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PROXIMAL FEMORAL FRACTURE REHABILITATION:  
**A RANDOMISED CONTROLLED TRIAL  
OF ELECTRICAL STIMULATION OF THE  
QUADRICEPS**

*A thesis submitted for the degree of MSc (Med Sci) by Research*

*Glasgow University*

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*2003*

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# ABSTRACT

## Introduction

Proximal femoral fracture is associated with high levels of residual physical disability. Quadriceps weakness may be a factor in poor outcome. This research project was an investigation into whether electrical stimulation of the quadriceps of the fractured leg of patients rehabilitating after fixation of proximal femoral fracture increases leg extensor power and decreases disability.

## Methods

A systematic search and structured review of the literature paying explicit attention to study design quality was carried out and a pilot study was undertaken using a case control series design. This was followed by a pragmatically designed, randomised controlled trial of elderly post-surgical proximal femoral fracture patients, that compared 6 weeks of supplementary electrical stimulation (15 patients, mean age 81 years) to standard physiotherapy alone (11 patients, mean age 80 years). The electrical stimulation on: off cycle was 7:23 seconds. The dosage was 36 cycles per session, delivered daily as an in-patient and twice weekly after discharge to the highest intensity patients would tolerate. The primary outcome measure was leg extensor power (Nottingham Power Rig) at 6 weeks (the end of the intervention). Functional mobility (Elderly Mobility Scale), disability (Barthel Index) and perceived health status (Nottingham Health Profile) were also measured.

## Results

The pilot study indicated a potential benefit of the treatment, however the results of the subsequent RCT did not. The RCT sample size had 80% power to detect a significant difference in change in LEP of 0.14W/kg at week 6 compared to baseline. Eleven (73%) of the intervention patients in the RCT tolerated sufficient stimulation intensity to produce only palpable or visible contractions, but no leg movement at initial ES set up. A median of 10 (IQR 6, 17) electrical stimulation sessions were given to those who reached the 6 week assessment (13 (87%)). There were no significant differences in improvement in leg extensor power for either the fractured or non-fractured leg at week 6 or week 14 compared to baseline between the groups. At week 6, the primary end point, the ES group improved fractured leg LEP by a median of 0.20 W/kg (interquartile (IQR) range 0.14, 0.32) compared to 0.22 W/kg (IQR 0.1, 0.43) in the controls. Non-fractured leg LEP improved by a median of 0.18 W/kg (IQR 0.08, 0.38) versus 0.13 w/kg (IQR 0.03, 0.22), respectively. There were no significant differences in change of Elderly Mobility Scale or Barthel score or Nottingham Health Profile between the two groups at any point of assessment.

## Conclusion

ES of quadriceps did not promote increased leg extensor power or reduce disability following proximal femoral fracture. Low stimulation tolerance levels may explain the lack of effect.

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## PRESENTATIONS AND PUBLICATIONS

This body of research has resulted in the following to date:

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Oral/ Platform presentation at the National Congress of Chartered Society of Physiotherapist, Birmingham, October 2001.  
Braid VH, Barber M, Mitchell SL, Martin BJ, Grant SJ, Granat MH, Stott DJ. *Proximal Femoral Fracture Rehabilitation: A Randomised Controlled Trial Of Electrical Stimulation Of The Quadriceps.*

Oral/ Platform presentation at the Scottish Physiotherapists Research Forum, Stirling, July 2001  
Braid VH, Barber M, Mitchell SL, Martin BJ, Grant SJ, Granat MH, Stott DJ. *Proximal Femoral Fracture Rehabilitation: A Randomised Controlled Trial Of Electrical Stimulation Of The Quadriceps.*

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## LIST OF MAIN ABBREVIATIONS

CSA	Cross Sectional Area
ES	Electrical Stimulation
HHD	Hand Held Dynamometer
Hz	Hertz
IQR	Interquartile Range
LEP	Leg Extensor Power
MVC	Maximum voluntary Contraction
MVIC	Maximum Voluntary Isometric Contraction
NHP	Nottingham Health Profile
NPR	Nottingham Power Rig

# CONTENTS

<b>CHAPTER 1: INTRODUCTION</b>	<u>Page</u>
1.1. Proximal Femoral Fracture: A Critical Area for Research	1
1.2. Quadriceps Weakness and the Role of Electrical Stimulation	1
1.3. Research Aims	2
<b>CHAPTER 2: BACKGROUND</b>	
2.1. Proximal Femoral Fracture	3
2.1.1. Definition	3
2.1.2. Epidemiology & Risk Factors	3
2.1.3. Management	5
2.1.4. Mortality	6
2.1.5. Morbidity	6
2.2. Limitation of Mobility after PFF	7
2.2.1. Definition of Mobility	7
2.2.2. Evidence of Mobility Impairment after PFF	8
2.2.3. Impaired Quadriceps Function and Mobility after PFF	9
2.2.4. Aetiology of Quadriceps Impairment	11
2.2.5. Quadriceps Training in the Elderly and After PFF	13
2.3. Electrical Stimulation to Improve Skeletal Muscle Function	14
2.3.1. Overview	14
2.3.2. Definition of terms	14
2.3.3. Motor Stimulation Currents	17
2.3.4. Technical Parameters	19
2.3.5. ES Training Protocols	24
2.3.6. Potential Mechanisms of Effect	25
2.4 Summary of Chapter	26
<b>CHAPTER 3: ES OF NORMALLY INNERVATED QUADRICEPS</b>	
3.1. Systematic Search Methodology	27
3.1.1. Electronic	27
3.1.2. Hand Search and Compilation	28

	<u>Page</u>
3.2. Structured Review Methodology	28
3.2.1. Scope of Review	28
3.2.2. Review Criteria	30
3.2.3. Critical Review Issues	31
3.3. Training Effects of ES of the Quadriceps in Younger Populations	32
3.3.1. Young Healthy Populations	32
3.3.2. Younger Clinical Populations	34
3.3. Training Effects of ES of the Quadriceps in Older Populations	39
3.4.1. Older Healthy Populations	39
3.4.2. Older Clinical Populations	40
3.5. Summary of Chapter	44
 <b>CHAPTER 4: RESEARCH OBJECTIVES, DESIGN AND METHODOLOGY</b>	
4.1. Research Objectives	47
4.2. Methodology	47
4.2.1. Design	47
4.2.2. Recruitment Procedures	47
4.2.3. Treatment Protocol	48
4.2.4. Outcome Measures	52
4.2.5. Assessment Protocol, Data Collection and Recording	55
 <b>CHAPTER 5: PILOT STUDY</b>	
5.1. Aims	56
5.2. Methodology	56
5.2.1. Design and Personnel	56
5.2.2. Recruitment Procedures	56
5.2.3. Treatment Provision, Outcome Measures & Assessment	57
5.2.4. Statistical Analysis	57
5.3. Results	58
5.3.1. Recruitment	58
5.3.2. Baseline Characteristics & Follow Up	58
5.3.3. Treatment Pragmatics	60
5.3.4. Outcomes	60
5.3.5. Process	64

	<u>Page</u>
5.4. Discussion	64
5.4.1.Principal Findings	64
5.4.2.Review of Methodology	65
5.4.3.Review of Findings	66
5.4.4.Potential Mechanism of Effect	68
5.4.5. Conclusion	69
 <b>CHAPTER 6: RANDOMISED CONTROLLED TRIAL OF ES OF QUADRICEPS</b>	
6.1. Aims	70
6.2. Methodology	70
6.2.1. Design and Personnel	70
6.2.2. Recruitment Procedures	70
6.2.3. Treatment Provision	71
6.2.4. Outcome Measures & Assessment	71
6.2.5. Statistical Analysis	72
6.3. Results	
6.3.1.Recruitment & Follow Up	73
6.3.2.Baseline Characteristics	73
6.3.3.Treatment Pragmatics	73
6.3.4.Outcome Measures	76
6. 4. Discussion	81
6.4.1.Principal Findings	81
6.4.2.Review of Methodology	81
6.4.3.Review of Findings	83
6.4.4.Potential Mechanism of Lack of Effect	84
6.4.5.Future Research	85
6.4.6. Conclusion	86
 <b>CHAPTER 7: FINAL SUMMARY</b>	
Appendices	89
References	98

## Tables, Figures and Plates

		<u>Page</u>
Table 1:	Classification of PFF Fracture Types	4
Table 2:	ES Regime Intensity: Contributing Factors	24
Table 3:	Literature Table: Young Clinical Populations (no immobilisation)	36
Table 4:	Literature Table: Young Clinical Populations (POP immobilisation)	38
Table 5:	Literature Table: Older Clinical Populations	41
Table 6:	Pilot: Comparison of Baseline Characteristics by Group.	59
Table 7:	Pilot: Improvements in Leg Extensor Power (LEP), Elderly Mobility Scale (EMS) and Barthel score at Week 6 (End of Intervention) and Week 14, Compared to Baseline.	61
Table 8:	Pilot: Changes in Total Domain Scores of the Nottingham Health Profile At Week 6 (End of Intervention) and Week 14, Compared to Baseline.	63
Table 9:	RCT: Comparison of Baseline Characteristics by Group.	75
Table 10:	RCT: Improvements in Leg Extensor Power (LEP), Elderly Mobility Scale (EMS) and Barthel score at Week 6 (End of Intervention) and Week 14, Compared to Baseline.	78
Table 11:	RCT: Changes in Total Domain Scores of the Nottingham Health Profile at Week 6 (End of Intervention) and Week 14, Compared to Baseline.	80
Figure 1:	Clarification of ES Terminology	16
Figure 2:	Motor Stimulation Currents	18
Figure 3:	Electrical Pulses	21
Figure 4:	Breakdown of Systematic Literature Search Results by Study Type	29
Figure 5:	Criteria for Structured Literature Review	30
Figure 6:	RCT: Initial Power Calculations	72
Figure 7:	RCT: Flow of Patients Through the Study	74
Figure 8:	RCT: Revised Power Calculation	76
Plate 1:	Electrical Stimulation in Situ	51
Plate 2:	Nottingham Power Rig	53

## *Chapter 1*

# INTRODUCTION

### **1. 1. Proximal Femoral Fracture: A Critical Area for Research**

Proximal femoral fracture (PFF) or, as it is more commonly referred to, hip fracture has been described as the most common serious and the most serious common injury in the elderly. Its incidence has reached epidemic proportions and is likely to grow. Despite the development of alternative routes of care (geriatric orthopaedic rehabilitation units and early supported discharge initiatives) patients with PFF occupy 25% of the total number of acute orthopaedic beds in the UK. The estimated in-patient cost of each patient is between £5000 and £6000, accounting for a total of £30,000,000 of health spend in Scotland in 1997 (1). Rehabilitation is likely to be important influence on outcome, since the aim of all involved services is to decrease pain, promote functional recovery and minimise dependence. However, rehabilitation outcomes are poor, resulting in a significantly increased burden on to social services and informal carers. The Scottish Hip Audit is a world leader with 80% coverage and 98% follow up. Initially focused on acute and surgical treatment, it was recently advised to shift its emphasis from surgical and peri-operative procedures towards measurement and evaluation of rehabilitation, long term outcomes and the 'whole person' experience of care (2). Potential methods for improving rehabilitation outcomes after surgical fixation of hip fracture are thus a critical area for research.

### **1. 2. Quadriceps Weakness and the Role of Electrical Stimulation**

PFF is associated with substantial residual decline in physical function in survivors (3) and weakness of the quadriceps muscles may be an important factor in poor performance (4). Progressive, high-intensity quadriceps training increases leg extensor power and decreases disability following PFF (5), but is a rehabilitation regime that requires a high degree of patient motivation and supervision. Electrical stimulation of skeletal muscle groups may be a useful tool in the rehabilitation of normally innervated quadriceps for a number of reasons. Firstly, it has been suggested that full activation of quadriceps muscle group can not be achieved voluntarily (6), (7). Secondly, electrical stimulation has been used to overcome reflex inhibition associated with post-surgical pain and effusion (8). Third, electrical stimulation may effect improvement in muscle function via neurological modulation (9). Finally, electrical stimulation has the theoretical advantage of requiring no patient motivation. Despite these potential benefits, there is little consensus regarding the optimal stimulus parameters or programme

content for muscle strengthening regimes. Furthermore, comparatively little research has been carried out using electrical stimulation on the quadriceps of elderly patients, although those studies that exist suggest that it is tolerated(10), (11),(12),(13),(14),(15). A low intensity regime of electrical stimulation has been demonstrated to be of benefit in quadriceps training in healthy elderly men (15). Electrical stimulation may also attenuate atrophy of quadriceps associated elderly orthopaedic conditions or post-surgical catabolic states (16),(17). A systematic search of the English language literature identified only one study that addressed the use of electrical stimulation to improve quadriceps function and disability following PFF (18). The results suggested a beneficial effect of patterned low frequency electrical stimulation in regaining pre-injury levels of mobility.

### **1. 3. Research Aims**

The primary aim of this research project was to evaluate the effects of a supplementary program of ES of quadriceps of the affected leg, in terms of impairment, disability and perceived health status and to investigate whether any benefits would be maintained after electrical stimulation treatment was stopped. The target population was elderly West of Scotland patients rehabilitating after recent surgical fixation for PFF.

Two supporting aims were to comprehensively search the literature concerning electrical stimulation of normally innervated quadriceps using an explicit, systematic search strategy, and to review the results of this search using a structured approach paying explicit attention to study design quality.

## *Chapter 2*

# **BACKGROUND**

## **2.1. Proximal Femoral Fracture**

### **2.1.1. Definition**

Proximal femoral fracture (PFF) is defined as any fracture of the femur from the femoral head to a level 5cm below the lesser trochanter (19). A primary distinction is made between intracapsular and extracapsular fractures. These occur proximal and distal to where the joint capsule attaches to the femur respectively. Not only are they anatomically distinct, but it is recommended that they receive different surgical treatment (19). Further sub-types of PFF exist and a variety of sub-classification systems feature in the literature. SIGN Guideline No. 56, Prevention and Management of Hip Fracture in Older People, recommends a cross European description and coding system for sub-type classification as outlined in Table 1 (20). Hip fracture is a widely accepted, synonymous term for PFF.

### **2.1.2. Epidemiology and Risk Factors**

PFF can occur at any age, but is largely a pathology of the elderly (21). The two primary risk factors are increased skeletal fragility secondary to osteoporosis and an increased risk of falling, both of which are associated with ageing (19). Moreover, with increasing age comes increasing rate of incidence (19),(22). Ninety percent of patients with PFF are over 65 years of age; 75% of them are over 75 years of age (23). More of these patients are women than are men. The lifetime risk in industrialised societies is 18% for females and 6% for men (19). The incidence is 3/100 between the ages of 65 - 74 years, which rises to 12.6/100 for women aged 85 years and over (24).

Most commentators agree there was an explosion in age-stratified incidence during the second half of the twentieth century in northern industrialised countries, with an increasing incidence at all ages (19). In the North East of Scotland between 1970 and 1993 there was a 101% increase in PFF admissions that coincided with a 158% increase in PFF in patients aged over 75 years (25). There is controversy, however, as to whether this increase in age-stratified rate of incidence is now slowing down or indeed has come to a halt (25),(23). Nonetheless, it seems certain that the absolute numbers of PFF are set to rise given the predicted demographic skew towards an ever-ageing population.

**Table 1. Classification of PFF According to SIGN Guideline No. 56, Prevention and Management of Hip Fracture in Older People (20).**

\*Trochanteric are also termed intertrochanteric or pertrochanteric

<b>Capsular Site</b>	<b>Details</b>	<b>Code</b>
Intracapsular	Undisplaced (subcapital or cervical). Garden grade 1 or 2.	1
	Displaced (subcapital or cervical). Garden grade 3 or 4.	2
Extracapsular	Basocervical (basal).	3
	Trochanteric* two fragments (a two part fracture, stable fracture).	4
	Trochanteric* multi-fragments (the extra fragments are generally the greater or lesser trochanter or both).	5
	Subtrochanteric (any number of fragments)	6

According to the 1997 Scottish Needs Assessment Programme (SNAP) report on hip fracture, Scotland alone will see a 25% increase, 95% of which is predicated on the rise in numbers of elderly per se (1). The 1999 the Scottish Hip Audit reported that the incidence is probably still rising with the case mix tending to older and frailer patients (2). If risk of falling is a major predictor of PFF then the multiple factors associated with this, as well as the development of osteoporosis will also be associated with risk of PFF. Rose et al detail an expanded list of risk factors for PFF: neuromuscular impairment; visual impairment; pre-existing medical conditions; dementia; alcohol intake; smoking; immobilisation; institutionalisation. They note that thinner people are also more at risk, since there is less overlying tissue to act as a shock absorber or force dissipater (26). Armstrong et al add that poor muscle strength or falls may more important risk predictors than bone density in the over 75 age group (22), which, as detailed above, accounts for three quarters of PFF patients.

