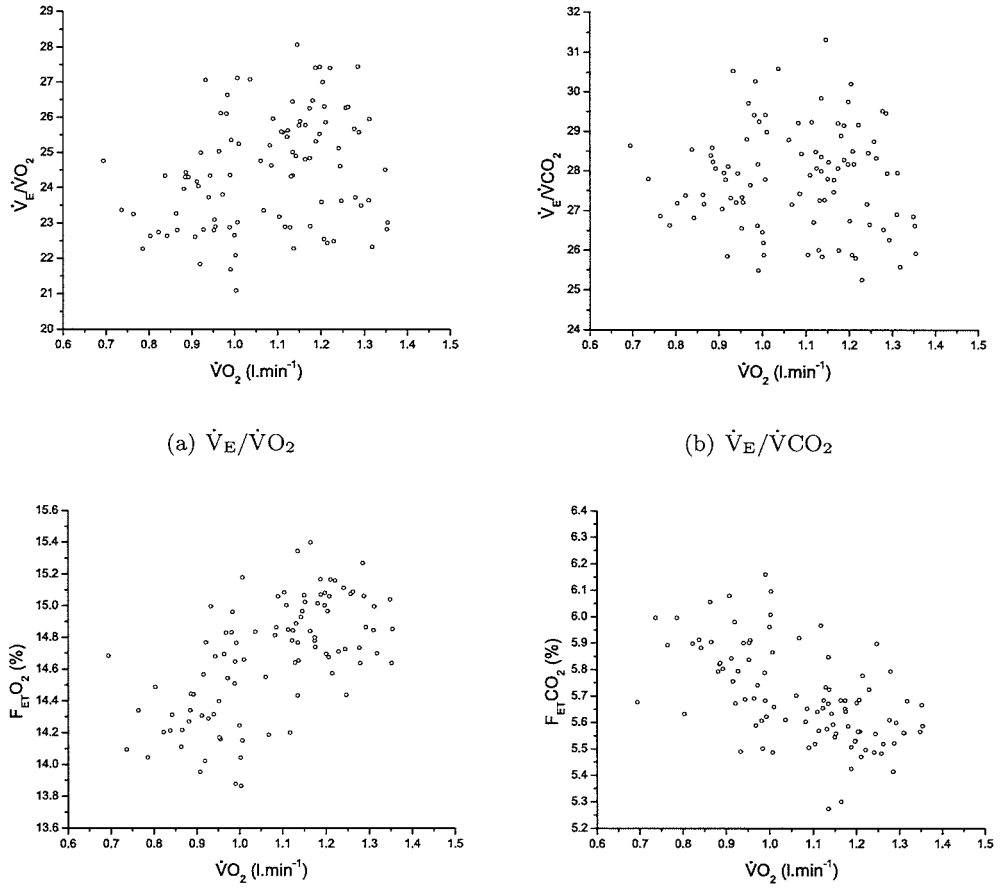


(a) $\dot{V}_E/\dot{V}O_2$ (b) $\dot{V}_E/\dot{V}CO_2$

(c) $F_{ET}O_2$ (d) $F_{ET}CO_2$

Figure B.5: Respiratory variable responses during the ramp phase of subject B's incremental exercise test at test point 5. Kinetic phase not removed. 2 breath averaged plots.

B.6 Test Point 3B

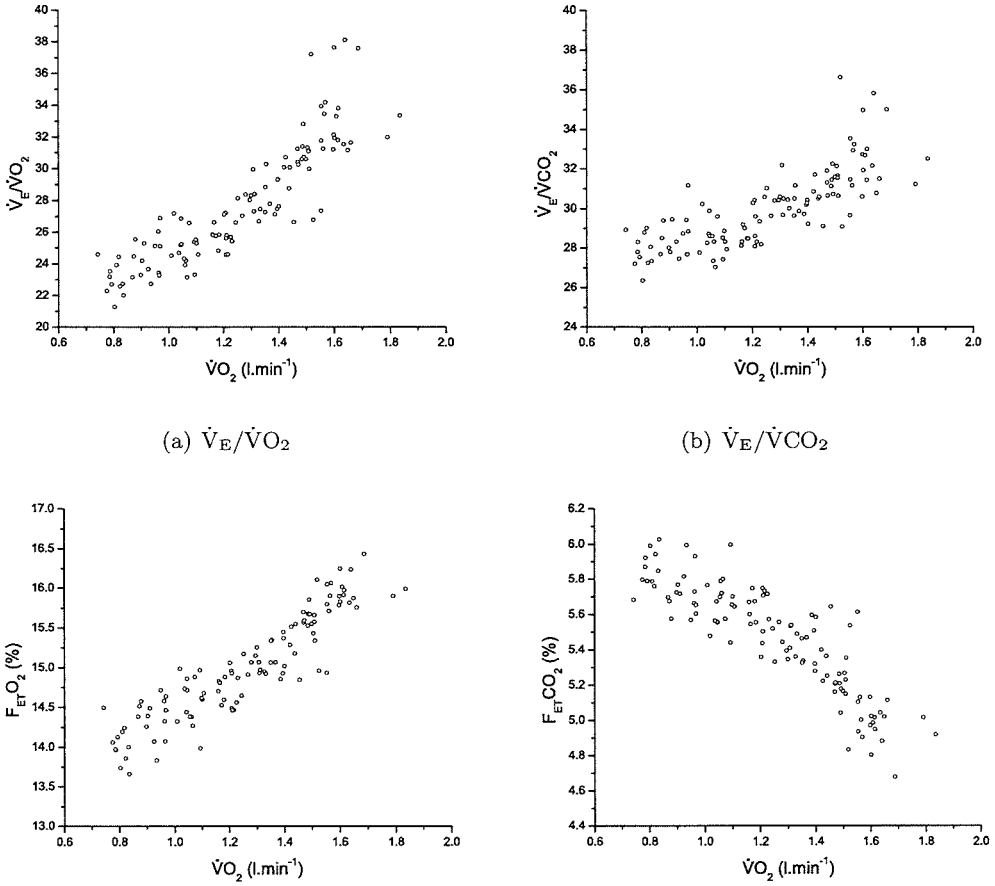


(a) $\dot{V}_E/\dot{V}O_2$ (b) $\dot{V}_E/\dot{V}CO_2$

(c) $F_{ET}O_2$ (d) $F_{ET}CO_2$

Figure B.6: Respiratory variable responses during the ramp phase of subject B's incremental exercise test B at test point 3. Kinetic phase not removed. 2 breath averaged plots.

B.7 Test Point 4B



(a) $\dot{V}_E/\dot{V}O_2$ (b) $\dot{V}_E/\dot{V}CO_2$

(c) $F_{ET}O_2$ (d) $F_{ET}CO_2$

Figure B.7: Respiratory variable responses during the ramp phase of subject B's incremental exercise test B at test point 4. Kinetic phase not removed. 2 breath averaged plots.