Development and Assessment of Methods for Arm-Cranking Exercise Assisted by Functional Electrical Stimulation (FES) in Tetraplegia

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A thesis submitted for the degree of Doctor of Philosophy (PhD)

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February 2005

Abstract

Tetraplegia is at least as common as paraplegia in the spinal cord injured population. The consequences of a cervical spinal cord injury (SCI), leading to tetraplegia, are numerous. They include loss of (or greatly reduced) function of the limbs and organs supplied below the level of the injury, but also health problems, such as an increased risk of cardiovascular disease. Exercise prescription may be one way of tackling some of these secondary health issues in tetraplegia, but the current options are limited. The idea of enabling exercise involving paralysed limbs, through the use of functional electrical stimulation (FES), has been explored over the past two decades for use in SCI. The FES-exercise systems produced to date have tended to recruit muscles of the lower limbs, for FES cycling, treadmill walking or rowing.

In this pilot study, a new avenue for exercise in tetraplegia, involving FES applied to upper limb muscles, is suggested. The main motivation for developing methods for FES-assisted arm-cranking exercise is to provide an exercise modality specifically designed for tetraplegia that might address cardiopulmonary issues, as well as work with remaining voluntary control of upper body musculature. One primary aim of this thesis was to determine the feasibility of using these systems in tetraplegia. To investigate this, standard protocols for exercise training, and incremental and constant-load exercise testing, were adapted to make them suitable for this population and this exercise modality. These novel protocols are described here, and represent one of the contributions of the thesis.

The implementation of these protocols for an experimental evaluation of the proposed systems for FES-assisted arm-cranking exercise makes up the main part of the thesis. Five volunteers with tetraplegia participated in this experimental evaluation, and their data are presented as two main case studies, and additional case reports. The first outcome of this evaluation is that it shows the feasibility of the proposed methods for FES-assisted arm-cranking exercise training and testing in tetraplegia. Secondly, benefits of regular use of the systems are illustrated for some individuals with tetraplegia, based on key indicators of cardiopulmonary fitness and measures of upper limb strength. Thirdly, the limitations of the current set-up for FES-assisted arm-cranking exercise in higher level tetraplegia are identified.

In summary, this thesis describes new systems and protocols for FES-assisted arm-cranking exercise in tetraplegia, and provides a preliminary assessment of these methods.

Acknowledgements

First of all, I should like to thank Ken Hunt for his supervision, constant support and encouragement throughout my time at the Centre for Rehabilitation Engineering. Many thanks also to Henrik Gollee, my thoroughly Scottish German colleague, who has taught me so much over the past few years. I enjoyed working with you on this project.

Of course, nothing would run smoothly without the behind-the-scenes magic of Elaine McNamara. Thanks for always sorting things out, and for doing so ever so efficiently. Thanks to Nicola also, for organising trips to some instructive and enjoyable conferences.

At the Queen Elizabeth National Spinal Injuries Unit at the Southern General Hospital, I should like to extend my greatest thanks to Alan McLean and Matthew Fraser, as well as David Allan, who have encouraged collaborative research with the University of Glasgow and provided the space and clinical support for experimental work. It is only with this kind of approach that such a multidisciplinary team can work towards the common goal of developing much-needed rehabilitation and exercise options for people with spinal cord injury. As they are now my colleagues, I should also like to thank them for the chance they are giving me to transfer my new skills to the clinical environment and to continue to work with such a motivated team.

Although the consultants were instrumental in allowing the clinical aspect of the project to go forward, a number of other people at the spinal unit have contributed to the smooth-running of the work there: by helping to identify potential candidates for the project, allowing me to use gym and office space, or helping me to arrange transport for external volunteers. In particular, my sincerest thanks go to Willie Stewart and Jon Hasler in physiotherapy, to Joyce and Sam at reception, to Irene and Anne for their administrative support, and to the nurses whom I have pestered.

To all the volunteers at the spinal unit, and from outside the unit, who so enthusiastically took part in the project: thank you for coming through to the gym to do your exercises, even when you really didn't feel up to it, through rain (mostly) or shine. Thank you for being so patient through any technical glitches. I hope you enjoyed taking part in the project as much as I enjoyed working with you.

For the financial support for this project, I would like to acknowledge the EPSRC and the EC.

In the early stages of my work, I learned a great deal from Sue Ward and Andy Cathcart, now at the University of Leeds. Without your invaluable tutoring, I could not have made sense of the complexities of exercise physiology.

In addition, I have to acknowledge countless people who have helped me through my three years at Glasgow University. Firstly, those in my group at the CRE, and especially the people who have undertaken a PhD: thanks for your moral support, and good luck with your own work. I hope you can lean on me through the difficult periods of your PhD's, as I have leaned on you through mine. Thanks also to those students who came from abroad, for injecting a bit of spice into the group and for bringing out my Mediterranean side, especially The Franceschi. Most of all, out of the group, the greatest thanks go to Barry. We've been through this together, and we are still close friends. Thanks for always being there.

I greatly appreciate the patience of those who have shared a flat with me over the years. Thank you to Kev, Esti and Ste for helping me through the first few months of my PhD work, when I was settling into my new environment. You were great fun to live with, and I have cherished your friendship. More recently, Ben has taken over as flatmate, and doing a great job! Ben, thank you for understanding that this writing phase is stressful, and for making it easier for me.

To my great friends who have been in Glasgow, by my side, throughout these years. Flora and Yiannis, I wish you wouldn't leave me to go back to Greece: you will be missed. Carolyn and Mark, you gave me emergency accommodation, made me laugh and forget about the stresses of the PhD work: who could ask for better friends?

To my great friends who aren't in Glasgow with me, but who are as dear to me as ever. I miss you enormously, and hope that you forgive me neglecting you somewhat over this past year. Especially to Sarah and Phil, thanks for going through this with me in spirit.

Finally, to the most important people in my life, my family, I wish to express my greatest gratitude. *Maman, Papa, Florence et Claire - je vous adore de tout mon coeur. C'est grâce à vous que j'y suis arrivée. Cette thèse est dédiée à vous.*

Thesis Outline

Chapter 1: This thesis begins by identifying the primary and secondary consequences of spinal cord injury (SCI), and illustrating the need for new technology to tackle secondary health issues in cervical SCI. In particular, the issue of reduced cardiopulmonary fitness is emphasised. The principles of exercise testing and training are then explored, to determine how they may be applied to address problems of low cardiopulmonary fitness in tetraplegia.

Chapter 2: The few options for voluntary exercise in tetraplegia are given here, illustrating a possible role for FES-exercise. The principles of FES-exercise, how it differs from voluntary exercise, and its potential limitations, are also described. Currently available systems for FES-exercise in SCI are discussed.

Chapter 3: This chapter includes a description of the novel systems and set-up for FES-assisted arm cranking exercise, for people with C4–C6 SCI. Relevant protocols for implementing these systems for exercise training, and for assessing their potential benefits experimentally, are also provided. The testing protocols are for two types of test: incremental exercise tests and constant-load exercise tests.

Chapters 4 & 5: The main part of the evaluation of the proposed methods for FES-assisted arm-cranking exercise training and testing is presented in the form of two individual case studies. These case studies detail the experimental results obtained with two volunteers with C6 SCI who have undertaken a period of exercise training using the new systems. Changes in upper limb strength are indicated by changes in the peak power production by the subjects at monthly test points over the period of participation. Through the analysis of the recorded cardiopulmonary responses to programmed changes in work rates at these test points, potential cardiopulmonary benefits of the exercise in tetraplegia are also illustrated.

Chapter 6: The final part of the assessment of these systems is provided using data and observations from additional case reports with volunteers with a higher level of injury, allowing the limitations of the systems and set-up to be identified.

Chapter 7: The analyses of the experimental results are brought together and discussed, to give a balanced preliminary assessment of FES-assisted arm crank exercise for use in tetraplegia.

Chapter 8: The exercise limitations in tetraplegia are clear from the results of this work and so, in this chapter, a brief summary of the challenges of exercise prescription in tetraplegia is provided.

Chapter 9: The main conclusions of the thesis are summarised here.

Contributions

- This thesis describes new apparatus and control systems for high precision work rate control during FES-assisted arm-cranking exercise tests. Such precision is especially important when testing in populations with severe exercise limitation (as in tetraplegia), as the working range of power production is typically small.

- New protocols for cardiopulmonary testing to estimate key markers of cardiopulmonary status are also described. To apply testing protocols to this severely physically disabled population and thereby enable a useful evaluation of the FES-ACE, a number of adaptations to standard protocols were required. The modified protocols are described here for incremental and constant load cardiopulmonary exercise tests.

- The indicator of strength used in this study is torque (and power) produced by the upper limbs at the cranks. This thesis introduces novel software for presenting and analysing the torque, crank angle and crank velocity data to monitor changes in upper limb strength.

- By illustrating successful application of the novel apparatus and training and testing protocols in an experimental evaluation with tetraplegic subjects, a key contribution of this thesis is proof of feasibility.

- The demonstration of beneficial training effects using the data obtained with tetraplegic subjects provides evidence for a possible future role of FES-assisted arm-cranking exercise in rehabilitation and home-training in tetraplegia.

- The limitations of the present methods are identified. In addition, suggestions are given for improvements that could be incorporated in future developments. If these potential improvements can be explored further, they may enable a wider range of individuals to benefit from the proposed exercise modality.

Publications

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2. S. Coupaud. Development of control systems for electrically stimulated arm crank ergometry. *Postgrad. Symposium, UKACC Conf. Control*, Sheffield, U.K., September 2002.

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Chapter 1

Introduction & Background

1.1 Summary

This chapter provides some background information on spinal cord injury (SCI) and its classification. This serves to illustrate that those individuals who have the greatest need for new assistive technology and rehabilitation interventions are those with higher SCI lesions. Tetraplegia results from cervical SCI, leaving the individual with vastly reduced function in the upper limbs, lower limbs and many organs of the body. A technique known as functional electrical stimulation (FES) has been used over the past few decades in systems designed to tackle some of these functional limitations. The principles of FES, and examples of FES-systems developed for people with SCI, are therefore described in this chapter. As exciting and necessary as these developments in functional systems are, solutions to secondary health issues following SCI are additionally needed. The health issues facing people with tetraplegia are described here, and are related to the decreased levels of physical activity that result from the injury. The idea of overcoming some of these problems through exercise is introduced. The final section of this chapter describes the principles of exercise physiology and prescription, to determine how these may be applied in tetraplegia.

1.2 Spinal Cord Injury

Spinal Cord Injury (SCI) is one of a number of causes of paralysis in the human body. Stroke also leads to paralysis, and is even more prevalent in the western world than SCI. However, in contrast to stroke, SCI most commonly affects people at a relatively young age, and hence at a very active stage of their life. Indeed, the majority of cases of traumatic SCI in the U.K. (and in many developed countries [4]) occur in males of 15-35 years of age. Medical advances over the past few decades

have considerably reduced the rates of mortality and morbidity in the SCI population [59]. Nevertheless, even though the extent of paralysis varies considerably from one individual with SCI to another, the resulting disability can be devastating. It is not only the loss of limb function (and loss of sensation) below the level of injury which affects the individual physically, physiologically and psychologically. Some of the most difficult consequences of SCI that the person has to deal with are the loss of (or impaired) control of the bladder and bowel, and of sexual function.

In addition to these primary functional issues, there are a number of secondary health consequences of SCI. Together with the loss of functional capability comes a less active lifestyle. This reduced activity often leads to low cardiopulmonary fitness, which imposes health risks to the SCI population. The problems include elevated risk of heart disease, blood disorders, loss of bone integrity and skin degradation. These issues need to be addressed.

1.2.1 Prevalence of SCI

In Britain, there are over 50,000 people with SCI (of whom 3,500 are in Scotland). Ninety-five new neurological cases of SCI were recorded at the Queen Elizabeth National Spinal Injuries Unit [1] for Scotland for the year 2002–2003. Figures provided by the Spinal Injuries Association[1] for the UK and Ireland in the year 2000 show that 633 new patients were admitted in the British Isles. In comparison, the data for the United States of America, published by the National Spinal Cord Statistical Center[2] in 2001, reveal an average of 11 000 new cases per year (equivalent to around 40 cases per million). The estimated number of people in America with spinal cord injuries lies between 183,000 and 250,000.

The distribution of causes of SCI in Scotland closely matches that for the U.K. as a whole, as summarised for 2000–2001 in Table 1.1. Falls are the primary cause, followed by Road Traffic Accidents (RTA) and then sports injuries. Other causes include violence and SCI resulting from medical problems (such as viral diseases or progressive medical conditions). In contrast to the U.K., violence is the second greatest source of spinal cord injury in the U.S., after road traffic accidents.

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[1] http://www.spinal.co.uk/publications/

[2] http://images.main.uab.edu/spinalcord/pdffiles/factsfig.pdf

Region	Year	Causes			
		Falls	RTA	Sports	Others
Scotland	2000–01	42%	30%	8%	20%
U.K. (inc. Scotland)	2000	42%	37%	12%	9%
U.S.A.	2001	22%	39%	7%	32%

Table 1.1: Main causes of SCI in the U.K. and the U.S.

1.2.2 Paralysis resulting from SCI

The extent of paralysis affecting an individual with SCI is dependent on both the level of the lesion and the completeness of the injury to the spinal cord.

Levels of injury

A lesion to the spinal cord is described as occurring at the cervical (neck), thoracic (chest), lumbar or sacral region. Within each section of the spine, different levels of the lesion (or injury) are defined. The neurological levels at which SCI can occur, and examples of the muscles innervated at various levels, are illustrated in Figure 1.1. The extent of impairment increases as the level of the SCI progresses towards the cranium because the neural supply to a larger part of the body is interrupted.

An injury to the spinal cord is described according to sensory and motor levels. Furthermore, right and left sides of the body may be scored differently. For the classification of neurological level of injury, four separate segments may be identified: Right-sensory (R-sensory), Left-sensory (L-sensory), Right-motor (R-motor) and Left-motor (L-motor). Where right and left sides are not described separately, the guidelines from the International Standards Classifications of SCI [68] provide the following definitions. The *sensory level* describes 'the most caudal segment of the spinal cord with normal sensory function on both sides of the body', whilst the *motor level* is similarly 'the most caudal segment of the spinal cord with normal motor function on both sides of the body'.

Completeness of injury

As well as the level of the spinal cord at which the damage occurs, the extent of this damage determines the severity of the motor deficit, loss of sensation throughout the body, and autonomic dysfunction. The injury is classified as clinically complete if no motor or sensory function is preserved in the sacral segments S4–S5. However, even

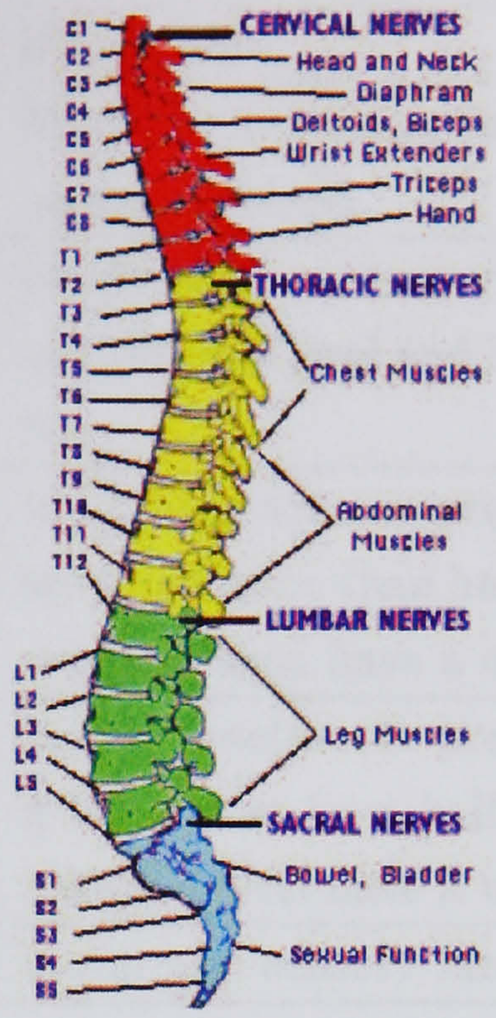

Figure 1.1: Diagram showing the spinal nerves in the cervical, thoracic, lumbar and sacral regions (taken from http://www.spinalinjury.net).

with a clinically complete SCI, some pathways may be preserved. The completeness of the injury is commonly described on a five category scale: the ASIA impairment scale (see Table 1.2), based on sacral sparing. The ASIA scoring chart is shown in Figure 1.2.

Spastic and flaccid SCI

Lesions of the upper motoneurone (UMN) lead to spastic paralysis, as the motor, sensory, and autonomic reflexes remain intact below the level of injury, even though they are no longer under the command of the brain. However, lesions of the lower motor neurone (LMN) result in flaccid paralysis and denervation, as central nervous system (CNS) control of sensorimotor functions is lost. Although this thesis focuses on spastic SCI, it is important to bear in mind that "injuries to the cord at any site resulting in damage to the reflex arc can leave a denervated (areflexic) segment among neighbouring segments that remain spastic" [55].

1.2.3 Tetraplegia

Paraplegia occurs with an injury to the thoracic, lumbar or sacral segments of the spinal cord. In cases of paraplegia, voluntary control of the upper limbs is maintained, but function of the trunk, legs and pelvic organs may be impaired.

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

Table 1.2: ASIA Impairment Scale, produced by the American Spinal Injuries Association [68].

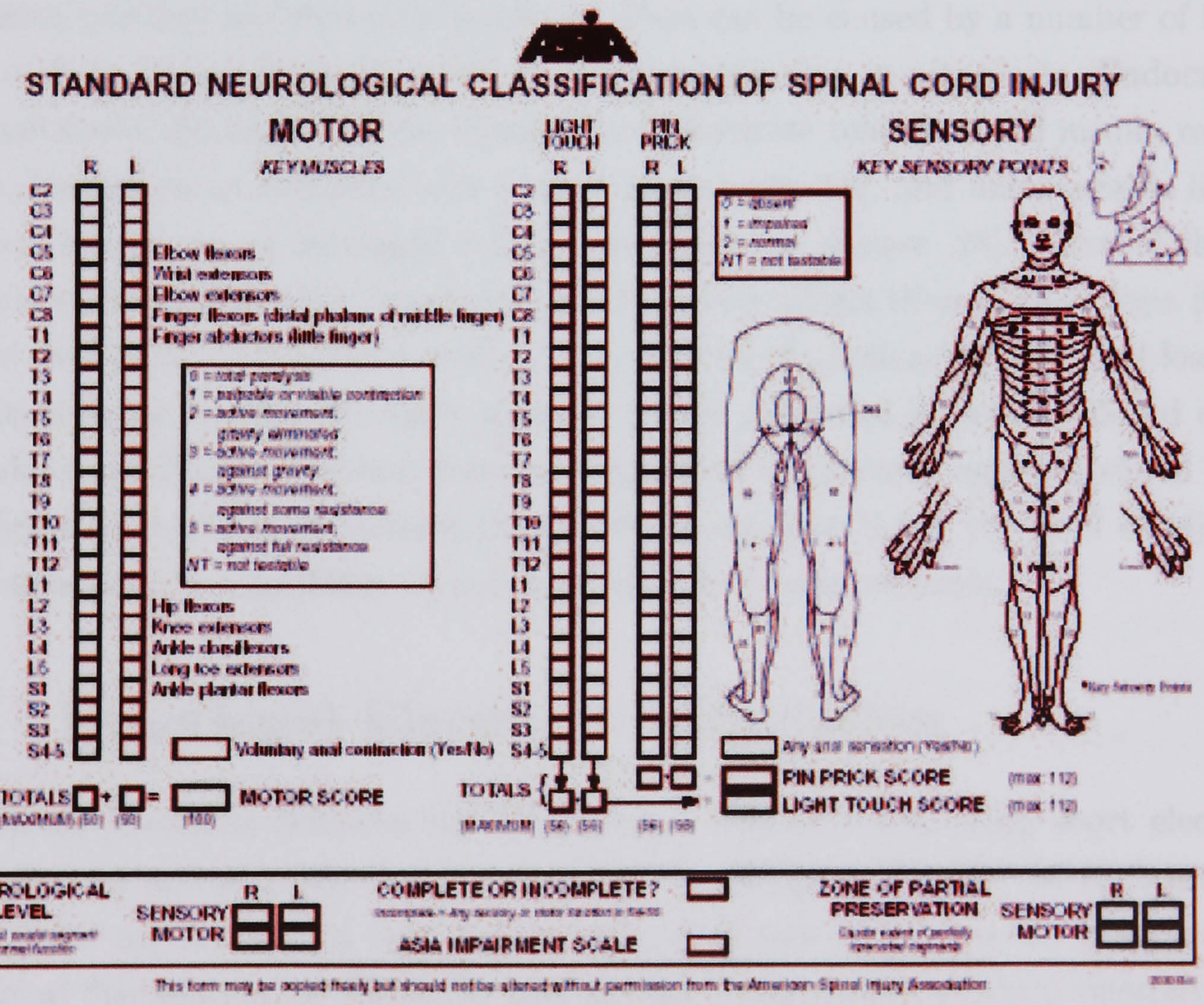

Figure 1.2: The ASIA scoring chart for neurological classification, produced by the American Spinal Injuries Association [68].

Resulting from a higher level of injury, tetraplegia is more debilitating than paraplegia. Tetraplegia (also referred to in some literature as 'quadriplegia'), is defined as the impairment or loss of motor and/or sensory function in the cervical segments of the spinal cord due to damage of neural elements within the spinal canal [68]. Function of the arms, legs, trunk and pelvic organs is affected as a result. The extent of remaining function in the upper limbs of people with tetraplegia depends on the level of the cervical injury. For example, a person with a C4 (complete) level injury shows full paralysis of the muscles in the arms and hands, with some remaining control of shoulder muscles. With a lower level complete C5 or C6 SCI, elbow flexors, but not elbow extensors, remain under voluntary control. The obvious implications of tetraplegia are in terms of function: most activities of daily living require the help of carers, at least with an injury level above C7.

In addition, there are secondary medical complications that arise from SCI [90]. In both paraplegia and tetraplegia, problems with spasticity, pain, endocrine and metabolic disorders are common. Spasticity interferes with the person's comfort, but also with mobility and everyday activities. Pain can be caused by a number of factors, and can be a more severe problem in tetraplegia than in paraplegia. Endocrine and metabolic disorders include impaired carbohydrate tolerance and insulin resistance, leading to an increased risk of type II diabetes [58], and unfavourable lipid profiles, leading to an increased risk of cardiovascular disease [28]. Most of these medical complications of SCI are more severe in tetraplegia than in paraplegia [90]. Other secondary consequences of the reduced levels of physical activity, and loss of sensation following SCI are rapid atrophy of the paralysed muscles, reduced cardiopulmonary fitness, reduced bone integrity with subsequent osteoporosis in the paralysed limbs [20] and reduced blood flow to the skin below the level of injury with associated susceptibility to the development of pressure sores.

1.3 Functional Electrical Stimulation

Functional Electrical Stimulation[3] (FES) is a method of delivering short electrical pulses to activate motor nerves innervating paralysed muscle. In contrast to therapeutic applications of electrical stimulation (often referred to as Therapeutic Electrical Stimulation, or TES), the aim of FES is to generate a muscle contraction which leads to a functional movement, thus temporarily restoring function to an affected organ or limb [95].

[3]Functional Neuromuscular Stimulation (FNS) is used synonymously with Functional Electrical Stimulation in some of the literature.

1.3.1 Principles of FES

Under certain conditions, paralysed muscle can retain its capacity to contract in SCI. even if the signals from the brain cannot travel to the peripheral nerves innervating a muscle supplied below the spinal cord lesion. Indeed, where there is no extensive LMN damage (either directly at the time of injury, or following extensive atrophy leading to denervation), the paralysed muscle can retain its capacity to contract because there is an intact connection to the cell body in the spinal cord. FES systems can be used as the external source of electrical signals to trigger action potentials in the motor neurones and control contractions in the innervated muscle.

Activating paralysed muscle

FES is delivered through electrodes placed on the skin (referred to as surface or transcutaneous stimulation), inserted through the skin (in percutaneous stimulation), or placed directly on, in or adjacent to the nerve (in implanted systems) [80]. The principle of activation of paralysed muscle is illustrated for surface stimulation in Figure 1.3. When the peripheral nerve to be stimulated lies within the electric field created between two electrodes (anode and cathode), action potentials can be triggered in the motor neurones, thus mimicking what would occur naturally in voluntary muscle contraction.

However, unlike a voluntary activation, the action potential will propagate in both directions from the site of stimulation. The electrical stimulus needs to be sufficiently large to elicit an action potential in the nerve. The minimum stimulus level required to elicit the action potential response is referred to as the threshold [85]. With the short pulses typically used in FES, this threshold is lower for large diameter motor neurones than for small diameter ones, which essentially means that the former are recruited first in FES. This is one of the main differences between FES-activation and voluntary activation of muscular contraction. In the voluntary case, the 'size principle' of recruitment applies, with smaller diameter fibres being recruited before larger ones.

Stimulation parameters

The precise pattern and level of recruitment are determined by a number of parameters of the applied stimulation [81]. Basic physiological properties of the tissue being stimulated, however, determine which combinations of electrode type, stimulus waveform, regulation and modulation are most appropriate for a particular task.

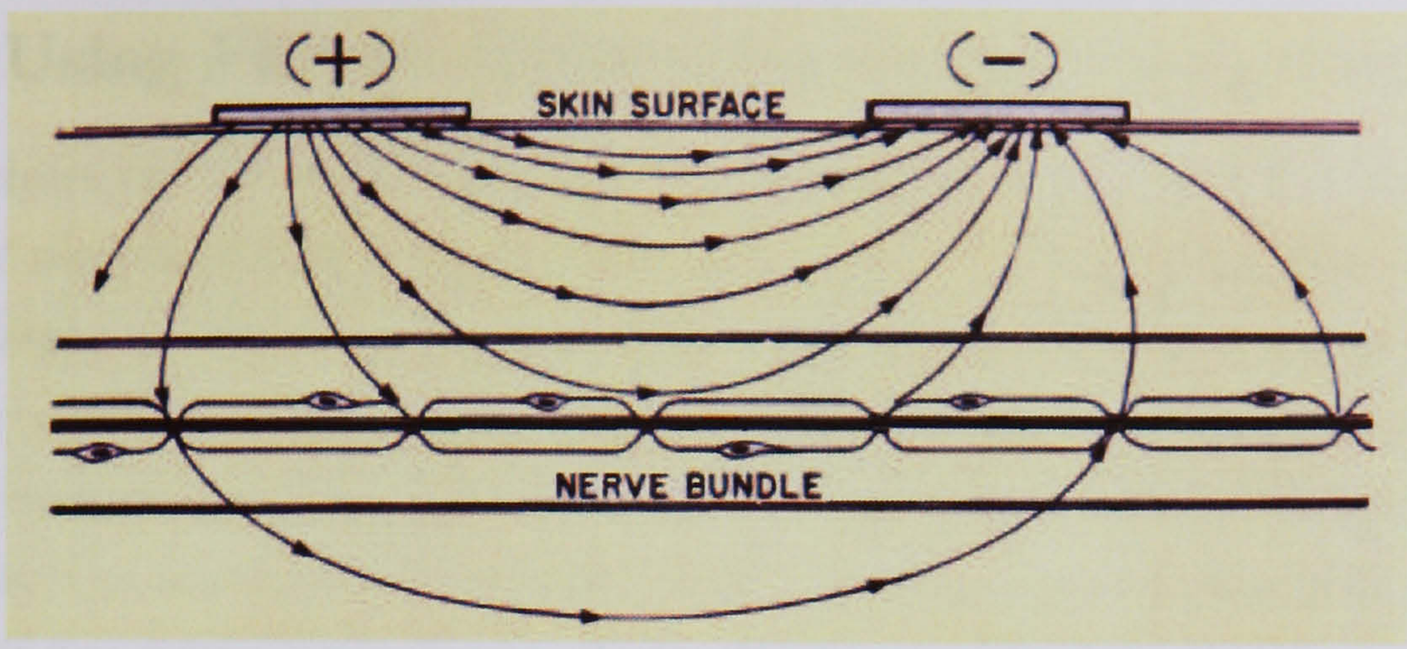

Figure 1.3: Diagram to illustrate the principle of motor nerve stimulation through surface FES (taken from [12]). With the motor nerve lying in the electrical field created between the two surface electrodes, action potentials can be generated in the nerve fibres.

In the development of multi-channel FES systems, two types of electrode configurations have typically been produced: bipolar configurations and monopolar configurations. In the case of bipolar stimulation, two electrodes are placed in the vicinity of the target nerve, forming a closed electrical circuit between the two electrodes. In contrast, monopolar stimulation uses active electrodes and one common electrode. The former are placed in the vicinity of the target nerve, whilst the latter is situated further away (but nevertheless along the neural pathway).

The stimulators may be either current-regulated or voltage-regulated. Current regulation allows for precise control of the charge delivered to the tissue, regardless of the changes in electrode properties. In contrast, with voltage-regulated stimulation, the charge delivered depends on the impedance of the electrode-to-tissue interface, thus resulting in an uncontrolled electrical current [85].

The effect on the stimulated structure also depends on the stimulus waveform. Properties of the stimulus waveform include its shape, its directionality, and the current amplitude, stimulation frequency and stimulation pulsewidth. Rectangular waveforms are mostly used. Biphasic (or bidirectional) stimulation is generally recommended, instead of monophasic (or unidirectional) stimulation. In surface stimulation, the reasons for this preference include greater comfort (although this can be a minor issue when used in sensory complete SCI), and reduced likelihood of tissue damage with biphasic waveforms [86]. Skin management is extremely important to individuals with SCI, and so every effort should be made to minimise the risk of tissue damage.

1.3.2 Using FES to Address Functional Requirements

The principles of FES were first applied to paralysed muscle over 40 years ago. with the aim of restoring some function [43, 111]. Most of the systems developed to date for tetraplegia provide hand grasping [75, 84], with some additionally incorporating elbow extension to allow for reaching [71]. A number of commercial FES-hand grasping systems are currently available. For example, a widely used surface stimulation system is the NESS Handmaster [76], whereas one with implanted electrodes and stimulator is the NeuroControl[4] Freehand [60, 47]. In addition to surface and implanted systems, there is the option of percutaneous stimulation, but this is less practical and so is usually used in a research context rather than in commercial systems (see [85] for review).

The provision of hand grasping has successfully given a group of tetraplegic individuals usage of the upper limb to carry out some activities of daily living (ADL) either without or with less assistance from carers [106]. Evidently, FES research has progressed considerably in addressing the issue of reduced upper limb function in this population.

Other FES systems available to the SCI population include systems for bladder and bowel control (using sacral anterior root stimulation [26, 56]), breathing (using phrenic nerve stimulation [30]) and walking [42, 87]. For all of these functional systems, it is clearly important to have accurate controllers so that they may be of maximum benefit to the users. Extensive work has been done on control methods for both upper limb and other functional FES systems [3, 5, 24, 25, 48, 65, 102].

In addition, FES has been applied clinically to other groups. The peroneal nerve stimulator is prescribed in stroke (as well as incomplete SCI) for the correction of drop-foot [66]. FES systems are also used for cardiac pacemakers, cochlear implants, and visual cortex implants (see review by Rushton [95]).

1.3.3 Using FES to Address Exercise Requirements

It is perhaps of little surprise, therefore, that the potential of FES to activate paralysed muscle has more recently been considered as a tool for exercise in spinal cord injured populations [83]. In comparison with the widespread use of functional systems, FES systems for exercise in SCI are, in the main, at a developmental stage. The motivation behind producing FES-exercise systems is to tackle secondary com-

[4]This system was recently removed from the market.

plications of SCI, such as reduced cardiopulmonary fitness, susceptibility to pressure sores, and bone demineralisation in individuals who lead a sedentary lifestyle as a result of their paralysis. Although individuals with paraplegia can manually propel their wheelchairs and perform voluntary upper body exercises, many people with tetraplegia cannot achieve even this level of activity due to the extent of their paralysis. Instead, passive forms of exercise (to help maintain range of motion of the joints) may be available, but this does not address the need to stress the cardiopulmonary system regularly to maintain a basic level of fitness.

Progress in the field of FES-cycling has already been achieved [57], but with systems which have predominantly been aimed at the paraplegic population. However, bearing in mind that approximately half of all spinal cord injuries result in tetraplegia, the potential for FES-exercise in the tetraplegic population needs to be explored further. In an era where people in the western world are made increasingly aware of the importance of maintaining a reasonable level of general fitness through regular exercise, the question of how individuals with tetraplegia (even more so than with paraplegia) could also address this issue has become a challenge for clinicians and researchers.

1.4 Exercise

Prior to tackling the issue of reduced fitness in SCI (and, more specifically, in tetraplegia), the causes of the exercise limitation need to be explored. With the extent of paralysis encountered in tetraplegia, a number of the systems normally involved in the control of breathing during exercise and in the increased circulation required for the delivery of oxygen to the exercising muscle are compromised, in addition to the muscles required for the work being paralysed. In order to understand the extent of the problem, it is useful first of all to look at the normal response of the healthy human body to exercise at the cellular and whole body levels.

1.4.1 Exercise Responses

'Normal' response to exercise

During dynamic exercise, stress is placed on the human body. If the body is intact and free from disease, the response to this stress is a well coordinated series of changes in breathing and blood circulation to achieve what is demanded in terms of extra work in the exercising muscles (see Figure 1.4).

In order to meet the demands of exercise, the muscles require a system that not only provides sufficient energy for this work, but also removes any waste products that would accumulate as a result of performing the work. Muscle contractions are fuelled by the release of energy that occurs when Adenosine Triphosphate (ATP) is broken down, through the cleavage of its high-energy bond. There are a number of potential sources of ATP, which can be used at different stages of the exercise, and for different intensities of exercise.

In the early phases of exercise, local phosphocreatine (PCr) stores in the muscles are usually the immediate source of ATP regeneration, not requiring the use of oxygen (anaerobic). The main mechanisms of ATP regeneration to maintain the supplies to the exercising muscles during the subsequent phases of exercise include aerobic and anaerobic metabolism of available substrates. By definition, for cells to produce ATP aerobically, oxygen needs to be supplied to those cells, for oxidation of carbohydrates and fatty acids. Aerobic metabolism is the predominant method of supplying the fuel for the exercising muscles as long as the rate of uptake of oxygen at the lungs ($\dot{V}O_2$), consequent distribution of oxygen via the blood, and oxygen utilisation are adequate to sustain this. Hence, aerobic metabolism is the mechanism involved in maintaining sustained exercise of moderate intensity[5]. Anaerobic glycolysis of glucose or glycogen contributes more significantly to the ATP generation for the working muscles at exercise intensities that can no longer be maintained through aerobic metabolism alone. Indeed, in the absence of adequate oxygen utilisation, anaerobic energy transfer is required to sustain the ATP production rate [123]. Anaerobic glycolysis leads to the production of ATP without the use of oxygen, but at the cost of a build up of lactate. Blood lactate concentration is an index of anaerobic metabolism: increased lactate levels in muscle and blood indicate an anaerobic supplement to the aerobic production of ATP [7]. The concept of the *anaerobic threshold* has been developed, based on an exponential increase in blood lactate concentration when exceeding a certain rate of exercise or oxygen uptake. Similarly, the *lactate threshold* has been defined as the exercise $\dot{V}O_2$ that can be achieved without a sustained increase in blood and muscle lactate concentration [123].

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[5]Throughout this thesis, **moderate** intensity exercise refers to the range of work rates at which there is no sustained elevation of arterial blood lactate concentration, **heavy** exercise is the range in which there is a sustained elevation of arterial blood lactate concentration, and **severe** exercise occurs at work rates at which the concentration continues to increase, and results in fatigue [120].

Extensive research has been done to further our understanding of the normal gas transport mechanisms at the whole body level, involved in maintaining the muscle respiration during exercise. Gas exchange (O_2 consumption and CO_2 production) is affected in a different way and in a characteristic pattern according to which of the three sources of ATP (or combination of these) is being used to fuel the muscular work [116]. Figure 1.4 illustrates the coupling of pulmonary to cellular respiration by the circulation. This shows how measurements of oxygen uptake ($\dot{V}O_2$) and carbon dioxide output ($\dot{V}CO_2$) made at the lung give us an indication of the underlying processes occurring at the cellular level. These principles are exploited in exercise testing.

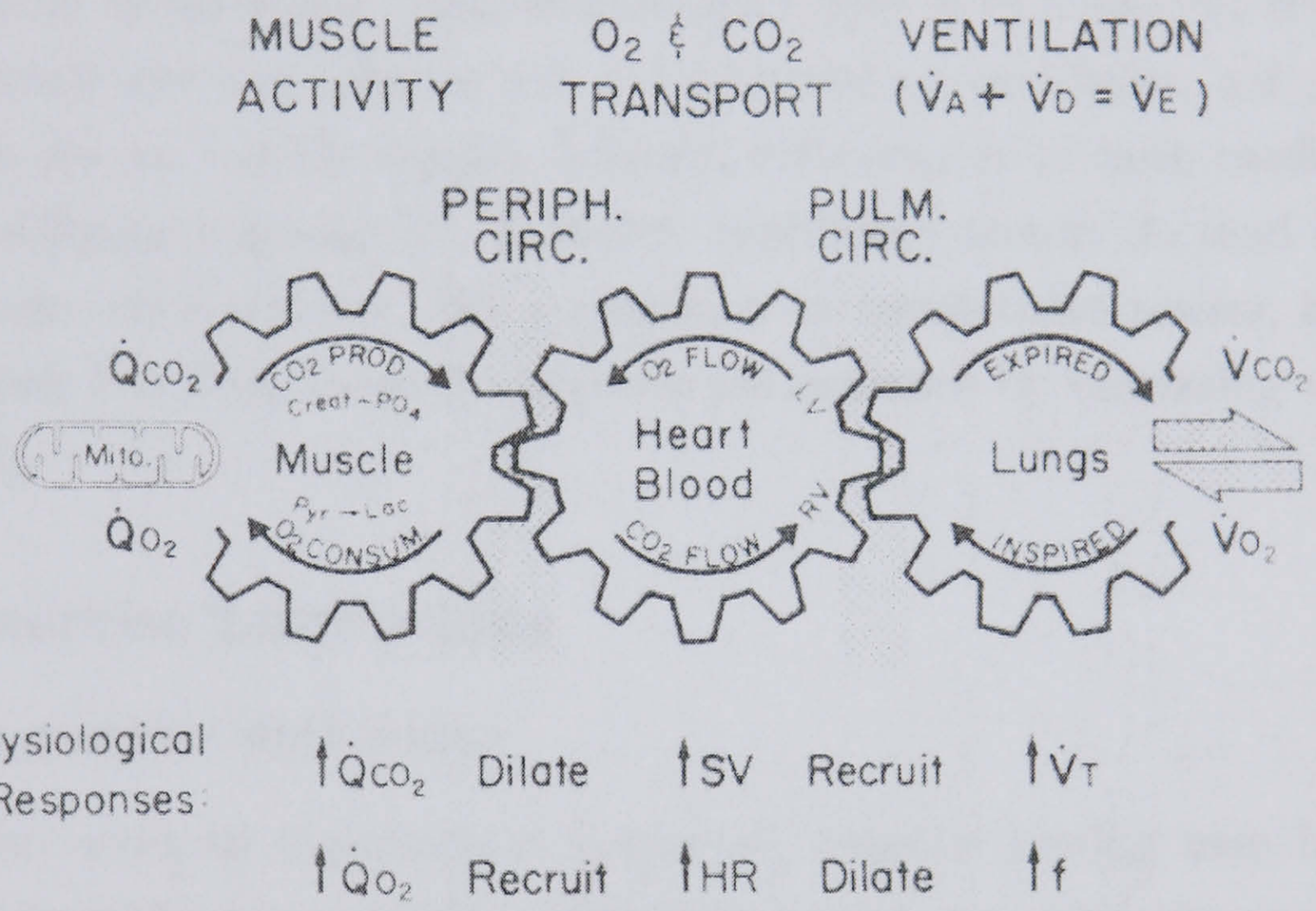


Figure 1.4: Diagram (taken from [116]) depicting the gas transport mechanisms for coupling cellular to pulmonary respiration. The gears illustrate the coordination between the components of the system. $\dot{Q}_{O_2}$ and $\dot{Q}_{CO_2}$ represent oxygen utilisation and carbon dioxide production by the contracting muscles, respectively. For these to increase, changes in both peripheral circulation (PERIPH. CIRC.) and pulmonary circulation (PULM. CIRC.) are involved. Increases in cardiac output (the product of stroke volume (SV) and heart rate (HR)) are coupled with increases in pulmonary blood flow, and ventilation (the product of tidal volume (VT) and breathing frequency (f)). $\dot{V}_E$ represents the minute ventilation, which includes the alveolar ventilation ($\dot{V}_A$) and dead space ventilation ($\dot{V}_D$). The rate of oxygen uptake by the alveoli ($\dot{V}_{O_2}$) and rate of carbon dioxide output ($\dot{V}_{CO_2}$) are measured at the lung to infer what is happening at the cellular level.

Maximal exercise

Considering the number of systems involved in sustaining exercise (and their complexity), a few processes could potentially limit maximal exercise: ventilation, pulmonary gas exchange, oxygen delivery, a combination of these, or some other factors. There is evidence for cardiovascular coupling to metabolism from the dependence of oxygen supply to the muscle cells on a number of factors, which include: (i) cardiac output (Q), (ii) distribution of perfusion to the tissues in need of O_2, and (iii) the partial pressure profile of O_2 in the capillary blood. Ventilatory coupling to metabolism also appears necessary, as the blood passing through the lungs must be arterialised to: (i) eliminate the added CO_2, (ii) replenish the O_2 consumed, and (iii) achieve homeostasis. Numerous studies have shown that, in healthy individuals, maximal exercise appears not to be limited by ventilation nor pulmonary gas exchange *per se*, but by oxygen delivery, with respect to both cardiac output and muscle diffusion capacity [2]. However, ventilatory factors do tend to become limiting in some elite athletes. For example, with competitive rowers, inspiratory muscle training has been shown to improve performance by increasing ventilatory capacity [115].

1.4.2 Exercise Limitations

Identifying exercise limitations

In cases where exercise limitation is suspected, exercise testing may be used to identify and quantify the problem. Breath-by-breath gas exchange measurement systems are now commonly used for this purpose. A volume transducer allows for measurement of flow, and a gas sample line feeds samples of air at the mouth to the gas analysers, to determine the characteristics and composition of each breath. Although the measurements are of gas exchange at the mouth, these can be used to infer what is happening at the cellular level.

In this way, the functional status of the cardiovascular system and the ventilatory system, and the degree of matching of ventilation to perfusion can be established non-invasively during exercise. Indeed, gas exchange will be affected in different ways depending on the defects in the coupling of external (airway) to cellular (mitochondrial) respiration. As a consequence, the pattern of gas exchange at the airway can be used to diagnose pathophysiology [116].

To explore possible exercise limitations, the gas exchange data and heart rate data

obtained during exercise testing, together with pulmonary function measurements recorded at rest, are usually summarised in a set of tables and plots. These are then compared to predicted values and characteristic response patterns to identify the problems. The main diagnostic response patterns used are: (i) maximum/peak O_2 uptake, (ii) heart rate response, (iii) ventilatory response, and (iv) the lactate (or anaerobic) threshold.

Determining causes of exercise limitations

One starting point is to look at the magnitude of the maximum (or peak) oxygen uptake reached during an incremental exercise test. The maximal oxygen uptake ($\dot{V}O_{2max}$) is defined as "the highest oxygen uptake the individual can attain during exercise" [7]. During tests in which oxygen uptake is measured for progressively increasing exercise work rates (during incremental exercise testing), the subject may not reach $\dot{V}O_{2max}$. In this case, the highest value during the test is recorded as a peak oxygen uptake ($\dot{V}O_{2peak}$) instead [92]. Additionally, when oxygen uptake is measured using exercise modalities that do not involve the large muscles of the legs (for example, in arm-cranking exercise), the highest oxygen uptake reached is also referred to as a peak, not a maximum.

At rest, a person consumes around 0.25 l/min of oxygen. If this person leads a sedentary lifestyle, oxygen consumption can increase to around 2.5 to 3.0 l/min in an incremental treadmill or leg-cycle ergometry exercise test. For an athlete, values of up to 5.5 l/min can be reached. Maximum or peak oxygen uptake is considered to be a good indicator of cardiopulmonary fitness, as it reflects the maximal functional ability of the circulation. When this is clearly lower than predicted, other indicative values need to be looked at to explore the exercise limitation further. Series of flowcharts, such as those produced by Wasserman *et al.* (one of which is given in Figure 1.5) facilitate the interpretation of the data obtained through exercise testing. This is a useful starting point, but it is important to remember that exercise limitation in patients with a reduced peak oxygen uptake is "complex, often multifactorial, and as such not limited by any single component of the O_2 transport/utilization process, but rather by their collective quantitative interaction(s)" [2].

1.4.3 Exercise Training

When the causes of exercise limitation have been identified through exercise testing, the information can be used to determine the course of rehabilitation and exercise

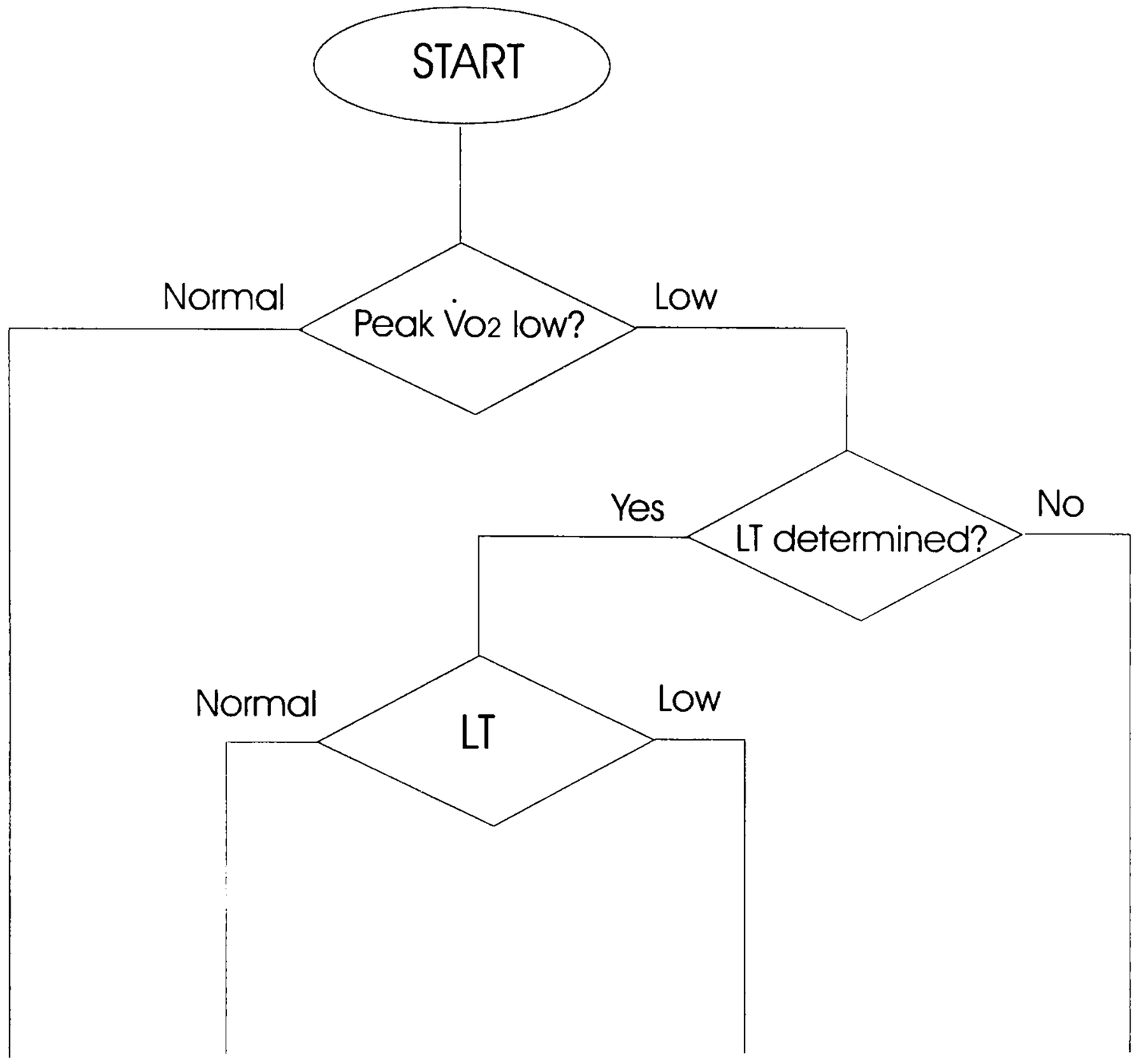


Figure 1.5: Flowchart for the differential diagnosis of the cause of exercise limitation in the general population (adapted from [116]); LT: lactate threshold. To discriminate between the different diseases, additional flowcharts (see [116]) that refer to other diagnostic cardiopulmonary data can be used.

prescription for each individual. Indeed, the data obtained in the exercise test give a good indication of the work rates to be incorporated in an exercise training programme for that person. It is generally accepted that, in the general population, individuals classified as average for $\dot{V}O_{2max}$ can improve aerobic power between 5 and 25% during a 12-week aerobic training programme [69] through appropriate choice of exercise intensities used in the training.

Methods of exercise prescription

A popular method of exercise prescription is to set the exercise work rate in relation to the lactate threshold, as determined by a baseline maximal exercise test. It is important that the exercise test used to calculate this threshold is performed on the same exercise modality (or at least using the same muscles) as will be used for the training. Knowing the oxygen uptake (and hence work rate) at which the lactate threshold is reached means that the exercise training intensity can be set within a domain of work rates that is known to be below this threshold (ie. moderate intensity, see footnote in Section 1.4.1). The lactate threshold can be increased significantly by endurance training. This means that there is a work rate domain in the trained state in which blood lactate concentration is not increased but within which it was increased in the untrained state [121].

An alternative exercise prescription method, based on the assumption of a linear relationship between the heart rate and the oxygen uptake with increasing work rate [34], is to train at a percentage of maximum heart rate. This method, however, cannot be confidently applied to populations for which this assumption of linearity is not valid. Such is the case in tetraplegia, where a so-called blunted heart rate response is observed, making the heart-rate-based determination of training intensity in this group inappropriate[6].

Goals of exercise training

Generally, the goals of exercise training are [69]:

1. to enhance the central circulation's capacity to deliver oxygen (through *central adaptations*), and

2. to develop the active muscles' capacity to consume oxygen (through *peripheral adaptations*).

[6]The reasons for this blunted heart rate response are described in later sections.

In terms of *central adaptations*, appropriate choice of exercise can increase the volume-load on the heart and stress the cardiovascular system to lead to [35]: (i) higher peak stroke volume (SV) and cardiac output ($\dot{Q}$) (reflecting an increased capacity to circulate blood), and/or (ii) lower heart rate (HR) at rest and during submaximal exercise (reflecting an increased cardiovascular reserve and decreased relative intensity).

Peripheral adaptations include increased concentrations of mitochondria, myoglobin, and oxygen storage, oxidative enzyme concentration and activity, as well as muscle fibre size and capillary density, which facilitate oxygen utilisation at the muscle level. Furthermore, endurance training can lead to a favourable change in histochemical profile of the muscle fibres to predominantly slow twitch characteristics with high oxidative capacity, and in an increase in the vascular bed supplying the trained muscles. Hence, the capacity of the exercising muscles for oxidative metabolism improves, and the oxygen cost of doing the same level of work in the exercising muscles decreases as a result of training (even though the metabolic cost is unchanged).

Where the exercise regime undertaken is appropriately designed, the exercise intensity and frequency of exercise determine the extent of the improvement (although there may be other limiting factors, as in disease or illness).

The application of these principles of exercise training is not so straightforward in a group of people with a blunted heart rate response and a limited capacity for aerobic exercise training, as is the case in tetraplegia [70]. Hence, there is a considerable challenge for researchers and clinicians to find effective ways of improving the cardiopulmonary fitness and general health of tetraplegics.

Chapter 2

FES-Exercise in Tetraplegia

2.1 Summary

The sedentary lifestyle imposed on tetraplegics as a result of their extensive paralysis presents them with serious health problems [35, 113], one of which is an elevated risk of cardiovascular disease. This problem has only surfaced relatively recently: ever since the mortality and morbidity rates immediately following a cervical SCI were considerably reduced through changes in medical and rehabilitation practices, first introduced by Guttman (in the U.K.) and Bedbrook (in Australia) [59].

With reference to the general population, the common approach to reducing the risk of developing cardiovascular disease is to prescribe regular aerobic exercise; but this is not easily implemented in tetraplegia. The idea of applying FES to paralysed muscles may be an appropriate avenue for allowing this population to exercise and to maintain an adequate level of activity and cardiopulmonary fitness. However, the obvious limitation of muscle paralysis *per se*, addressed by the use of FES, is not the only issue. There are a number of other limitations to exercise in SCI, and further problems in tetraplegia (compared with paraplegia). With injuries to the spinal cord at the cervical levels, a number of key cardiovascular responses normally observed during exercise in the healthy intact body are impaired.

Bearing in mind the goals of exercise training, a number of challenges emerge. Firstly, with an SCI at the cervical level and the implications of such extensive disruption of information flow between the CNS and the peripheral nervous system, can the capacity of central circulation to distribute oxygen to the exercising muscles be altered through training? Secondly, with the large muscles of the arms and legs usually involved in aerobic exercise paralysed, is it possible (and useful in the

long-term) to have exercise modalities that will allow these paralysed muscles to perform the required work? Finally, even if this can be achieved, can such exercise modalities be developed to the extent that they are made easily available to the tetraplegic population? The aim of this chapter is to identify some of the major problems associated with implementing exercise regimes when working with people with tetraplegia, to present and criticise some of the modes of FES-exercise that have been developed to date in an attempt to overcome some of the highlighted issues, and to propose a novel method of exercising in tetraplegia.

2.2 Options for Voluntary Exercise in Tetraplegia

In the planning of rehabilitation of acute SCI, it is important for the individual to start physiotherapy as soon as is practicable. Once the person is stable, there is some urgency in rebuilding muscles that remain under voluntary control, and in maintaining the range of motion of the joints. The reasons for this include the extensive muscle atrophy (referred to as 'disuse atrophy') that can occur within weeks of the injury, and the development of contractures of the joints. If muscle atrophy is allowed to continue for too long, there is a real threat of the muscle wasting becoming so extensive as to be irreversible.

The possibilities for tetraplegics to perform *voluntary exercise* are clearly restricted to some upper limb work. Therapeutic exercises have traditionally been used in rehabilitation to improve voluntary function of residual intact musculature [35]. However, there is an additional limitation to exercise in cervical SCI. This is a ventilatory limitation which results from paralysis of accessory muscles of respiration. Purely diaphragmatic breathing is sufficient at rest and at low exercise work rates, but accessory muscles of respiration are usually used in neurologically intact people exercising at increasing work rates. Nevertheless, even considering this ventilatory limitation, the lower the level of the lesion, the greater the number of exercise modalities available to the individual.

In the case of a complete injury above C4, voluntary exercise is not an option. With a C4 SCI, some of the shoulder musculature can still be used voluntarily, potentially allowing shoulder elevation and depression exercises (also referred to as 'shoulder shrugging') to be carried out [14]. Good biceps control should remain in C5 and C6 injuries, allowing for biceps strengthening exercises in this group of tetraplegics. By maintaining the biceps muscle strength, there is potential to increase the functionality of the arms to some extent. To make up for the lack of triceps function.

tendon transfer surgery may be undertaken. Through the learning of compensatory techniques [16], some manual wheelchair propulsion and hence mobility can be regained in this group.

The most functional use of the upper limbs in tetraplegia is clearly found in cases of C7 and C8 SCI. Upper body exercises involving strengthening of the biceps (and other elbow flexors), triceps, and shoulder muscles are possible. The ability to perform transfers and manually propel a wheelchair results in a considerably greater level of daily physical activity than with higher level injuries [32].

In the case of complete cervical SCI, a reasonable level of cardiopulmonary stress during voluntary upper-body exercise can therefore only really be achieved in tetraplegia with a C7 or C8 injury, and to a lesser extent in C5 or C6 tetraplegia.

2.3 Physiological Constraints on FES-Exercise

The introduction of FES-exercise options to the tetraplegic population could compensate to some extent for the lack of options for voluntary exercise modalities.

2.3.1 Physiology of FES-Exercise

Before considering the potential for FES-exercise in tetraplegia further, a number of points regarding the physiology of FES-exercise, and how this differs from exercise under voluntary control, need to be highlighted.

Recruitment

FES-stimulated muscle contracts in much the same way as voluntarily controlled muscle through the propagation of action potentials along motor neurones. However, some differences exist in the pattern of recruitment in electrically stimulated muscle, with important consequences for the application of FES in exercise training.

The main difference relates to the order of recruitment of fibres. In a *voluntary* muscle contraction, type I slow-twitch fibres tend to be recruited first. These highly oxidative fibres are innervated by motor neurones with small diameters and a relatively low threshold for excitation. When more rapid muscle force generation is required at higher work rates, the type II fast-twitch, fibres are then recruited. Their motor neurones tend to be of larger diameter, with a higher threshold for excitation. This is the "size principle of recruitment" [121, 123]. In this way, during exercise,

moderate levels of work can be maintained by the high-oxidative type I fibres. At the higher exercise intensities, the type II fibres (with a lower potential for oxidative metabolism, but fast rate of glycogen metabolism) then play a significant role in fulfilling the increased demands for muscular work. This, however, is accompanied by increased lactate production, which is associated with muscle fatigue.

In contrast, it is generally accepted that in *FES-induced* muscle contraction the type II fast-twitch fibres are preferentially recruited. These have larger diameter motor neurones, which have a lower threshold for artificial electrical activation than small diameter motor neurones. The type II fibres which they innervate utilise more oxygen for a given tension development than would type I fibres [8]. With these low-oxidative fibres involved in the muscular work early on, the muscular action is inefficient, and the muscle fatigues rapidly. Indeed, the absence of an adequate number of mitochondria for ATP production requirements of the exercise results in increased rates of glycolysis and increased lactate production, even if an excess of O_2 is available to the muscle cells. Elevated levels of lactate production therefore result when muscle power is produced by type II fibres rather than type I fibres — other factors being equal [121].

However, it is important to note that type II fibres can be further classified according to their histochemical profiles, into type IIa and type IIb fibres. Type IIb fibres have fast fatiguable (denoted FF) characteristics, whereas type IIa fibres are intermediate between type I (slow, oxidative or SO) and type IIb, in that they are fast, oxidative glycolytic (FOG) [93]. These fibre types have been repeatedly identified through histochemical and immunohistochemical typing using a variety of techniques [103]. Furthermore, there is some apparent plasticity in muscle. This is illustrated by studies showing that disuse can lead to changes from predominantly slow to predominantly fast characteristics, whereas factors such as endurance training can have the opposite effect.

Implications for FES-exercise training

In the healthy and intact human body, training can lead to a favourable change in the muscle composition (see section 1.4.3). Indeed, "endurance training can markedly increase the concentration of oxidative enzymes, the number of mitochondria and the capillary density in both fiber types (but appreciably more in type I fibers) leading to greater sustainability of a given work rate" [121]. On the other hand, inactivity (for example, during a period of bedrest), leads to a reversal of that effect, with a reduction in exercise capacity. This is often referred to as the detraining

effect. Muscle atrophies at such a high rate that even short periods of bedrest can lead to a considerable reduction in bulk of the inactive muscles. Furthermore, the muscle composition changes to predominantly type II fibres [73, 94].

As Barstow *et al.* [8] point out, SCI is an extreme form of the detraining condition, and the reduction in aerobic capacity of the paralysed muscle over time since injury is paralleled with changes in mitochondrial density and capillarity of skeletal muscle. The study by Burnham *et al.* [18] suggests that changes in the fundamental properties of muscle probably occur as early as 4–6 weeks post-injury. A few studies have investigated whether or not the muscle fibre composition can be favourably altered through FES-exercise training of the paralysed muscles, in an attempt to replicate the training effect that can be achieved in the general population through endurance training.

Chilibeck *et al.* [21] found that eight weeks of FES-leg cycling training in SCI achieved a significant increase in the number of capillaries per fibre, capillary contacts per fibre, and fibre area of the stimulated muscle. Nevertheless, capillarisation remained well below that in healthy intact subjects. Furthermore, fibre-type composition did not change significantly, so that a high proportion of type II fibres still made up the muscle under investigation (91.3± 3.6% pre-training, compared to 88.0±2.6% post-training). The choice of staining technique of the muscle sections, however, did not allow for the different subtypes (a and b) of type II fibres to be distinguished. In contrast, an earlier study by Mohr *et al.* [73], looking at the muscle fibre composition following 12 months of FES-leg cycling training, was able to show a change from the IIb fast-glycolytic to the IIa fast-oxidative subtypes.

Mohr *et al.*'s work demonstrated the potential for the fibre-type composition to change favourably within the type II subgroup with FES-exercise training, but these muscle fibres still fatigue more rapidly than type I fibres. This consequently limits the endurance capabilities of the muscle during FES-exercise, when compared with exercise under voluntary muscular control. Nevertheless, any histochemical changes in the muscle fibre composition leading to greater oxidative capacities and increased vascularisation of the muscles involved in the exercise should enable them to better maintain sustained contractions over longer periods of time following long-term FES-exercise [42].

2.3.2 Physiological Limitations in Tetraplegia

In addition to the altered pattern of recruitment in FES-induced muscle contractions during exercise, there are other factors which distinguish exercise responses in SCI from exercise responses in the healthy able-bodied person. In SCI, the system is lacking both central command of the contracting muscles, and afferent feedback from the contracting muscles, both of which normally have important roles in the regulation of cardiovascular responses during exercise [72]. Further limitations are imposed on circulation in high-thoracic paraplegia and tetraplegia, compared to low-thoracic and lumbar paraplegia because of the level of the injury in relation to the level of sympathetic outflow to the heart.

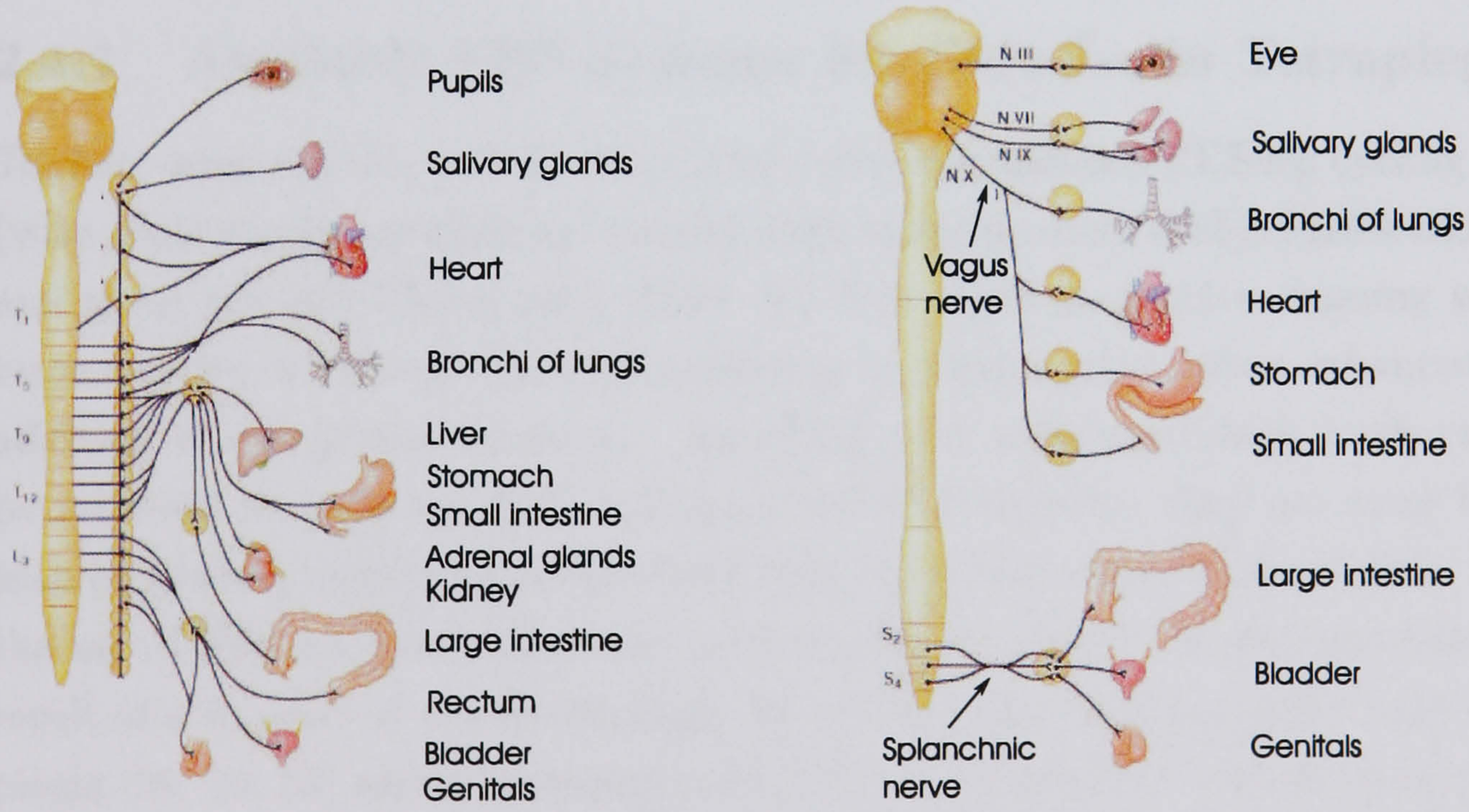
Lack of Central Command and Afferent Feedback

If central command and afferent feedback are important in the regulation of cardiovascular responses, both oxygen transport and utilisation should be affected by the injury [50]. The importance of central command and afferent feedback for the regulation of exercise responses was investigated in a key study by Kjaer *et al.* [61]. The investigators looked at the cardiovascular and ventilatory responses to dynamic electrically-induced leg exercise in the absence of both central command and neural feedback from contracting muscle. This was achieved by blocking afferent neural influences from the legs of eight healthy (neurologically intact) males through epidural anaesthesia at L3–L4, resulting in cutaneous sensory anaesthesia below T8–T9 and complete paralysis of the legs. Each subject performed leg-cycling exercise under two conditions: voluntarily controlled cycling (without anaesthesia) and FES-induced cycling (with anaesthesia). Comparing the results between normal cycling and cycling with FES during the temporary paralysis, the study found that, for a similar measured $\dot{V}O_2$ (up to around 2 l/min), heart rate (HR) and cardiac output (CO) were similar under the two conditions. However, minute ventilation ($\dot{V}E$) was higher in FES-induced cycling (54 l/min with FES, compared with 45 l/min without). Furthermore, the change in systolic blood pressure (SBP) was clearly different: the SBP in voluntary exercise sessions increased, as expected, from rest (93mmHg at rest, compared with 119mmHg during voluntarily controlled exercise), whereas the SBP in FES-exercise remained relatively unchanged (93 mmHg at rest, compared with 95 mmHg during FES-exercise). The study also found that mean arterial pressure (MAP) increased only in response to voluntary exercise, whilst it stayed at resting values in FES-exercise. Kjaer et al. put these results forward as supporting evidence that the neural input from working muscle is crucial for the normal blood pressure response to exercise, but also as being suggestive of other

haemodynamic and/or humoral mechanisms involved in the control of HR, CO and $\dot{V}E$ during dynamic exercise with large muscle groups [61].

Impaired Sympathetic Autonomic Activity in Tetraplegia

When reviewing findings from studies investigating possible physiological explanations for exercise responses in SCI, it is important to determine whether or not the investigators have grouped their subjects appropriately. An example of a study that was otherwise well-designed, but where this grouping was not observed, was that by Mutton *et al.* [74]. The result is that the usefulness of its findings is limited. This is because SCI responses where the lesion is *above* the level of sympathetic outflow to the heart differ from SCI responses where the lesion is *below* that level. With cervical injuries, all tetraplegics (at least with complete transection of the spinal cord) fall into the former group, as sympathetic outflow to the heart is found at thoracic segments of the cord (see Figure 2.1 (a)). Consequently, tetraplegics have an inadequate input to the cardiac plexus for sympathetic acceleration of the heart rate [54]. The commonly observed blunted heart rate response (a decreased maximal heart rate) in tetraplegia when compared to paraplegia, in voluntary upper-body exercise, has long been speculated to be attributable to this reduced sympathetic stimulation [23, 113].



(a) Sympathetic (b) Parasympathetic

Figure 2.1: Illustration of sympathetic and parasympathetic pathways of the autonomic nervous system (adapted from http://soma.npa.uiuc.edu/courses/bio303/).

Other consequences of the loss of supraspinal control of the sympathetic nervous system after high level SCI include orthostatic hypotension (with associated dizziness, nausea, light-headedness), low resting blood pressure and loss of diurnal fluctuation of blood pressure [107].

The problems faced in trying to tackle cardiovascular fitness in the tetraplegic population are summarised by Figoni in a flowchart, shown in Figure 2.2 [35].

2.4 Potential for FES-Exercise in Tetraplegia

Considering that the normal response to exercise involves the integration of cardiovascular and pulmonary responses, the loss of a number of regulatory mechanisms in tetraplegia clearly leads to exercise limitations. Despite the physiological constraints imposed on individuals with tetraplegia that limit the potential benefits of exercise training in this group, the introduction of FES-exercise systems could nevertheless address some of the health issues in the tetraplegic population. The challenge is to ensure that, where possible, these FES-exercise modalities can provide measurable and clinically useful improvements in remaining function and cardiopulmonary condition, through peripheral and possibly central adaptations.

2.4.1 Available FES Systems for Exercise in Tetraplegia

To date, work relating to FES-exercise systems has included FES-leg cycling [51, 82] (with some stationary systems commercially available since 1985), FES-walking [53], and more recently FES-rowing [119]. All these systems involve training with the large muscles of the legs (mostly quadriceps and hamstrings, often enhanced by the addition of the gluteal muscles). Assuming that sufficiently high work rates can be achieved through the FES-induced lower limb exercise, they are more likely to lead to notable central training effects than voluntary upper-limb exercise. Indeed, the use of FES leg-cycling exercise has been encouraged in the SCI population as a result of a number of studies highlighting its potential health benefits both in paraplegia [29, 33, 57] and in tetraplegia [33, 35, 82]. It should be noted, however, that people with tetraplegia have tended to perform FES-leg cycling at slightly lower power outputs, and proportionally lower levels of physiological responses, than people with paraplegia [35].

There are good reasons for giving people with SCI the option of exercising the lower limbs using electrical stimulation. Firstly, in terms of achieving central adap-

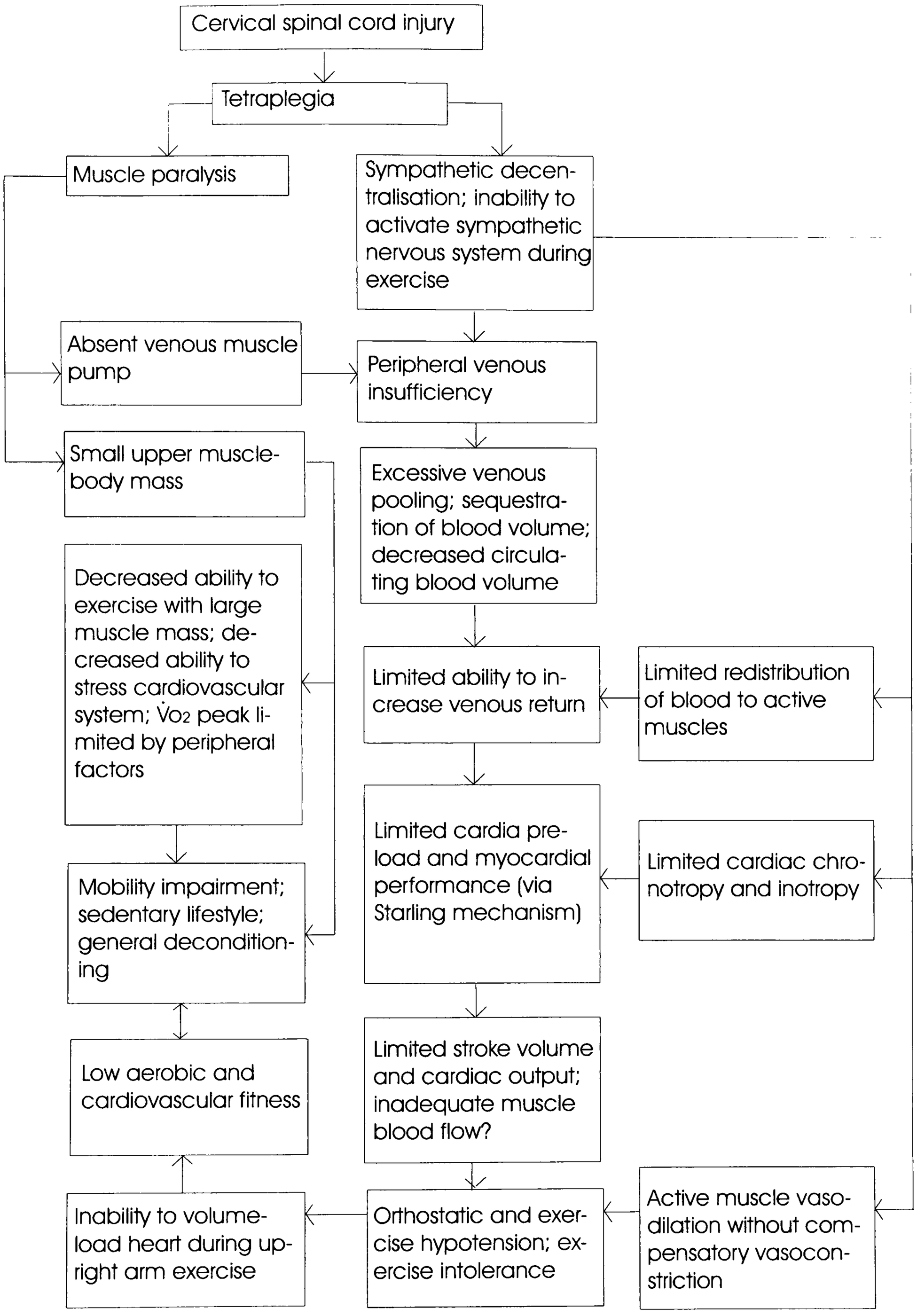


Figure 2.2: Flowchart of factors that may influence cardiovascular fitness in tetraplegia resulting from SCI (adapted from [35]).

tations, the cardiovascular system can potentially be stressed more through exercise involving the larger muscles of the legs rather than with the smaller muscles used during arm exercises. Typically, even in able-bodied individuals, the peak oxygen uptake in arm-cranking exercise is around 30% lower than the maximum oxygen uptake in leg-cycling, or treadmill exercise [7, 13, 69, 116]. Consequently, even wheelchair athletes (who can be considered to be at the highest levels of cardiopulmonary fitness in the SCI population) cannot attain peak oxygen uptake levels through upper limb exercise that are comparable to those potentially reached by neurologically intact people during leg cycling exercise.

Secondly, in individuals with SCI, a haemodyamic response known as "circulatory hypokinesis" is observed during arm-cranking exercise. This refers to the reduced cardiac output, and the impaired ability to distribute blood throughout the vascular system effectively [54]. In the intact human body, with increasing intensity of upper-body exercise, reflex control of the distribution of cardiac output causes some characteristic changes in blood pressure and vascular resistance. Local mediators in the exercising muscles cause intense vasodilation that increases blood flow to support metabolic demands. At the same time, the muscles that are not involved in the exercise (such as the large muscles of the legs, during upper-body exercise) are vasoconstricted from reflex increases in sympathetic nerve activity. In this way, systemic vascular resistance falls, but systolic blood pressure typically rises progressively with an increase in $\dot{V}O_2$ [2]. Hence, in able-bodied individuals performing upper-body exercise, the muscle pump in the legs maintains adequate venous return to the heart. However, in SCI, this muscle pump in the legs is absent. The lack of venous return from the paralysed lower limbs in SCI is therefore thought to contribute significantly to the observed circulatory hypokinesis during upper-body exercise, as the heart rate consequently needs to increase in order to maintain the cardiac output [50]. Studies combining voluntary arm-cranking with FES-leg cycling (hybrid exercise) in tetraplegia [49, 82] and paraplegia [74, 91] claim to reduce this effect.

In their study comparing the metabolic and haemodynamic responses of tetraplegics performing voluntary arm crank ergometry (ACE) alone, FES-leg cycle ergometry (FES-LCE) alone, and hybrid exercise (ACE + FES-LCE), Hooker *et al.* [49] illustrated that the oxygen uptake achieved during hybrid exercise could be increased significantly from that elicited during either of the individual exercise modalities during submaximal exercise.

This type of hybrid exercise could potentially lead to central cardiovascular adaptations, thereby increasing the cardiac output produced, compared with ACE alone or FES-LCE alone. Hooker *et al.* suggest that this is due to an increase in HR and SV, and a decrease in total peripheral resistance. However, although it has been shown that hybrid exercise can induce relatively high peak physiologic responses and may place the optimal load on the cardiovascular system of individuals with tetraplegia, it seems that the two exercise modes may interfere with one another at higher power output levels and may not be tolerated by some individuals [35, 49]. A possible reason for this is that, when the legs and arms are working concurrently, the "legs may not compete successfully with the arms for their limited share of blood flow" [35]. This may be exacerbated in tetraplegia due to excessive venous pooling and limited venous return.

2.4.2 Maximising the Potential for FES-Upper Body Exercise in Tetraplegia

Many of the studies discussed so far have investigated the use of FES-exercise in the lower limbs (with or without voluntary arm-cranking) to encourage central adaptations. However, peripheral adaptations through training (even in the general population), are known to be modality-specific [69]. Therefore, individuals with SCI can train up the leg muscles through lower-limb FES exercise, but the increase in $\dot{V}O_{2max}$ would not translate to increased exercise capacity of muscles in the upper limbs during upper body activity. This is not of primary concern in paraplegia where there is ample opportunity to maintain upper body fitness and strength through wheelchair propulsion, wheelchair sports, and other voluntary upper-body exercise training.

In contrast, the importance of developing peripheral adaptations in the upper limbs through the chosen FES-exercise modality is much greater in tetraplegia, where the exercise could build on any remaining voluntary control of upper body musculature. The extent to which this can be achieved clearly depends on the exact level of the lesion, and on whether or not the cervical lesion is complete or incomplete, but by developing a system that is adaptable (to take into account the extent of remaining upper body function), the potential benefits of regular use of the system could be maximised for each individual.