### **2.1.3. Management**

#### *2.1.3(i) Surgical*

PFF usually presents as an emergency. Recent SIGN guidelines provide clear guidance on the protocols to follow concerning surgical and peri-operative care (20). Despite the rarity of large, well controlled randomised controlled trials to compare different surgical treatments, it has been reported that immediate outcomes of surgical fixation have improved considerably in terms of survival after surgery and immediate and subsequent stability of fixation (27). It has also been observed that despite improvements in implant technology, operative technique and rehabilitation protocols, elderly PFF patients often experience outcomes that fall short of expectations (28).

#### *2.1.3(ii) Rehabilitation*

Rehabilitation post PFF can take place in a variety of settings and following a range of care models including: acute orthopaedic wards, geriatric orthopaedic rehabilitation units (GORU), hospital at home schemes, early supported discharge schemes and in out-patient clinics. The superiority of one type of in-patient setting to another has not been established (23),(19). Early discharge schemes have not been shown to produce faster or greater functional improvement for patients than in-patient care (23). SIGN Guideline No. 56 recommends GORU transfer for patients with co-morbidity, poor functional ability and low mental test scores prior to admission (20). It is recommended that rehabilitation should start early and be of a multi-disciplinary nature, however the precise content and intensity of therapeutic programs have been less well researched. This will be expanded later in section 2.2.5.

#### **2.1.4. Mortality**

Hip fracture is not only a common pathology in the elderly, but a major cause of morbidity and mortality (21). Precise death rates vary across different epidemiological studies depending in part on different time points of assessment as well as different population demographics. Hospital mortality rates in the Northern Hemisphere range from 7 – 36%. Fixed period mortality rates for all types of PFF range from 19% to 44% at 6 months and from 12% to 37% at 12 months (21). In Scotland, the mortality rate after one year is approximately 30% (20). Half of those who die within a year are over 90 years of age (23). Intra and extracapsular fractures may be associated with different risk of death (26), (29). Patients with an extracapsular fracture are at a greater risk of dying within 12 months of surgery than those with an intracapsular fracture (29). Given reported improvements in surgical care, as outlined in 2.1.3 above, and decreasing mortality rates immediately post fixation (27) it could be argued that morbidity (a larger rehabilitation population) is now becoming a more pressing problem than mortality.

#### **2.1.5. Morbidity**

Morbidity after PFF is harder to quantify, however, since recovery is subjective and specific to the individual. It can be measured at the level of impairment, e.g. joint range of motion, lower limb muscle performance, pain). It can be measured at the level of disability, e.g. mobility, activities of daily living or extended activities of daily living. Or it can be measured at the level of handicap, e.g. place of residence, increased costs of social support, quality of life. One broad definition of the goal of rehabilitation following any injury is to return the patient to his or her pre-injury level of mobility and independence as quickly as possible, without jeopardising the chances of successful treatment of the particular injury. According to these criteria, PFF survival is associated with high levels of surgical success (27), but substantial physical decline (3), (30), (31) and loss of independence (24),(30), (31). It is claimed that 30% of PFF patients in Scotland, admitted from home, require a subsequent move to long term residential or nursing home care (1) and of those already in long-term care, 25% require a higher level of support (19). Those who do return to community living have greater difficulties with activities of daily living than age and sex matched contemporaries (19),(24).

Of course, there are different interpretations, and degrees, of functional independence and mobility. This is reflected in the proliferation of outcome measures for each, applied at differing short, medium and long term points of assessment. This makes meta-analysis of outcome studies and predictor of outcome studies difficult. Furthermore, from a review of the literature on outcomes post hip fracture, it is clear that mobility itself (or, its components, e.g. transfers or

gait) may be both an outcome and a predictor of other outcomes, e.g. functional ability, health, and death (30), (32).

This study is particularly interested in leg extensor power as a contributor to recovery after PFF fixation. The broader the outcome domain, the harder it will be to demonstrate direct association of lower limb power with positive outcome, since there will be an ever increasing number of compounding influences. The following section will therefore restrict itself to an examination of morbidity outcomes post PFF primarily in terms of mobility, and to the potential role of lower limb function therein. Specifically, it does not address balance impairment per se or its influence on mobility, although this is recognised as an important factor. Axiomatic though it may be, it has also been clearly stated that ambulatory outcomes feature strongly in the list of key outcome indicators suggested by all researchers or commentators in the area of PFF (33).

## **2. 2. Limitation of Mobility after PFF**

### **2.2.1. Definition of Mobility**

Before looking at the evidence for mobility limitation post PFF, the term mobility and the phrase independent mobility require definition. Mobility at its most basic means the ability to move. Concerning human beings, there can be mobility of a part (a joint or limb) or the mobility of the whole. Problems with mobility of a part fall into the category of impairment whereas of the whole, they fall into the category of disability. Providing the environment is appropriate and the required mechanical assistance available, it is possible for human beings to be independently mobile, as a whole, without the use of their legs. Independence in mobility is a graded phenomenon and for any particular individual may depend on their environment and on the particular task imposed. Ideologically, there is no reason why concepts of independent mobility should be downgraded for the elderly. However, where the clinical assessment of elderly frail and/ or patient populations is concerned, most mobility scales, or mobility items within basic activity of daily living scales, tend to address only a limited range of basic activities and have very definite ceiling effects. Mobility outcomes are limited to the ability to move into and out of the basic human positions of lying, sitting and standing together with the ability to walk indoors and climb stairs. Nonetheless, adequate lower limb function is one pre-requisite for independent mobility described even in such basic terms. An elderly patient will be classed as independently mobile if they are able to rise, stand, walk and, should their home environment require it, able to ascend and descend stairs without assistance. Where external support is required from a walking aid, the person may be considered independently mobile with an aid.

### **2.2.2. Evidence of Mobility Impairment after PFF**

The evidence to support the view that PFF is often associated with a long-term decline in mobility, as defined above, comes from a diverse body of research. Mobility status has been investigated pre and post PFF, using between and within subject comparisons, experimental correlation and case controlled designs, and employing a diverse range of measures, measurement tools and assessment schedules. Measures of mobility range from simple to complex, from nominal outcomes to detailed scales, from standardised tools to apparently one-off, study specific measures and from self-reported ability to observer rated measures (34). Examples include comparison of pre and post fracture gait independence and walking aid use, carefully delineated gait tasks (set time or set distance walking tests), transfer tasks (chair rise time), composite tasks (timed up and go) or specific mobility scales, e.g. the Elderly Mobility Scale (35). Also, mobility outcomes are often subsumed within scales for measuring basic activities of daily living, e.g. the Barthel (36).

There is research evidence to support the following. After hip fracture, people rise from a chair and walk more slowly (18). They are more dependent on walking aids for the first time or more dependent on a higher category of walking aid than before (37). They are less able to climb stairs (31), (3) or walk outside and they are unable to walk as far as they did before (3). In Scotland, only 40-45% of patients had the same measured walking ability at 4 months post PFF as pre PFF and furthermore this was at the expense of increased use of walking aids (2). Elsewhere it has been reported that as many as 66% of PFF patients still suffer impaired mobility at six months post surgery, compared to pre-fracture state (23).

The causes of impaired mobility post PFF are poorly understood (23). They are likely to be many in number, physical, psychological and social in origin and they may vary between individuals. However, there is strong evidence to support the presence of significant quadriceps weakness within patients who have undergone surgical fixation after PFF. As one of the major leg extensors, weakness of it may be an important contributor to disability after proximal femoral fracture (3), (4). The nature of this weakness and the argument as to why it may be an important factor in poor mobility post PFF fixation will be outlined in the next sub-section.

### 2.2.3. Impaired Quadriceps Function and Impaired Mobility after PFF

Before discussing the nature and evidence of impaired quadriceps function and its relationship to mobility after proximal femoral fracture, two broad, but overlapping concepts of muscle function require clarification: strength and power,

#### *2.2.3(i) Strength versus Power*

Strength is an umbrella term, often used in a non-specific and therefore non-technical manner, to refer to different aspects of skeletal muscle force production and also to overall physical ability. In engineering terms, however, the strength of a material refers to its ability to withstand force or stress (be this as the result of shear, tension, or torsion) before breaking. Put simply, one material is stronger than another if it can withstand a higher total amount of the stress in question. For this reason, perhaps, the most commonly used measure for skeletal muscle strength is force of maximum voluntary isometric contraction (MVIC). Isometric pertains to production of force without movement around a joint and isometric effort over time equates to static muscle work. Isotonic strength refers to force generating capacity under concentric or eccentric contraction conditions, i.e. where joint movement together with muscle shortening or lengthening are involved, and is commonly measured by the maximum load that can be moved in one or ten repeated maximal efforts. Thus muscle strength can refer to force generating capacity in static or dynamic conditions.

Muscle power is a different, but related and potentially overlapping concept. It is defined as the capacity of a muscle to do work and is measured as the product of forces generated and velocity of movement or velocity of force generation (38). Thus, measures of power relate to strength development over time. Unlike 'inert' materials, the different metabolic processes (anaerobic or aerobic) that support the development and maintenance of muscle tension further complicate the specifics of human performance. Therefore, in physiological or biomechanical investigations, it is good practice to define the type of muscle performance under investigation. This will involve a precise description of what is being measured in terms of muscle contraction type or motor task, force generated, range of movement, time frame and whether single, repeated or sustained effort. Thus measures of muscle performance range from the simple to the complex. Examples of simple measures include MVIC at a specified joint angle, one repeated maximal effort (1RM) or peak isokinetic muscle contraction of a specified type (concentric/ eccentric) at a constant and named angular velocity. Some examples of more complex measures are maximal rate of force rise time or force frequency relationships for given actions. Where maximal effort is elicited, researchers should distinguish whether they are recording the peak or average value of a

specified number of maximal attempts and also the specified time frame within which each maximal tension generating effort is made.

### *2.2.3.(ii). LEP and Quadriceps Impairment in the Elderly*

According to the above, there are numerous ways of measuring and thus defining impaired quadriceps function. Leg extensor power (LEP) is a commonly used measure in elderly, frail elderly and proximal femoral fracture (PFF) research. LEP is a measure of the speed and force of concentric contraction of the extensor muscles of the lower limb. The primary extensors are the gluteus maximus at the hip and the quadriceps femoris at the knee. Optimisation of LEP will depend to a lesser extent on the muscles that stabilise around the hip, trunk, tibia and foot. As a delineated measure of muscle performance, LEP is useful in that it reflects the fact that composite leg extensor activity is required for basic mobility. However, as scientific terminology it lacks precision. LEP is required for rising from a chair, walking, stair climbing and stamping on the break pedal for an emergency stop when driving, for example. But in each of these activities the nature of the LEP involved differs according to the start and stop position of the joints around which extensor force is exerted and the required speed of the action. Accordingly, LEP can be measured in a number of different ways. It can be assessed via functional tests such as timed stair climbing or maximal vertical jump off a force plate. The latter involves hip extension towards neutral, but is less suitable for the elderly, and as a measure of LEP may be polluted by poor balance reactions. Or it can be measured by the Nottingham Power Rig (see 4.2.4.). This device measures maximal explosive LEP (the data reflects maximal extensor force generation during the first second of effort) (39). This device measures LEP with the hip maintained in a flexed seated position, such that only the knee moves into full extension, which therefore places increased emphasis on the knee extensor element of LEP. The quadriceps muscle group acts as the primary knee extensor. Frail elderly people have been shown to have reduced quadriceps strength and decreased explosive LEP compared to age-matched healthy elderly people (3), (4). LEP values for patients recovering after PFF fixation have also been reported (18), (5) and these compare poorly to the normative values reported for healthy elderly subjects (40).

### *2.2.3.(iii). LEP, Quadriceps Strength and Impaired Mobility in the Elderly*

Several studies using elderly subjects have shown that LEP is a determinant of many tasks required for basic independent mobility. Peak maximal leg press power, together with physical activity were independent predictors of self-reported functional status in a correlation study of 80 community-dwelling women, mean age of 75 ( $\pm 5$ ) years and mean number of chronic diagnoses of 3.2 ( $\pm 1.9$ ) (41). In this study, LEP was measured as dynamic concentric lower limb

extension effort in a single repeated maximal (1RM) leg press test. Maximal explosive LEP as measured by the Nottingham Power Rig, has been associated with gait speed, stair climbing speed and step up power in very elderly men and women (39) and when standardised for body weight to influence chair rise time and step height (42). Quadriceps strength (MVIC) and LEP and have been shown to be predictors of sit to stand time, gait speed and stair climbing time in elderly women (mean age 80 years) with a previous hip fracture (4). Fractured limb LEP one week after PFF fixation has been shown to be a key determinant of walking speed and stair climbing time (43).

Intuitively muscle power relates more closely than isometric strength to the mobility demands of everyday living, however the two concepts are not unrelated and a strong quadriceps, i.e. a quadriceps that can demonstrate a higher isometric contraction force is also likely to be a more powerful one. Several studies have examined the impact of quadriceps strength on mobility tasks in the elderly. A large cross-sectional study of 230 subjects, randomly selected from the population register and aged 75 years, were tested for MVIC of knee flexion and extension using an isokinetic dynamometer, the gold standard instrument for muscle testing. It was found that increased lower limb strength correlated with faster gait speed and longer step length (44). In a controlled intervention trial 100 subjects, functionally impaired and aged above 65 years, had the isokinetic and isometric strength of their knee and ankle extensors and flexors measured using similar equipment. After a 10 weeks home program of lower limb resistive training (the control group were instructed not to initiate any new exercise regime during this time), lower extremity strength gain was associated with gains in chair rise performance, gait speed and in transfers and stair climbing (45).

#### **2.2.4. Aetiology of Quadriceps Impairment**

The vast majority of hip fracture patients are elderly (see 2.1.3 above) and this has implications for the state of their muscles. Aged skeletal muscle appears to differ from young skeletal muscle not only in terms of its reduced functional ability, but also in its physiology and histology. Aged muscles show similarities with, and differences to, muscles that have atrophied through disuse.

##### *2.2.4.(i). Aged Muscle*

Research in the field of aged muscle seeks to distinguish the effects of ageing per se from the effects of the chronic conditions associated with old age and from the effects of the reduced physical activity that often, but not necessarily, accompanies old age. In order to differentiate the effect of ageing from any concomitant impairment due to co-morbidity, some studies have particularly selected elderly subjects to meet strict health criteria. Studies of the quadriceps

function in such healthy elderly have shown a decrease in strength and even greater decrease in power with increasing age. Estimates for the change from youth to middle and old age have been derived from both cross-sectional and longitudinal designs in different countries and using different measures of assessment. Inevitably, results vary. In one such cross sectional study of healthy subjects aged from 65 to 89 years of age, maximum voluntary isometric contraction (MVIC) of the knee extensor muscle appears to decline by 1-2% per year of a 77-year-old's value (42). According to the same cross sectional study, with age there comes an even greater reduction of knee extensor power with associated losses of 3-4% of a 77-year-old's value per year. Cross sectional studies are open to the confounding influence of cohort effects such as systematic lifestyle variance between different eras. However, the longitudinal and within subject studies of strength and power that exist appear to concur with the principle of decline. Men and women both suffer an age related decline in strength and power and healthy elderly women have been shown to have lower power to weight ratio than aged matched healthy elderly men (46).