In a study looking to develop a system specifically aimed at the tetraplegic group, Needham-Shropshire *et al.* [77] investigated the use of electrical stimulation of the triceps applied during arm-cranking exercise in a group of tetraplegics. Following

a period of training with the system, a significant increase in manual muscle grade scores was shown, demonstrating a functional benefit of FES-assisted arm-cranking exercise.

Potential additional benefits of regular FES-assisted arm-cranking exercise in tetraplegia above the C7 level may include cardiopulmonary and other health benefits. which were not explored in the Needham-Shropshire *et al.* study. Although the muscles involved in arm-cranking are smaller than in leg-cycling, improvements in peak oxygen uptake measured during the exercise would be associated with beneficial peripheral adaptations in the arms, and possibly even some central adaptations.

The exercise responses in tetraplegics able to perform voluntary arm-crank ergometry were compared to those in paraplegia and able-bodied individuals in a study by Van Loan *et al.* [113]. The study showed a much reduced peak oxygen uptake in the group of tetraplegic individuals, when compared with both the paraplegic and able-bodied group, during voluntary arm-cranking exercise. A system that builds up the upper body musculature through regular FES-assisted arm-cranking training could increase peak oxygen uptake during this type of exercise, involving muscles that are required for the limited remaining function of the upper body in the C4–C6 group. In this way, even if predominantly peripheral as opposed to central training adaptations could result from the FES-assisted upper-body exercise, they would be valuable in terms of functionality, in so much as they might facilitate activities of daily living requiring muscular endurance or high peak force (such as wheelchair propulsion, transfers, and pressure relieving exercises).

Could regular sessions of exercise achieved through electrical stimulation of key upper limb muscles address both health and functionality deficits present in the tetraplegic population, thus resulting in multiple potential benefits of FES-arm cranking exercise? This idea is explored in the following chapters, which detail the development and assessment of methods for FES-assisted arm-cranking exercise in tetraplegia.

Chapter 3

Methods

3.1 Summary

This chapter introduces the systems for FES-assisted arm-crank ergometry, and the protocols for their evaluation with tetraplegic volunteers. The chapter begins by providing details of the hardware, software and set-up which make up the systems that were assessed. The protocols used for the experimental evaluation are described: protocols for muscle strengthening, exercise testing (incremental and constant-load), exercise training and data analysis. The methods were based on standard exercise evaluation methods, but incorporate necessary novel modifications for use with the target C4–C6 SCI population.

3.2 Methods for FES-ACE

The system assessed here for its potential as an FES exercise modality in tetraplegia was developed by Gollee *et al.* [41]. Based on an instrumented commercial arm crank ergometer, it allowed for both active and passive exercises. The instrumentation enabled measurement of torque at the cranks and generated power output. This system of FES-Arm Crank Ergometry is referred to as FES-ACE in the remainder of this thesis.

3.2.1 Apparatus & Set-up

The general set-up, illustrated in Figure 3.1, consisted of the ACE device, the neuromuscular stimulator and the pattern generator (implemented in software).

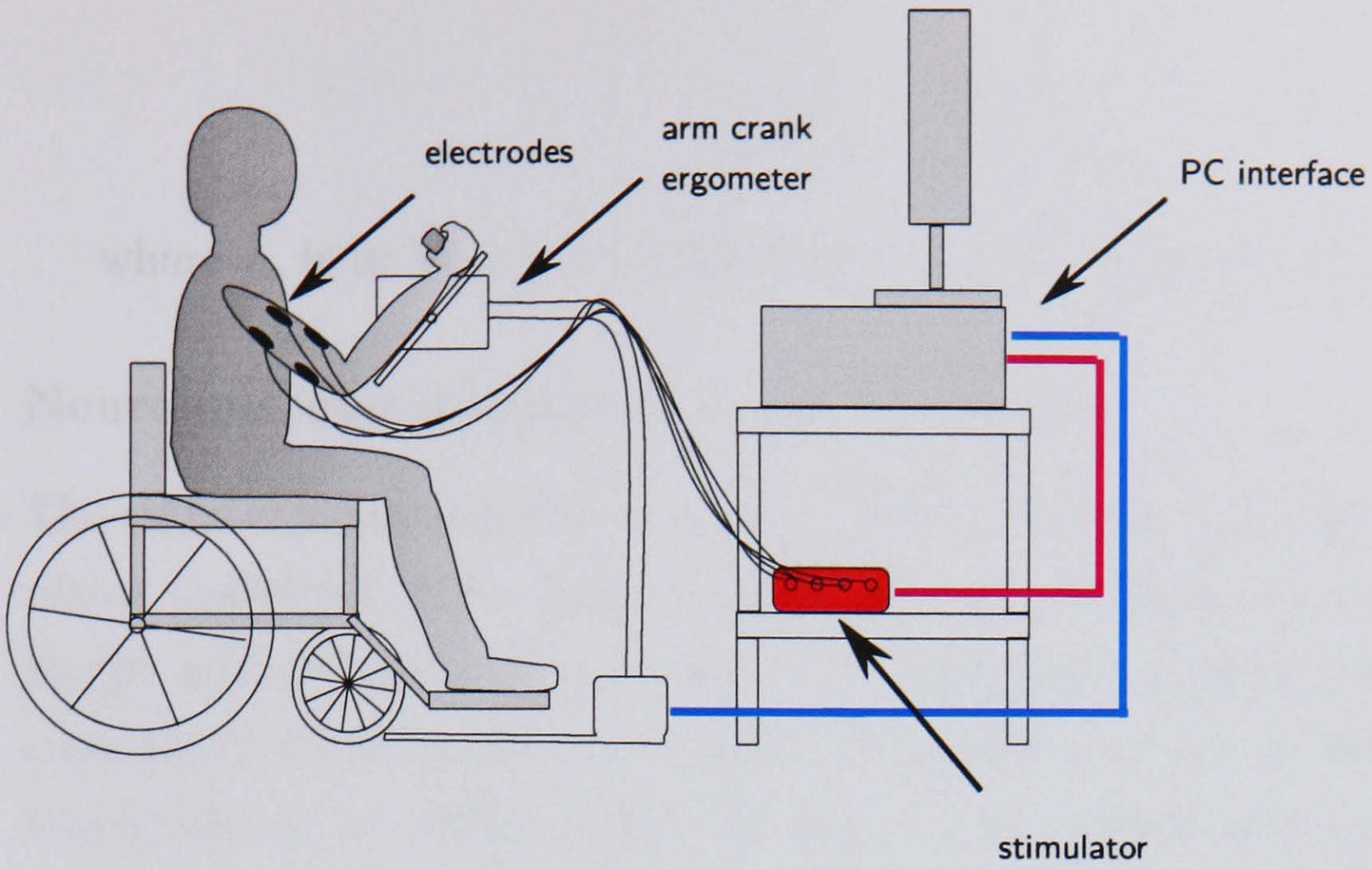


Figure 3.1: Set-up for FES-ACE sessions.

Instrumented ACE

The arm crank ergometer (ACE) used here was the TheraVital trainer (Medica Medizintechnik, Germany). The ACE device provided measurements of the crank angle, θ, the angular velocity, ω, and the motor torque, m_o, via a serial communication interface. The cadence was recorded as the number of revolutions per minute (rpm) of the right crank arm. The arm-rests were bolted to the cranks at their pivot point. The pivot point on the arm-rests formed a circular motion during the arm-cranking exercise. However, due to the positioning of the arms in the arm-rests, and the positioning of the subject in relation to the ergometer, this resulted in an eliptical motion of the hands.

The extension and flexion moment induced by the muscular contractions at the elbow generated a force at the cranks of the ACE device that induced an external moment, m_e. For a constant cadence, the torque generated by the motor, m_o, was equal to the external moment applied at the cranks, m_e. In this case, the motor torque was used as a measurement of the external moment, m_e. The motor torque, m_o, was derived from measurements of the current through the motor. It had been calibrated in such a way that it was zero when no external torque was applied. If an external resistance was applied at the cranks and the motor had to generate an active torque, then $m_o > 0$. If the cranks were propelled actively by the subject and the motor had to generate a resistive torque then $m_o < 0$. Power output, p_e, was computed from the torque, m_e, and cadence, c, as shown in equation 3.1.

$$p_e = \frac{2\pi}{60} c m_e \tag{3.1}$$

where p_e is in W, c is in revolutions per minute (rpm), and m_e is in Nm.

Neuromuscular stimulator & gel electrodes

The eight-channel stimulator used in all FES-ACE sessions was the Stanmore Stimulator (Salisbury, UK). Four of these stimulation channels were used: left and right biceps and left and right triceps. The stimulation pulses produced were current-controlled, monophasic rectangular. Frequency was set at 20Hz, with the current amplitude set at either 30mA or 40mA (the current could potentially be varied in 10mA steps up to a maximum of 130mA). Pulsewidth was adjustable in steps of 0.5μs, and was varied using a throttle, implemented as a potentiometer. During individual sessions, only the stimulus pulsewidth was varied between 0μs and a maximum safety limit of 500μs. This was the only stimulation variable used to control the stimulation intensity during FES-ACE sessions.

The gel electrodes used here were the 50mm diameter round PALS Ultraflex (Axelgaard, California, U.S.A.). These were placed over the bulk of the *biceps brachii* and of the *triceps brachii* (lateral or medial head).

Software implementation

The pattern generator drove the neuromuscular stimulator via an isolated RS232 link. The pattern generator was implemented in software in Matlab/Simulink (The Mathworks, Massachussets, U.S.A.) and used an algorithm in which, for each muscle group, a nominal angular stimulation range was defined. These ranges are shown in Figure 3.2, and were such that the appropriate muscles were stimulated during each part of the cycle for a smooth cranking motion. In addition, a speed correction factor was incorporated to compensate for the delay between stimulation and muscle contraction: hence, the stimulation ranges were brought forward as the cadence increased.

The PC Matlab Simulink interface provided real time graphical displays of target and actual cadence, stimulation levels to each of the four muscles, crank position, torque and power output generated.

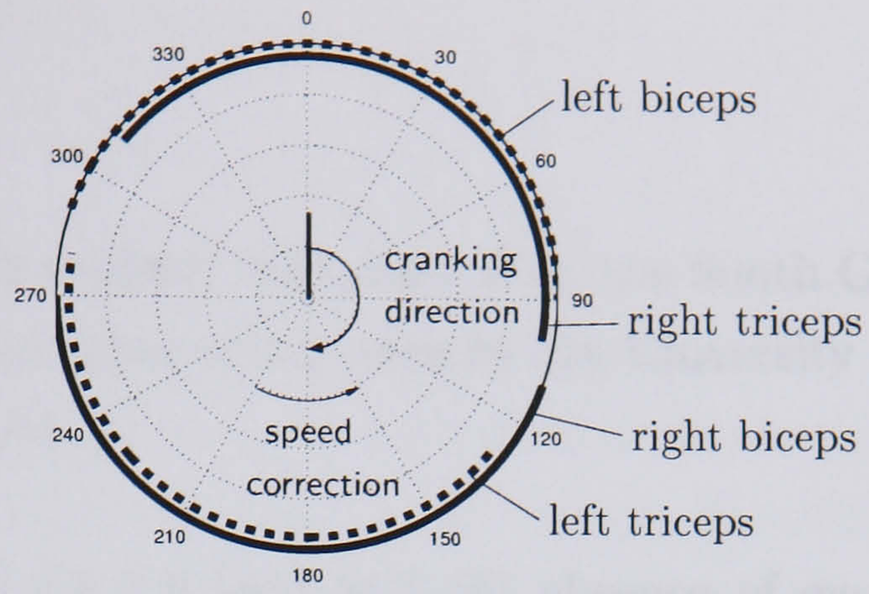


Figure 3.2: Nominal stimulation ranges [41]. The angle is shown as the position of the right crank arm.

Control systems

During training sessions and, more importantly, during exercise tests, it was necessary to control the work rate accurately at all times. In exercise testing, physiological responses are dependent on work rate. The power output (or work rate) was computed as the product of the cadence and torque applied at the cranks by the subject, and so both these inputs needed to be controlled.

1. **Cadence -** Visual feedback was provided on the PC screen with a real-time display of target cadence and actual cadence. To maintain the desired cadence, the subject was encouraged by the investigator to put in maximal effort using remaining voluntary control of upper body musculature. In addition, the investigator used the visual feedback to control the stimulation intensity to the biceps and triceps muscles, using a manual throttle[1].

2. **Torque -** There were two feedback loops for motor torque control: an 'Active Torque Controller' and a 'Resistive Torque Controller'. A Controller Switch was used to switch between the two. The inputs to the 'Active Torque Controller' were: torque reference, motor torque (averaged over one revolution), and switch output. The output was the active motor torque. The inputs to the 'Resistive Torque Controller' were: torque reference and external torque (produced by the subject). The output was the resistive motor torque. This allowed smooth transition between active and passive FES-ACE.

[1]This manual method of control of cadence differed from some FES-cycling studies in which feedback control of cadence incorporated automatic control of stimulation intensity [51, 52]. One reason for using manual stimulation control here was for patient comfort: some subjects included in this pilot study were sensory incomplete and could therefore feel the stimulation. The second reason was to allow for varying levels of voluntary input from the subject.

3.2.2 Subjects

Candidate selection

Full ethical approval for this project[2] was granted by the South Glasgow University Hospitals NHS Trust, and for parts of the work by the University of Glasgow Ethics Committee (see Appendix A).

Inclusion criteria were: (i) C4–C6 level SCI (ii) absence of excessive upper-limb spasticity (< 2 on the Modified Ashworth Scale, see Appendix A), (iii) absence of significant upper-limb joint contractures, (iv) absence of significant denervation of biceps and triceps muscles, (v) no history of significant postural hypotension, (vi) no history of significant autonomic dysreflexia, and (vii) neurological stability.

Candidates were given a patient information sheet and asked to provide informed consent (see Appendix A) prior to evaluation of muscle response to electrical stimulation.

Additional requirements for inclusion were: (i) satisfactory outcome of assessment of biceps and triceps response to FES, and (ii) ability of the candidate to give the time commitment for the proposed training programme.

Subjects included in the study

The details of the subjects who were recruited for the study are given in Table 3.1. 'Age' and 'Time since injury' are as at the beginning of each person's participation.

Subject	Age	Sex	Level of injury	Time since injury
A	38	M	C6 (incomplete*)	18 years
B	52	F	C6 (complete)	7 months
C	23	M	C5 (complete)	4 years
D	17	M	C4 (incomplete*)	6 months
E	33	F	C4/5 (complete)	16 years

Table 3.1: Details for subjects recruited for the FES-ACE pilot study; M: male, F: female, *: motor and/or sensory incomplete SCI.

[2]This formed part of the work funded by the UK EPSRC (Grant GR/R30730) and by the European Commission (Grant MCFI 2000-02190), on the "Development of Systems for Tetraplegic Arm Cranking using Functional Electrical Stimulation: a pilot study".

3.2.3 Procedures

General set-up and FES-ACE procedures

The general set-up that was used for FES-ACE sessions is shown in Figure 3.1. The subject remained in his/her wheelchair, and was positioned so that the centre of the cranks was horizontally aligned with the shoulders of the individual [13]. The height of the ergometer could be altered to achieve this. The distance between the wheelchair and the ergometer was chosen so that the elbows were slightly flexed at the maximal extension of the cranks [54].

Bandages were used to secure the hands to the armrests, for subjects who were not able to grip the handles due to the paralysis of finger flexors. Straps kept the arms in the arm rests for cranking motion to be restricted to the parasagittal plane. Padding was placed underneath the straps to reduce the risk of marking the skin.

Muscle assessment procedures

The initial muscle assessment involved simply applying surface electrical stimulation over the motor points of the target muscle. For this, a probe was used, and the stimulation intensity was increased until the desired muscle response was observed. The pulsewidth required to achieve this was noted for each muscle individually.

Muscle assessment was also performed prior to each FES-ACE session, to determine the range of pulsewidths to be used in that session. In contrast to the initial muscle assessment, a probe was not used. Instead the electrodes were placed over the muscle bulk and the surface stimulation was applied until the desired response was observed. During these muscle assessments, if the response of the muscle was not ideal, the electrodes were moved and the procedure was repeated until a better response resulted.

Muscle strengthening procedures

Following the initial muscle assessment, to determine the muscle response to stimulation, the next step was to use the FES-ACE to build up the muscles before beginning the formal exercise training programme. In cases of sensory incomplete SCI, this also served to get the subject used to the sensation of the stimulation.

FES-ACE at low cadence (20–30 rpm) and with no resistance (passive training) was used in the initial phase of muscle strengthening. At the start, the subject

underwent sessions of just 5 minutes, twice weekly. Muscle strengthening took place over 4-6 weeks, or until the muscles were strong enough to maintain zero load arm-cranking at 50 rpm (ie. without using the motor assistance to maintain this cadence). During this phase, the length and frequency of the sessions and the target cadence were progressively increased. By the end of the muscle strengthening phase, the subject was required to be able to tolerate 10 minutes of continuous FES-ACE at 50 rpm, at no (or minimal) resistance, in order to progress to the next stage of the programme.

Exercise training procedures

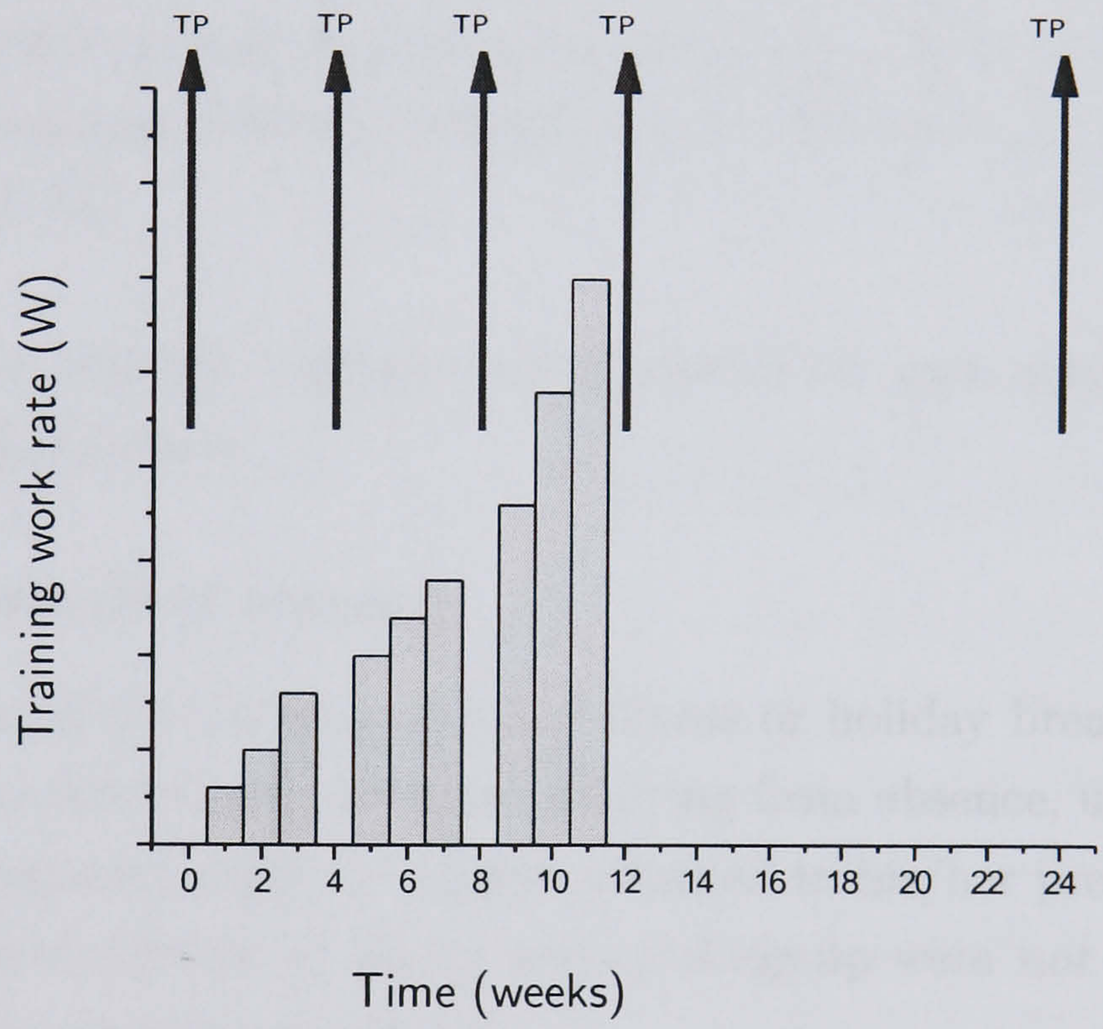


Figure 3.3: General exercise training and testing schedule; TP: test point.

The general timetable of FES-ACE exercise training and testing used with the subjects involved in this pilot study, after successful completion of the muscle strengthening phase, is illustrated in the graph in Figure 3.3. It consisted of:

1. Baseline exercise testing prior to starting the formal exercise intervention.
2. 12 weeks of FES-ACE exercise intervention, using a progressive exercise regime.
3. Repeat exercise testing in weeks 4, 8 and 12 of the exercise programme.
4. Post-training exercise testing in week 24.

The specifics of the chosen FES-exercise training regime were important in determining its efficacy in improving cardiopulmonary fitness. As McLean *et al.* [70] point out, using the popular method of training at a certain percentage of maximum heart rate is of limited use in tetraplegia, due to the severely blunted heart rate response.

Here, training intensity was set in terms of the estimated lactate threshold. The moderate training work rate (below the lactate threshold) chosen by the investigator was based on the subject's most recent incremental exercise test. Both the work rate and the session duration were then progressively increased over the subsequent training period. Over the training programme, the subject worked towards an average of three sessions per week, with each session involving approximately 30 minutes (usually in two bouts of 15 minutes, separated by a few minutes of rest) of FES-assisted arm-cranking at a moderate work rate. This was a similar training protocol to that used in FES leg cycling studies, such as those by Faghri [32, 33] and Barstow *et al.* [9].

The details of the training regimes, individualised for each subject, are given in each case study that follows.

Dealing with periods of absence

Periods of absence of the subject included illness or holiday breaks. To deal with the interruption to the training schedule resulting from absence, upon the subject's return, training resumed until the subject returned to his/her pre-absence training level. The combined periods of illness and catching-up were *not* counted as being part of the exercise intervention period.

Practical considerations

A practical problem which resulted from the compromised blood pressure regulation in tetraplegia was the risk of autonomic dysreflexia (or hyperreflexia). FES applied below the level of the lesion in cases of SCI above the T6 level could theoretically trigger the onset of autonomic dysreflexia [6] [3], but there were no incidences of it over the course of this study. Although candidates with a history of recurrent autonomic dysreflexia were excluded from the study, there was still a risk to any individual

[3] "Stimuli below the level of the lesion that are perceived as noxious, including FES, can cause spinal-cord-level vasoconstrictor reflexes and acute hypertension. This in turn elicits a bradycardia via normal baroreceptor feedback. This autonomic dysreflexia has been reported in patients with SCI performing FES leg extension exercise [9]."

with tetraplegia during FES-exercise. Both the subjects and the investigator were, however, aware of the symptoms. These include a severe headache, heavy sweating (face, neck and shoulders), pale cold skin below the level of the lesion, reddened skin and goose bumps above the level of the lesion, blurred vision and a feeling of anxiety. A bout of autonomic dysreflexia could be life-threatening. If the symptoms and cause had been identified, the trigger for this reflex response would have been removed (the FES, or, for example, a blocked catheter could be the trigger). If removing the source was not sufficient to reduce the blood pressure, medical staff were at hand to administer antihypertensive drugs.

An additional practical consideration during both training sessions and exercise testing was that, with the body under cardiopulmonary stress, the subjects may have had severely impaired thermoregulation [35, 89, 107] due to the level of their injury. Overheating, especially in the warmer months of the year, was therefore monitored. An electric fan was used if necessary to cool the subject down externally.

3.3 Methods for Cardiopulmonary Assessment

The methods developed in this study to assess the potential cardiopulmonary benefits of FES-assisted exercise in the tetraplegic population were derived from standard techniques used in exercise testing during upper body exercise [98]. In parallel with the 4–6 weeks of muscle strengthening that each subject was required to complete, the subject was familiarised with the equipment for physiological assessments, and the testing environment, before the baseline tests were performed.

3.3.1 Familiarisation

Familiarisation was important to make the subject feel as relaxed as possible when formal exercise testing subsequently took place. During exercise testing, the subject wore a mask that covered the mouth and nose. It was common for a subject to hyperventilate when the mask was first put on. During the test, the only influences on the subject's breathing needed to be the physiological stresses placed on the body during exercise. It was therefore important that the subject had become used to wearing the mask and being surrounded by the machines used for recording and monitoring, and that distractions were kept to a minimum [116]. Furthermore, the subject needed to feel that he/she was able to communicate to the investigator if there were any problems during the test. During familiarisation sessions, therefore,

the investigator periodically asked the subject if he/she was feeling 'ok'. and the subject practised how to respond with a single clear blink of the eyes for a 'yes' answer and two clear consecutive blinks of the eyes for a 'no'. This method replaced the thumbs-up and thumbs-down replies used by able-bodied or paraplegic subject during exercise tests.

3.3.2 Apparatus for Exercise Testing

The specifications for each of the devices used for cardiopulmonary measurements and monitoring during exercise testing are given in Appendix A.

Portable breath-by-breath cardiopulmonary measurement

During exercise testing, the MetaMax 3B (Cortex Biophysik, Germany) portable cardiopulmonary measuring system was used. This provided breath-by-breath data on oxygen uptake ($\dot{V}O_2$, in l/min), carbon dioxide output ($\dot{V}CO_2$, in l/min), minute ventilation ($\dot{V}E$, in l/min), respiratory exchange ratio (RER), tidal volume (VT, in l), breathing frequency (fb, in breaths/min), end-tidal tension of oxygen ($PETO_2$, in mmHg) and end-tidal tension of carbon dioxide ($PETCO_2$, in mmHg).

For this, the volume transducer (turbine) and gas sample line were attached to a Hans-Rudolph mask (available in three sizes), which was fitted over the mouth and nose, and tightened to create a good seal. All the gases breathed in and out therefore passed through the mask and transducer. Samples of air traveled down the sample line to the base system, which contained the gas analysers. The composition of the air was determined for oxygen and carbon dioxide.

In this portable system, the oxygen analyser is made up of an electro-chemical cell, based on the principle that chemical reactions between O_2 and a substrate generate a small electric current. The generated current is proportional to the rate of O_2 molecules reacting with the substrate. The carbon dioxide analyser measures absorption by CO_2 over a range of wavelengths of infrared light. Infrared light passes through a cell containing the sampled gas, and the amount of light transmitted is compared to a reference value: absorption is proportional to the fraction of CO_2 in the sample of gas [116].

Spirometer

Resting spirometry data were recorded prior to each exercise test using the MicroLoop Spirometer (Micro Medical, UK). The data of interest were collected during

maximal expiratory effort, to determine Forced Vital Capacity (FVC, in l), Forced Expiratory Volume in the 1^{st} Second (FEV_1. in l). and Peak Expiratory Flow (PEF. in l/s).

For these measurements, the subject wore a noseclip (to ensure that all the air flow was at the mouth), and was asked to take a maximal inspiration before sealing his/her lips around the mouthpiece and blowing into the spirometer for a Forced Vital Capacity test. The subject was instructed to blow as hard, as fast, and for as long as possible until he/she could not blow any more air out. After a short rest, two repeat measurements were made. The best of the three blows was recorded.

Mouth pressure meter

Mouth pressure measurements were made prior to each exercise test using the MPM Mouth Pressure Meter (Micro Medical, UK). During maximal inspiratory effort, maximum inspiratory pressure (PI_{max}, in cmH_2O) was measured. During maximal expiratory effort, maximum expiratory pressure (PE_{max}, in cmH_2O) was measured.

A nose clip pinched the subject's nostrils shut. The valve for 'Expiratory' measurements was attached to the mouthpiece, which allowed the subject to inspire fully through the valve, which then closed during the expiration effort to allow the measurement of expired pressure. The subject was instructed to insert the mouthpiece into the mouth, position the lips around the flange, with the bite blocks between the teeth. The subject was asked to inhale to total lung capacity and then exhale with maximal effort for as long as possible. The PE_{max} was recorded. The valve was then changed to the inspiratory one, which allowed the subject to expire fully, but then closed during the inspiratory effort to allow measurement of the inspired pressure. The subject was instructed to position the mouthpiece in the same way into the mouth, to exhale to residual volume and then inhale with maximal effort for as long as possible. The PI_{max} was recorded (and was the minimum pressure that was sustained for one second).

Pulse oximeter

The 3800 Pulse Oximeter (Datex-Ohmeda, UK) enabled simultaneous recordings of pulse rate (PR, in beats/min)[4] and oxygen saturation of the blood (SpO2, in %),

[4]Ideally, heart rate would have been recorded with a heart rate monitor. A Polar heart rate monitor was used initially during exercise testing familiarisations. However, when the stimulation to the muscles was switched on, this interfered with the signal from the belt worn by the subject

through a RS232 connection to the PC. An ear probe was used with tetraplegic subjects performing arm-cranking exercise, due to limited access to the finger, and the possibility of movement artefacts preventing the use of a finger probe. Readings were recorded every 2 seconds. The pulse rate was used in this study as a measure of heart rate (HR, in beats/min).

Ratings

Subjects were asked to indicate their Rating of Perceived Exertion (RPE) and Rating of Perceived Breathlessness (RPB) from the two scales shown to them during the last 30 seconds of each minute of incremental exercise testing. Ratings of Perceived Exertion were determined using the 15-point Borg Scale [7] shown in Table 3.2, and Ratings of Perceived Breathlessness, using the 12-point scale shown in Table 3.3. The method used for indicating ratings in this study was eye-blinking. The investigator pointed to the chart and moved down the list of ratings. The subject gave a single clear blink of the eyes when the correct rating was reached. This method was chosen as the subject was unable to point to a chart.

6	
7	Very, very light
8	
9	Very light
10	
11	Fairly light
12	
13	Somewhat hard
14	
15	Hard
16	
17	Very hard
18	
19	Very, very hard
20	

Table 3.2: Borg Scale of Ratings of Perceived Exertion.

around his/her chest, preventing us from recording HR in this way.

0	Nothing at all
0.5	Very, very slight
1	Very slight
2	Slight
3	Moderate
4	Somewhat severe
5	Severe
6	
7	Very severe
8	
9	Very, very severe
10	Maximum

Table 3.3: Scale of Ratings of Perceived Breathlessness.

3.3.3 Frequency of Exercise Testing

Following the initial 4–6 week phase of muscle strengthening, a baseline set of tests (Test Point 1, Week 0) was performed with FES-ACE. This could only be carried out with individuals whose muscles were at least strong enough to perform zero-load arm-cranking at 50 rpm for ten consecutive minutes. During the three-month training programme, further exercise tests took place during Weeks 4, 8 and Week 12 (Test Points 2, 3 and 4, respectively). The subject was then asked to return for a final set of tests three months after the end of the training period (Test Point 5). At each Test Point, at least one incremental and at least one submaximal constant load test were carried out, in random order. The tests were performed on different days, ideally with one day of rest between them.

Descriptions follow of the general protocols used in this pilot study. Any variations on these protocols are described individually for each subject in the case studies that follow.

3.3.4 Protocols for Incremental Exercise Testing

A continuous protocol was chosen for incremental exercise testing [98]. The target cadence throughout the tests was set at 50 rpm (but the actual cadence was allowed to vary between 50 and 60 rpm). A sustained drop in cadence below 35 rpm was considered to be the point at which that particular work rate was not successfully achieved by the subject.

Calibration

A volume calibration (using a 3-litre syringe) of the volume transducer and a two-point calibration of the gas analysers of the cardiopulmonary measurement system were carried out prior to each test.

Subject instructions

The subject needed to be familiar with all the equipment, the setting, and the methods prior to the baseline test. This was to ensure that the subject was as relaxed as possible in the testing environment. The subject was asked to refrain from eating, smoking and drinking coffee for 2 hours prior to the test. The subject was also asked to ensure that his/her urine bag was empty before starting. Ideally, the subject should not have performed strenuous exercise for 24 hours prior to the test.

Testing protocol

1. **Rest 1**: When the investigator was satisfied that the subject was relaxed, resting variables were recorded. These resting variables were: (i) FVC, (ii) FEV_1, (iii) heart rate, and (iv) maximum inspiratory and expiratory pressures.

   Once these recordings had been made, the mask was placed over the subject's face and tightened to prevent leakage of air around the mask. The system set-up is shown in Figure 3.4. The mask was connected to the breath-by-breath analysis system once the subject had had a few minutes of quiet rest.

   The subject breathed normally, whilst stationary. until consecutive $\dot{V}O_2$ readings over three minutes were within 5% of each other, and there were no signs of hyperventilation. At this point, recording of resting $\dot{V}O_2$ and monitoring of heart rate began. This recorded resting period lasted at least 3 minutes.

2. **Passive arm-cranking**: Maintenance of the desired cadence of 50 rpm during this initial phase of passive arm-cranking was achieved by using motor power. There was no input from the subject and no FES applied. This phase lasted for 3 minutes and was intended for loosening of the muscles.

3. **Rest 2**: The arms were brought back to rest, and recording of cardiopulmonary data continued whilst the subject was stationary. This phase lasted for 3–4 minutes.

Figure 3.4: Set-up for breath-by-breath measurements during exercise.

4. **Arm-cranking at 'zero load'**: The subject was asked to move the cranks round up to the target cadence of 50 rpm. The FES was only applied at this stage if necessary to maintain the target cadence. Visual feedback of target cadence and actual cadence were continuously provided on the PC screen. Zero load was the work rate at which the subject produced just enough power to turn the cranks round at the desired cadence, without any additional resistance[5]. The subject maintained this work rate for 3 minutes.

5. **Incremental phase**: The FES was switched on, and the resistance was automatically stepped up every minute to increase the work rate in pre-programmed equal steps. The size of the steps in work rate varied between tests. The incremental phase generally lasted 8–10 minutes. In order to maintain the cadence at increasing work rates, the stimulation intensity was increased when appropriate: this was achieved by the investigator, using the throttle.

   During the last 30 seconds at each work rate, RPE and RPB were recorded.

6. **Active Recovery**: The point at which the load was reduced back down

[5]The power required to achieve this was equivalent to approximately 2W (although there was some slight inter-subject variability according to the weight of the subject's arms). The system had been calibrated so that the zero load work rate gave a power output of 0W. The range of passive arm-cranking, during which there was motor assist, was from -2 to 0W.

to 'zero-load' was when the specified cadence could no longer be maintained (when the cadence dropped to below 35 rpm and the stimulation could not be further increased to correct this). The electrical stimulation was gradually turned off during this part of the recovery. This phase lasted for 2–4 minutes (depending on how the subject was feeling).

7. **Passive Recovery**: 'Zero-load' arm-cranking stopped and passive recovery began, with the arms stationary. Recording stopped when values returned to pre-exercise resting levels.

Determination of work rate increments

The work rate increments were set so that the whole incremental phase of the test lasted (ideally) between 8 and 10 minutes [100]. Performance of the subject in the week prior to exercise testing allowed the investigator to determine the appropriate step size. The step sizes used for each incremental test are stated in each case study.

3.3.5 Protocols for Constant Load Exercise Testing

Calibration

A volume calibration (using a 3-litre syringe) of the volume transducer and a two-point calibration of the gas analysers of the cardiopulmonary measurement system were carried out prior to each test.

Subject instructions

The subject instructions were the same as for Incremental Exercise Testing (see previous section).

Testing protocol

1. **Rest 1**: When the investigator was satisfied that the subject was relaxed, resting variables were recorded. These resting variables were: (i) FVC, (ii) FEV_1, (iii) heart rate, and (iv) maximum inspiratory and expiratory pressures.

Once these recordings had been made, the mask was placed over the subject's face and tightened to prevent leakage of air around the mask. The mask was connected to the breath-by-breath analysis system.

The subject breathed normally, at rest, until consecutive $\dot{V}O_2$ readings over

three minutes were within 5% of each other, and there were no signs of hyperventilation. At this point, recording of resting $\dot{V}O_2$ and monitoring of heart rate began. This recorded resting period lasted at least 3 minutes.

2. **Passive arm-cranking**: Maintenance of the desired cadence of 50 rpm during this initial phase of passive arm-cranking was achieved by using motor power. There was no input from the subject and no FES applied. This phase lasted for 3 minutes and was intended for loosening of the muscles.

3. **Rest 2**: The arms were brought back to rest, and recording of cardiopulmonary data continued whilst the subject was stationary. This phase lasted for 3–4 minutes.

4. **Arm-cranking at 'zero load'**: The subject was asked to move the cranks round up to the target cadence of 50 rpm. The FES was only applied at this stage if necessary to maintain the target cadence. Visual feedback of target cadence and actual cadence were continuously provided on the PC screen. Zero load was the work rate at which the subject produced just enough power to turn the cranks round at the desired cadence, without any additional resistance. The subject maintained this work rate for 5 minutes.

5. **Constant load phase**: The FES was switched on, and the resistance was automatically stepped up to one constant work rate. This constant load was maintained for 12–15 minutes. In order to maintain the cadence at the specified work rate, the stimulation intensity was increased if necessary.

6. **Active Recovery**: The point at which the load was reduced back down to 'zero-load' was either at the end of the set constant load phase (12–15 minutes), or if fatigue set in before this was completed, and the specified cadence could no longer be maintained (when the cadence dropped to below 35 rpm) even with increased stimulation. The electrical stimulation was gradually turned off during this part of the recovery. This phase lasted 2–4 minutes (depending on how the subject was feeling).

7. **Passive Recovery**: 'Zero-load' arm-cranking stopped and passive recovery began, with the arms stationary. Recording stopped when values returned to pre-exercise resting levels.

Determination of 'constant load' work rate

The work rate for each constant load test was chosen to be submaximal and below the estimated lactate threshold, in the moderate exercise intensity range.

3.3.6 Outcome Measures

- **Graphical representation of data**

  Graphical representation of the cardiopulmonary data was based on the 9-panel array of graphs recommended by Wasserman *et al.* [116]. Here, the cardiopulmonary data are presented in a 10-panel array (to include RPE and RPB) which consists of the following graphs:

  1. $\dot{V}E$ (l/min) vs. power output (W)
  2. HR (beats/min) vs. power output (W)
  3. $\dot{V}O_2$ and $\dot{V}CO_2$ (l/min) vs. power output (W)
  4. $\dot{V}E$ (l/min) vs. $\dot{V}CO_2$ (l/min)
  5. HR (beats/min) and $\dot{V}CO_2$ (l/min) vs. $\dot{V}O_2$ (l/min)
  6. Ventilatory equivalents for O_2 and CO_2 vs. power output (W)
  7. VT (l) vs. $\dot{V}E$ (l/min)
  8. RER vs. power output (W)
  9. $PETO_2$ and $PETCO_2$ (mmHg) vs. power output (W)
  10. RPE and RPB vs. power output (W)

  Although all these variables were plotted, not all of the results in these plots are discussed here (for example, RPE and RPB), in order to focus the thesis on the most informative outcome measures.

- **Peak power output**

  The peak power output was taken to be the mean power output of the last (or highest) completed stage of the incremental FES-ACE exercise test.

- **Peak $\dot{V}O_2$**

  According to the guidelines recently provided by the American Thoracic Society and the American College of Chest Physicians [2], "the peak value reported should represent the mean of the last completed stage or all of the data collected during the final stage, but preferably for not less than 30 seconds". Here, the mean $\dot{V}O_2$ was calculated for the last thirty seconds of the last (or highest) completed stage of the incremental test.

- **"Lactate" threshold**

  The lactate threshold was *estimated*, using the V-slope method [116]. This method is based on excess CO_2 being generated when lactate is increased during exercise, due to the bicarbonate buffering of lactic acid [11]. $\dot{V}CO_2$ was plotted against $\dot{V}O_2$, and the point of inflexion in the relationship between the two variables was taken to be indicative of the threshold. Here, the edited $\dot{V}O_2$ and $\dot{V}CO_2$ data were used, excluding the initial rest phase, and the final recovery phase. No blood lactate samples were taken to validate the estimation of the lactate threshold, due to the invasive nature of the blood lactate sampling technique.

- **Efficiency**

  Calculations to determine the efficiency of FES-ACE in tetraplegia were made from the constant load tests, all of which were chosen to be submaximal. The assumption was that the steady-state was reached in each test. Three efficiency calculations were made, namely: (i) gross efficiency (see equation 3.2), (ii) net efficiency (see equation 3.3), and (iii) work efficiency (see equation 3.4). These were determined for each constant load test, according to the following equations [38, 39, 104].

$$\text{Gross efficiency } (\%) = \frac{W}{E} \text{ x } 100 \tag{3.2}$$

$$\text{Net efficiency } (\%) = \frac{W}{(E - E_r)} \text{ x } 100 \tag{3.3}$$

$$\text{Work efficiency } (\%) = \frac{W}{(E - E_0)} \text{ x } 100 \tag{3.4}$$

where:

W = caloric equivalent of measured external work performed,
E = aerobic caloric expenditure of the subject during exercise,
E_r = aerobic caloric expenditure of the subject at rest,
E_0 = aerobic caloric expenditure of the subject during unloaded pedalling ("zero load").

- **Gas exchange kinetics**

  The time constants for $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}E$ were obtained from constant load tests. Where the constant load work rate was of moderate intensity, and hence

below the lactate threshold, a single exponential curve could be fitted to the plotted edited data to determine the time constant for each variable.

The first 25 s were not included in the analysis, as they were attributed to phase I kinetics. For the remaining data, the equation (see 3.5) used to fit the expected exponential response curve for $\dot{V}O_2$ was adapted from [123].

$$\Delta\dot{V}_{O_2}(t) = \Delta\dot{V}_{O_2}(ss) \text{ x } (1 - e^{-\frac{t}{\tau}}) \tag{3.5}$$

where:

$\Delta\dot{V}_{O_2}(t)$ = the increase in $\dot{V}O_2$ above the control value at time t,
$\Delta\dot{V}_{O_2}(ss)$ = the steady-state increment in $\dot{V}O_2$,
τ = the time constant of the response.

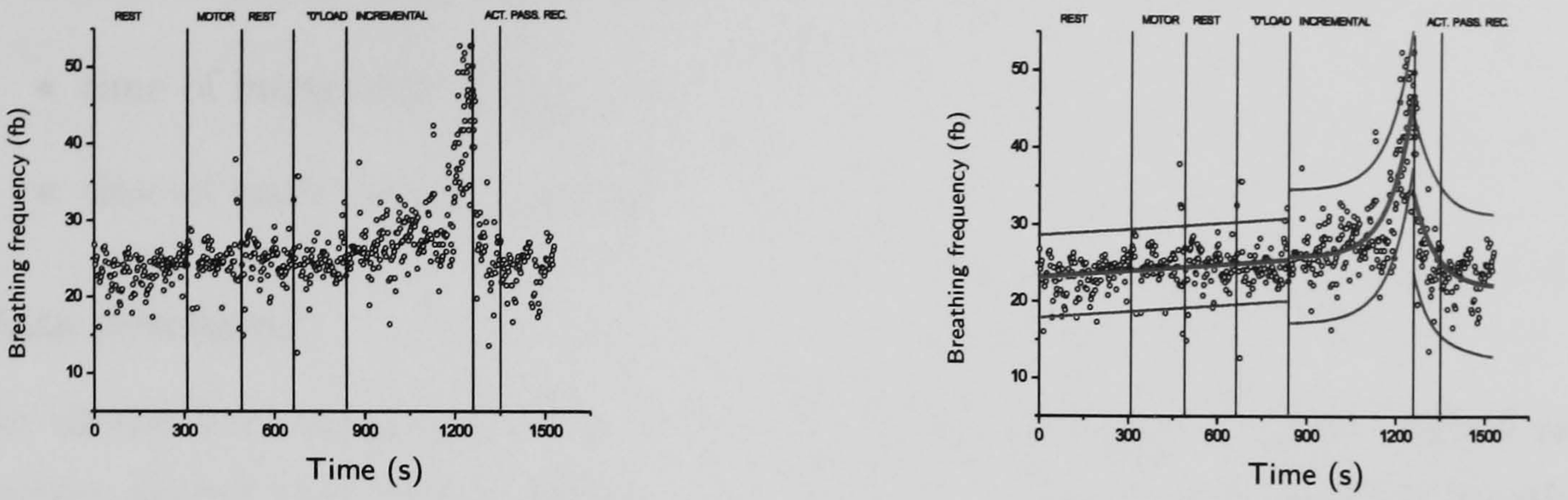
The same basic equation was used to determine the time constants for $\dot{V}CO_2$ and $\dot{V}E$, substituting the $\Delta\dot{V}_{O_2}$ terms in equation 3.5 with $\Delta\dot{V}_{CO_2}$ and $\Delta\dot{V}_E$, respectively.

3.3.7 Data Analysis

Raw gas exchange data

The raw gas exchange data obtained during exercise testing were displayed and recorded breath by breath. A number of primary variables were automatically determined from the measurements of air flow and time (from the volume transducer) and gas composition (from the oxygen and carbon dioxide analysers). These included tidal volume, breathing frequency, times of inspiration and expiration, inspired fractions of oxygen and carbon dioxide, and end-tidal tensions of oxygen and carbon dioxide. As an example, raw breath-by-breath data for one of these primary variables — breathing frequency (fb), in breaths/min — are shown graphically in Figure 3.5(a).

A number of derived variables were automatically calculated in software, according to algorithms detailed in [116]. These included oxygen uptake, carbon dioxide output, respiratory exchange ratio, and minute ventilation.



(a) Raw data for 'fb'.

(b) Data for 'fb', with best fit curves and 95% prediction bands superimposed, at ±2 standard deviations of the mean response.

Figure 3.5: Procedure for data editing, shown here for breathing frequency (fb) response by Subject B from an incremental exercise test. Points lying outwith the prediction bands were identified as outliers, and were subsequently deleted to produce the edited dataset.

Editing of gas exchange data

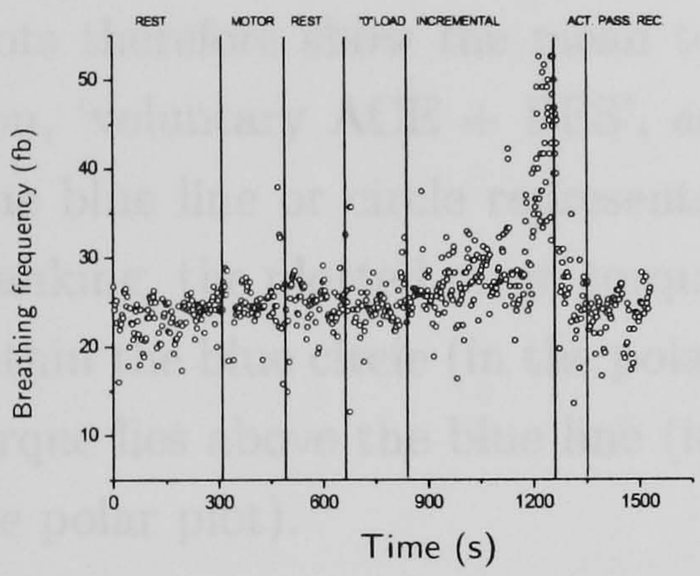
Editing was carried out, based upon the primary variables, using the Origin (Origin 7.5, OriginLab, Massachussets, US) statistical package. A linear (or cubic) best curve fit (using a 95% confidence limit) was determined for each step of the test. This method used the least sums of squares approach. Prediction bands were set at 95% which, in statistical terms, should have included datapoints within ±2 standard deviations [97] of the estimated mean. An example of this procedure is given in Figure 3.5(b). Data points lying outwith the 95% prediction bands were deleted, to produce the edited dataset, before any averaging of the data was performed. The curve fitting and prediction band delineation were performed on the following primary variables:

- breathing frequency (fb)
- tidal volume (VT)
- end-tidal oxygen tension ($PETO_2$, in mmHg)
- end-tidal carbon dioxide tension ($PETCO_2$, in mmHg)
- fractional concentration of oxygen in inspired gas (FIO_2)

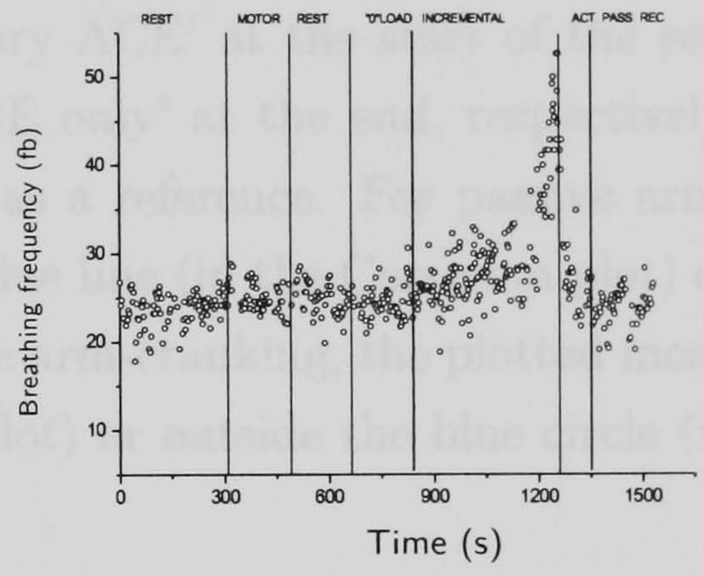
- fractional concentration of carbon dioxide in inspired gas ($FICO_2$)
- time of inspiration (T_{insp}, in s)
- time of expiration (T_{exp}, in s)

Data averaging

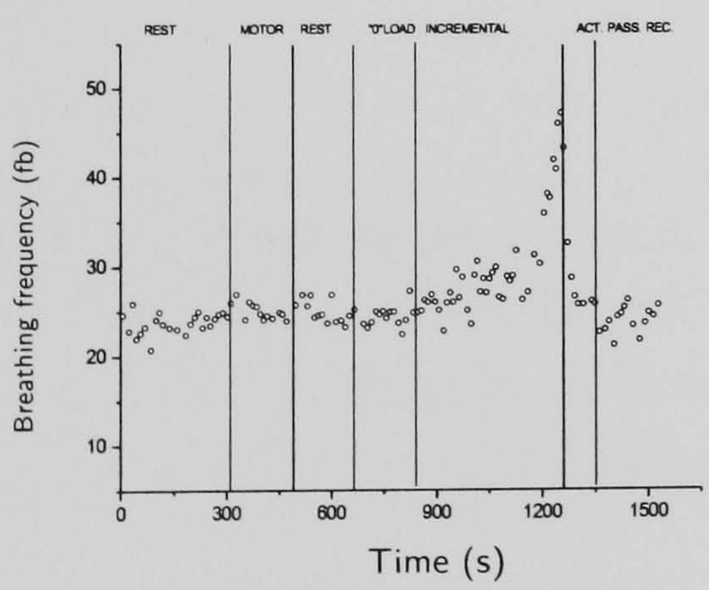
For clearer representation of the data to illustrate the trends in physiological responses during incremental exercise (see Figure 3.6), averages of consecutive breaths were taken, based on the edited data. 4-breath and 8-breath averages were calculated in each case (see Figure 3.6(c) and 3.6(d)). The 4-breath averaged data were arbitrarily chosen for clear graphical representations of the data in most cases (except for unusually long tests, for which 8-breath averages were presented instead).



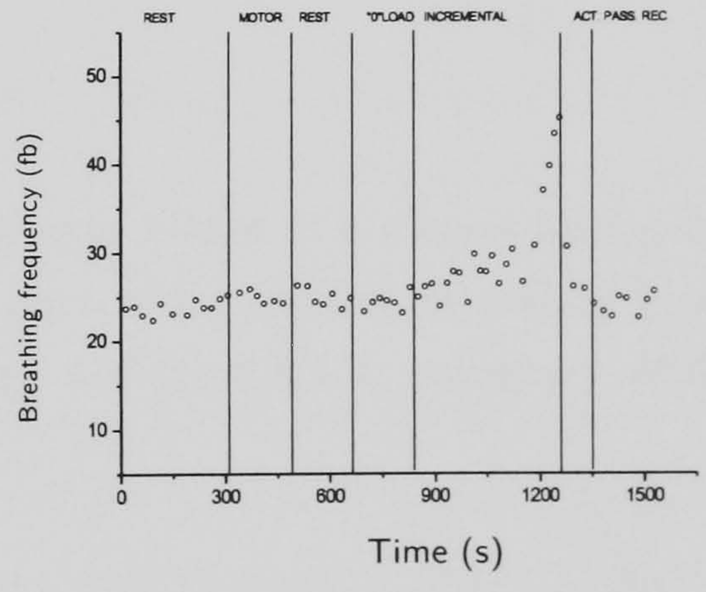
(a) Raw data.



(b) Edited data (outliers removed).



(c) Edited, 4-breath average.



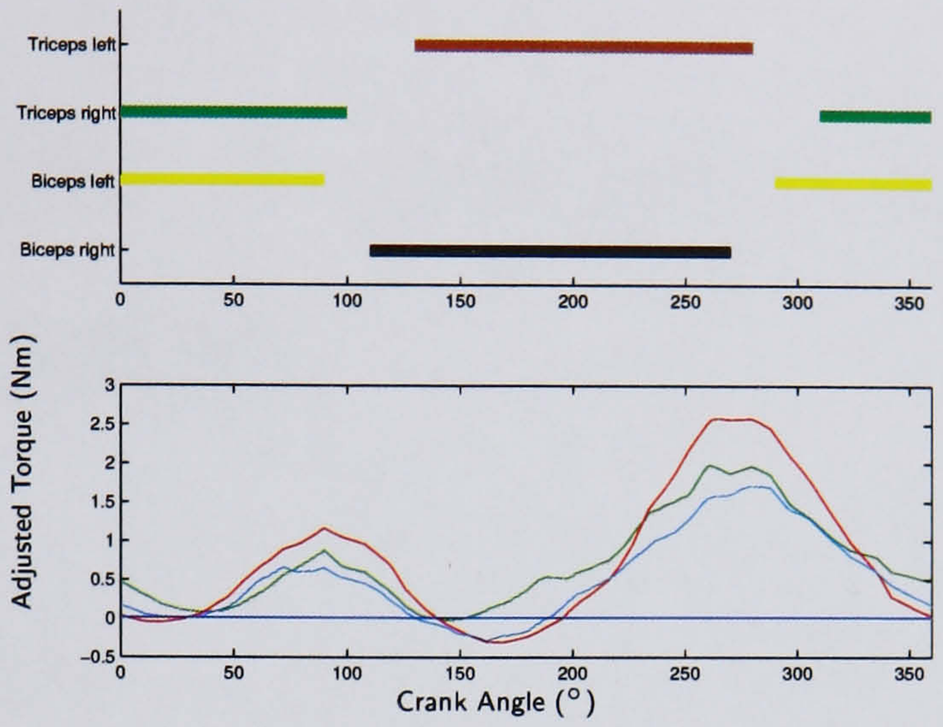
(d) Edited, 8-breath average.

Figure 3.6: Graphical display of the process of data editing and averaging, using real data for breathing frequency (fb) obtained from an incremental test with Subject B.

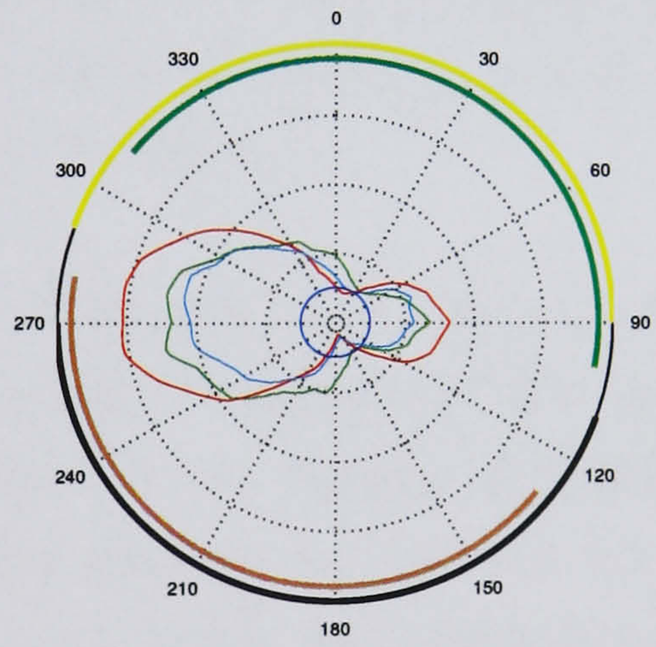
In Figure 3.7, the raw data (stimulation intensity, crank angle, torque, cadence and power) are presented in relation to time. The software, developed by Gollee [41], allowed different parts of the session to be selected for subsequent plots of mean values.

Analysis was performed separately on each selected phase of the training session (each represented by a different colour - green, red and cyan). For each phase, the mean torque was automatically calculated and plotted in relation to the crank position in a Cartesian plot in Figure 3.8(a) and in a polar plot in Figure 3.8(b).

The colours on the top graph of Figure 3.8(a) and on the outside edge of the circle in Figure 3.8(b), represent the stimulation ranges for each of the four target muscles (triceps left, triceps right, biceps left and biceps right). The colours on the bottom plot of Figure 3.8(a) and within the circle in Figure 3.8(b) refer back to the three phases selected from the raw data plot in Figure 3.8. The green, red and cyan data plots therefore show the mean torque for 'voluntary ACE' at the start of the session, 'voluntary ACE + FES', and 'voluntary ACE only' at the end, respectively. The blue line or circle represents the 'zero-load', as a reference. For passive arm-cranking, the plotted mean torque lies below the blue line (in the Cartesian plot) or within the blue circle (in the polar plot). For active arm-cranking, the plotted mean torque lies above the blue line (in the Cartesian plot) or outside the blue circle (in the polar plot).



(a) Cartesian plot of torque



(b) Polar plot of torque

Figure 3.8: Mean torque per cycle, plotted for each selected phase of a muscle strengthening session performed by Subject C. For the torque data plots, the colour coding is as follows. GREEN: voluntary ACE only; RED: voluntary + FES; CYAN: voluntary ACE only. The BLUE line or circle represents 'zero load'.)

Chapter 4

Case Study 1 - Subject A, C6 (Incomplete)

4.1 Summary

The primary aim of this chapter is to provide a preliminary evaluation of the systems and protocols for FES-ACE exercise training and testing with a tetraplegic volunteer. Additional goals include identifying possible benefits to the individual of the regular use of the exercise modality.

The subject for this case study was male, with a chronic C6 (incomplete) SCI. He took part in a programme that consisted of five weeks of muscle strengthening, a baseline set of exercise tests, three months of FES-assisted ACE training (three times per week), and repeat exercise tests at the end of each month of training, and again post-training. The exercise tests provided measurements of upper limb strength (peak power output), cardiopulmonary fitness (peak oxygen uptake, lactate threshold, response kinetics, efficiency) and pulmonary function (lung capacity, peak expiratory flow, respiratory muscle power), allowing us to monitor these outcome measures over the period of participation. Data from incremental exercise tests with this subject revealed increases in both upper limb strength and cardiopulmonary fitness as a result of the exercise intervention. Peak power output increased by 450% over the three month period, with an associated increase in peak oxygen uptake of 50%. Furthermore, the subject was able to maintain the positive effects of training after FES-ACE training intervention ended. Vital capacity (measured at rest) was generally unaffected by training, but peak expiratory flow and respiratory muscle power increased over the exercise period. In contrast to incremental tests, data obtained from constant load tests were less informative about a possible training

effect, as response kinetics could not be extracted for each test point. However, the data were used to estimate indices of efficiency. Gross and net efficiency seemed to improve over the training period.

This case study provides an initial experimental evaluation of the novel systems and protocols developed in this project. It shows that the FES-ACE can be used by people with tetraplegia as an exercise modality. Furthermore, it demonstrates that the exercise training and testing protocols developed in this study are appropriate (although some aspects of constant load testing may require modification). Using these training and testing protocols, even with a short three-month training intervention, benefits of the regular use of the FES-ACE methods are illustrated for an individual with chronic C6 (incomplete) SCI. Training effects are demonstrated mainly through increases in peak power output and peak oxygen uptake. This case study highlights the feasibility of using such systems and protocols in tetraplegia, and the potential for follow-on studies to be performed.

4.2 Methods

4.2.1 Subject Details

The details of the subject described in this case study are given in Table 4.1. This was a 38-year-old male with chronic SCI, 18 years post-injury, and training status prior to participation in this pilot study which could be classified as extremely sedentary [55]. The table also shows the subject's neurological status.

Subject A	
Age	38
Time since injury	18 years
Sex	Male
Neurological status	C6 (incomplete); good voluntary control of biceps right (BR) and biceps left (BL), weak triceps right (TR), very weak triceps left (TL)

Table 4.1: Details for Subject A ('Age' and 'Time since injury' are as at the start of participation in the study).

4.2.2 Details of Training & Testing Programme

The general timetable and protocols for exercise training and testing followed those described in Section 3.2.3. Any additional details of the training programme used with this individual are given in Tables 4.2 and 4.3. The schedule for exercise testing is given in Table 4.4. These regularly repeated tests were used to monitor indicators of cardiopulmonary fitness over the course of the training programme, and to identify either positive potential carry-over effects or unfavourable de-training effects post-training.

	Week -5	**Week -4**	**Week -3**	**Week -2**	**Week -1**
Number of sessions	2	2	2	2	3
Session duration	10 mins	15 mins	20 mins	25 mins	20 mins
Work rate	-2W*	-2W*	-2W*	0W	0W

Table 4.2: Muscle strengthening programme used with Subject A. (* The -2 W work rate refers to 2 W power produced by the motor, and not the subject, for passive arm-cranking.)

	Weeks 1-3	**Weeks 5-7**	**Weeks 9-11**
Number of sessions	3	3	3
Session duration	20 mins	25 mins	2 x 15mins
Work rate (start)	3W	10W	18W
Work rate (end)	8W	14W	30W

Table 4.3: FES-ACE training programme used with Subject A.

Test Point	**Week 0 TP1**	**Week 4 TP2**	**Week 8 TP3**	**Week 12 TP4**	**Week 16 TP5**	**Week 24 TP6**
Increments for IC test	1W	1W	2W	4W	4W	4W
Work rate for CL test	-	8W	12W	22W	22W	22W

Table 4.4: FES-ACE testing schedule used with Subject A (IC: Incremental; CL: Constant Load).

The time-line for this exercise training and testing is illustrated in Figure 4.1. As this shows, Subject A did voluntary arm-cranking exercise at home between TP5 and TP6, but no written record was kept of the frequency (although it was about 2 to 3 times per week) and work rates used during that period. The work rates could not be easily determined with the commercial arm-crank ergometer that the subject had at home. Instead, the subject exercised at a level that seemed to him to replicate a similar level of work as he had reached at the end of FES-ACE training.

Although the provisional timetable of testing and training had included three months without exercise between TP4 and TP5 (to observe any potential de-training effects), a deviation is to be noted here. The investigator felt it unfair and perhaps unreasonable to prevent the subject from continuing arm-cranking exercise and at least maintain (if not improve upon) the new levels of upper body strength and cardiopulmonary fitness reached through the FES-ACE training programme, if he so desired. The parties therefore agreed that this three-month break from exercise would be reduced to one month, which gave the subject time to purchase a commercial ACE for home use before the post-training test (TP5) was performed, and voluntary arm-cranking exercise could begin.

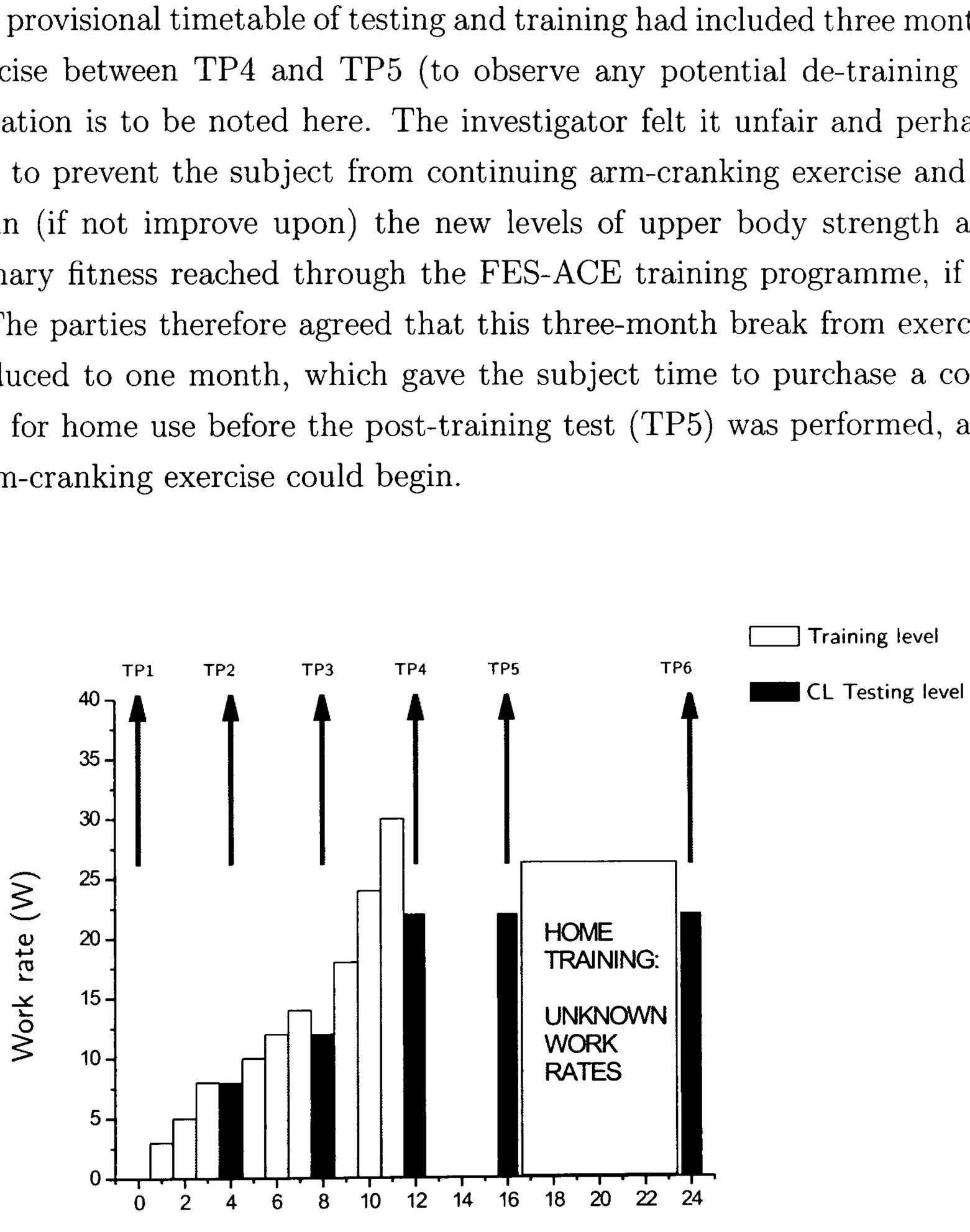


Figure 4.1: Training and constant load testing schedule used with Subject A; CL: Constant Load.

In terms of percentage of peak power output that each of the constant load work rates represented, they were 40 to 45% for TP2, TP3 and TP 6, and 55% for TP4 and TP5.

4.3 Results

The results are given separately for: (i) incremental tests, (ii) constant load tests, and (iii) lung function tests.

4.3.1 Incremental Tests

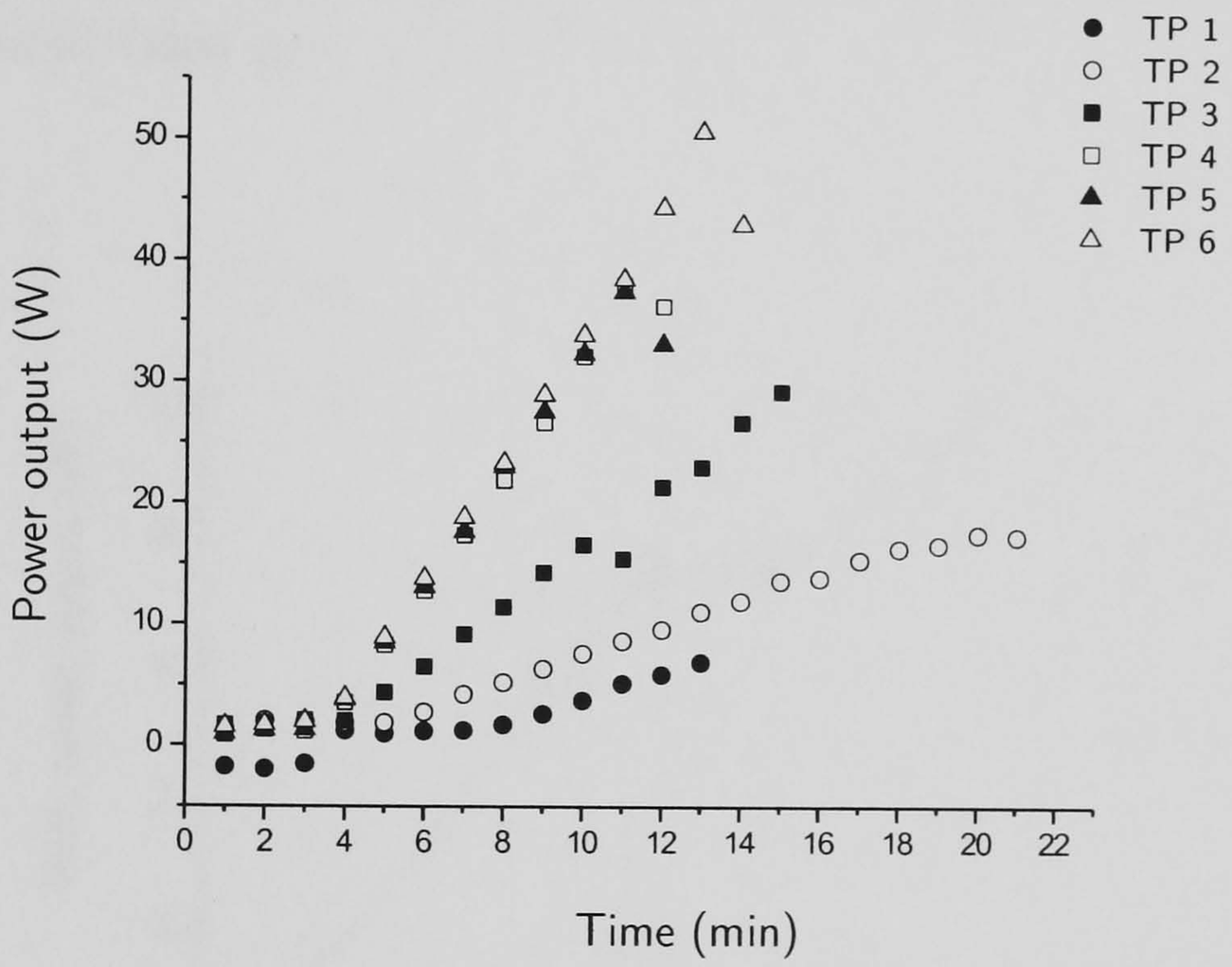


Figure 4.2: Profile of increasing work rate (power output) for each incremental test performed by Subject A.

The progressive increase in work rate followed by Subject A during each incremental FES-ACE test is shown in Figure 4.2. The graph illustrates that, following recorded rest periods, each incremental test began with arm-cranking at zero load for three minutes. Thereafter, the work rate was incremented in equal steps every minute within each test, until the subject could no longer continue to maintain a cadence of around 50 rpm. At each test point, the size of the increment was chosen so that the incremental phase would last between 8 and 12 minutes. This was successfully achieved for most test points, except TP2, for which the incremental phase lasted

considerably longer (17 minutes). The investigator, based upon the training in the week prior to the test at TP2, had not anticipated that the subject would do so well and reach such a high peak power output at this point.

The work rate profile additionally illustrates the effect of spasm on the power output during the test. This is clear for TP3 where, between minutes 10 and 12, there was a transient drop in power production during a period of spasm. The subject, when asked, indicated that he would work through it, which he did satisfactorily.

Peak power output

The 60s-mean power outputs produced in the last (or, for TP4, TP5 and TP6, the highest) completed stage of each incremental exercise test are shown in Figure 4.3, and summarised in Table 4.5.

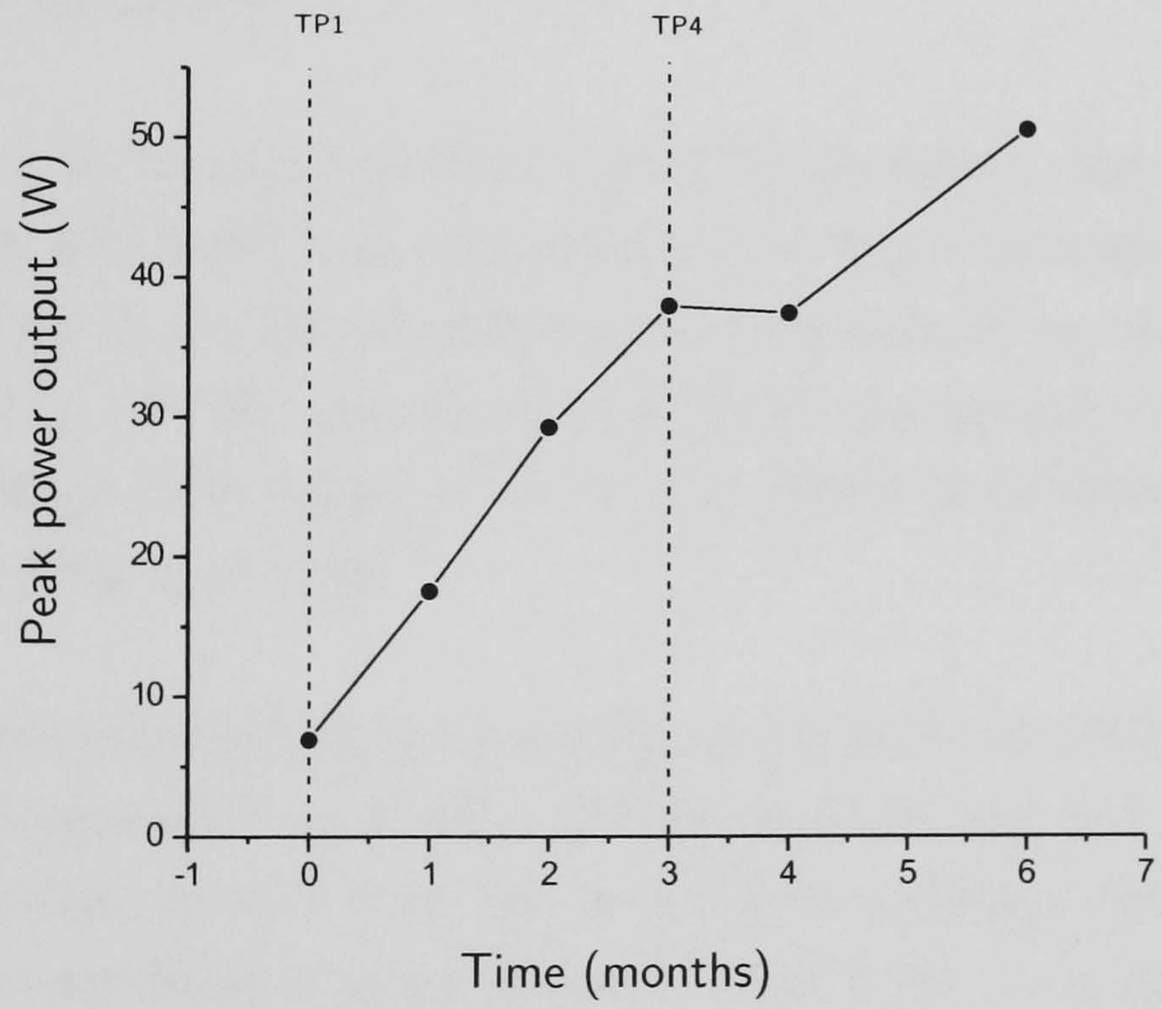


Figure 4.3: Peak power output achieved by Subject A at each test point. TP1 and TP4 are shown to highlight the start and end of FES-ACE exercise intervention. For each test point, the peak power output was calculated as the mean power output during the last (or highest) completed stage of the incremental test.

At TP1, and hence prior to any exercise intervention, this person was able to produce a baseline peak power output of 7 W during the incremental FES-ACE test. From this baseline, Subject A's peak power output increased at a rate of approxi-

Test Point	Training status	Peak Power Output (W)	Change in Peak Power Output (W)
1	**Baseline** (no prior training)	**6.9**	–
2	+1 month FES-ACE	17.6	+ 10.7
3	+2 months FES-ACE	29.3	+ 11.7
4	**+3 months FES-ACE**	**38.0**	+ 8.7
5	+1 month post-training (no exercise)	37.5	- 0.5
6	+3 months post-training (voluntary ACE)	50.7	+ 13.2

Table 4.5: Peak power output data for Subject A. The data for TP1 and TP4 are highlighted, as the start and end of FES-ACE intervention.

mately 10 W per month of training, so that by the end of the FES-ACE programme, he was able to produce 38W.

With this subject, it was also possible to track the changes in the outcome parameters after the end of FES-ACE exercise intervention. In the first month post-training (leading up to TP5 tests), the subject did not take part in any form of exercise at home. Tests at TP5 revealed that the level of power production capability had been maintained (37 W at TP5, compared to 38 W at TP4), illustrating some carry-over potential of this type of exercise.

Taking the investigation further, we were able to re-assess the subject's capabilities in the FES-ACE ergometer two months after the post-training test point. The difference at TP6 was that, by this time, the subject had purchased an un-instrumented active arm-crank ergometer for use at home. This relied on voluntary input only. Hence, the subject was able to resume a two- or three- session-per-week training regime over this period, but this time with no FES-assistance. At TP6, two months into the home exercise routine, there was a further increase in peak power output when compared to the end of FES-ACE training, to a new peak of 51 W. Averaging at 6.5 W increase per month of voluntary arm-cranking training, this was a slightly reduced rate of improvement than with the FES-ACE training. Even so, this showed that Subject A had the potential to improve further, and the willpower to adhere to an exercise regime that had been initiated in this pilot study.

Peak oxygen uptake

The mean resting oxygen uptake, peak oxygen uptake and slope of oxygen uptake against power output (over the linear portion of the relationship only) are shown for each test point in Table 4.6. The resting oxygen uptake was calculated as the mean of the last three minutes of the recorded resting phase data. For the peak oxygen uptake, the mean of the last thirty seconds of the last (or highest) completed stage of the incremental test is given. The peak oxygen uptake is plotted for each test point in Figure 4.4.