A strong quadriceps can generate a large amount of extensor force and a powerful quadriceps can generate large amounts quickly. Muscles consist of a mixture of different fibre types: Type I slow twitch fibres, Type IIa fast twitch oxidative fibres and Type IIb fast twitch glycolytic fibres. The latter rely on an anaerobic metabolic pathway and are primarily responsible for the generation of large amounts of force quickly (47). Since the proportion of Type IIa to Type IIb varies among individuals (46), the more power a quadriceps muscle exhibits, the more likely it is to have either a predominant proportion, or selective hypertrophy (or both) of its Type IIa fast twitch fibres. Conversely, it might be expected that the weaker it is, the lower the number of Type II fibres and at the smaller their CSA. It is certainly known that the total CSA of the quadriceps muscle group is highly correlated to the maximal amount of isometric force it can generate (47). The data from the age-related muscle performance studies presented in the previous paragraph is endorsed, therefore, by the results of laboratory tests based on biopsies of the human vastus lateralis. It should be pointed out that there are potential methodological issues in these biopsy studies (46), not the least concerning histological stain tests to identify Type I, IIa or IIb muscle fibres; elderly skeletal muscle appears to have more hybrid fibres (48). Nevertheless, they provide some evidence of the following changes in elderly muscle physiology. In elderly muscle there is a reduction in overall mass as measured by cross sectional area (CSA). This loss of mass is due to a reduction in the total number of fibres and is consistent with long standing, progressive and only partially compensated denervation at the spinal cord (46), (49). Although motor units increase in size, there are fewer of them (50). Also, there may be more fat or connective tissue within the CSA, resulting in a lower specific strength,

which is defined as force per unit of CSA (51). Although the relative proportions of Type I and II remain the same, specific strength may also diminish partly because of a selective decrease in the size of Type II fibres. Elderly men have been shown to have a reduced size and CSA of Type II fibres (52) and in the quadriceps of female PFF patients, there is evidence of a smaller cross sectional area of these fibres compared to age matched contemporaries (53). In vitro, these Type II fibres have been shown to contract more slowly than Type II fibres from younger muscles, which may be due to slower  $Ca^{2+}$  channel release rate in their sarcoplasmic reticuli (Del Bonoo 1995 cited by Harridge and Young (54)).

Most patients who break their hips are not just elderly, but also frail elderly. One reason why many PFF victims do not recover their pre fracture mobility and related functional independence, or do so quite slowly, may be because their age pre-disposes them to a greater number of co-morbid conditions. Co-morbidity is defined as multiple, simultaneous, interactive pathology (55). Eighty percent of PFF patients have hypertension, diabetes mellitus, Parkinson's disease or dementia (23). Thus, it is possible that PFF victims are inherently less healthy, and have lower physical reserves, than their age matched contemporaries. This frailty may reduce physical activity and therefore lead to muscle detraining effects in addition to those of ageing and morbidity. Many patients pre PFF may be operating at the threshold levels of muscle power needed for their daily lives with little or no reserve. Hip fracture may simply be the catalyst for functional decline selecting out the elderly of indifferent health who then may then be at a recuperative disadvantage. The impact of co-morbidity may be reflected in pre fracture functional status. Indeed, there is evidence to suggest that pre fracture ability to perform the activities of daily living, measured either specifically or via reliance on external help reflected in residential status, is a predictor of PFF rehabilitation outcomes (3),(37),(56).

## **2. 2. 5. Quadriceps Training in the Elderly and After PFF fixation**

While the context of rehabilitation has been relatively well investigated, the content of in-patient rehabilitation has been poorly described (57) and under-researched (20), (58). PFF rehabilitation should be multi-disciplinary and most members of the team will contribute to early weight bearing and mobilisation. Specific responsibility for focal mobility re-education and practice and muscle training interventions are addressed by physiotherapists. There is strong evidence that the performance of elderly muscle can be improved through training, even for the frailest of adults (59), (60). In our own department progressive, high-intensity quadriceps training after PFF has been shown to increase leg extensor power and decrease disability (5). However this approach does require a degree of patient motivation. The next section of this chapter addresses

electrical stimulation in skeletal muscle training. This modality may be a useful adjunct to rehabilitation and may negate or supplement the need for patient effort.

## **2. 3. Electrical Stimulation to Improve Skeletal Muscle Function**

### **2.3.1. Overview**

The effects of the application of externally applied electric current to normally innervated human quadriceps have been investigated in a variety of laboratory and clinical situations, using healthy subjects and those with orthopaedic conditions, and in subjects drawn from different age groups. Clinical research is dominated by studies based on young populations and their pathologies, but there are some studies which have specifically addressed clinical conditions that affect the middle aged and elderly populations, such as arthritis. There is also a small body of research pertaining solely to the effects of electrical stimulation in very elderly populations.

Therapeutic electrical stimulation is a subject laden with specialist technical terms that are used neither consistently nor discretely (61). Furthermore, it has been stated that, 'Selecting optimal stimulus characteristics for strength training in weakened and normal musculature presents the investigator with a complex task. Present indications are that there is likely to be considerable subject variation in response to electrical stimulation and optimisation may relate more to the subject than the stimulus parameters themselves (62). Therefore, this section necessarily begins with some definitions, before providing an overview of the variety of motor stimulation currents available and a review of the individual current and training regime parameters to consider when setting a training protocol. Chapter 3 then present the results of a systematic search and structured review of the literature on training studies of ES of normally innervated quadriceps, with a particular focus on clinical populations.

### **2.3.2. Definition of terms**

Electrotherapy is the umbrella term for any application of electrical forces to bring about therapeutic change. Although the term pulsed electric stimulation has been used to refer to short wave diathermy, a thermal modality which targets collagenous tissue, more commonly electrical stimulation refers specifically to the stimulation of excitable tissue, i.e. human muscle or nerve (61). Technically, it is possible to directly trigger skeletal muscle action potentials, via the depolarisation of the sarcolemma of muscle fibres. However, since the fibres have an increased impedance and thus higher threshold to activation than the motor nerves, the latter are first depolarised causing subsequent effect in the former (63). Therefore, in practice any reference to

muscle stimulation in normally innervated subjects is a technically incorrect; it is the motor nerve that is the target of stimulation (61), (63). For this reason several authors prefer to use 'neuromuscular electrical stimulation' to describe the treatment. Sundry other terms are current in the literature: electromyo-stimulation, electro-motor stimulation, functional electrical stimulation and, rarely, transcutaneous electrical nerve stimulation (TENS). Functional electrical stimulation is most commonly used to refer to use of more complex, multi-muscle electrical stimulation used to produce composite functional actions in denervated subjects, e.g. sit to stand in paraplegics. TENS has come to pertain almost exclusively to specific low intensity, battery operated sensory nerve stimulators used for pain management (61). Normally innervated skeletal muscle is also stimulated most commonly by means of transcutaneous electrodes (as opposed to via percutaneous needles or implanted electrodes). Thus, the most accurate label for the intervention being investigated in this research project would be transcutaneous neuromuscular electrical stimulation or TNMES. However, for simplicity, the term electrical stimulation and the acronym ES will suffice.

Definition of terminology becomes more complicated when comparing the detail of ES protocols, i.e. current specifics. Most commentators rue the lack of reporting standardisation in both clinical and laboratory trials (8),(64),(62),(61). Treatment labels have come to have specific meanings which are neither informative, nor used consistently (e.g. Galvanism or Faradism). Technical vocabulary appears blurred with different writers using the same word to mean different things. One example of this is the use of the words pulse, burst and train. An electrical pulse could refer to a single electrical waveform (or phase or cycle), i.e. to the single basic unit of current. Or it could refer to a burst of current, i.e. a brief on time. Without clear definition, it is difficult to know whether pulse frequency (i.e. pulses per second or pps) pertains to the basic current frequency or to a burst frequency (i.e. bursts per second or bps) produced by modulation. Pulse duration might refer to something quite distinct from burst duration, just as pulse shape might from burst shape. Additionally, a pulse train may be the same thing or something different to a current burst. A pulse train refers to a discrete series of pulses (single electrical phases) grouped together and followed by a distinct rest interval. Thus, a single burst of current might contain a single or several pulse trains. If the definition of the word pulse is not made clear from the start (and often one writer's pulse is another's burst), the inevitable result is obfuscation. In the absence of a universal nomenclature imposed by a global ES standards board, this paper will adhere to the language usage set out in Figure 1.

**Figure 1. Clarification of ES Terminology**

<p><b>Electric Current:</b> a flow of electrical charges subject to a superimposed voltage</p> <p><b>Direction:</b> monophasic (unidirectional, i.e. direct current) or biphasic (alternating current)</p> <p><b>Continuity:</b> continuous (constant) v. interrupted (sometimes called pulsed)</p> <p><b>Current Intensity:</b> the rate of flow of electrons (Amps) or amount of charge (Volts)</p> <p><b>Amps = Volts (electric pressure)/ Ohms (resistance to flow)</b></p> <p><b>Power = Volts x Amps (Watts)</b></p> <p><b>Pulse or Wave or Cycle:</b> the single, basic unit of current</p> <p><b>Duration:</b> pertains to the temporal width of the basic unit of current</p> <p><b>Shape:</b> the shape of the rise and fall of the basic unit of current</p> <p><b>Frequency:</b> number of pulse repetitions per second (Hz).</p> <p><b>Interval:</b> the rest time between single pulses</p> <p><b>Phase:</b> one segment of a multi-segment pulse</p> <p><b>Train:</b> a discrete group of single pulses</p> <p><b>Duration:</b> pertains to the temporal width of the train</p> <p><b>Shape:</b> the shape of the rise and fall of the train</p> <p><b>Frequency:</b> number of train repetitions per second (Hz).</p> <p><b>Interval:</b> the rest times between separate trains</p> <p><b>Burst:</b> a short interval of current on time at a micro level (Hz)</p> <p><b>Duration:</b> pertains to the temporal width of the burst</p> <p><b>Shape:</b> the shape of the rise and fall of the burst</p> <p><b>Frequency:</b> number of burst repetitions per second (Hz).</p> <p><b>Interval:</b> the rest times between separate burst</p> <p><b>On: off cycle:</b> current 'on' time in seconds to current 'off' time in (usually seconds)</p> <p><b>Duty cycle:</b> the ratio of current on: total cycle time (usually seconds)</p>
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another problem area arises with the broad classification of currents by low, medium and high frequency bands. One writer's high frequency can be another's low. For example, the motor nerve stimulation range is commonly accepted to lie between 20 and 100Hz (61), yet there are obviously low, medium and high options within this range. In turn, the entire motor stimulation range itself may be described as low frequency when compared to medium range frequencies (which some would describe as being 100Hz and over, but which most commonly refer to frequencies in the thousand of Hz band) and high range frequencies (millions of Hz). Not all writers quantify what they mean by their chosen band descriptor. Thus, when high frequency currents are stated to cause greater muscle fatigue, without quantification of the actual frequency involved, no useful scientific statement is made

### **2.3.3. Motor Stimulation Currents**

Low and Reid detail a comprehensive list of all therapeutic currents that have been used in physiotherapy (61). The wide ranges of currents that have been used to stimulate skeletal muscle have been extrapolated from this list and are detailed in Figure 2.

From figure 2, it is clear that electrical pulses or bursts of different duration, shapes and frequencies and delivered by currents that may be direct or biphasic, continuous or interrupted, single or combined can all produce muscle contraction. Single pulse duration according to the above can vary from 0.1ms to 1000 ms and pulse intervals from 1ms to several seconds. While frequency appears to vary from 30Hz to 4000Hz, the motor stimulation range (which could be the pulse frequency, the burst frequency or, in the case of interferential current, the beat frequency) is limited to between 30 and 100Hz (see 2.3.4.).

This variety raises the question of how comparable different ES muscle stimulating regimes are, not least because they also vary beyond the parameters discussed so far. Further considerations include: uniform or variable frequency; duty cycle variation; current ramp variation; repetitions per session; variation in session frequency and total number per course of treatment; variations in number, size and type of electrodes and coupling medium used; type of generating unit; target level of intensity and position of limb during stimulation. Not surprisingly, it is generally agreed that the ideal set of motor stimulation Parameters for muscle training has not been established. The main problems (quality of experimental design aside) appear to be there are too many variables for one study to address and that many studies do not outline the intervention in sufficient detail for comparison.

**Figure 2. Motor Stimulation Currents**

Extracted from Low and Reid, page 33 (61)

1. Interrupted direct current with long duration (1 to 600ms) square wave pulses and pulse intervals from 1millisecond to several seconds.
2. Interrupted direct current with short duration (0.1-1ms) faradic type pulses at frequencies between 30 and 100Hz.
3. High voltage galvanic (continuous direct current) or high voltage pulsed galvanic (similar to 1. above).
4. Faradic current: asymmetrical biphasic waveforms of short pulse duration (0.1ms to 1ms) at frequencies of around 60Hz.
5. Sinusoidal currents (evenly alternating sine waves) with pulse duration of 10ms delivered at 50Hz as per the UK mains, but at no more than 80V.
6. Diadynamic currents (similar to 5. above): simply rectified and modified mains alternating current with 10 ms pulse duration and frequencies of 50 or 100 Hz.
7. Russian current: an interrupted sinusoidal current with a short pulse duration of 0.4ms alternating at the much higher frequency of 2500Hz and interrupted 50 times per second to provide a burst duration of 10ms and a burst interval of 10ms (i.e. medium frequency current delivered in low frequency bursts).
8. Interferential current: two alternating sine wave currents of about 4000Hz (therefore pulse duration of 0.2ms) interfering to produce a lower frequency (10 - 130Hz), physiologically active current called the 'beat' frequency response to ES of different individuals (62). This section therefore moves on to a more detailed consideration of the individual items that should be considered when setting an ES muscle training protocol. Parameters will be considered under the following headings: technical parameters (current and application specifics) and training regime parameters.

#### 2.3.4. Technical Parameters

In electrically stimulated muscle contraction, motor neuron action potentials are triggered by an electrical current that flows through the tissues in a complete circuit between two (or more) electrodes. Similar to principles of voluntary muscle strength or power training, training effects via ES may arise directly as a result of the level of muscle tension generated by electrical means (36). Therefore when using ES as a training modality with the aim of producing chronic augmentation of muscle performance, the objective is to produce as strong a tetanic contraction as possible within subject tolerance and that causes no adverse muscle damage. This requires sufficient charge to de-polarise the motor neurons supplying as many of the motor units as possible at an optimal tetanising frequency. The technical parameters that contribute to this end effect are a) the current characteristics and b) the application method.

##### *2.3.4. (i). Current Characteristics*

The basic unit of the current is its pulse, although the basic unit of stimulating current may be a train or burst comprising a series of pulses (as defined in Figure 1 earlier). It has been suggested that various features of an electrical current may be manipulated to produce a more efficient or acceptable stimulation effect. These are its pulse shape and duration (A) and its pulse or burst frequency (B), the two latter of which demonstrate a certain degree of inter-dependency in effect. Current intensity (C) is another important characteristic to consider.

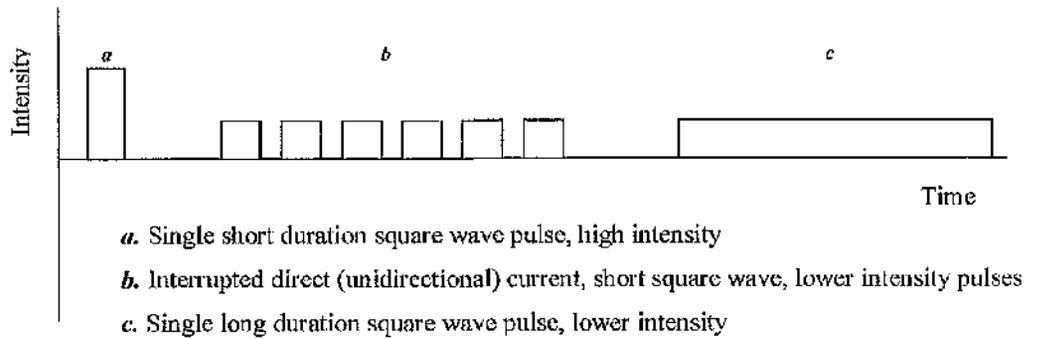
**A. Pulse shape and duration:** The shape and duration of an electric pulse reflect whether the current is monophasic or biphasic, how the electron flow (i.e. charge) rises and falls within each pulse and the time course of charge delivery. The area under the pulse curve represents its total amount of charge. Although monophasic (most commonly known as direct) currents have been used for motor stimulation, alternating current is often preferred to avoid the potential risk of chemical damage at the electrode site from unidirectional ionic flow (36), (61). Where alternating currents are concerned, it is the positive segment or phase of a biphasic pulse that acts on the motor neuron. The negative phase merely reverses the current flow to ensure a net nil flow of charge. By this point, of course, the neuronal action potential, which is an all or nothing event, has been triggered. Shape of the activation phase of the electrical pulse does not appear to be a critical factor other than that the rise time should be as fast as possible (62).

Hence the frequent use of square or rectangular shapes as shown in Figure 3 (i). Asymmetrical biphasic square waves deliver the de-polarising charge in a short sharp package, then reverse the electrochemical flow in the tissues over a longer period as shown in Figure 3 (ii). Pulse duration, or in the case of biphasic pulses, activation phase duration, seems a more important issue. Shorter duration activation phases are preferred for motor stimulation for reasons of comfort. First, they preferentially target the larger diameter and thus faster conducting motor nerves, compared to slow conducting pain fibres; second, they reduce skin impedance and therefore require less charge in order to penetrate subcutaneous tissue to reach the motor fibres. Therefore most effective pulse duration for targeting motor nerves can be as short as 0.05 to 0.02 ms (61). Continuous currents with pulses of these short lengths fall into what has been described as the 'medium' frequency range. In order to stimulate motor nerves effectively these 'carrier' currents are then modulated by means of interruption or interference to produce lower burst or beat frequencies as described earlier, see Figure 3 (iii).

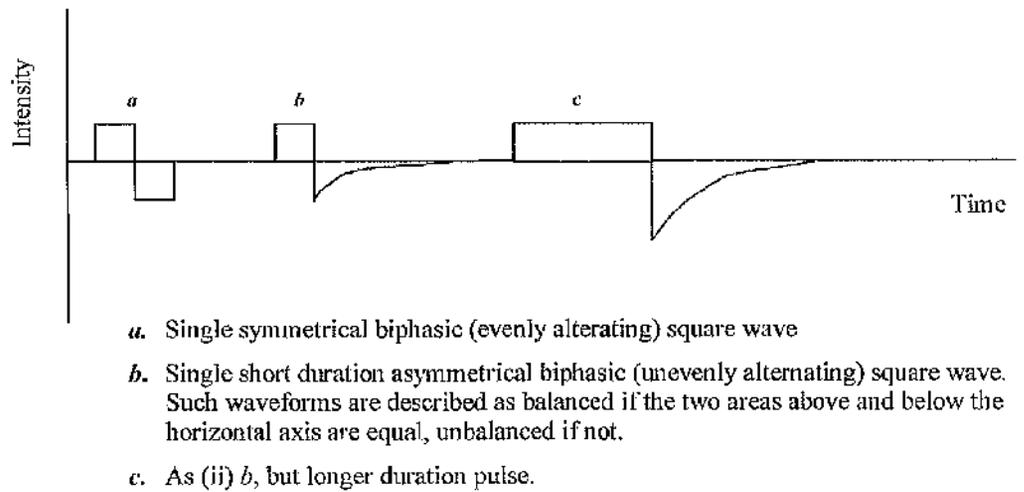
**B. Pulse or burst frequency:** Frequency appears to be one of the most debated current specifics in motor stimulation research. The upper limit for an maximally effective stimulation frequency (i.e. produces maximal muscle contraction force) would be dictated by the maximal firing frequency of the target motor units in their un-fatigued state. This is dictated by the time-course of the muscle fibre action potentials (to be differentiated from the motor neuron action potentials), from the initial de-polarisation to the end of the absolute refractory period. For a given current intensity and pulse duration, strength of effect depends on frequency of firing. As described by Tortora, at 1Hz there will be a twitch, at 10 Hz there may be several twitches (tremor) and around 30Hz tetanic contraction will begin (65). Without altering the current intensity, contraction strength then increases with rising frequencies up to 100Hz. Thereafter subsequent pulses (depending on their duration) fall into the absolute refractory period and have no effect. Thus, the tetanising motor stimulation range, depending on the target muscle, is normally accepted as being from 30Hz up to 100Hz. For a given pulse duration, higher frequencies in this range require less current to produce the same effect as the lower frequencies, since the same amount of charge is being delivered at more frequent intervals. No apparent consensus appears as to the optimum frequency, which may vary by muscle group and by individual, but the most commonly used frequencies appear to lie between 30-50Hz (64),(62). It is scientifically rigorous to identify whether a carrier frequency is being modulated to deliver lower frequency bursts of stimulating current. However the difference between a motor stimulation frequency produced by single pulses or by modulated bursts of higher 'medium'

**Figure 3. Electrical Pulses (adapted from Low and Reid (61))**

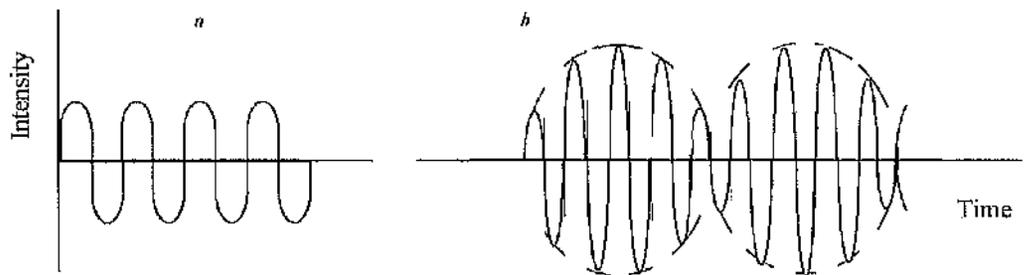
**(i) . Monophasic square waves**



**(ii) Biphasic symmetrical and asymmetrical square waves**



**(iii) Sine wave pulse shape and currents**



- a.* Continuous, evenly alternating sine wave current at 2,500Hz (i.e. 'medium' frequency)  
*b.* Sine wave current as above, but modulated to 48Hz.

frequency current has been viewed as being not very obvious in practice (62). Although there appears to be controversy over whether higher frequencies of ES produce greater muscle fatigue, the literature is unclear as to the precise nature of 'higher' (i.e. 100's or 1000's of Hz). There is a long chain of electro-chemical-mechanical events that takes place in between motor neuron depolarisation and eventual muscle contraction. Fatigue is the result of failure of one or more of these linked events (66). Electro-chemical fatigue has been said to occur when failure occurs prior to the release of the  $\text{Ca}^{2+}$  ions in the muscle fibres; mechanical or metabolic fatigue when failure occurs thereafter (66). It is beyond the scope of this thesis to systematically review the theoretical and laboratory investigations into what is a highly complex area. Although ES induced fatigue may be qualitatively similar to that produced by voluntary work (67), one cautious approach to frequency selection might be to use the minimum necessary to produce the maximal force output (68). There is some consensus that longer rest intervals between contractions, i.e. smaller ES on: off ratios may also mitigate fatigue effects (69), (70), (71). One further question is whether varying, as opposed to maintaining a fixed frequency during one session may be more effective at maintaining force of contraction over treatment time (i.e. reducing the effects of fatigue) (66).

**C. Current intensity:** The area under the pulse curve that results from plotting amount of electron flow (mA) against time represents the total amount of charge delivered to the tissues by successive pulses. Current flow is synonymous with intensity. Electron flow is determined by conductor resistance (Ohms) and voltage (electrical pressure to flow, often likened to hydrostatic pressure). For a given resistance, intensity can only be increased by increased voltage; for a given voltage, increased intensity can only be produced by decreased resistance. It is commonly accepted that, within safety limits, higher current intensity produces greater intensity of ES induced muscle contraction. The reasons for using as high as possible current intensity are as follows. 1) In transcutaneous stimulation cutaneous sensory nerves are always be affected first and the deeper motor nerves only be stimulated with greater intensities. 2) When electrical charge is delivered during the relative refractory phase of a motor neuron, further action potentials can only be triggered by a supra-threshold stimulus and therefore require a higher intensity of stimulation (65). 3) Providing sufficient charge is delivered to de-polarise the motor neuron cell membrane to its threshold value, a higher intensity will have no further effect on that cell (action potentials are an all or nothing event). However, the surplus charge may ensure that more fibres are reached, resulting in stronger and more widespread muscle contractions. In practice, however, it is subject tolerance that mostly determines the maximum intensity that can be applied via ES (62), (72). For this reason, it is important to optimise all features of ES application that contribute to comfort. One technical parameter that may help is the addition of a

current ramp leading up to the stimulating intensity. Some writers describe this as current modulation. Essentially it means that successive pulses during the first few seconds of on time in any one duty cycle are delivered with a graduated increase in intensity. If rate of rise of current is very slow, however, there is the potential for the motor neuron cell membrane to accommodate.

Not all generator units allow a full choice of current specifications (i.e. manipulation of ramp settings, pulse shapes or pulse durations). The efficacy of mains units have been contrasted with battery operated ones, which patients can be taught to apply and use for themselves. It has been suggested that there is little effective difference in force production between 'low' and 'medium' frequency generators (62).

#### *2.3.4. (ii). Method of Application*

Electrical stimulation of normally innervated quadriceps is near exclusively applied via transcutaneous electrodes. Various alternatives for electrode positioning exist. The active electrode may be placed over the lumbosacral nerve, the femoral nerve or the motor point of the muscle itself (73), (74), (69). The dispersive electrode is positioned distally on the quadriceps muscle group. Since the area of highest current density is the site of greatest effect, the more accurate the location of the active electrode over the trigger point, the less charge and the smaller area of current density will be required (61). Anatomical references exist for the approximate location of motor points for different muscle groups. However, there will always be individual variation and the most effective way of determining the most effective site will be through systematic individual trial and error (36).

Before siting the electrodes, the patient should be positioned in a comfortable manner with the knee flexed to lengthen the quadriceps muscle towards mid range, where it is at its angle of mechanical advantage and generates maximal force (8). This is commonly perceived to be in 60° of flexion (75) (64), although some commentaries have suggested less than this dependent on hip joint angle (8). ES may be more effective at increasing isokinetic muscle strength if ES is applied to a free limb that is able to move during contraction (64). There are a variety of different electrode sizes, materials, attachment methods and conduction mediums available. Electrode size is dependant upon the size of the target muscle, too small an electrode will increase discomfort as it will require a higher intensity of charge, too big an electrode will risk stimulation of the antagonist muscle (36). The trend has been towards self-adhesive, single patient use electrodes that combine adhesion and conduction medium in one. They are clean, durable and easy to apply, although their conduction efficacy in comparison to the older style

carbon electrodes and conduction gels has been questioned (76). Correct skin preparation has been shown to decrease impedance and thus contribute to comfort and optimal effect. This will be outlined in 4.3.3.

### 2.3.5. ES Training Protocols

Two basic types of ES training protocols have been differentiated in the literature. These are the "more muscle-endurance-type regimen" and the "more typical muscle-strength-training regimen" (77). The former are typified by 'lower' frequencies (defined as 50 - 200Hz), short rest intervals of equal length to the contraction time, but longer sessions and thus greater total ES on time. The latter are typified by longer rest intervals and higher frequencies (e.g.2500Hz). An alternative and more up to date analysis differentiates 'tonic' from 'phasic' style regimens. Tonic regimens feature prolonged ES sessions of up to 8 hours, undertaken during normal daily activity, using very low stimulation frequencies (below the accepted motor stimulation range and around 10Hz) and requiring only low levels of muscle contraction intensity. Phasic regimens fit with the more typical muscle-strength-training regimens above. They use motor stimulation frequencies in the 30 to 100 Hz band (64), sometimes produced via modulation and sometimes not, a limited number of repetitions (normally 10), aim for the highest possible contraction intensity and use longer rest intervals between repetitions. Program intensity is the sum of a number of different factors, which are tabled below (Table 2). Contraction or training intensity is described in various ways as also outlined in the table. It is sometimes measured as a percentage of the individual's MVIC and other times quantified by current intensity at maximally tolerated or maximally comfortable levels. Most often it is governed by what can be achieved practically, with this with notable individual variation (62).

**Table 2. ES Program Intensity: Contributing Factors**

ITEM	MEASURED	EFFECT ON INTENSITY
Contraction intensity	current intensity (mA or mV) or or % MVIC or in terms of patient tolerance (comfortable/ maximal)	Greater contraction intensity increases overall regime intensity.
Contraction duration	Seconds	Greater length of contraction increases overall regime intensity
Rest interval between contractions	Seconds	Shorter rest intervals increase overall regime intensity.
Number of contractions (repetitions) per session	Count	Greater number increases overall regime intensity
Rest interval between sessions	Normally deduced from sessions/ week data	Shorter intervals increase overall regime intensity.
Number of sessions	Number of sessions/ week x weeks of treatment	Greater number increase overall regime intensity.

### 2.3.6. Potential Mechanisms of Effect

Two different mechanisms by which ES training can produce improvement in muscle performance have been proposed. (36). The first is similar to that of the overload principle of resisted voluntary exercise, where a low number of repetitions and a high external load, relative to the maximum the untrained muscle is capable of acting on, are used to produce a high intensity of muscle contraction (8). It is proposed that only by stressing the contractile elements will they adapt to produce greater ability. That the superimposition of ES has in some instances appeared to augment the force produced by a maximal voluntary contraction has led to the proposition that a force deficit exists for such voluntary effort (6), (78). If ES can be used to produce stronger than maximal voluntary contractions, theoretically it might be considered a superior technique for strength training (62). There are an impressive number of studies that have found the ES induced contraction force, be this via stand alone or superimposed ES, to be less than maximal voluntary force (8) (64). However, providing ES can produce sufficiently high levels of muscle contraction, there is no need for it to produce stronger than maximal voluntary contractions to be a viable training medium where voluntary exercise is not possible or desirable for whatever reason. Several studies have reported ES induced training intensities (ie intensity of contraction as opposed to current intensity) as measured either by isometric mode isokinetic dynamometer or by strain gauge tensionometer. Variation in ES-induced contraction intensity expressed as percentage MVIC has been reported between studies, within studies and within individuals. Reported levels range from 25% to 104% of MVIC (62),(64).

The second theory of effect concerns potential neural effects of ES that could lead to improved performance. These are posited from studies that report significant gains in muscle performance after ES training, but with no associated muscle hypertrophy. In one such study greater force producing capacity was associated with higher intensities of ES. A clear cross transfer effect, which did not vary with intensity, was also demonstrated (9). These findings have led to the proposition that ES might produce enhanced performance via increased activation of anterior horn cells (accounting for the cross transfer effect), long term potentiation with increased synapse sensitivity, synchronisation of motor unit firing patterns and selective targeting of Type II motor units.

Laboratory studies have supported the view that motor unit recruitment order with ES is different to voluntary exercise. In the latter, initial recruitment of Type I (slow oxidative) fibres appears to progress to Type II fibres with greater effort (Anderson & Sjogaard 1976, Milner-

Brown et al 1973 and Gollnick et al cited (79)). The order reverses when activation is via ES (Garrett & Stephens 81, similarly cited (79)). Additionally, after sub-maximal ES of the quadriceps muscle specific Type II fibre glycogen depletion has been demonstrated, albeit in a small preliminary study (79). It has also been proposed that transcutaneous ES lowers the threshold of high threshold motor units (Garrett & Stephens 81). This might explain why ES protocols involving an intensity of muscle contraction lower than voluntary exercise, might produce increases in MVIC.

## **2. 4. Summary of Chapter**

PFF is a significant problem for patients and their carers, the health care system and social services. It produces major functional deficits that have been associated with impairment of quadriceps muscle performance. Quadriceps biopsy of female PFF patients has shown smaller cross sectional area of Type II fibres. While voluntary exercise has been shown to be of benefit, it does require motivation and sustained effort in an already frail population. ES is an accepted muscle training modality in some areas of physiotherapy and may depend to a lesser extent on patient motivation than voluntary exercise. It can, but does not always, produce a strong involuntary tetanic muscle contraction. However neither optimum ES stimulation parameters, nor the mechanisms by which any chronic effects result are clear. Chapter 3 proceeds to a review of the literature on training studies that have investigated the effect of ES on normally innervated quadriceps of young and old, healthy and clinical populations.