Test Point	**Resting $\dot{V}O_2$ (l/min)**	**Peak $\dot{V}O_2$ (l/min)**	**Gradient of slope of $\dot{V}O_2$ vs. PO**
1	**0.270**	**0.708**	**0.026 (R^2=0.40)**
2	0.173	0.875	0.023 (R^2=0.75)
3	0.254	0.891	0.024 (R^2=0.76)
4	**0.230**	**1.054**	**0.015 (R^2=0.87)**
5	0.215	1.085	0.017 (R^2=0.87)
6	0.260	1.206	0.017 (R^2=0.87)

Table 4.6: Oxygen uptake data for Subject A. Correlation coefficients are given for the gradient of the linear approximation of oxygen uptake against power output.

Looking at the baseline cardiopulmonary fitness value (at TP1), peak oxygen uptake was calculated at 0.71 l/min. From this baseline (TP1) to the end of FES-ACE training (TP4), a 50% increase was observed, to 1.05 l/min. As with changes in peak power output, the progression in peak oxygen uptake was gradual over the three-month FES-ACE exercise intervention period.

Subject A maintained this higher cardiopulmonary fitness over the month with no exercise intervention: the re-test peak oxygen uptake at TP5 was 1.09 l/min. In the same way as the peak power output was unaffected by one month without training, there was a carry-over of the improved cardiopulmonary fitness over that month.

In concert with the pattern in power production, a further increase in peak oxygen uptake was recorded in TP6, at 1.21 l/min, in response to two additional months of exercise training (this time performing voluntary arm-cranking exercise at home).

Oxygen uptake is plotted against power output for the incremental test at each test point in Figure 4.5. The linear approximation of the relationship between $\dot{V}O_2$

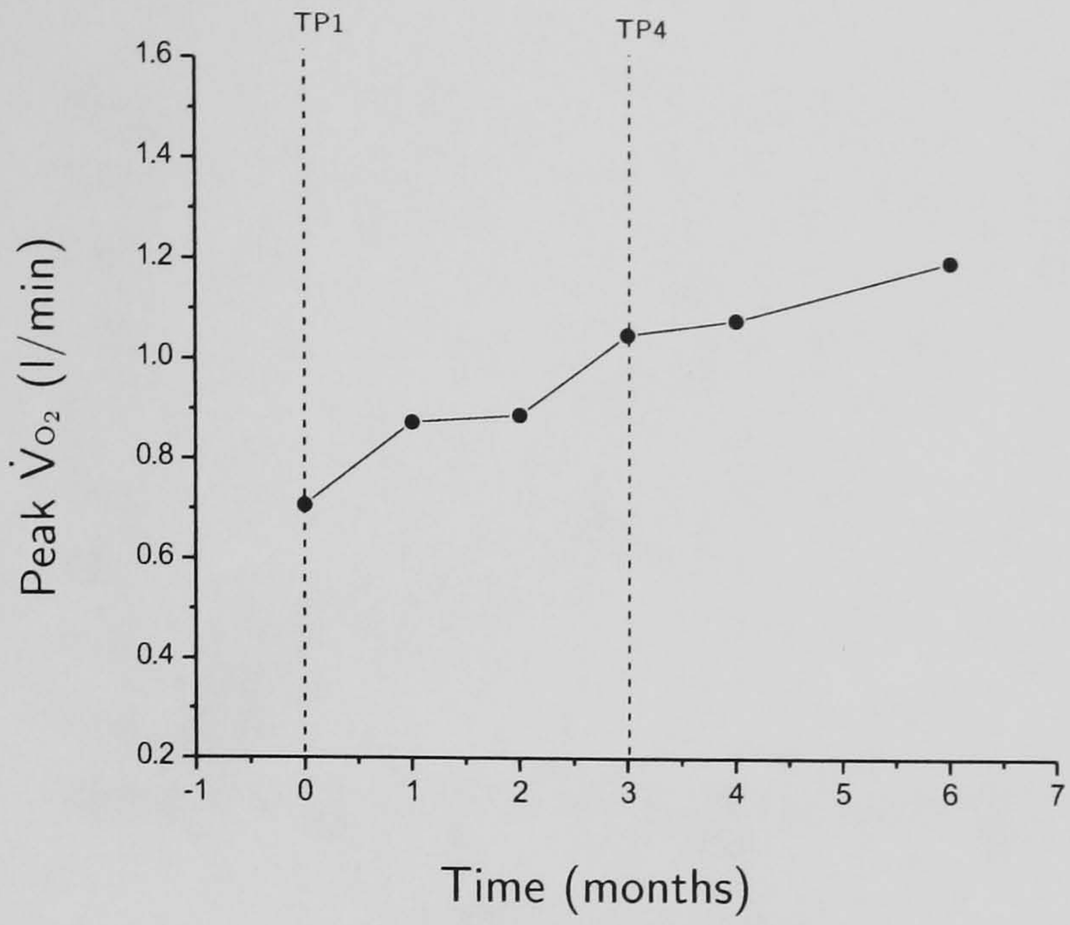


Figure 4.4: Peak oxygen uptake for Subject A at each test point. TP1 and TP4 are shown to highlight the start and end of FES-ACE intervention. For each test point, the peak oxygen uptake was calculated as the mean of the last thirty seconds of the last (or highest) completed stage.

and power output was estimated for each test point for Subject A, as shown in the graph in Figure 4.6. For TP3–TP6, the linear approximation was fitted only to the earlier part of the $\dot{V}O_2$ – power output relationship, as the linear relationship did not appear to hold at higher power outputs. Correlation coefficients for these linear approximations varied from $R^2 = 0.40$ at TP1 to $R^2 = 0.87$ at TP4, TP5 and TP6. The gradient of the slope decreased considerably overall, from 0.026 at baseline to 0.015 at end of training (see Table 4.6). This slope increased slightly to 0.017 during the month without exercise, which was then maintained when exercise resumed. The y-intercept of the linear relationship decreased between TP1 and TP4, suggesting that the oxygen cost of performing the exercise at a particular work rate decreased with training.

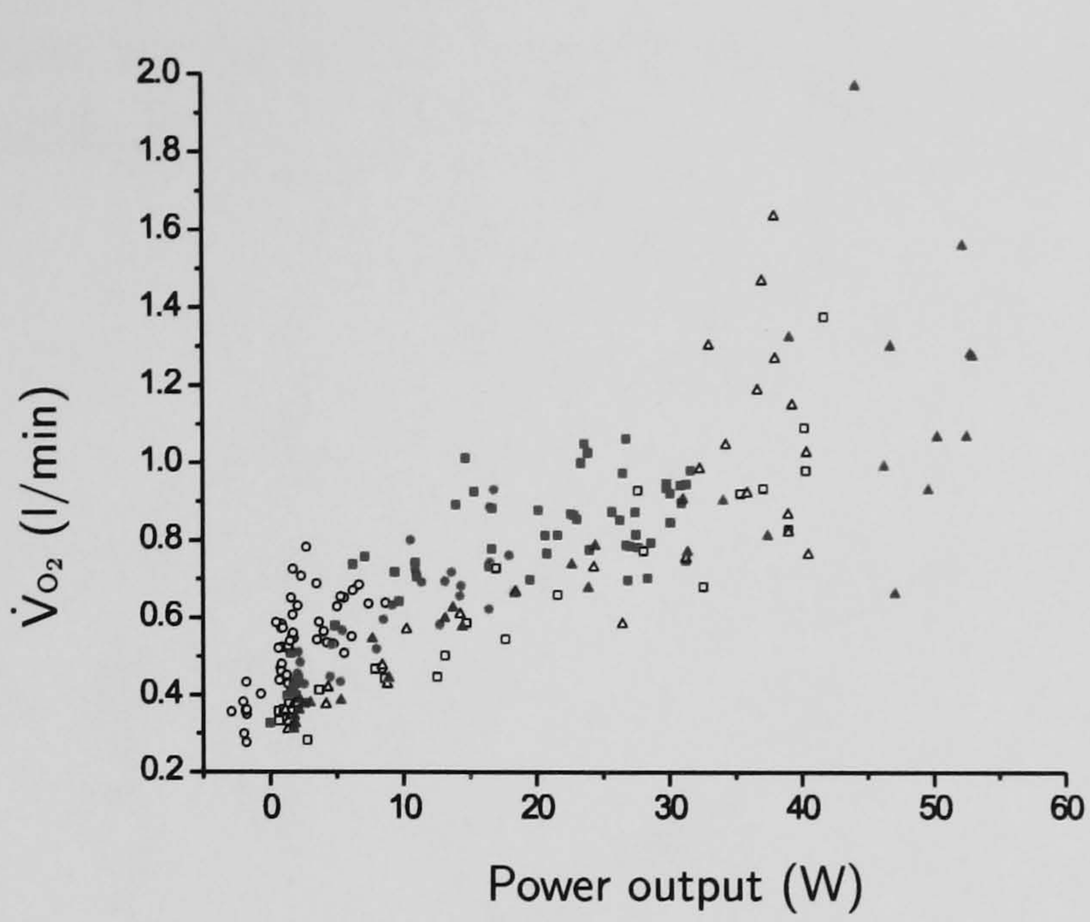


Figure 4.5: Oxygen uptake plotted against power output for Subject A for the incremental test at each test point. The oxygen uptake data have been edited and either 4-breath or 8-breath averaged.

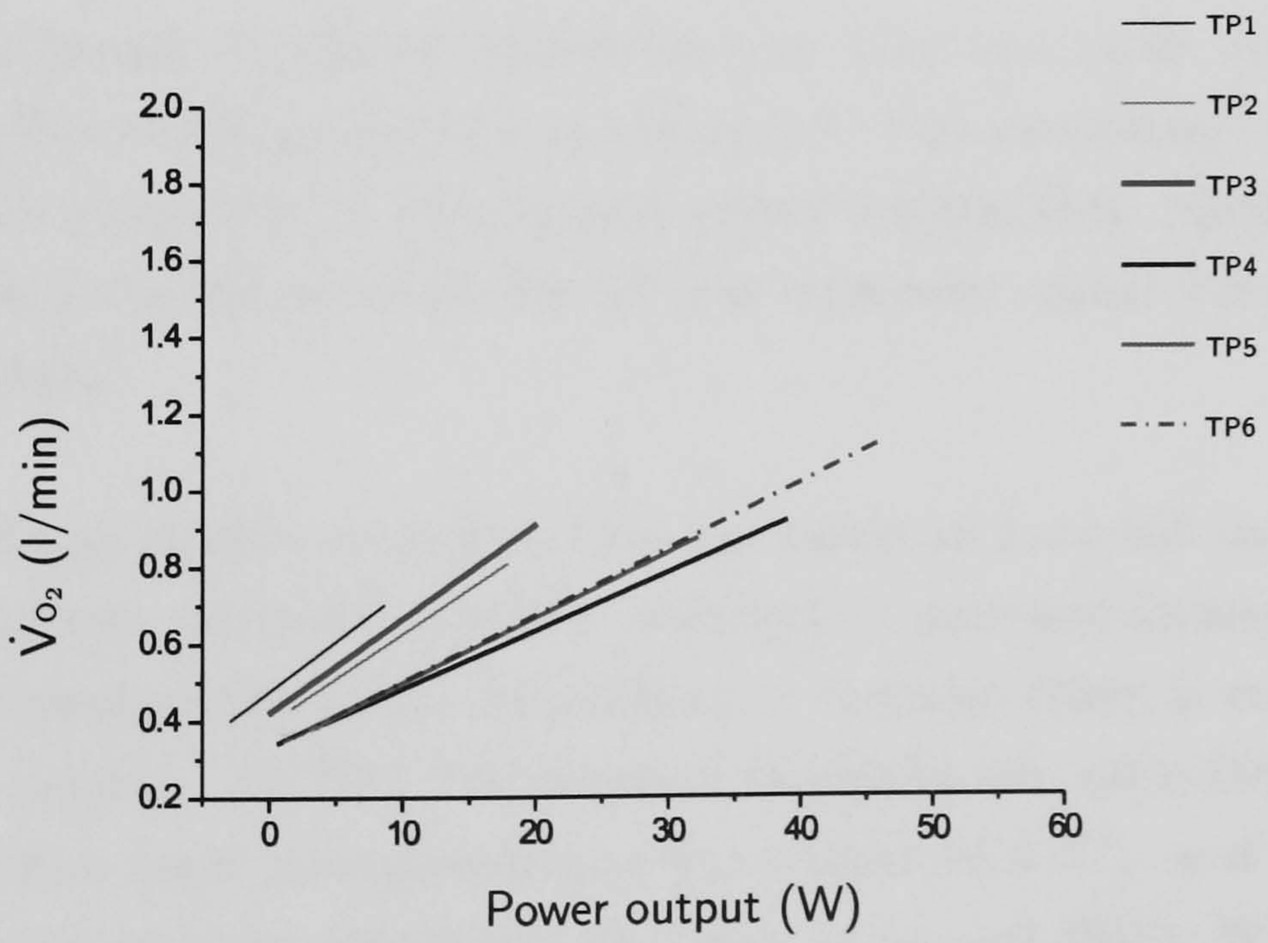


Figure 4.6: Linear approximation of oxygen uptake against power output for Subject A at each test point. For TP3–TP6, the linear fit was performed only on the early portion of the test as the linearity was not evident at higher power outputs.

Lactate threshold

An example of the use of the V-slope method to determine the lactate threshold is given for TP2 in Figure 4.7.

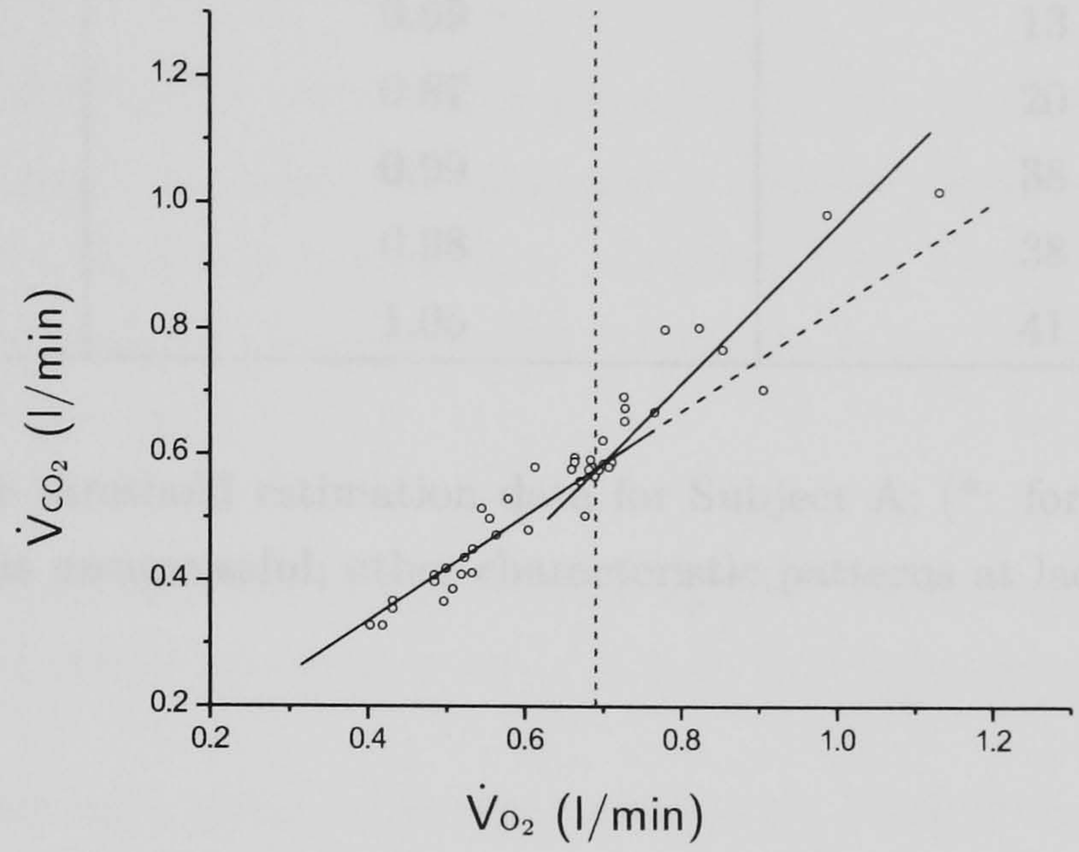


Figure 4.7: Illustration of the V-slope method, shown for data for Subject A, at TP2.

The estimated lactate thresholds determined for each test point are presented in Table 4.7 and illustrated graphically in Figure 4.8. The percentage of peak oxygen uptake that the estimated LT represented varied considerably, ranging from 43 to 100%. The power output at which the LT was estimated varied from 87 to 98% or peak power output.

In so far as the thresholds estimated here are taken to have the same descriptive value as the lactate threshold typically observed in maximal incremental exercise testing with neurologically intact individuals, a training effect is once more illustrated in this subject. At TP1, the baseline threshold was estimated at a $\dot{V}O_2$ of around 0.62 l/min (and corresponding power output of 3 W), and this gradually increased over the training period to 0.99 l/min (at around 38W). With only a negligible dip to 0.98 l/min one month post-training, this lends further support to the idea that Subject A was able to maintain the new level of cardiopulmonary fitness reached through FES-ACE training. The additional two months of unassisted arm-cranking training at home then seemed to lead to a further increase in this threshold to around 1.05 l/min (with a power output of 41 W).

Test Point	Estimated value of $\dot{V}O_2$ at threshold (l/min)	Estimated value of PO at threshold (W)
1	0.62	3
2	0.69	13
3	0.87	20
4	0.99	38
5	0.98	38
6*	1.05	41

Table 4.7: Lactate threshold estimation data for Subject A; (*: for this test point, the V-slope method was unsuccessful; other characteristic patterns at lactate threshold were therefore used).

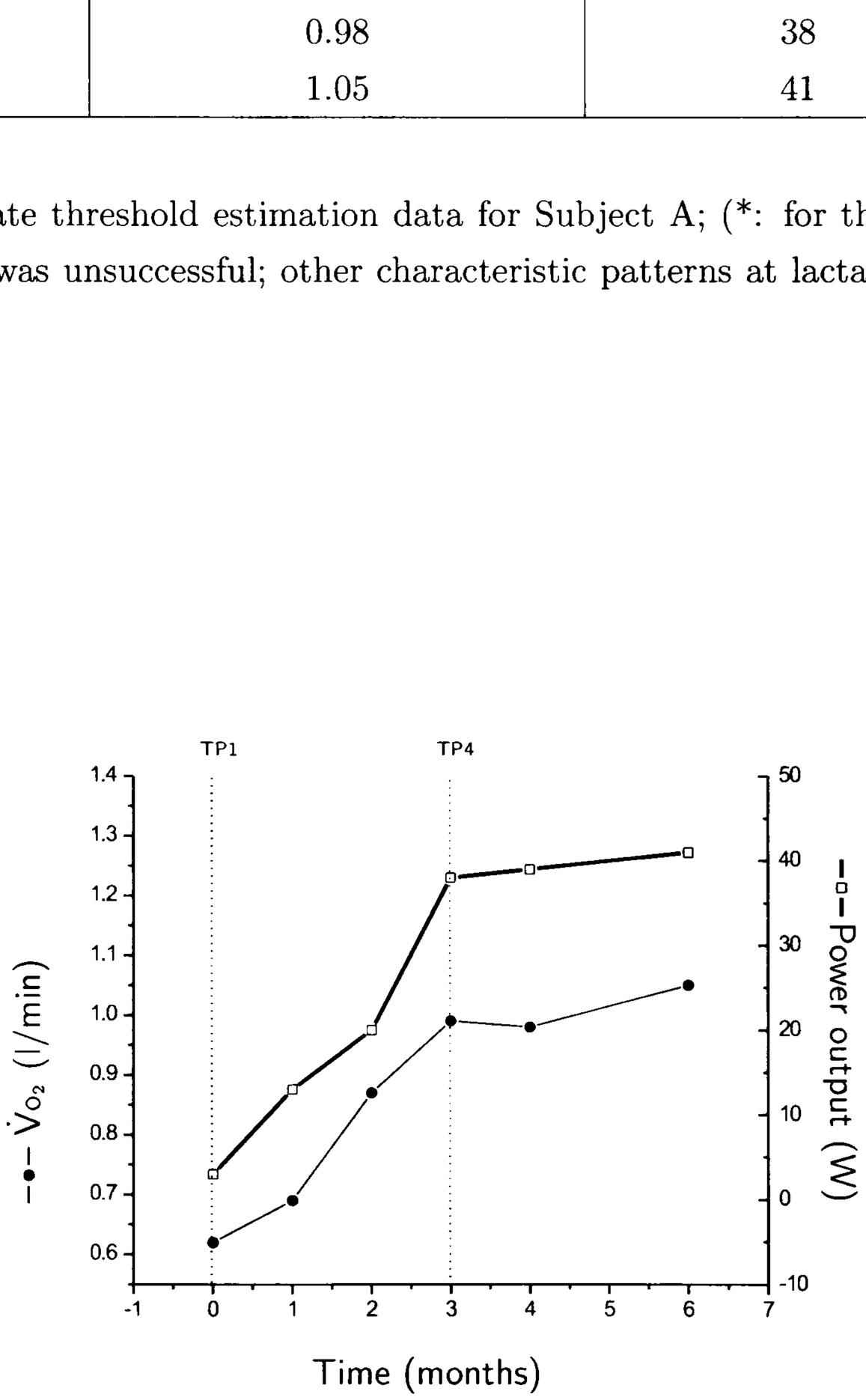


Figure 4.8: Value (or range) of oxygen uptake and power output at the estimated lactate threshold for Subject A at each test point.

In summary, the three main outcomes of the incremental tests — namely, peak power output, peak oxygen uptake and estimated lactate threshold — were shown to improve gradually and considerably for this subject over the course of his arm-cranking training.

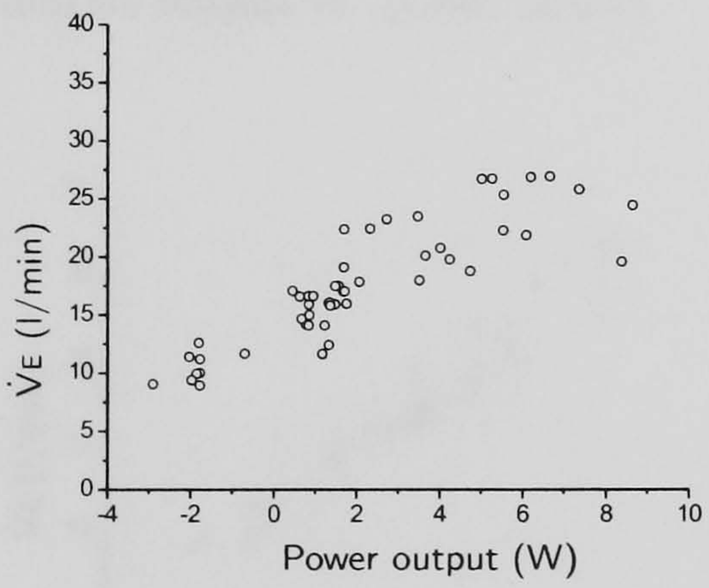
Graphical representation of data

The 10 panels displaying the cardiopulmonary data for test points 1 and 6 are given as examples in Figure 4.9. Here, the plots are presented side-by-side for TP1 (left) and TP6 (right) to facilitate comparison. It should be noted that these are not drawn to the same scales. The equivalent 10-panel arrays for all other test points are given in Appendix B.

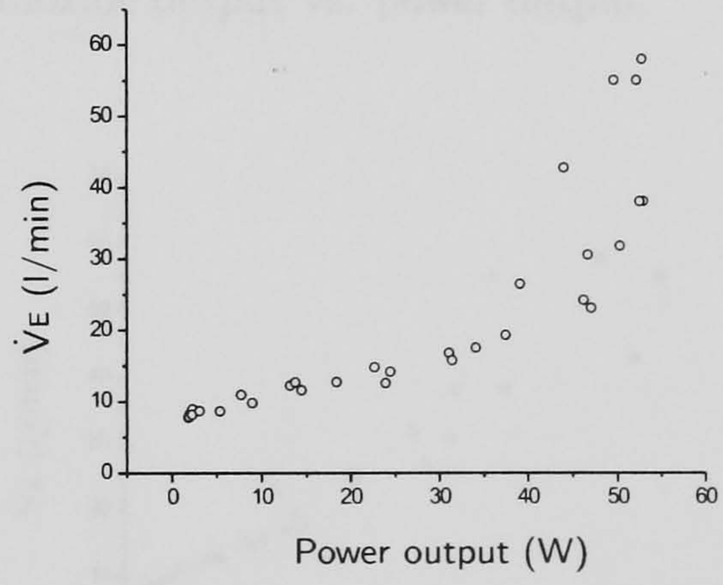
Although an in-depth analysis of the full dataset for each test point is beyond the scope of this thesis, some interesting observations are highlighted here:

1. There was no indication of severe ventilatory limitation, as ventilation increased in accordance with the ventilatory requirements of the exercise from TP1 (Figures 4.9(a) and 4.9(m)) to TP6 (Figures 4.9(b) and 4.9(n)).

2. There was a clear increase in peak heart rate from baseline (Figure 4.9(c)) to the end of participation (Figure 4.9(d)).

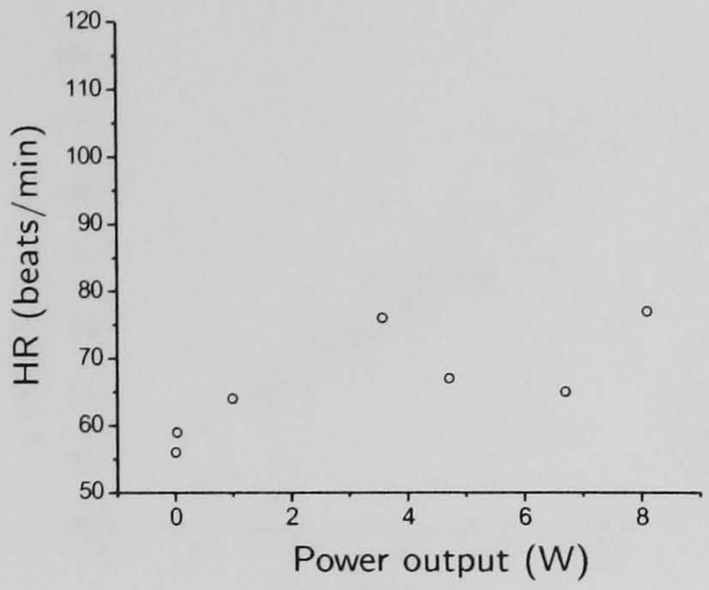


(a) TP1: Ventilation vs. power output

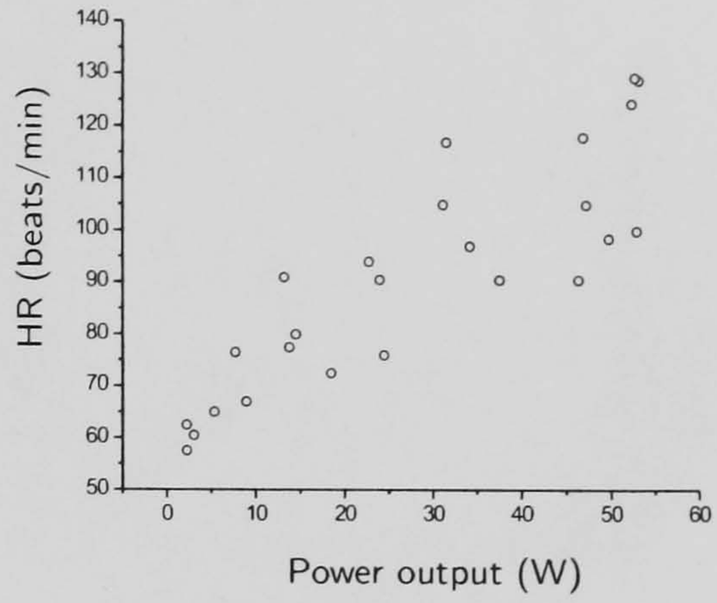


(b) TP6: Ventilation vs. power output

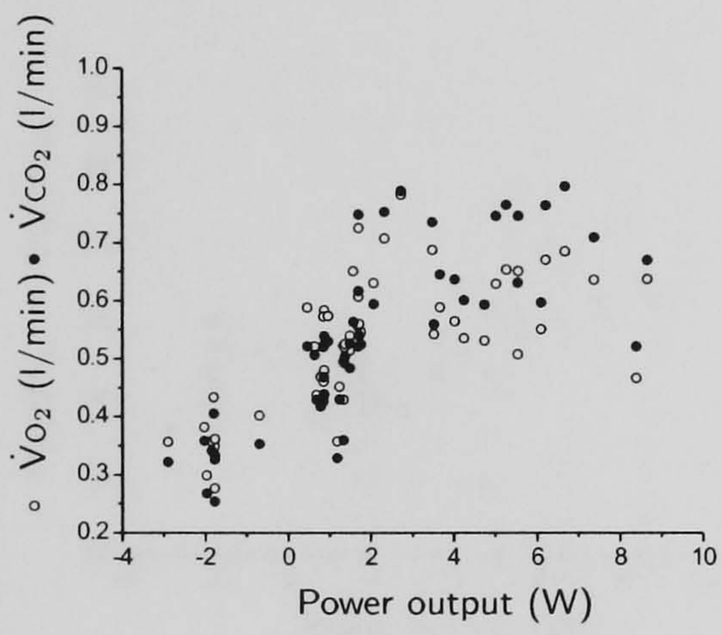
Figure 4.9: Graphical representation of cardiopulmonary data for Subject A, from incremental FES-ACE exercise testing at TP1 (left) and TP6 (right). The data have been edited and 4-breath averaged.



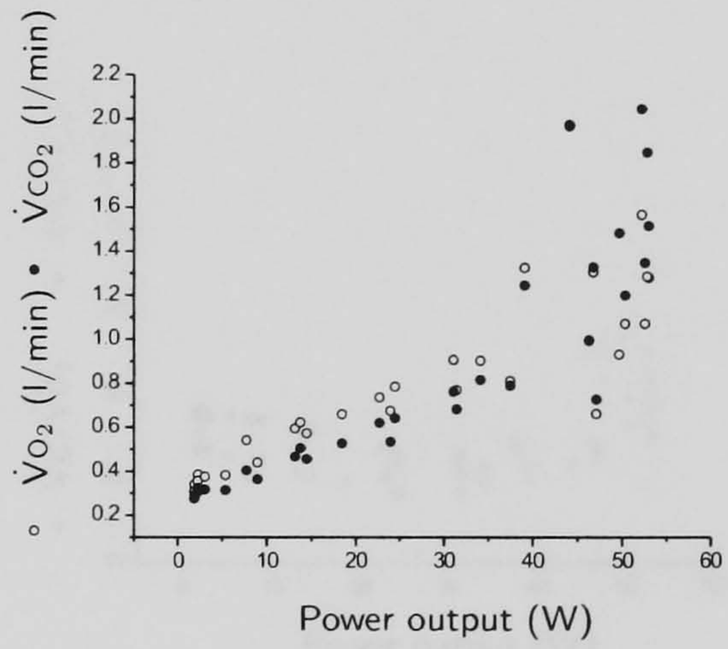
(c) TP1: Heart rate vs. power output



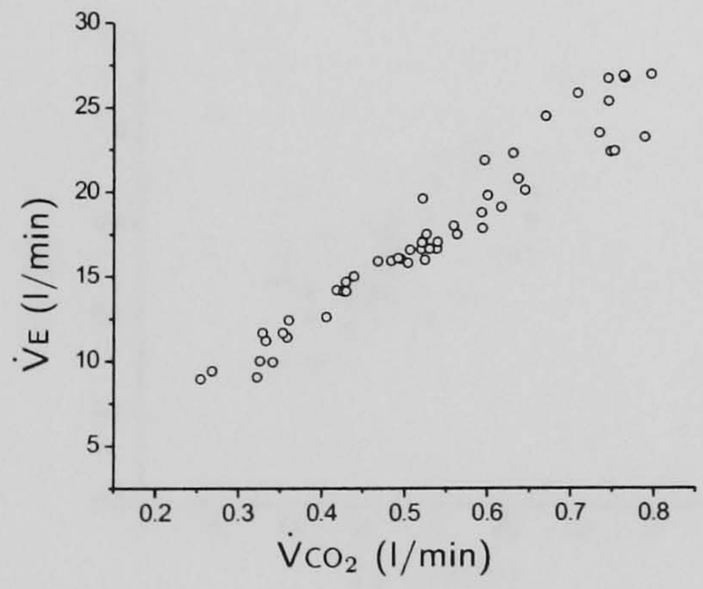
(d) TP6: Heart rate vs. power output



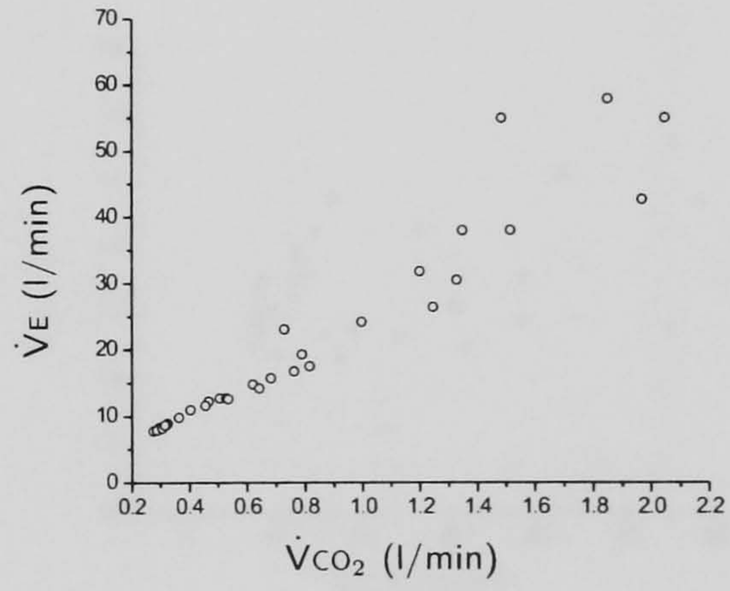
(e) TP1: Oxygen uptake and carbon dioxide output vs. power output



(f) TP6: Oxygen uptake and carbon dioxide output vs. power output

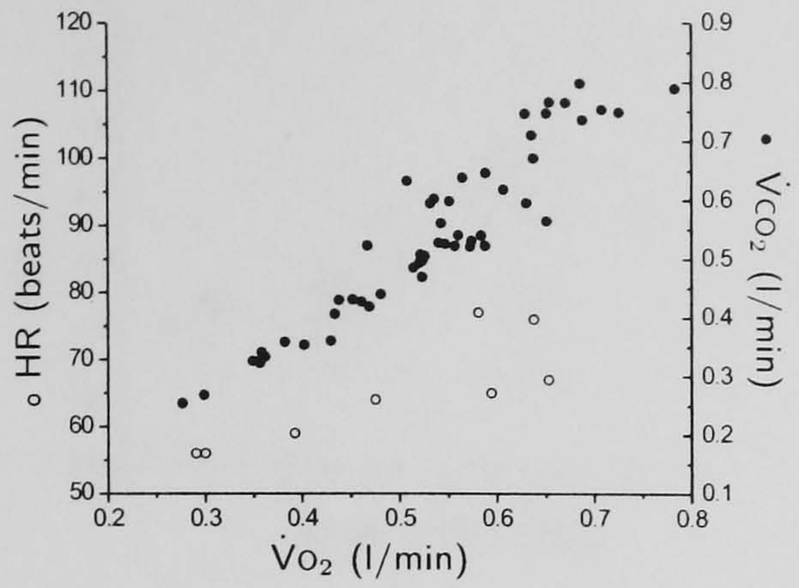


(g) TP1: Ventilation vs. carbon dioxide output

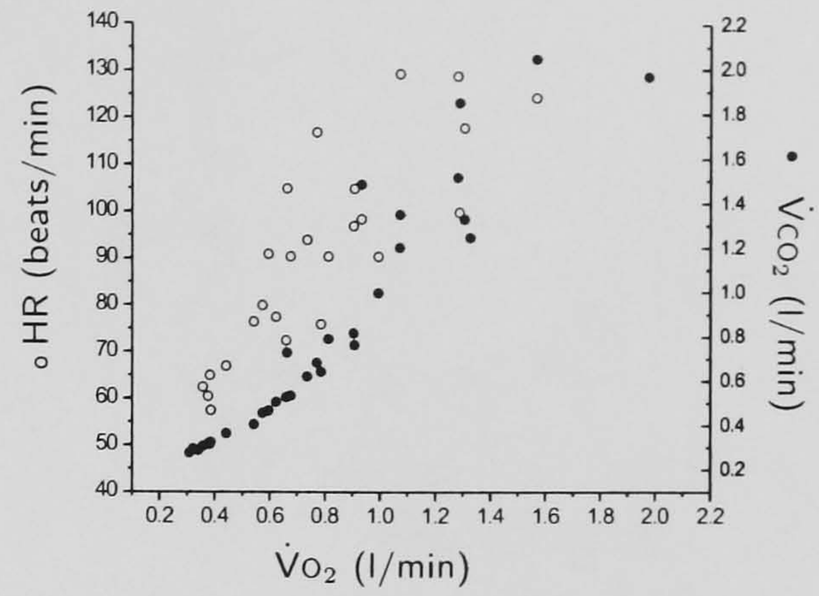


(h) TP6: Ventilation vs. carbon dioxide output

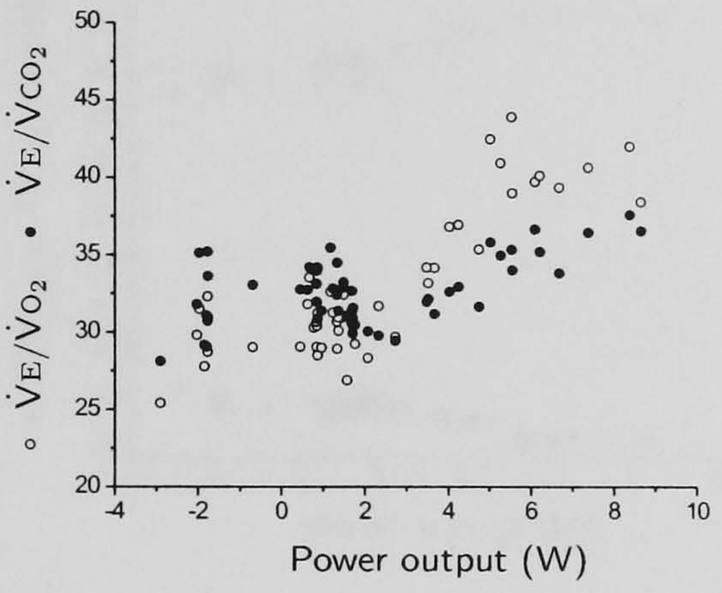
Figure 4.9: (cont.)



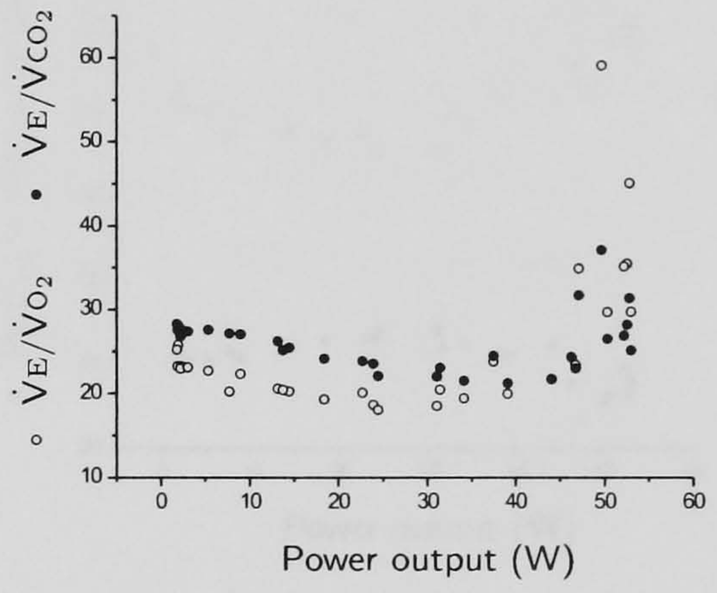
(i) TP1: Heart rate and carbon dioxide output vs. oxygen uptake



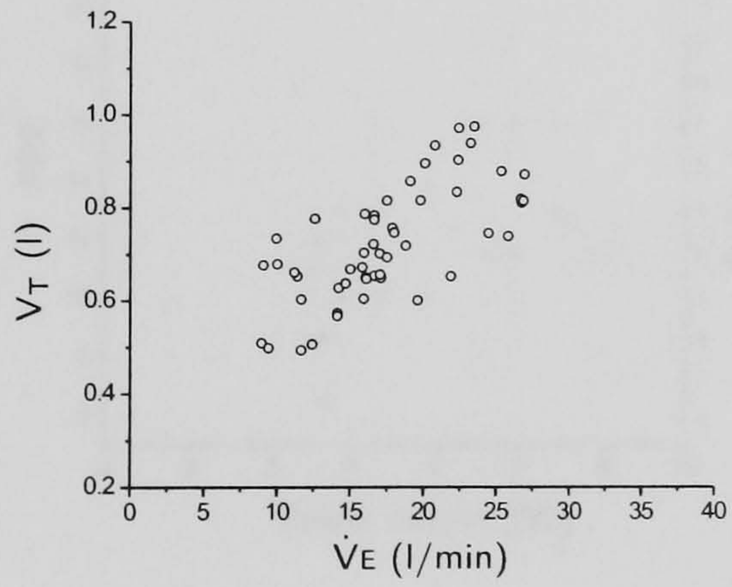
(j) TP6: Heart rate and carbon dioxide output vs. oxygen uptake



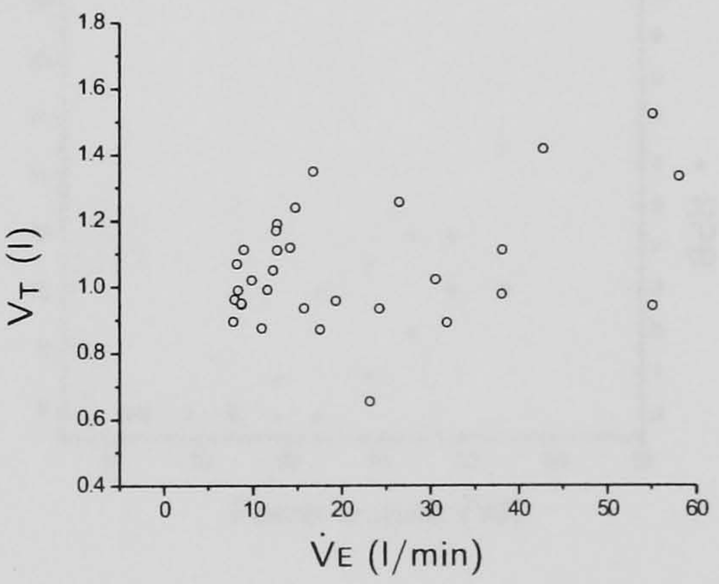
(k) TP1: Ventilatory equivalents vs. power output



(l) TP6: Ventilatory equivalents vs. power output

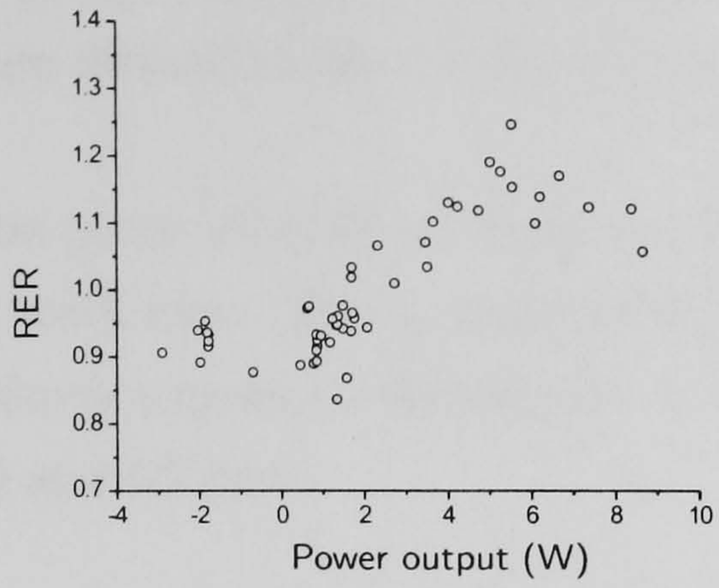


(m) TP1: Tidal volume vs. ventilation

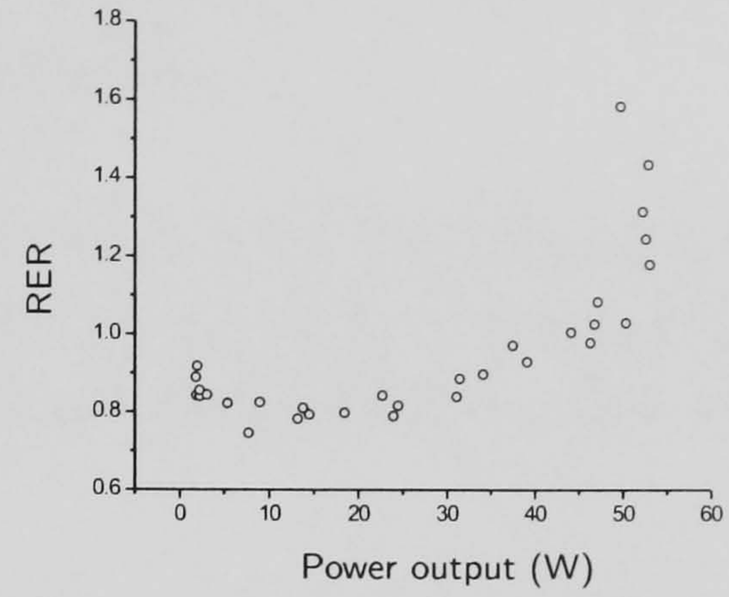


(n) TP6: Tidal volume vs. ventilation

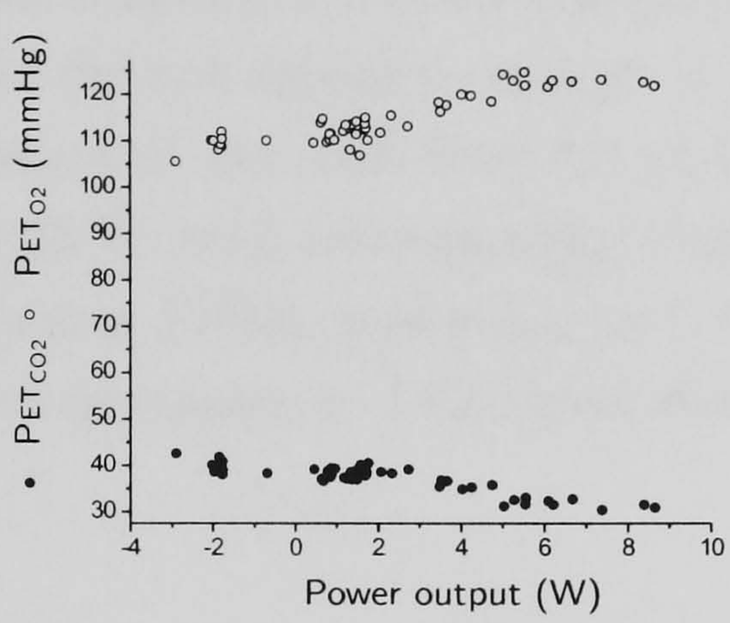
Figure 4.9: (cont.)



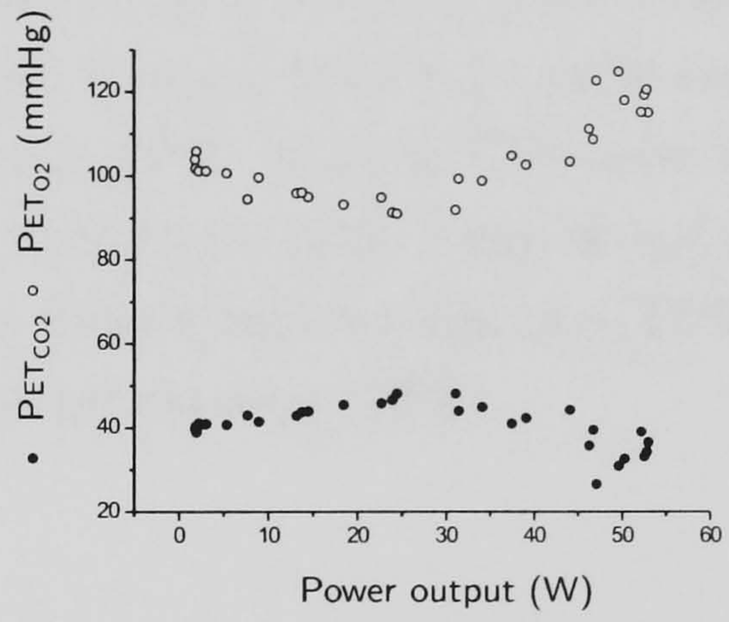
(o) TP1: Respiratory exchange ratio vs. power output



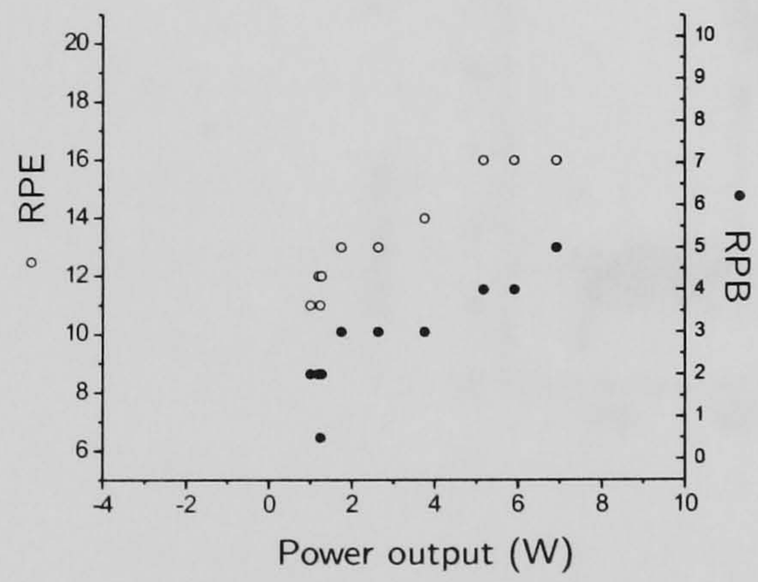
(p) TP6: Respiratory exchange ratio vs. power output



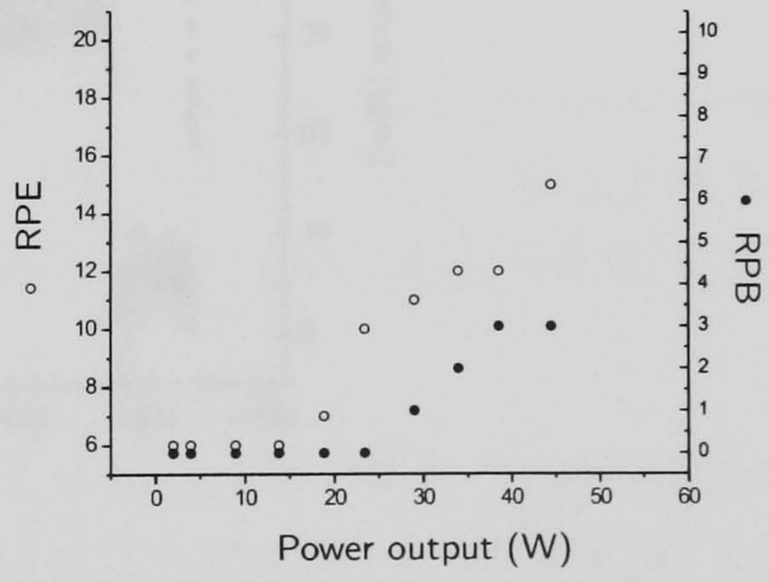
(q) TP1: End-tidal tensions vs. power output



(r) TP6: End-tidal tensions vs. power output



(s) TP1: Ratings of Perceived Exertion and Breathlessness vs. power output



(t) TP6: Ratings of Perceived Exertion and Breathlessness vs. power output

Figure 4.9: (cont.)

4.3.2 Constant Load Tests

Although constant load tests were carried out at each test point, the data from TP1 were discarded due to the test being of insufficient quality.

The power control is shown for TP2 in Figure 4.10, to show the clear step increase in work rate. The cadence maintained by the subject is also shown. Although the reference given to the subject was 50 rpm, the cadence was allowed to vary between 50 and 60 rpm.

The steady-state oxygen uptake and respiratory exchange ratio data for each stage of the constant load tests are summarised in Table 4.8. Steady-state values for oxygen uptake at rest were similar between test points. The oxygen cost of zero-load arm-cranking decreased with training from 0.44 l/min at TP1 to 0.38 l/min at TP4, and did not appear to change at TP5 and TP6. The constant load work rates were not set at the same level for all test points. However, TP3, TP4 and TP5 were all at 22 W, with corresponding oxygen costs at this work rate of 0.96 l/min at end of training (TP4), increasing to 1.27 l/min after one month without exercise (TP5), and decreasing to 1.02 l/min after the subject resumed training (TP6).

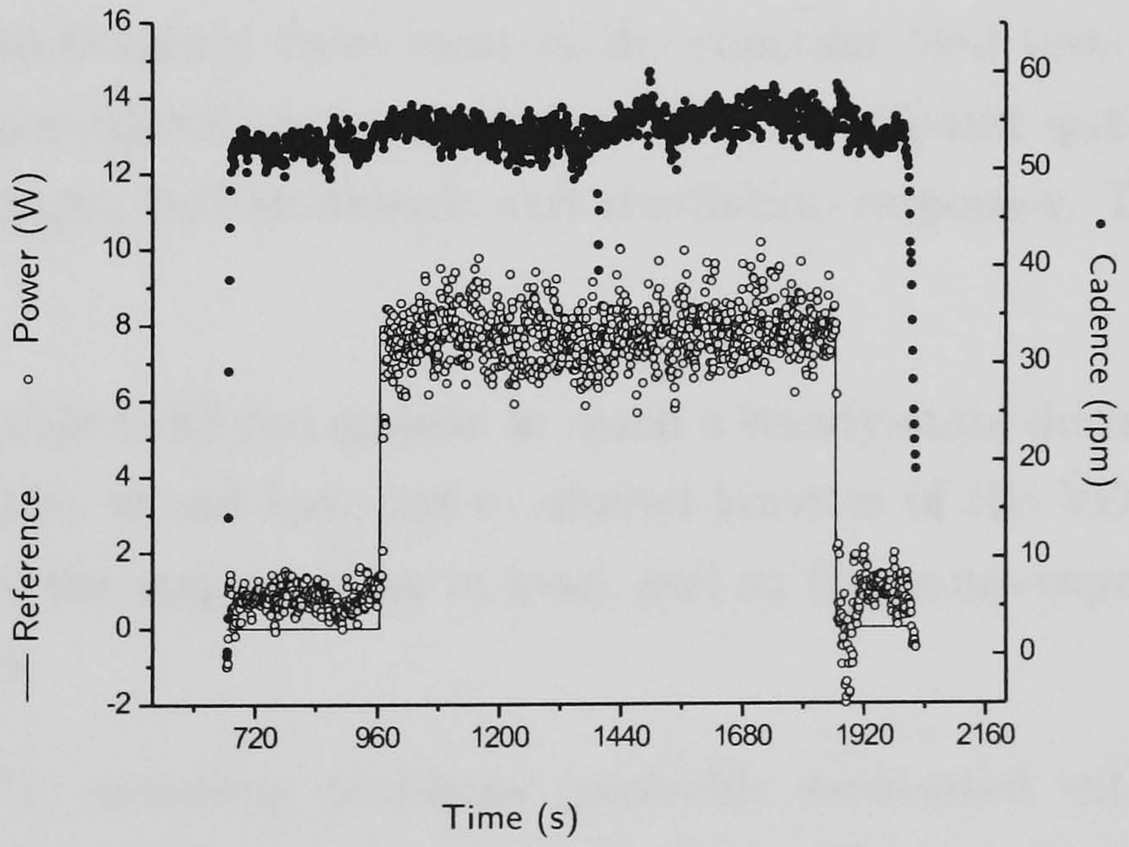


Figure 4.10: Power output, power reference and cadence data plotted against time for Subject A, for 8 W constant load FES-assisted ACE exercise testing at TP2 (+ 4 weeks training).

Test Point	Work Rate (W)	Resting		Zero Load		Constant Load	
		$\dot{V}O_2$ (l/min)	RER	$\dot{V}O_2$ (l/min)	RER	$\dot{V}O_2$ (l/min)	RER
1	-	-	-	-	-	-	-
2	8	0.269	0.81	0.440	0.81	0.656	0.87
3	12	0.250	0.82	0.419	0.90	0.915	0.73
4	22	0.261	0.79	0.384	0.78	0.958	0.93
5	22	0.255	0.74	0.385	0.77	1.272	0.91
6	22	0.280	0.79	0.393	0.78	1.020	0.87

Table 4.8: Gas exchange data for each stage of constant load testing for Subject A, for each test point. Steady-state is assumed, and data are shown as the mean of the last three minutes of each stage.

Time constants

Ideally, for each constant load test, time constants for $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}E$ would have been determined by fitting the typical first-order exponential response that is expected for a step increase in work rate (where the subject is working below the lactate threshold).

However, the data obtained from most of the constant load tests carried out with Subject A were considered to be, in the main, of insufficient quality to determine the kinetics of oxygen, carbon dioxide and ventilation responses. The issues were as follows:

1. TP2: the subject did not appear to reach a steady-state during zero-load arm-cranking. This would have led to altered kinetics of the $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}E$ responses to the step increase in load, and so the mono-exponential fit would not be valid.

2. TP4 & TP5: sampling problems (probably associated with excessive head movement during the constant load exercise pulling on the sampling line and volume transducer cable by the subject) exacerbated the noise levels in the breath-by-breath data. Even after editing, this extent of noise in the data made line fitting problematic.

3. TP6: a successful exponential fit could only be made to the $\dot{V}O_2$ data. Time constants could not be determined for $\dot{V}CO_2$ and $\dot{V}E$.

Therefore, in this case study, there was only one constant load test for which these problems were considerably reduced, namely the test at 12 W for TP3. The TP3 data are consequently used here to illustrate the feasibility of this type of testing, exponential curve fitting and time constant analysis. Figure 4.11 shows the response kinetics for $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}E$. The estimated time constants were 99 s. 129 s and 162 s, respectively, which are much slower than those expected in healthy neurologically intact individuals. The time constants could not be tracked through the time course of Subject A's training programme. Therefore, no information could be gleaned here about longitudinal changes in kinetics that would otherwise have provided another marker of changes in cardiopulmonary fitness in this subject.

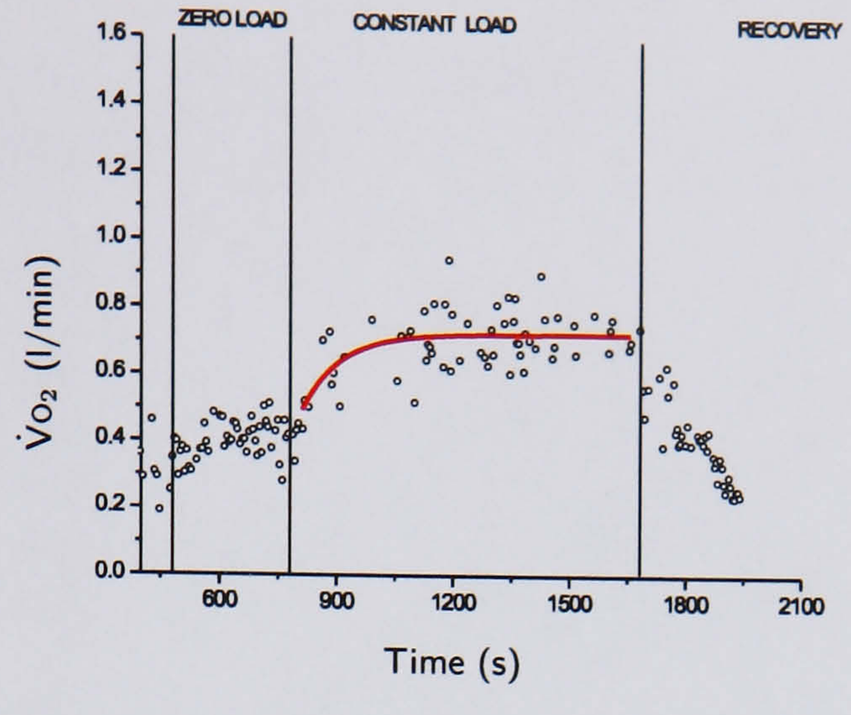
Efficiency

Although most of the constant load datasets could not be used to extract information about the kinetic responses, they were nevertheless used for efficiency calculations for FES-ACE exercise (except for TP1). This is because the data used for efficiency calculations were averaged over the last three minutes of each stage (rest, zero-load arm-cranking, constant-load arm-cranking), thus reducing some of the effect of the noise. The estimated efficiencies for each test point are summarised in Table 4.9 and displayed graphically in Figure 4.12.

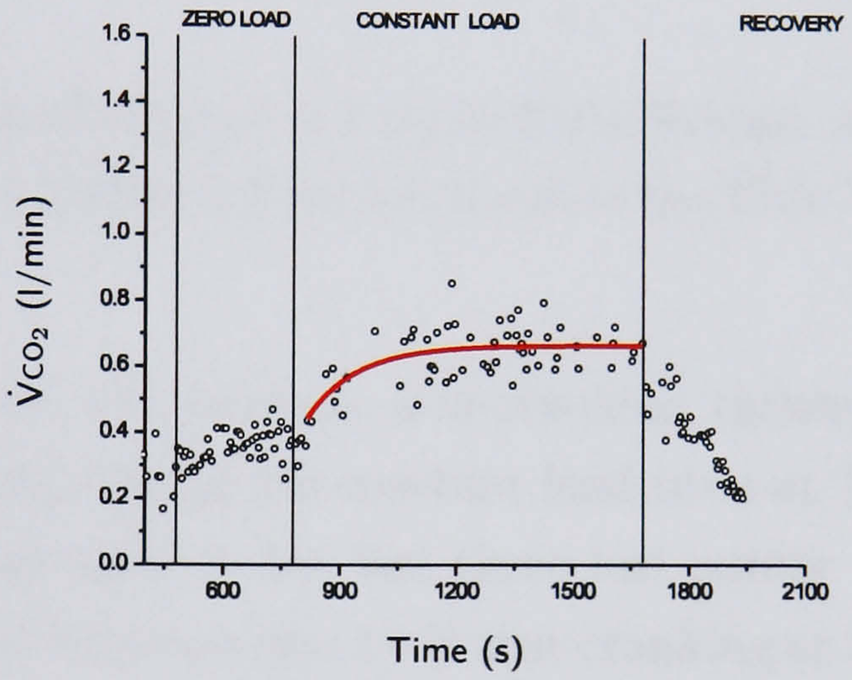
Test Point	Work Rate (W)	Gross Efficiency (%)	Net Efficiency (%)	Work Efficiency (%)
1	-	-	-	-
2	8	3.9	6.5	11.5
3	12	5.4	8.2	12.8
4	22	6.8	9.2	11.1
5	22	5.3	6.6	7.5
6	22	6.7	9.2	10.8

Table 4.9: Efficiency data for Subject A at each test point.

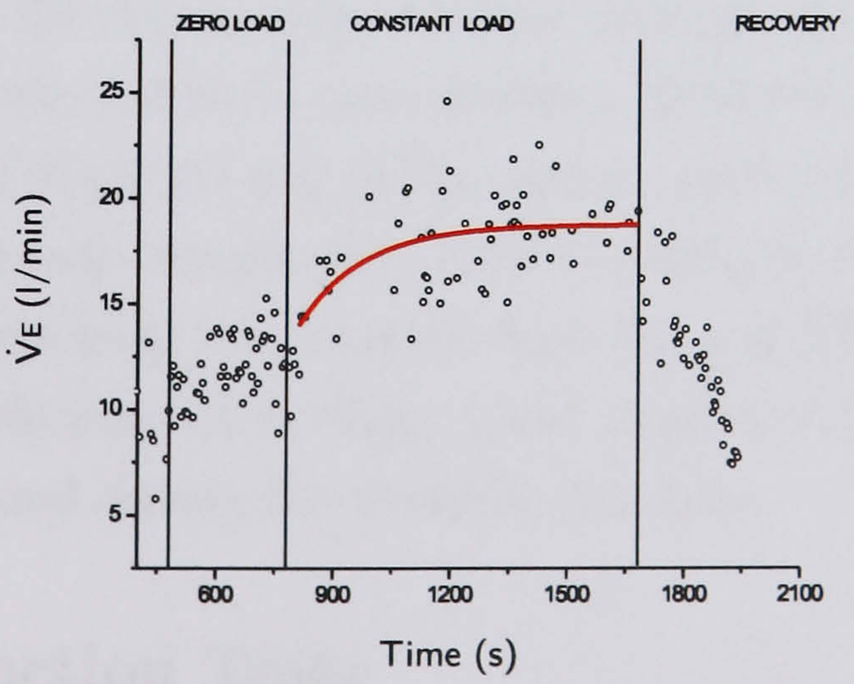
Taking the data from TP2 to TP6 into account, a different pattern was observed for *work* efficiency, compared with *gross* efficiency (GE) and *net* efficiency (NE). Both GE and NE increased gradually over the training period, dipped to a lower value after one month without exercise (TP5), and then (TP6) returned to previous end-of-training (TP4) values once arm-cranking training resumed. WE showed no discernible pattern.



(a) TP3: $\dot{V}o_2$ kinetics, time constant = 99 s.



(b) TP3: $\dot{V}co_2$ kinetics, time constant = 129 s.



(c) TP3: $\dot{V}E$ kinetics, time constant = 162 s.

Figure 4.11: Example of exponential curve fitting to determine response kinetics at TP3. The data were edited prior to fitting. The first 25 s (phase I) of the kinetic response to the step increase in work rate from 0 W to 8 W were not included.

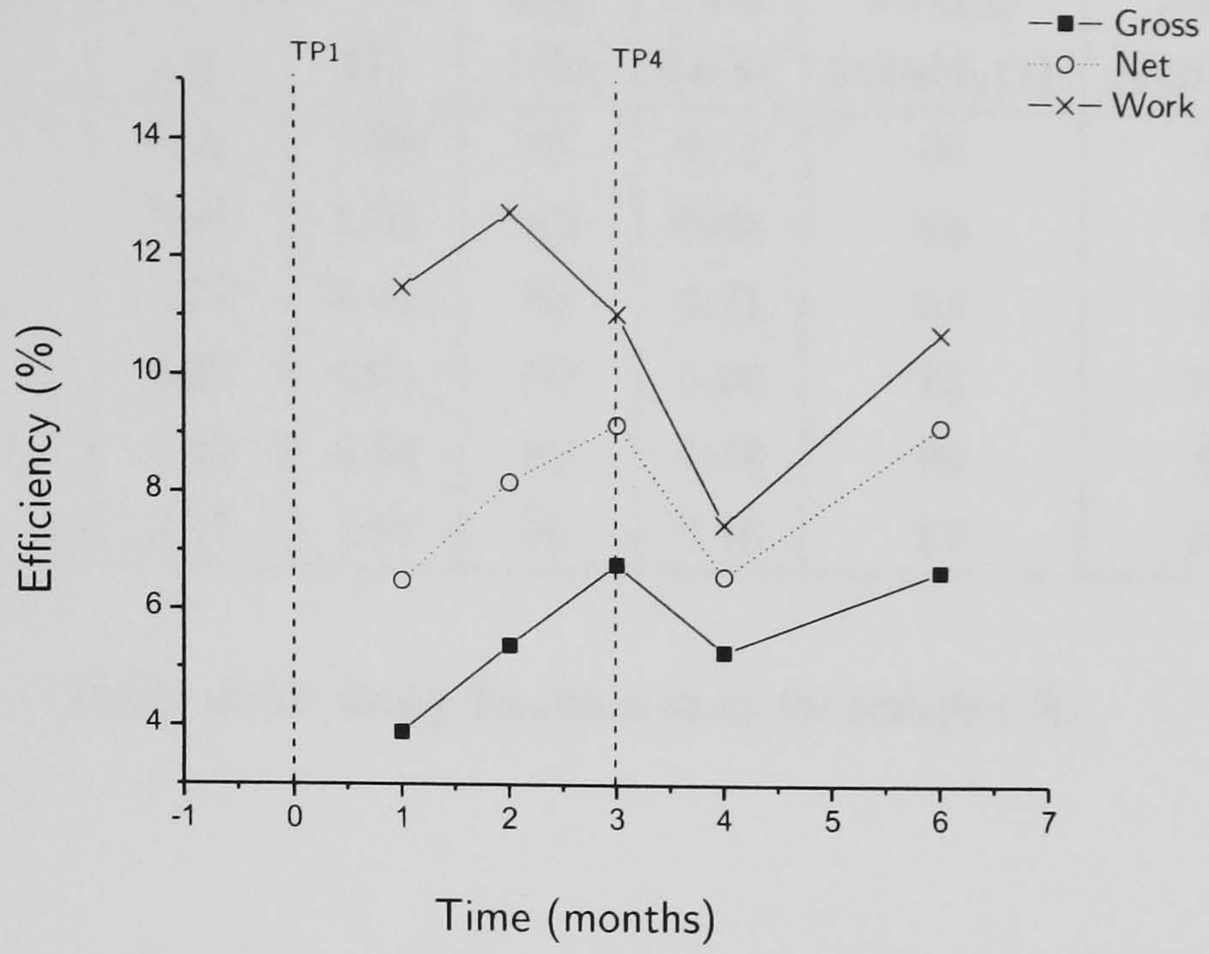


Figure 4.12: Estimated efficiencies of FES-ACE for Subject A at each test point. TP1 and TP4 are shown to highlight the start and end of the FES-ACE intervention period.

It should be noted that the average arm-cranking cadence was around 55 revolutions per minute (rpm) during the constant load tests at TP2 and TP3, but closer to 60 rpm in those performed at the last three test points. There is some evidence that the efficiency of cyclical exercise, be it arm-cranking or leg-cycling, is dependent on cadence [38, 88], due to the increased cost of moving the limb masses at higher cadences.

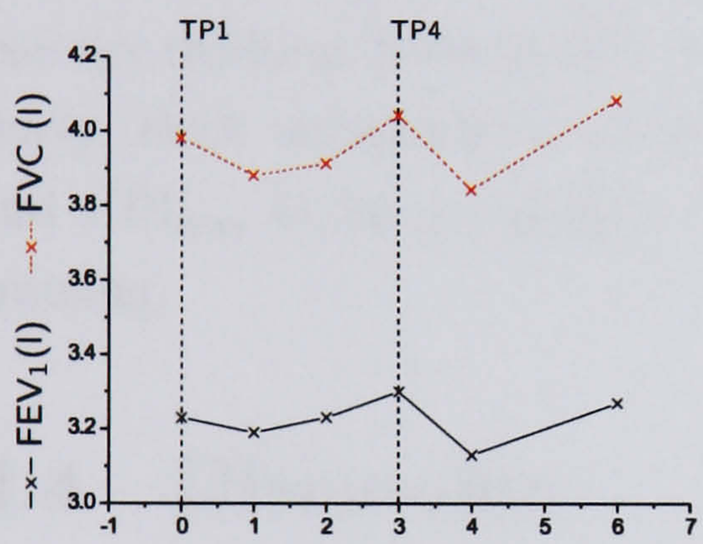
In summary, the constant load tests were, in the main, too noisy and/or did not fulfill the requirement for steady-state exercise thus preventing useful estimation of response kinetics over the subject's participation. However, the time constants from one test were given to illustrate feasibility, and to show the greatly reduced speed of response in gas exchange compared to reference data from healthy, neurologically intact people. The data from the constant load tests at TP2 to TP6 were used to estimate changes in efficiency that might point towards a beneficial change within the working muscles used during the exercise over time.

4.3.3 Lung Function Tests

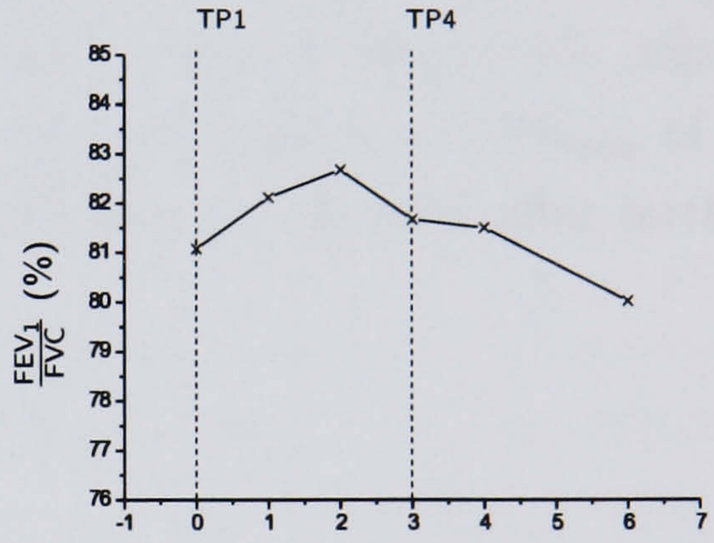
Pulmonary function data, collected at each test point, are presented for Subject A in Table 4.10, and illustrated graphically in Figure 4.13.

Test Point	FEV_1 (l)	FVC (l)	$\frac{FEV_1}{FVC}$ (%)	PEF (l/s)	PE_{max} (cmH_2O)	PI_{max} (cmH_2O)
1	3.23	3.98	81	6.11	66	85
2	3.19	3.88	82	6.43	66	76
3	3.23	3.91	83	6.71	59	82
4	3.30	4.04	82	6.92	83	109
5	3.13	3.84	82	6.78	69	98
6	3.27	4.08	80	7.18	87	103

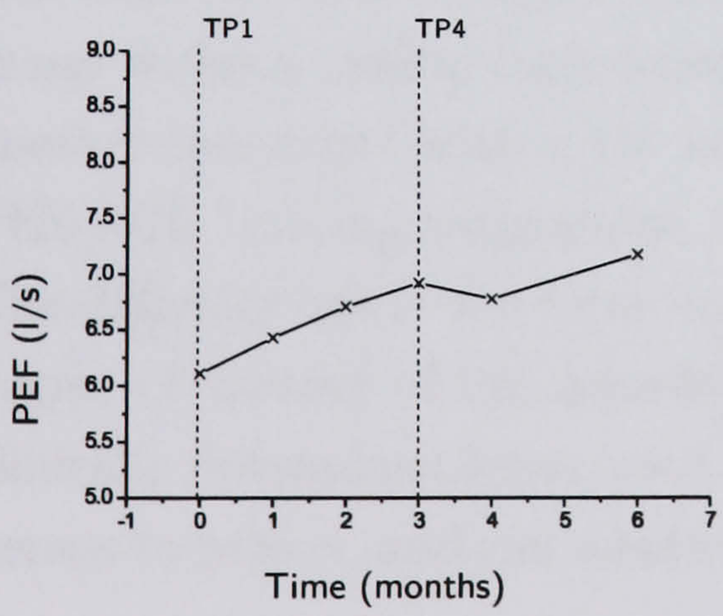
Table 4.10: Lung function data for Subject A.



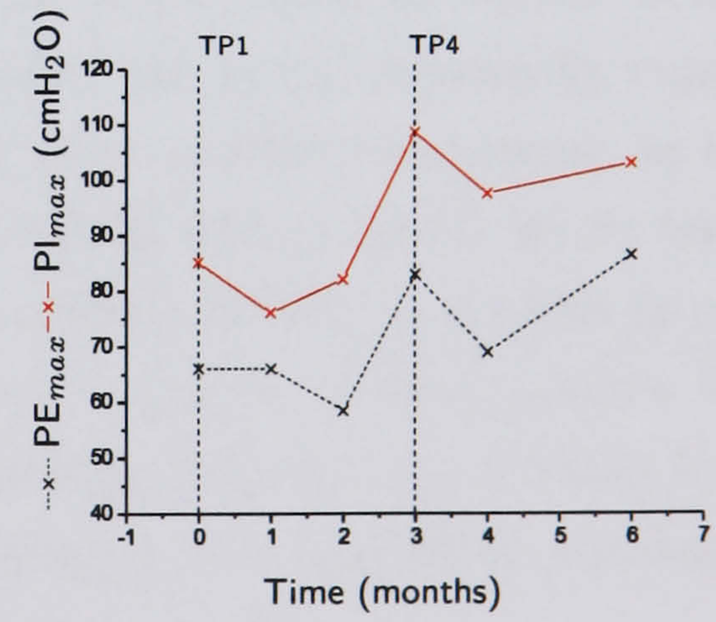
(a) FEV_1 and FVC



(b) $\frac{FEV_1}{FVC}$



(c) PEF



(d) PE_{max} & PI_{max}

Figure 4.13: Lung function data for Subject A. TP1 and TP4 are shown to highlight the start and end of the FES-ACE intervention period.

These indices of pulmonary function, measured at rest, were monitored over the subject's participation. The data for Subject A show that there were no substantial changes in forced vital capacity (FVC), which ranged from 3.84 to 4.08 l. During the spirometry tests, the subject typically expelled around 80% of this volume in the first second following maximal inspiration: a near-normal ratio.

Although the lung capacity did not appear to improve with exercise training, peak expiratory flow increased with every month of training, from a baseline of 6.11 l/s, up to an end-of-training value of 6.92 l/s. This dropped slightly post-training to 6.78 l/s at TP5, but then increased again with two additional months of arm-cranking training, reaching 7.18 l/s at TP6.

Both maximal expiratory and maximal inspiratory power increased overall through exercise training, from baselines of 66 and 85 cmH_2O, to 83 and 109 cmH_2O, respectively. Both transiently decreased in the month without training to a PE_{max} of 69 and a PI_{max} of 98, going back up to 87 and 103 cmH_2O, respectively, after further training.

4.4 Discussion

Before exploring the training effects identified for Subject A in detail, it is useful to explore to what extent Subject A's profile is representative of the wider C4–C6 tetraplegic population targeted in this pilot study. We propose that any extrapolation from the data obtained with this subject should not be made to the rest of this group without careful consideration. This is because one would reasonably expect another individual with a C6 incomplete SCI to show a different response to the FES-ACE training programme, let alone an individual with a higher lesion level. The difficulty lies in the term 'incomplete', when applied to SCI, as it refers to any degree of sparing of the neurological (motor and/or sensory) pathways below the clinically determined lesion level. This degree of sparing can vary considerably from person to person, and can additionally involve sparing of some autonomic pathways.

Consequently, the author presents the positive training outcomes of this case study in this light. Nevertheless, a number of clear goals were reached here, namely: the development of systems for FES-assisted ACE, the determination of training and exercise testing protocols specific to this exercise modality, and the preliminary evaluation of the potential benefits to the C4–C6 tetraplegic population of taking part in an FES-ACE training programme. Although the changes in upper limb strength

and cardiopulmonary fitness observed with Subject A as a result of training are in themselves substantial and informative, perhaps more importantly they demonstrate feasibility of the approach, and the potential benefits of this exercise modality for this population.

4.4.1 Peak Power Output

Here, we can analyse the impact that the FES-assisted arm-cranking exercise regime had on Subject A's peak power output (our indicator of upper limb strength). First of all, it is useful to report this person's neurological, physical and physiological condition before participating in the exercise programme. With a well-established chronic C6 incomplete lesion of 18 years, even before introducing electrical stimulation, Subject A was able to produce useful and strong contractions of the biceps in both arms, only weak contraction of the triceps in the right arm, and a barely discernible twitch of the triceps in the left arm during voluntary effort. Together with full use of shoulder musculature and some wrist control, this gave Subject A a considerable degree of remaining upper body function. Although activities of daily living were not recorded in this study, the anecdotal evidence is that this person was only limited in performing tasks which required elbow extension, manual dexterity, or significant upper limb strength and endurance.

Therefore, prior to training, Subject A was already able to manually propel his wheelchair over a number of surfaces, but would require assistance up slopes and over long distances. Without effective elbow extension, activities of daily living which were difficult to perform effectively without assistance included transfers, pressure-relieving lifts and any tasks requiring overhead reaching. In addition, certain hobbies were made difficult. This individual enjoyed fishing, but was limited in his ability to fish due to his weak triceps. He therefore hoped that participation in FES-assisted arm-cranking exercise would help him perform these activities more effectively.

Needham-Shropshire *et al.* [77] demonstrated the effectiveness of adding elbow extension through electrical stimulation of the triceps for arm-cranking exercise in tetraplegia. This led to increased muscle strength, as determined through manual muscle testing. In our pilot study, the upper limb strength was measured from the torque produced at the cranks. The limitation of this was that any change in force production by any single muscle group could not be identified, as the biceps of one arm was usually working simultaneously with the contralateral triceps at any one

point in the crank cycle.

Nonetheless, we can look at the changes in Subject A's peak power production in the upper limbs to infer changes in muscle strength in the muscles involved in the exercise. With Subject A, any improvements in peak power output recorded over the period of participation could be attributed almost exclusively to the result of FES-ACE training (although it is not possible to estimate the extent to which the electrical stimulation itself contributed to the changes, in relation to the voluntary input). This is because the FES-ACE exercise was the only intervention (over and above the subject's usual daily activities) during the three-month training period that would have altered this capacity for upper limb power production.

From his baseline peak power output of 7 W, Subject A was able to increase upper limb power production at a rate of approximately 10 W per month of training so that, by the end of the FES-ACE training, he was able to produce 38W. Encouragingly, the higher level of peak power production reached at the end of FES-assisted arm-cranking training was carried over post-training, with no apparent decrease after one month without training. Although it would have been of interest to track changes for a period of time (for example, 3–6 months) after removing arm-cranking intervention, the results obtained following two additional months of arm-cranking exercise training without FES are also interesting in themselves.

Although, in absolute terms, the end-of-training peak may still appear to be low in comparison to that which an able-bodied person could produce, it nevertheless represented almost a 450% increase in peak power for this individual. Furthermore, this increase in upper body strength could translate to a considerable increase in functional capability of the limbs, for tasks involving the muscles that remain under voluntary control by this individual. Such tasks would include wheelchair propulsion, pressure-relieving lifts in the wheelchair, and any other activities requiring upper body strength (for example, with this subject, the hobby of fishing would be facilitated).

In terms of the contribution of FES to the changes, it was presumed that the benefit of adding electrical stimulation to recruit a greater proportion of muscle units in the relevant upper limb muscles during the exercise was mostly within the first few weeks of exercise training. Thereafter, the voluntary input was a more significant contributor. Data collected following voluntary arm-cranking training with Subject A lend support to this idea. Prior to the re-assessment of the subject's capabilities

in the FES-ACE ergometer at TP6, the subject had been able to resume a two- or three-session-per-week training regime over the two-month period at home. The further increase in peak power output recorded when compared to the end of FES-ACE training, to a new peak of 51 W, illustrated a number of points. Averaging at 6.5 W per month of voluntary arm-cranking training, this was a reduced rate of improvement than with the FES-ACE training (which had been at 10 W per month). Even so, this highlighted the potential for Subject A to increase his upper body strength further through this manageable routine of exercise at home. This case study therefore also illustrates that it would be realistic for people with Subject A's level of injury (and resulting paralysis) to take part in such a training programme in the comfort of their own home. This, of course, assumes a similar level of motivation of the individual to do the exercise at the required frequency and intensity. Furthermore, the FES-ACE systems would need some further development to facilitate donning and doffing and operation of the FES equipment.

4.4.2 Peak Oxygen Uptake

Although the increase in upper body strength has been demonstrated in this case study, the idea of improving strength of the key upper limb muscles used in arm-cranking by adding electrical stimulation is not new. In contrast, a new aspect of this FES-ACE was the investigation into the possibility that positive cardiopulmonary changes could result from regular use of such systems by people with tetraplegia. Looking at Subject A specifically, we can illustrate the potential cardiopulmonary benefits in an incomplete C6 SCI individual, as a result of a three-month FES-assisted ACE intervention.

Prior to the endurance training, Subject A completed a phase of muscle strengthening which was not considered to stress the cardiopulmonary system to any great extent, as it involved arm-cranking with FES only at low cadence and no (or minimal) resistance. This phase was also used to familiarise the subject with the equipment and procedures which would later be used for exercise testing.

At baseline, with a peak oxygen uptake of 0.71 l/min, Subject A was within the range of normal values, when compared to a group of 13 C5–C8 SCI people performing voluntary arm-cranking exercise, for whom $\dot{V}O_2$ averaged at 0.8±0.2 l/min (mean±sd), in a study by Van Loan *et al.* [113]. Comparing our values with a separate study by Burkett *et al.* [17], looking at untrained tetraplegics during wheelchair ergometry exercise, it would seem that Subject A was above average for peak $\dot{V}O_2$,

even before training. Whether Subject A's baseline cardiopulmonary fitness was in line with, or slightly above, the average for the tetraplegic group, it is important to note that 0.71 l/min was still extremely low when compared with otherwise healthy, sedentary neurologically intact individuals.

Although the precise determination of the sources of exercise limitation in Subject A is beyond the scope of this thesis, it was likely that at least one component would be the central limitation imposed on most[1] tetraplegics due to the fact that the level of the lesion is above the level for sympathetic outflow to the heart, as part of the 'decentralisation' of the sympathetic nervous system [32, 49, 55]. It was unlikely that any exercise regime, involving either the small muscle mass of the arms or the larger muscles of the legs (through, for example, FES-cycling), could be expected to reduce this effect. If, however, there had been some peripheral components to the exercise limitation, it was anticipated that the FES-assisted arm-cranking training regime may be able to reduce their effect.

With Subject A, the training regime did appear to tackle some peripheral factors. After three months of training, a 50% increase in peak oxygen uptake was observed, from 0.71 to 1.09 l/min. This brought Subject A closer to the lower range of what a paraplegic subject could produce during voluntary arm-cranking exercise. This is again based on the Van Loan *et al.* data, which found that the mean peak oxygen uptake in a group of T4-L3 paraplegics during arm-cranking was 1.5±0.6 l/min [113].

In agreement with the pattern of power production, a further increase in peak oxygen uptake was recorded with Subject A at TP6, at 1.21 l/min, in response to two additional months of exercise training (this time performing voluntary arm-cranking exercise at home). Therefore, this case study illustrates that cardiopulmonary fitness can be improved with a realistic training regime in this particular individual with C6 incomplete tetraplegia, by setting the training work rates below the estimated lactate threshold (at moderate intensity). It is speculated here that some of this change was due to peripheral adaptations in the muscles involved in the exercise, and through improved oxygen delivery to those muscles. Whether there may also have been central adaptations over the training period is less clear: some possibilities include an increase in cardiac output resulting from an increase in stroke volume and/or peak heart rate.

Relative to the levels that a healthy able-bodied person should reach as a result

[1] With an incomplete SCI, the effect may be reduced.

of a similar period of training, the final peak $\dot{V}O_2$ value of 1.21 l/min is still comparatively low. Indeed, this represents a cardiopulmonary fitness level equivalent in the general population to that of a sedentary or extremely inactive person. Whether the improvement in cardiopulmonary fitness resulting from the FES-assisted ACE exercise intervention in this individual would be considered sufficient to reduce the risk of developing cardiovascular disease is not yet known, and would require further investigation.

4.4.3 Efficiency

In the general population, the oxygen uptake-work rate relationship for progressively increasing work rates is expected to be linear up to the maximum $\dot{V}O_2$. The slope of this relationship is similar between healthy individuals, with a gradient of around 0.01 l/min per Watt for leg-cycling exercise. Only the position of the relationship tends to vary with body weight. This is illustrated in Figure 4.14. Generally, the slope is not affected by training, age or gender, so that the work efficiency of the use of oxygen by the working muscles is unchanged. With training, a person may move further up the slope, but with no change in the gradient. However, in this case study, we observed a 450% increase in power output over three months, accompanied by only a 50% rise in peak $\dot{V}O_2$, suggesting some increased 'efficiency' of the exercise with training.

If the change in slope is a true pattern in this subject, it suggests that training has enabled the exercising muscles to produce a greater total force per unit of oxygen taken up. This could have been achieved through peripheral adaptations to the FES-ACE exercise, perhaps with gradual changes in the oxidative capacity of the exercising muscles and/or improved blood flow to the muscles. Prior to the exercise training programme, Subject A would be expected to show the typical pattern of disuse atrophy in the elbow extensors, and even to some extent in the elbow flexors, seen in many tetraplegics. As Stein *et al.* [105] point out, "loss of muscle bulk, associated reductions in force, and increased fatigability have all generally been found after spinal cord injury." In addition to this atrophy, following injury the composition of the muscles in the upper limb would have changed from predominantly type I to predominantly type II fibres [18, 67, 94].

We are therefore suggesting here that, through the FES-assisted arm-cranking exercise (relying mostly on the FES for the triceps activation, but on voluntary input for the biceps contractions), a gradual increase not only in peak force of the exercising

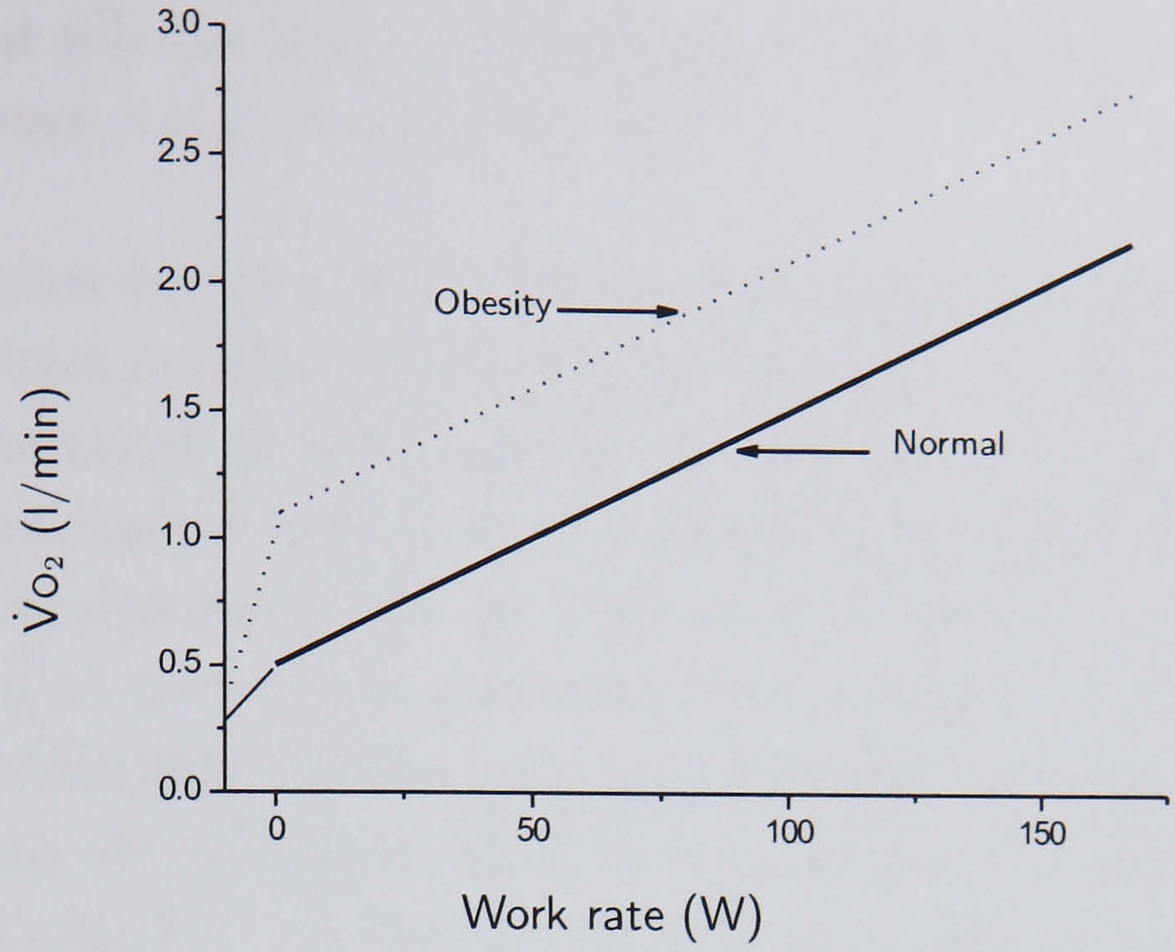


Figure 4.14: The normal $\dot{V}O_2$ - WR relationship (irrespective of age, gender or training), and the corresponding relationship in the case of obesity (reproduced from Wasserman *et al.* [116]).

muscles, but also in the aerobic capacity of those muscles was achieved. With a greater aerobic capacity of the exercising muscles (possibly through an increase in numbers of capillaries supplying the muscle fibres, and an increase in mitochondria per unit area), endurance would be improved. In functional terms, taking wheelchair propulsion as an example, the benefits would not simply be greater force production in short spurts (large force, short duration) — which would facilitate overcoming obstacles — but also greater endurance (medium force, long duration) for sustained periods of wheelchair propulsion.

This can be investigated in greater detail by considering different indices of efficiency (with or without baseline correction) calculated for constant load exercise. For these calculations to be valid, we are assuming that metabolic steady-state was reached both during zero-load arm-cranking and during arm-cranking at the selected constant load work rate.

However, the constant load test at TP2 did not fulfill this requirement, as the subject had not reached steady-state during zero-load arm-cranking. Instead, the oxygen uptake was still rising in the last three minutes of zero-load arm-cranking, so that the calculated mean would have been lower than if the subject had been allowed

to continue to steady state. This error would not affect the gross and net efficiency calculations, but only the work efficiency index (as the baseline subtraction for the latter is the energy cost of zero-load exercise).

The patterns observed with Subject A for gross and net efficiency indices were suggestive of a training effect. Both increased gradually over the training period, dipped after one month without exercise, and then increased back to pre-training values after two further months of arm-cranking exercise. The absolute difference in these two efficiency indices at any one test point was consistent, with net efficiency (NE) tending to be about 2–3% higher than gross efficiency (GE). NE, calculated with baseline subtraction of resting oxygen uptake, removed the resting metabolism component of the oxygen uptake during exercise, whereas GE was calculated without baseline subtraction. As the resting metabolism was apparently stable over the period of participation, it is of no surprise that the gross and net efficiency indices changed in parallel with each other over time (see Figure 4.12). In contrast, when the baseline subtraction was made using the oxygen uptake during zero-load arm-cranking, the pattern was less obvious, but work efficiency did dip one month post-training, and increased again after two months of voluntary ACE training. The problem with zero-load values at TP2 has already been identified as a contributing factor.

The usefulness, and even the validity, of baseline subtractions has been debated, and so the efficiency indices which rely on such subtractions should be considered with caution, and with an understanding of what each index does and does not indicate [46, 104, 116]. Stainbsy *et al.* argue against the use of baseline subtractions, as "the efficiency of muscle is determined by the efficiency of the processes that provide energy and convert energy to work" [104]. Indeed, it seems that work efficiency is generally unaltered by training status, age, or gender [116], thus reflecting the basic biochemical energy-yielding reactions needed for muscle contraction. A further argument against baseline subtraction, where the baseline is of zero-load work rate, is that "the $\dot{V}O_2$ of the "unloaded" ergometer can vary considerably from one subject to another because of differences in subject size and actual work rate of the "unloaded" cycle."[116]

The work efficiency data obtained for Subject A illustrate this last point. The baseline subtraction for this index was the energy expenditure at zero-load arm-cranking. However, the level of 'zero-load' arm-cranking was variable between tests, which imposed an error on the work efficiency values obtained at different test points.

Therefore, although the work efficiency appeared to change with training, and post-training, some of the differences would be attributable to the variability in unloaded arm-cranking.

One further aspect of differences in efficiency over time is the possibility that an increase in efficiency could have been due to an improvement in technique. However, even if there was some component of increased skill, it would not likely have continued over the whole period of training. Hence, the author postulates that, if at all, changes in efficiency resulting from better skill in performing the arm-cranking exercise would have been manifest only early in the training. Furthermore, based on observation by the investigator during training and testing sessions with the subject, there seemed to be no visible change in Subject A's technique over time.

4.4.4 Response Kinetics

There were considerable problems with the quality of the cardiopulmonary data collected during the constant load tests with Subject A. An aspect of this person's technique when working at a steady and relatively high work rate was that he moved his head from side to side during the arm-cranking motion. This probably pulled on the cables and sample line in such a way that the sampling was impaired. Consequently, no useful kinetic information with respect to possible effects of training could be gleaned from Subject A's constant load datasets. Only one set, for TP3, fulfilled the requirements for calculating the kinetics, and so was used as an example. Estimates for the time constants for $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}E$ at TP3 were presented, to show that the time constants are slower than in able-bodied people, and to demonstrate feasibility of the approach.

A mono-exponential equation (see Section 3.3.6) was fitted to the data (excluding the first 25 s, or Phase I response), as used to describe the kinetics of these variables for a step change in work rate (for submaximal exercise) in the general population [116, 121]. However, this may not be appropriate for people with SCI. Indeed, in one of their studies, Barstow *et al.* [8] suggest that a straight line fit may be more appropriate for the 'on' phase, with the kinetics being considerably slower in SCI during FES-leg cycling than in the intact healthy human. It would be reasonable to assume that the kinetics would be even slower in tetraplegia than in low paraplegia, due to the disruption to the sympathetic pathways.

Due to the low quality of the data obtained in most of the constant load tests

carried out with Subject A, it was not possible to identify potential effects of training on the speed (and possibly shape) of the kinetics for $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}E$ in tetraplegia. Had there been a training effect of the FES-assisted ACE intervention, one would have expected the kinetics to become progressively faster and hence the time constants to become shorter. This idea is based on studies looking at the effect of training on gas exchange kinetics in able-bodied individuals. For example, Hagberg *et al.* [44, 45], showed that $\dot{V}O_2$ kinetics are faster following training.

4.4.5 Lung Function

At baseline, Subject A seemed already to have a high enough vital capacity (VC) to cope with the normal range of ventilatory requirements in a non-athlete during exercise. Subject A had higher values at the start of training than the average for the tetraplegic population. Van Loan *et al.* [113] provide average values of VC for C5–C8 tetraplegics of 3.1±0.2 l (mean±sd). However, a more recent study by Tow *et al.* [110] present lower average values, at 2.5–2.8 l, depending on the time since injury. At 3.98 l, Subject A's baseline VC was clearly above both these estimates. Indeed, it was closer to normal lung capacity in a healthy neurologically intact male (4.92 l in trained young males, but can be as low as 3.94 l in sedentary young males [7]). At around 80%, the ratio of FEV_1 to FVC for Subject A was also within the normal range even at the start of participation.

In functional terms, this points towards at least partial voluntary control of respiratory muscles other than the diaphragm, such as the intercostals and the obliques. Had Subject A's SCI been clinically complete, these muscles would not remain under voluntary control. Therefore, even from the baseline exercise test, these values allowed us to confidently rule out ventilatory requirements as being a main factor limiting the exercise capabilities for this particular subject.

The influence of the exercise training programme used with Subject A on his resting lung capacity values was not convincing. The fact that this person was able to increase his peak oxygen uptake without any corresponding change in vital capacity lends support to the idea that lung capacity requirements were not a limiting factor from the start.

In contrast, changes were observed in peak expiratory flow and maximum inspiratory and expiratory muscle power over the training period. These all increased overall during that time. This may show that FES-assisted arm-cranking exercise

performed three times per week for a number of weeks led to some conditioning of the respiratory muscles still under voluntary control in this individual. However, this had no detectable effect on the volume of air that could be expelled from the lungs at rest.

4.5 Conclusions

This case study provided a preliminary evaluation of the new systems and protocols developed for FES-ACE training and testing, and demonstrated their feasibility. The training and testing schedule allowed us to monitor a number of outcome measures, and to produce a profile of upper limb strength and cardiopulmonary fitness for the subject over the FES-ACE training period. Furthermore, by implementing the FES-ACE training and testing with a subject with a chronic C6 (incomplete) SCI injury (18 years post-injury) who could otherwise be classified as extremely sedentary, any positive changes in the outcome measures could be directly attributed to the exercise intervention. In this case, there was a combination of voluntary and FES-induced activation of the biceps and triceps muscles involved in the exercise, but the relative contributions of these two inputs could not be ascertained.

Nevertheless, training effects were demonstrated, with peak power output during FES-ACE increasing by 450% over the three-month FES-ACE intervention period, and peak oxygen uptake increasing by 50%. In addition, there was evidence of increased efficiency of the exercise over time. Therefore, we were able to demonstrate some important positive training effects overall as a direct result of FES-ACE training in this individual with chronic tetraplegia.

The protocols for incremental exercise testing were proven to be suitable to determine key cardiopulmonary fitness markers in individuals with tetraplegia. In contrast, we propose that the protocols for constant load exercise testing were appropriate for investigating response kinetics, but practical problems during the execution of these tests made interpretation difficult.

Chapter 5

Case Study 2 - Subject B, C6 (Complete)

5.1 Summary

The purpose of the second case study, presented in this chapter, is to provide further evaluation of the FES-ACE training and testing methods, by testing them with a subject with a greater extent of disability than Subject A. By combining these case study results, we can build a more representative picture of the potential benefits of FES-ACE exercise to the wider C6 SCI population. However, extrapolation of the benefits identified in C6 subjects cannot confidently be applied to C5 and C4 SCI at this stage, due to the heterogeneity of this group.

The subject (Subject B) for this case study was female, with a complete C6 SCI, in the sub-acute phase of injury. She completed the same period of muscle strengthening and FES-ACE exercise intervention as Subject A, with a similar exercise testing schedule. The main difference was that Subject B's FES-ACE training was carried out in parallel with other rehabilitation exercises during her inpatient stay at the spinal injuries unit. Upper limb strength, cardiopulmonary fitness and pulmonary function were monitored throughout her participation in order to identify potential benefits of FES-ACE training in complete C6 SCI. Subject B showed a 150% increase in peak power output over the FES-ACE intervention period, but with no discernible increase in peak oxygen uptake (or other indicators of cardiopulmonary fitness). The increase in peak power output was suggestive of some peripheral adaptations within the exercising muscles as a result of training. Positive changes in cardiopulmonary fitness seemed to have been prevented by central limitations. Severely compromised lung function was identified as a contributing factor, resulting in ventilatory limi-

tation. Indeed, lung capacity at rest (and tidal volume during exercise) was lower at all test points than the average published in the literature for individuals with similar neurology. A second limiting factor was related to the inability to increase cardiac output sufficiently to meet the demands for oxygen delivery, probably as a result of extensive autonomic dysfunction that is commonly observed with a cervical SCI. Nevertheless, over time, this person was able to perform the FES-ACE exercise more efficiently, as determined by the change in the oxygen uptake-work rate relationship, as well as other indices of efficiency. It is speculated here that such improvements in muscle performance would translate to functional benefits during everyday activities involving the upper limb muscles still under voluntary control.

This case study provides further evidence for the feasibility of using the FES-ACE systems and protocols in the target population. However, it also highlights some of the problems of the testing protocols and the challenge of prescribing exercise for those with severe exercise limitation, as is the case for many individuals with cervical SCI. Combined with the results of Case Study 1, these findings prove that the methods described in this thesis are applicable to some extent to tetraplegia, and illustrate some of the potential benefits and limitations of FES-ACE in this population.

5.2 Methods

5.2.1 Subject Details

The details of the subject described in this case study are given in Table 5.1. This was a 52-year-old female with sub-acute SCI, 7 months post-injury (at the start of participation in the project). The table also summarises this subject's neurological status at that time. As an inpatient in the Queen Elizabeth National Spinal Injuries Unit, this subject was undergoing the FES-ACE training programme in parallel with daily rehabilitation.

5.2.2 Details of Training & Testing Programme

The general timetable and protocols for exercise training and testing followed those described in Section 3.2.3. Any additional details of the training programme used with this individual are given in Tables 5.2 and 5.3.

The schedule and work rates used for exercise testing, to monitor indicators of car-

Subject B	
Age	52
Time since injury	7 months
Sex	Female
Neurological status	C6 (complete); good voluntary control of biceps right (BR) and biceps left (BL), no voluntary triceps right (TR) or left (TL)

Table 5.1: Details for Subject B ('Age' and 'Time since injury' are as at the start of participation in the study).

	Week -5	**Week -4**	**Week -3**	**Week -2**	**Week -1**
Number of sessions	2	2	2	2	3
Session duration	10 mins	15 mins	20 mins	25 mins	20 mins
Work rate	-2W*	-2W*	-2W*	0W	0W

Table 5.2: Muscle strengthening programme used with Subject B (* The -2 W work rate refers to 2 W power produced by the motor, and not the subject, to maintain the arm-cranking motion).

	Weeks 1-3	**Weeks 5-7**	**Weeks 9-11**
Number of sessions	3	3	3
Session duration	15 mins	18 mins	2 x 10 mins
Work rate (start)	2W	4.5W	7W
Work rate (end)	4W	6.5W	8.5W

Table 5.3: FES-ACE training programme used with Subject B.

diopulmonary fitness over the course of the training programme, and to identify either positive carry-over effects or negative de-training effects post-training, are given in Table 5.4.

Test Point	**Week 0 TP1**	**Week 4 TP2**	**Week 8 TP3**	**Week 12 TP4**	**Week 16 TP5**
IC test increments	0.5W	1W	1W	1.5W	1W
CL test work rate(s)	1.5W	1.5W,3W	3W	3W	3W

Table 5.4: FES-ACE testing schedule used with Subject B. (IC: Incremental; CL: Constant Load)

The work rates for the constant load tests were set at either 1.5 W or 3 W, to facilitate interpretation of the data. The time-line of training and testing is also illustrated in the bar chart in Figure 5.1. The testing programme was altered slightly from the original schedule, so that the post-training dataset (TP5) was collected only one month after the end of the training period, instead of three. This was because the subject was an inpatient of the spinal injuries unit and was due to be discharged before the end of the three-month post-training period. As well as being at an inconvenient moment, the distance for the subject to travel back to the unit precluded this last scheduled set of tests.

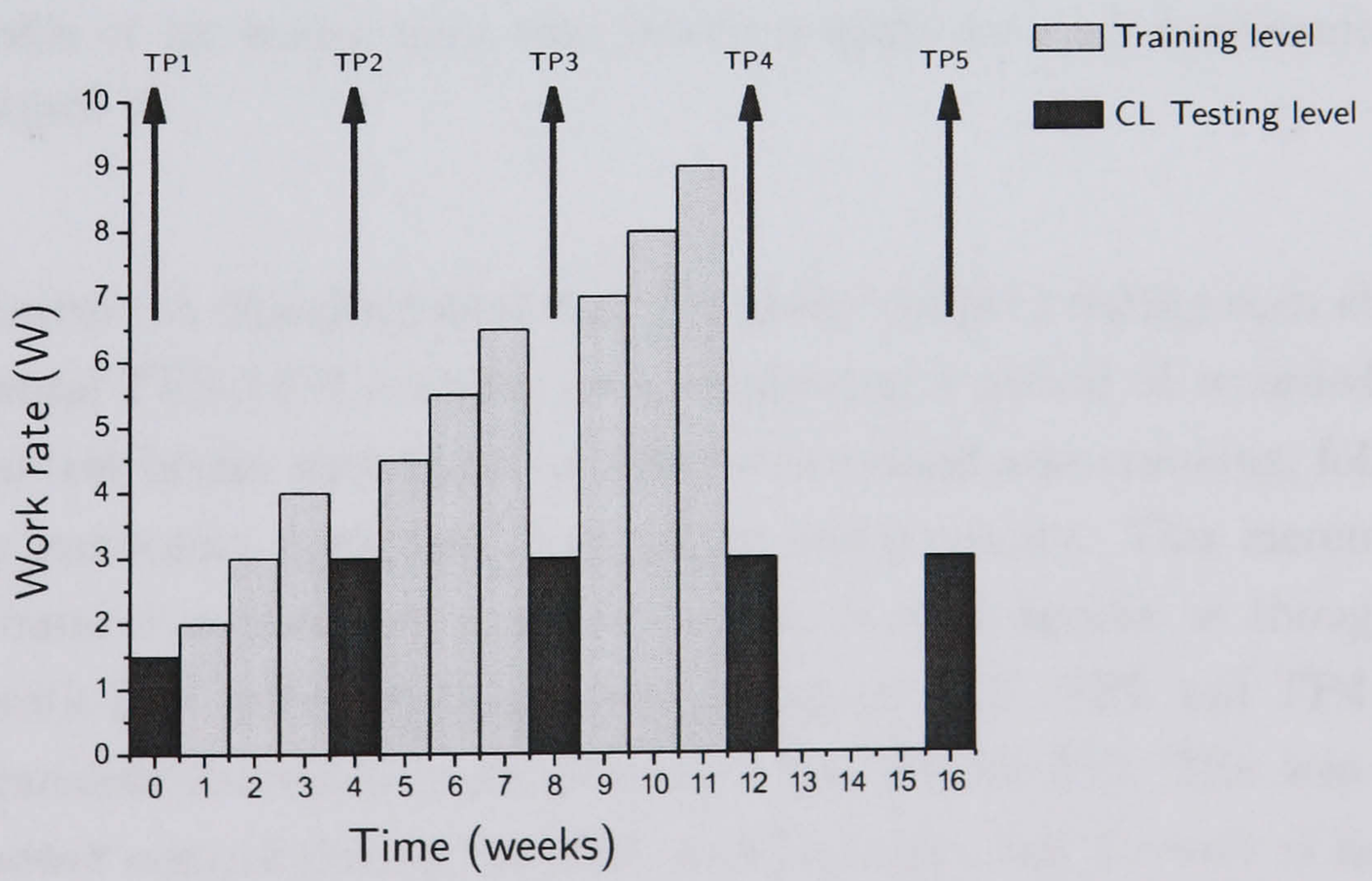


Figure 5.1: Training and constant load testing schedule used with Subject B; CL: Constant Load.

5.3 Results

The results are given separately for: (i) incremental tests, (ii) constant load tests, and (iii) lung function tests.

5.3.1 Incremental Tests

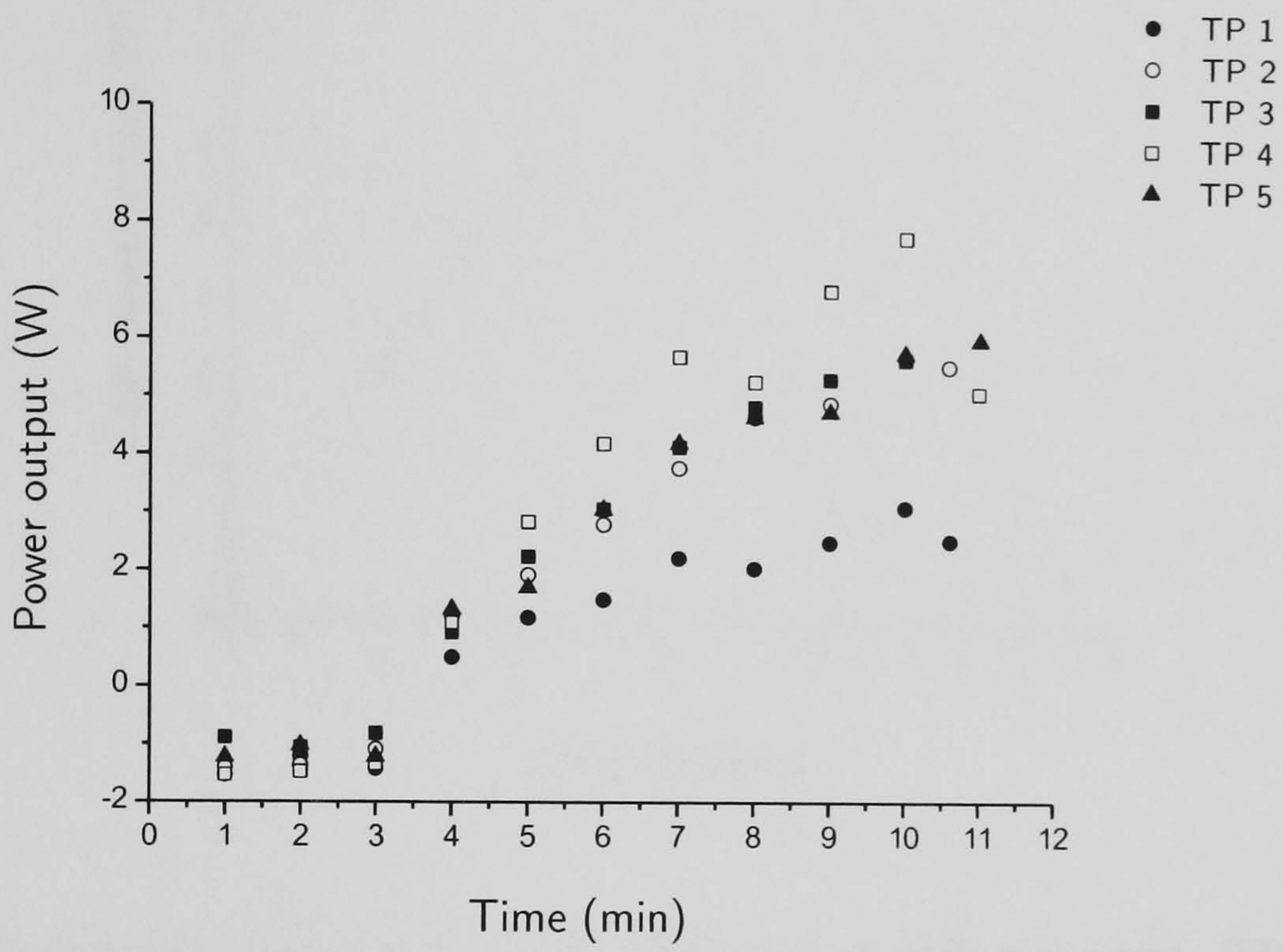


Figure 5.2: Profile of increasing work rate (power output) for each incremental test performed by Subject B.

Figure 5.2 illustrates the changing work rate (or power output) during each of Subject B's incremental FES-ACE exercise tests. Following a period of recorded rest, each incremental test began with three minutes of zero-load arm-cranking, followed by progressively increasing work rate, stepped up every minute. This incremental phase lasted around 8 minutes at each test point. It may appear as though the increments in work rate were not equal within each of TP1, TP2 and TP4, suggested by the transient decreases in power output (see Figure 5.2). This was not a feature of the power control during the FES-ACE exercise, but a result of periods of spasm during the test when power production at the cranks was momentarily compromised. In all cases, the subject was asked to signal (through the eye-blinking system) whether or not she was able to continue. She signalled that she could, and successfully worked through these spasms to complete the tests.

Peak power output

The 60s-mean power outputs produced in the last (or highest) completed stage of each incremental exercise test are shown in Figure 5.3, and summarised in Table 5.5.

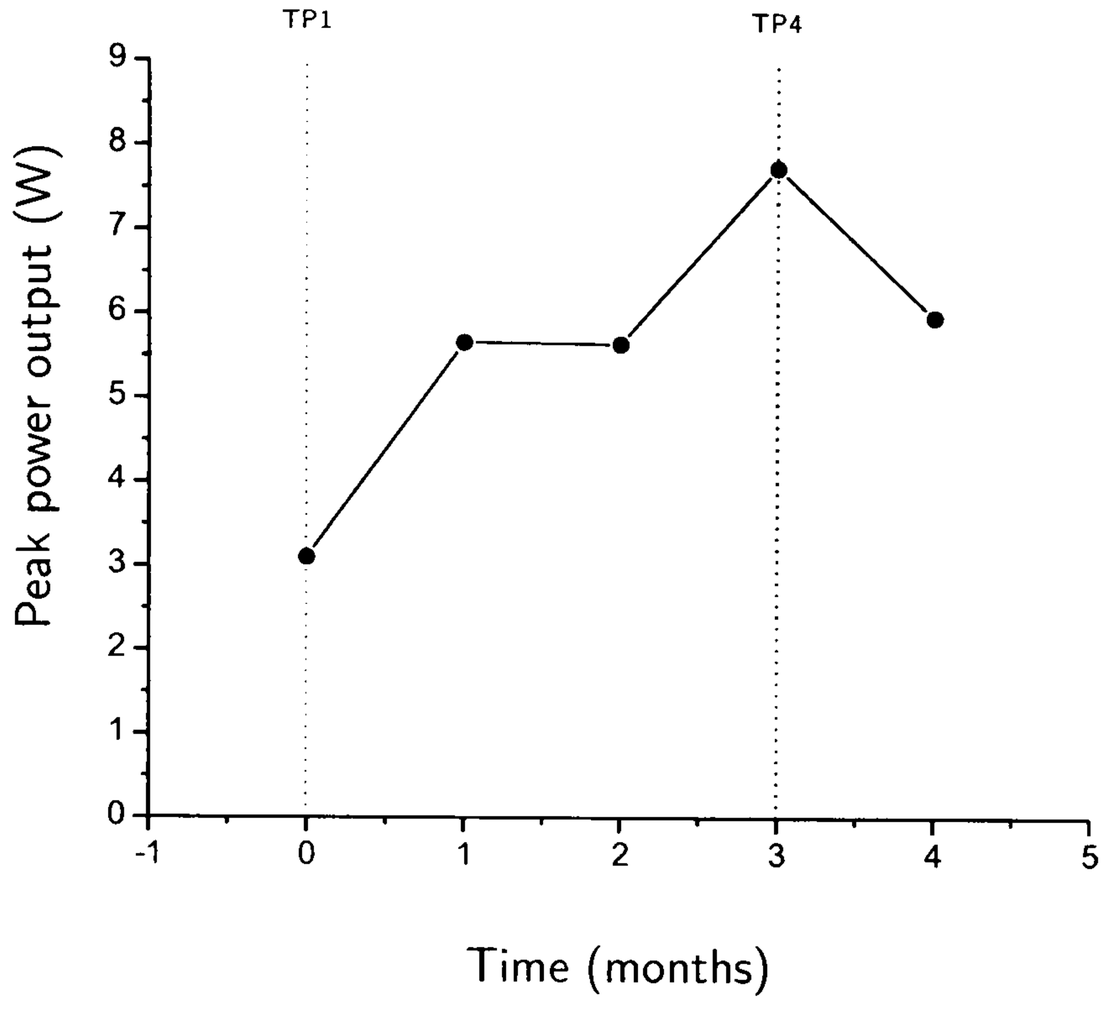


Figure 5.3: Peak power output achieved by Subject B at each test point. TP1 and TP4 are shown to highlight the start and end of FES-ACE exercise intervention. For each test point, the peak power output was calculated as the mean power output during the last (or highest) completed stage of the incremental test.

As Figure 5.3 shows, the peak power produced by Subject B increased from a baseline (TP1) of 3 W to an end-of-training value of just under 8 W (at TP4). There was no change in peak power output between TP2 and TP3.

The data suggest that Subject B was then unable to maintain the level of power production of the upper limbs between TP4 and TP5, when she was not using the FES-ACE exercise modality for one month. During this month, however, she had replaced this FES-ACE activity with other upper-limb rehabilitative work in the gym during the remainder of her inpatient stay at the spinal unit. There was a decrease in peak power output over this month from around 8 W at TP4 to 6 W at TP5. This may suggest that there was a de-training effect with Subject B when the FES-ACE exercise routine had been removed from her programme of rehabilitation. A further set of tests two months after TP5 may have either confirmed or refuted

Test Point	Training status	Peak Power Output (W)	Change in Peak Power Output (W)
1	**Baseline** (no prior training)	**3.1**	–
2	+1 month FES-ACE	5.7	+ 2.6
3	+2 months FES-ACE	5.7	0
4	**+3 months FES-ACE**	**7.7**	**+ 2.1**
5	+1 month post-training (no exercise)	6.0	- 1.8

Table 5.5: Peak power output data for Subject B.

this theory. In addition, repeatability tests would have been needed to identify whether differences as small as 2 W between test points could have been explained by overall test-to-test variation. Such repeatability tests were not performed. The main reason for this was to minimise the number of tests that the subject had to undertake. Indeed, the tests were time-consuming, and needed to be timetabled around daily rehabilitation activities.

An interesting point to note is that, in the incremental exercise test at TP4, Subject B was unable to exceed the power outputs (8.5 W) which had been maintained in 15-minute sets during training sessions in the week leading up to the test (see Table 5.3). This could be interpreted as a limitation of the incremental exercise testing protocol, as the peak power output reached during the test by this subject did not seem to reflect true peak capability of the muscles.

Peak oxygen uptake

The mean resting oxygen uptake, peak oxygen uptake and the gradient of the slope of oxygen uptake against power output are shown for each test point in Table 5.6. The resting oxygen uptake values are the mean of the last three minutes of the recorded resting phase data. For the peak oxygen uptake, the mean of the last thirty seconds of the last (or highest) completed stage of the incremental test is given. The peak oxygen uptake calculated is plotted for each test point in Figure 5.4.

With Subject B, there was no clear pattern of change in peak oxygen uptake over the three-month FES-ACE training programme. There was a noticeable decrease in peak oxygen uptake with this subject at the end of the first month of training from a baseline value of 0.53 l/min (at TP1) to 0.41 l/min at TP2. Over the next

Test Point	Resting $\dot{V}O_2$ (l/min)	Peak $\dot{V}O_2$ (l/min)	Gradient of slope of $\dot{V}O_2$ vs. PO
1	0.287	0.526	0.029 (R^2= 0.63)
2	0.265	0.413	0.019 (R^2= 0.61)
3	0.265	0.484	0.026 (R^2= 0.78)
4	0.277	0.539	0.019 (R^2= 0.51)
5	0.298	0.547	0.024 (R^2= 0.70)

Table 5.6: Oxygen uptake data for Subject B.

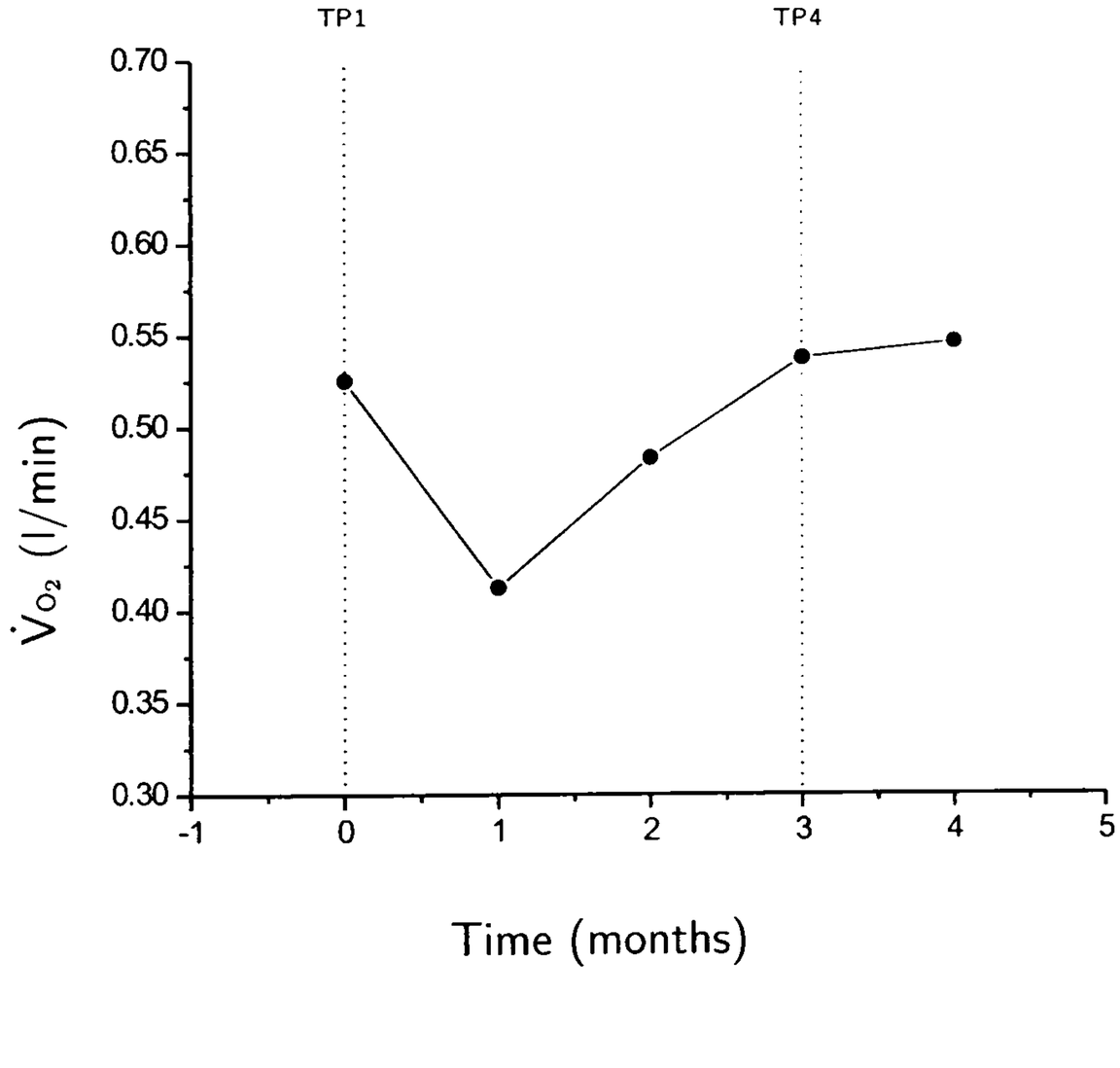


Figure 5.4: Peak oxygen uptake for Subject B at each test point. TP1 and TP4 are shown to highlight the start and end of FES-ACE intervention. For each test point, the peak oxygen uptake was calculated as the mean of the last thirty seconds of the last (or highest) completed stage.

two months, this gradually increased again back to a peak $\dot{V}O_2$ of 0.54 l/min at TP4. One month without training with FES-ACE apparently had no effect on peak oxygen uptake in this subject, which was 0.55 l/min at TP5.

However, the pattern of use of the oxygen by the exercising muscles during the FES-ACE exercise may have changed in some way, as the power production increased over the training period even though the peak oxygen uptake did not. To illustrate this, oxygen uptake is plotted against power output for each test point in Figure 5.5. The linear approximation of the relationship between oxygen uptake and power output was fitted for each test point, and plotted in Figure 5.6. It should be noted that the correlation coefficient for these fitted linear relationships was variable (from only R^2= 0.51 at TP4 to R^2= 0.78 at TP3, as shown in Table 5.6). Even so, there seemed to be an overall decrease in the gradient of the slope of $\dot{V}O_2$ against power output, from the start of training (gradient of 0.029 at TP1) to the end of training (gradient of 0.019 at TP4), and a return to a slightly steeper slope after a month without training (gradient of 0.024 at TP6). As well as the change in gradient, the position of the slope shifted downwards considerably after the first month of training, suggesting that the oxygen cost of unloaded cycling had decreased.

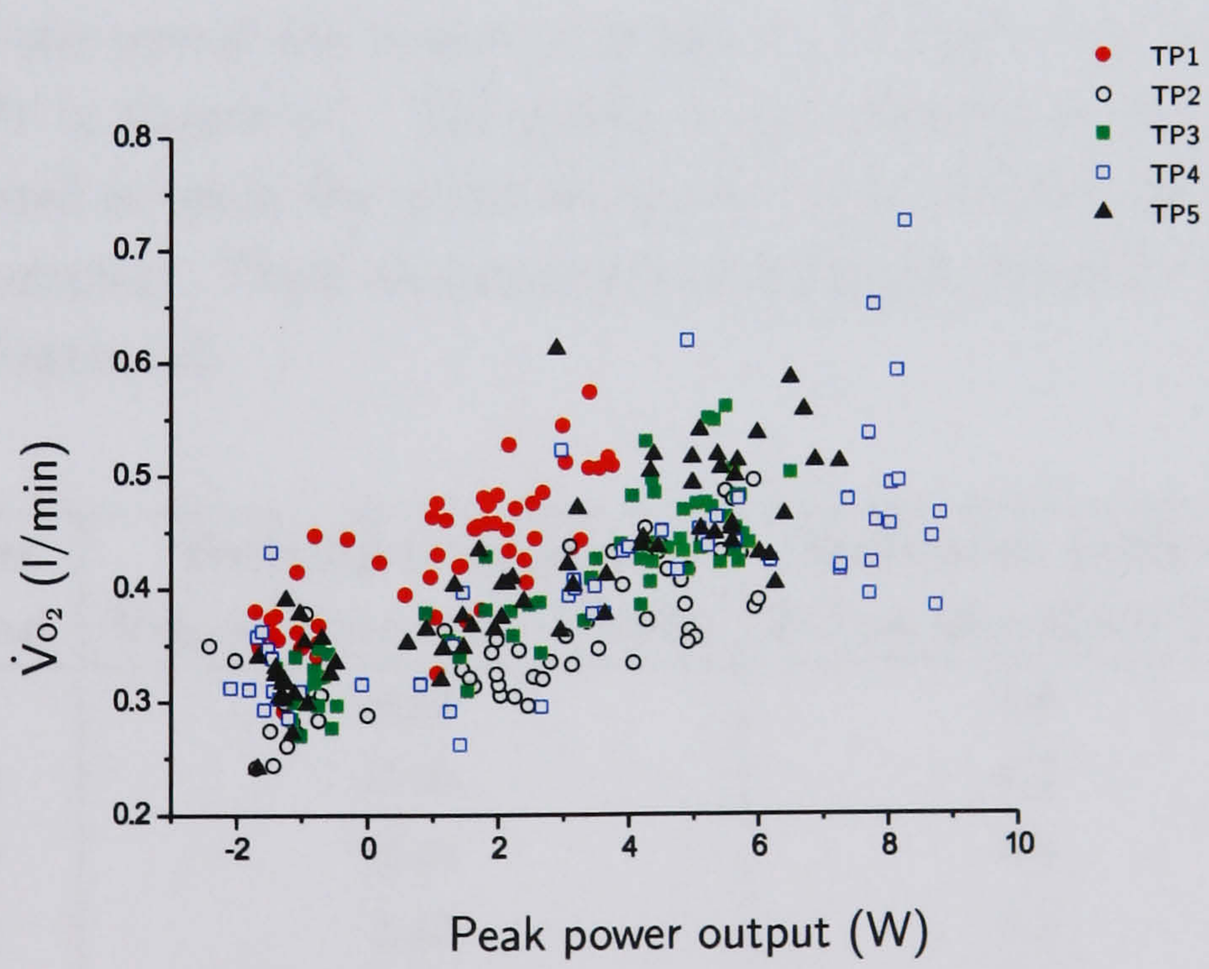


Figure 5.5: Oxygen uptake plotted against power output for Subject B for the incremental test at each test point. The oxygen uptake data have been edited and either 4-breath or 8-breath averaged.

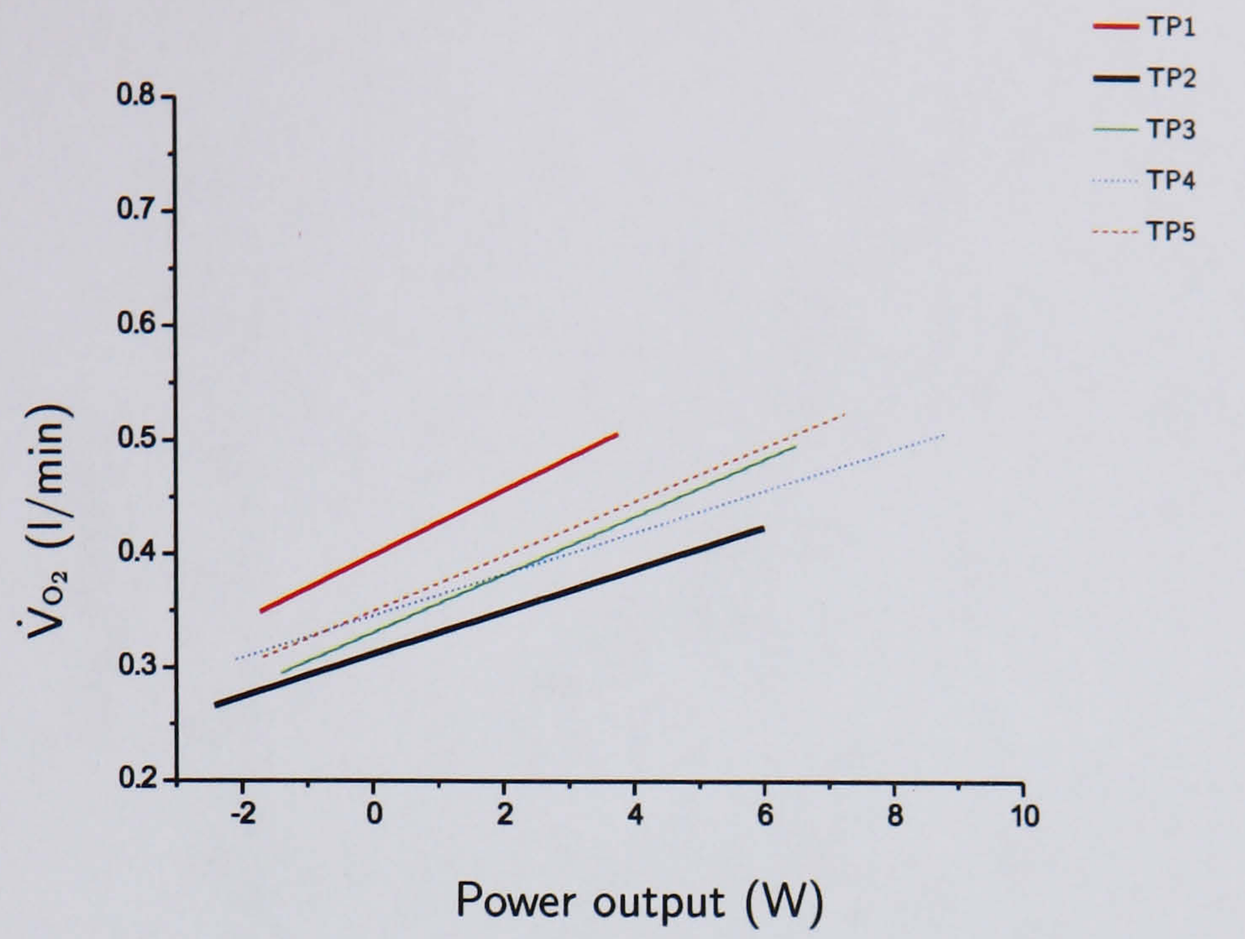


Figure 5.6: Linear approximation of oxygen uptake against power output for Subject B at each test point.

Lactate threshold

An example of the use of the V-slope method to determine the lactate threshold is given for TP1 in Figure 5.7. The points taken to represent the lactate threshold were estimated for each test point using the V-slope method (in the absence of blood lactate samples). These estimates are presented in Table 5.7 and illustrated graphically in Figure 5.8.

Test Point	**Estimated value of $\dot{V}O_2$ at threshold (l/min)**	**Estimated value of PO at threshold (W)**
1	0.49	2.4
2	0.40	4.4
3	0.45	4.6
4	0.45	5.7
5	0.50	3.9

Table 5.7: Lactate threshold estimation data for Subject B.

If these characteristic breakpoints in the gas exchange can be considered as representative of the lactate thresholds, it seems that there was no clear pattern in the oxygen uptake at lactate threshold over Subject B's period of participation. Indeed,

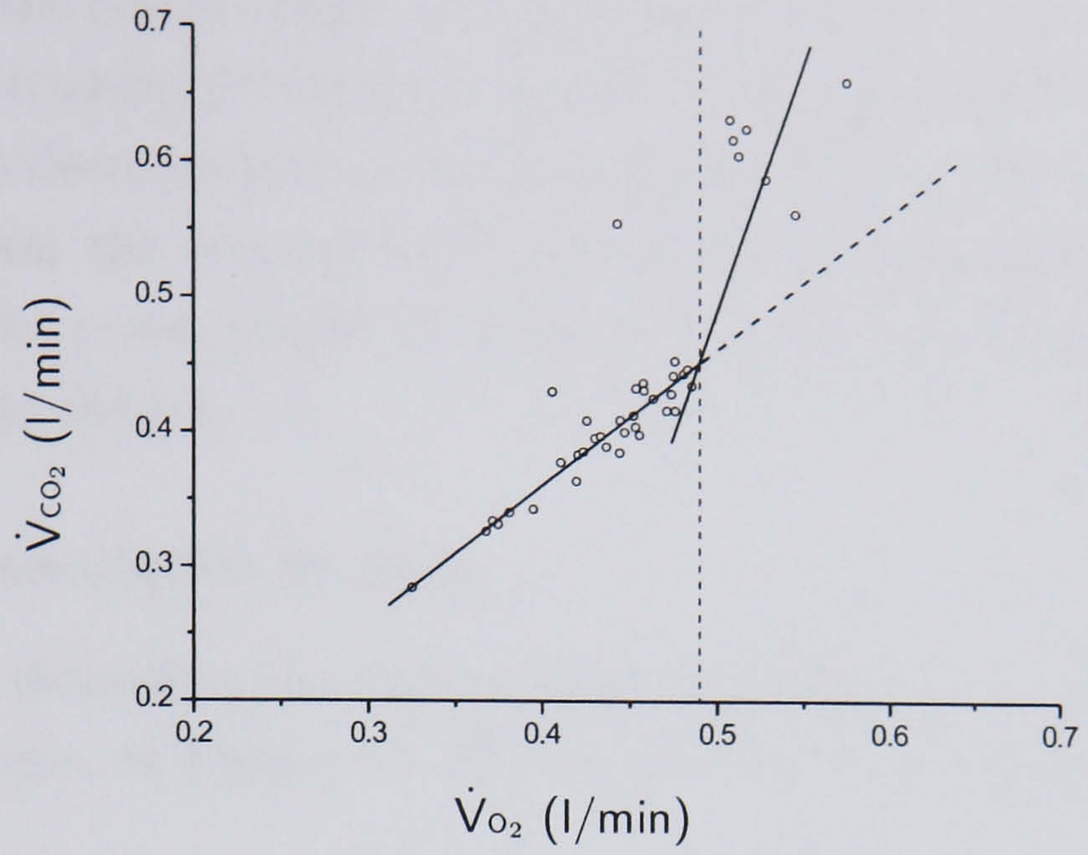


Figure 5.7: Illustration of the V-slope method, shown for data from TP1, with Subject B.

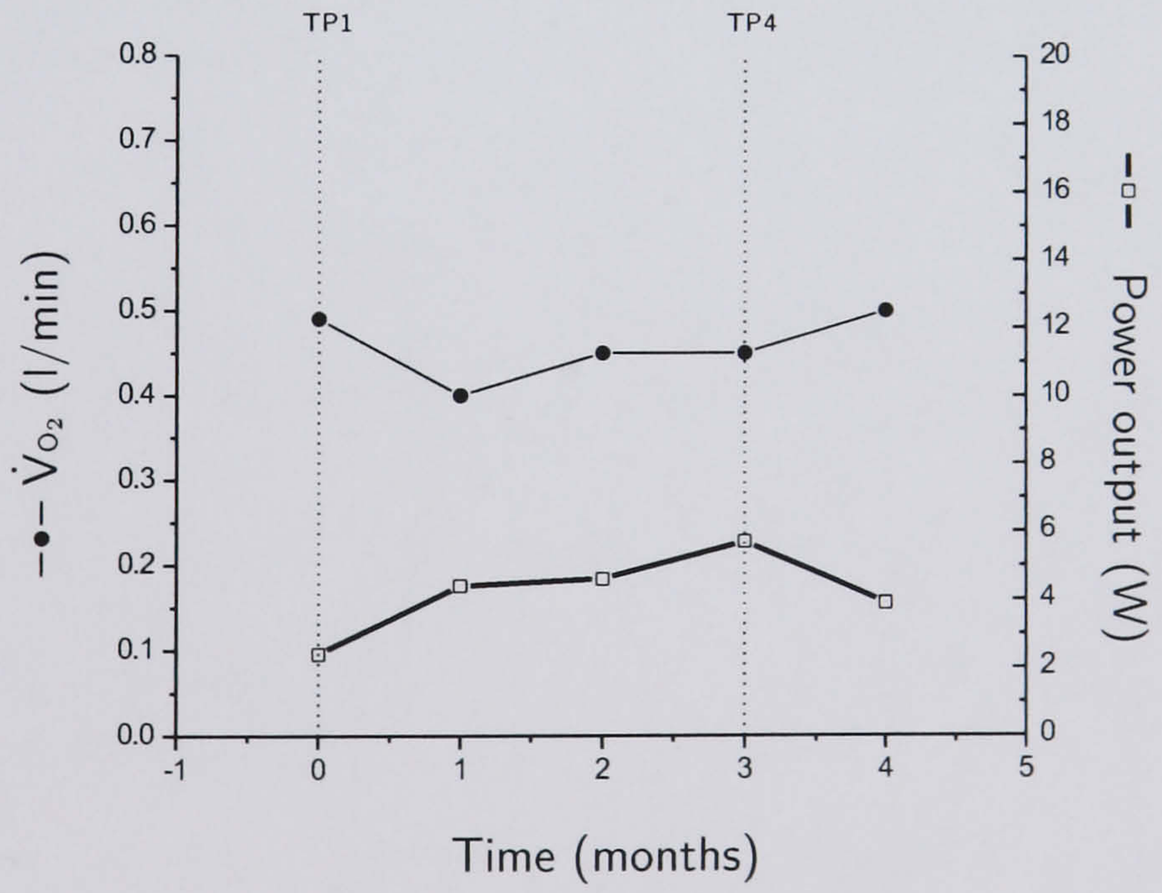


Figure 5.8: Oxygen uptake and power output at estimated lactate threshold for Subject B, at each test point.

as with peak oxygen uptake, the lactate threshold decreased after the initial month of FES-ACE exercise intervention, but then increased again before the end of training. In contrast, the power output at which this threshold was reached did seem to increase over the training period from around 2.4 W at baseline (TP1), to 5.7 W at TP4, and then to decrease post-training to 3.9 W at TP5. The percentage of peak oxygen uptake that the estimated LT represented was consistently high (ranging from 83–98%). The power output at which the LT was estimated varied from 65 to 81% of peak power output.

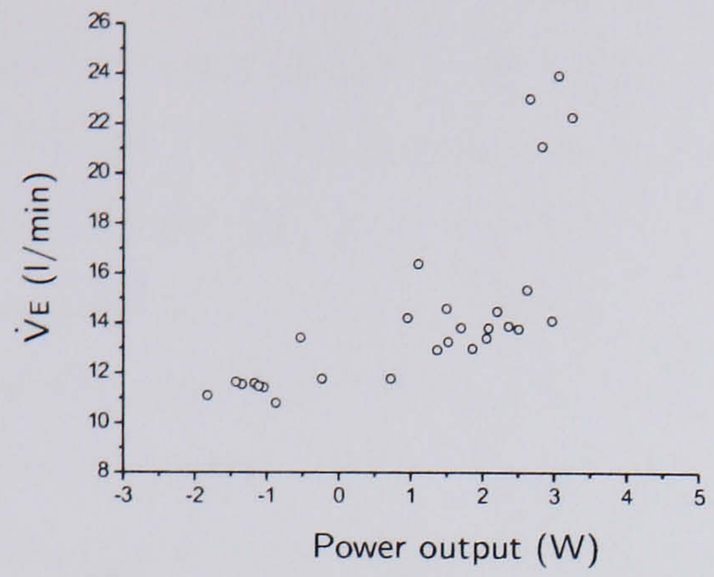
Graphical representation of data

A 10-panel array displaying the cardiopulmonary data for test point 1 (baseline) is given as an example, in Figure 5.9. There are two main points to note from this panel.

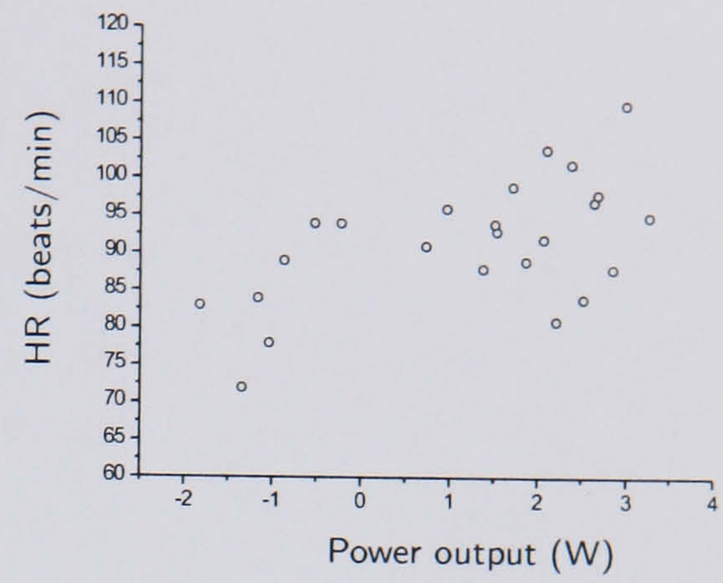
1. Heart rate remained below 115 beats/min (Figure 5.9(b)).

2. During peak effort, tidal volume did not exceed 0.58 l (Figure 5.9(g)).

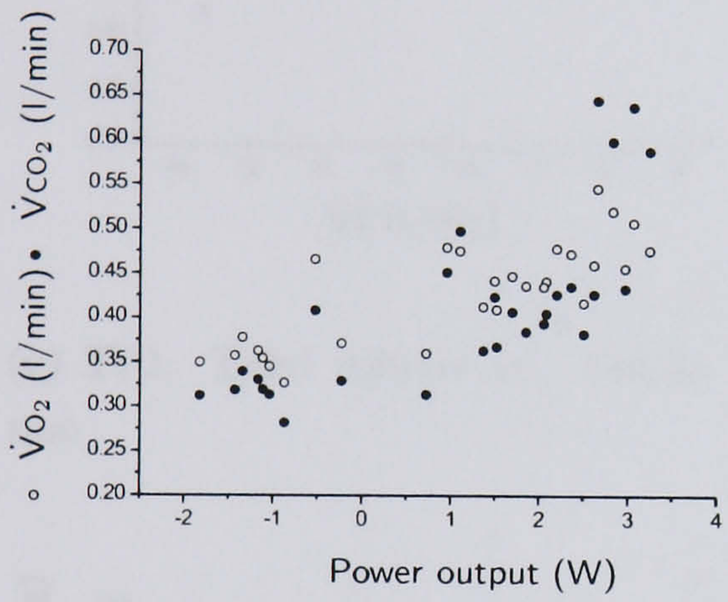
The equivalent plots for each of the other test points for Subject B can be found in Appendix B.



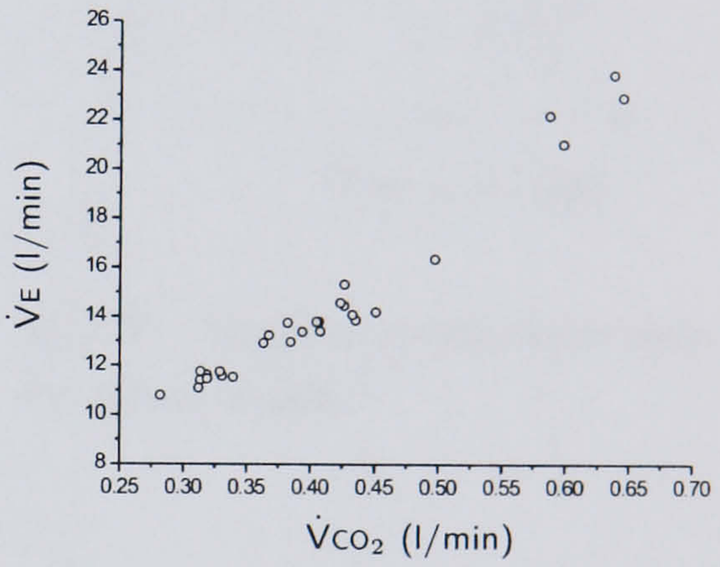
(a) TP1: Ventilation vs. power output



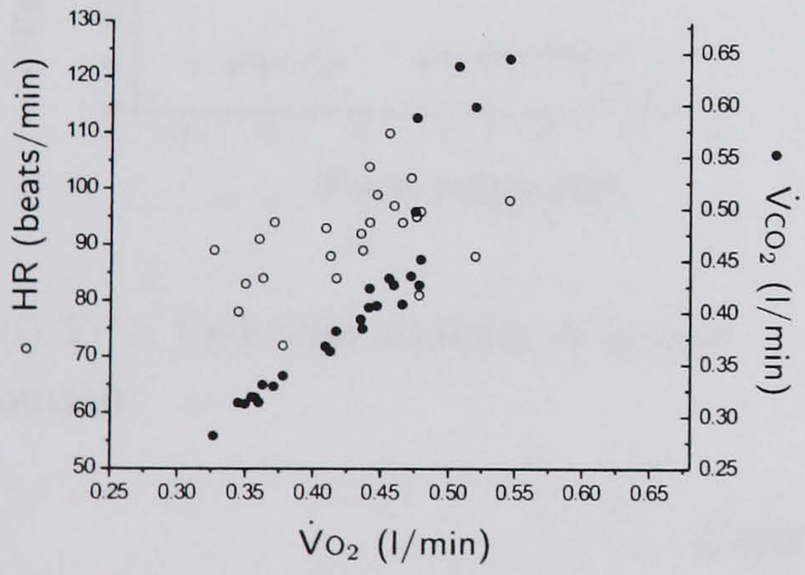
(b) TP1: Heart rate vs. power output



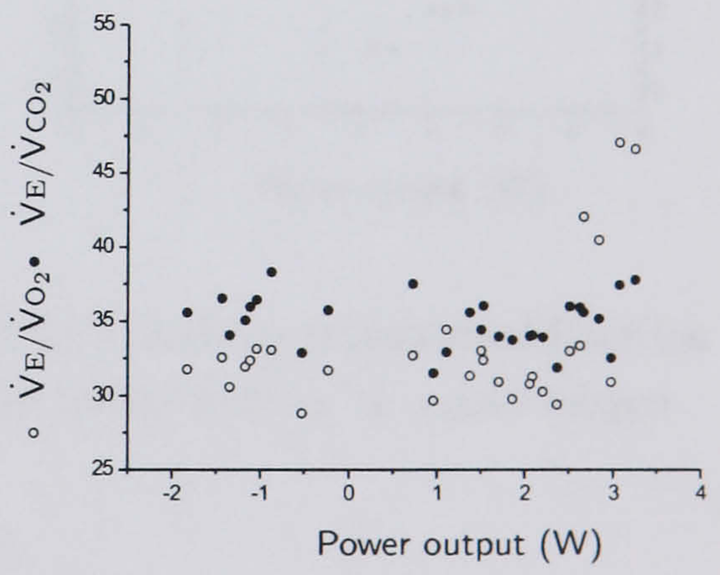
(c) TP1: Oxygen uptake and carbon dioxide output vs. power output



(d) TP1: Ventilation vs. carbon dioxide output

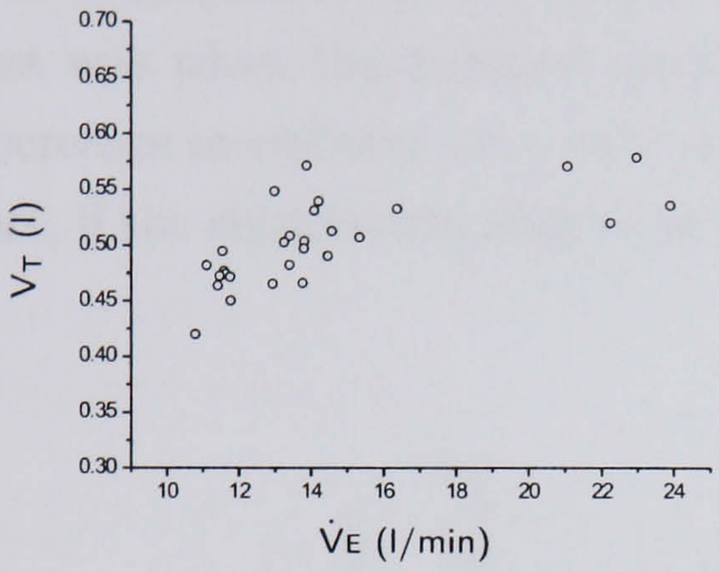


(e) TP1: Heart rate and carbon dioxide output vs. oxygen uptake

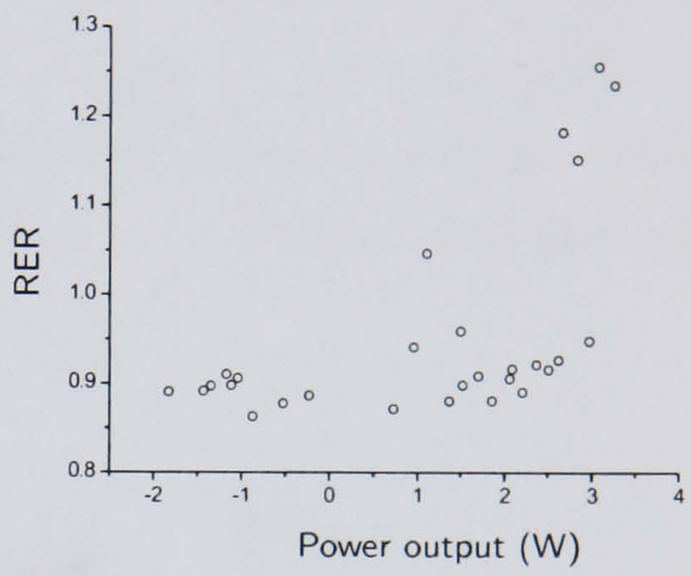


(f) TP1: Ventilatory equivalents vs. power output

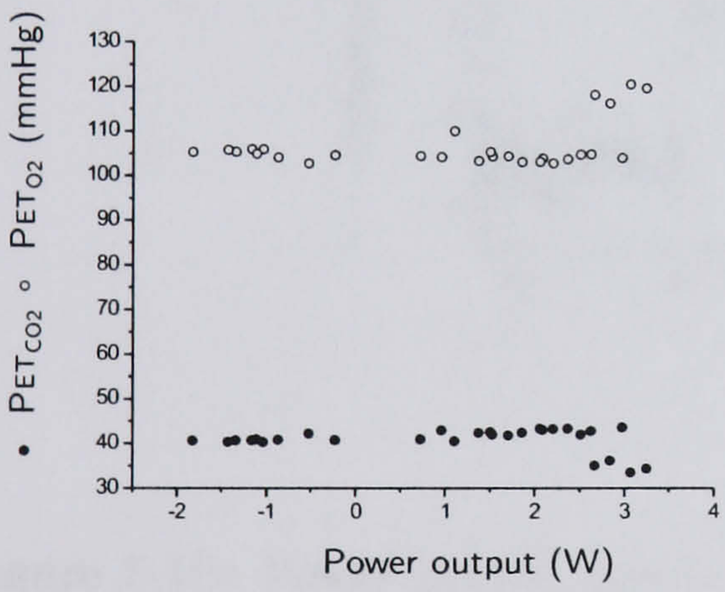
Figure 5.9: Graphical representation of cardiopulmonary data for Subject B, from incremental FES-ACE exercise testing at Test Point 1 (Baseline). The data have been edited and 8-breath averaged.



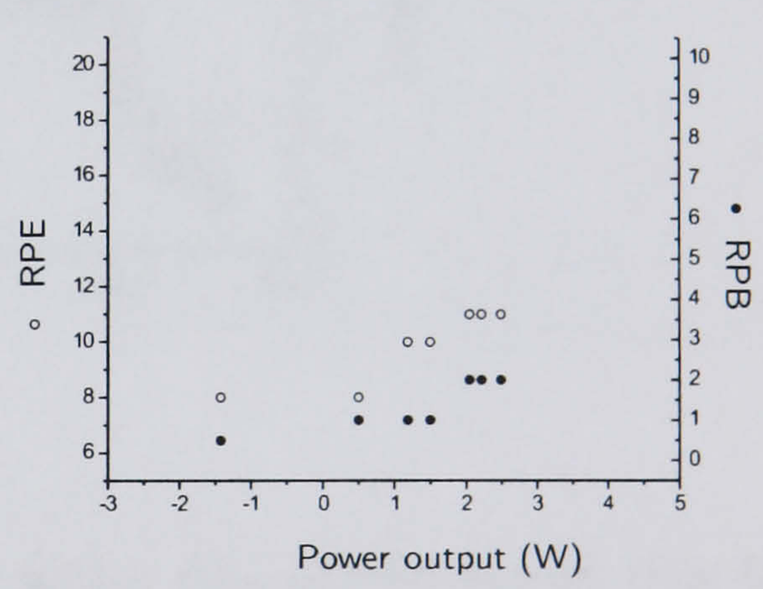
(g) TP1: Tidal volume vs. ventilation



(h) TP1: Respiratory exchange ratio vs. power output



(i) TP1: End-tidal tensions vs. power output



(j) TP1: Ratings of Perceived Exertion and Breathlessness vs. power output

Figure 5.9: (cont.)

5.3.2 Constant Load Tests

An example of the power control during constant-load exercise testing is given for TP3 (at 3 W) in Figure 5.10, to show the step change in work rate from zero-load to the chosen constant load. The plot for this test point was chosen as an illustration because it not only highlights the difficulties of controlling power output at such low values, but also clearly shows the points during the test when the subject experienced spasms. Such points can be identified by a momentary decrease in cadence, and consequently, power output. One of the criteria for terminating an exercise test was when the cadence decreased below 35rpm. However, in these tests, such decreases in cadence were only transient in nature when caused by spasms. Therefore, if the subject was able to work through the spasms, the exercise test continued.