## Chapter 3

### LITERATURE REVIEW

#### ES TRAINING STUDIES OF NORMALLY INNERVATED QUADRICEPS

##### 3.1. Systematic Search Methodology

A systematic search of the English language literature was undertaken to identify studies of the application of ES to normally innervated human quadriceps muscle. A comprehensive list of key search terms was compiled from the range of alternatives used for ES described earlier in chapter 2.3.2. These terms were then used to survey the literature using both electronic and hand search methods as described below.

##### 3.1.1. Electronic Search

The list of key terms formed the basis of six customised search strings specific to the workings of the following electronic databases: Medline, Cinahl, AMED, Sportdiscus, Best Evidence and the Cochrane Collaboration. The 'generic' search string was as follows: [electric(al) stimulation OR electric(al) stimulator OR neuromuscular stimulation OR neuromuscular stimulator OR muscle stimulation OR muscle stimulator OR electomyostimulation OR electromyostimulator] AND [quadriceps OR rectus femoris OR vastus lateralis OR vastus medialis] NOT [spinal cord injury OR stroke OR cerebral vascular accident]. The six specific search strings and their results are displayed in Appendix A. Two levels of search were undertaken from 1977 to 2000.

##### 3.1.1.(i). Focal Search

A narrowly focused search applied the above string with two additional specifiers: either to include [hip fracture OR proximal femoral fracture] or with the application of an age limit to subjects aged over 65 years. This search produced only two references. The first was a conference proceeding extract presenting the results of an RCT concerning a study of low frequency, chronic quadriceps ES to women rehabilitating after fixation of proximal femoral fracture. It was possible to trace the thesis in which the full study had been published. In the month of this thesis submission, this study was published as a journal article (80). The second was a reference to a study comparing the effect of voluntary exercise with the effect of ES in healthy elderly males.

### *3.1.1.(ii). Broad Search*

A wider search was then undertaken without the above age and pathology delimiters. This produced considerably more material. From detailed reading of the references produced eight further studies were identified where subjects were over 65 years or suffering clinical conditions common to older patients.

### **3.1.2. Hand Search & Compilation**

A hand search was undertaken of the contents of the five years of publication, from 1995 - 2000, of two journals, 'Clinical Rehabilitation' and 'Age and Ageing'. A copy of the thesis by Lamb was also procured and scanned for additional material.

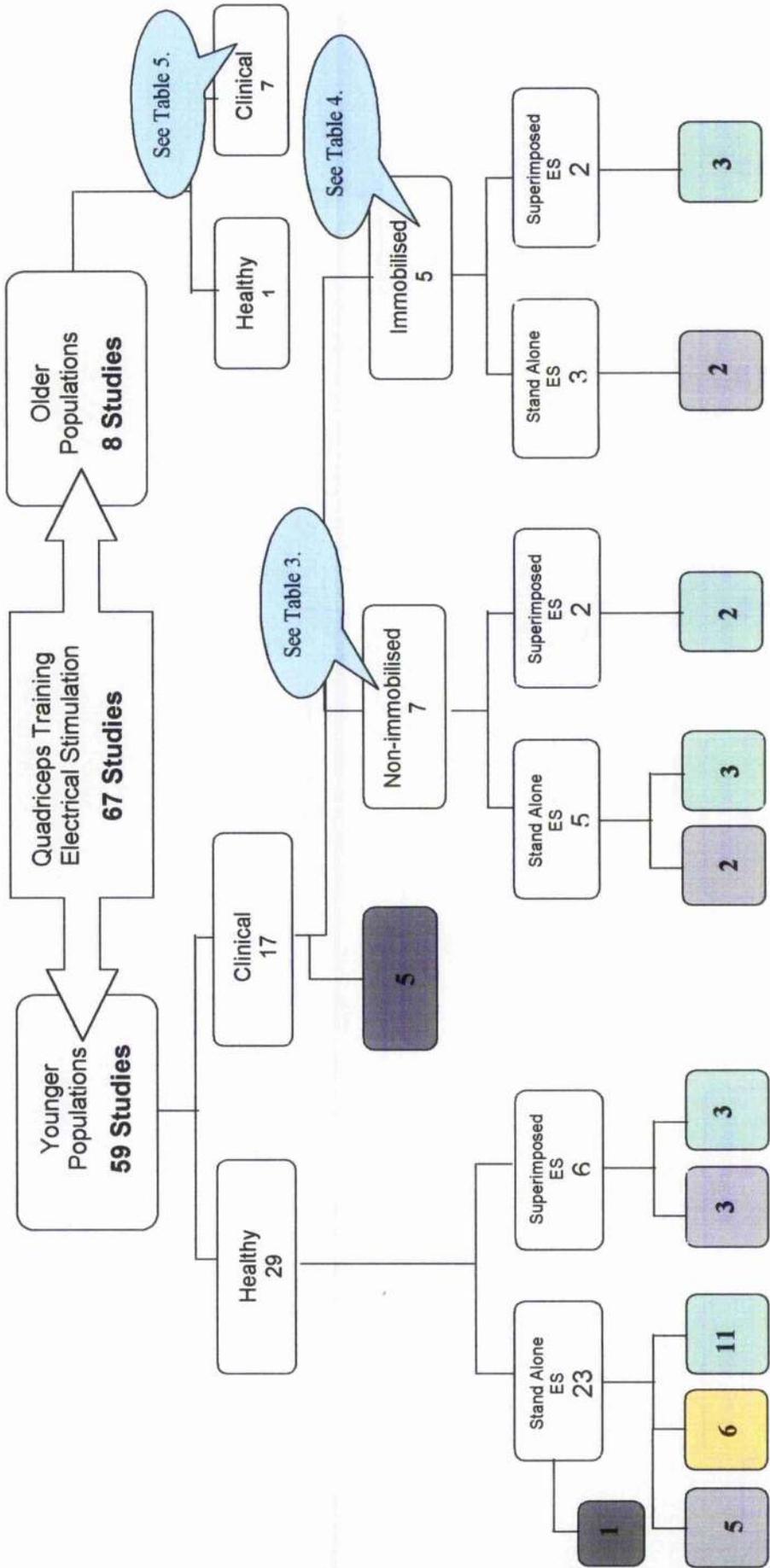
All titles and abstracts (where available) were compiled into a Reference Manager database, electronically searched to eliminate duplications, then visually scanned to exclude irrelevant citations, e.g. the use of ES in the treatment of incontinence, or duplicates missed in the electronic scan. The results were then classified firstly by type of ES application, laboratory style one off intervention or training study, and then by four population sub types: young healthy, younger clinical, old healthy and older clinical. The young healthy were mostly physical education or physiotherapy students aged in their twenties. The majority of young clinical were patients with orthopaedic knee conditions, tending to a predominance of anterior cruciate ligament repair studies. The older healthy were men aged over 70 years. The older clinical were mostly patients with osteoarthritic knees before or after total knee replacement, but also included one study of frail elderly female patients after PFF fixation and one study on patients post abdominal surgery (age range 25 – 73 years).

## **3.2. Structured Review Methodology**

### **3.2.1. Scope of Review**

It was beyond the scope of this thesis to undertake a structured, critical review of the entire body of research produced by the search strategy above, which included a large volume of laboratory style studies. Therefore, the following section is restricted to the literature pertaining to ES training studies, with a particular focus on ES training in clinical populations. A training study is defined as one that involves repeated application of ES with the aim of producing chronic effects in quadriceps muscle function or physiology. Figure 4 presents a flowchart breakdown of the 67 training studies sourced through the systematic search, by type and design basics.

Figure 4. Breakdown of Systematic Search Results by Study Design Basics



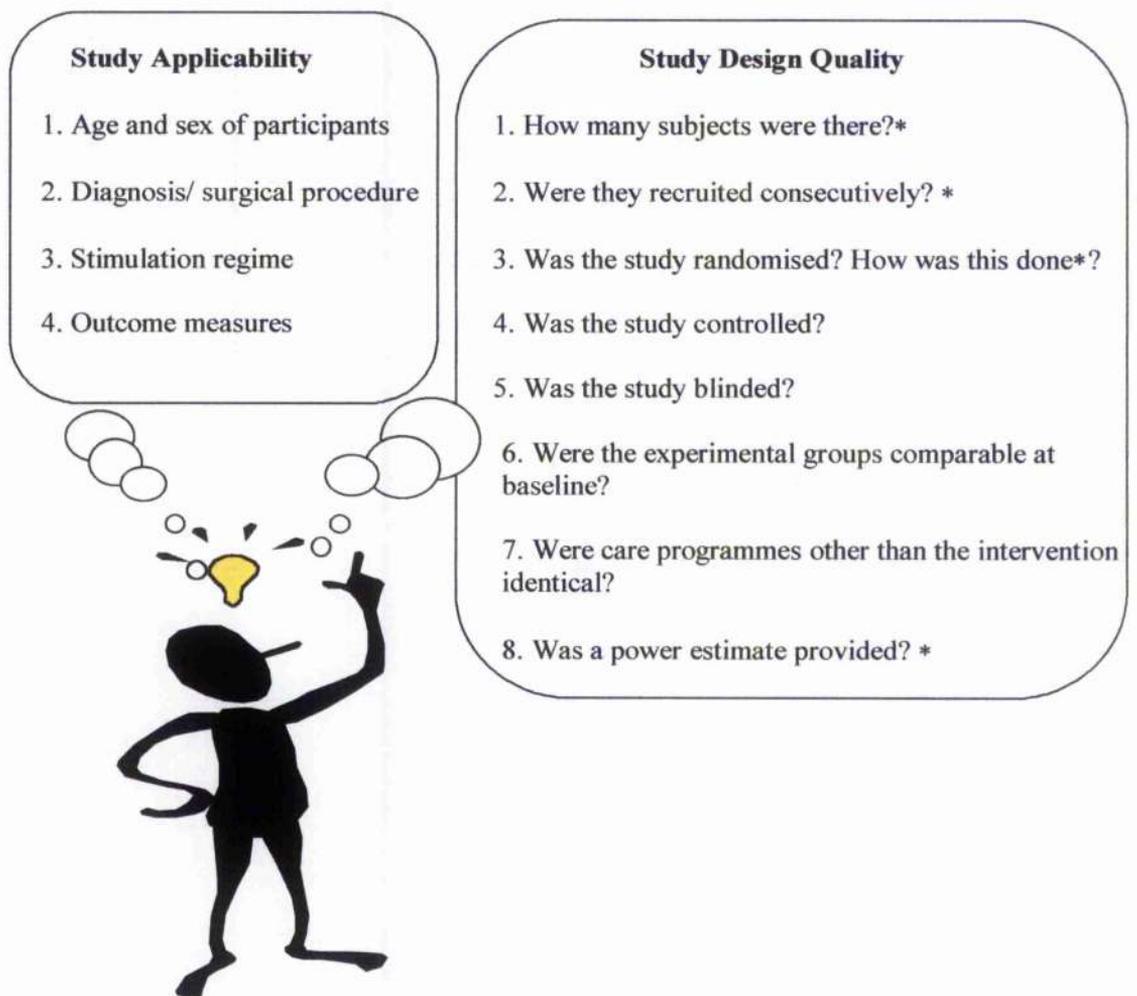
**COLOUR CODING**

- Rejected (single case etc)
- Rejected (inadequate controls)
- Controlled by contra-lateral limb
- Randomised and controlled

### 3.2.2. Review Criteria

The material was divided into research into young healthy, younger clinical, older healthy and older clinical populations as defined above (3.2.1). In order to facilitate the comparison of quality and applicability, all the studies were tabled using criteria based on a review of the literature by Lamb (18), but expanded to include some additional quality indicators, which are highlighted with an asterisk in Figure 5. Only the comparative tables for the trials in younger and older clinical populations are reproduced in this review. While blinding is an important quality indicator for the purposes of reducing observer bias, in many rehabilitation trials involving physical modalities, blinding of patient and treatment provider is difficult (81). Independent assessment is the most important form of blinding and becomes even more so where provider and patient blinding is not possible (33).

**Figure 5. Criteria for Structured Literature Review**



### 3.2.3. Critical Review Issues

Interpreting the results of ES training studies of normally innervated quadriceps in different populations, healthy or clinical, is complicated. Study comparison is fraught with difficulty for a number of reasons that will be outlined briefly.

First, there are noticeable deficits in the generic scientific quality standards of many clinical studies. Not all are randomised, assessor blinding is mainly absent, baseline comparison of study groups is rarely provided, sample sizes are small, power calculations rarely undertaken, sometimes the statistical analyses undertaken are inappropriate and often precision in reporting terminology is lacking. For these reasons alone the data from some trials might be considered uninterpretable.

Second, outcome measures vary both in their nature, which makes comparison of results difficult, and in the level of detail with which they are reported, which opens them to question over their reliability and validity. Some measures are crude, such as tape measured thigh girth, while others are gold standard (isokinetic dynamometry). However, even where the latter is the case, many studies attempt to evaluate some aspects of maximal muscle function without full reporting of testing procedures, e.g. warm up procedures, practice sessions, patient feedback details, level of verbal encouragement given etc. Where histochemical analyses are concerned, the validity and reliability of muscle biopsy techniques are rarely referenced and detail concerning the depth from which the sample is taken is often missing.

Third, there is often inadequate detailing of ES intervention protocols: various details concerning current type, electrode type, electrode placement and patient set up may be missing or unclear. Fourth, from those studies where appropriate reporting of such detail occurs, it is apparent that there is great variation in protocol detail, such as in length of duty cycles, number of repetitions, intensity of contraction and number of sessions across number of weeks.

This raises the final question and that concerns applicability. Where studies investigating the effects of ES are well designed and comprehensively reported, how comparable are they when different pathologies and ages of population are concerned, even within the limits of normally innervated quadriceps? The effects of ES on younger individuals, whether healthy or with orthopaedic knee conditions, may not be so readily transposed to older patients with different pathologies. It is with these points in mind that the following review was undertaken.

### 3. 3. Training effects in Younger Populations

#### 3.3.1. Young Healthy Populations

##### *3.3.1. (i). Stand-alone ES*

For the purposes of this thesis, stand-alone ES refers to ES applications where muscle contraction is evoked entirely by means of ES. This contrasts with applications where ES is superimposed on voluntary contraction, i.e. superimposed ES. Stand-alone ES can be provided instead of active exercise or supplementary to active exercise. The systematic search identified twenty-three training studies that investigated the effects of stand-alone ES on the quadriceps of healthy, young subjects and that were sourced as full text articles. None of them featured blinded assessment. Twenty-two of them featured a control group in the form of a no exercise group or a voluntary exercise group, or sometimes both. Eleven (50%) featured random allocation.

Five (45%) of the randomised trials tested an ES regime that featured a current frequency of 50 or 60Hz (82) (83) (84) (85) (86) and reported isometric knee extensor torque as an outcome. Two further trials featured the same frequency and outcome measure, but use the contra-lateral leg as a control (87) (88). Thus of 22 controlled trials, there was a homogeneous core of 7 (33%) that tested similar phasic style ES regimes (see 2.3.4) using isometric quadriceps extensor torque outcomes and which were considered to be adequately comparable.

Of the seven, one trial compared ES to voluntary exercise (89), three trials compared ES to no exercise (84), (88), (87), and three trials compared ES to both no exercise and voluntary exercise (82), (85) ,(86). Four of the six studies that used a no treatment group reported a statistically significant positive effect of ES compared to no treatment (82), (84) ,(86) ,(88). Three of the four studies that used a voluntary exercise group reported an equally positive effect of ES when compared with voluntary exercise (82) ,(90) ,(85). Therefore the results of the majority, 5 (71%) of this core group concur that phasic style ES may be more effective at increasing quadriceps isometric torque than no exercise, and as effective as voluntary isometric exercise.