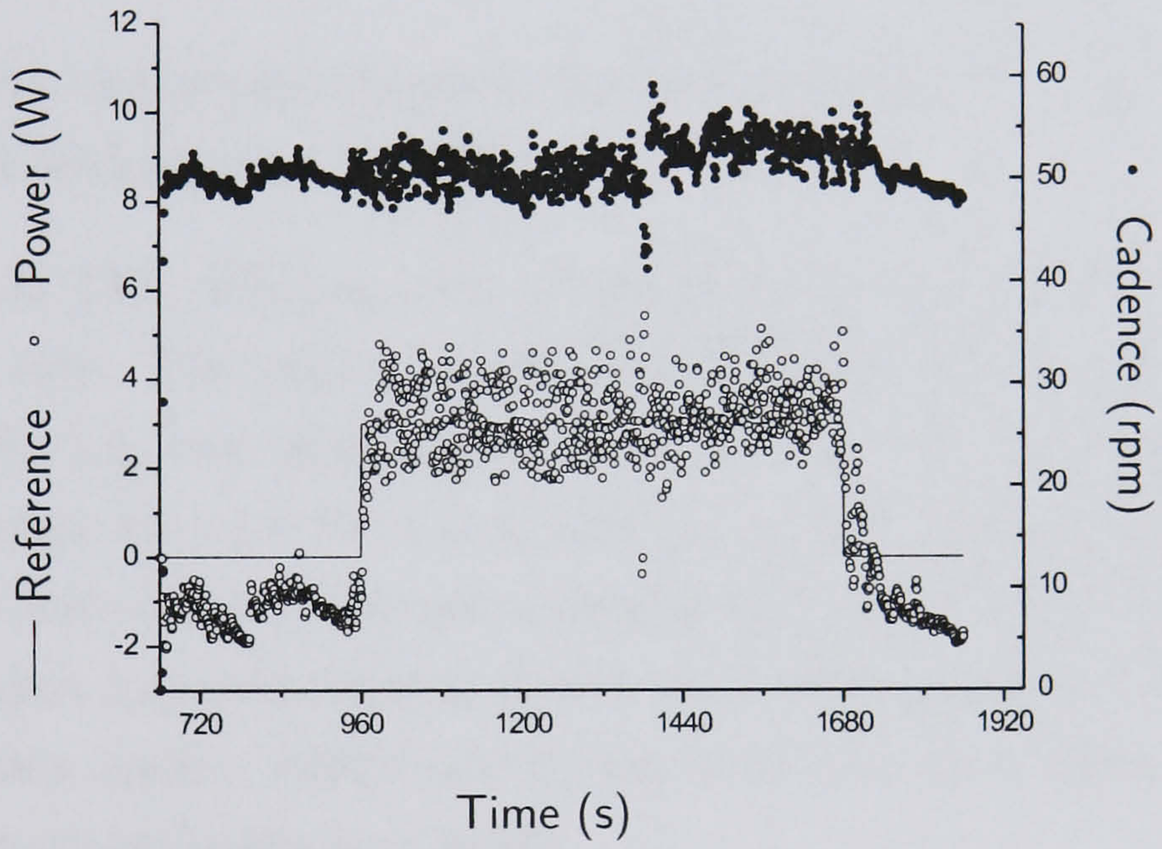


Figure 5.10: Power output, power reference and cadence data plotted against time for Subject B, for a 3 W constant load test at TP3.

The steady-state oxygen uptake and respiratory exchange ratio data for each stage of the constant load tests are summarised in Table 5.8.

Time constants

For the constant load test data, an attempt was made at fitting the first-order exponential to the response of each of $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}E$ (all edited, but unaveraged), to determine their time constants. However, the validity of the resulting time constants is questionable. Although the constant load work rate had been

Test Point	Work Rate (W)	Resting		Zero Load		Constant Load	
		$\dot{V}O_2$ (l/min)	RER	$\dot{V}O_2$ (l/min)	RER	$\dot{V}O_2$ (l/min)	RER
1	1.5	0.262	0.71	0.337	0.84	0.429	1.08
2	1.5	0.232	0.77	0.290	0.83	0.413	1.12
2	3	0.236	0.67	0.315	0.79	0.376	0.89
3	3	0.229	0.72	0.294	0.86	0.438	0.95
4	3	0.270	0.81	0.353	0.93	0.425	1.03
5	3	0.252	0.76	0.288	0.84	0.457	1.01

Table 5.8: Gas exchange data for each stage of constant load testing for Subject B. for each test point. Steady-state is assumed, and data are shown as the mean of the last three minutes of each stage.

chosen to be below the lactate threshold for each test, there was a recurrent pattern with this subject with respect to RER:

1. TP3, TP4 & TP5: RER seemed to transiently exceed 1.0 during the constant load work rate. The subject would initially maintain the constant work rate at an RER<1.0, but after approximately 5 minutes at this work rate, RER would increase to >1.0 for a few minutes, before coming back down to <1.0 before the end of the 12 minute constant load period. This may be explained by the subject hyperventilating after 5 minutes at the higher work rate, before settling down again. Alternatively, the work rate may have been above the lactate threshold (supra-threshold).

2. TP1 & TP2 (1.5 W): RER was consistently above 1.0, for the duration of the constant load phase, which suggests either that the exercise was supra-threshold (for TP1, but not for TP2 (1.5 W)[1]) at that work rate, or that the subject was a consistent hyperventilator.

Assuming the lactate threshold concept was valid here, the only constant load test which fulfilled all the requirements for fitting the basic mono-exponential curve was that carried out at TP2, at 3 W. Here, the subject maintained the 3W for 12 minutes with an RER below 1.0. The subject additionally seemed to be in a metabolic

[1]The fact that the subject had an RER below 1.0 during the 3 W test at TP2, but above 1.0 during the 1.5 W test at the same test point, gives weight to the idea that, at least for the 1.5 W test TP2 (and possibly also for TP3, TP4 and TP5), the work rate was sub-threshold, and the person was hyperventilating for other reasons. The two tests at TP2 were carried out on different days.

steady-state in the last three minutes of the zero-load and the 3 W constant load phases. Therefore, only the data from the TP2 (3 W) constant load test would have been valid for the determination of mono-exponential kinetics of gas exchange response to a step increase in work rate. Fitting of the mono-exponential curve was therefore attempted for TP2 (3 W), but was unsuccessful for all three variables.

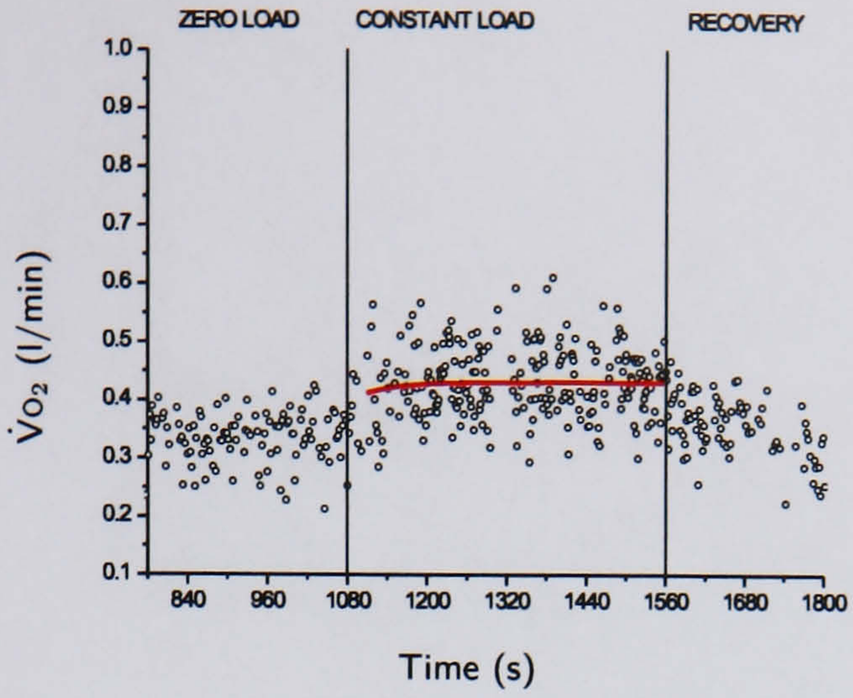
Nevertheless, to illustrate feasibility of the approach, curve fitting is shown for TP1 (at 1.5 W) in Figure 5.11, and for TP4 (at 3 W) in Figure 5.12. These would represent the response kinetics for the start and end of training, if the analyses were valid. The exponential curve fitting (having removed the first 25s of the responses, which should represent phase I kinetics), produced the results shown in Table 5.9. In terms of the relative speed of response of $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}E$, TP4 shows the more typical pattern for sub-threshold exercise, with $\dot{V}O_2$ responding faster to the step change in work rate, and $\dot{V}CO_2$ and $\dot{V}E$ lagging. At TP1, the relative speed of the response of the three variables, however, was more consistent with supra-threshold kinetics (with $\dot{V}CO_2$ and $\dot{V}E$ being faster than $\dot{V}O_2$), which implies that the kinetic analysis results of the two tests are not comparable.

Test Point	Time constant for $\dot{V}O_2$ (s)	Time constant for $\dot{V}CO_2$ (s)	Time constant for $\dot{V}E$ (s)
1	54	33	41
4	86	131	241

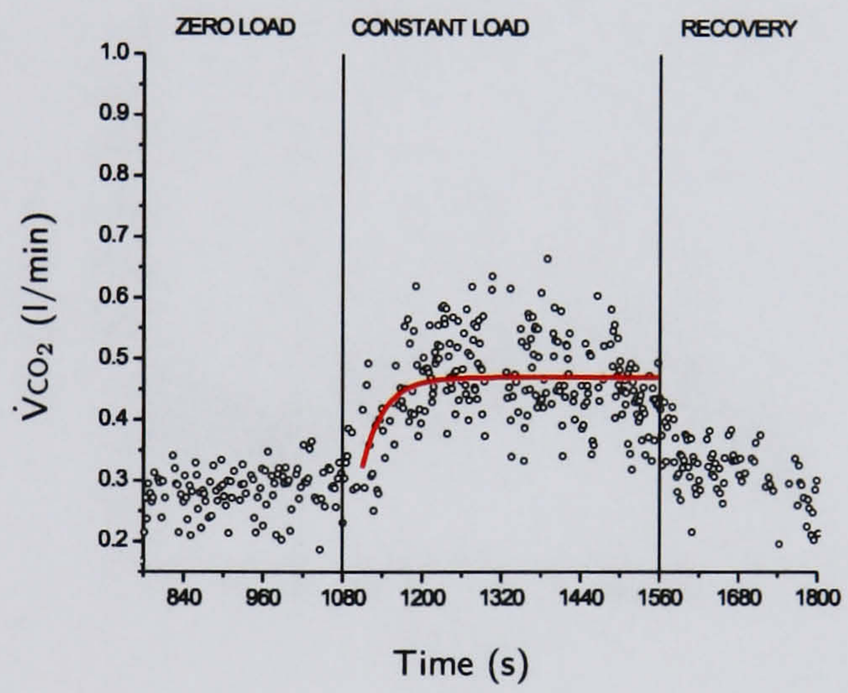
Table 5.9: Estimated time constants for $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}E$ at the start (TP1) and end of training (TP4) for Subject B.

Efficiency

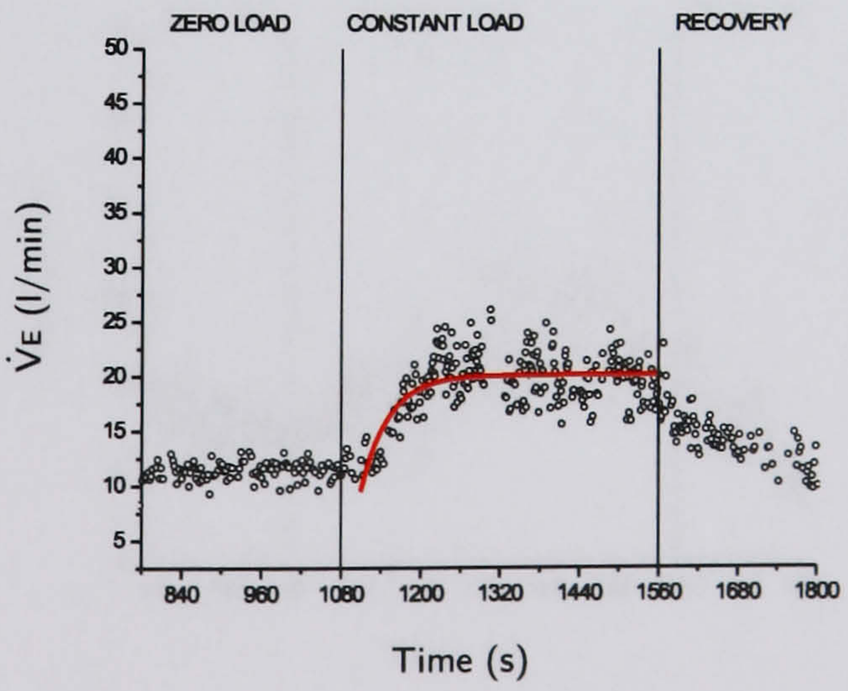
As with the determination of response kinetics, efficiency calculations also require that the subject has reached steady-state. All the constant load tests carried out with Subject B seemed to fit this criterion. However, TP1 may have violated a different condition for efficiency calculations, namely that the subject should be exercising below the 'lactate threshold'. From the RER recordings, it appears that Subject B might not have been exercising below this threshold in the test at TP1. Nonetheless, estimated efficiency indices are summarised for all test points in Table 5.10 and displayed graphically in Figure 5.13 (for TP2, efficiency values calculated at both 1.5 W and 3 W are given).



(a) TP1: $\dot{V}o_2$, time constant = 54 s.

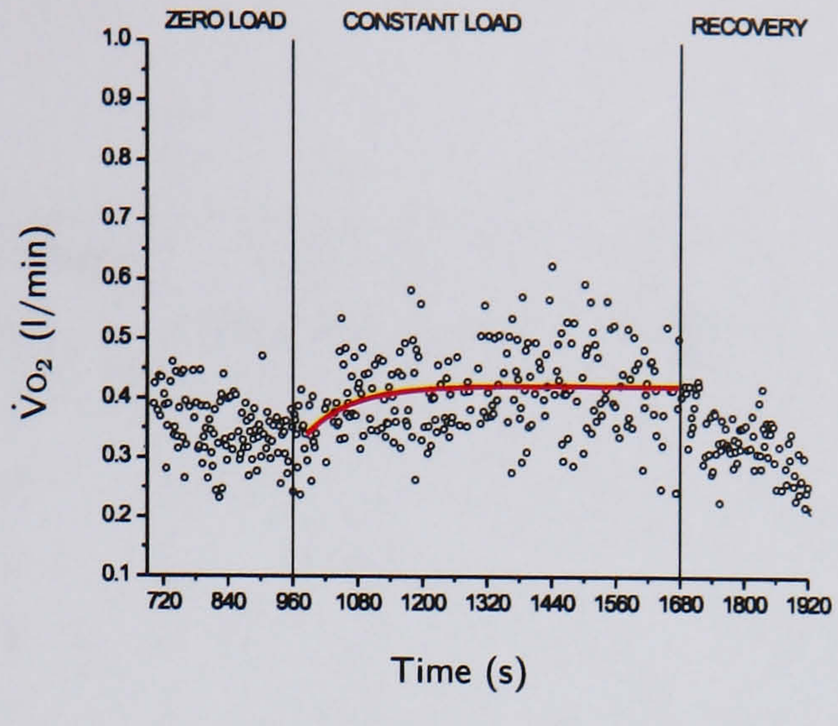


(b) TP1: $\dot{V}co_2$, time constant = 33 s.

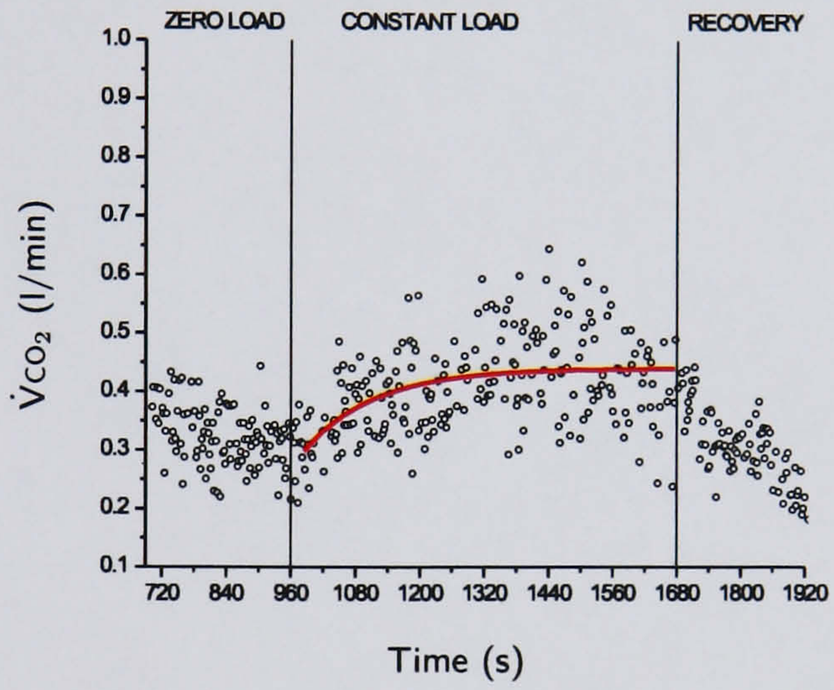


(c) TP1: $\dot{V}_E$, time constant = 41 s.

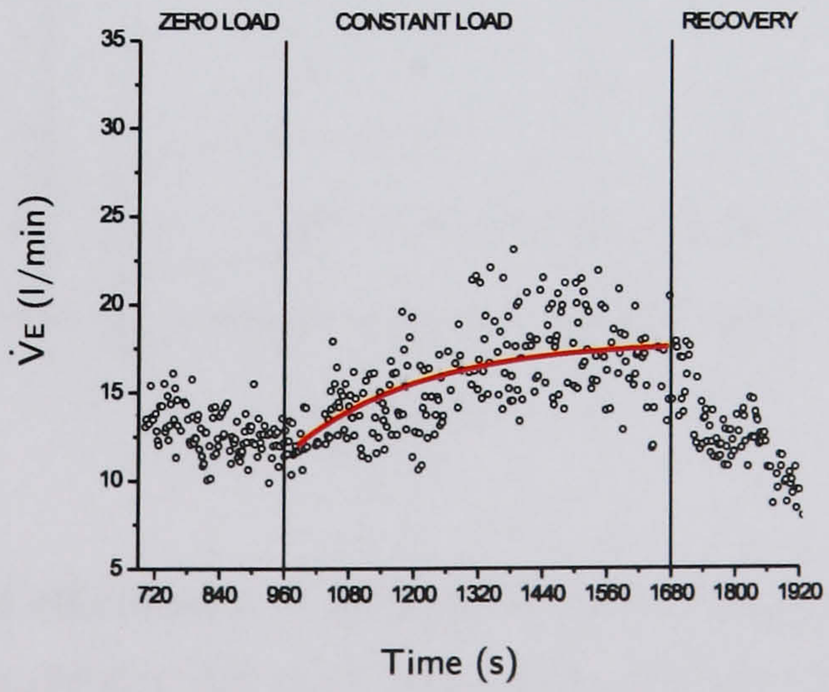
Figure 5.11: Exponential curve fitting to determine response kinetics at TP1.



(a) TP4: $\dot{V}o_2$, time constant = 86 s.



(b) TP4: $\dot{V}co_2$, time constant = 131 s.



(c) TP4: $\dot{V}_E$, time constant = 241 s.

Figure 5.12: Exponential curve fitting to determine response kinetics at TP4.

Test Point	Work Rate (W)	Gross Efficiency (%)	Net Efficiency (%)	Work Efficiency (%)
1	1.5	0.8	1.9	3.4
2	1.5	1.3	2.9	4.1
2	3	2.2	5.5	12.0
3	3	2.1	4.1	6.0
4	3	2.1	5.2	11.0
5	3	2.0	4.1	5.0

Table 5.10: Efficiency data for Subject B.

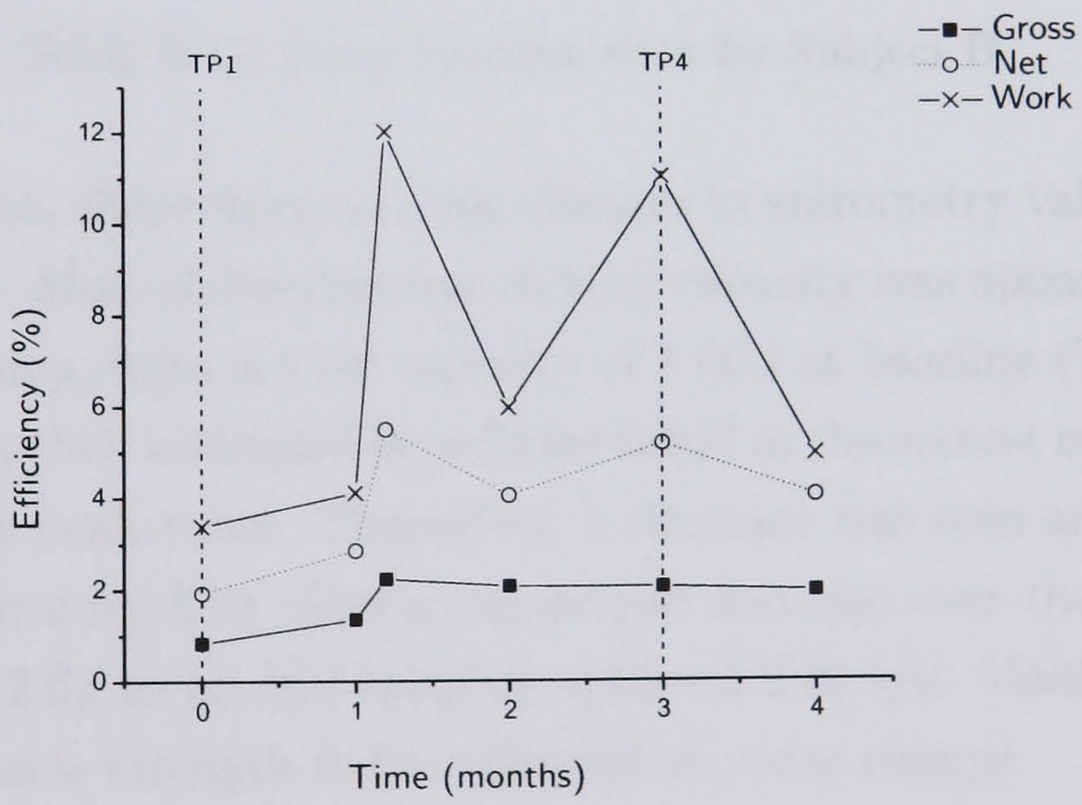


Figure 5.13: Estimated efficiencies of FES-ACE for Subject B at each test point. TP1 and TP4 are shown to highlight the start and end of the exercise intervention period.

Gross efficiency values were the most stable, ranging only from 0.8% (at baseline) to 2.2% (at TP2, 3 W). Net efficiency ranged from 1.9% (at baseline) to 5.5% (at TP2, 3 W). Work efficiency values varied considerably from one test to the next (even at the same test point, but at different work rates), ranging from 3.4% (at baseline) to 12.0% (at TP2, 3 W). The variability in work efficiency values could be explained by the differences in the oxygen cost of 'zero-load' arm-cranking from one test to another. This is discussed in greater detail in Section 5.4.3.

5.3.3 Lung Function Tests

Lung function data, collected at each test point, are presented for Subject B in Table 5.11, and illustrated graphically in Figure 5.14.

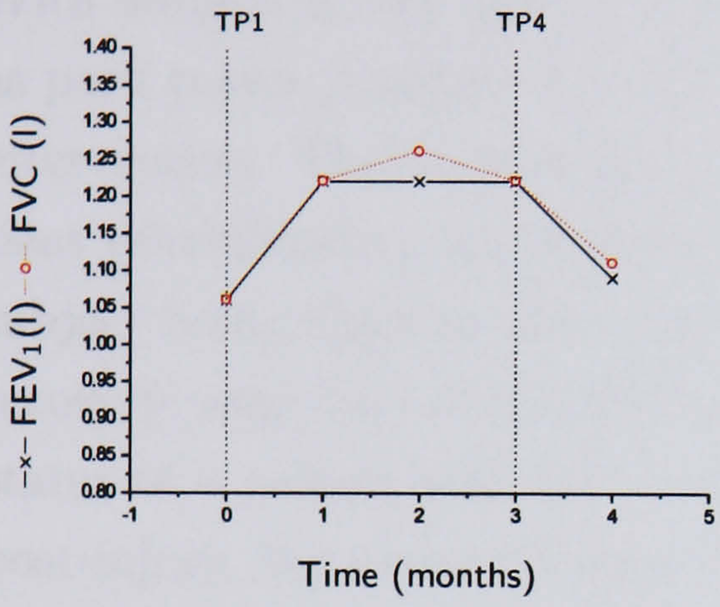
Test Point	**FEV_1** (l)	**FVC** (l)	**$\frac{FEV_1}{FVC}$** (%)	**PEF** (l/s)	**PE_{max}** (cmH_2O)	**PI_{max}** (cmH_2O)
1	1.06	1.06	100	2.62	16	19
2	1.22	1.22	100	2.90	19	21
3	1.22	1.26	97	3.20	19	20
4	1.22	1.22	100	2.86	20	16
5	1.09	1.11	98	2.30	19	15

Table 5.11: Lung function data for Subject B.

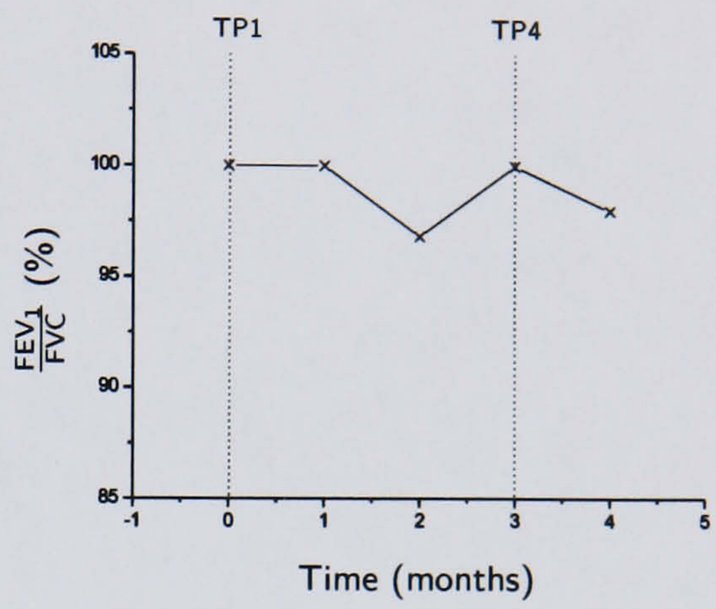
As Figure 5.14 shows, there were no clear changes in spirometry values over Subject B's training period. Most of the increase in lung capacity was apparently within the first month of training, from a vital capacity of 1.06 l at baseline (TP1) to 1.22 l at TP2. Vital capacity then increased by another 0.04 l in the second month of training, where it reached its peak value. Thereafter, a decrease was seen at TP4, and again at TP5. Peak expiratory flow showed an overall increase over the training period from a baseline of 2.62 to an end-training value of 3.20 l/s. Maximum expiratory and inspiratory muscle strength indices showed no clear change.

5.4 Discussion

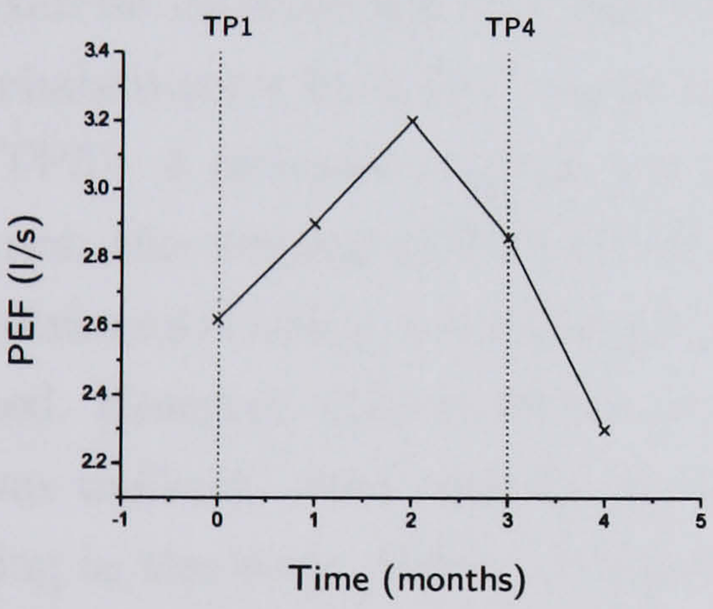
It is useful to be reminded of Subject B's capabilities prior to FES-ACE exercise intervention. With shoulder muscle control, weak voluntary biceps control and no clear voluntary control of triceps contraction, no finger flexion/extension for handgrip, and only weak wrist control, upper limb function was severely limited. In terms



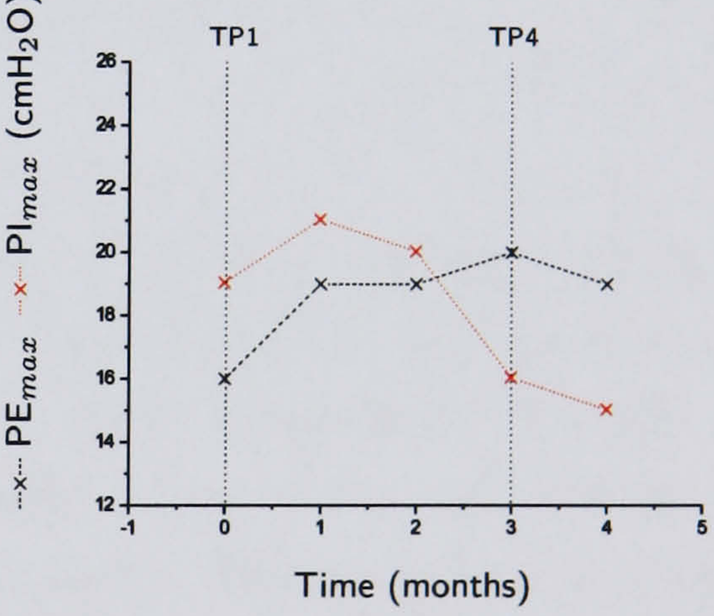
(a) FEV_1 and FVC



(b) $\frac{FEV_1}{FVC}$



(c) PEF



(d) PE_{max} & PI_{max}

Figure 5.14: Lung function data for Subject B. TP1 and TP4 are shown to highlight the start and end of the FES-ACE intervention period.

of physical activity, although she could propel her own wheelchair in small spurts. she mostly required someone to push her wheelchair for her. Potentially, she could have gained from building up upper limb strength and endurance through FES-ACE training.

5.4.1 Peak Power Output

With Subject B, any observed improvements in upper limb strength, measured here as peak power production, could not be attributed solely to the FES-ACE exercise intervention. The three-month training programme was held in parallel with inpatient rehabilitation, involving one or two daily gym sessions. Moreover, with this subject being eight months post-injury at the start of participation, some 'natural recovery' may have still been occurring. Indeed, although most of the neurological status of a person with SCI is considered to be well established by about 3 weeks post-injury, there may be some form of recovery for up to a year following the initial trauma [59].

Nevertheless, one may speculate about the relative contributions of the FES-ACE exercise intervention and the traditional physiotherapy exercises used for inpatient rehabilitation from the repeat tests performed one month post-FES-ACE training (TP5). A decrease in peak power output at TP5 may have been interpreted as follows: the removal of FES-ACE as a component of Subject B's rehabilitation had a detrimental effect, even though the remainder of rehabilitation exercises had continued. However, this would assume that all other factors had remained equal, which was unlikely. One such factor was the possibility of some natural recovery occurring in the early phases of the FES-ACE programme. The second factor related to the normal pattern of improvement during inpatient rehabilitation. Even without FES-ACE intervention, improvements in upper limb strength would likely have increased at a greater rate at the initial phase of rehabilitation, even in traditional physiotherapy. With this traditional therapy, a plateau would then be expected at the end of the inpatient rehabilitation phase. The end of the FES-ACE intervention probably coincided with this plateau (because the subject was nearing the end of her inpatient rehabilitation), when little improvement in upper limb function and/or strength would be expected anyway.

The peak power output of Subject B increased overall by around 150% from the start (3 W) to the end (8 W) of the three-month FES-ACE exercise intervention. However, the progress was not linear over the training period. Instead, peak power

appeared to improve in the first month, remain stable in the second, and then increased further in the last month of FES-ACE training. Repeatability tests would have been required to identify whether changes in peak power outputs of just 2 W from one test point to another could simply be attributed to test-to-test variation. However, the investigator was confident, in the main, that the peak power outputs achieved during testing were representative of Subject B's capability (based upon her performance in the training sessions in the week prior to testing). One notable exception was at TP4. The peak power output calculated at TP4 (8 W) was slightly less than the training work rate that had been used in the week prior to testing (8.5 W). One possible explanation for this is that the incremental test protocol used was perhaps not suited to obtaining maximal exercise responses in this individual. This may indeed be a problem with people with cervical SCI who exhibit clear autonomic dysfunction and severely compromised ventilatory capacity.

Another point to note is that incremental exercise testing was possibly not the most appropriate form of testing to monitor improvements in this individual. The incremental exercise tests, and especially the use of peak power output during these tests as the indicator peak muscle capability, may not have been sensitive enough to the small changes in peak responses that were achievable by this individual. To assess peak muscle forces more precisely in future developments of FES-ACE training and testing, a possible alternative for measuring the peak force production of individual muscles used in the exercise would be to use a dynamometer. This would allow more accurate measurement of the force production capability of each of the muscles involved in the exercise at the different stages of training[2].

Nevertheless, if we assume that the recorded changes in peak power production over the training period were true changes, it is clear that such changes were small in relation to what a neurologically intact person performing arm-cranking would expect to achieve. Nevertheless, even small changes could have useful consequences to the tetraplegic individual. Building up the muscles still under volitional control in the upper limbs may have facilitated the use of assistive tools for daily tasks such as tooth-brushing, hair-combing and feeding[3].

In addition, the increased power production may have translated to more effective wheelchair propulsion. However, during wheelchair propulsion, the individual must overcome a number of forces resisting the movement. Such forces include rolling

[2]A dynamometer was not available for these measurements at the time of the study.

[3]These activities of daily living (ADL) outcomes were not measured in this pilot study.

friction, air friction and internal friction (of the wheelchair parts) [112]. These can vary considerably between different surfaces and different environments. In addition. the angle of the slope on the ground affects the difficulty of wheelchair propulsion. Thus, absolute changes in peak power production of only 5 W are unlikely to facilitate wheelchair propulsion on anything other than low friction surfaces, with no (or minimal) incline.

One month without FES-ACE training had an apparent negative effect on upper body strength (with a 2 W reduction in peak power output), so that peak power output at TP5 was down to 6 W. The FES-ACE exercise performed by Subject B was very much a combination of voluntary input (for the biceps) and FES (which the operator set at higher intensity in the triceps, to compensate for the greatly reduced volitional control of this muscle group) throughout the period of FES-ACE training. Although at the end of FES-ACE training this subject was continuing with other upper body exercise in her rehabilitation, she was unable to maintain the upper body strength recorded at TP4. In absolute terms, the drop in power production from the upper limbs was only 2 W. In relative terms, however, this represented a 25% drop from TP4. If this rate of decrease in peak power output had continued, it would only have taken a further two months for this person to regress back to baseline values. The author speculates that, had the FES-ACE training regime been maintained, the loss in peak power output would not have occurred. Instead, the upper limb strength could have been built up further over time.

5.4.2 Peak Oxygen Uptake

At baseline (TP1), Subject B showed severe exercise limitation, achieving a peak oxygen uptake of only 0.53 l/min. This was just below the lower end of the range recorded by Van Loan *et al.* [113] for C5–C8 tetraplegics performing voluntary arm-cranking. However, this value was in the normal range, if compared with the values given by Burkett *et al.* [17] for tetraplegics (recorded during wheelchair ergometry).

Training three times per week with FES-ACE did not make a positive impact on this subject's peak oxygen uptake. On the contrary, after the first month of training, a decrease to 0.41 l/min was recorded. Thereafter, peak oxygen uptake did gradually recover over the next two months of FES-ACE training to 0.54 l/min at the end of FES-ACE exercise intervention. There was then no clear change in peak oxygen uptake after a month without the training, to a final value of 0.55 l/min.

These data, averaged over the last thirty seconds of the last completed work rate, suggest that, unlike the overall increase observed with peak power output, Subject B showed no clear improvement in peak oxygen uptake as a result of FES-ACE training. However, it could be argued that the 30s-averaged data for peak oxygen uptake were not entirely representative of the subject's capabilities. By looking at the four-breath averaged oxygen uptake plotted against power output in Figure 5.5, it seems that Subject B was actually capable of oxygen uptake values of around 0.73 l/min at TP4. This should be borne in mind before discounting the possibility of a training effect in this subject.

Even if we assume that the thirty-second average could have resulted in an underestimate of Subject B's peak oxygen uptake, it is clear that, even after training, this person still exhibited severe exercise limitation. With a complete C6 SCI, probable central limiting factors would have been:

- impaired cardiac output due to disrupted sympathetic outflow to the heart, and
- impaired ventilation due to extensive paralysis of respiratory muscles.

Of course, these central limitations were in addition to the peripheral limitations caused by extensive muscle atrophy following the SCI, with the typical preferential reduction (and sometimes even complete loss) of type I muscle fibres (slow, high-oxidative), as evidenced from muscle biopsies taken from the paralysed muscles of SCI individuals [18, 94].

With only some voluntary control of the muscles and a large component of the muscle force during FES-ACE resulting from recruitment of motor units through the electrical stimulation, speculation can be made here about the muscle composition following training. The voluntary component would have encouraged development of the slow motor units, with a tendency towards greater oxidative capacity of the exercising muscle during endurance training. However, the FES component was presumably preferentially recruiting the fast units (with motor neurones of large diameter), with a less oxidative (and more glycolytic) capacity. One could argue that, when the FES-ACE was removed from the weekly timetable of rehabilitation, Subject B's capacity for prolonged exercise at submaximal levels may have been maintained through alternative exercise modalities; however, without the FES component of exercise, the peak muscle force may have decreased, leading to a reduced peak power production. This idea is speculative at this stage.

This case study would suggest that FES-ACE is perhaps not an effective means of improving cardiopulmonary fitness to any great extent in a complete C6 SCI individual. With severe central limitations to the exercise, however, this would be true of any exercise modality (the same problems would be faced in FES-cycling, for example). We can speculate that a large part of the limitation in this subject was a direct result of impaired sympathetic pathways, so that the normal feedback mechanisms to the heart and lungs during exercise were not available to this individual. Therefore, improvements with Subject B may have been limited to some peripheral adaptations in the exercising muscles themselves. As peripheral adaptations are local in nature, it is still useful to encourage any form of exercise which involves the muscles remaining (even if only partially) under voluntary control, as these are the muscles that the person is able to use for any remaining upper body function. The author therefore suggests that, by continuing the programme of FES-ACE training over a longer period, with progressive increases in work rate, Subject B could have shown further peripheral adaptations and continued to improve on peak power output, even if peak oxygen uptake remained relatively unaffected.

In addition, the ventilatory limitation in this subject was also clear. The subject was unable to move sufficiently large volumes of air in and out of the lungs during exercise (as evidence by low tidal volume and low minute ventilation), which was probably a result of the purely diaphragmatic breathing that is typical in complete cervical SCI (as accessory muscles of respiration, which are mostly innervated in the thoracic region of the spine) are no longer under voluntary control). Further evidence of this ventilatory limitation is given in Section 5.4.5.

5.4.3 Efficiency

Overall, as Subject B progressed through her FES-ACE training there was a decrease in the gradient of slope of oxygen uptake plotted against power output for incremental tests. This implies that each unit of oxygen taken up during the exercise at the end of the training regime was used for greater force production by the muscles involved in the arm-cranking motion, when compared to the start of training. In the general population of neurologically intact people performing voluntary exercise, this slope would not change appreciably with training [116].

Improved technique and skill in arm-cranking could have contributed to Subject B's apparent increased efficiency over the training period. Alternatively, the changes could have been linked to the relative contributions of high-aerobic and high-glyco-

lytic fibres in the FES-ACE exercise during any one test.

There was a transient increase in the gradient of the slope of oxygen uptake against power output seen at TP3. The hypothesis that this reflected a reduced efficiency of the exercise at that point in the training programme was strengthened by the efficiency data obtained from the constant load test at the same test point.

The calculations made using the constant load test data relied on the assumption that Subject B was exercising at steady-state during zero-load arm-cranking, and then reached a steady-state at the chosen constant load work rate. If this assumption held true (which it appeared to do for all test points with Subject B), it seems that gross efficiency (GE) was the most robust index, varying only slightly over the subject's participation between 0.8 and 2.2%.

Net efficiency (NE), calculated with a baseline subtraction of resting energy expenditure, tended to increase with training. NE increased from 1.9 % at TP1 to 5.2 % at TP4, and decreased slightly one month post-training, at TP5.

Work efficiency was the most variable index of efficiency, but this was largely an artefact of the changing baseline. The baseline correction for work efficiency was energy expenditure during zero-load arm-cranking, but this seemed to vary considerably from test to test, and with no clear pattern.

Based on the results obtained with Subject B, we would agree with Hintzy and Tordi's [46] conclusions (who evaluated efficiency indices applied to wheelchair ergometry in SCI) that gross and net efficiency indices provide more useful information about the mechanical efficiency of the exercise modality being investigated than work efficiency, especially when there seems to have been a shifting baseline for the work efficiency calculation.

An interesting result obtained here related to the difference in efficiencies obtained at the same test point (TP2), but at different work rates. The data suggest that the subject was exercising with greater efficiency (according to all three indices calculated here) at the higher than at the lower work rate. The idea that efficiency of cyclical exercise varies with work rate has already been demonstrated for able-bodied individuals for both arm-cranking [88] and leg-cycling [38].

Another factor that could explain the apparent difference in work efficiency at 1.5 W

and at 3 W (at the same test point) may be the very small step change in work rate from 'zero-load' to 1.5 W. Such a small step from a baseline of '0 W' results in a very low signal to noise ratio, thus making calculations of efficiency at this low work rate problematic.

5.4.4 Response Kinetics

The quality of the data obtained from constant load tests with Subject B was questionable, due mainly to the noisiness of the breath-by-breath gas exchange data obtained. One component of this variability was related to the small range of power output, and hence small range of oxygen uptake, involved. Throughout her participation, Subject B was only able to exercise at power outputs of -2 W to no more than 10 W. The small steps in work rate used for constant load testing (from zero load to either 1.5 W or 3 W) were accompanied by only small changes in oxygen uptake (and carbon dioxide output and ventilation). The low signal to noise ratio of the cardiopulmonary data made it difficult to separate the kinetic response from the natural breath-by-breath variability. As a result, even following data editing, fitting of the expected mono-exponential curve was largely unsuccessful.

Nevertheless, two examples were given here of curve-fitting, to produce time constant estimates for $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}E$ at the start (TP1) and end of training (TP4). In neurologically intact, healthy people performing exercise below the lactate threshold, the normal value is around 30 s for $\dot{V}O_2$, although this is reduced in fitter subjects [121, 123]. The time constant for $\dot{V}CO_2$, although less predictable and less reproducible than for $\dot{V}O_2$, tends to be somewhat longer at around 50 to 70 s. In terms of ventilation, the evidence points to the time constant for $\dot{V}E$ being similar (although slightly lagging) that for $\dot{V}CO_2$. These are the values expected for exercise performed below the lactate threshold. The pattern for higher relative work rates (supra-threshold) tends to be different, with the time taken for $\dot{V}O_2$ to reach steady-state (if at all) being longer [122] than at work rates below the lactate threshold. Additionally, in supra-threshold exercise, carbon dioxide output and ventilation kinetics tend to be faster than oxygen uptake kinetics [123].

With Subject B at TP1, the absolute values seemed not to be considerably slower than for able-bodied people. However, the relative values were suggestive of supra-threshold exercise, as the responses of carbon dioxide output and ventilation were faster than that of oxygen uptake. In contrast, at TP4, the relative values pointed to sub-threshold response kinetics, but with much slower responses than would be

seen in able-bodied individuals during sub-threshold exercise. No positive training effect could be demonstrated from these data.

5.4.5 Lung Function

The spirometry data, giving information about the lung volumes available to the subject both at rest (for quiet breathing) and during exercise (when the ventilatory requirements are augmented), could provide part of the explanation for the negligible change in cardiopulmonary fitness over the three-month FES-ACE training period used here.

Astrand and Rodahl [7] provide spirometric reference data collected in 1982, for trained young members of the general population. Typical vital capacity (VC) is in the region of 4.05 l for trained young females, compared to 4.92 l for trained young males. The authors suggest these values can be reduced by as much as 20% in the sedentary members of the population, bringing these values down to around 3.24 and 3.94 l in sedentary females and males, respectively. Correspondingly, the typical maximum tidal volume (VT) recorded during maximal exercise testing in the same group was at 2.23 l in trained females, and 3.23 l in trained males. Again, for sedentary young people, this would be expected to be lower, down to around 1.78 l in females and 2.58 l in males. In addition, it is known that lung capacity at rest and during exercise is age-dependent, tending to decrease with age. These data suggest that, in the neurologically intact population, lung capacity can vary greatly depending on gender, training status and age. In addition, during exercise, tidal volume appears not to exceed around 45% of vital capacity.

If we take the case of Subject B, and compare her values to those of the able-bodied population, we see that her vital capacity at the start of participation, at 1.06 l, was much lower than that of a sedentary young female. At 52 years old, we would expect vital capacity to be somewhat lower than for a young female, but not to the extent seen here. Subject B was not a smoker either before or after her injury, and had been quite active prior to the SCI (a regular hill-walker), and so we would assume that the reduced pulmonary function was a direct consequence of the SCI. With a VC of 1.06 l, Subject B initially had a greatly reduced lung capacity even when compared with reference values from the tetraplegic population: Van Loan *et al.*'s study gives a mean for the C5–C8 group of 3.1 l [113], whilst Tow *et al.* estimate VC at around 2.5 l [110] for tetraplegics at the end of their inpatient rehabilitation following SCI.

In relation to exercise, if we take the pattern seen in the able-bodied population, where only about 35–45% of VC is used in maximal tidal volume, this would have been equivalent to 0.37–0.48 l with Subject B. Taking TP1 as an example, we can look back to the graph of tidal volume against ventilation in Figure 5.9(g), showing that Subject B was able to use 0.55 l at maximum tidal volume (equivalent to 58% of FVC).

With training, a slight improvement in FVC, and consequently FEV_1, was recorded to peaks of 1.26 and 1.22 l, respectively. Although this represented almost a 20% increase in FVC, it was not sufficient to bring Subject B into the normal range, even for a person with C6 tetraplegia. Furthermore, there did not seem to be a carry-over effect of this improved pulmonary function one month post-exercise, when FVC decreased again to 1.09 l.

The reduced lung volumes available for ventilation during exercise could clearly have been a source of exercise limitation. From TP1 to TP5, exercise tidal volume never exceeded 0.62 l (see Appendix B). The suggestion here is that, without tackling the issue of reduced vital capacity in this subject, she could perhaps not be expected to improve cardiopulmonary fitness overall, despite the rigorous training regime imposed.

In agreement with the idea that Subject B had extensive paralysis of many of the muscles usually involved in respiration during exercise, peak inspiratory and expiratory power was greatly impaired. With values not exceeding 20 cmH_2O, this is less than 25% of average values for females in the general population.

Relying solely on the diaphragm (innervated by the phrenic nerve mainly at C3–C5 and hence under at least partial voluntary control in all our subjects) for respiratory power even during exercise, Subject B was unable to move a large enough volume of air into and out of the lung to meet ventilatory requirements during increasing FES-ACE work rates. The alternative to increasing tidal volume during exercise is to increase breathing frequency, but faster breathing cannot fully compensate for reduced tidal volume.

With this subject, it may have been beneficial to provide some inspiratory muscle strengthening prior to (and probably simultaneously with) the FES-ACE training. This could have been achieved using surface electrical stimulation of abdominal mus-

cles, which has the potential to increase both tidal volume and peak expiratory flow in tetraplegia [40]. For this, surface electrodes are placed over the rectus abdominal muscles and the external oblique muscles. With appropriate controllers, the stimulation of these muscles can be synchronised with the subject's own breathing.

5.5 Conclusions

In this case study, the FES-ACE methods were evaluated further with an individual whose status differed significantly from that of the subject described in the previous chapter (Subject A). Here, the subject (Subject B) was an inpatient at the spinal injuries unit in the sub-acute phase of injury (7 months post-trauma), and classified as a complete C6 SCI. This had two main implications for the experimental evaluation of FES-ACE. Firstly, the injury was complete, thus giving increased weight to the applicability of the results to other individuals with complete C4–C6 SCI. This is in contrast to results obtained for individuals with incomplete injuries, as they make up a very heterogeneous group. The second implication was related to the fact that the FES-ACE training occurred at the same time as other rehabilitation exercises, and during a phase of possible natural neurological recovery. One may argue that changes in the outcome measures monitored throughout our training programme were not entirely attributable to the FES-ACE intervention.

Bearing these points in mind, Subject B showed an increase in peak power production over the period of FES-ACE training, from a baseline of 3 W to an end-of-training value of 8 W, but with no overall change in cardiopulmonary fitness. Severe limitations to exercise response in this individual were apparent, both in terms of ventilation and cardiac output. Even so, the increased peak power output with no associated increase in peak oxygen uptake provided evidence for peripheral adaptations following training. The muscles were apparently using the oxygen more efficiently for force production, and/or the peripheral circulation of blood to deliver oxygen to the exercising muscles had improved.

Therefore, this case study illustrates that FES-ACE can be used in tetraplegia to produce some positive peripheral adaptations in the exercising limbs despite significant central limitation to exercise in complete cervical SCI. However, the training effect was limited.

Some issues with the exercise testing protocols also emerged. The incremental test protocol may not, in its current form, be the most effective way of assessing the

tetraplegic individual's peak capabilities in the case of severe circulatory and respiratory limitation.

Furthermore, extracting response kinetics from constant load test data proved only partly successful. We propose that the low signal to noise ratio in the gas exchange data during these tests with very small step changes in work rate was a significant limiting factor for the analysis.

It may be that more simple tests could be devised to determine, in the first instance, the extent of autonomic dysfunction and of ventilatory limitation, and then to measure peak force production by each of the exercising muscles individually. Exercise testing may be of more benefit in assessing those tetraplegic individuals with less restricted central responses to exercise than the subject in this case study.

Chapter 6

Additional Case Reports

6.1 Summary

The FES-ACE methods developed and evaluated in this pilot study were intended for use in C4–C6 SCI. The aim of this chapter is to investigate the potential for the systems to be used in SCI above C6 (as a complement to the two C6 SCI case studies presented in previous chapters). Limitations of applying the present methods for FES-ACE to higher lesion levels are explored. Possible solutions for overcoming some of these issues are also given.

Three subjects with SCI at C4 and C5 were involved in part of the experimental evaluation of the systems and protocols for FES-ACE. Muscle strengthening sessions, using FES-ACE at low cadence and low work rates (mostly in the passive range), were carried out with each subject. At the end of the muscle strengthening phase, only those who were able to maintain unloaded cycling (without motor assist) for a number of minutes were eligible to proceed to the formal phase of FES-ACE exercise training.

Spirometry was carried out periodically to assess pulmonary function. Muscle torque data were recorded during FES-ACE sessions with each subject. These torque data were plotted against crank angle (using novel polar and Cartesian plots), to monitor upper limb strength over time, and to compare upper limb strength with and without electrical stimulation. Subject C, with a C5 (complete) SCI, showed improvements in upper limb torques over time, and would have been able to proceed to formal exercise testing and training, but he was unable to commit to the intense training schedule. In contrast, at the end of their muscle strengthening periods. Subjects D and E were still unable to maintain unloaded FES-ACE exercise for ten

consecutive minutes, and so cardiopulmonary testing and formal FES-ACE training did not take place. For Subjects D and E, cadence and work rate needed to be kept low due to problems (common at this level of injury) of shoulder instability and shoulder pain. The shoulder issue would need to be addressed in further developments of the FES-ACE systems in order to make them applicable to the C4 SCI group. Nevertheless, torque data were recorded for these subjects, showing the positive effects of electrical stimulation on upper limb torques.

This chapter illustrates the use of the FES-ACE apparatus. and the presentation of torque and crank angle data in polar and Cartesian plots as a means of monitoring upper limb strength and performance during the exercise. This chapter also highlights some of the limitations of applying FES-ACE systems to individuals with SCI above C5. Possible solutions to these problems are suggested. These findings provide an important complement to the positive training outcomes revealed in the previous two case studies.

6.2 Methods

The apparatus and set-up for FES-ACE were as described in Section 3.2.1. However, the protocols for training and testing differed from the original plans. An explanation for this is given in the sections that follow.

6.2.1 Subject Details

The details of the subjects who were initially included in the study, but who did not proceed further than the muscle-strengthening phase, are given in Table 6.1.

6.2.2 Muscle-Strengthening Protocol

Subjects C, D and E all began the muscle-strengthening protocol with 5–10 minute sessions, twice a week. Over the 6 weeks that followed, the length of the sessions was gradually increased for each subject. In addition, by the end of this muscle-strengthening period, the frequency of training for Subject C had been increased to three sessions per week.

During this muscle-strengthening phase, the passive mode of the FES-ACE system was used to maintain a set cadence. Each session would begin with arm-cranking at a low cadence (30 rpm), with full motor assist, for 3–5 minutes. Then. electrical stimulation was added at low intensity to begin building up the muscles. As the

Subject	Age	Sex	Level of injury	Time since injury	Voluntary control of target muscles
C	23	M	C5 (complete)	4 years	Good voluntary control of biceps right and biceps left, very weak triceps right, very weak triceps left
D	17	M	C4 (incomplete)	6 months	No voluntary control of biceps right, very weak biceps left, no voluntary triceps right, and no voluntary triceps left
E	33	F	C4/5 (complete)	16 years	No voluntary control of biceps right, weak biceps left, no voluntary control of triceps right, and no voluntary triceps left

Table 6.1: Details for Subjects C–E; M: Male, F: Female.

weeks progressed, and FES-activated muscle contractions became stronger, it was possible with some subjects (C and E) to increase the cadence and/or reduce the contribution of the motor assist. This was achieved by having a 'passive controller' and an 'active controller' and a switching algorithm for the transition from one to the other.

6.3 Results

Subject	Status	Reason(s) for not continuing
C	Completed MS phase successfully	Unable to commit to training schedule
D	Unable to complete MS phase successfully	Shoulder joint problems prevented progression to next phase
E	Unable to complete MS phase successfully	Shoulder and trunk stability problems prevented progression to next phase

Table 6.2: Reasons for the subjects not continuing to the next phase of the FES-ACE programme.

The reasons for terminating each of subjects C, D and E's participation in the pilot study are summarised in Table 6.2. The subjects did not progress to FES-ACE exercise testing for baseline measurements or formal training. The data collected

for each subject therefore included torque data (recorded during each session) and lung function data (spirometry carried out at rest), but no other measurement of cardiopulmonary fitness.

6.3.1 Torque Data - General

During the muscle strengthening sessions, torque, cadence, crank angle and stimulation intensity were recorded continuously. Within any particular session, this allowed us to observe the effect of stimulation on torque resulting from the action of the biceps and triceps muscles. Furthermore, by comparing torque (and power) produced by the subjects between sessions, we were able to infer whether or not there had been any changes in upper limb strength for each individual subject.

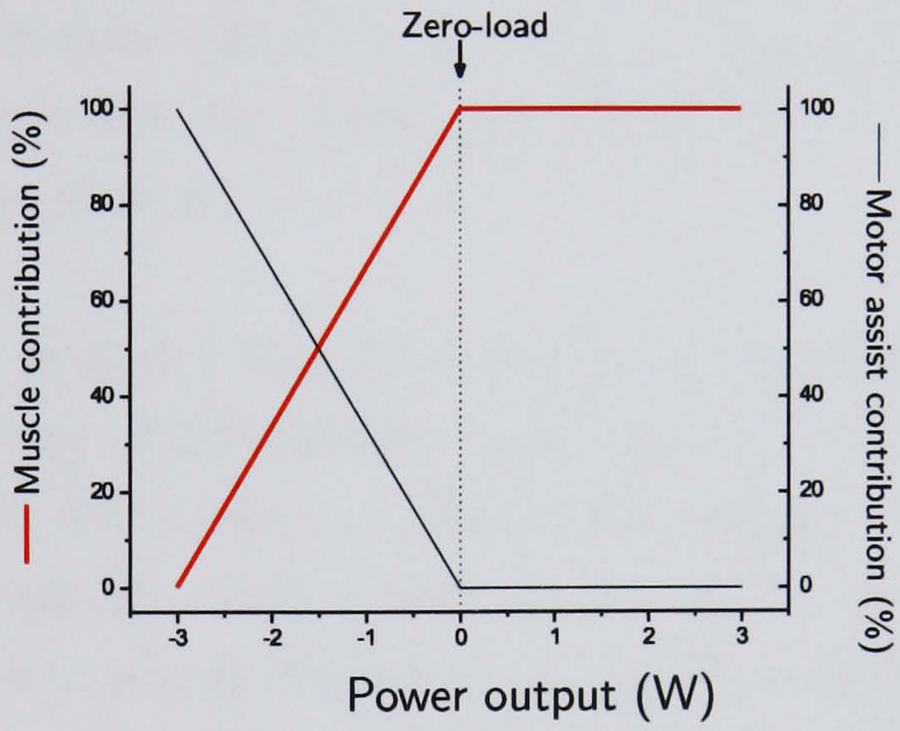


Figure 6.1: An illustration of the concept of the 'negative power output range'.

In most subjects, as the muscle strengthening period progressed, even where no resistance could be added for the muscles to work against, the electrically stimulated muscles gradually contributed a greater percentage of the torque (and hence power) required to maintain the arm-cranking motion, thus reducing the extent of motor assist needed. This concept of working in the 'negative power output range' is illustrated graphically in Figure 6.1 (for a full description of power control in this negative range, see Hunt *et al.* [52], with reference to FES leg cycling). Data from a muscle-strengthening session carried out with Subject E are provided here to illustrate how this negative power range was used in FES-ACE muscle strengthening. The data were plotted using software developed by Gollee *et al.* [41], and are presented in Figure 6.2.

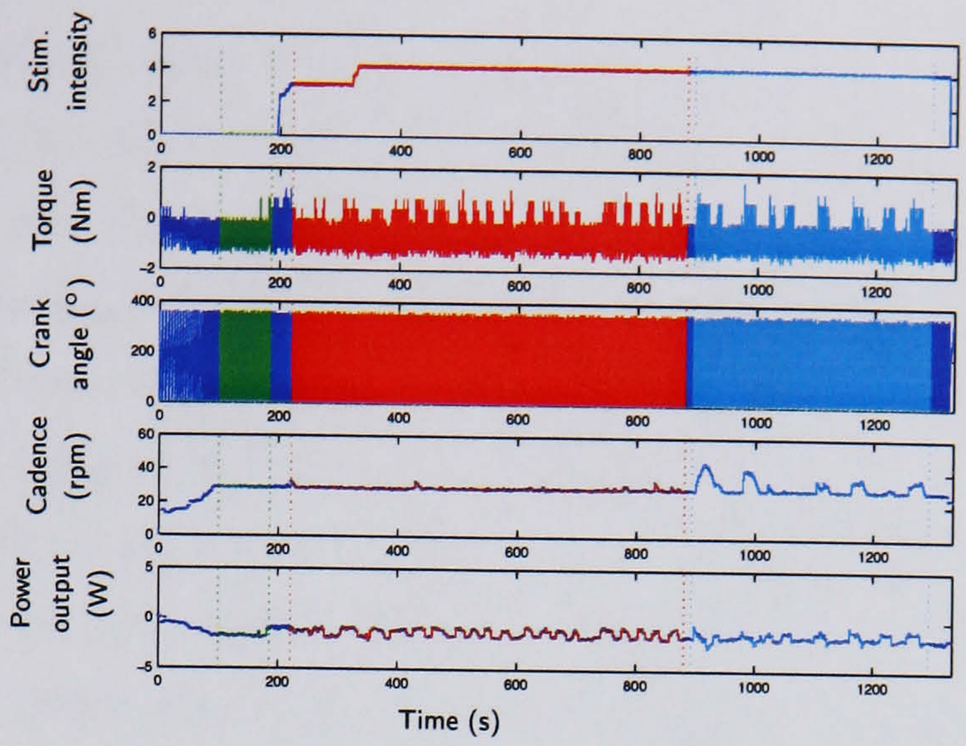
There are a few points to note in the interpretation of the muscle strengthening data plots that follow.

1. The polar and Cartesian plots are of mean torque (averaged over a number of cycles) in relation to the point in the 360° cycle at which it was produced.
2. In the polar and Cartesian plots of torque against angle, the blue line represents 0 Nm (or 'zero load').

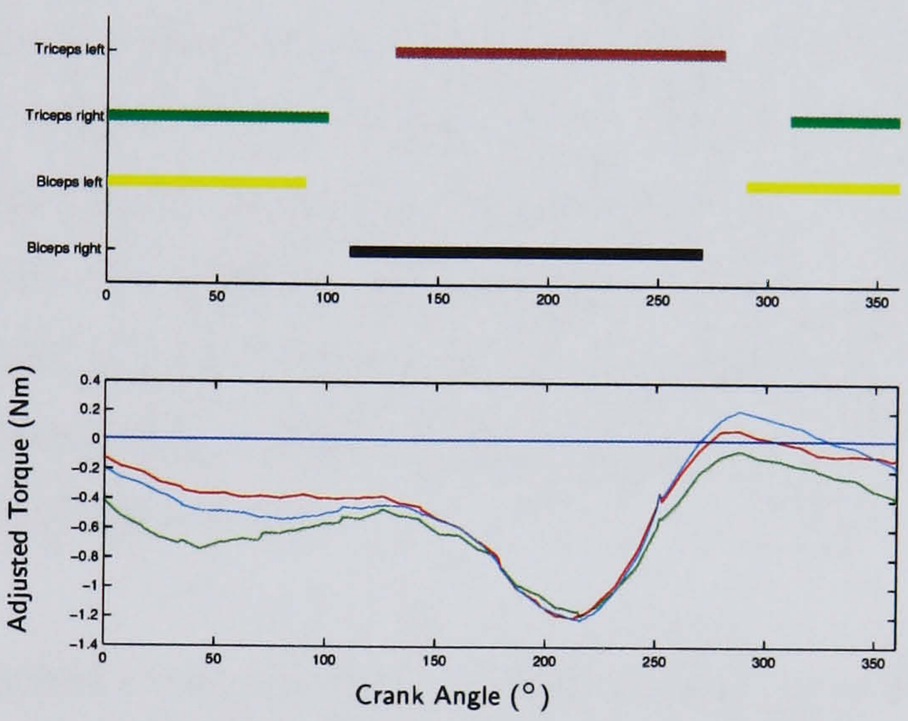
Figure 6.2 can be used to emphasise a number aspects of interpretation of the data. Plot 6.2(a) gives an overview of all the data, plotted against time, over the duration of the whole session of muscle strengthening. This can be used for a general description of the session. For example, we can see that the average cadence in this session was around 30 rpm, and that the power output was in the negative range throughout (indicating that the motor was contributing to the torque required to maintain the cranking motion).

The data presented in plot 6.2(a) formed part of the display on the PC screen during a training session. This illustrates how the plots can be used as an incentive to the subject. As the PC screen is visible to the subject as he or she is exercising (to monitor actual cadence, with respect to the target cadence), the torque and power plots can also be used by the subject as visual feedback of the effort that the muscles are putting in (through combined voluntary and FES inputs). This shows the subject when the motor is doing all the work (totally passive arm-cranking), and when the muscles are contributing to moving the arms round (progressing through the negative range, to get closer to zero-load arm-cranking). As training progresses, the visual display can provide encouraging positive feedback to subjects, to show them when they were achieving the transition from passive arm-cranking to active arm-cranking.

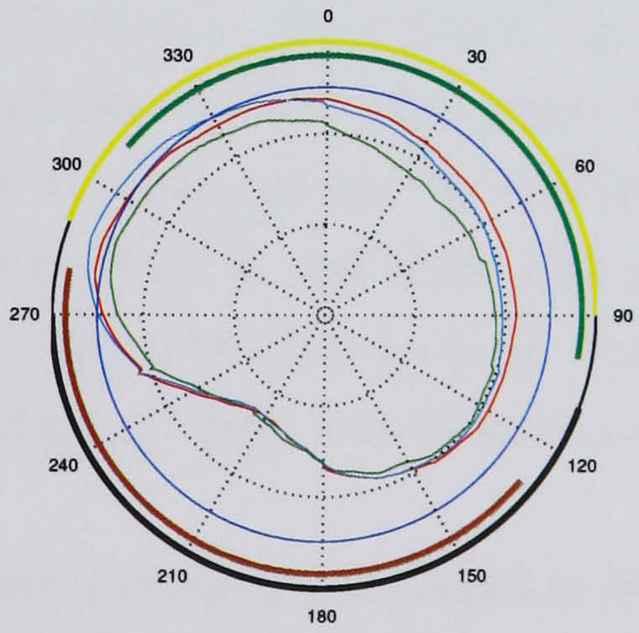
After a session is finished, the software also allows different parts of the session to be analysed separately. The parts of the session (in plot 6.2(a)) that have been selected here are as follows. The *green* section represents the initial motor-assist phase, with no contribution from the muscles. In the *red* section, the motor-assist is still maintaining the cranking motion, but stimulation to the muscles is added. In the *cyan* phase, spurts of voluntary activity from the subject are added, so that there are contributions from the motor-assist, FES-activation of the muscles and voluntary control of the muscles.



(a) Raw FES-ACE data



(b) Cartesian plot of torque



(c) Polar plot of torque

Figure 6.2: Muscle strengthening data from a session with Subject E. (For the torque data plots, green: motor assist only; red: stimulation added; cyan: voluntary input added in small spurts of activity; blue: 'zero load'.)

The muscle stimulation range is shown for each biceps and triceps muscle in the upper part of plot 6.2(b), and on the perimeter of plot 6.2(c). Plots 6.2(b) and 6.2(c). provide Cartesian and polar plots of the mean torque produced (averaged by the number of cycles completed in the selected phase), in relation to the position of the right crank. These show that the mean torque production was mostly in the negative range throughout the session (below the blue line in the Cartesian plot, and within the blue circle in the polar plot, both of which represent 'zero load'). One point to note is that the pattern of torque production with stimulation (red and cyan) followed the same shape as torque production without stimulation (green). We can imply from this that the stimulation ranges used mimic the natural ranges adequately. By adding stimulation and some voluntary input from the biceps, the magnitude of the negative torque was reduced. Addition of stimulation resulted in a torque (and power) output that was getting closer to unloaded arm-cranking, thus gradually moving from totally passive exercise to more and more active exercise. For some parts of the cycle, the addition of stimulation and some short spurts of voluntary input from the left biceps brought Subject E into the positive range, showing that the person was producing a high enough torque at that part of the cycle to not require the assistance of the motor.

The data also show some asymmetry in torque production between the two halves of the cycle, not only during muscle activation (which may suggest some of the muscles being stimulated were stronger than others), but also when only the motor was performing the cranking motion. We can speculate that there was some physical resistance to the motion on one side (for example, as a result of contracture or scoliosis) contributing to the asymmetry. In addition, in the case of Subject E, extensive disuse atrophy of muscles in the right arm may have contributed to the asymmetry (because, even with stimulation, there was little increase in the force produced when the right biceps or right triceps were activated).

The plots shown illustrate the amount of information that can be extracted from the muscle strengthening data. Therefore, even for tetraplegics with very weak upper limb muscles, plots such as the ones described here could provide useful information about upper limb strength, and the effects of stimulation during FES-ACE exercise.

The expectation had been that, over time, the FES-ACE muscle strengthening sessions would increase in duration and work rate (moving from the negative power output range to zero-load arm-cranking) and cadence (from 30 rpm to 50 rpm).

However, out of Subjects C–E, the increase in work rate over time was only possible with Subject C.

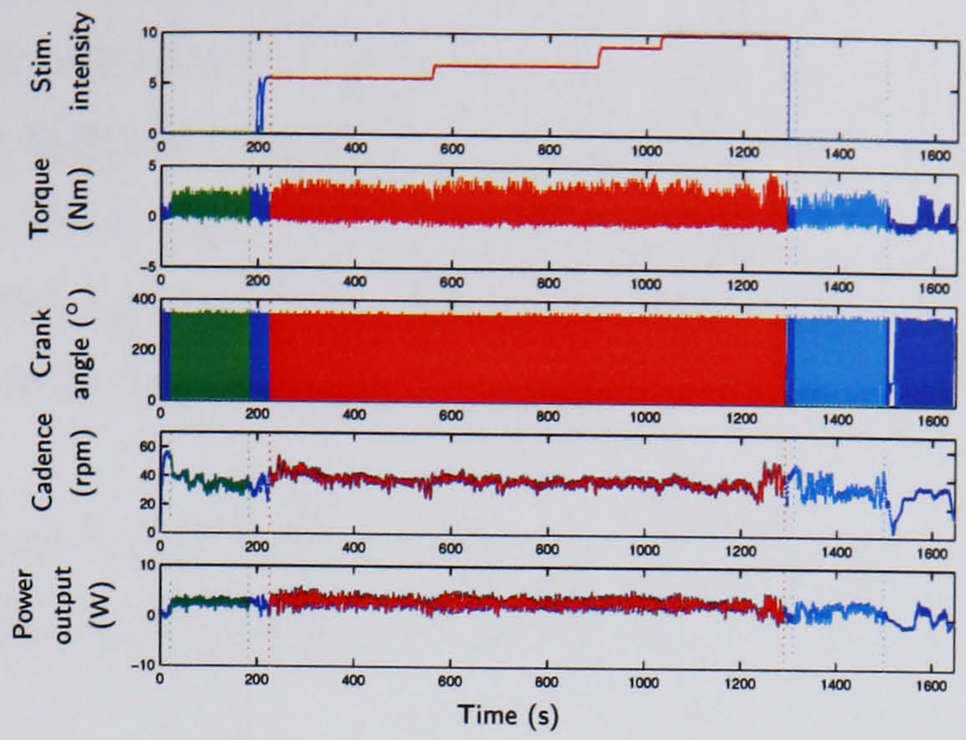
6.3.2 Torque Data - Subject C

With a C5 SCI, Subject C was able to show considerable improvement in his torque and power production at the cranks over the muscle-strengthening phase of the programme. This subject progressed to the stage where the motor assist could be turned off completely, and he could perform the arm-cranking motion in the positive output range.

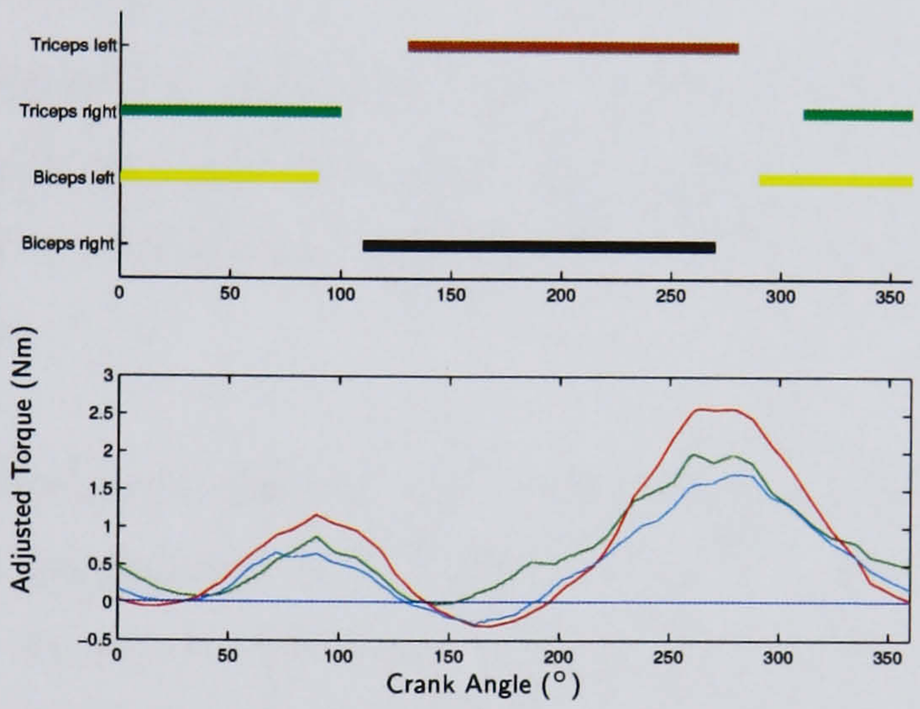
Furthermore, Subject C was able to work progressively higher in the positive output range so that, by the end of the muscle-strengthening phase, he was reaching up to 3 W and maintaining this for up to 30 minutes. To achieve this, Subject C had conditioned his upper limbs through a combination of his own voluntary control of biceps muscle function, and surface stimulation of the biceps and triceps (with higher intensity of stimulation being delivered to the latter). For these sessions, an example of which is given in Figure 6.3, the subject would usually begin arm-cranking without stimulation, at around 2 W and 40 rpm (see 6.3(a)).

In 6.3(a), the different colours relate to different time periods in the session: *green* representing the initial period in which Subject C was producing all the torque required for the cranking motion using voluntary control of the muscles; *red* representing the period in which stimulation was added, and gradually increased to maintain that level of work; and *cyan* representing the final period when the stimulation was switched off, but the subject continued to work at that level until he could no longer carry on. During the period of stimulation, the stimulation intensity (varied here by changing the stimulation pulsewidth only) was increased manually by the operator when drops in torque production, suggestive of muscle fatigue, were observed. Through the combination of voluntary input and electrical stimulation, Subject C was able to maintain a positive power output of around 3 W for over 25 minutes in this particular session (see 6.3(a)).

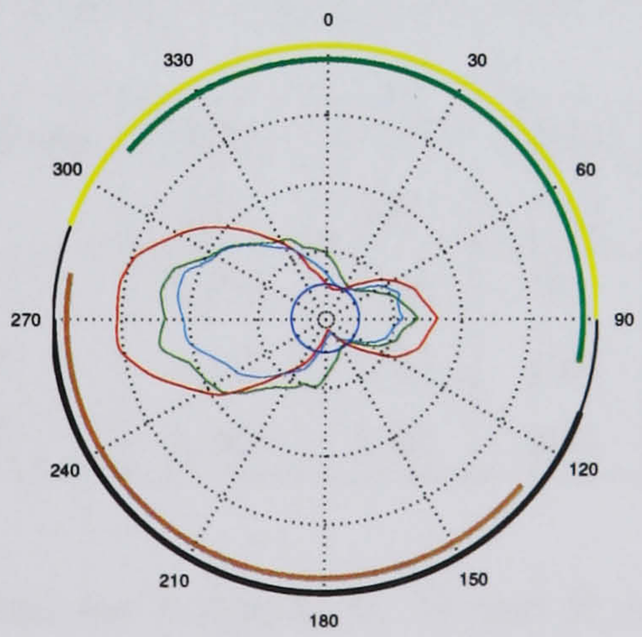
The plots in 6.3(b) and 6.3(c) also show that, by adding the FES. the average torque produced by the subject at the crank was increased during some parts of the cycle. There was some asymmetry between the torque production in one half of the cycle and the other. This subject had good voluntary control of the biceps muscles in both arms, but the asymmetry may have been a reflection of the stronger biceps



(a) Raw FES-ACE data



(b) Cartesian plot of torque



(c) Polar plot of torque

Figure 6.3: Muscle strengthening data from a session with Subject C. (For the torque data plots, green: voluntary ACE only; red: voluntary + FES; cyan: voluntary ACE only; blue: 'zero load'.)

of one arm compared to the other. (Clearly, this asymmetry in strength of the upper limbs is also seen in many able-bodied people, who tend to have a dominant arm.) For Subject C, the highest torque was produced at the end of left triceps and right biceps stimulation. A second, but lower peak in the torque production occurred at the end of left biceps and right triceps stimulation. There were parts of the crank cycle when little power was being produced (between 115° and 170°).

These data can further be used to highlight another point about Subject C's capabilities: the subject was unable to exceed a mean cadence of 40 rpm at work rates above 2 W.

6.3.3 Lung Function

Although none of Subjects C, D and E were able to proceed to the formal training phase of the FES-ACE programme, they had been familiarised with the exercise testing equipment and procedures in anticipation of progression to baseline FES-ACE exercise testing.

Resting spirometry data were collected for each subject over the muscle strengthening period. The data are presented in Table 6.3, as the mean of the values recorded throughout each person's participation (excluding the values from the first two sessions, which were considered as familiarisations with the spirometer). The values for FEV_1, FVC and PEF were noticeably higher for the subject with C5 SCI (Subject C) than for the two subjects with C4 SCI (Subjects D and E).

Subject	**FEV_1** (l)	**FVC** (l)	**$\frac{FEV_1}{FVC}$** (%)	**PEF** (l/s)
C	1.95	1.98	99	5.02
D	1.43	1.43	100	3.71
E	1.46	1.46	100	3.09

Table 6.3: Lung function data for Subjects C, D and E, shown as mean values over the muscle strengthening phase.

6.4 Discussion

6.4.1 FES-ACE Exercise in C5 SCI

We propose that there is potential for the use of FES-ACE as an exercise modality in C5 tetraplegia. However, this potential could not be demonstrated here as the only C5 subject in this feasibility study felt he had to pull out. The reason given was that he could not commit the time required for the intense exercise training programme.

Even so, one practical problem (in terms of the FES-ACE set-up) which had not affected the C6 subjects, but which was an issue with Subject C, was trunk instability. This was easily solved by applying a strap around the subject's chest to secure the person to his wheelchair and prevent excessive medio-lateral movement (but without being so tight as to restrict the arm-cranking motion, or breathing during the exercise).

In addition, had this subject been able to proceed to the next phase of the programme, some modifications to the exercise testing protocols may have been required to accommodate lower cadences of FES-ACE arm-cranking. Subject C was consistently cranking at cadences of 40 rpm or below. Although this was acceptable for muscle strengthening (see Fornusek and Davis [36]), it would have proven problematic for exercise testing, at least according to the protocols used for testing in this pilot study. At present, the protocols state that an exercise test should be terminated if the cadence falls below 35 rpm (unless this is only transient, due to spasm). This problem was encountered by McLean *et al.* [70] in their study: their solution was simply to allow subjects who could not reach higher cadences to perform the exercise tests at low cadence. A lower target cadence can easily be programmed with the FES-ACE software prior to exercise testing. The problem would only relate to the interpretation of the cardiopulmonary data at these lower cadences, especially if these are to be compared with data from other studies using cadences of 50 or 60 rpm.

6.4.2 Limitations of FES-ACE Exercise in C4 SCI

Trunk instability

Trunk instability was initially a problem with all subjects with a C4 SCI, but, for Subject D, the use of a chest strap was sufficient to overcome this. However, with

Subject E, the issue of trunk instability was combined with a problem of scoliosis. The scoliosis had developed over the course of the 16 years since injury (which had occurred at childhood). This combination created significant problems for seating position. The challenge was to try to minimise discomfort, without seriously compromising arm-cranking motion. In the end, attempts to address this were largely unsuccessful. Severe scoliosis may therefore be a contraindication to FES-ACE exercise.

On the whole, in the absence of severe scoliosis, a chest strap should be sufficient to minimise undesirable trunk movement during FES-ACE exercise in most subjects with C4 SCI.

Shoulder joint instability

With an SCI at C5 or below, full use of the shoulder musculature remains and so, where there is sufficient opportunity for the individual to exercise these muscles, shoulder joint instability should not be a problem. Indeed, in this pilot study, our C5 subject did not experience shoulder instability issues.

In contrast, an SCI at C4 or above leaves the individual with paralysis of many of the muscles involved in stabilising the shoulder joints (for example, the rotator cuff muscles: infraspinatus, supraspinatus, subscapularis and teres minor), even though individuals with C4 SCI can achieve shoulder shrugging, using the levator scapulae and upper trapezius muscles [101]. Problems with the shoulder mechanism occur more than at any other joint in a person with high tetraplegia. In the neurologically intact human body, the shoulder mechanism permits high mobility and range of motion, at the expense of stability. Some 17 muscles cross the joints of the shoulder mechanism [114], a proportion of which are involved in keeping the ball of the humerus in the glenohumeral socket. Therefore, when atrophy of those muscles occurs following spinal cord injury, the support mechanism at that joint breaks down, and the humerus may become displaced from its articulation with the scapula[1]. Subjects D and E in this pilot study both showed signs of shoulder instability. As a precaution, therefore, the investigators were unwilling to put excessive strain on those joints and so decided to keep the arm-cranking motion at minimal cadence, and with no resistance.

[1]In high tetraplegia, where the muscle atrophy around the joint becomes too severe, shoulder subluxation can result.

Shoulder pain

Pain is notoriously difficult to quantify. In tetraplegia (and SCI in general). the causes of pain are often multifactorial, making pain management even more challenging. Shoulder pain has been shown to affect a high percentage of all individuals with tetraplegia during the acute phase of injury [96], and is often an issue in the long-term. In our pilot study, shoulder pain was only reported by those subjects with C4 SCI, namely Subjects D and E. This was not necessarily induced by the FES-ACE, but the presence of pain did restrict the arm-cranking cadence and work rate that could be used. This was a further reason why Subjects D and E could not progress to the formal FES-ACE training part of the programme.

Some of the shoulder pain may have been related to the shoulder instability (sometimes referred to as musculoskeletal pain). If this was the main cause of pain, excessive, repetitive movement at the glenohumeral joint through arm-cranking exercise may not have been advisable. However, in addition to musculoskeletal pain, neuropathic and root pain would have been likely contributors. With these, activity (possibly combined with drug treatment) may actually have helped to alleviate their intensity.

6.4.3 Potential for FES-ACE Exercise in C4 SCI

The author consequently believes that, if FES-ACE were to be of benefit to individuals with a C4 SCI, the shoulder muscles would need to be strengthened before starting any regime of arm-cranking exercise. In particular, to increase stability at the shoulder complex and to overcome the effects of gravity pulling down on the upper limbs, the rotator cuff muscles would need to be targeted. In a similar manner to the therapeutic use of FES in treating shoulder subluxation in hemiplegia following stroke [63], we suggest that a programme of shoulder FES could benefit certain individuals with high tetraplegia. Infraspinatus, supraspinatus, subscapularis and teres minor are rotator cuff muscles. These act to stabilise the shoulder, and may be accessible through surface stimulation. Over time, these could be built up, and some stability may be restored to the shoulder complex. Only if this could be achieved, and pain could be managed, should FES-ACE be considered. Even then, it is proposed that stimulation of some shoulder muscles would probably need to be added to the pattern of biceps and triceps stimulation used in this pilot study in order to maintain shoulder strength and to contribute to the arm-cranking motion. For this, the best muscles to stimulate during arm-cranking would not necessarily be the rotator cuff muscles.

To identify which muscles would be most suitable for stimulation during FES-ACE. a useful starting point would be to record the activity of different shoulder muscles during arm-cranking in neurologically-intact subjects. This could be achieved by recording electromyographic (EMG) signals from individual muscles during the ACE motion. The shoulder muscles with the highest EMG activities could then be selected[2], and the ranges of the ACE crank cycle over which they act could be recorded. This information could then be transferred to the pattern generator in the FES-ACE software, and the appropriate shoulder muscle stimulation incorporated in the sequence.

We postulate that there may be additional benefits to stimulating shoulder muscles during the exercise. The involvement of other muscles may provide additional torque at parts of the cranking cycle that may otherwise be problematic (with an appropriate pattern and sequence of stimulation). Indeed, if sufficient torque could be added to the arm-cranking motion in C4 SCI, it may be possible to increase the cadence at which the exercise is performed from 30 rpm up to 50 rpm. The next step, assuming all the stimulated muscles (at the shoulder, as well as the biceps and triceps) could be strengthened sufficiently, would be to progress to endurance training, where resistance could gradually be added. Not only would greater power production result, but, with a larger muscle bulk involved in the exercise, the cardiopulmonary system would be stressed to a greater extent, thus potentially increasing peak oxygen uptake during FES-ACE exercise in C4 SCI.

It is speculated here that FES-ACE (with shoulder stimulation) for C4 tetraplegia would be most beneficial if it could be initiated in the sub-acute phase of the injury, when the individual is undergoing intensive rehabilitation. Used at this stage, it may help prevent, or slow down, the atrophy of shoulder musculature, thus maintaining some shoulder stability. Remaining shoulder function, in the form of shoulder shrugging, may also be enhanced. By dynamically loading the humerus and radius through regular FES-ACE exercise, it may even be possible to slow the rate of loss of bone mineral density in the upper limbs. Improved bone integrity, as a result of a programme of FES-cycling training, has been demonstrated in the tibia and femur of paraplegic individuals [73].

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[2]The addition of too many shoulder muscles to the set of muscles being stimulated may require a very complex controller (as it would need to be based on a more complex model). and lead to unreasonable donning and doffing times.

6.5 Conclusions

The systems and protocols for FES-ACE were initially designed with the C4–C6 SCI population in mind. Data for individuals with C4 and C5 SCI using the FES-ACE were therefore provided here to complement the two case studies already discussed. The three subjects included in this part of the evaluation, Subjects C, D and E, did not proceed to the formal FES-ACE training phase. Nevertheless, useful torque data were collected during muscle strengthening sessions. Torque data were plotted using informative polar and Cartesian plots which, we propose, are an innovative way of presenting upper limb strength information. Such plots could be used to monitor changes in upper limb strength over time, and to compare torque production under different conditions (for example, at varying levels of stimulation) and at different parts of the arm-cranking cycle.

As no exercise testing was performed, the cardiopulmonary fitness status of Subjects C, D and E could not be determined here. However, pulmonary function data were collected at rest, indicating vital capacities in the range of 1.4 to 2.0 l.

Subject C, with a C5 SCI, had reached sufficient levels of upper limb torque and power production at the end of the muscle strengthening phase to proceed to FES-ACE training, but decided to pull out of the project. For Subjects D and E, the problem was a practical one, indicating some limitations of FES-ACE in C4 SCI. This was due to instability and/or joint pain at the shoulder, thus limiting the FES-ACE cadence, work rates and stimulation intensities that could be used. Suggestions for tackling this issue in further developments of the FES-ACE systems, for use in C4 SCI, include the addition of electrical stimulation of key shoulder muscles to better support the shoulder structure.

Chapter 7

Discussion: FES-ACE in Tetraplegia

7.1 Summary

The findings of the two case studies evaluating FES-ACE systems and protocols in C6 SCI, and the summary of additional trials performed with individuals with C4 and C5 SCI, are combined here for a detailed analysis of the potential benefits of FES-assisted arm-cranking exercise for use in tetraplegia. One of the additional aims of this chapter is to determine the value of developing the methods described in this thesis further, in a follow-on study, to work towards systems and protocols for routine use in both inpatient rehabilitation (for sub-acute tetraplegia) and home use (for chronic tetraplegia).

7.2 Evaluation of the Potential Benefits of FES-ACE Exercise

We propose that FES-ACE training could have a useful role to play in tackling some of the secondary complications of tetraplegia resulting from SCI. This would not only be applicable to those in the sub-acute phase of rehabilitation (during their inpatient stay in hospital), but also to those with chronic SCI who are in apparent need of cardiopulmonary and/or upper limb conditioning. This pilot study has illustrated the potential for positive training effects following an intensive programme of FES-ACE exercise, in certain individuals with C4–C6 tetraplegia.

The study has also highlighted the variability of response to FES-ACE exercise even within this sub-group of individuals with tetraplegia targeted here.

7.2.1 Peak Power Output

One of the main functional outcomes of this feasibility study was peak power output, which represented the rate of work that the muscles of the upper limbs could produce at a certain point in time. Hence, regular recording of peak power output during FES-ACE exercise every four weeks allowed us to monitor upper limb strength over the training phase, and for a period of time after cessation of exercise intervention. In both case studies presented here for C6 SCI subjects, clear overall increases in peak power production, following FES-ACE training intervention, were demonstrated.

With Subject A, the effectiveness of a progressive FES-ACE training programme was evident from the steady increase in peak power output at a rate of approximately 10 W per month. This was achieved over a relatively short programme (three months). We can therefore speculate that, had this intervention period been extended, the rate of improvement could have been maintained (although a plateau would eventually have been reached, beyond which no further increase could have resulted). This makes the case for individuals with similar neurological deficits following their SCI potentially being able to benefit from regular use of FES-assisted ACE, in order to improve the strength of upper limb muscles (including those still under voluntary control). However, care would need to be taken after a long period of training that adverse degenerative effects at the shoulder did not develop.

With a greater degree of initial impairment than Subject A, Subject B gained upper limb strength over the period of FES-ACE training, but at a slower rate of improvement[1]. Starting with a baseline peak power output of 3 W, and with an average increase of only around 1.5 W per month, it would have taken Subject B longer (and/or a more intensive training schedule) to achieve the end-of-training peak power output of 38 W that Subject A had reached. Nevertheless, Subject B may have had potential to improve further, assuming no other limiting factors.

For Subjects C, D and E, the effect of a formal training intervention with FES-ACE on power production could not be investigated. Nevertheless, we can speculate that Subject C, with a C5 SCI, could have shown a level and rate of improvement similar to Subject B, had he progressed to the next phase of the

[1]The difference was too large to have been explained by other factors alone, such as sex, age, and arm girth prior to training.

programme. The muscle-strengthening period was successful in building up Subject C's upper limb muscles to the extent that he could have performed the initial baseline FES-ACE exercise tests (although protocols for exercise testing may have needed modification to accommodate this subject's lower cranking speeds). However, the subject's decision to pull out of the project after the muscle-strengthening phase prevented us from investigating the possibility further.

In contrast to C5 and C6 SCI, the development of upper limb strength in C4 SCI through FES-ACE proved problematic, as seen with Subjects D and E. The main issues were concerned with the shoulder mechanism, which seemed too weak (and the source of too much pain) to cope with the strain of arm-cranking exercise. Those sessions that were performed with the C4 subjects did, nevertheless, clearly show a positive torque produced when the muscles were being stimulated, thus showing that the biceps and triceps muscles had the ability to do useful work under artificial control.

In summary, therefore, we have demonstrated in this pilot study that FES-ACE systems, when used for regular and progressive training, can build up upper body strength in individuals with C5 or C6 SCI. However, the completeness of the injury, degree of disuse and denervation atrophy of the upper limb muscles at the start of training, and the level of motivation of the individual, are all likely to influence the potential for improvements in power production in this group.

7.2.2 Cardiopulmonary Fitness

Peak oxygen uptake

Maximum oxygen uptake is a widely accepted measure of cardiopulmonary fitness in the general population [7, 69]: the higher the value, the fitter the individual. However, one criterion for a true *maximum* is that the exercise modality used for testing should involve large muscles (usually of the legs). Here, *peak* oxygen uptake values were given instead as, although these were the highest $\dot{V}O_2$ values within any particular incremental test, they were recorded during arm-cranking exercise (which uses a small muscle mass). Moreover, in groups of individuals in which severe exercise limitation is suspected, the term "peak" tends to be used even for lower-limb exercise, as another criterion for a true *maximum* is generally not met. This criterion is the attainment of a plateau in oxygen uptake with further increases in work rate.

In this study, peak oxygen uptake (together with other indicators of cardiopulmonary fitness) was assessed by means of breath-by-breath gas exchange measurements made during FES-ACE exercise. Whether a result of natural breath-by-breath variation, of the monitoring system itself, of limitations of the set-up used for exercise testing in this pilot study, or a combination of these factors, there were some issues with the quality of the cardiopulmonary data obtained.

The most significant problem was related to the extent of noise in the data. In *absolute* terms, the noise in the data obtained in this pilot study may have been comparable to the natural breath-by-breath variation seen with neurologically intact, healthy people during exercise. In *relative* terms, in the case of our tetraplegic subjects, the noise represented a large percentage of mean oxygen uptake at any point in time, resulting in a low signal to noise ratio. Therefore, the small range of oxygen uptakes involved could have explained, to some extent, the relatively high levels of noise in the breath-by-breath data here.

Even so, systematic editing and averaging allowed comparisons of peak oxygen uptake, estimated lactate threshold, and estimated efficiency to be made between test points.

The cardiopulmonary data collected for Subjects A and B during the course of their FES-ACE training revealed useful information about the potential for cardiopulmonary fitness training in C6 tetraplegia. (Any extrapolation to benefits in C5 tetraplegia are purely speculative at this stage.) The results obtained with Subject A showed a clear and gradual increase in peak oxygen uptake over the course of the FES-ACE exercise intervention period. His initial baseline peak, at 0.7 l/min, was within the normal range for tetraplegics performing voluntary arm-cranking [113]. Three months of FES-assisted arm-cranking training then succeeded in bringing this individual to a new peak of 1.1 l/min: above the average for tetraplegics, and into the lower range of what paraplegics would achieve during voluntary arm-cranking exercise [113].

In contrast, Subject B did not show such an improvement. With a baseline value of 0.5 l/min, this person started the programme with a peak oxygen uptake below average for the tetraplegic group, according to the study by Van Loan and colleagues [113]. In contrast, Burkett and colleagues [17] provide data suggestive of Subject B's peak oxygen uptake being average for the tetraplegic group (even though this was determined for wheelchair ergometry, and not arm-cranking

exercise). Even so, Subject B's peak oxygen uptake did not increase discernibly over her training period, remaining low even after three months of training with FES-assisted ACE three times per week.

No cardiopulmonary data, as determined through exercise testing, could be given for the remaining subjects, as they did not take part in the formal training. Subjects D and E were not strong enough to complete even a baseline incremental exercise test to give pre-training values, and so only resting data could have been collected. However, this would have been of limited use because the resting values for oxygen uptake do not give an indication of cardiopulmonary fitness. Indeed, differences in resting values of oxygen uptake tend to be related to body weight, rather than training status. In agreement with this, the data collected during the resting phase of exercise tests with Subject A and Subject B were within the normal range, and so, in themselves, would not have provided useful information about the subjects' fitness levels.

The very different cardiopulmonary responses to training with FES-ACE in two different people with the same level of cervical SCI illustrate some important points:

1. The variability of exercise responses in tetraplegia, even between individuals with the same lesion level. Much of this variability may be related to the completeness of the injury.

2. The likelihood of severe central limitations to exercise, which may be more important in complete SCI, and reduced in some cases of incomplete SCI.

3. The need for diagnostic tests prior to exercise prescription in tetraplegia.

Lactate Threshold

Within each case study presented in this thesis, a lactate threshold was estimated indirectly for each test point. The lactate threshold, or anaerobic threshold, is defined as the "level of work or O_2 consumption just below that at which metabolic acidosis and the associated changes in gas exchange occur" [117]. The direct method of measuring the lactate threshold is through blood sampling of lactate, to find the highest $\dot{V}O_2$ at which there is no sustained increase in blood and muscle lactate concentration. As no blood sampling was carried out in this pilot study, characteristic changes in gas exchange were identified instead, to determine the lactate threshold indirectly, using the V-slope method.

However, this noninvasive determination of the lactate threshold is problematic, as one needs to be able to show that the more rapid rate of change of $\dot{V}CO_2$ or $\dot{V}E$ is a consequence of the developing metabolic acidosis, and not the result of some other possible causes of hyperventilation [92]. In this pilot study, the information obtained from the V-slope method was correlated with characteristic changes in the respiratory exchange ratio, and in the end-tidal tensions and ventilatory equivalents for oxygen and carbon dioxide, to increase the confidence that the threshold represented metabolic acidosis.

One *caveat* is that the validity and usefulness of the lactate threshold in FES-exercise are perhaps questionable. Let us consider the now widely-accepted phenomenon that the physiological characteristics of most muscles no longer under voluntary control change following SCI: from predominantly type I prior to injury to predominantly type II muscle fibres post-injury (due to preferential atrophy of the former) [18, 67]. With the latter mostly being the high-glycolytic fibres, there is little remaining potential for the muscle to perform the work required during FES-induced exercise without a significant anaerobic component. Furthermore, as previously mentioned, there is evidence that the pattern of nerve fibre recruitment in the muscles stimulated by external electrical pulses is the inverse of the natural pattern seen in voluntary muscular contraction. With the high glycolytic (type IIb) fibres preferentially recruited during FES-exercise (due to the lower activation threshold of their motor neurones, which are typically of large diameter), one would expect a strong anaerobic component to the metabolic activity of the working muscles early on in the FES-exercise. The high oxidative (type I) fibres (with smaller diameter motor neurones) may then be recruited to a greater extent later on in the exercise, after the fast fibres have fatigued. If this were the case, would FES-exercise be expected to result in a reverse lactate threshold? This may be so for exercise relying solely on electrical stimulation for contraction of the muscles involved in the exercise. However, in our application of FES-assisted arm-cranking exercise in C6 SCI, the exercise was performed through a combination of the remaining volitionally controlled input and the artificially controlled stimulation input, thus making the interpretation of the 'lactate threshold' even less straightforward.

Nonetheless, although purely speculative, the suggestion here is that the lactate thresholds estimated for FES-ACE in this study may be more a feature of the artificial control of stimulation and activation of the fibres through FES, rather than a true representation of the aerobic capacity of the muscles being stimulated.

Hence, the lactate threshold may not be representative of cardiopulmonary fitness in individuals performing FES-ACE exercise, or any other form of FES-exercise.

Kinetics

In a study of five healthy men who were confined to bed rest for seven days, Convertino *et al.* [22] demonstrated slowed oxygen uptake kinetics during upright exercise, suggestive of a detraining effect. A similar, but more marked slowing of $\dot{V}O_2$ kinetics has been demonstrated by Barstow and his team [8, 9] for individuals with SCI during FES-leg cycling. They suggest that we can consider the effect of the sedentary lifestyle that SCI imposes on the person to be like an extreme form of detraining and deconditioning.

In this pilot study, we had hoped to show two main points with respect to the gas exchange kinetics of our tetraplegic subjects performing FES-ACE exercise. Firstly, we aimed to illustrate the slowed kinetics in tetraplegia, compared to neurologically intact people during arm-cranking. Secondly, we anticipated that training with FES-ACE may, in time, have led to faster kinetics, which we would have taken to be another indicator of improved cardiopulmonary fitness, as has been shown for paraplegics after FES-leg cycling training [10].

However, the data collected during constant load testing were considered to be of insufficient quality to determine the kinetics of oxygen uptake, carbon dioxide output and ventilation responses. This was mainly a result of the low signal to noise ratio in the data used to determine the kinetics, as a result of the small magnitude of the steps in work rate. The effect of the noise was even more pronounced than with incremental exercise test analyses, as kinetics were extracted from un-averaged data. A second problem was that, for many of the tests, the subject did not appear to reach a steady-state, either during the zero-load arm-cranking phase, or during the constant-load phase. In addition, although the work rates had all been chosen to be below the lactate threshold[2], many of the gas exchange responses exhibited by the subjects during these tests were suggestive of supra-threshold exercise (or other causes of hyperventilation). The results of curve fitting for some test points (despite the questionable validity of the kinetic analyses) were given merely as examples to show:

1. The feasibility of the approach, but also the problems associated with it.

[2]See previous discussion arguing against the validity of the lactate threshold concept in FES-exercise.

2. The slowed kinetics shown by people with tetraplegia during arm-cranking exercise, compared to neurologically intact individuals (even untrained, sedentary people) during cyclical exercise.

Efficiency

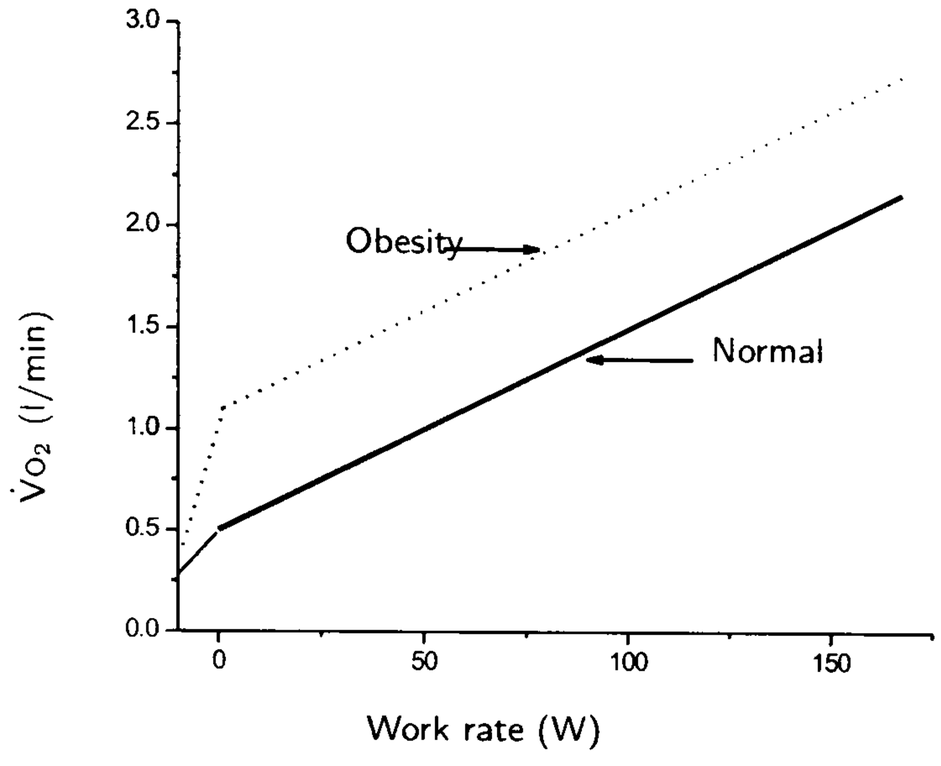


Figure 7.1: The normal $\dot{V}O_2$ - WR relationship (irrespective of age, gender or training), and the corresponding relationship in the case of obesity (reproduced from Wasserman *et al.* [116]).

In the able-bodied population, one would expect most healthy people (regardless of age, sex or training status) to follow a rather robust $\dot{V}O_2$-WR relationship for any specific exercise modality. The position of the slope should not alter dramatically from person to person, except in the case of obesity (see 7.1), due to the increased oxygen cost of maintaining the higher mass of the limbs in motion at any particular work rate. Positive training effects would normally allow the trained individual to work to a higher level up that slope (which is approximately 0.01 l/min of $\dot{V}O_2$ per W for leg-cycling), but with no obvious change in the gradient of that slope. This is because the gradient is representative of the efficiency of the exercise, which should reflect the underlying metabolic requirements for the muscles to perform that work [104]. Nevertheless, some possible reasons for this efficiency to change with training in the general population have been proposed. These include:

1. Improved skill and better technique in performing the exercise after training, suggestive of a greater mechanical efficiency of the body as a whole in the approach to the exercise. (Through this mechanism, muscular efficiency itself would be unchanged.)

2. An initial limitation in the muscle, or in the delivery of oxygen to the muscle, preventing it from working effectively prior to training, which has then been addressed through training. (In this case, muscular efficiency may be affected.)

In our study, we did observe an apparent change over time in the slope of the relationship between oxygen uptake and work rate during incremental exercise testing, suggestive of some kind of change in efficiency, either related to improved technique or to changes within the muscles performing the work. This finding was confirmed through constant load exercise testing, which allowed us to determine more specific indices of efficiency: gross, net and work efficiency. With FES-ACE training, both Subject A and Subject B showed a decrease in the gradient of the slope of the $\dot{V}O_2$-Work Rate relationship (derived from incremental tests), and an increase in gross and net efficiency over the training period (derived from constant load tests). It is unlikely that this was due to improved technique, as each subject had used the FES-ACE set-up for up to six weeks prior to baseline testing, and so would have been expected to adjust to the exercise modality over that muscle-strengthening phase. Instead, the extensive muscle atrophy in the upper limbs, and the predominance of high glycolytic fibres in the atrophied muscles, may have been the initial limitation preventing the muscles involved in the exercise from performing the work effectively. Adaptations within the muscle may then have occurred over the training period to change this, and hence alter the aerobic capacity of the trained muscles.

An additional explanation for differences in efficiency, specific to FES-exercise in SCI, was proposed by Theisen *et al.* [108]: that the lack of central command removes the direct neural control during exercise so that the normal and well-matched response to work intensity is absent. Thus, differences in efficiency between our different tests may have been an artefact of the external control of muscle activity. This artificial control may have led to sub-optimal activation patterns and consequently inefficient muscular contractions in certain tests, thus explaining, in part, some of the variability in efficiency between tests.

It is nevertheless interesting to compare the range of efficiencies estimated here for FES-ACE exercise in tetraplegia with other FES-exercise modalities, such as FES-cycling, and voluntary modalities such as arm-cranking, wheelchair ergometry and leg-cycling in other groups. Such data are summarised in Table 7.1. For each study, the efficiency indices for two different work rates are given to illustrate typical patterns of variation in efficiency. An important point to bear in mind is the apparent work-rate dependency of certain efficiency indices, which

Exercise Modality	Study	Subject Group	Work Rate (W)	Cadence	Gross Eff. (%)	Net Eff. (%)	Work Eff. (%)
FES-ACE (TP2)	Present	T(A)	8	50 rpm	3.9	6.5	11.5
FES-ACE (TP4)	Present	T(A)	22	50 rpm	6.8	9.2	11.1
FES-ACE (TP1)	Present	T(B)	1.5	50 rpm	0.83	1.92	3.38
FES-ACE (TP4)	Present	T(B)	3	50 rpm	2.05	5.19	11.03
FES-LCE (min)	Theisen [108]	LP	5	50 rpm	3.3	-	-
FES-LCE (max)	Theisen [108]	LP	8	50 rpm	4.7	-	-
Vol-WCE	Hintzy [46]	AB	23	1.11 m/s	6.5	9.9	16.8
Vol-WCE	Hintzy [46]	AB	38	1.11 m/s	7.9	10.7	14.5
Vol-ACE	Powers [88]	AB	15	50 rpm	7	-	29
Vol-ACE	Powers [88]	AB	30	50 rpm	13	-	28
Vol-LCE	Gaesser [38]	AB*	33	40 rpm	12.0	18.8	24.8
Vol-LCE	Gaesser [38]	AB*	65	40 rpm	17.0	22.9	26.9

Table 7.1: Efficiency indices for different exercise modalities; TP: test point; T: tetraplegia; LP: low paraplegia; AB: able-bodied; (A): Subject A; (B): Subject B; ACE: arm-crank ergometry; LCE: leg-cycling ergometry; WCE: wheelchair ergometry; *: trained; Eff.: efficiency.

renders the comparison between the efficiency of FES-ACE (typically performed at low work rates) and the efficiency of voluntary forms of exercise in able-bodied people (generally at higher work rates than FES-exercise) difficult (see Table 7.1).

Perhaps the most useful and valid comparison of efficiencies is between our study and that by Theisen *et al.*, who estimated FES-cycling gross efficiency in paraplegia at around 3.3% at 5 W, increasing to 4.7% at 8 W [108]. However, it should be pointed out that the RER was consistently above 1.0 during these tests, which, if indicative of exercise above the lactate threshold, may reduce our confidence in these efficiency estimations. In a similar way, in our pilot study, constant load tests from which efficiency values were calculated were often performed at work rates which appeared to lie above the lactate threshold (assuming the lactate threshold concept applies to FES-exercise). This is not ideal for efficiency calculations, as the anaerobic contributions are neglected, thus giving an over-estimate of efficiency [39]. Nevertheless, here we compare our gross efficiency values with those provided by Theisen and colleagues for FES-leg cycling. Gross efficiency of FES-ACE with Subject A was estimated at 3.9% near the start of training (at 8 W). and rose to 6.8% at the end of training (at 22 W). Lower values were obtained for Subject B,

whose gross efficiency during FES-ACE varied from 0.8% at the start to training (at 1.5 W), to 2.2% (at TP2, 3 W). However, it has already been pointed out that, in our studies, the accuracy of the control of work rate was around ±0.5 W. Therefore, those efficiency values calculated from very small step increases in load in this pilot study (e.g. from unloaded to 1.5 W) may not be credible due to the high percentage error in work rate, and in $\dot{V}O_2$.

To compare efficiency indices for FES-ACE with those for voluntary exercise modalities in neurologically intact individuals, we can use the values from Powers *et al.* [88] for voluntary arm-cranking, from Gaesser *et al.* [38] for voluntary leg-cycling, and from Hintzy and Tordi [46] for wheelchair ergometry. These are summarised in Table 7.1. In their study with able-bodied subjects, Powers *et al.* calculated efficiency indices for arm-cranking exercise at different cadences (50, 70 and 90 rpm) and work rates (15, 30, 45 and 60 W). As our subjects were performing FES-ACE at 50 rpm, and at work rates below 30 W, the values from the Powers *et al.* study [88] at 50 rpm for 15 W and 30 W are given here for comparison. As with the latter study, it seems from our data that gross efficiency of FES-ACE was work-rate dependent (alternatively, it may have been training-status dependent), going from around 1-2% at 3 W, up to around 4% at 8 W and to 7% at 22 W. This gross efficiency of 7% at 22 W is comparable to that calculated for wheelchair ergometry (in able-bodied subjects) by Hintzy and Tordi [46], but slightly lower than for voluntary arm-cranking exercise (again, in able-bodied subjects).

The most notable difference is between the work efficiency (WE) indices for FES-ACE and for voluntary ACE (and, to a lesser extent, for voluntary WCE). This may, in part, be due to a discrepancy in the baseline correction for unloaded (or 'zero-load') exercise for each of the different exercise modalities in the separate studies. Let us assume here that the baseline correction is valid (but see Stainsby *et al.* [104] for criticism of this): with voluntary ACE giving values of 28-29% for WE, this is considerably higher than the highest WE values reached by Subject A and Subject B in FES-assisted ACE, which were 12.8% and 12%, respectively. Even though work efficiency values calculated in our study showed great variability, it is interesting to note how much lower they were overall for FES-ACE in tetraplegia compared to voluntary ACE in able-bodied individuals. This probably reflects not only the inefficiency of the FES-component of the exercise, but also the significantly altered cardiopulmonary response to exercise in tetraplegia.

An additional point to make is that in the efficiency calculations made in

this study, and in the other studies used here for comparison, there is no consideration of the negative power output range (see Section 6.3.1). In FES-ACE, the range of negative power outputs with our tetraplegic subjects was from around -2 to 0 W. For Subject B, this represented a considerable proportion of her total power range (even at the end of training). It may be useful to have an additional index of efficiency in FES-exercise in SCI that uses a new baseline correction to take the negative power output range into account. This is even more applicable to FES-cycling, in which the negative power output range can extend to -12 W.

Improved pulmonary function

By comparing the spirometric values obtained for each of the five subjects in this pilot study, we can note the variability in remaining pulmonary function following cervical SCI. Subject A showed only slight impairment in FVC and FEV_1, with a near-normal percentage of FVC expired in the first second (~80%). In contrast, Subjects B, C, D and E all had clearly reduced FVC and, consequently, reduced FEV_1 volume (with Subject B having the lowest values of the four). The fact that, on average, Subjects B–E expired 100% of FVC in the first second after a maximal inspiration suggests that the main limitation was the lung volume that was accessible for ventilation. This was probably a feature of the purely diaphragmatic control of ventilation in complete tetraplegia. Tow *et al.* [110] investigated the vital capacity of tetraplegic patients at different stages following SCI. At the end of initial rehabilitation, the mean vital capacity was 2.6 l, at 10 years post-injury, 2.8 l, and 20 years post-injury, 2.5 l. It was also noted in that study that women with tetraplegia had significantly lower mean vital capacities than their male counterparts. In terms of our study, Subject A (18 years post-injury) had a vital capacity considerably higher than average for 20 years post-injury (ranging from 3.8-4.1 l for Subject A, compared to the 2.5 l average). In contrast, Subjects B, C, D and E all had lower-than-average values, with Subject C closest to the mean proposed by Tow *et al.*. However, according to the mean derived by Van Loan *et al.* [113] of 3.1 l, all subjects other than Subject A were well below expected for the tetraplegic population.

It is clear that, compared to neurologically intact people, individuals with cervical SCI have significantly reduced vital capacities, and, more generally, altered breathing mechanics. This is due to "the abnormally high extra-pulmonary work of breathing attributable to the use of the diaphragm as the main source of ventilation" [110]. In the case of Subject A, the high vital capacity even prior to exercise intervention may have reflected the incompleteness of the injury; some

pathways controlling accessory respiratory muscles (i.e. other than the diaphragm) may have remained under central control. This could explain why ventilatory limitations were unlikely to have been an issue for Subject A, but probably a significant component of the exercise limitations observed with Subject B during the course of FES-ACE training.

7.3 Limitations of FES-ACE Exercise

The issues limiting the usefulness of FES-ACE in C4–C6 tetraplegia are discussed here. Some of these issues are *general* exercise limitations in tetraplegia, and others are limitations that are *specific* to arm-cranking exercise in tetraplegia.

7.3.1 General Exercise Limitations

Sympathetic Nervous System Dysfunction

One of the major factors limiting cardiovascular responses to exercise in tetraplegia is the extent of dysfunction of the sympathetic nervous system (SNS) which results from the SCI. The effects of SNS dysfunction below the level of injury tend to become more pronounced, the higher the lesion [107].

The secondary complications associated with SNS dysfunction need to be borne in mind when considering exercise prescription in tetraplegia. One aspect of this SNS dysfunction, which mostly affects those with a lesion above T5, is that both resting systolic and diastolic blood pressure are lowered in tetraplegia (and high paraplegia). In addition, during exercise, there is an impaired cardiovascular response to the requirements for increased blood flow and oxygen delivery to the exercising muscles. This is evident from the blunted heart rate response that results from reduced sympathetic activity [10, 99].

The variability of the blunted heart rate response between different individuals with tetraplegia was emphasised by McLean *et al.* [70]. This could be related to large variability in the extent of the SNS dysfunction in this group. Although, in most cases of clinically complete SCI leading to tetraplegia (as determined through ASIA scores), a significant amount of SNS dysfunction is expected, there may be some preserved sympathetic pathways [19]. In incomplete injuries, this likelihood is increased even further. However, there is no reliable clinical test in routine use today that can identify the extent of SNS dysfunction in SCI. Indeed, in a study by Curt *et al.* [27], the investigators found that, with incomplete SCI lesions,

"the clinical examination can predict the severity of impairment of the spinal sympathetic system in only about 50% of patients" [27]. The need for diagnostic tests relating to SNS dysfunction is being addressed by a team led by Ellaway [31].

7.3.2 Exercise Limitations in Upper-Body Exercise

Venous pooling

In individuals with normal SNS function, there is a clear disparity in both cardiorespiratory and haemodynamic responses to arm exercise versus leg exercise at identical work rates [37, 53, 54]. Usually, with increasing intensity of upper-body exercise, reflex control of the distribution of cardiac output causes some characteristic changes in blood pressure and vascular resistance. Local mediators in the exercising muscles cause intense vasodilation that increases blood flow to support metabolic demands. At the same time, the muscles that are not involved in the exercise (such as the large muscles of the legs, during upper-body exercise) are vasoconstricted from reflex increases in sympathetic nerve activity. In this way, systemic vascular resistance falls, but systolic blood pressure typically rises progressively with an increase in $\dot{V}O_2$ [2]. Hence, in able-bodied individuals performing upper-body exercise, the muscle pump in the legs maintains adequate venous return to the heart.

In people with high paraplegia and tetraplegia, even at rest in the sitting position, SNS dysfunction leads to orthostatic hypotension[3], which is related to "pooling of blood in the viscera and dependent extremities in the absence of SNS efferent activity and reflex arterial and venous vasoconstriction in SCIs above the thoracic SNS outflow" [107]. What this additionally means during upper-body exercise performed in the sitting position, is that the lack of muscle pump in the legs decreases the venous return to the heart, causing the heart rate to increase in order to maintain the cardiac output [50].

Circulatory function during arm-cranking exercise in tetraplegia is therefore limited as a result of the impaired sympathetic activity below the level of the lesion (this effect is often referred to as "circulatory hypokinesis"[54]). The cascade of implications for the use of upper-body exercise in tetraplegia is summarised by Figoni [35]: peripheral vascular insufficiency and inactivity of the skeletal muscle venous pump may cause excessive venous pooling in the legs and abdomen, reduce the circulating blood volume, and diminish venous return.

[3]Hypotension is defined as at least two consecutive systolic blood pressure measurements of <90mmHg [107].

thereby limiting stroke volume, cardiac output. and blood flow to exercising arm muscles. Although blood pressure and cardiac output were not measured directly in this pilot study, it is likely that the impaired circulatory function during upper-body exercise would have affected the tetraplegic subjects involved in this project, who performed the FES-assisted upper limb exercise from a sitting position.

These effects could potentially be reduced by:

- The use of drug treatments to reduce the effects of orthostatic hypotension.
- Adapting the systems so that they can be used in the supine position.
- The use of alternative exercise modalities that involve the muscles in the legs, such as FES-cycling, to induce blood flow in the lower limbs.

The Shoulder Issue

Problems at the shoulder joints have already been discussed, with reference to Subjects D and E, who had C4 level SCI. The issues included shoulder pain and shoulder instability. Shoulder pain is unfortunately almost an accepted consequence of tetraplegia. Furthermore, its causes appear to be multifactorial [96]. Shoulder instability can be related to extensive muscle atrophy in the upper limbs and in many of the muscles usually involved in supporting the complex structure that makes up the shoulder mechanism. The altered musculoskeletal arrangement at the shoulder joints in SCI at C4 limits the usefulness of FES-ACE systems as they are. Further developments would be necessary to overcome this problem. One suggestion provided in this thesis is the addition of stimulation of key shoulder muscles prior to, and during, FES-ACE training.

Even with individuals with full voluntary control of shoulder musculature, it is important to emphasise that problems associated with chronic use of the upper limbs for wheelchair propulsion and arm-cranking exercise can develop, as is seen in low tetraplegia, and paraplegia. This is because these individuals are at high risk of developing degenerative changes in the shoulders, as a result of altered function of upper extremities following SCI: the shoulders become weight-bearing, instead of being used predominantly for prehensile and placement activities [64]. Consequently, although an intense FES-ACE routine may initially be beneficial to individuals like Subject A in our pilot study, the FES-ACE training programme may need to be limited to only a few months at a time. After this, instead of

continuing on an intense arm-cranking regime, the individual may benefit from changing to a combined programme of arm-cranking and FES-cycling, for example.

7.4 Other FES-Exercise Options in Tetraplegia

The idea of using FES exercise in SCI has been explored for the past two decades, mostly in relation to FES-leg cycling [83]. Indeed, benefits of regular training with FES-leg cycle ergometry have already been identified, not only in paraplegia, but also in certain individuals with tetraplegia.

It should be noted that many of the central limitations resulting from SNS dysfunction apply to lower-limb FES-exercise in tetraplegia, as well as for FES-ACE. However, for those individuals with some remaining SNS function, the cardiopulmonary responses to FES-leg cycling are expected to be greater than with arm-cranking alone, due to a number of factors. First of all, the venous pooling and associated circulatory hypokinesis observed in upright FES-ACE exercise would not affect lower-limb cycling. Another reason is that the larger muscle bulk involved in lower limb cyclical exercise, compared to upper limb cyclical exercise, requires a higher oxygen uptake to supply the exercising muscles, allowing the cardiopulmonary system to be stressed to a greater extent.

Therefore, for those tetraplegic individuals who are able to perform FES-cycle ergometry exercise from their wheelchairs, this may be the best exercise modality if the main goal of exercise is to stress the cardiopulmonary system as much as possible.

However, if one of the goals of the exercise is to build up strength and endurance in those muscles in the arms still under voluntary control in tetraplegic individuals, thus requiring peripheral adaptations, we propose that arm exercises (with or without FES-assistance, depending on the level of the lesion) would generally be the best option (except possibly in SCI at C4 and above).

Another option may be FES-rowing [118], but the present set-up used with paraplegics would have to be modified significantly to accommodate tetraplegics. This would mostly relate to the seating used for this exercise modality.

Alternatively, a combination of the higher cardiopulmonary workout from the legs and the upper limb strengthening could be achieved through hybrid training, involving arm-cranking and leg-cycling simultaneously. Such hybrid systems have

been tested with tetraplegic subjects (voluntary ACE together with FES-LCE), but with varying levels of success, as there is some suggestion that the arm and leg exercises carried out concurrently may interfere with each other in some way [35, 49]. Another solution might therefore be to have a hybrid training programme, instead of a hybrid exercise modality, so that the individual performs sessions of voluntary or FES-assisted arm-cranking exercise on some days, and FES-leg cycling exercise on others.

It is clear that further investigation into the options for exercise in tetraplegia is required.

Chapter 8

Further Work...

...On Exercise Prescription in Tetraplegia

8.1 Summary

The responses to exercise in tetraplegia are not only dependent on the level of the injury, but also on the completeness of the injury. This chapter makes the case for working towards a systematic method of identifying the precise causes of exercise limitation. This should allow exercise prescription to be determined in tetraplegia on a case-by-case basis. We suggest that a number of tests need to be included to build up an individual's profile, but not all of these tests are in routine clinical use at present. In addition to identifying each person's exercise limitations, the goals of exercise training need to be made clear before a useful training programme can be drawn up for the individual.

Finally this chapter provides some recommendations for further work on FES-ACE systems for use in tetraplegia. With some modifications and further evaluation, FES-ACE could eventually be one of the exercise options considered as part of a systematic approach to exercise prescription in this population.

8.2 Identifying Exercise Limitations in Tetraplegia

A recent review by Jacobs and Nash [55] highlights the complications and dangers of prescribing exercise to individuals with SCI. and especially with tetraplegia, without

first considering the specific consequences of the SCI to the individual. Clearly, a systematic assessment of individuals with tetraplegia is required to determine the extent and source of exercise limitation, before proceeding to exercise prescription. A much-needed battery of tests is being developed by a team led by Ellaway [31].

Use of the SSR test

One of the tests being developed by Ellaway and colleagues, is a test of SNS dysfunction, referred to as the sympathetic skin response (SSR) test [19, 27]. If such a test could be incorporated in the clinical assessment of people with SCI, instead of relying solely on the present norm of manual muscle test scores (e.g. ASIA score), a more accurate and more descriptive picture of each person's neurology could be built up. This would allow the clinician or physiotherapist to determine the most suitable approach to tackling the exercise limitation in that individual.

Use of clinical exercise testing

Exercise testing is used clinically to identify sources of exercise limitation, and to determine the best course of action to rectify these. Simple exercise tests need to be identified for the initial assessment of individuals with tetraplegia. Whether these should be submaximal tests, incremental tests, or a combination, and which exercise modality (or modalities) would be most informative and practicable in tetraplegia, need further investigation. Noonan and Dean [79] suggest that predictive, submaximal tests should be used to determine peak $\dot{V}O_2$ in populations with severely compromised exercise capacity due to disease or musculoskeletal limitations. The main motivation would be to increase safety and minimise unnecessary strain to the individual. This would seem applicable to tetraplegia, and the SCI population as a whole. However, the great variability in exercise responses seen in individuals with tetraplegia, depending on the level of injury, the completeness of the injury, and the degree of remaining SNS function, make it very difficult to produce predictive equations for peak $\dot{V}O_2$. Clinical exercise testing in able-bodied groups sometimes uses heart rate response as a predictor of $\dot{V}O_2$ response. Problems with using heart rate response to predict oxygen uptake response in tetraplegia have already been identified by McLean *et al.* [70].

Use of spirometry evaluations

Could spirometry values be used as part of an initial assessment before determining the best course of action for tackling the exercise limitation in a person with tetraplegia? It may be that, if the lung capacity accessible to the individual through

purely diaphragmatic breathing is extremely low, then this issue needs to be tackled as the factor limiting ventilatory requirements even before oxygen uptake capability is assessed. If this were the case, the time-consuming incremental tests would be postponed until a solution could be found for increasing available lung volumes to meet ventilatory requirements during exercise. One way to increase tidal volume during exercise could be through abdominal FES, which has been shown to be successful during quiet breathing (and coughing) at rest [40].

Use of nerve conduction and EMG tests

If the clinician is considering using FES to assist the tetraplegic person to perform exercise, it is useful to perform a preliminary test of the muscles to be stimulated, to determine whether there has been any lower motor neurone (LMN) damage to the nerves supplying those muscles (using nerve conduction tests), or to quantify any remaining activity in the muscles (using EMG tests).

Re-assessment of level of impairment

In addition to diagnostic tests, Jacobs and Nash [55] suggest that a full neurological re-assessment of the individual with SCI should be made prior to exercise testing and training.

8.3 Tackling Exercise Limitations in Tetraplegia

The evaluation of an individual with tetraplegia considered for exercise prescription clearly needs to begin with a systematic determination of motor, sensory and SNS impairment, even before any form of diagnostic exercise testing is performed. The resulting profile will undoubtedly vary considerably from one case to another, so that the approach to tackling exercise limitation needs to be tailored to the particular individual's capacity and motivation. Knowing the individual's exercise limitations in detail before prescribing exercise would ensure that there are no unreasonable expectations for his or her potential for improvement following exercise intervention.

If these initial evaluations identify a potential for improving strength of muscles still under voluntary control, and/or for improving cardiopulmonary fitness, the next step would be to identify the goal(s) of exercise for that particular individual.

One important goal of exercise training in tetraplegia should be to reduce the risk of cardiovascular disease, type 2 diabetes. and insulin resistance syndrome

(also known as the metabolic syndrome) [58]. The challenge here is: in terms of reducing the risk of developing cardiovascular (and other) diseases in tetraplegia, how much exercise is enough?

In some cases, the goal may be weight loss (which, if successful, could reduce the risk of cardiovascular disease by reducing the resting load on the heart). In the general population, in order to burn subcutaneous fat, endurance exercise at low to moderate intensities is generally recommended, but the problems of applying similar principles to the well-trained, let alone the untrained, SCI individual have recently been highlighted by Knechtle *et al.* [62].

For those individuals who have very marked SNS dysfunction, and so may be considered to have little scope for marked cardiopulmonary improvements, a solution needs to be found. How do we tackle the central limitations to exercise imposed by extensive SNS dysfunction? One route may be the use of pharmacologic treatments to provide an artificial stimulus for an increase in blood pressure, and hence blood flow, during exercise. Clearly, their safety and efficacy would need to be tested. Promising preliminary investigations into the use of Midodrine, to increase BP during exercise in tetraplegia, have been performed by Nieshoff and colleagues [78]. The idea of increasing BP during exercise is already exploited by some wheelchair athletes who make use of autonomic dysreflexia to enhance performance, through a technique referred to as "boosting"; but this is not recommended as it is clearly dangerous.

Finally, which exercise protocols should be used in tetraplegia? The exercise modality options have already been discussed, but once those are chosen, exercise training intensity needs to be set. This depends, among other things, upon the need for increased endurance versus the need for high peak force production. Whether exercise training regimes used with people with SCI should aim to increase peak muscle force, or improve endurance, is still a subject of debate [109], but is clearly dependent on the main goal of training. For endurance training in the general population, exercise intensity is usually set at a work rate that elicits a desired percentage of peak oxygen uptake or peak heart rate, or at a work rate below the lactate threshold. Problems with use of the heart rate or the lactate threshold in FES-exercise have already been alluded to. Setting exercise intensity at a percentage of peak oxygen uptake may therefore be the best global solution for exercise prescription in SCI.

8.4 A Future Role for FES-ACE?

Does FES-ACE have a role in exercise prescription in tetraplegia? The results of the pilot study of the proposed systems for FES-ACE provide evidence for benefits of their regular use in some individuals with C4–C6 SCI. However, further modifications to the systems and protocols would be required in order to: (i) make the system applicable to a wider range of individuals in the target group. and (ii) work towards a full experimental evaluation of FES-ACE, possibly as part of a home-based research study. Some ideas for modifications of the FES-ACE systems are provided here.

The FES-ACE set-up could be modified to make it more adaptable to the level of impairment of the individual. A choice of which muscle groups to include for electrical stimulation would be particularly useful, so that only biceps and triceps groups would be switched on for C5 and C6 SCI, but additional shoulder muscle stimulation would be incorporated in C4 SCI.

A simple grading system for the biceps, triceps and any stimulated shoulder muscles, similar to the MRC grades used for muscles of the hand, could be a useful additional tool. Such a scale, applied to each muscle independently, could be used in parallel with the torque and power measurements to monitor changes in upper limb muscle strength with training. As an alternative (or as a complement). tests of peak muscle force from individual muscles of the upper limbs could be performed using a dynamometer.

Additional tests, relating to functional outcomes, may provide a more clinically useful evaluation of FES-ACE. Functional Independence Measures (FIM) and Activities of Daily Living (ADL) are examples of such tests.

To reduce donning and doffing time of the electrodes and cables, a jacket or pair of sleeves could be designed which house the electrodes, thus requiring only some conductive gel between the sleeve and skin surface at the electrode positions. This would be similar to the shorts already used by some paraplegics for FES cycling.

Finally, it may be useful to investigate an alternative FES-ACE system that can be used in the supine position. This would be favourable in cases of severe trunk instability in the upright position, or scoliosis. Exercise performed in the supine position may also result in higher cardiopulmonary responses than in the

upright position.

Following some of these modifications, a full evaluation of FES-ACE for use in tetraplegia would need to be performed, to include a larger number of subjects. By implementing a longer training intervention with these subjects, longer-term effects of the FES-exercise could be investigated.

8.5 Conclusions

In summary, there are a number of areas which need to be explored in greater detail to work towards systematic exercise prescription in tetraplegia. The first of these would involve setting up a set of diagnostic tests for routine clinical evaluation of exercise limitation(s). This would provide a profile for the individual upon which decisions regarding exercise prescription would be based. The next step would be the definition of the goals of training for the individual, and the determination of the most appropriate exercise modality (or combination of modalities) and training programme to address the goals of training.

In tetraplegia, one of the most significant sources of limitation to exercise is probably the extent of SNS dysfunction following cervical SCI. An investigation into possible solutions for increasing exercise responses in cases of severe SNS dysfunction seems warranted.

Provided exercise is recommended to the individual with tetraplegia, FES-ACE should be considered as an option. Although further developments are needed for its applicability to higher lesion levels, there seems to be a future role for this exercise modality in tetraplegic rehabilitation and home-use.

Chapter 9

Conclusions

To enable an experimental evaluation of FES-ACE, we developed the technical set-up and control systems. The data presented here show that these developments resulted in high precision systems for exercise training sessions and for exercise testing. The accurate control of power output during FES-ACE permitted incremental and constant load exercise testing with tetraplegics, who typically can only perform the exercise at work rates of very low magnitude, and within a narrow range.

Even with the exercise systems in place, standard cardiopulmonary testing protocols used with neurologically intact subjects during voluntary exercise would not have been suitable for this group of individuals with extensive physical disability. Thus, the protocols needed to be adapted for this target group before the physiological assessment could begin. The results for two case studies demonstrate that the modified protocols presented in this thesis, in the main, are appropriate for people with tetraplegia.

Results from incremental exercise testing provided the most comprehensive information on cardiopulmonary fitness. This included peak oxygen uptake, an estimate of lactate threshold, and an indication of efficiency from the oxygen uptake-work rate relationship. Useful kinetic response data, which can usually be used to identify training effects, was less consistently obtained from the constant load tests with tetraplegic subjects. We would argue that the constant load testing protocols are nevertheless applicable, but the low signal to noise ratio makes the extraction of response kinetics problematic. Steady-state cardiopulmonary data from the constant load tests were useful in identifying patterns of efficiency at different phases of training. Such data are also useful for comparison with efficiency values provided in the literature for other exercise modalities.

The overall experimental evaluation was carried out with five tetraplegic subjects. Two completed the full programme of FES-ACE training and testing, and their results were presented as case studies. This allowed the exercise responses and training effects of two people with different neurological status at the start of participation to be described. The first case study centered around an individual with chronic incomplete C6 SCI. Any effects of training in this chronic SCI subject could be attributed directly to the exercise intervention. Although incomplete injuries make up around 40% of SCI in the U.K., people with incomplete lesions at the same level can have very different neurologies, with differences in the extent of remaining voluntary control of muscles and sensation below the level of injury, and in the extent of autonomic system dysfunction. In the first case study presented, we were able to demonstrate upper limb strength and cardiopulmonary fitness benefits to the individual as a result of the FES-ACE exercise intervention. In order to assess the potential of FES-ACE in the wider C4–C6 SCI population, the investigators identified the need to test the FES-ACE methods in complete SCI.

In the second case study presented in this thesis, the subject had a complete C6 SCI. Unlike the previous case study, there were some confounding factors relating to this subject's sub-acute condition and primary care. With sub-acute SCI, this subject could have shown some natural recovery (which can occur for up to one year post-injury) and some improvements in upper body strength and cardiopulmonary fitness through other rehabilitation exercises. These exercises were performed as part of primary care during the subject's inpatient stay, with the FES-ACE exercise intervention running in parallel. Nevertheless, we can argue that changes observed in the outcome measures recorded here would be at least partly attributable to the FES-ACE training.

Positive effects of training were apparent in both case studies: both showed improvements in peak power output, and one showed associated increases in cardiopulmonary fitness. This provides evidence that FES-assisted arm-cranking exercise could benefit the individual in the long term, providing appropriate training schedules are implemented. However, the cases taken together illustrate the variability of physiological responses between individuals with tetraplegia, which represents a significant problem for broad exercise prescription in this group.

In this pilot study, we were also able to identify the limitations of the current set-up and systems, in relation to C4 SCI. The suggestions given here for possible developments to rectify some of these issues should be investigated further in follow-on studies.

Even for those who could not progress to formal exercise training, the software presented in this thesis for representation of the stimulation data, in relation to the data recorded from the instrumented arm-crank ergometer, provides a useful tool. The polar and Cartesian plots allow us to visualise the variation in torque production over the crank cycle, and relate this to the use of different muscles (with or without stimulation). As these same plots can be generated for each session, the software enables us to monitor changes in torque (and power) production by the upper limb muscles over time.

In conclusion, we have identified a need for novel exercise modalities aimed specifically at people with tetraplegia, and for appropriate methods of evaluating them. We have presented systems and protocols for FES-ACE systems and their evaluation in C4–C6 SCI, and identified some of the benefits and limitations associated with FES-ACE. Ideas for further work in the area of exercise prescription in tetraplegia, and a possible future role for FES-ACE, have been provided.

Appendices

Appendix A

A.1 Ethical Approval NHS

A.2 Ethical Approval GU

A.3 Modified Ashworth Scale

A.4 Patient Information Sheet

A.5 Patient Consent Form

A.6 Equipment Specifications

A.1 Ethical Approval NHS

South Glasgow
University Hospitals
NHS Trust

Trust Headquarters

Our Ref ETNOVLET.FMcG.LC
(Direct Line) 0141 201 1150

29 November 2000

Professor K Hunt,
Professor of Mechanical Engineering
University of Glasgow,
Glasgow

Dear Professor Hunt,

DEVELOPMENT OF SYSTEMS FOR TETRAPLEGIC ARM CRANKING USING FUNCTIONAL ELECTRICAL STIMULATION: A PILOT STUDY
PAPER NO. EC/00/5/95

Further to your recent application for approval of the above study, I am pleased to advise that full ethical approval was granted by the Ethics Committee at its meeting held on Tuesday 28 November 2000.

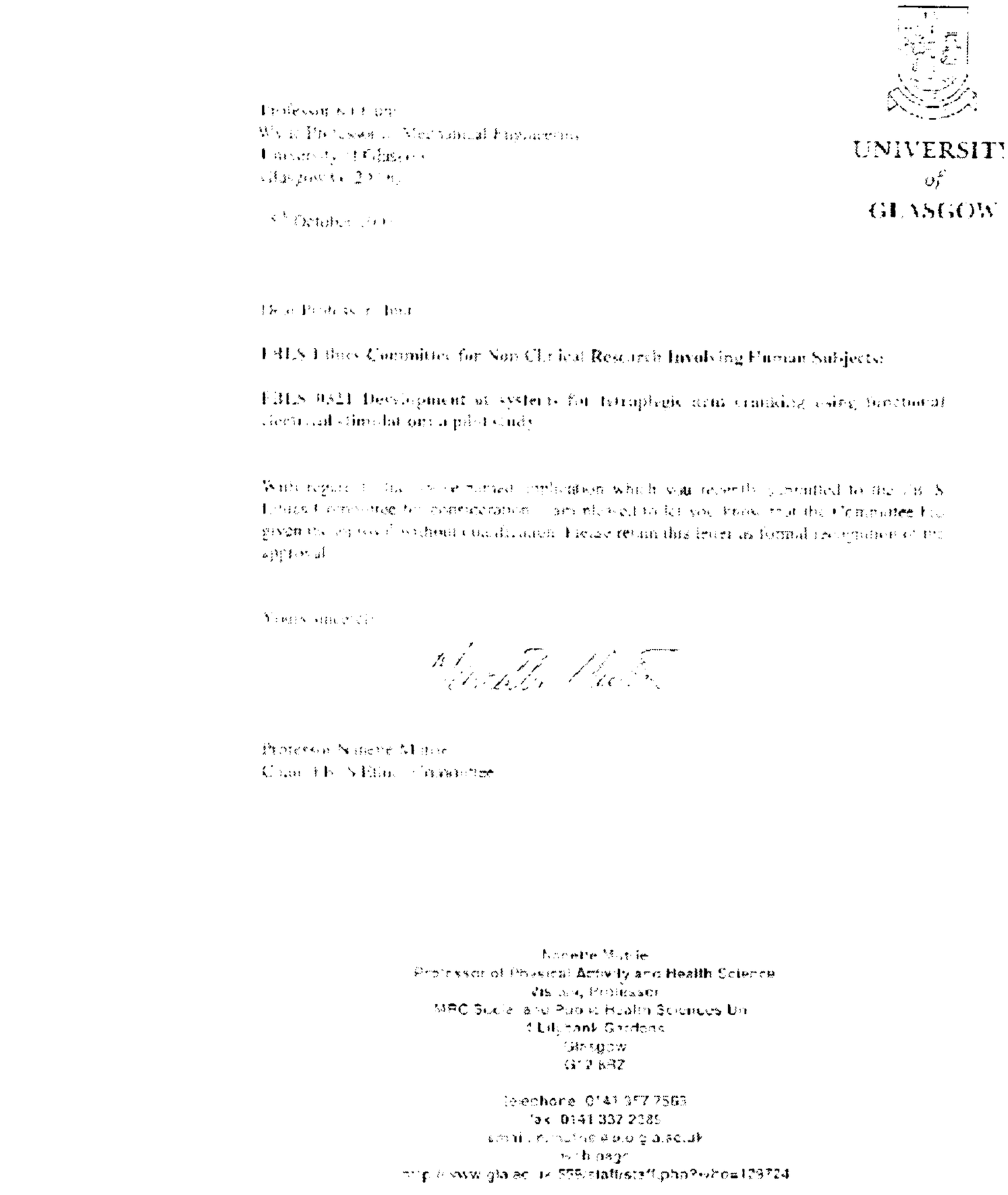
On behalf of the Committee, may I take this opportunity to wish you every success with the trial and request that on the conclusion of this study a full report is forwarded to the Ethics Committee.

Yours sincerely,

.....
Frank McGuire
SECRETARY - ETHICS COMMITTEE

Figure A.1: Full Ethical Approval, granted by the South Glasgow University Hospitals NHS Trust, Glasgow.

A.2 Ethical Approval GU



UNIVERSITY of GLASGOW

Professor N Mutrie
Professor of Physical Activity and Health Science
Visiting Professor
MRC Social and Public Health Sciences Unit
4 Lilybank Gardens
Glasgow
G12 8RZ

Telephone 0141 357 7563
Fax 0141 337 2389
email n.mutrie@educ.gla.ac.uk
web page
http://www.gla.ac.uk/55/staff/staff.php?who=139724

5th October 2011

Dear Professor Mutrie

FBLS Ethics Committee for Non Clinical Research Involving Human Subjects

FBLS 0421 Development of systems for tetraplegic arm cranking using functional electrical stimulation: a pilot study

With regard to the above-named application which was recently submitted to the FBLS Ethics Committee for consideration, I am pleased to let you know that the Committee has given its approval without conditions. Please return this letter as formal recognition of this approval.

Yours sincerely

Professor Nanette Mutrie
Chair, FBLS Ethics Committee

Figure A.2: Ethical Approval for part of the work, granted by the University of Glasgow.

A.3 Modified Ashworth Scale

The following scale was taken from [15].

0 = No increase in muscle tone.

1 = Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end range of motion when the affected part is moved in flexion or extension (abduction or adduction, etc.).

1+ = Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM.

2 = More marked increase in muscle tone through most of the ROM, but the affected part is easily moved.

3 = Considerable increase in muscle tone, passive movement is difficult.

4 = Affected part is rigid in flexion or extension (abduction or adduction, etc.).

A.4 Patient Information Sheet

SGH

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PATIENT INFORMATION SHEET

1. Study Title: Development of Systems for Tetraplegic Arm Cranking using Functional Electrical Stimulation: a pilot study

Investigators: Dr Alan McLean, Mr Matthew Fraser (Spinal Injuries Unit, SGH)
Prof Kenneth Hunt, Dr Stan Grant (University of Glasgow)

2. Invitation: You are invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and those responsible for your medical care if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Consumers for Ethics in Research (CERES) publish a leaflet entitled "Medical Research and You". This leaflet gives more information about medical research and looks at some questions you may want to ask. A copy may be obtained from CERES, PO Box 1365, London, N16 0BW.

Thank you for reading this.

3. Purpose of the study: Functional electrical stimulation (FES) has for many years been widely used to retrain paralysed muscle and achieve, at least partially, useful functions such as hand grasping, standing, stepping and cycling.

We are currently recruiting subjects for a study investigating the feasibility of using FES of the paralysed arm muscles to assist in arm-cranking exercise. Subjects will be tetraplegic patients with a neurological injury level between C4 and C6, inclusive. We will be developing systems for both arm-crank ergometry (a static arm cranking device) and arm crank wheelchair propulsion (a wheelchair fitted with a hand cycling accessory). This project is a pilot study which will allow us to develop and evaluate the basic methods for FES-assisted arm cranking for C4-C6 tetraplegic patients. Our longer term goal is to assess the feasibility of moving the FES arm cranking system and methods into daily practice, for example within the tetraplegic patient's acute rehabilitation programme. We hope that the type of exercise which these systems offer will lead to general improvements in the quality of the upper limbs, in the execution of several important daily activities (transfers etc.), and in general fitness and health.

(a) Page 1

Figure A.4: Patient information sheet.

4. Selection of Participants: we aim to recruit a total of three volunteer patients for this study. Potential candidates have been selected from the current in-patients of the Spinal Injuries Unit and are being invited to consider if they wish to participate.

5. Do you have to take part?: Taking part in the research is entirely voluntary. It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. This will not affect the standard of care you receive.

6. Procedures: This research study will last a total of two years, but each individual subject will be asked to participate for a period of up to four months, with one further measurement session required three months following the end of the exercise period. The study will take place in the rehabilitation gymnasium at the Spinal Injuries Unit.

You will first undergo a one-month programme of muscle strengthening using daily FES of the paralysed upper-arm muscles. Stimulation will be applied via adhesive electrodes placed on your skin. Stimulation pulses are generated by an electronic stimulator, which is controlled by a PC. Muscle strength will be measured using an instrumented arm-crank ergometer apparatus at the start, throughout the month, and three months after the end of the exercise programme.

You will then take part in up to three months (12 weeks) of regular (3 or 4 times per week) FES arm-crank exercise using the arm-crank ergometer device. Tests will be carried out at the start of weeks 1, 4, 7, and 10, and at the end of week 12 (these are called the "Test Points"). The following tests will be carried out at each Test Point: (i) Sub-maximal test: you will exercise at pre-defined (sub-maximal) loads and duration; (ii) Maximal power test: you will exercise at slowly increasing load until maximal power output is determined. During both types of test your heart rate, blood pressure, exhaled air, Rating of Perceived Exertion (RPE), and Rate of Perceived Breathlessness (RPB) will be monitored. Tests (i) and (ii) will be performed on successive days at each Test Point. Resting variables to be measured are vital capacity, forced expiratory volume in one second, mouth pressure (these tests involve blowing as hard as you can into a tube), heart rate and blood pressure. If at any time during an experimental session you wish to stop, you will be completely free to do so. Exhaled air will be collected throughout the tests and will be analysed by a computer. To measure the exhaled air, you will wear a nose clip and breathe through a rubber mouthpiece, which is connected to the computer by plastic tubing.

Regular measurements will also be made during the exercise programme, using the instrumented arm-crank ergometer, to measure the evolution of muscle strength, mechanical power output capability, and endurance. The effect on voluntary range of motion will be assessed in standardised functional (reaching) tests. If judged to be sufficiently strong, you will be invited to do regular sessions of FES-assisted arm-crank wheelchair propulsion on the arm-crank wheelchair apparatus (a wheelchair with an instrumented hand cycling attachment).

7. Possible Risks: Electrical stimulation has been used in rehabilitation as a therapy for spinal cord injured persons for many years. Electrical stimulation via surface electrodes at the levels intended is widely used, is not known to be harmful to muscle, or to present risk of injury.

(b) Page 2

Figure A.4: (cont.)

Using FES on the paralysed muscles of your arms for arm cranking will introduce strain at the joints, with the potential for musculo-skeletal injury, and will also stress the cardiovascular system. However, during the selection process you will be carefully assessed by physiotherapists and clinicians within the Unit to help ensure that your musculo-skeletal and cardiovascular capabilities are not likely to be exceeded during this programme. A physiotherapist will also be present during all experimental sessions.

8. Possible Benefits: During this study we may see general improvements in your fitness and in the condition and strength of your upper-arm and shoulder musculature. However, since this is a short-term pilot study it is unlikely that there will be long-lasting beneficial effects after the study is completed. By carrying out this study we hope to gain information which will allow us to improve procedures and apparatus for upper-limb FES-assisted arm cranking exercise. In the longer term we hope to be able to offer systems for therapy and exercise which when regularly used can produce significant and sustained improvements to fitness and health.

9. What if something goes wrong?: The potential risks involved in your participation in the study have been outlined above. If you are harmed by taking part in this research project there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms may be available to you.

10. Confidentiality: All information which is collected about you during the course of the research will be kept strictly confidential. Any information about you which leaves the hospital/Unit will have your name and address removed so that you cannot be recognised from it.

11. Publication of Results: It is likely that the results of the study will be published in scientific peer-review journals. Your identity will not be revealed in dissemination of the results. Any photographic material recorded during experimental sessions will only be published with your prior consent.

12. Organisation and Funding of the Research: The study is being jointly organised by the National Spinal Injuries Unit (Southern General Hospital) and the Department of Mechanical Engineering at the University of Glasgow. The work is funded by the Engineering and Physical Sciences Research Council and the European Commission. The funding covers only the necessary research expenses such as physiotherapists and engineers time, and apparatus. The investigators will not be paid for carrying out this study or for including you in it.

13. Who has reviewed this study?: This study has been reviewed and approved by the Ethics Committee of the Southern General Hospital NHS trust.

(c) Page 3

Figure A.4: (cont.)

14. Contact for Further Information:

If you would like further information, or if you would like to discuss any aspect of the study, please do not hesitate to contact one of the investigators listed below.

Dr Alan McLean
Spinal Injuries Consultant
National Spinal Injuries Unit
Southern General Hospital NHS Trust
1345 Govan Road
Glasgow G51 4TF
Tel: 0141 201 1100

Mr Matthew Fraser
Spinal Injuries Consultant
National Spinal Injuries Unit
Southern General Hospital NHS Trust
1345 Govan Road
Glasgow G51 4TF
Tel: 0141 201 1100

Professor Ken Hunt
Department of Mechanical Engineering
University of Glasgow
Glasgow G12 8QQ
Tel: 0141 330 4340

Dr Stan Grant
Institute of Biomedical and Life Sciences
University of Glasgow
Glasgow G12 8QQ
Tel: 0141 330 6490

Thank you very much for considering participation in this study.

Patients will be given a copy of the Patient Information Sheet and a signed Consent Form to keep.

(d) Page 4

Figure A.4: (cont.)

A.5 Patient Consent Form

SGH

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CONSENT FORM

Title of Study: Development of Systems for Tetraplegic Arm Cranking using Functional Electrical Stimulation: a pilot study

Names of Researchers: Dr A McLean; Mr M Fraser; Prof K Hunt; Dr S Grant

To be completed by the Patient

	Please Tick Yes	No
. I confirm that I have read and understand the Patient Information Sheet dated November 2001 (Version 2.0) for the above study and have had the opportunity to ask questions.	☐	☐
. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	☐	☐
. I understand that sections of my medical notes may be looked at by responsible individuals from the Southern General Hospital or Glasgow University or from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to my records.	☐	☐
. I agree to take part in the above study.	☐	☐

Name of Patient..... Signature..... Date.....

Name of Person taking consent..... Signature..... Date.....

Researcher..... Signature..... Date.....

1 for patient; 1 for researcher; 1 to be kept with hospital notes

Figure A.5: Patient consent form.

A.6 Equipment Specifications

MetaMax 3B specifications

Volume transducer	Type	Triple-V® turbine, digital
	Range	0.05-20 l/s
	Resolution	7ml
	Accuracy	2%
	Resistance	>0, 1 kPA/l/s at 16l/s
O_2 analyser	Type	electro-chemical cell
	Range	0-35 % O_2
	Response time (t_{90})	100ms
	Accuracy	0.1 Vol.%
CO_2 analyser	Type	ND infrared
	Range	0-13 % CO_2
	Response time (t_{90})	100ms
	Accuracy	0.1 Vol.%
Temperature sensor	Type	NTC Thermistor
	Range	$-55°C - +155°C$
	Accuracy	1°C
Pressure sensor	Type	Silicon
	Range	200-1050 mbar
	Accuracy	1.8%

MicroLoop Spirometer specifications

Resolution (volume)	10ml
Resolution (flow)	0.03 l/s
Accuracy	±3%
Resolution	±3%

MPM Mouth Pressure Meter specifications

Operating pressure	$\pm 300 cmH_2O$
Burst pressure	$\pm 700 cmH_2O$
Accuracy	±3%
Resolution	$1 cmH_2O$

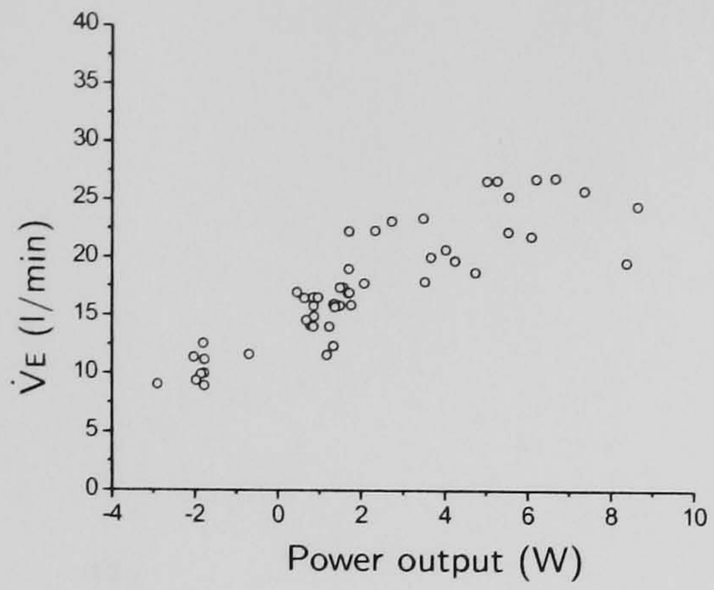
3800 Pulse Oximeter specifications

$SpO2_2$	Range	0 to 100%	
	Accuracy (±1 SD)	80 to 100%	±2%
		60 to 79%	±3%
		Below 60%	unspecified
	Resolution	1%	
Pulse rate	Range	20 to 255 bpm	
	Accuracy	40 to 235 bpm	±1.7% of reading
	Resolution	1bpm	

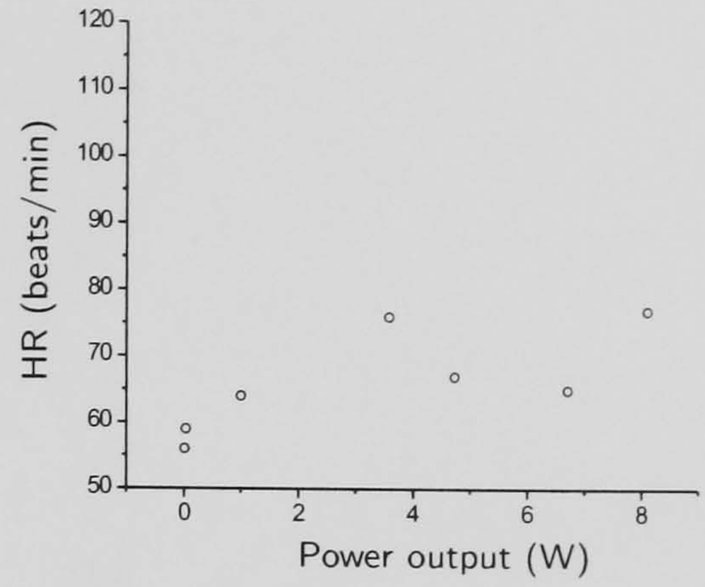
Appendix B

B.1 Cardiopulmonary Data, Subject A

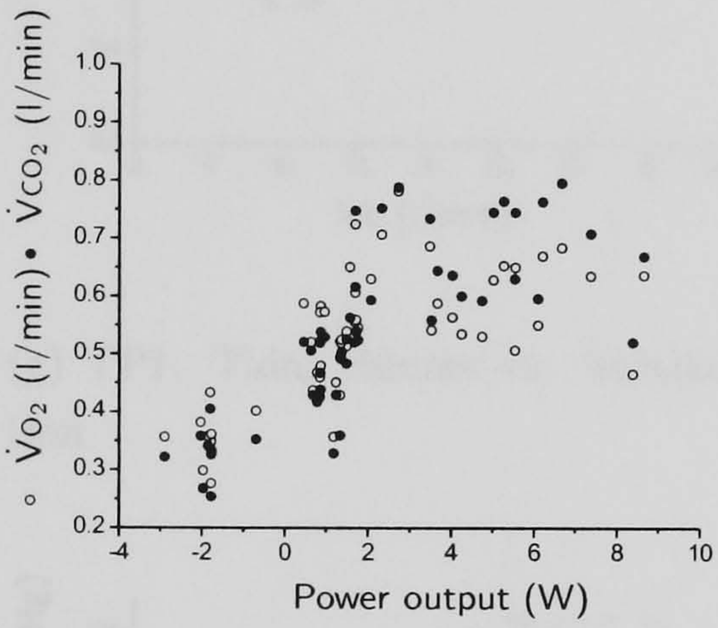
B.2 Cardiopulmonary Data, Subject B



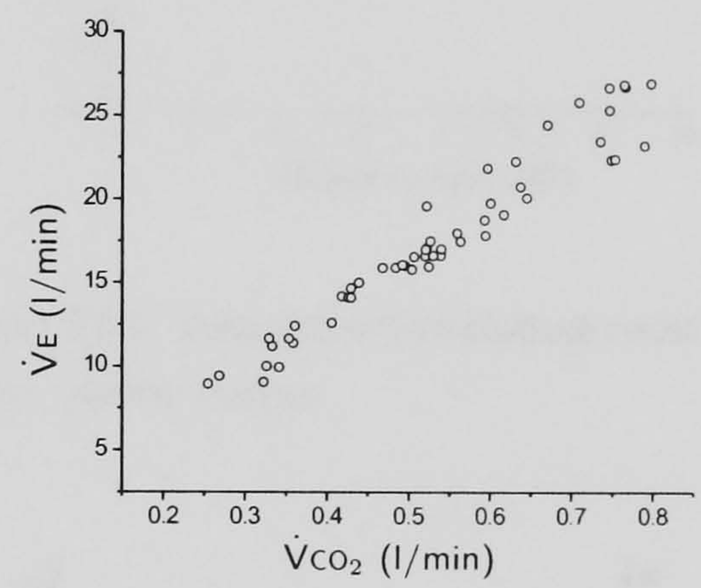
(a) TP1: Ventilation vs. power output



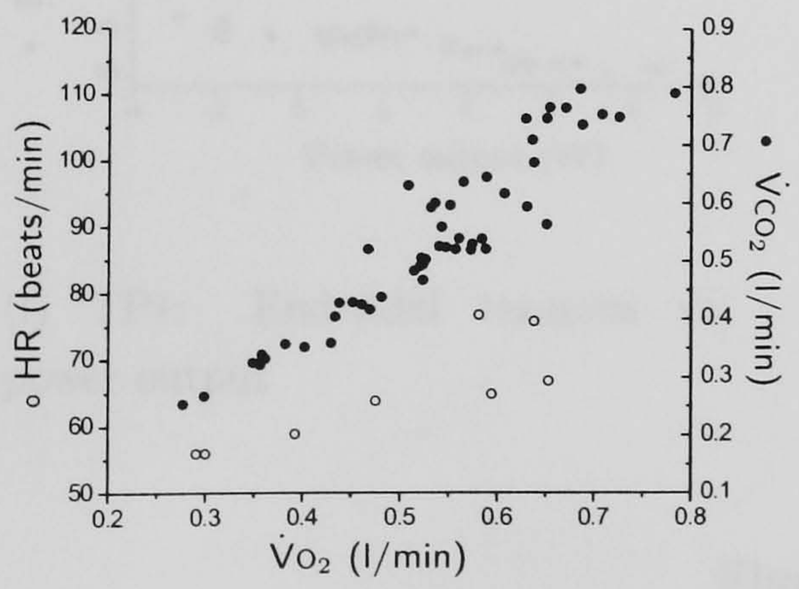
(b) TP1: Heart rate vs. power output



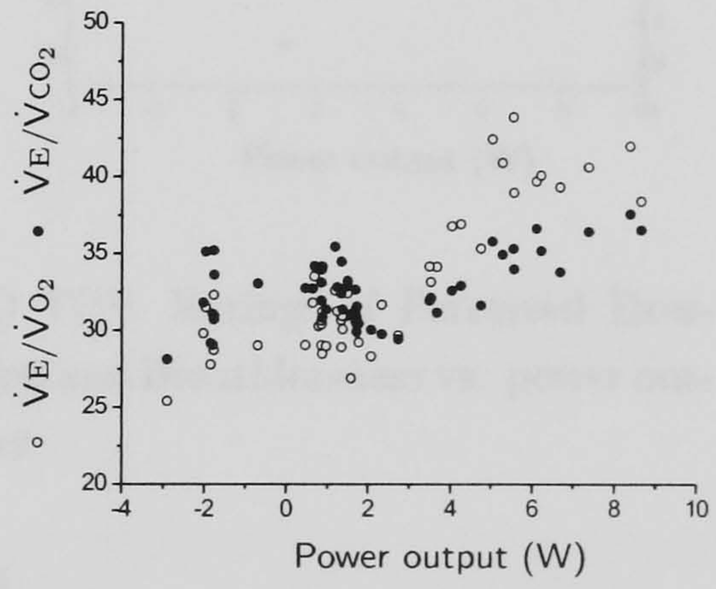
(c) TP1: Oxygen uptake and carbon dioxide output vs. power output



(d) TP1: Ventilation vs. carbon dioxide output

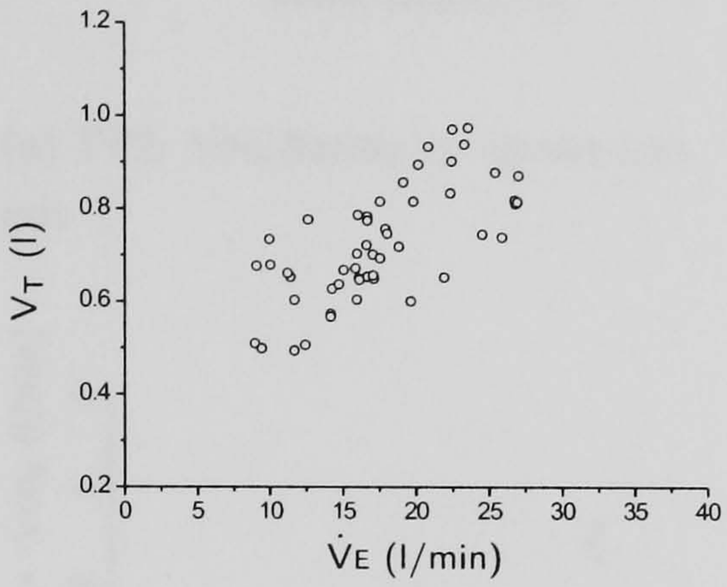


(e) TP1: Heart rate and carbon dioxide output vs. oxygen uptake

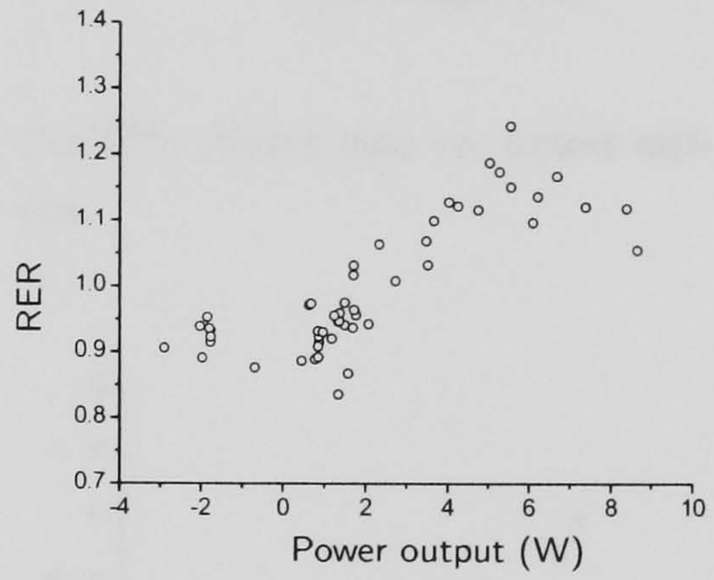


(f) TP1: Ventilatory equivalents vs. power output

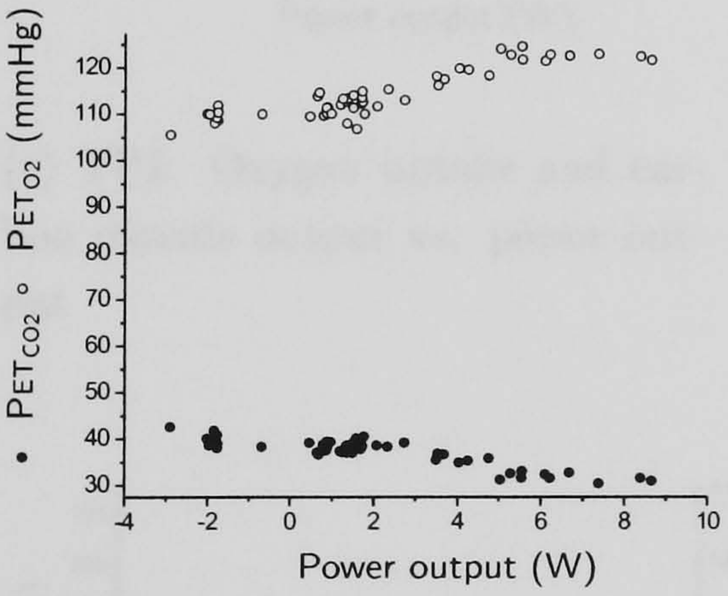
Figure B.1: Graphical representation of cardiopulmonary data for Subject A, from incremental FES-assisted ACE exercise testing at Test Point 1 (Baseline). The data have been edited and 4-breath averaged.