Although there were two negative effect studies, their results may be explained by some exceptional points of methodology (85),(87). In the first one by Mohr et al (85), a 50 pps frequency was delivered via high voltage, monophasic current using a twin peak waveform with a on:off cycle that featured a much shorter off phase of 10 seconds as opposed to 50 seconds. These current parameters are generally deemed a far less comfortable form of ES and the much shorter rest intervals may have produced an increase rate of fatigue. In the second one by

Farrance et al (87), ES was applied to a fully shortened quadriceps using an exceptional treatment position of full extension in long sitting (compared to the more common 60° of knee flexion that puts quadriceps in its mid range). Furthermore, the knee angle of 90° flexion used for isometric assessment was completely different to the treatment angle. Since strength training tends to show specificity of effect, it might be expected that training in a shortened position would not produce increased function in a lengthened position.

Isokinetic outcomes following ES training were reported by three of the 11 randomised, controlled studies. One was the negative study by Farrance et al, discussed above, whose outcomes also included peak concentric torque from 90° to 0°. The other two by Lai et al and Romero et al reported more positive findings (88), (91). A study by Lai et al measured isokinetic 'strength' as the area under the strength curves produced by peak efforts of maximal concentric and eccentric knee extension, at an angular velocity of 60° per second (88). The study compared two levels of ES training intensity (described as the amount of muscle force produced during the training sessions). Subjects were randomised to either high intensity (50% of MVIC) or low intensity (25% of MVIC) or no exercise. Their contra-lateral leg served as control. Both ES groups produced a statistically significant effect compared to no exercise and the high intensity group showed greater increases compared to the low intensity group. The ES regime used a frequency of 50 Hz, 30 repetitions per session of an on: off cycle of 5s: 5s with a one-minute inter-set rest between sets of 10 repetitions. Thus the on: off cycle and number of repetitions differ to the other positive 50Hz studies which mostly use an on: off of 10s: 50s and just one set of 10 repetitions. The other positive isokinetic study was by Romero et al (91), who tested an ES regime described as 'alternating, surging, interrupted faradic current of 2000Hz in an on: off cycle of 4s: 4s' that ran continuously for 113 repetitions in each 15 minute session, 10 times in 5 weeks. In the treatment group, both the dominant and non-dominant quadriceps were stimulated. Compared to a no treatment control, there was a statistically significant improvement in peak torque measured at an angular velocity of 30°/sec, but not at 60°/sec, and this only in the non-dominant leg. This study also reports statistically significant isometric increases in both the dominant and non-dominant leg associated with ES treatment. It was not included in the cluster of studies reviewed above, however, because although faradic current is often delivered at 60Hz, the description of the current parameters did not state the frequency of the interrupted current.

### *3.2.2. (ii). Superimposed ES*

Three randomised, controlled training studies were identified that tested ES superimposed onto a voluntary muscle contraction (92),(93),(94). All reported that superimposed ES was no more effective than voluntary exercise alone, regardless of outcome measure (MVIC, isokinetic knee extension at 30° and 180° per second and measures of squat performance).

### *3.2.3. (iii). Summary*

There appears to be a reasonable consensus in the results from non-blinded, but randomised and controlled trials of ES at 50 Hz in young healthy people. This is that a training course of ES is likely to improve quadriceps torque at least to an equal effect as voluntary isometric exercise, when applied to the normally innervated quadriceps in a flexed knee position. While there is a core cluster of trials in young healthy individuals that feature the same frequency and duty cycle to number of repetitions formula, variation increases when all positive studies are taken together. Positive outcomes have been found in randomised controlled trials using frequencies ranging from 20 to 60Hz. In these trials, total current on time (i.e. summed over total number of repetitions and treatment sessions) ranged from 20 to 47 minutes. Off time ratios ranged from 55% to 83% of the cycle. Training intensity is not always quantified or may be variably reported in terms of % of initial MVIC, or amount of current tolerated, or in terms of patient tolerance (which can be set at a comfortably tolerated or maximally tolerated level with differing effect (74)). Where quantified, intensity of muscle contraction under ES ranged from 5% to greater than 80% of initial maximal voluntary isometric contraction (MVIC) of quadriceps. This leads on to one final point of interest. One of the reasons that ES is proposed as a muscle strengthening modality is because it has been claimed that ES can produce a stronger than maximal voluntary contraction force (6),(7). Yet laboratory and training trials which have compared the maximal quadriceps contraction force by voluntary, electrically evoked or superimposed means conflict in their results. Of the training studies that have reported training intensity in terms of %MVIC, the values produced by ES alone have been reported as 5%, 25%, 40% , 50% and greater than 80% of MVIC.

## **3.3.2. Young Clinical Populations**

Clinically, involuntary quadriceps stimulation by ES may have advantages that do not depend upon its absolute force production exceeding that of voluntary effort, providing a level of contraction intensity is produced that is sufficiently high to produce a training effect. Also, ES may be useful to overcome the reflex inhibition associated with knee joint pain and effusion in order to re-educate a patient in quadriceps contraction (8). The systematic search identified 17

training studies of ES of the quadriceps of younger clinical populations that were sourced as full text articles. Five were excluded: two single case reports, two studies where quadriceps and hamstrings underwent conjoint ES and one study that was a subgroup analysis based one of the featured studies. The 12 remaining studies divided into those where the knee was either immobilised or non-immobilised during rehabilitation. Eight of these investigated the effect of ES on quadriceps after ACL reconstruction. In the earlier ones the limb was immobilised post operatively (95),(96),(97),(98), while later studies featured a protective limb orthosis that was removed for physiotherapy treatment (99),(100),(101). The other studies investigated ES in meniscectomy patients with no post-operative immobilisation (102),(103),(104) and tibial fracture patients during immobilisation (105). Eight of the studies were randomised, but the method of randomisation was not transparent and only one study featured blinded assessment (100).

### 3.3.2. (i). *ES Training of Non-Immobilised Quadriceps*

There were seven studies where ES was applied to non-immobilised quadriceps (Table 4). Five are randomised. Three of these compare normal treatment (i.e. voluntary exercise) to normal treatment supplemented with stand-alone ES (99),(102),(100). **Williams et al** used outcome measures of isokinetic peak torque of knee flexion/ extension at 120°, 180°, 240° and 300°/ sec and found a statistically significant increase within subjects for the ES group at all speeds, but only at slower speeds for the voluntary group (102). However, baseline comparability of subjects is not made clear (number of days post meniscectomy ranges from 16 - 88 for the total sample) and assessment was not blinded. The ES regime was a frequency of 50Hz, for 10 repetitions using an on: off cycle of 15: 50 seconds for 15 sessions over 3 weeks with current intensity set to "patient tolerance". In an assessor-blinded trial, **Snyder-Mackler et al** reported a statistically significant improvement as a result of high intensity ES compared to all other interventions using a homegrown outcome 'quadriceps index'<sup>1</sup>. The study compared four regimes: high intensity and low intensity stand-alone ES, a combination of them both and voluntary exercise alone (100). Statistical analysis was by ANCOVA that took ACL graft type (i.e. surgical procedure) into account. A weakness of this study was its tailor made (and therefore untested from a reliability and validity point of view) outcome measure. The high intensity regime consisted of ES at a frequency of '75 bps', for 15 repetitions of a duty cycle of 11: 120 seconds for 18 sessions in 6 weeks. The low intensity regime was a frequency of 55 bps, for 50 repetitions of an on: off cycle of 15: 50 seconds for 30 sessions across 6 weeks.

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<sup>1</sup>. The quadriceps index was MVIC of knee extension of the affected leg with superimposed quadriceps ES (for assessment procedure only) expressed as a percentage of the same measure for the uninvolved leg and then multiplied by 100.

**Table 3: ES Training Studies in Younger Clinical Populations (no limb immobilisation)**

DESIGN APPLICABILITY	Draper 97	Lieber 96	Synder-Mackler 95	Draper 91	Williams 86	Laimy 83	Godfrey 79
Age Male (m): female (f) Clinical status	Range 16 – 47 yrs 14 m: 15 f Acute rehabilitation after ACL surgery	Range 15 – 44 yrs Mixed, not stated Acute rehabilitation after ACL surgery	Range 14 – 43 yrs 80 m: 30 f Acute rehabilitation after ACL surgery	Range 15 – 44 yrs 16 m: 14 f Acute rehabilitation after ACL surgery	Range 18 – 45 yrs 18m: 3 f 16 – 88 days post arthroscopic meniscectomy	Not stated 6m, 2 f Post arthroscopic meniscectomy	Not stated Mixed, not stated PT referrals for strengthening after trauma or surgery
Stimulation regime Frequency Duty cycle (secs)	Superimposed ES 35 bps Medialis 2: 30 Rectus Femoris 9: 30	Stand alone ES 50 Hz 10: 20	High or low intensity ES 75 bps or 55 bps 11: 120 or 15:50	Superimposed ES 35 Hz 10: 20	Stand alone ES 50 Hz 15: 50	Stand alone ES 100 Hz 10: 50	Unclear if stand-alone Unclear 10: 50
Session length/content Total sessions/ weeks	9 x 10 reps 36 in 4 weeks	30 minutes 20 in 4 weeks	15 reps or 60 minutes 18 or 30 in 6 weeks	90 reducing to 30 mins 34 in 6 weeks	10 reps 15 in 3 weeks	2 x 10 reps 24 in 6 weeks	10 reps 15 in 3 weeks
ES intensity	Patient tolerance	Highest tolerable	Maximum tolerable	Maximum tolerable	Patient tolerance	Not stated	Not stated
Total subjects + groups Consecutive admissions? Randomisation method? Control group? Baseline comparability? Blinding? Similar care otherwise?	29 + 3 Not stated Random, not stated Voluntary exercise Uncertain None Apparently	40 + 2 Not stated Random, not stated Voluntary exercise Yes None Apparently	110 + 4 Not stated Random, not stated Voluntary exercise Uncertain Assessor blinding Yes, apart from surgery	30 + 2 Not stated Age & sex matched Voluntary ex + BFB Uncertain None Yes	21 + 2 Not stated Random, not stated Voluntary exercise Uncertain None Uncertain	8 Not stated Cross over design Voluntary exercise Uncertain None No	35 + 2 Not stated Not randomised Voluntary + placebo ES Balanced for condition Double Uncertain
Outcome measures	QF surface EMG Peak measure Time to peak measure Expressed as % deficit of involved to uninvolved leg.	MVC (concentric) [No protocol details]	'Quadriceps index' using MVIC with superimposed ES of involved compared to uninvolved leg, plus kinematics of knee joint during stance	Ratio of involved to uninvolved peak MVIC torque. Knee extension lag	Thigh girth Isokinetic peak torque of knee extension/ flexion at 120°, 180°, 240° & 300°/sec	MVIC	Isokinetic knee extension at speeds of 3, 10 & 25 reps/ min
Assessment schedule	Pre and post surgery at weeks 1, 2, 3 & 4	Pre and post intervention	Post intervention only	Pre and post for lag Post intervention for MVIC torque ratio	Within subject pre and post intervention	Pre intervention and post each cross over period	Pre and post
Statistical power	None reported Used $p \leq 0.10$	70% at $p \leq 0.05$ for MVC $\sigma = 32.6Nm$	None reported ANCOVA used graft type as co-variate	None reported	None reported	None reported	None reported
Results	Mean deficit of BFB group significantly less than other groups.  Mean deficit of superimposed ES group no different to that of voluntary exercise group.	No statistically significant difference between ES group and voluntary exercise group MVC in an ANCOVA that used total activity during treatment sessions as a co-variate.	Statistically significant improvement in quadriceps index and stance kinematics in groups using high intensity ES compared to other groups (low intensity ES and voluntary exercise alone).	Greater recovery in MVIC peak torque ratio by voluntary exercise + BFB group compared to + ES group.	Pre and post within subject statistically significant increase at all speeds for ES group, but only for slower speeds for voluntary exercise group. Pre and post within subject statistically significant increase for thigh girth	No effect of ES at any point.	Trend for increased peak torque for ES group compared to control at all speeds, however only statistically significant at ?  Girth measures not reported.

Most recently, however, Lieber et al report no statistically significant difference between ES and a voluntary exercise group in an ANCOVA that used total activity during treatment sessions as a co-variate (99). Although patient groups were comparable at baseline and power calculations are provided, measurement detail is lacking with reference to the main outcome of maximal voluntary concentric contraction of quadriceps extension. The ES regime was a frequency of 50Hz, for 60 repetitions using an on: off cycle of 10: 30 seconds for 20 sessions over 4 weeks with current intensity set to "highest tolerable".

### *3.3.2.(ii). ES Training of Quadriceps during Limb Immobilisation*

Five studies tested ES of the quadriceps of a limb immobilised in plaster (Table 4). Three were randomised, of which two found several positive maintenance effects in favour of ES (97),(95). Wigerstad-Losing et al used a frequency of 30Hz to deliver 37.5 repetitions of an on: off cycle of 6s: 10s for 72 sessions in 4 weeks with current intensity set to "highest tolerable" (97). Arvidsson et al used a frequency of 40Hz to deliver 33 repetitions of an on: off cycle of 20s: 35s for 115 sessions in 4 weeks with current intensity set to "highest tolerable" (97). The beneficial effects reported were a significantly smaller decrease in quadriceps C1' measured cross sectional area (97),(95), statistically significant smaller decreases in knee extensor MVIC and isokinetic torque (97) and statistically significant preservation of relative area of Type I fibres (97). However, neither trial reported baseline data for comparison, and in one of them, it is doubtful whether both groups received comparable care programs other than the intervention (97). Furthermore, the two trials conflict in their findings concerning measures of oxidative and glycolytic enzyme activity.

The third trial appeared to be of a more robust design, reporting adequate baseline compatibility and comparable care programmes. It found no statistically significant difference between ES and standard treatment groups in terms of quadriceps performance after taking athletic activity and time to surgery into account. Quadriceps performance was defined as ratio of torque to body weight in a MVIC measured by isokinetic dynamometer. The ES regime used a frequency of 40Hz to deliver 720 repetitions of an on: off cycle of 10s: 30s in 42 sessions in 4 weeks with current intensity set to "maximum comfortable". Although this was the better study design, it is still possible that 'maximum comfort' was a less effective ES setting than the 'highest tolerable' used in the two positive studies above.

**Table 4. ES Training Studies in Younger Clinical Populations (ES during limb immobilisation)**

	Gibson 88	Sisk 87	Wigerstad-Losing 86	Arvidsson 86	Morrissey 85
<b>DESIGN APPLICABILITY</b>	<p>Subjects age Male(m): female (f) Mean 26/ 48 yrs (ES/ control) Males only</p> <p>Surgical procedure/ diagnosis Immobilisation post tibial #</p> <p>Stimulation regime Stand-alone ES in POP</p> <p>Frequency 30 Hz On: off (s) 2: 9 60 minutes per day Daily for 6 weeks</p> <p>Intensity Visible contraction</p>	<p>Mean 24 yrs 13 m: 9 f</p> <p>Immobilisation post ACLR</p> <p>Stand-alone ES + Exercise in POP 40 Hz 10: 30 (R) 8 hours daily Daily for 6 weeks</p> <p>Maximum comfortable intensity + palpable contraction 22 + 2</p>	<p>Range 21 – 45 yrs 16 m: 7 f</p> <p>Immobilisation post ACLR</p> <p>Stand-alone ES + Exercise in POP 40 Hz 6: 10 (R) 4 x 10 minutes in a day 18 days across 6 weeks</p> <p>Maximum tolerance</p>	<p>Range 18 – 40 yrs 18 m: 20 f</p> <p>Immobilisation post ACLR</p> <p>Stand-alone ES + Exercise in POP 40 Hz 20: 35 (R) 3 x 30 minutes in a day Daily for 5.5 weeks</p> <p>Maximum tolerance</p>	<p>Range 17 – 31 yrs Males only</p> <p>Immobilisation post ACLR</p> <p>Stand-alone ES in POP 50 pps 10:50 8 hours per day Daily for 6 weeks</p> <p>Highest tolerable</p>
<b>DESIGN QUALITY</b>	<p>Total subjects + groups 21 + 2 (7, 14)</p> <p>Recruited consecutively Not stated</p> <p>Randomisation method Case control &amp; contralateral leg</p> <p>Control group Exercise (standard treatment)</p> <p>Baseline comparability Uncertain</p> <p>Blinding None</p> <p>Similar care otherwise No</p>	<p>Not stated</p> <p>Random, not stated</p> <p>Exercise (standard treatment) Yes None Yes</p>	<p>23 + 2</p> <p>Not stated</p> <p>Random, not stated</p> <p>Exercise (standard treatment) Uncertain None No</p>	<p>38 + 2 (1 subject moved group)</p> <p>Not stated</p> <p>Random, blocked by sex</p> <p>Exercise (standard treatment) Uncertain None Yes</p>	<p>15 + 2</p> <p>Not stated</p> <p>Not randomised</p> <p>No treatment Uncertain None Uncertain</p>
<b>DESIGN QUALITY</b>	<p>Outcome measures Ultrasonography CSA Muscle biopsy</p> <p>Assessment schedule Pre-post POP</p> <p>Statistical power None reported</p>	<p>MVIC by Kin Com as ratio of torque to body weight</p> <p>Post surgery at week 7, 8 &amp; 9</p> <p>None reported ANOVA</p>	<p>Muscle biopsy Computed tomography MVIC &amp; MV isokinetic torque</p> <p>Pre post</p> <p>None reported</p>	<p>Muscle biopsy Computed tomography CSA</p> <p>Pre and post surgery at week 1 and 6</p> <p>None reported</p>	<p>Thigh circumference Cybex II MVIC wearing de-rotational brace</p> <p>Pre and post surgery at weeks 6, 9 and 12.</p> <p>None reported</p>
<b>RESULTS</b>	<p>No statistically significant loss of CSA in ES group, but statistically significant loss in controls</p>	<p>No statistically significant difference between groups, taking athletic activity and time to surgery into account as covariates.</p>	<p>Statistically significant decrease in oxidative and glycolytic enzyme activity, relative area of Type I fibres and quadriceps CSA in control compared to ES group.</p> <p>Statistically significant greater decrease in knee extensor MVIC and isokinetic torque in controls compared to ES group.</p>	<p>Statistically significant greater decrease in CSA of ES group to controls (greater benefit seen in females compared to males)</p> <p>No difference in oxidative or glycolytic enzymes between the groups.</p>	

## 3.4. Structured Review of ES in Older Populations

### 3.4.1. Older Healthy Populations

In contrast to the volume of experimental work on ES quadriceps training in young, healthy subjects, there appear to be only two studies that investigate its effect on healthy, older people. One of them is a human performance, laboratory type trial by Hakkinen et al that compared voluntary and ES evoked muscle contraction force in men in their seventies with younger groups (10). It is included here as an exception to the scope limitations set earlier. The second was a study by Caggiano et al that compared a training course of stand-alone ES to voluntary isometric exercise in healthy, elderly men (15).

#### *3.4.1.(i). Comparison of Quadriceps ES in Different Ages of Men*

Hakkinen et al analysed differences in peak torque of quadriceps maximal isometric contraction under several conditions in a cross-sectional design that compared three different ages of men: in their thirties, in their fifties and in their seventies (10). Under voluntary conditions, the seventy-year-olds produced significantly lower unilateral maximum voluntary isometric contraction (MVIC) forces than the two younger groups, but under stand-alone ES conditions they produced the same percentage of MVIC (26%) as the men in their fifties. The three ages of men did not differ significantly with respect to the amount of current (measured in mA) that they could maximally tolerate. These results may suggest a decrease in maximal voluntary neural activation of the quadriceps muscle with increasing age in men. The study design appears reasonably robust. Measurement was by isokinetic dynamometer and although the authors did not use a random order of testing, they ensured sufficient recovery time between efforts. ES was a 2000Hz current modulated by a square pulse to 50Hz, with an on: off cycle of 2: 2 seconds using no ramp. Maximum current intensity was assumed to be the point where, 'clear muscle contraction occurred resulting in isometric force as high as possible but the subject did not yet feel too uncomfortable'.

#### *3.4.1.(ii). ES Training of Healthy Elderly Men*

Caggiano et al compare what is described as 'minimal' training of quadriceps using comparable training by stand-alone ES or voluntary quadriceps isometric exercise in a non-blinded, randomised trial (15). Their subjects were a volunteer group of 18 elderly men (mean age  $72 \pm 4$  years) classified by questionnaire response into three different, criteria defined, physical activity types: community active, moderate exercise or heavy exercise. Twelve training sessions over 4 weeks produced a significant difference in pre-test compared with post-test peak and average MVIC torque for the sample as a whole, but found no statistically significant difference in

improvement between the two groups. The average increase in torque post-training was 9%. In a post hoc analysis, the data were pooled and grouped according to physical activity level. A significant correlation was reported between activity level and percent peak torque achieved after training ( $n=18$ ,  $r=0.57$ ,  $p=0.01$ ) with the relationship between them accounting for 33% of the variance between these two variables. A 12% gain in peak torque following training of less active subjects was reported compared to a 5% gain in the subjects who continued their heavy exercise program outside the training session. This would seem to generate the hypothesis that low intensity training, whether by ES or voluntary means, produces more of an effect in sedentary elderly subjects than heavy exercisers.

There are additional points of methodological interest in this study. First, within limits, the researchers offered a flexible approach to the ES Parameters selected for each subject. The core regime was a symmetrical biphasic square waveform with phase duration of 100-113 $\mu$ s applied for 10 repetitions of an on: off cycle of 15: 50 seconds. The frequency was 25 pps, unless as the authors stated, 'additional current was needed to maintain the appropriate MVIC percentage; frequency was increased up to 50pps as needed'. They also stated that 'current intensity was adjusted and maintained at the appropriate percentage of MVIC, or to tolerance, during each contraction'. Therefore, it would seem that both frequency and current intensity were used to optimise charge delivery to the tissue and thus muscle contraction intensity. This was set at a target of 40% pre-test MVIC as measured by isokinetic dynamometer. In actuality, the elderly male subjects in the stimulation group tolerated an average intensity of 36% (range 23% to 43%) of their initial MVIC.

### **3.4.2. Older Clinical Populations**

Seven studies were identified that examined the ES quadriceps training in elderly clinical populations. A comparison of these training studies is presented in Table 5. One very recent study investigated the use of ES in females aged over 75 years after surgical fixation of proximal femoral fracture (18). Three studies investigated ES in conjunction with continuous passive movement (a standard modality) during acute rehabilitation following TKR surgery (11), (12) (13). Two studies investigated ES in patients with OA knees awaiting TKR (16), (14). The last study investigated the effect of ES in a group of patients with limited mobility due to being in the very acute stage post major abdominal surgery (17). These studies will be reviewed according to these four different patient types.

**Table 5: ES Training Studies in Older Clinical Populations**

	Lamb 98	Gottlin 94	Martin 91	Haug 88	Oldham 95	Gibson 89	Vinge	
<b>DESIGN APPLICABILITY</b>	<p>Subject age Male (m): female (f) Clinical Status Stimulation regime Frequency On: off cycle (secs) Session length/ content Total sessions/ weeks ES intensity</p>	<p>Mean 83.7±3.7 years Females only Early PFF rehabilitation Self applied PNMS mean 10 Hz 30:15 3 hours 42 in 6 weeks Palpable + visible contraction (5%MVIC)</p>	<p>Range 61-67 years Not stated Immediately after TKR for OA Superimposed on CPM 30Hz 10 s in each CPM cycle 1.5 hours daily 1 week (7 days) Tolerable limit (claims = visible contraction)</p>	<p>Mean 71±8, 67±9 16 m: 11 f Immediately after TKR for OA or RA. Superimposed on CPM 35pps 15: 20 then 65 45 reps x 3 daily 8 days Max tolerable</p>	<p>Median 69 years Not stated Atrophy due to OA (waiting TKR). Stand-alone ES (3 types) Mean 8.4Hz 30:15 3 hours 42 in 6 weeks Palpable + visible contraction</p>	<p>Mean age 69/74 Not stated Atrophy due to OA (28 days pre TKR). Stand-alone ES 30 Hz Duty cycle 2:9 1 hour 28 in 4 weeks Visible contraction (Claims = 5 %MVIC)</p>	<p>Range 27 - 73 6 males, 7 females Post major abdominal surgery. Stand alone ES 30 Hz Duty cycle 5:10 (R) 1 hour 15 in 5 days Visible contraction</p>	
<b>DESIGN QUALITY</b>	<p>Total subjects + groups Consecutive admissions? Randomisation method? Control group? Baseline comparability? Blinding? Similar care otherwise?</p>	<p>40 + 2 Volunteers Randomised, not stated Dummy electrodes Age, weight and AROM None Yes</p>	<p>16 + 2 Uncertain Randomised, not stated Standard treatment Uncertain None Yes</p>	<p>27 (28 knees) + 2 Uncertain Not randomised Standard treatment Uncertain None Uncertain</p>	<p>30 + 4 Uncertain Randomised, not stated Sham ES Uncertain Double blinded Yes</p>	<p>14+2 Uncertain Not randomised Complicated No (age difference) None Uncertain</p>	<p>13 ? Not randomised Contralateral leg Uncertain Assessor blinded Yes</p>	<p>Computed tomography CSA Muscle biopsy</p>
<b>RESULTS</b>	<p>Assessment schedule Statistical power</p>	<p>Extension lag by manual goniometre: 1) change in PROM 2) change in AROM, days discharge (able to walk 150ft using a stick ant to ascend and descend 5 steps independently) Pre surgery Day of discharge</p>	<p>Muscle biopsy: 1) analysis of muscle fibre type, 2) muscle fibre cross-sectional area</p>	<p>AROM knee extension, MVIC knee extension at 0°, -20°, -35° &amp; -90° extension, number of days to discharge, &amp; perceived pain.  Post surgery, day before PT referral, day before discharge</p>	<p>MVIC knee extension with ES interpolation. Sustained MVC, ultrasound X-sectional area, timed 10m walk, stride length, timed sit- stand.  W1, 2, 3, 4, 5, 6, 7, 8, 10, 12 &amp; 18, but pre and post test statistics.</p>	<p>MVIC knee extension at 90°knee flexion. Under ES stimulation, rates of muscle relaxation &amp; fatigue. Muscle biopsy: fibre type &amp; rate of muscle protein synthesis. Pre and post ES (strength tests for ES group), at surgery</p>	<p>Pre and post (day 6 post op)  None reported</p>	<p>None reported</p>
	<p>65% power to detect a change in gait speed of 0.14m/sec at 0.05 significance level</p>	<p>None reported</p>	<p>None reported</p>	<p>Trend for increased force ES compared to control  Increase AROM KE  Decrease pain</p>	<p>No stimulation pattern emerged superior and no significant.  No difference in NHP scores at any week.  Trend in PNMS groups (either of 2) for greater MVIC torque, better endurance and functional performance</p>	<p>Decrease in muscle protein breakdown ES compared to control.  Increase fibre diameters ES v. control</p>	<p>Statistically significant smaller reduction in CSA for ES group compared to control  Statistically significant preservation of muscle protein synthetic activity in ES group compared to control</p>	

#### *3.4.2.(i). ES Training in Frail Elderly Women Following PFF Fixation*

Lamb undertook a randomised, parallel group, double blinded and placebo controlled study that tested the effect of patterned neuromuscular electrical stimulation (PNMS) on 24 women aged over 75 years rehabilitating after fixation for PFF (18). PNMS involves a deliberate variation in frequency of current within a treatment session. In this study, PNMS was self administered for 3 hours daily for 6 weeks at a mean frequency of 101Hz with a continuous on: off cycle of 30: 15 seconds. The training intensity was reported as palpable and visible contraction analogous to 5% MVIC. The active and placebo intervention commenced one week after surgical fixation. Compliance was reported to be over 75% with no difference between groups.

The sample size was reported to have 65% power to detect a change of 0.14m/ sec in gait speed, the primary outcome measure, at a significance level of 0.05. Leg extensor power (LEP) was also measured. From baseline to the end of a 6-week period of intervention (week 7 following surgery) there was no statistically significant difference in change in gait speed between the two groups. However, a statistically significant greater percentage of the PNMS group were reported to have recovered their pre-injury level of mobility ( $p < 0.05$ ) at this point. At the same time point, there was a trend for the PNMS group to have a greater mean improvement in weight adjusted LEP for the affected limb (0.39 W/ Kg) compared to the placebo (0.26 W/ Kg). This trend was also seen in unaffected limb LEP, which improved by 0.17 W/ Kg and 0.08 W/Kg, similarly. At a follow up assessment 6 weeks after the end of treatment, a significant increase in gait speed was reported in the ES group compared to the placebo ( $p < 0.05$ ). These results merit further investigation.

#### *3.4.2(ii). ES Training with CPM in Patients Following TKR*

Gotlin et al compared dummy electrode placement with ES at a frequency of 35 Hz using an on: off cycle of 12s: 10s applied 2 x one hour daily during CPM to patients immediately post TKR for OA (11). Applying 80% of the current that produced a visible contraction in the contralateral quadriceps produced training intensity. The study was randomised and placebo controlled with a reasonable sample size. Baseline comparability of groups was reported in terms of age weight and AROM of affected leg knee extension. However, the outcome measures and assessment schedule were poor. These were ranges of motion by manual goniometry and number of days to discharge as defined by ability to reach certain mobility goals with assessment pre surgery and the day of discharge. Also, the overall duration of the ES treatment (i.e. number of weeks) was not reported. Thus, the findings (which were positive) must be viewed with considerable circumspection.

Martin et al reported a randomised trial that compared ES during CPM with standard treatment in a similar group of patients (12). A statistically significant loss of cross sectional area of Type I and II fibres was found in the control group compared to the ES group, but no power estimates are provided for the sample size of 16. The ES regime was a frequency of 30Hz and an 'on' time of 10s in every CPM cycle (the total cycle time was not provided). The treatment group had 1.5 hours of ES with CPM daily for 7 days consecutively. Contraction intensity was set at the tolerable limit for each patient at a level that produced visible contraction.

Haug et al reported a non-randomised, poorly described and inadequately assessed control group study of ES during CPM immediately after TKR for knees affected by either OA or RA (13). The assessment schedule varied between individuals. Pre-testing is described as taking place post surgery and posttests on the day before physiotherapy referral and the day before discharge. This is sufficient to render the results invalid. The ES regime was a frequency of 35pps at maximally tolerated current intensity for 45 repetitions x 3 daily for 8 consecutive days post-surgery using an on: off cycle which started at 15s: 20s, then progressed to 65s: 20s.

#### *3.4.2. (iii). ES Training in Older Patients Awaiting TKR for OA/ RA*

Oldam et al investigated the effect of three different sets of ES parameters compared to sham ES on the atrophied quadriceps of 30 subjects in a randomised, controlled and assessor blinded trial where baseline compatibility is not discernible and where the method of randomisation is not made clear (14). Power estimates are provided, but are inadequately reported and appear questionable given the sample size (n=30) divided into four intervention groups. No stimulation pattern emerged as superior, regardless of outcome, including the sham application. The outcomes included MVIC knee extension with ES interpolation superimposed, sustained MVC knee extension, ultrasound cross sectional area, timed 10m walk, stride length and timed sit to stand. The active frequencies under comparison were a uniform 8.4Hz and two forms of PNMS delivered at mean frequency of 8.4Hz, one that replicated the discharge of a fatigued muscle, while the other was patterned randomly. Each frequency was delivered using an on: off cycle of 30: 15 and self administered for 3 hours daily for 6 weeks at an intensity that produced a palpable and visible contraction.

Gibson et al report what appears to be a poorly controlled case study (16). For some measures an intervention group was compared with a control group. It is not clear whether this control was a historic or a parallel group, but the age range of its subjects was quite different (older). For other measures the control was the intervention groups contra-lateral leg. Pre and post intervention tests of MVIC knee extension, plus rates of quadriceps relaxation and fatigue under

ES, were compared between limbs for the intervention group only. Results of muscle biopsy taken from the affected limb at the time of surgery were compared between the groups. It was reported that there was a decrease in muscle protein breakdown and an increase in fibre diameter in the ES group compared to the control. The ES regime was a frequency of 30Hz and an on: off cycle of 2s:9s self applied to produce visible contraction for one hour daily for 28 consecutive days pre-surgery.