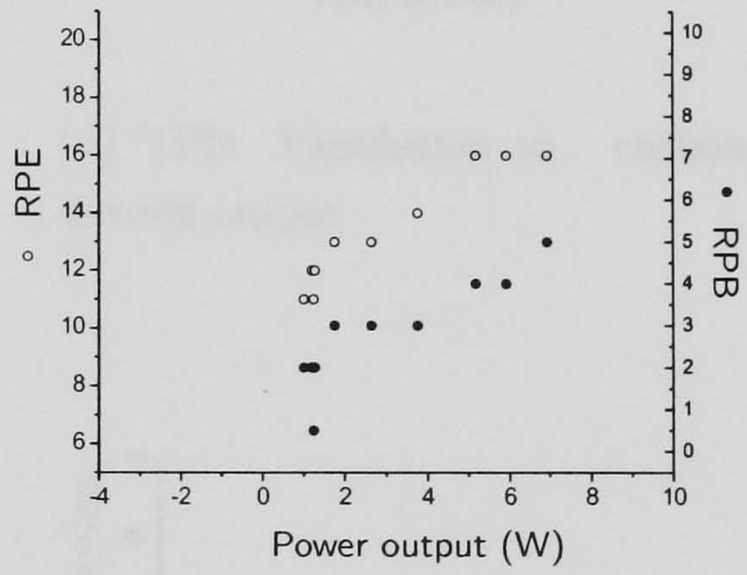
(g) TP1: Tidal volume vs. ventilation



(h) TP1: Respiratory exchange ratio vs. power output

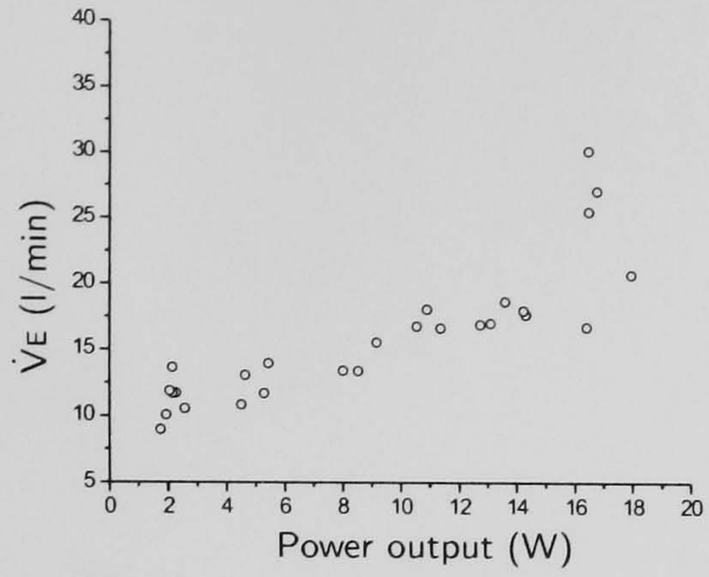


(i) TP1: End-tidal tensions vs. power output

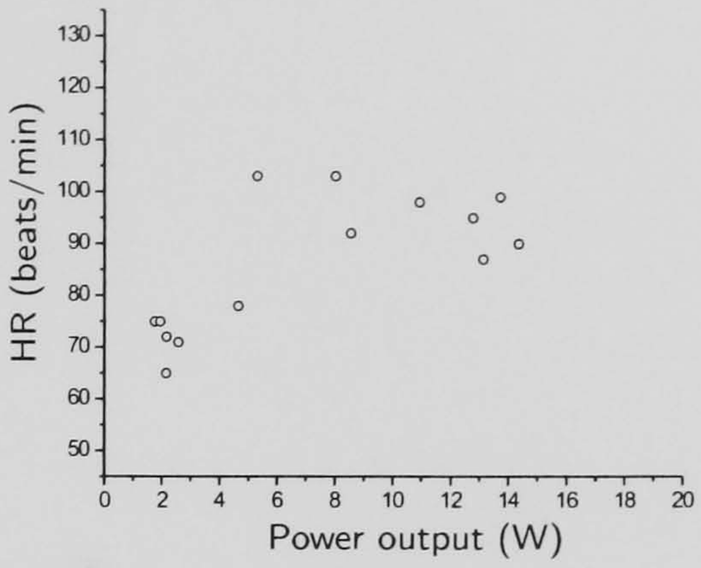


(j) TP1: Ratings of Perceived Exertion and Breathlessness vs. power output

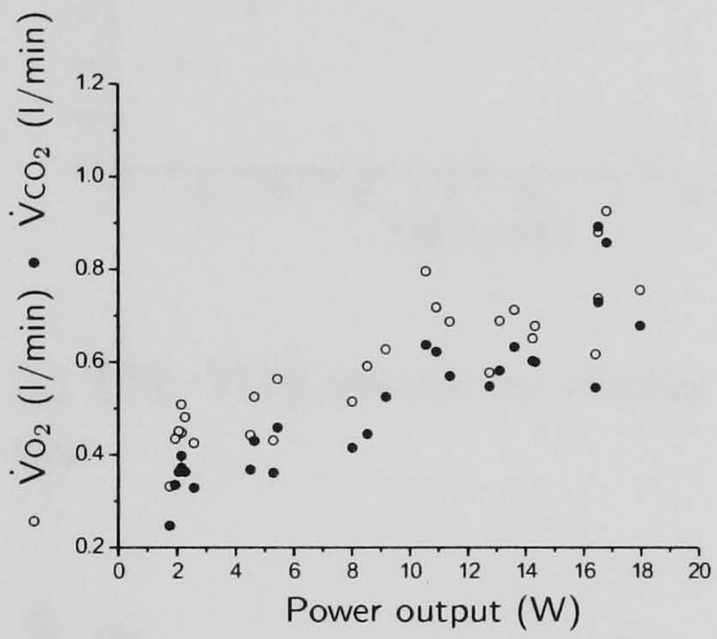
Figure B.1: (cont.)



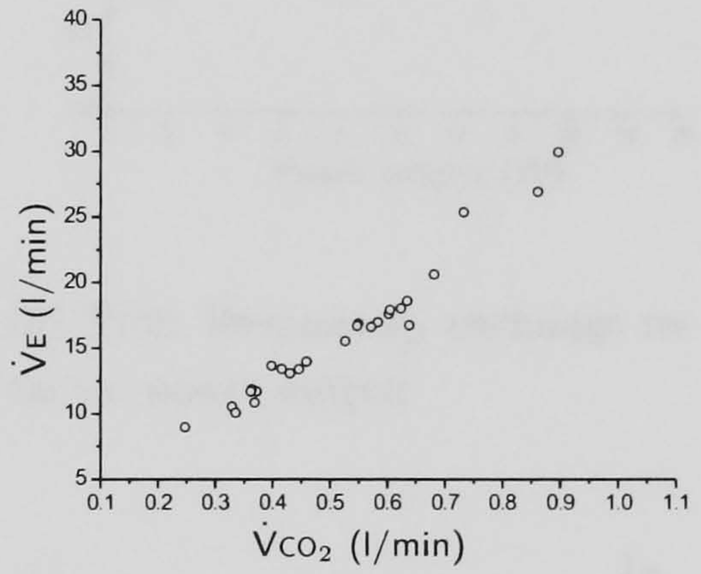
(a) TP2: Ventilation vs. power output



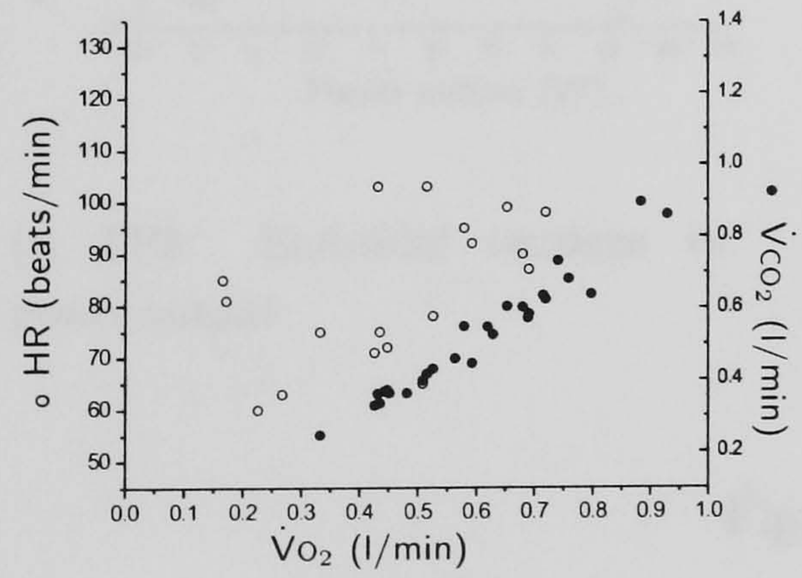
(b) TP2: Heart rate vs. power output



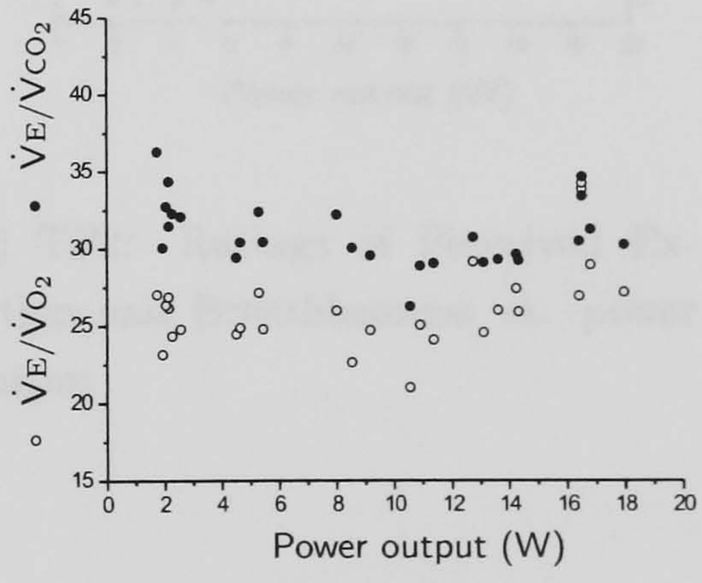
(c) TP2: Oxygen uptake and carbon dioxide output vs. power output



(d) TP2: Ventilation vs. carbon dioxide output

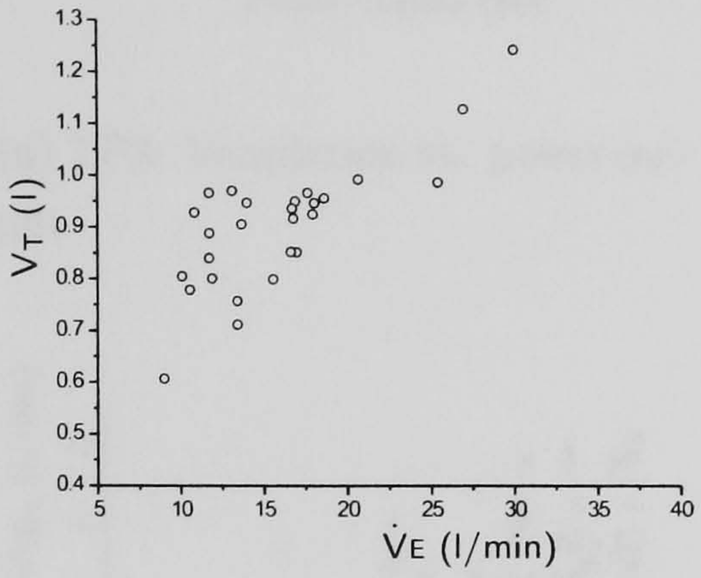


(e) TP2: Heart rate and carbon dioxide output vs. oxygen uptake

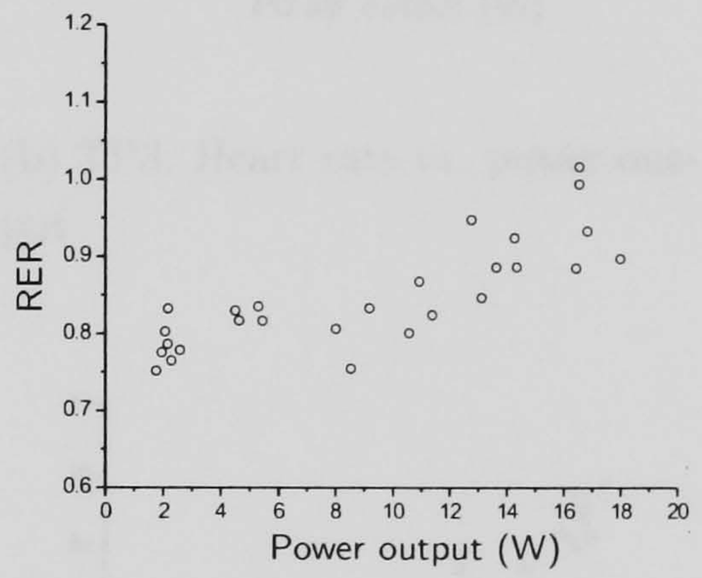


(f) TP2: Ventilatory equivalents vs. power output

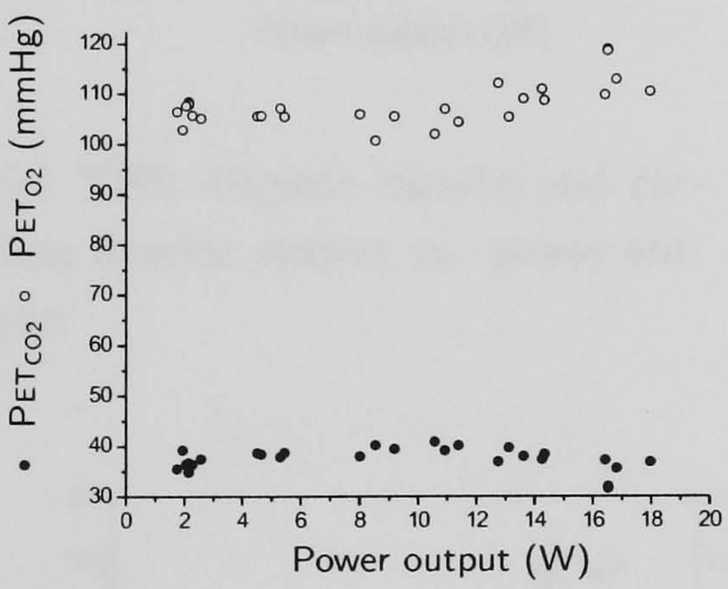
Figure B.2: Graphical representation of cardiopulmonary data for Subject A, from incremental FES-assisted ACE exercise testing at Test Point 2. The data have been edited and 8-breath averaged.



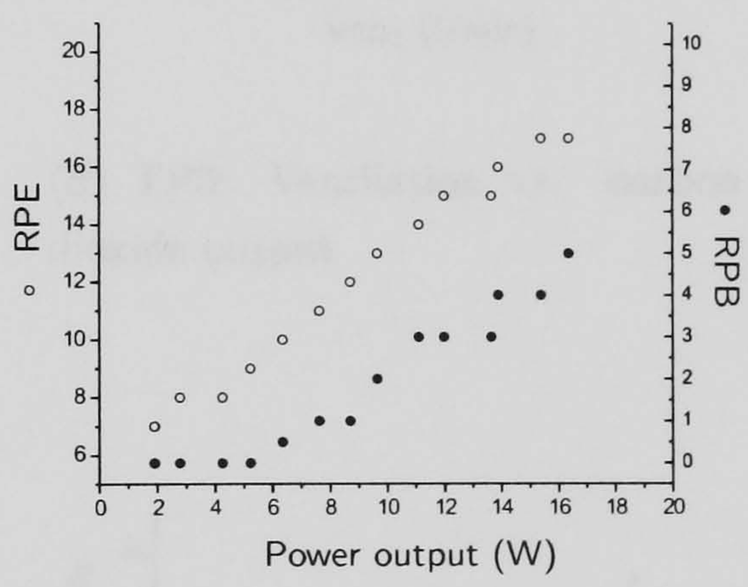
(g) TP2: Tidal volume vs. ventilation



(h) TP2: Respiratory exchange ratio vs. power output

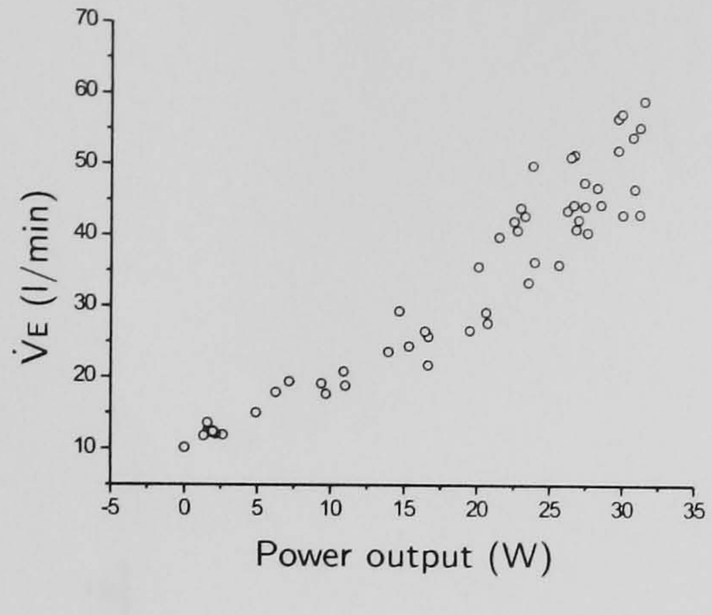


(i) TP2: End-tidal tensions vs. power output

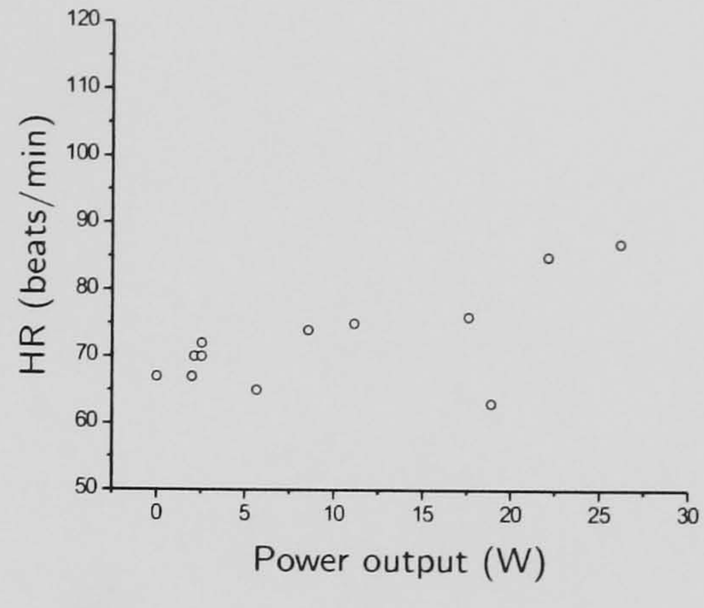


(j) TP2: Ratings of Perceived Exertion and Breathlessness vs. power output

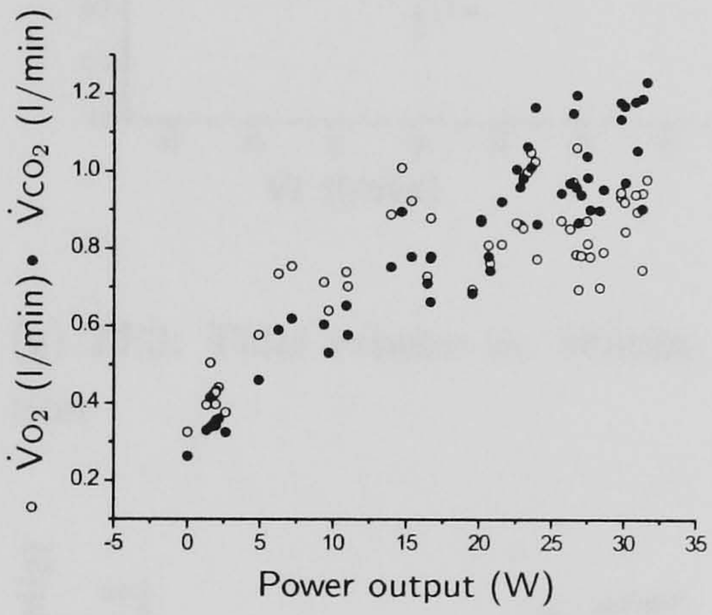
Figure B.2: (cont.)



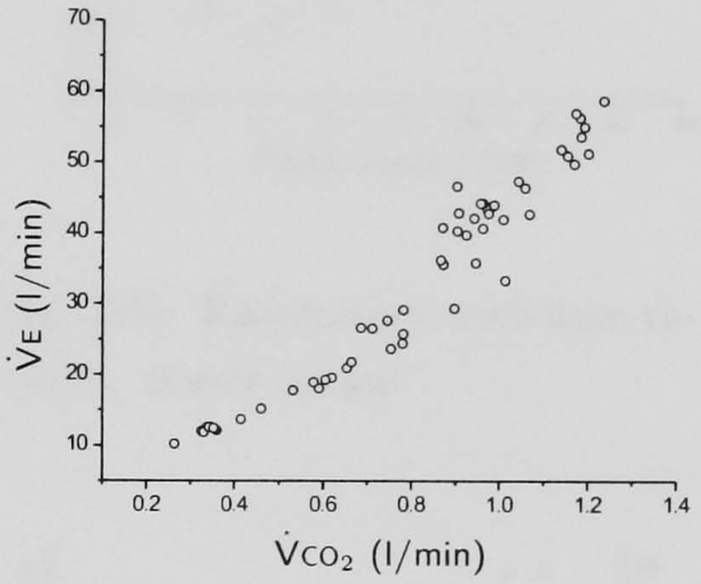
(a) TP3: Ventilation vs. power output



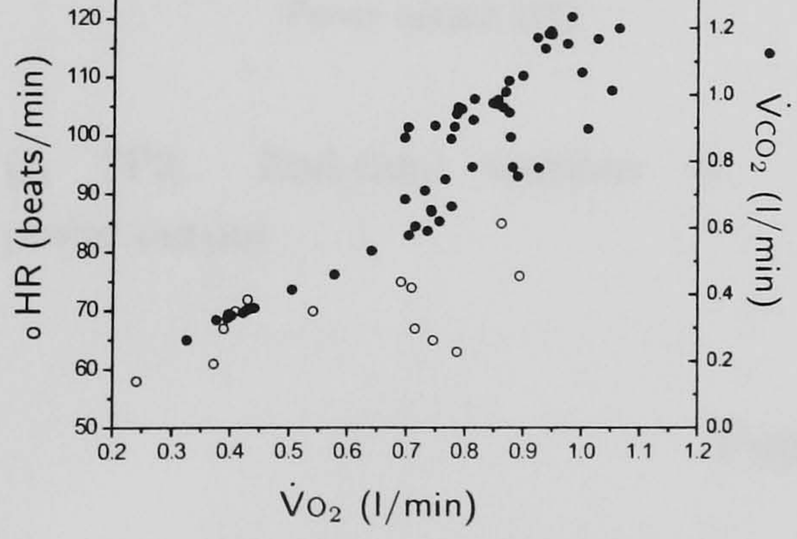
(b) TP3: Heart rate vs. power output



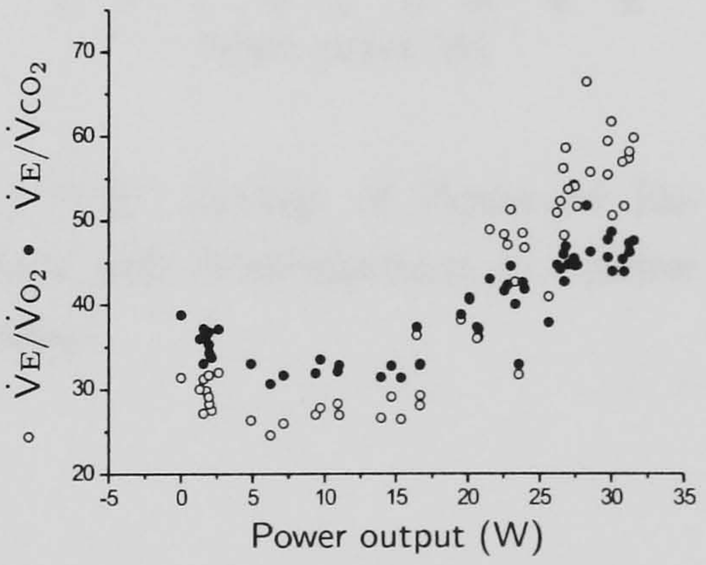
(c) TP3: Oxygen uptake and carbon dioxide output vs. power output



(d) TP3: Ventilation vs. carbon dioxide output

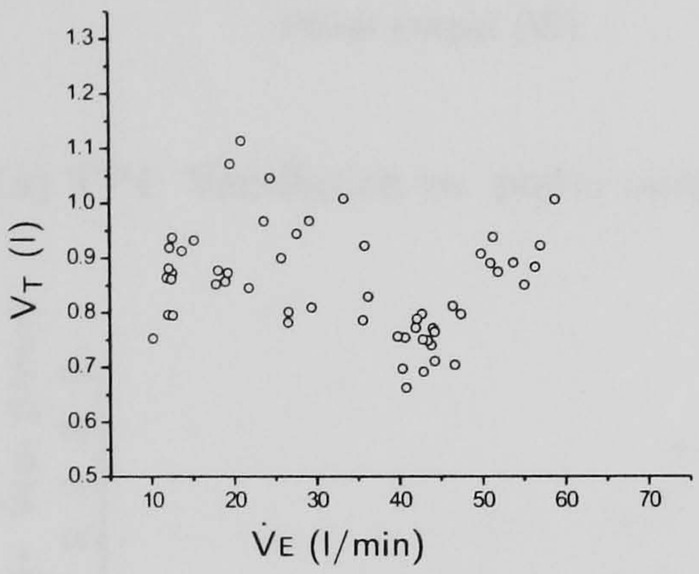


(e) TP3: Heart rate and carbon dioxide output vs. oxygen uptake

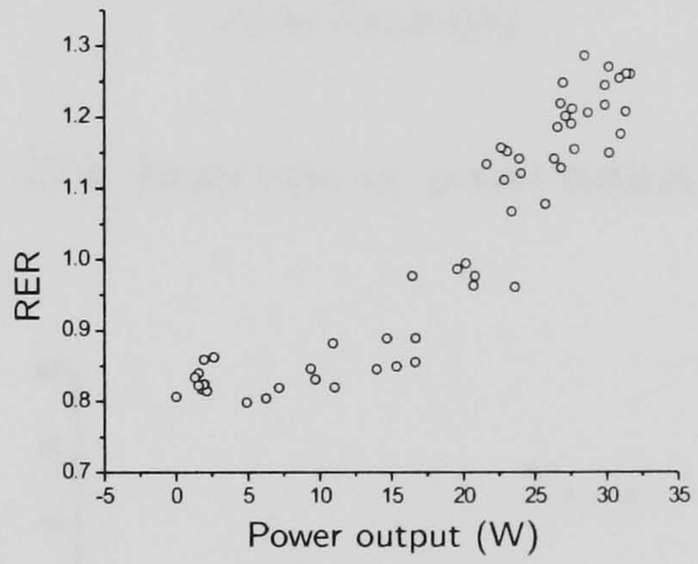


(f) TP3: Ventilatory equivalents vs. power output

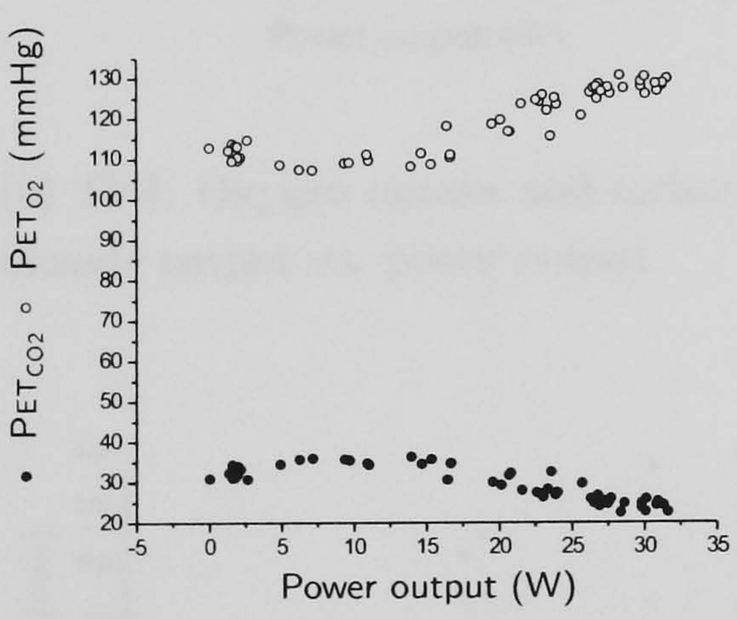
Figure B.3: Graphical representation of cardiopulmonary data for Subject A, from incremental FES-assisted ACE exercise testing at Test Point 3. The data have been edited and 4-breath averaged.



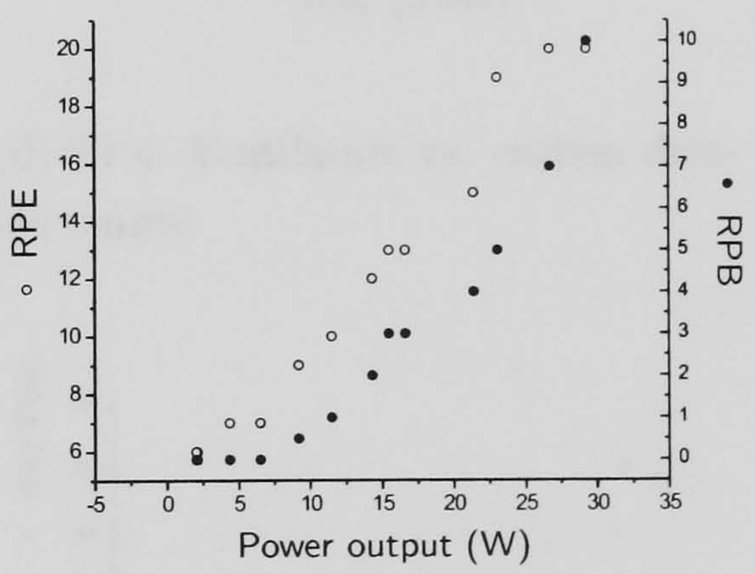
(g) TP3: Tidal volume vs. ventilation



(h) TP3: Respiratory exchange ratio vs. power output

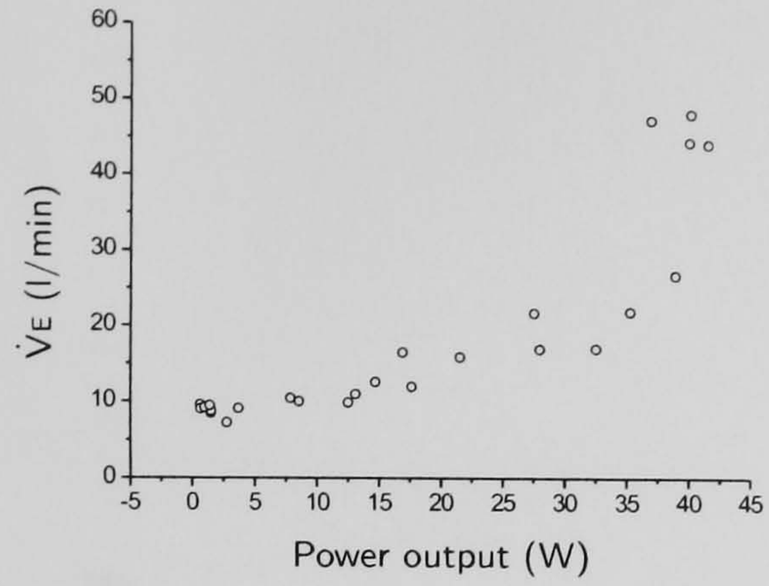


(i) TP3: End-tidal tensions vs. power output

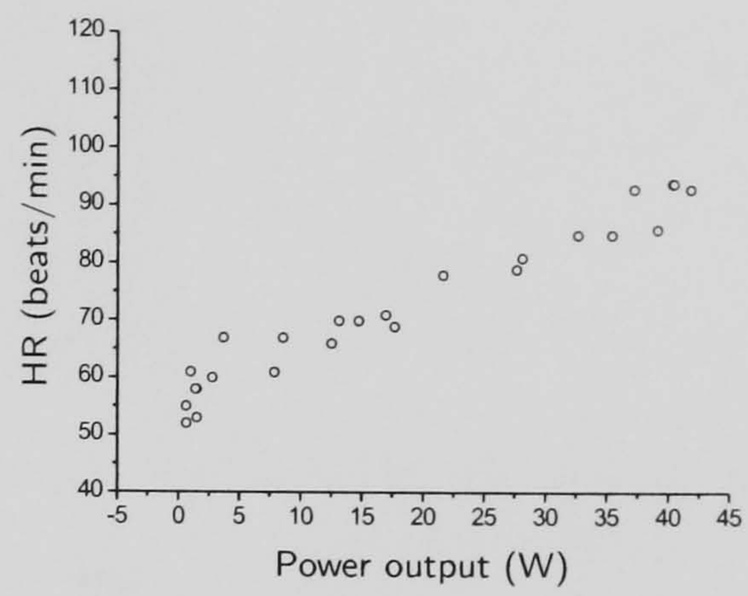


(j) TP3: Ratings of Perceived Exertion and Breathlessness vs. power output

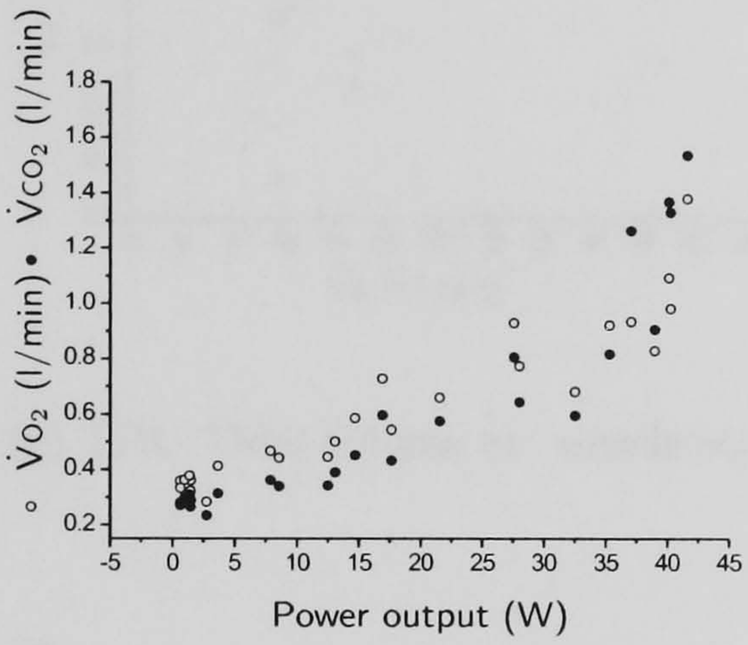
Figure B.3: (cont.)



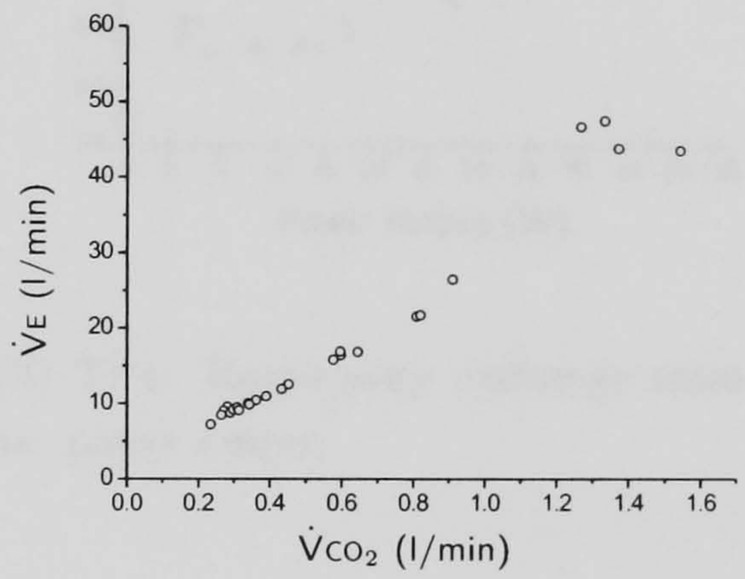
(a) TP4: Ventilation vs. power output



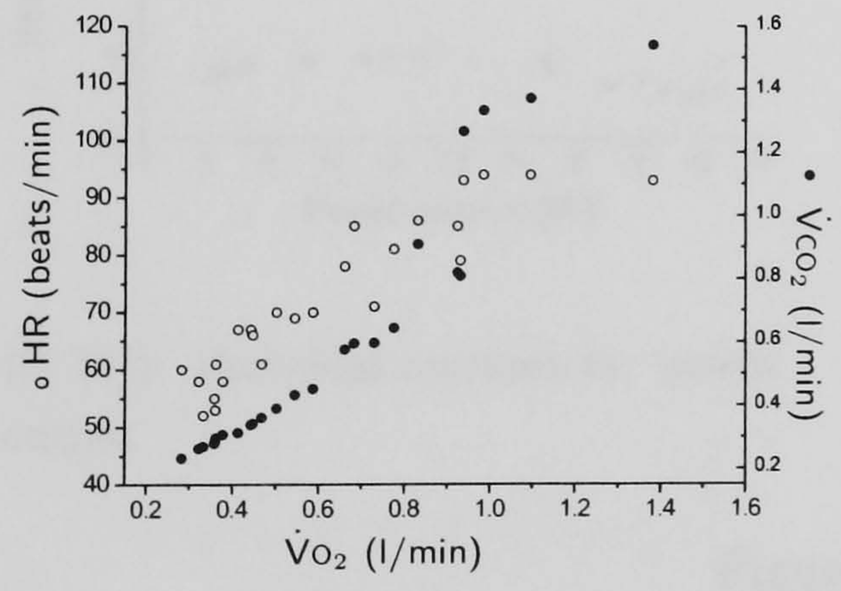
(b) TP4: Heart rate vs. power output



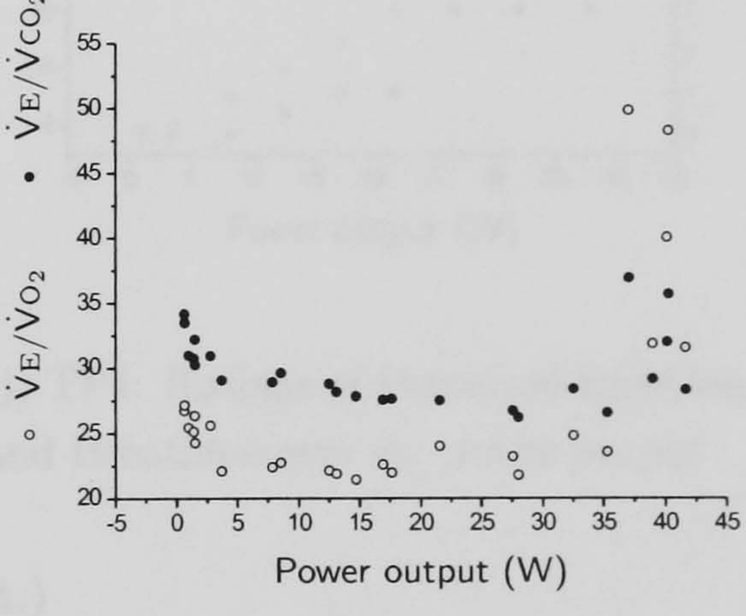
(c) TP4: Oxygen uptake and carbon dioxide output vs. power output



(d) TP4: Ventilation vs. carbon dioxide output

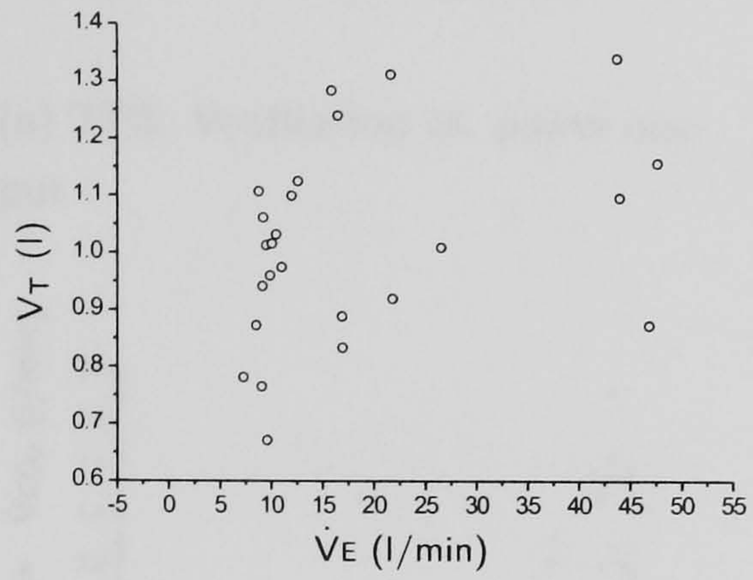


(e) TP4: Heart rate and carbon dioxide output vs. oxygen uptake

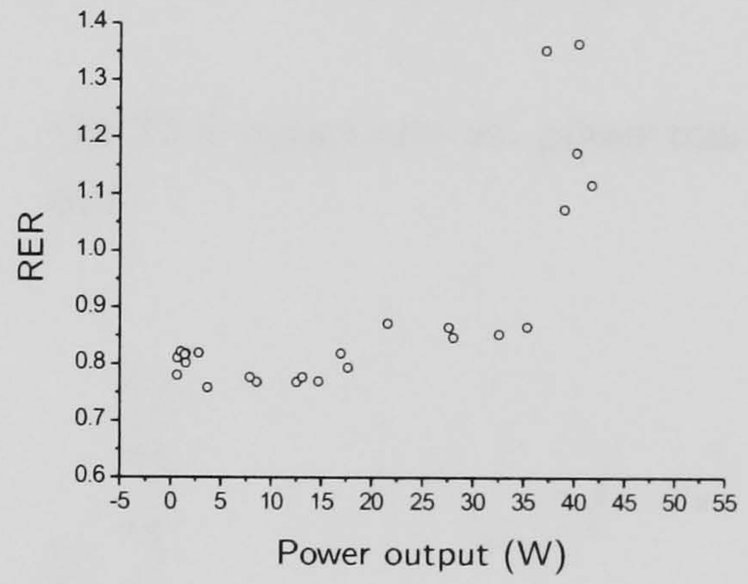


(f) Ventilatory equivalents vs. power output

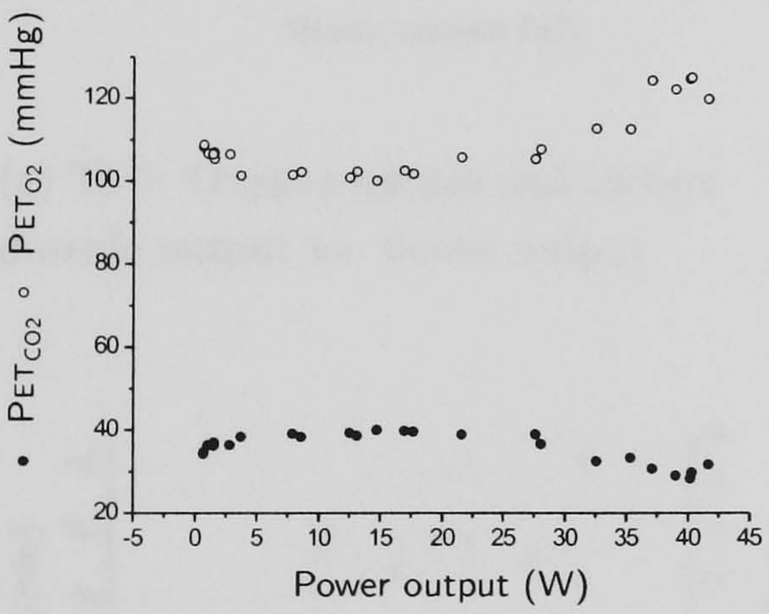
Figure B.4: Graphical representation of cardiopulmonary data for Subject A, from incremental FES-assisted ACE exercise testing at Test Point 4. The data have been edited and 4-breath averaged.



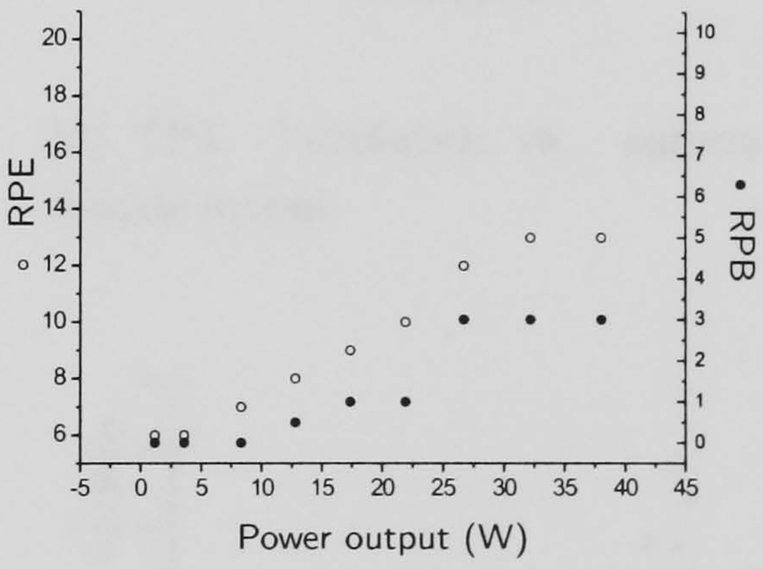
(g) TP4: Tidal volume vs. ventilation



(h) TP4: Respiratory exchange ratio vs. power output

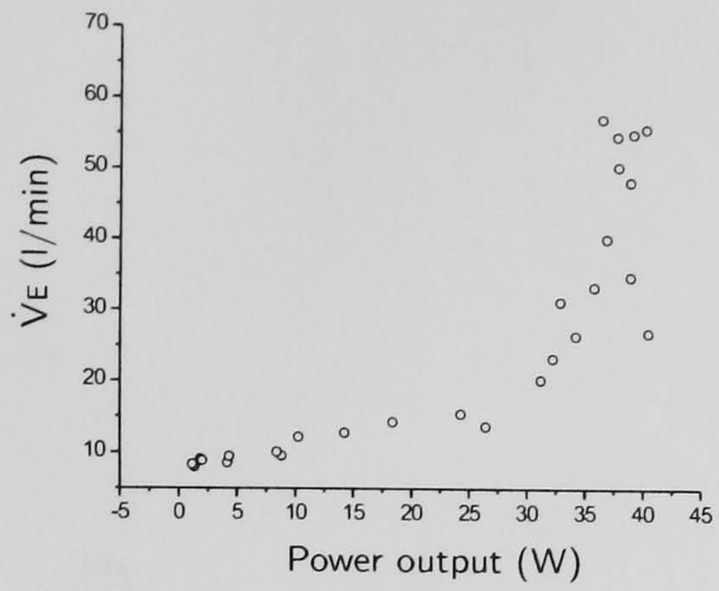


(i) TP4: End-tidal tensions vs. power output

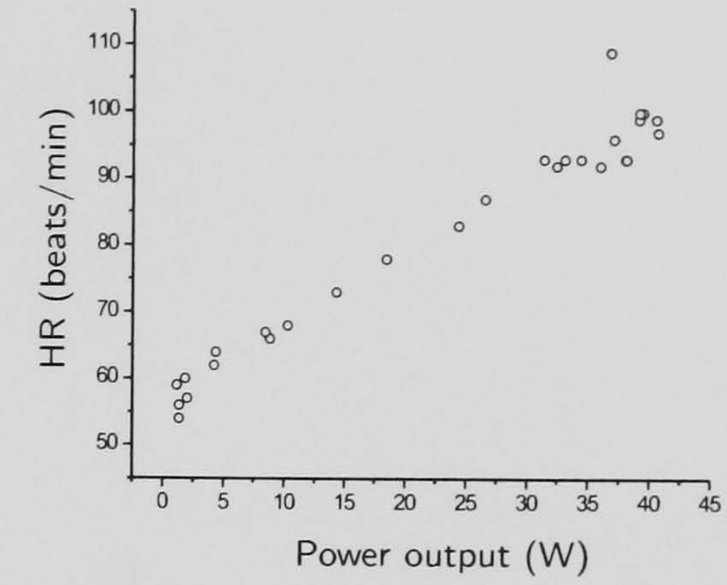


(j) TP4: Ratings of Perceived Exertion and Breathlessness vs. power output

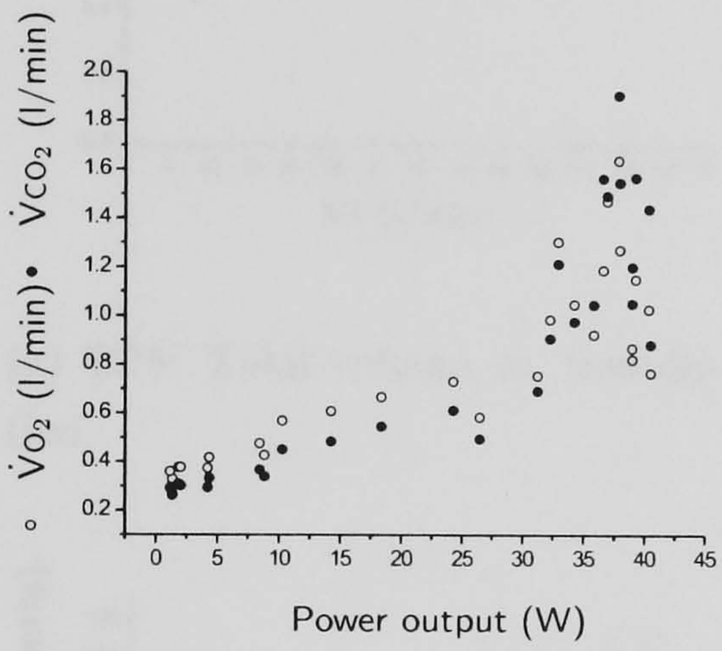
Figure B.4: (cont.)



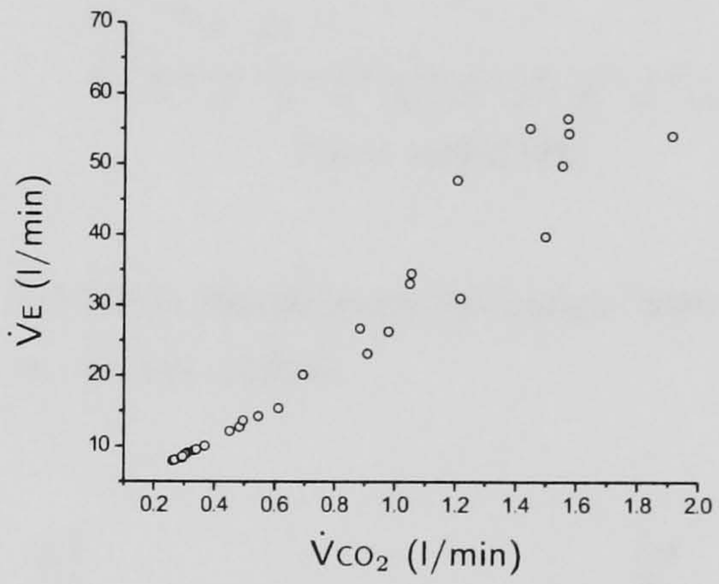
(a) TP5: Ventilation vs. power output



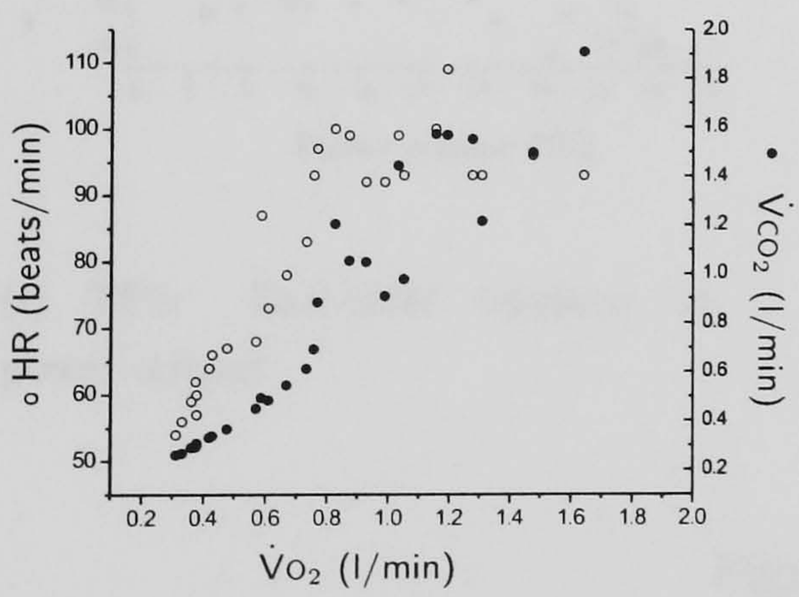
(b) TP5: Heart rate vs. power output



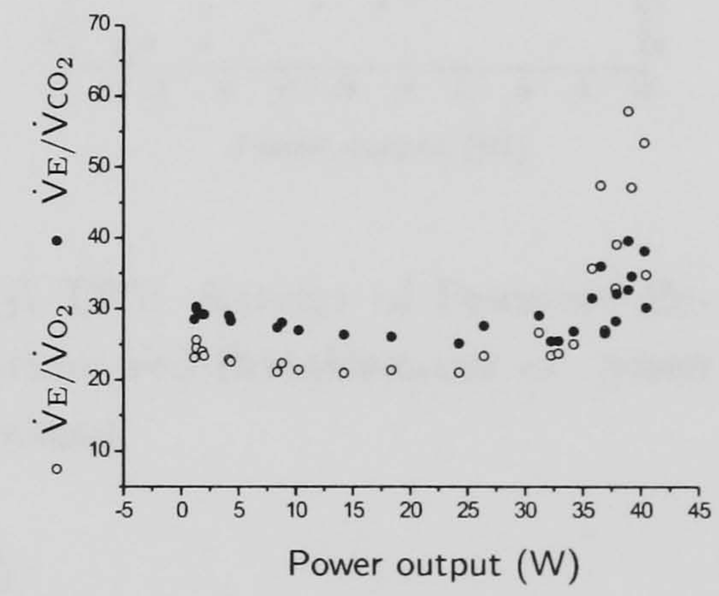
(c) TP5: Oxygen uptake and carbon dioxide output vs. power output



(d) TP5: Ventilation vs. carbon dioxide output

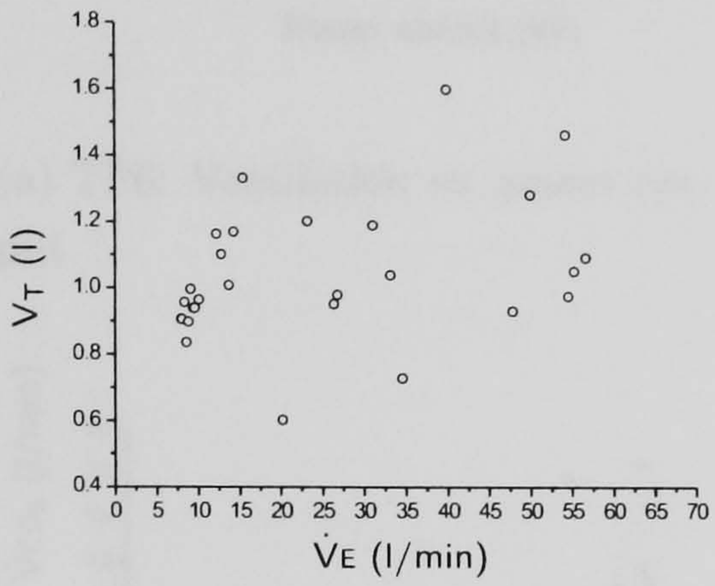


(e) TP5: Heart rate and carbon dioxide output vs. oxygen uptake

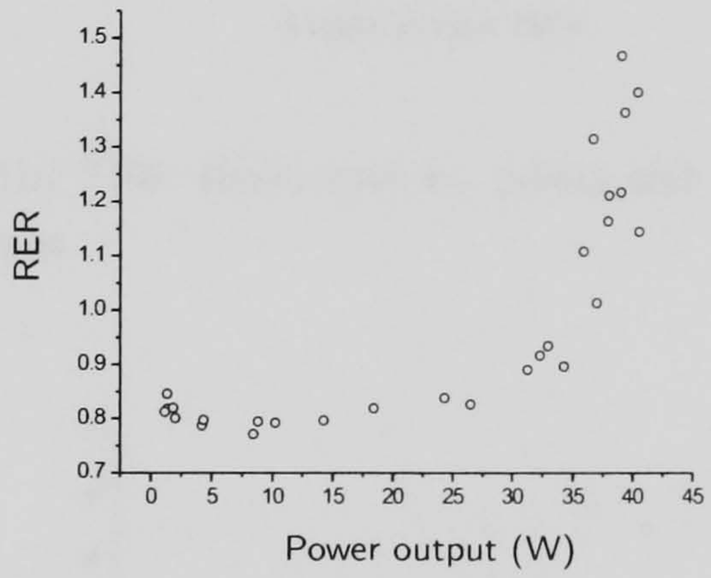


(f) TP5: Ventilatory equivalents vs. power output

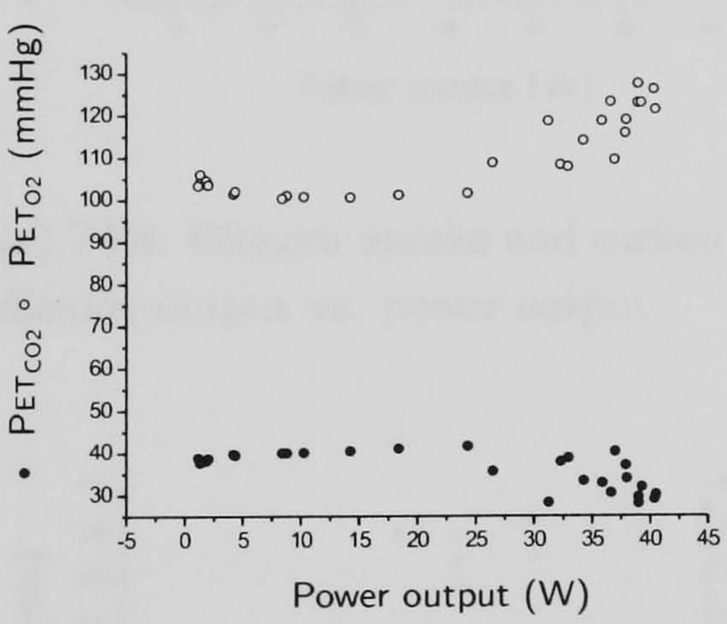
Figure B.5: Graphical representation of cardiopulmonary data for Subject A, from incremental FES-assisted ACE exercise testing at Test Point 5. The data have been edited and 4-breath averaged.



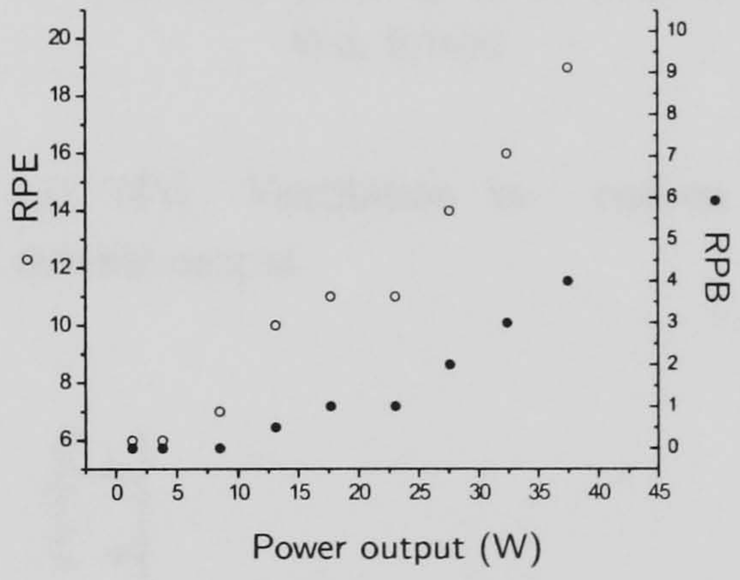
(g) TP5: Tidal volume vs. ventilation



(h) TP5: Respiratory exchange ratio vs. power output

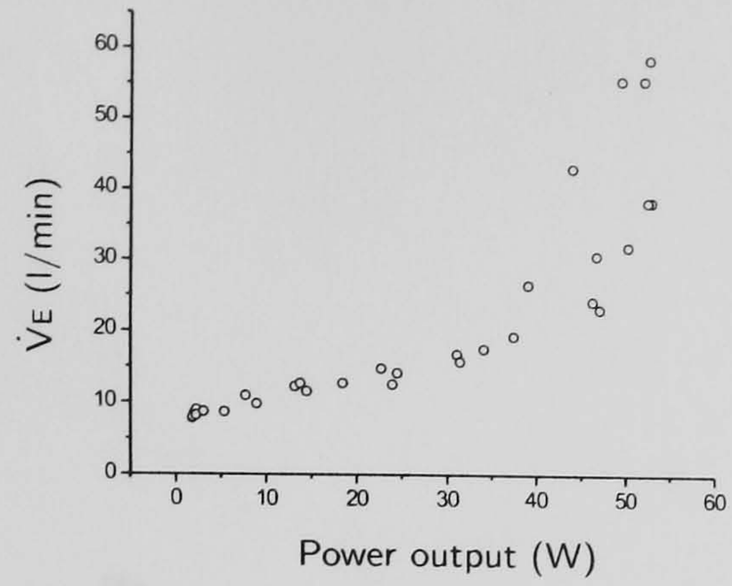


(i) TP5: End-tidal tensions vs. power output

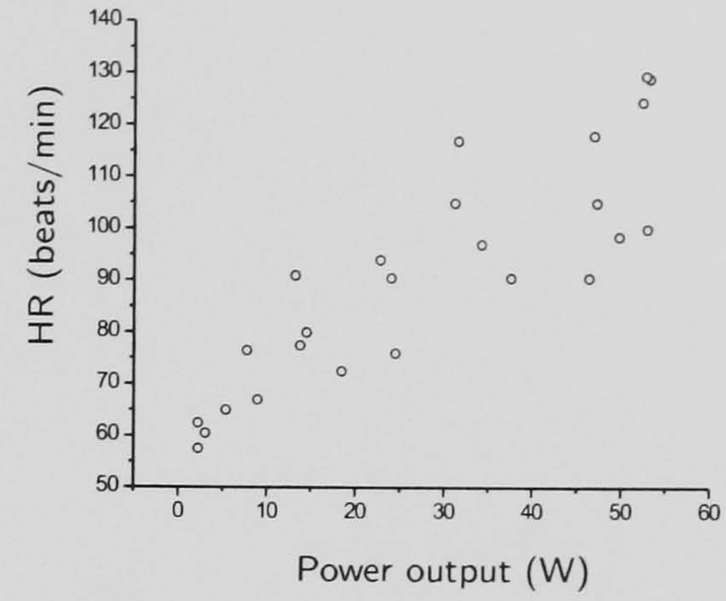


(j) TP5: Ratings of Perceived Exertion and Breathlessness vs. power output

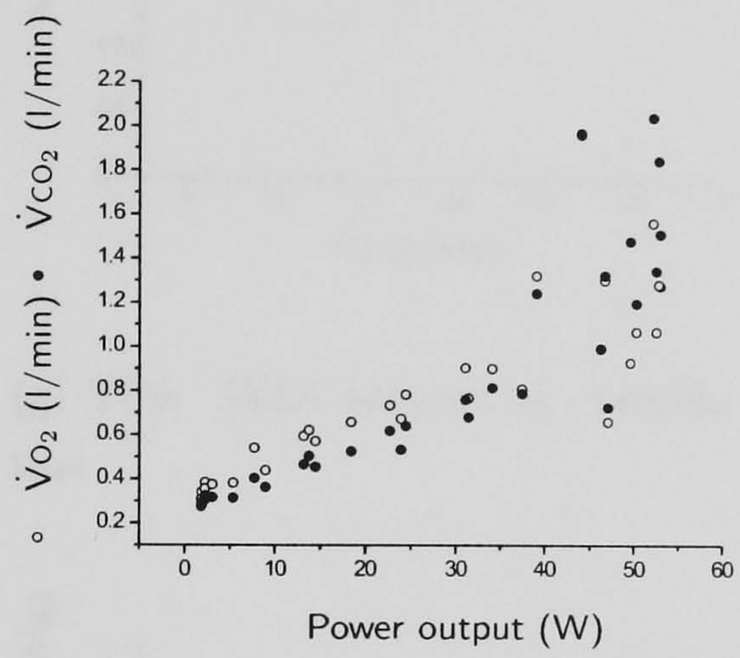
Figure B.5: (cont.)



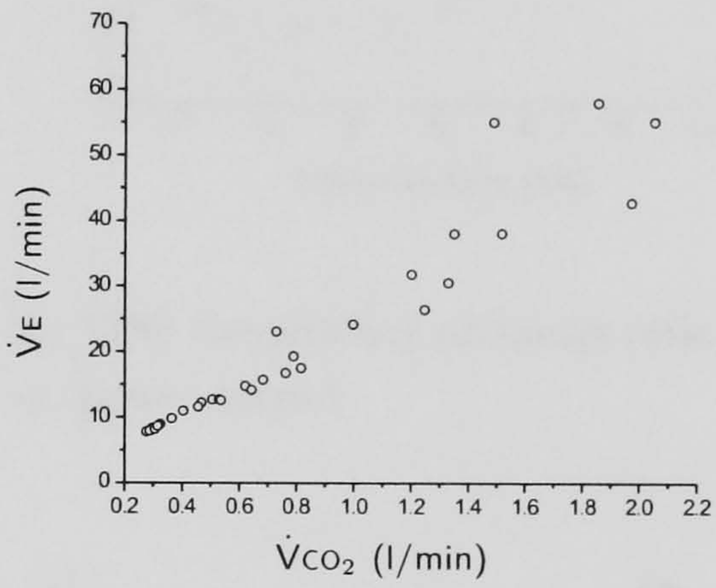
(a) TP6: Ventilation vs. power output



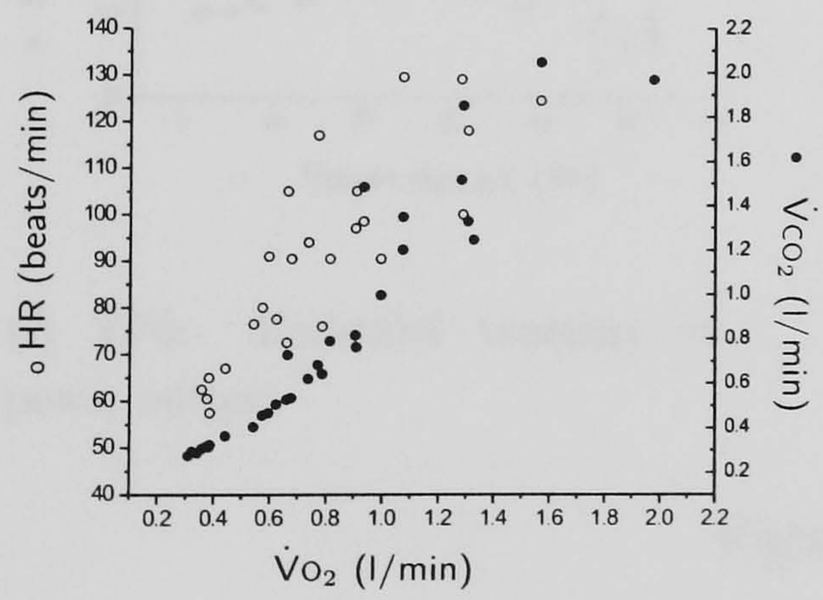
(b) TP6: Heart rate vs. power output



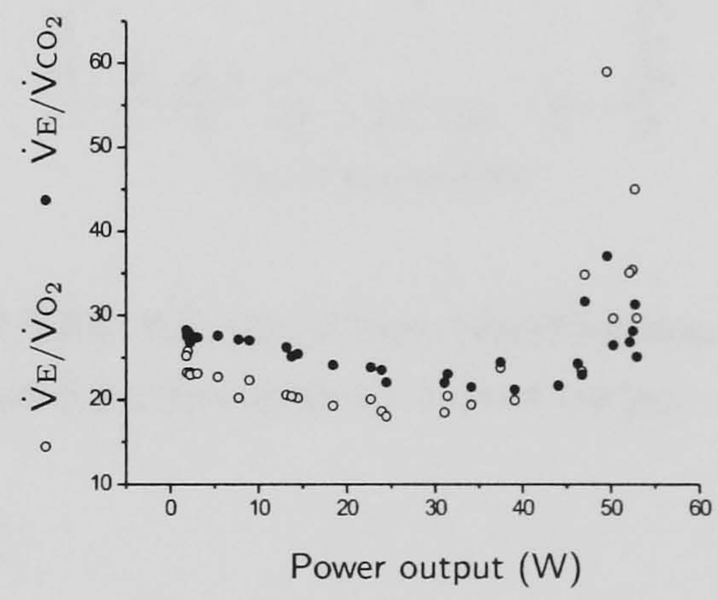
(c) TP6: Oxygen uptake and carbon dioxide output vs. power output



(d) TP6: Ventilation vs. carbon dioxide output

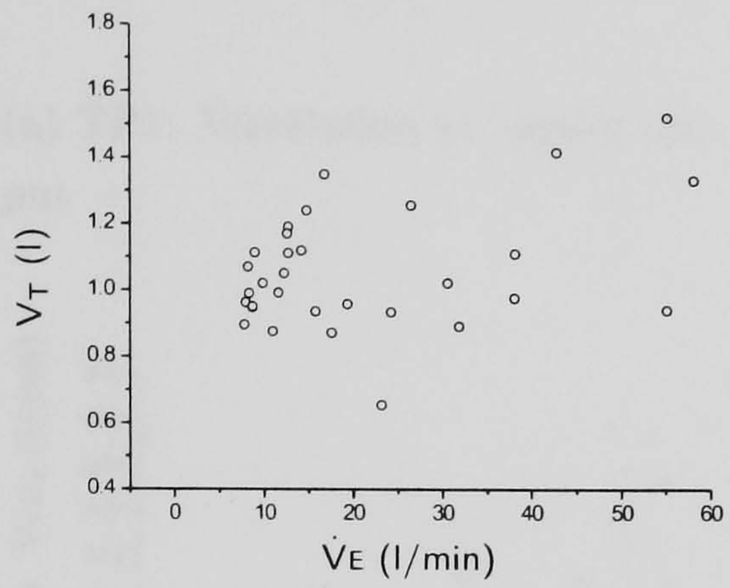


(e) TP6: Heart rate and carbon dioxide output vs. oxygen uptake

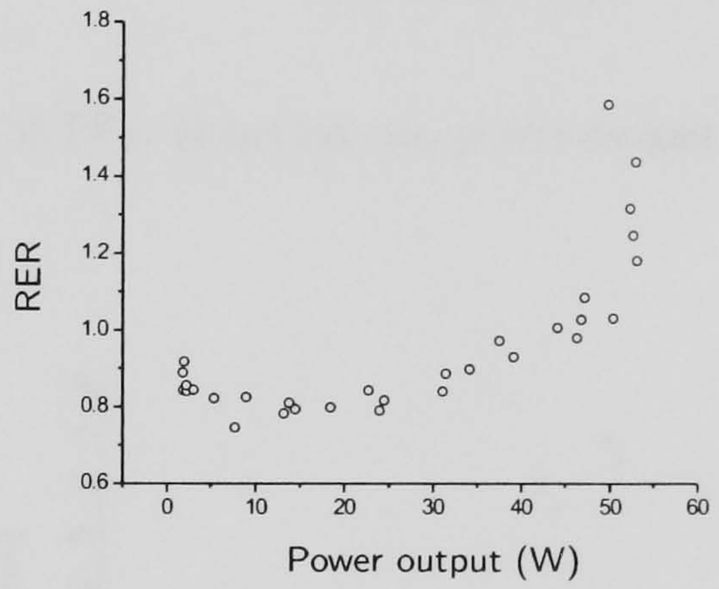


(f) TP6: Ventilatory equivalents vs. power output

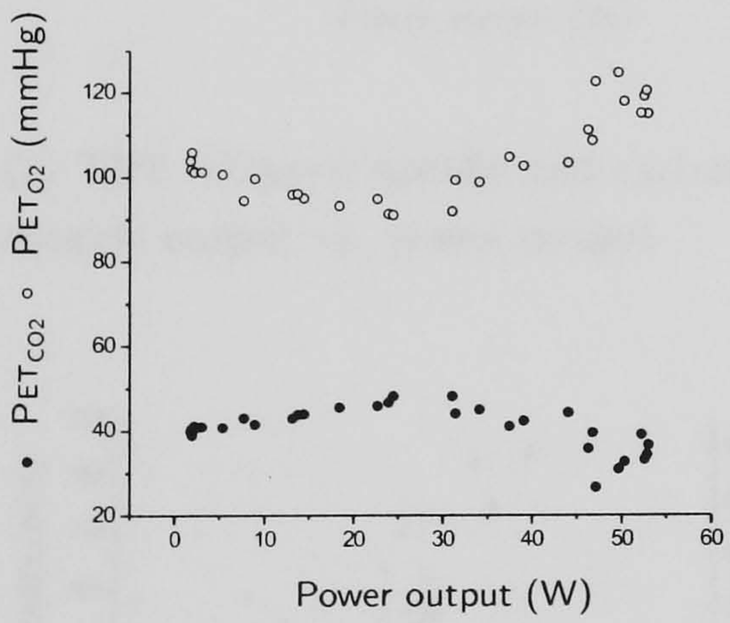
Figure B.6: Graphical representation of cardiopulmonary data for Subject A, from incremental FES-assisted ACE exercise testing at Test Point 6. The data have been edited and 4-breath averaged.



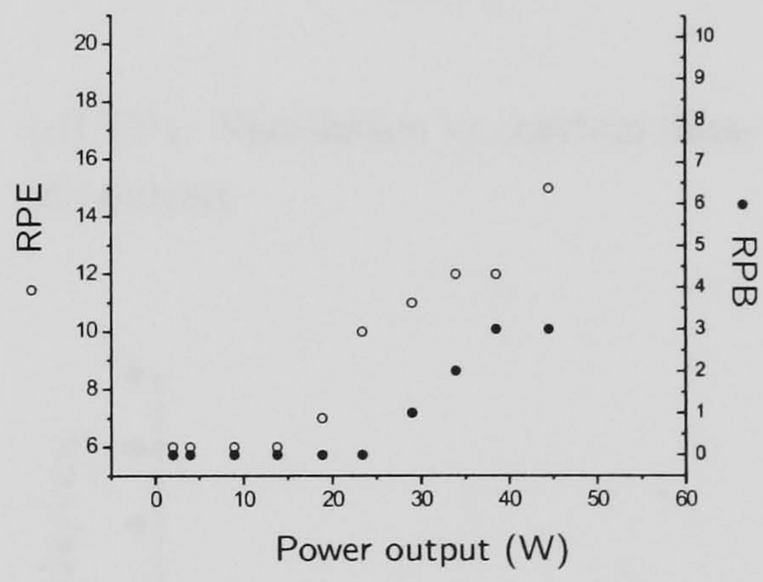
(g) TP6: Tidal volume vs. ventilation



(h) TP6: Respiratory exchange ratio vs. power output

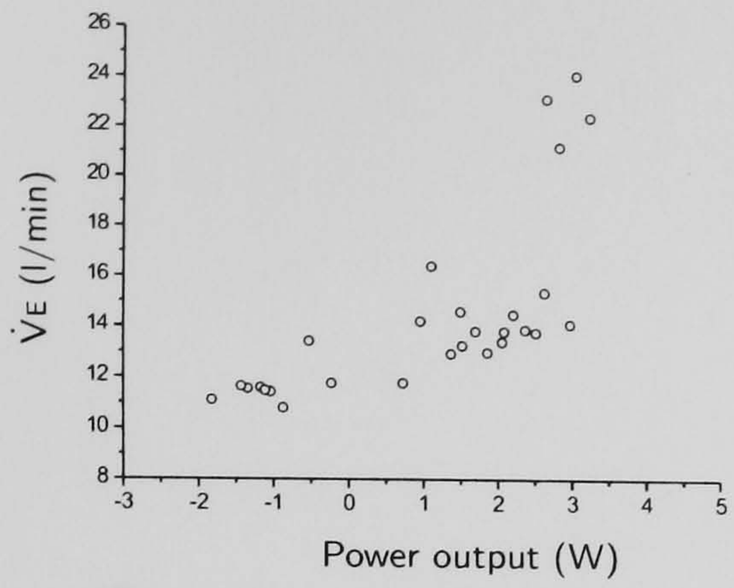


(i) TP6: End-tidal tensions vs. power output

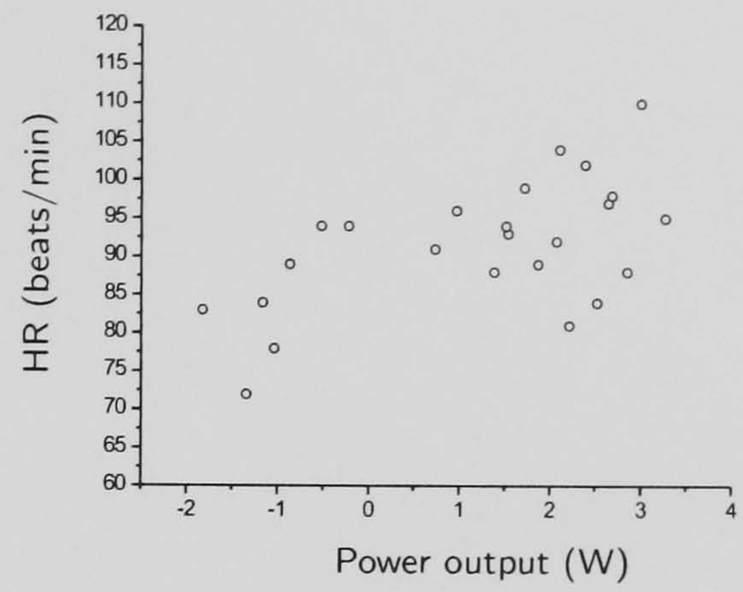


(j) TP6: Ratings of Perceived Exertion and Breathlessness vs. power output

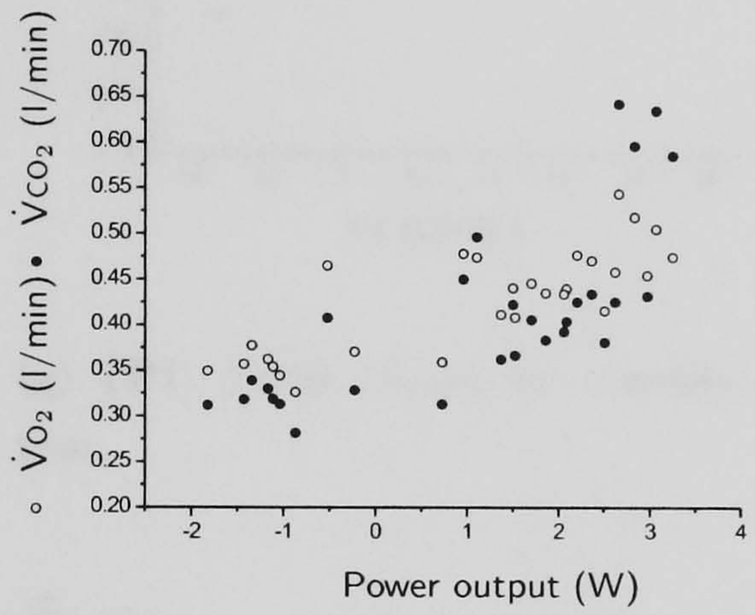
Figure B.6: (cont.)



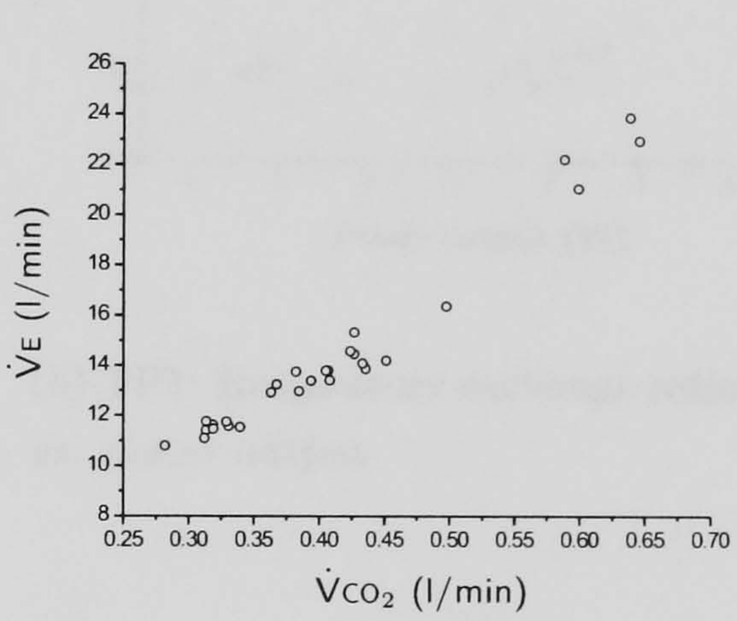
(a) TP1: Ventilation vs. power output



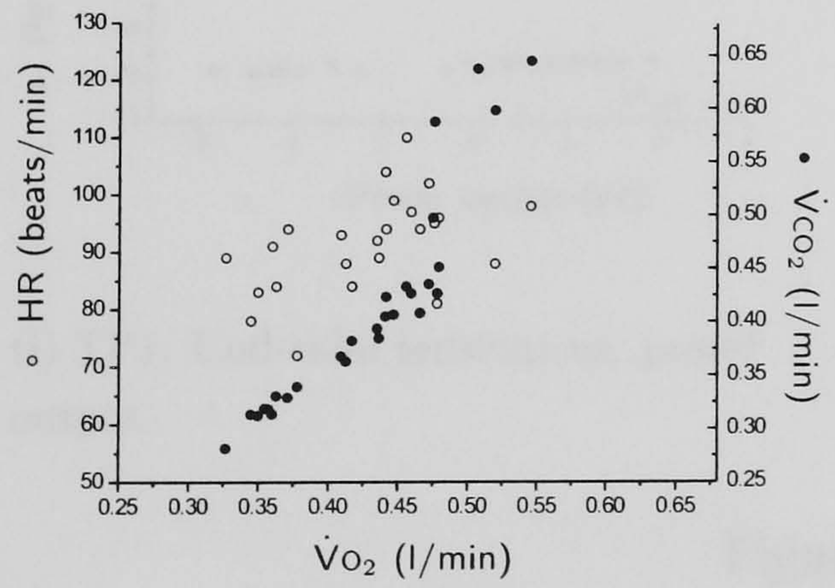
(b) TP1: Heart rate vs. power output



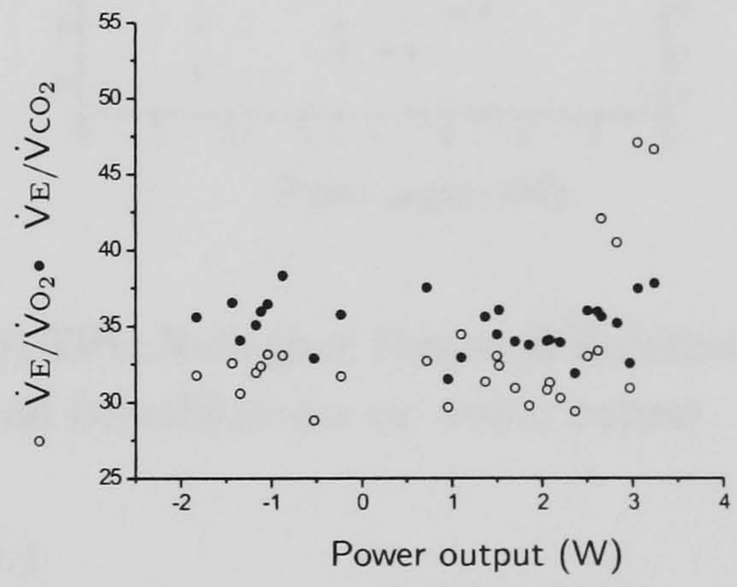
(c) TP1: Oxygen uptake and carbon dioxide output vs. power output



(d) TP1: Ventilation vs. carbon dioxide output

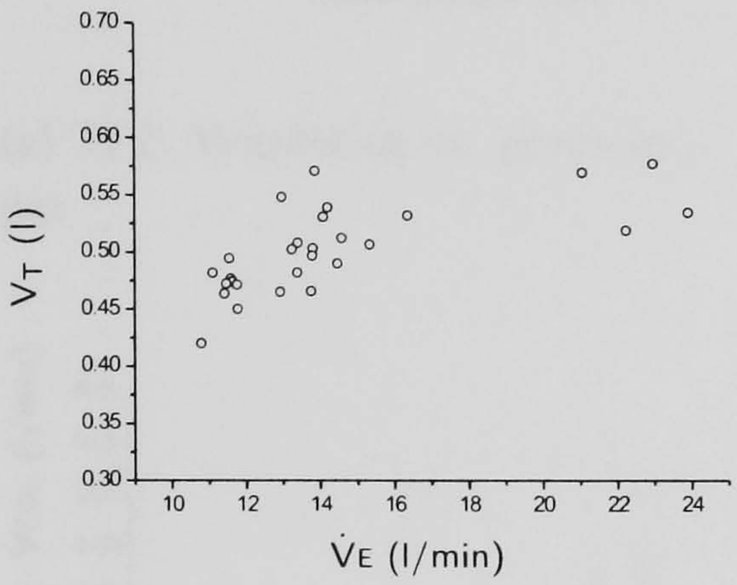


(e) TP1: Heart rate and carbon dioxide output vs. oxygen uptake

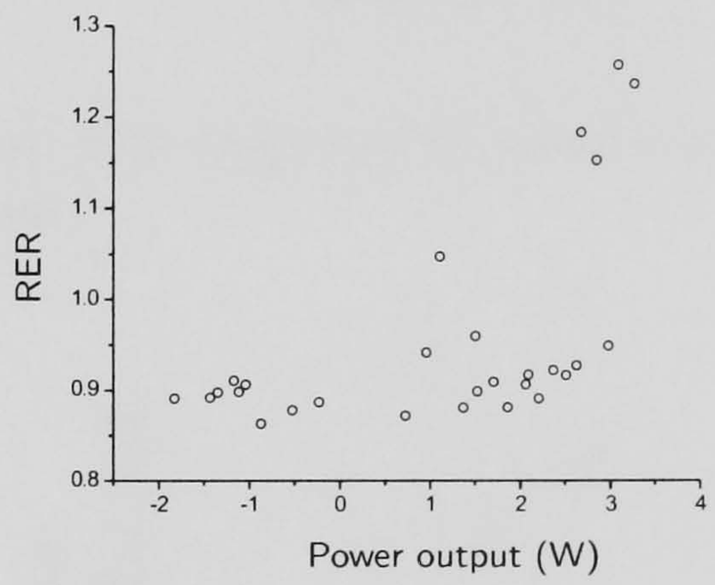


(f) TP1: Ventilatory equivalents vs. power output

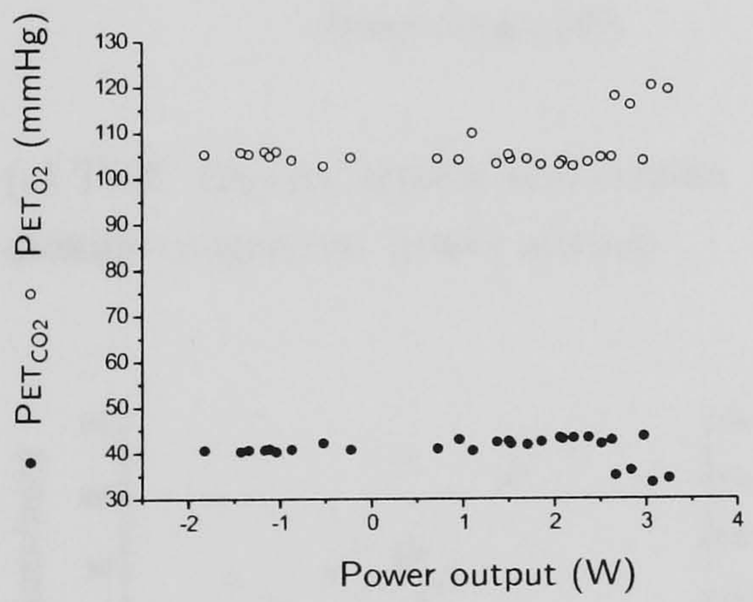
Figure B.7: Graphical representation of cardiopulmonary data for Subject B, from incremental FES-assisted ACE exercise testing at Test Point 1 (Baseline). The data have been edited and 8-breath averaged.



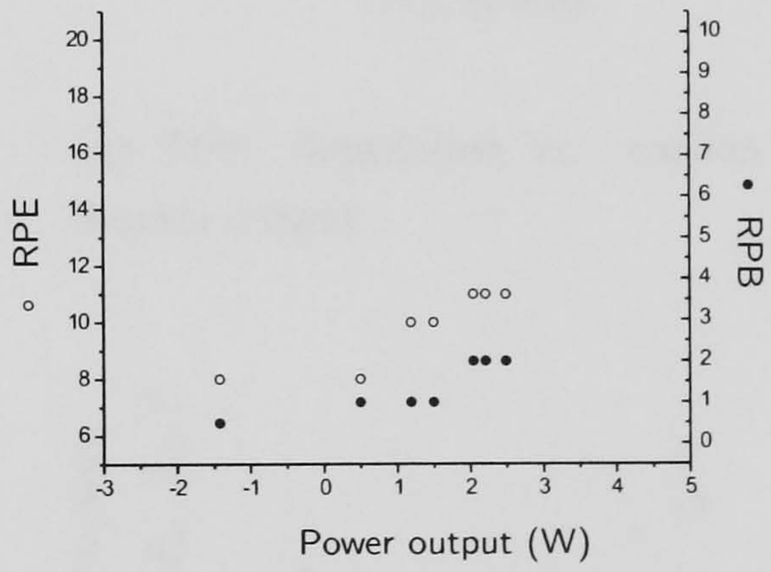
(g) TP1: Tidal volume vs. ventilation



(h) TP1: Respiratory exchange ratio vs. power output

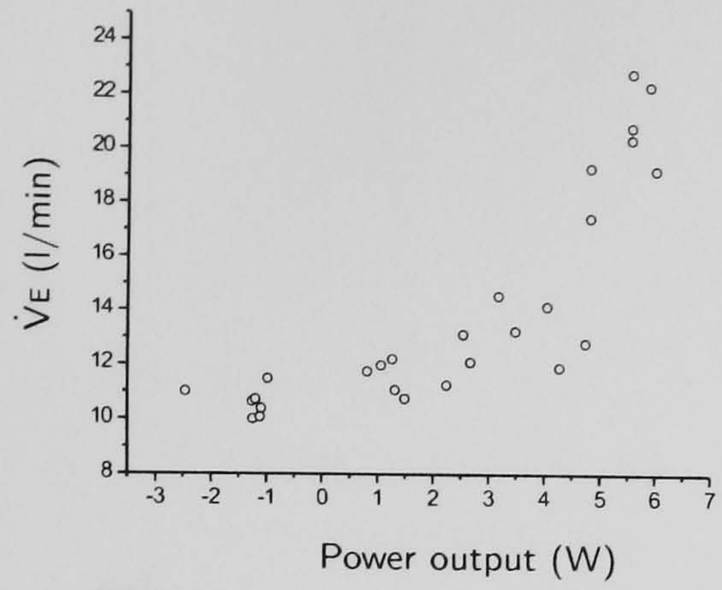


(i) TP1: End-tidal tensions vs. power output

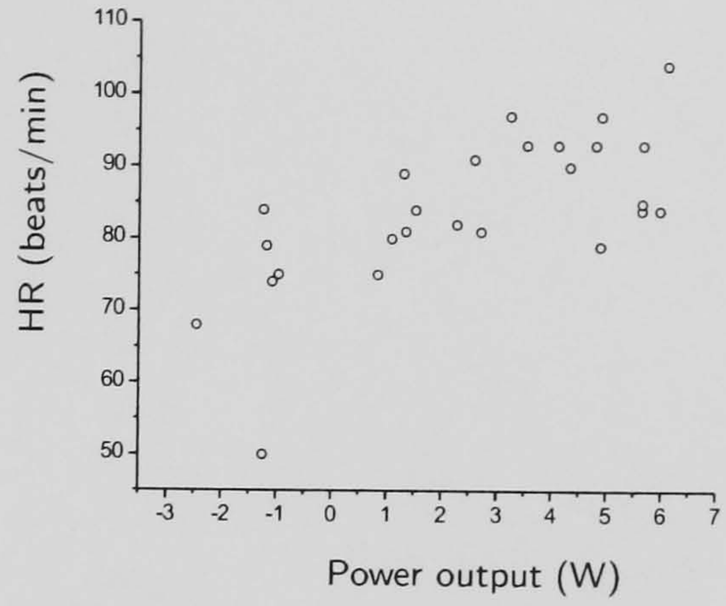


(j) TP1: Ratings of Perceived Exertion and Breathlessness vs. power output

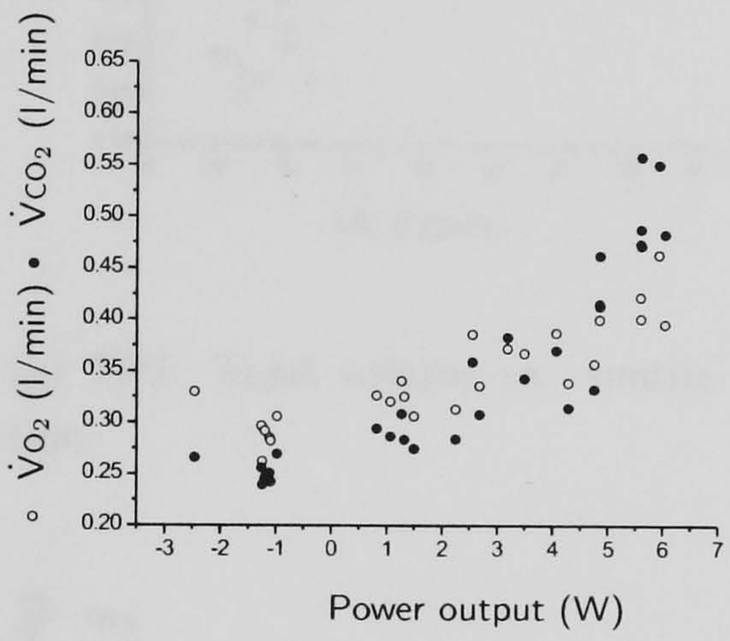
Figure B.7: (cont.)



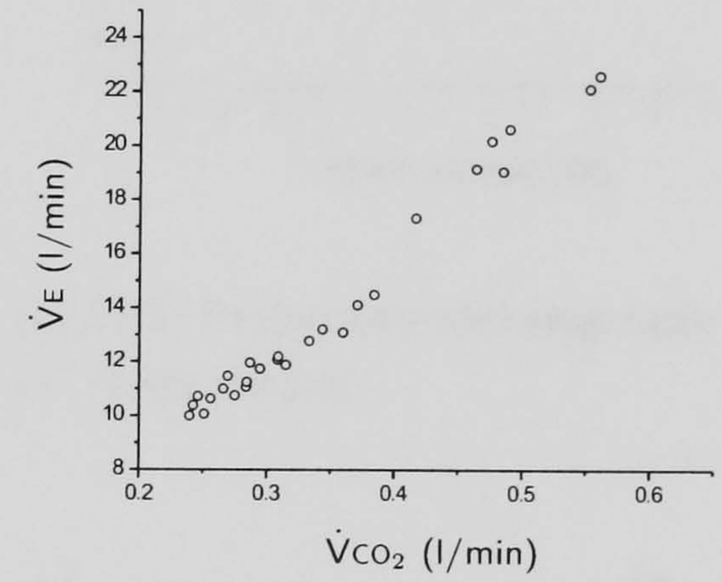
(a) TP2: Ventilation vs. power output



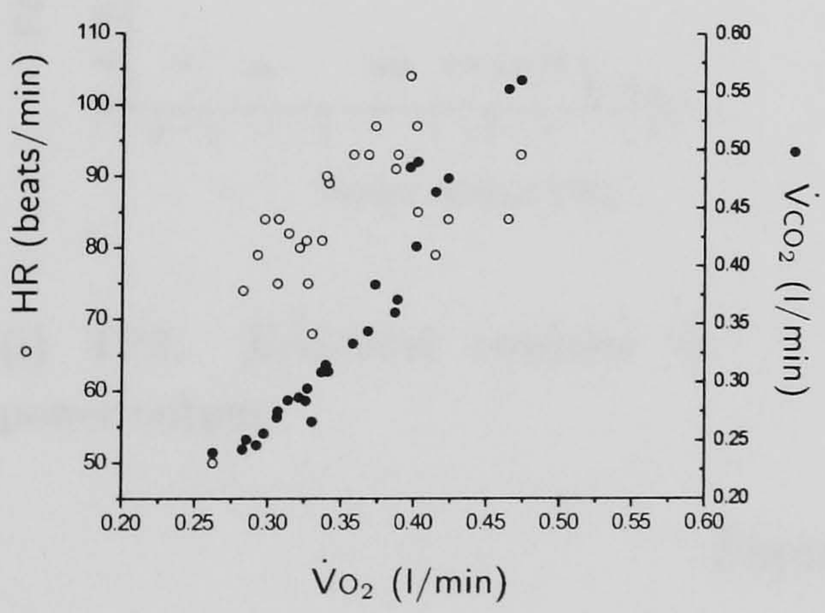
(b) TP2: Heart rate vs. power output



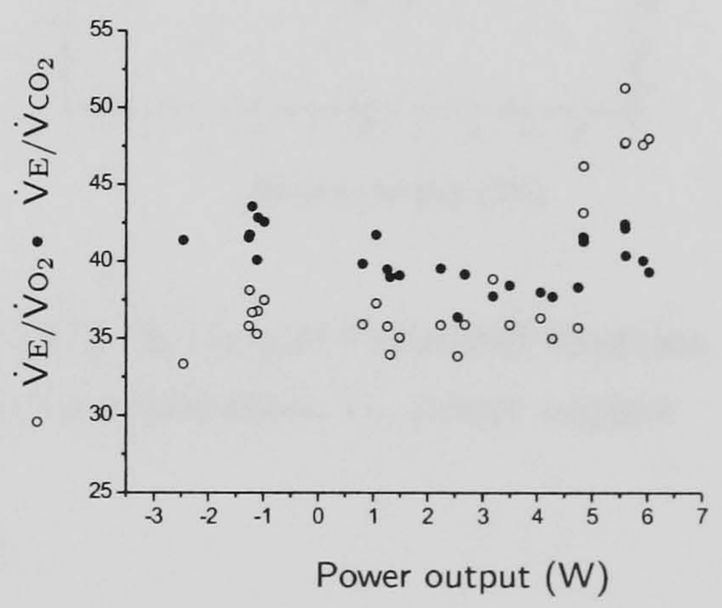
(c) TP2: Oxygen uptake and carbon dioxide output vs. power output



(d) TP2: Ventilation vs. carbon dioxide output

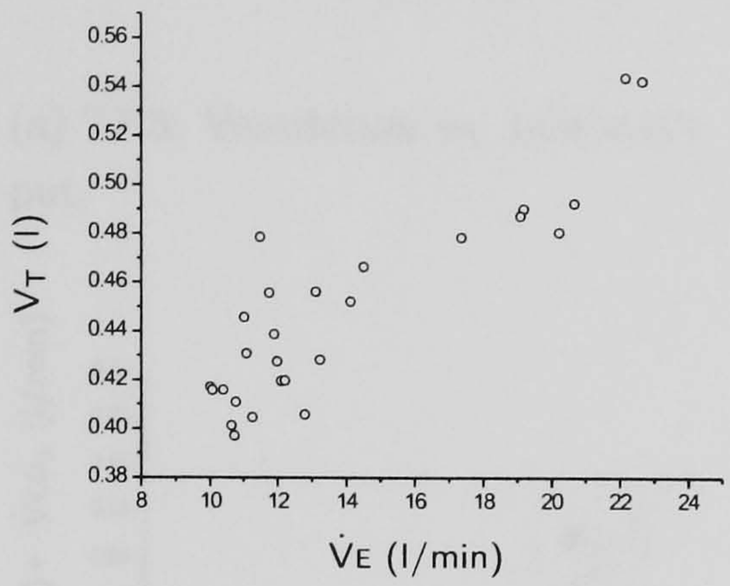


(e) TP2: Heart rate and carbon dioxide output vs. oxygen uptake

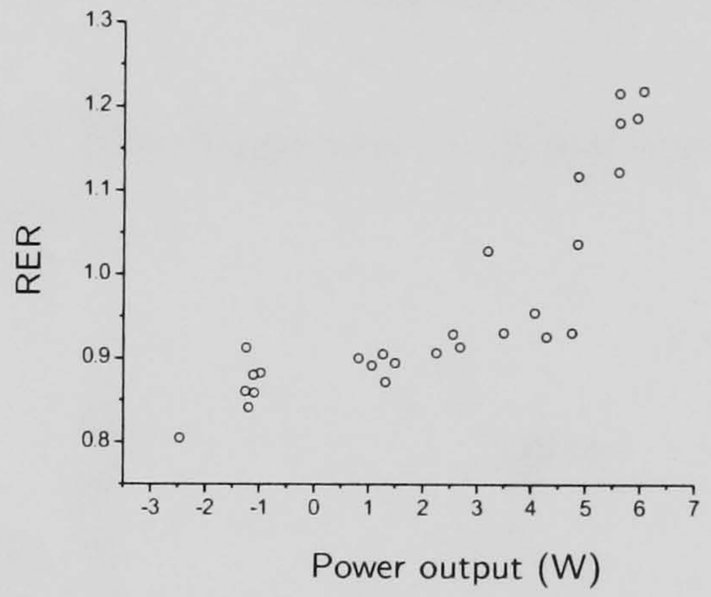


(f) TP2: Ventilatory equivalents vs. power output

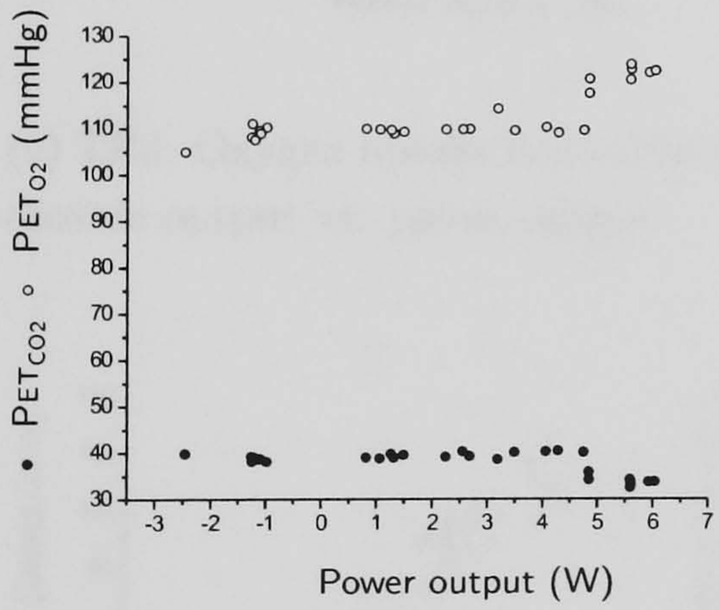
Figure B.8: Graphical representation of cardiopulmonary data for Subject B, from incremental FES-assisted ACE exercise testing at Test Point 2. The data have been edited and 8-breath averaged.



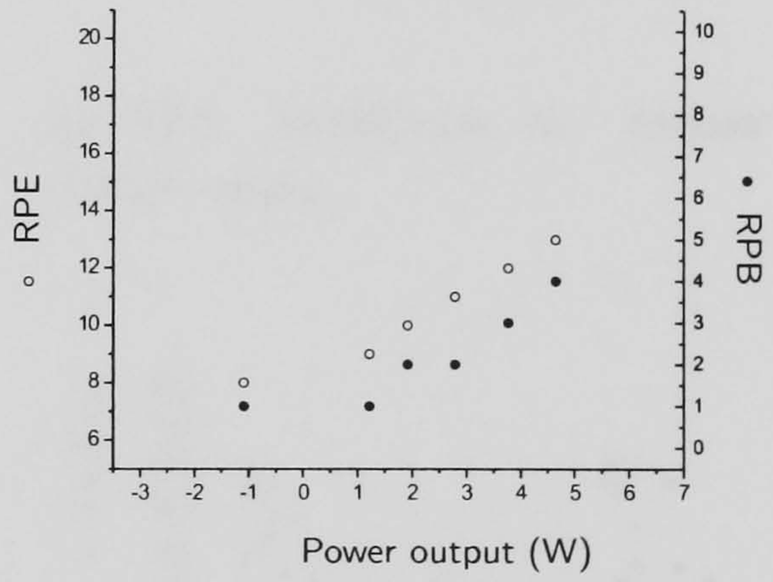
(g) TP2: Tidal volume vs. ventilation



(h) TP2: Respiratory exchange ratio vs. power output

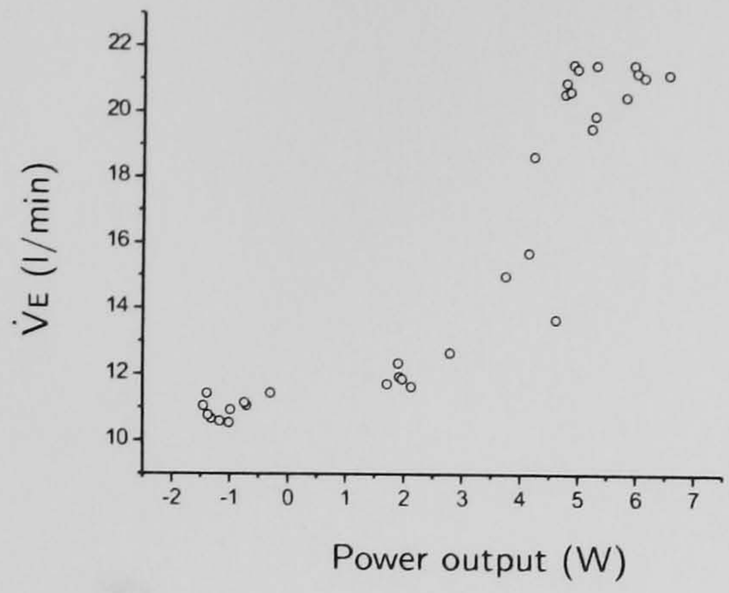


(i) TP2: End-tidal tensions vs. power output

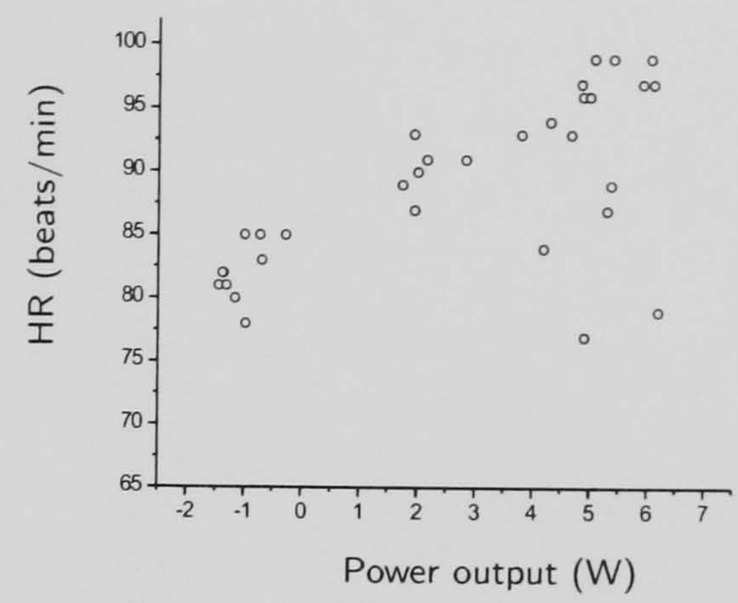


(j) TP2: Ratings of Perceived Exertion and Breathlessness vs. power output

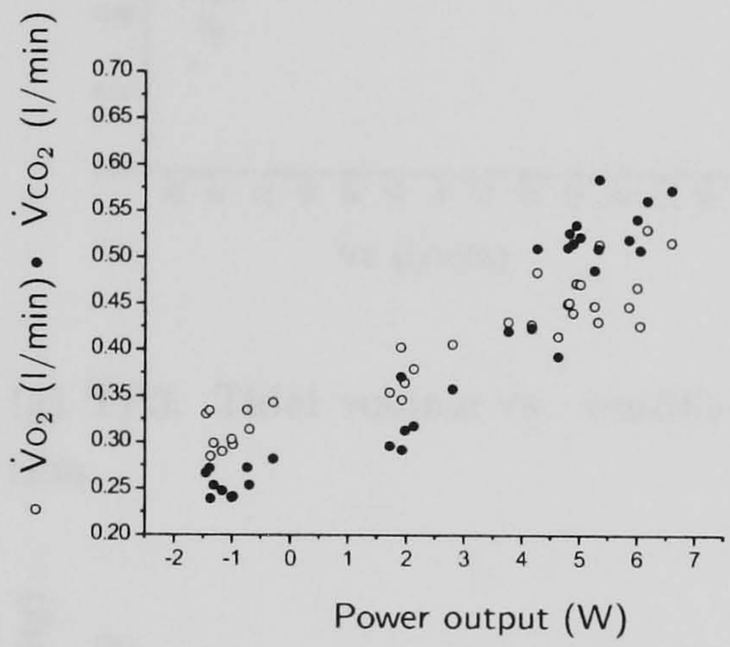
Figure B.8: (cont.)



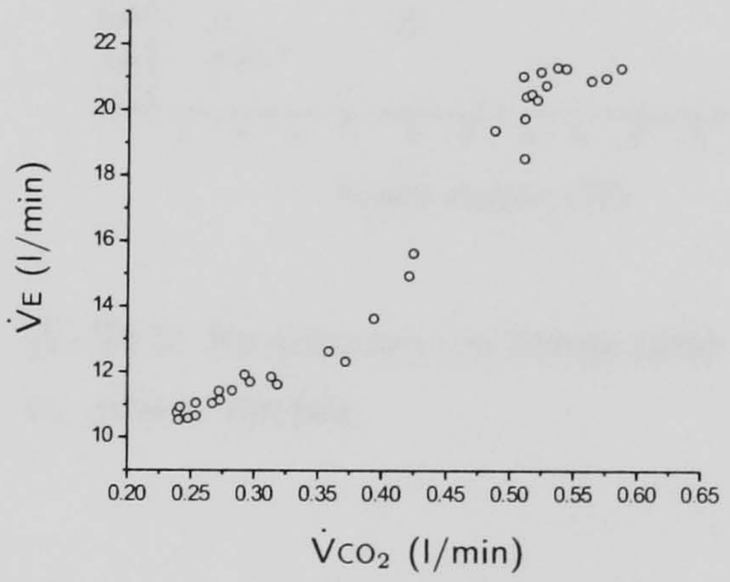
(a) TP3: Ventilation vs. power output



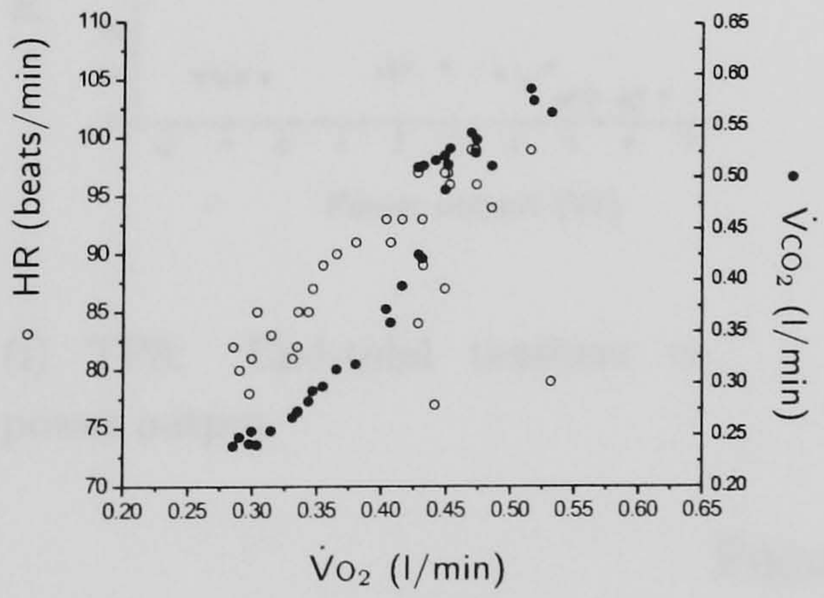
(b) TP3: Heart rate vs. power output



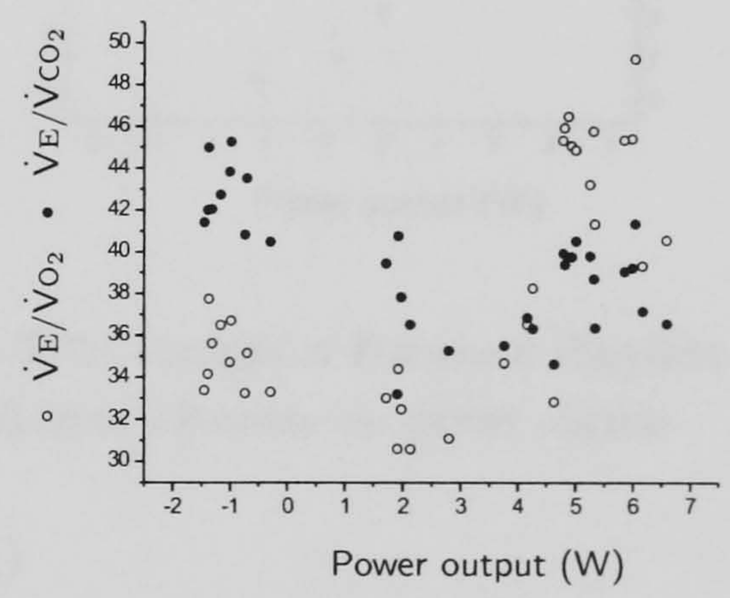
(c) TP3: Oxygen uptake and carbon dioxide output vs. power output



(d) TP3: Ventilation vs. carbon dioxide output

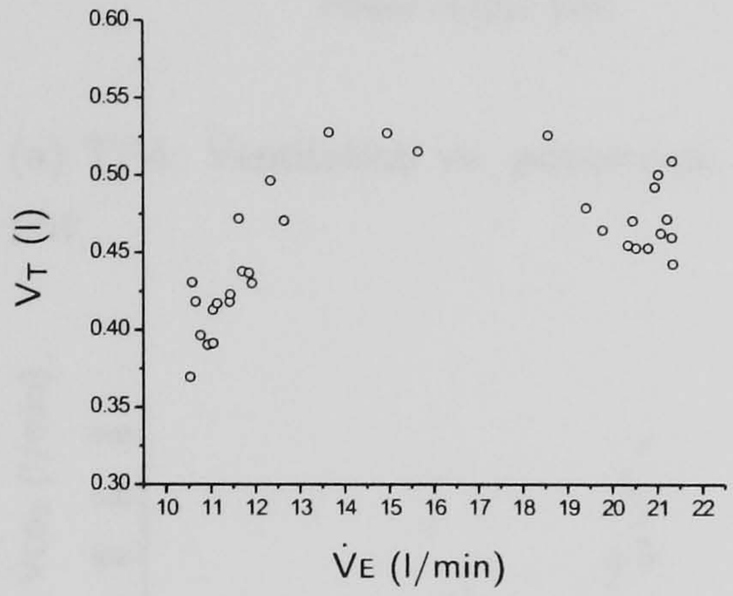


(e) TP3: Heart rate and carbon dioxide output vs. oxygen uptake

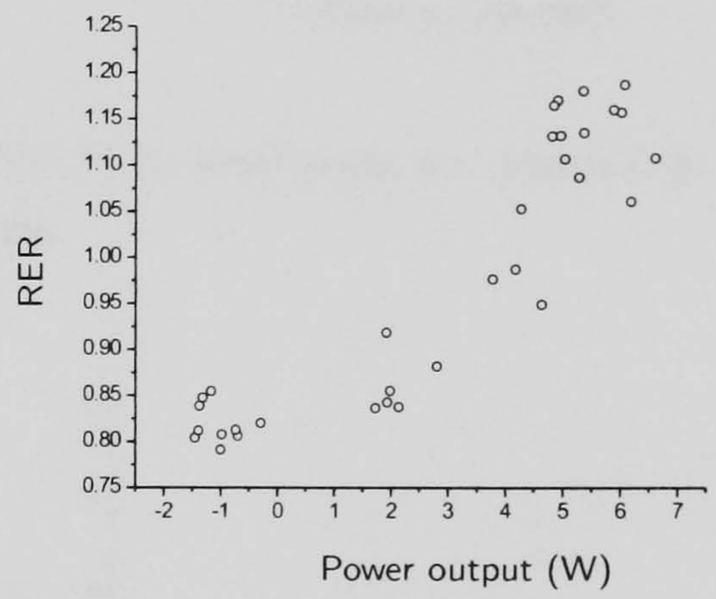


(f) TP3: Ventilatory equivalents vs. power output

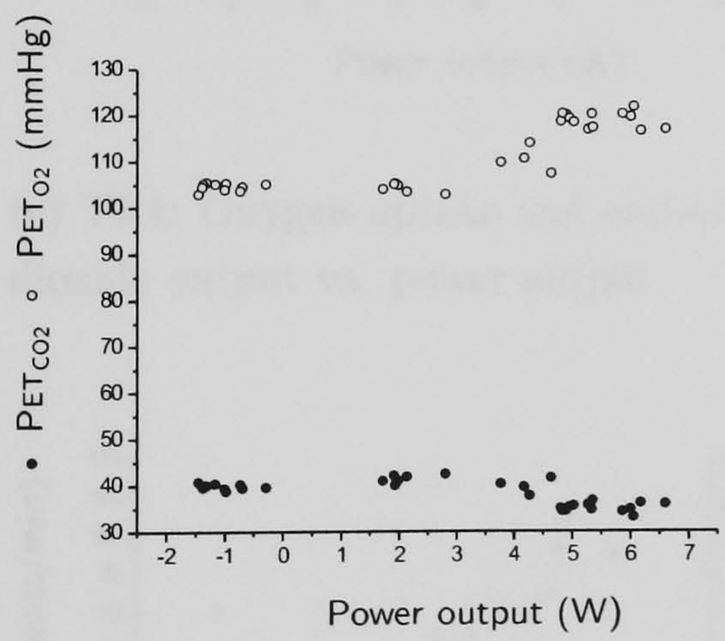
Figure B.9: Graphical representation of cardiopulmonary data for Subject B, from incremental FES-assisted ACE exercise testing at Test Point 3. The data have been edited and 8-breath averaged.



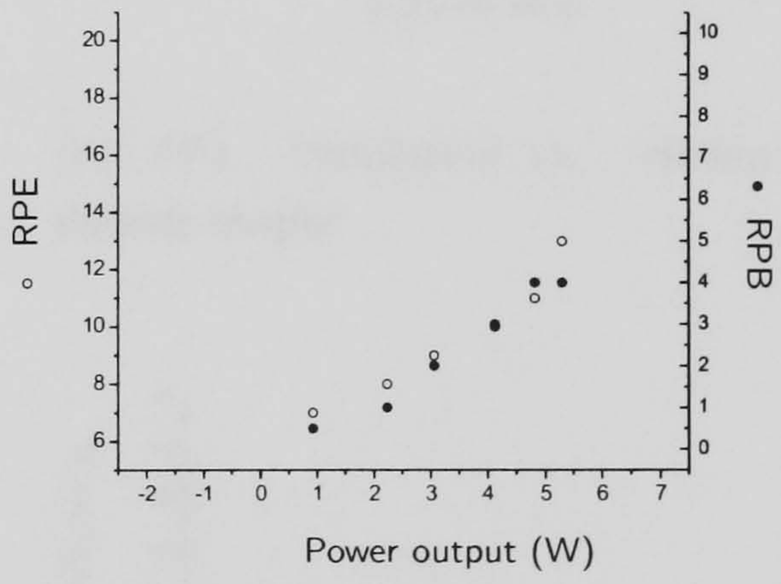
(g) TP3: Tidal volume vs. ventilation



(h) TP3: Respiratory exchange ratio vs. power output

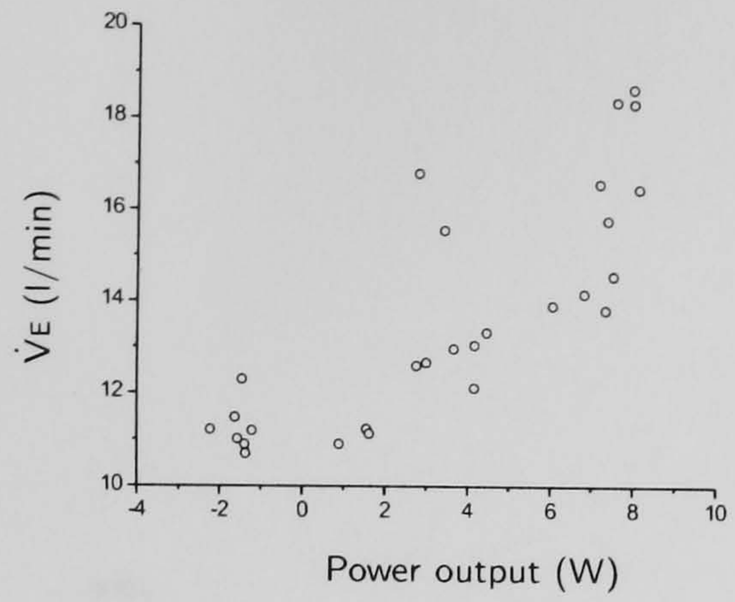


(i) TP3: End-tidal tensions vs. power output

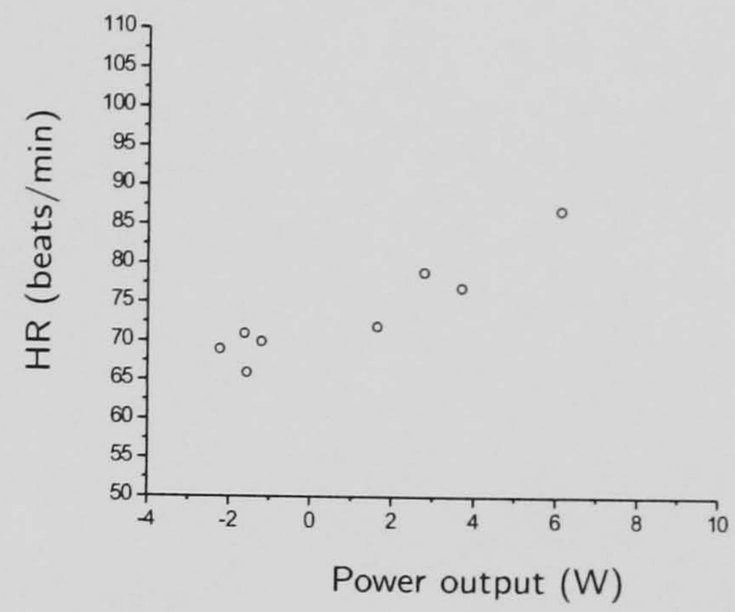


(j) TP3: Ratings of Perceived Exertion and Breathlessness vs. power output

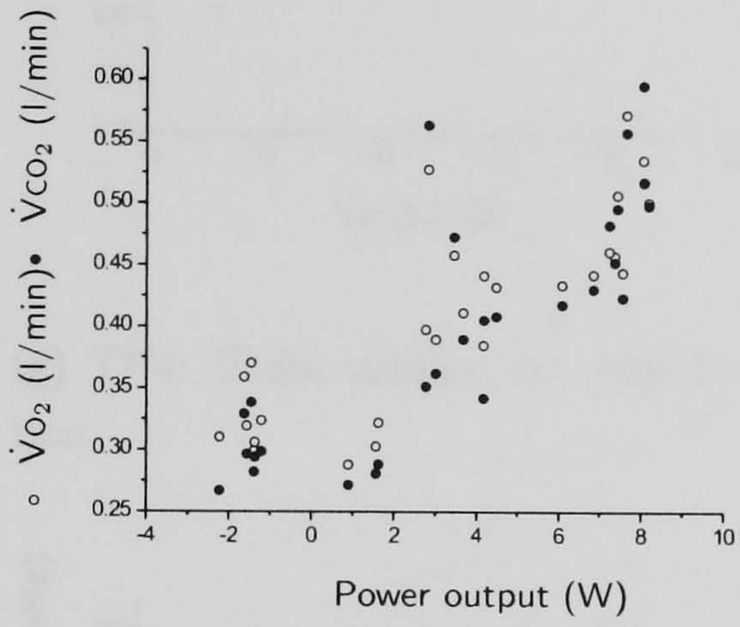
Figure B.9: (cont.)



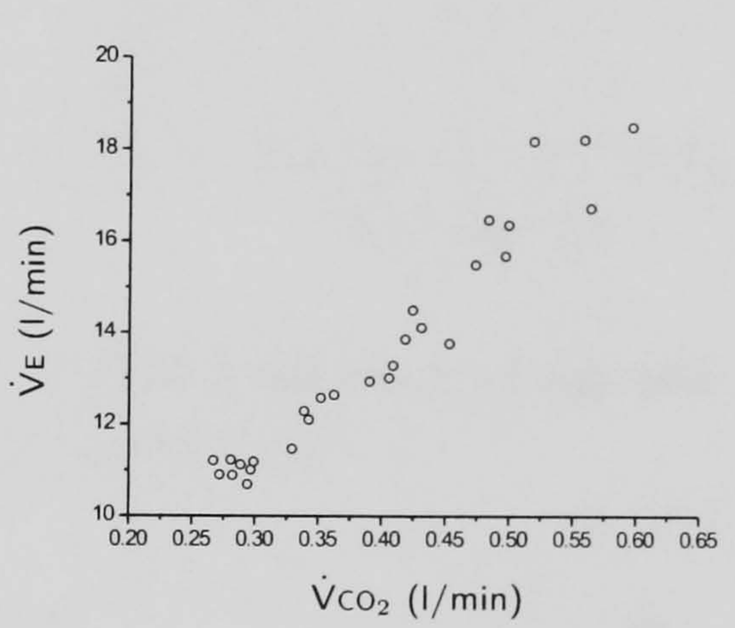
(a) TP4: Ventilation vs. power output



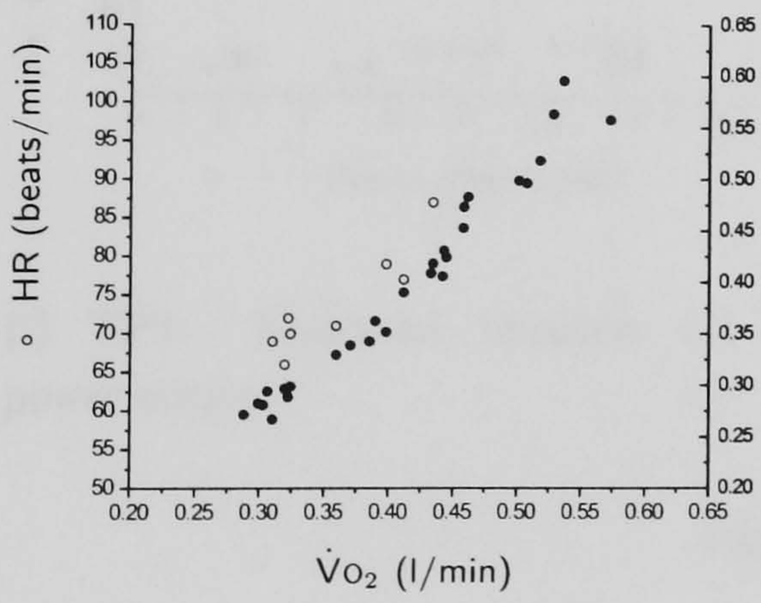
(b) TP4: Heart rate vs. power output



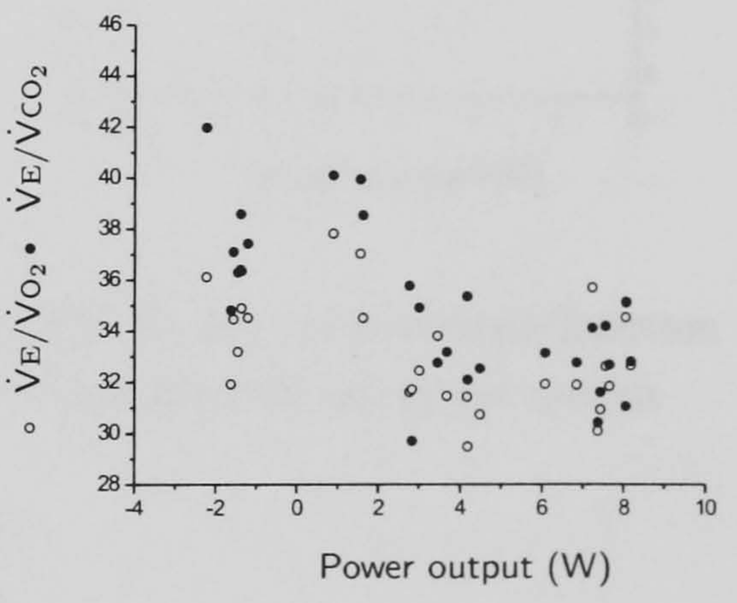
(c) TP4: Oxygen uptake and carbon dioxide output vs. power output



(d) TP4: Ventilation vs. carbon dioxide output

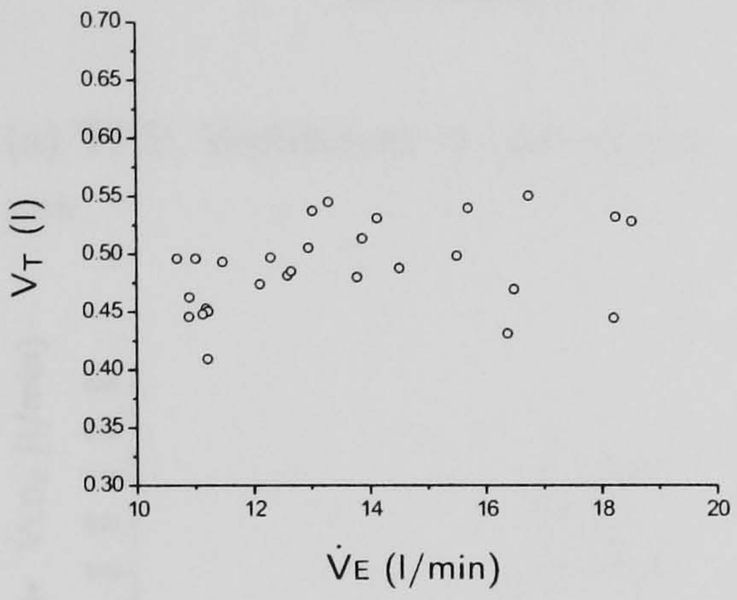


(e) TP4: Heart rate and carbon dioxide output vs. oxygen uptake

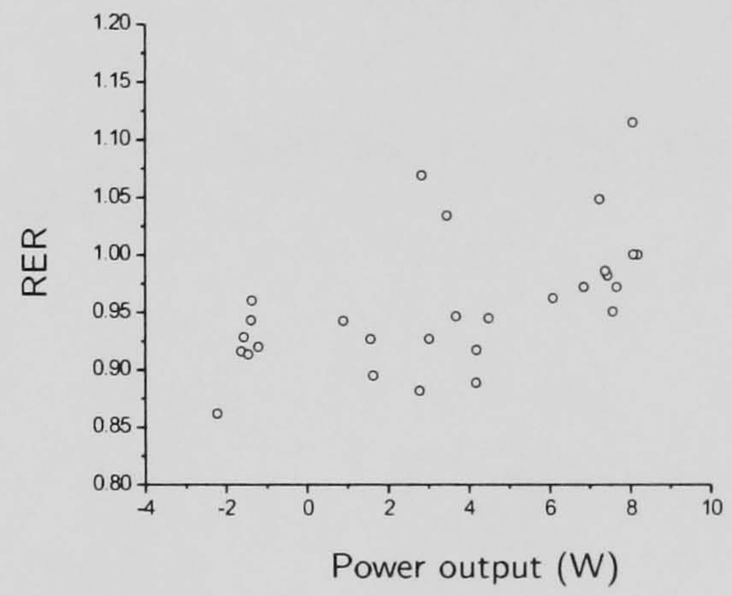


(f) TP4: Ventilatory equivalents vs. power output

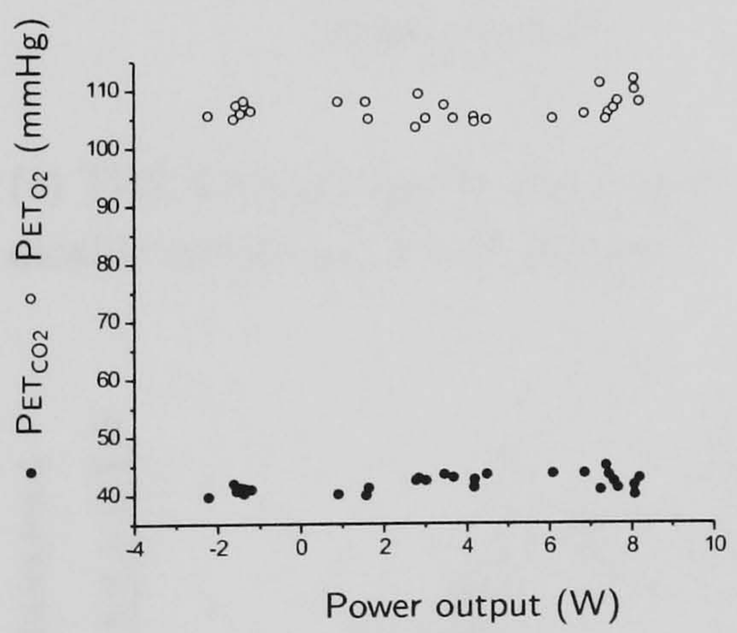
Figure B.10: Graphical representation of cardiopulmonary data for Subject B, from incremental FES-assisted ACE exercise testing at Test Point 4. The data have been edited and 8-breath averaged.



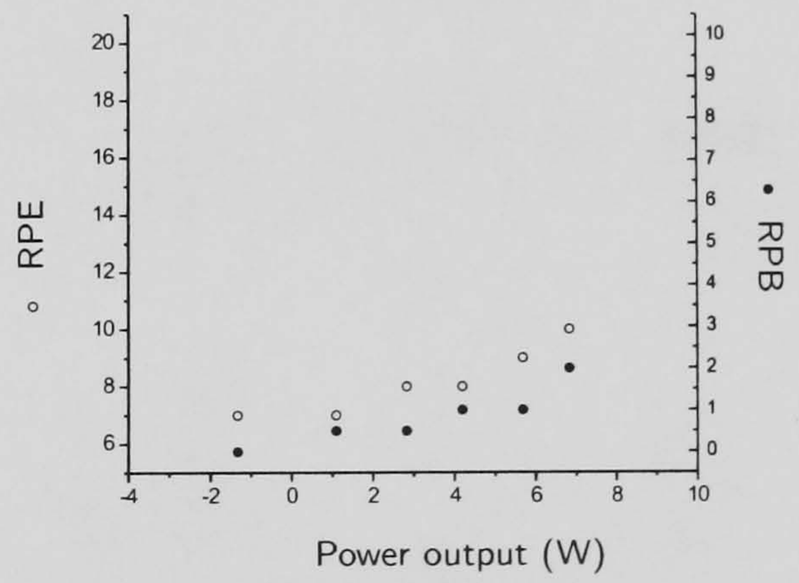
(g) TP4: Tidal volume vs. ventilation



(h) TP4: Respiratory exchange ratio vs. power output

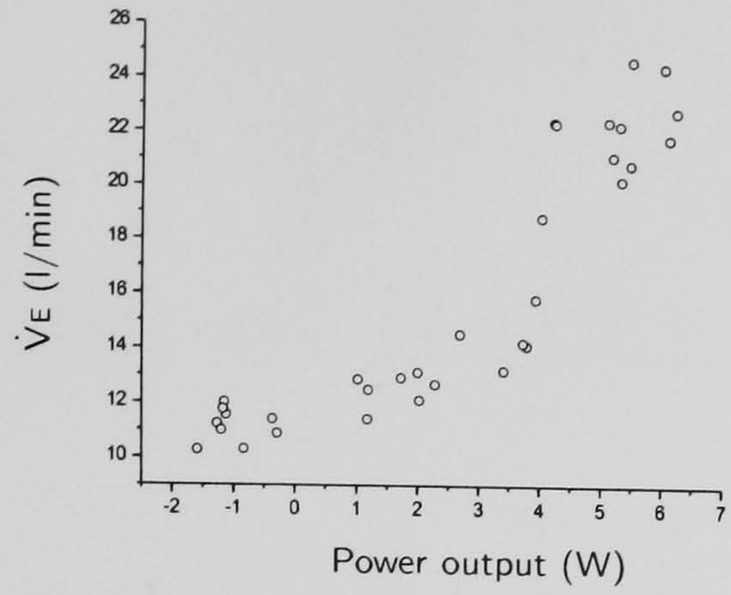


(i) TP4: End-tidal tensions vs. power output

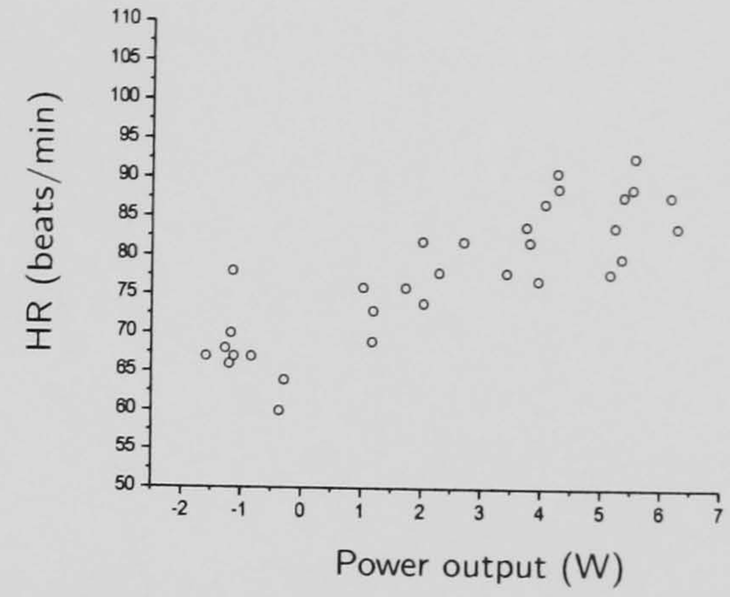


(j) TP4: Ratings of Perceived Exertion and Breathlessness vs. power output

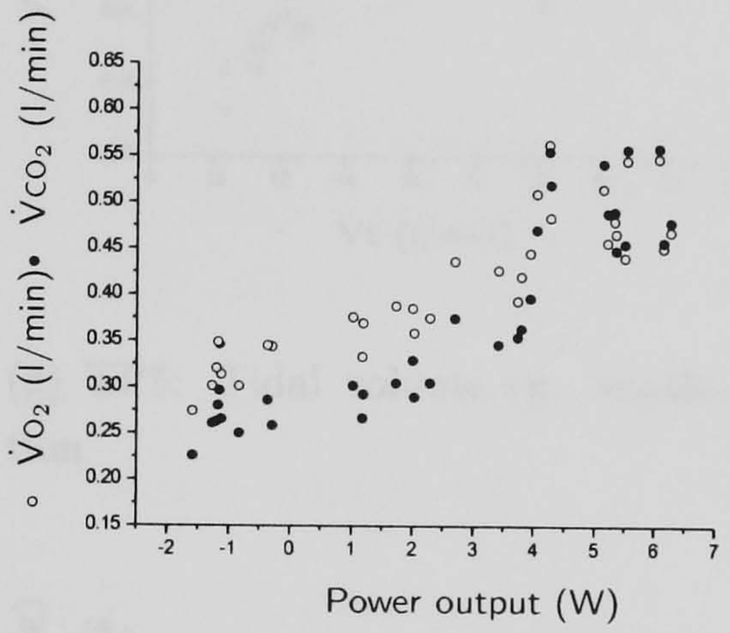
Figure B.10: (cont.)



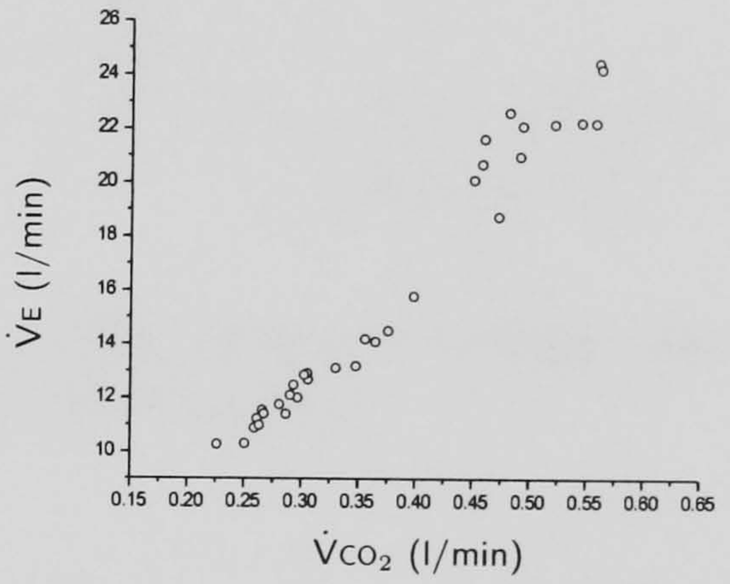
(a) TP5: Ventilation vs. power output



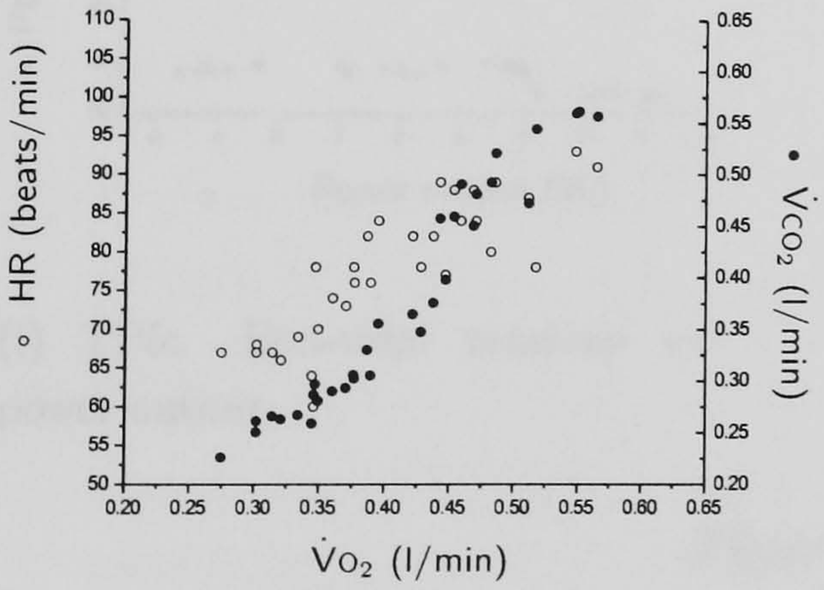
(b) TP5: Heart rate vs. power output



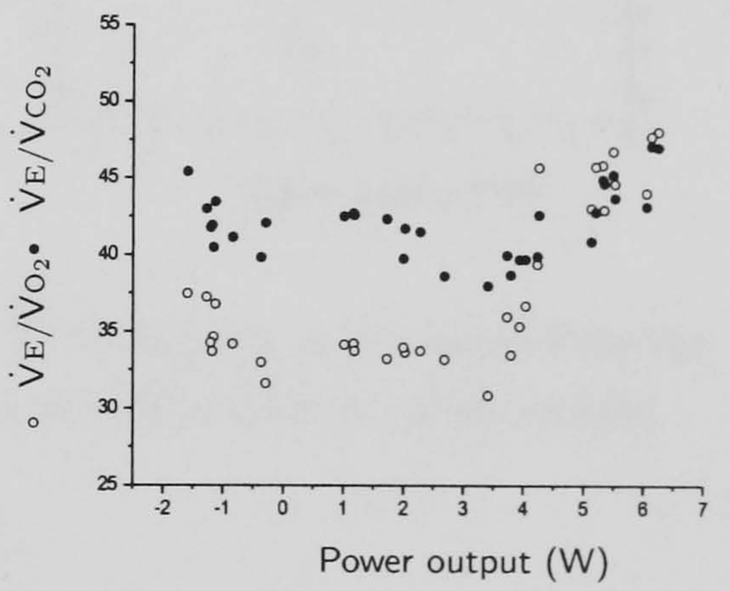
(c) TP5: Oxygen uptake and carbon dioxide output vs. power output



(d) TP5: Ventilation vs. carbon dioxide output

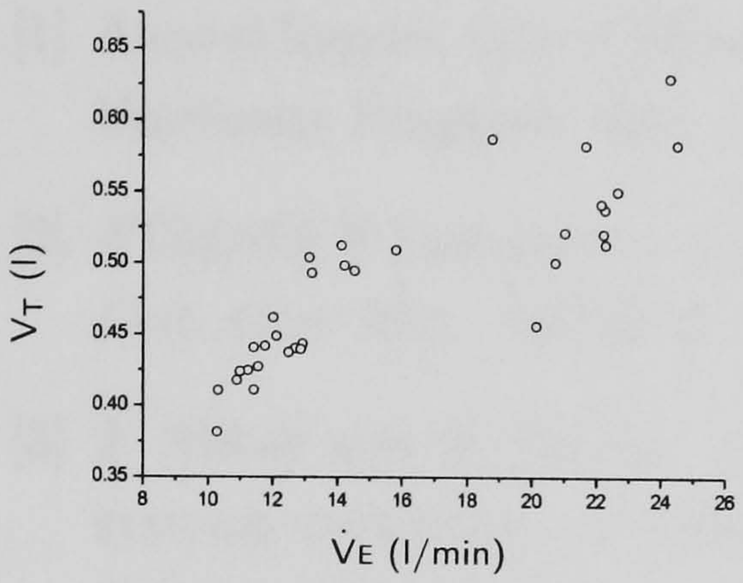


(e) TP5: Heart rate and carbon dioxide output vs. oxygen uptake

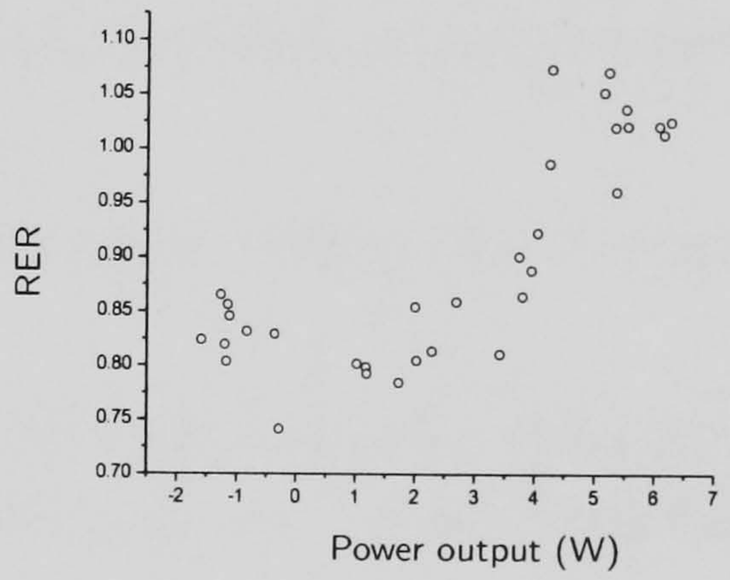


(f) TP5: Ventilatory equivalents vs. power output

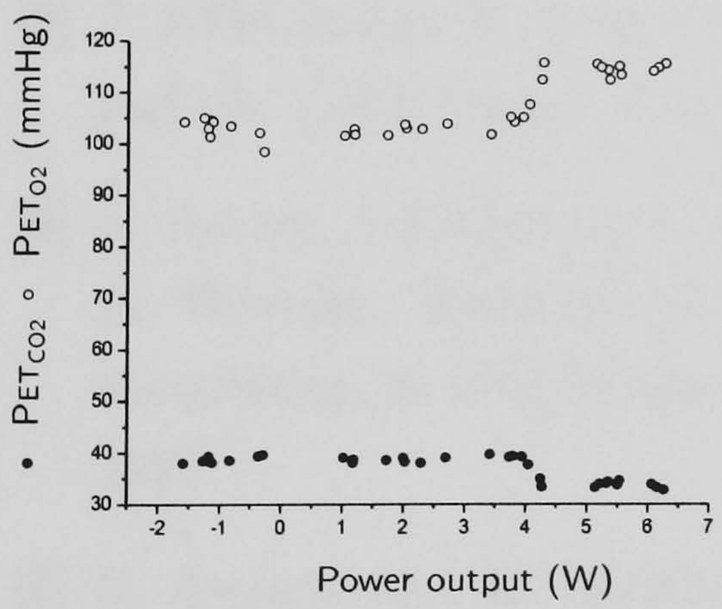
Figure B.11: Graphical representation of cardiopulmonary data for Subject B, from incremental FES-assisted ACE exercise testing at Test Point 5. The data have been edited and 8-breath averaged.



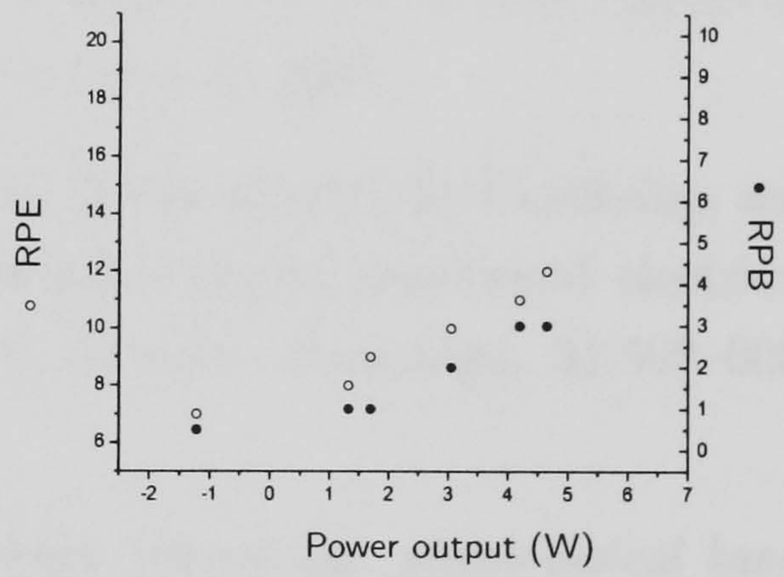
(g) TP5: Tidal volume vs. ventilation



(h) TP5: Respiratory exchange ratio vs. power output



(i) TP5: End-tidal tensions vs. power output



(j) TP5: Ratings of Perceived Exertion and Breathlessness vs. power output

Figure B.11: (cont.)

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