#### *3.4.2. (iv). ES Training in Patients Following Abdominal Surgery*

The quadriceps not only has a major atrophic response to knee surgery and orthopaedic immobilisation, but also to immobilisation or catabolic states associated with other major surgery. Using the contra-lateral quadriceps as a control, and a blinded assessor to assess outcome, Vinge et al applied ES to the quadriceps of one leg of thirteen abdominal surgical patients (age range 23-73 years). CT measured quadriceps cross sectional area and muscle biopsy count of polyribosomes decreased significantly less in the stimulated quadriceps compared to the control. A decrease in this count is an expression of a decrease in muscle protein synthesis activity, therefore the authors suggest that quadriceps ES might be a simple and effective method for improving muscle protein synthesis and muscle mass during the catabolic phase post abdominal surgery. The frequency was 30Hz and the on: off cycle was 5s: 10s applied continuously for an hour x 3 daily x 6 days post-operatively. Current intensity was set to produce a visible contraction.

### **3.4. Summary of Chapter**

ES has been tested in young healthy, younger clinical (with non-immobilised or immobilised knees), old healthy and older clinical populations (PFF, pre and post TKR OA knees, abdominal surgery) with mixed effect. Interpretation of findings and inter study comparison of results is mostly confounded by the reasons given in 3.2.2. However, within the young healthy trials, there appears to be some consistency in findings among randomised, controlled studies that compare what could be referred to as phasic style, stand-alone ES regimes. Such regimes involve 4 to 6 weeks of short, intermittent sessions (no more than 15 minutes, 2 to 3 times per week) of higher frequency current at maximally tolerated current intensity. In the majority of such trials ES appears to have a positive effect on MVIC force compared to no exercise controls and equal effect when compared with similarly drawn up isometric exercise regimes. Where training intensity has been quantified, it has ranged from 5% to over 80% of MVIC. Interestingly, one study found an equal improvement in outcome between a voluntary exercise group and a stand-alone ES group despite respective training intensities being 78% and 36% of MVIC (84). In this

study, it would seem that ES produced the same outcome for half the training intensity. For the same population, i.e. young healthy adults, there appears no support for any benefit of using superimposed compared to stand-alone ES.

Only two studies were identified that investigated the effect of ES on healthy elderly adults. From these it has been shown that individual elderly men have tolerated quadriceps stimulation of between 26% and 43% MVIC. The lower contraction intensities were produced in a study that used a very short and sudden on:off cycle (2s: 2s with no current ramp) (10). The higher ones were produced in a study that allowed flexibility of frequency choice and used a longer on: off cycle that included a current ramp (15). Ramp up time has been shown to add to the comfort of ES (36). In this latter study, ES was shown to be as effective as traditional training in increasing isometric quadriceps torque. From its results it could be suggested that sedentary elderly men might benefit more from ES in terms of improved MVIC of quadriceps extension than elderly active exercisers.

In clinical trials of quadriceps training by ES, it appears that tonic style ES interventions prevail, regardless of clinical subgroup. 'Tonic' regimes involve a high number of repetitions of the duty cycle in long, consecutive sessions (1 to 3 hours daily) of ES at lower frequencies and lower current intensities (visible contractions only, about 5% of MVIC). Duty cycles are typified by higher ratios of 'on time' to 'off time'. Such regimes have been applied either for short periods post operatively (up to a week) or for longer periods of between 4 to 6 weeks. The nature of such regimes means that ES is mostly patient, rather than therapist applied. Outcome measures have focused on physiological detail such as glycolytic and oxidative enzyme activity, muscle protein synthesis, fibre type ratio and size, muscle CSA by various means and surface EMG recordings. From such trials, there appears to be some weak evidence that ES can reduce disuse atrophy. However, there is a notable lack of trials that use functionally relevant outcome measures for muscle performance or basic general mobility. The one exception is the placebo group RCT by Lamb (18), which evaluated tonic style patterned ES in female patients following PFF fixation. Although this study did not report a significant change in the primary outcome variable (gait speed at the end of 6 weeks of intervention), a higher proportion of PNMS subjects had regained independent mobility compared to controls and there was a trend for increased fractured limb leg extensor power at this point. There was also a significant increase in gait speed at the long term follow up for the PNMS group compared to the controls (18).

Since progressive high intensity resistance training (a phasic style regime) has been tested on frail elderly populations using the same principles as used for muscle strengthening in young

healthy individuals (5), there may be potential in applying phasic style ES for a similar purpose. The added advantage of ES is that it can produce muscle contraction independent of volition and therefore may be attractive for a clinical population in whom the motivation to exercise is not always strong. It would therefore seem that there is an opportunity to develop the breadth and quality of the research base concerning the use of ES for quadriceps training, using a phasic style regime, in a group of patients during early rehabilitation following PFF. The following chapter proceeds to describe the research objectives and methodology for such research.

## Chapter 4

### RESEARCH OBJECTIVES & METHODOLOGY

#### 4.1. Research Objectives

There were three principal research objectives, which were as follows:

1. To test the viability, acceptability and potential effect of a pragmatic ES treatment protocol in a small number of patients.
2. To investigate the effect of ES of the quadriceps of the affected limb, in patients who have undergone recent fixation for PFF in a study which:
  - a) measures outcome at levels of impairment, disability and health related quality of life,
  - b) uses valid and reliable outcome measures and
  - c) has adequate power to detect a clinically significant effect.
3. To determine whether any improvements persist after ES treatment has stopped.

#### 4.2. Methodology

##### 4.2.1. Design

Research was undertaken in two stages. A pilot study was completed which took the form of a nested case controlled study, using historical controls. This was followed by a randomised, controlled trial (RCT). The following subsections describe the methodology so far as it was common to both the pilot and the RCT and which includes: recruitment procedures, treatment protocol, outcome measures, assessment protocol and data recording, equipment and statistical analysis.

##### 4.2.2. Recruitment Procedures

###### *4.2.2.(i). Inclusion/ exclusion Criteria*

Studies using elderly people as their subjects, particularly frail elderly adults, cannot afford to set such tight eligibility criteria that they render their results redundant for the vast majority of a population for whom an important defining feature is that of multi-pathology. Therefore,

eligibility criteria were set to be as inclusive as possible. There were two inclusion criteria: 1) patients were to be aged 65 years or over, and 2) were to have had PFF treated surgically less than 21 days prior to assessment. Verification of the existence of PFF, the date of surgery and whether the fracture was intra or extra capsular, was made on the basis of the surgical report in the medical notes. Only five exclusion criteria were set. These were based on treatment safety, ethical considerations and the ability to use and follow the assessment equipment and protocol. They were: terminal disease, abbreviated mental test score of less than 7 out of 10 (Appendix A), previous inability to walk, profound deafness or presence of a cardiac pacemaker. The status of each eligible patient in respect of these criteria was established by means of the medical notes and by mental testing by the primary researcher on initial screening for eligibility.

#### *4.2.2.(ii). Recruitment Sites*

Patients were to be recruited from consecutive admissions to a single geriatric orthopaedic rehabilitation unit in the east-end of Glasgow.

#### *4.2.2.(iii). Informed Consent*

A full and objective information sheet was produced in accordance with the GRI and ethics committee guidelines and all patients were encouraged to read it through with their relatives. One version was produced for the pilot study and a second for the RCT, adjusted to take account of the implications of randomisation (Appendix B). Twenty-four hours were allowed to elapse before written consent, thus informed, was sought. It was made verbally clear, and also through the typed information sheet, that all patients would have the right to withdraw from the experimental treatment at any point without jeopardising their right to continued standard treatment.

### **4.2.3. Treatment Protocol**

#### *4.2.3.(i). Standard Therapy (both groups)*

All subjects, both the historical controls and the RCT control group, were given standard physiotherapy as in-patients. This included a mix of balance training, work on transfers, progressive gait re-education and walking practice together with flexibility and strengthening exercises. Some of this physiotherapy treatment was provided in the ward and some of it in a gym. The therapists knew that their patients were undergoing supplementary ES treatment. Treatment was provided according to need and discharge was determined according to whether patients were able and confident of managing at home with or without informal or formal carer support and home adaptations according to need.

#### *4.2.3(iii) Electrical Stimulation (intervention group only)*

ES was given supplementary to standard physiotherapy to the intervention group only and applied only to the fractured leg. The specification of the electrical stimulation treatment was drawn up with the help of ES experts. The following subsections will cover: equipment, current parameters, application parameters, regime parameters and individual ES set up, i.e. the way ES parameters were prescribed for individual subjects in order to achieve best response to stimulation.

##### **A. ES Equipment**

Six portable, custom built, battery operated ES units were supplied by the Bioengineering Unit of Strathclyde University. The intensity dials of the units were calibrated from 1 to 10 reflecting increasing intensity of output current (mA). Although the units shared a similar output scale, the actual intensity for any given number was not identical between units. For this reason, the units were numbered and patients were allocated a dedicated unit from initial set-up to be used throughout the treatment program. The batteries of the units were changed on a regular basis every 2 weeks, regardless of use. The Bioengineering Unit of Strathclyde University provided a supply of PALS 7cm diameter, pre-gelled, self-adhesive and re-usable electrodes for single patient use, manufactured by Axelgaard Manufacturing Co., Ltd, USA.

##### **B. Current Parameters**

The current used was a continuous, alternating, balanced, asymmetrical square wave current with a pulse width of 300  $\mu$ secs and a frequency range of 40, 60, 80 or 100Hz. The aim was to produce the strongest tetanic quadriceps contraction within patient comfort levels. In testing the stimulator on two physiotherapists and one in-patient from the rehabilitation hospital before the pilot study, it appeared that the comfort of different frequencies was perceived differently by each individual, as the literature had suggested it might be (123), (124). Therefore selection from a range of frequencies was allowed in order to produce the strongest contraction within each individual's tolerance (see 4.3.3 (ii) which details individual set up). This mirrored the approach of Caggiano et al (15). It was not possible to record the charge delivered to the tissue in each treatment session or to measure objectively the % force of contraction achieved. However, quadriceps contraction intensity was monitored using a simple observational scale: no contraction, palpable, visible, partial extension, and full extension. ES intensity was increased in every session, and also as sessions progressed, according to patient tolerance.

### **C. Application Parameters**

**Electrodes:** The current was delivered to the quadriceps by two of the self-adhesive electrodes. The skin was prepared to reduce impedance by cleaning it with surgical spirit and, if necessary, shaving off any hairs before the application of the electrodes. The active electrode position varied between subjects in order to achieve a maximum contraction effect within comfort levels. It was either placed proximally over the femoral nerve before its branch or over the motor point of the vastus lateralis. The dispersive electrode was placed distally. Once the optimal placement was established, the sites were marked with indelible pen. **Patient position:** On initial set-up, subjects were seated in an armchair with their hips in 100° of flexion and the fractured leg positioned over a custom manufactured foam wedge so angled as to achieve 60° of free knee flexion. This is suggested to be the position of maximal mechanical advantage for the quadriceps. Thereafter, in-patient treatment sessions were given on the ward in the patient's dedicated armchair using an identical foam wedge leg support. Out-patient sessions were given using the same chair as the initial set up plus a foam wedge, or else in the patient's own home using whatever chair best equated to the target hip position plus the foam wedge (highly portable). Plate 1 shows the first pilot study patient undergoing ES. Her leg is resting on an adjustable support, positioned at 60°. This support was subsequently replaced with the customised wedge.

### **D. Regime Parameters**

**Session Content:** Each session consisted of 36 repetitions of an on: off cycle of 7:23 seconds. Intensity was set at the level recorded during initial set up for each subject (maximum tolerance) and increased as tolerance allowed during progressive sessions. The on time included a 2 second ramp up and a sustained current phase of 5 seconds, which was designed to replicate the 5 second hold time commonly used in voluntary strength training. The 23 seconds rest period was to allow adequate muscle relaxation time. Patient comfort was monitored in sessions 1 to 5 and in the final session with a brief questionnaire (Appendix C). **Number of Sessions:** The aim was to deliver 5 sessions per week as an in-patient and 2 sessions per week after discharge as an outpatient. It was anticipated that most patients would receive 2 weeks of treatment as an in-patient and 4 weeks as an outpatient. Thus it was projected that an average of 18 sessions would be delivered in total. Treatment was not given in the event of inter current illness or on patient refusal. A record of ES treatment given was kept for each patient in the intervention group. This was completed by the researcher for the pilot study, and by the research assistants for the RCT.

**Plate 1. Electrical Stimulation In Situ In The First Pilot Study Patient.**



ES Unit

Wire leading to the active electrode over femoral nerve

Prototype leg rest to ensure 60° initial knee flexion

Inactive electrode over distal quadriceps

### **E. Optimisation of ES Parameters by Individual**

ES assessment was undertaken individually to establish the optimum ES set up for every patient within one working day after completing the baseline outcome measures assessment, but prior to randomisation. Three parameters were adjusted following a set protocol with sufficient rests to allow for fatigue. These were electrode site, current frequency and current intensity. Electrode placement was established first, then maximum intensity for ascending frequencies noting the resultant contraction effect using the observational scale described above. The aim was to maximize muscle contraction intensity without generating significant local discomfort. In exceptional cases a second ES assessment session was required which followed within one working day of the first.

#### **4.2.4. Outcome Measures**

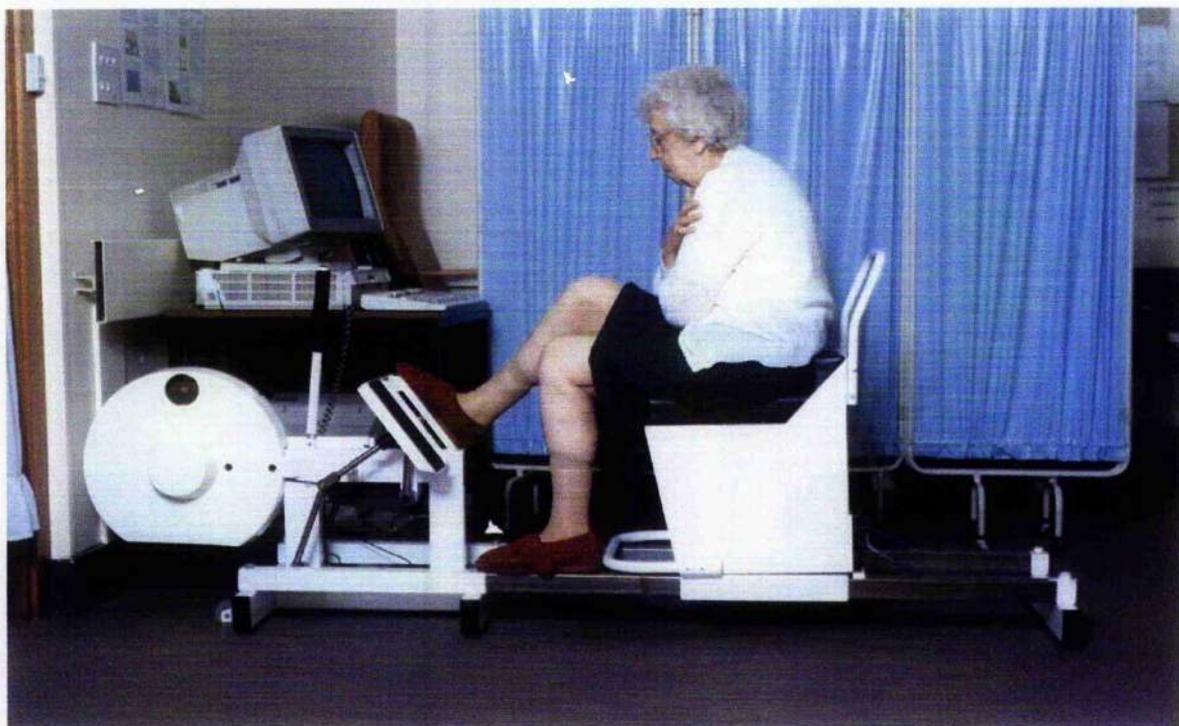
The measures used in this study are described below with specific reference to evidence of their performance in terms of reliability, validity, sensitivity and practicality for use with the elderly. All of them have also been used successfully with PFF patients (5), (18). In keeping with the WHO 1980 International Classification of Impairments, Disabilities and Handicaps (recently reworded), they were selected to reflect patient outcomes at all levels.

##### *4.2.4. (i). Impairment: Leg Extensor Power by Nottingham Power Rig*

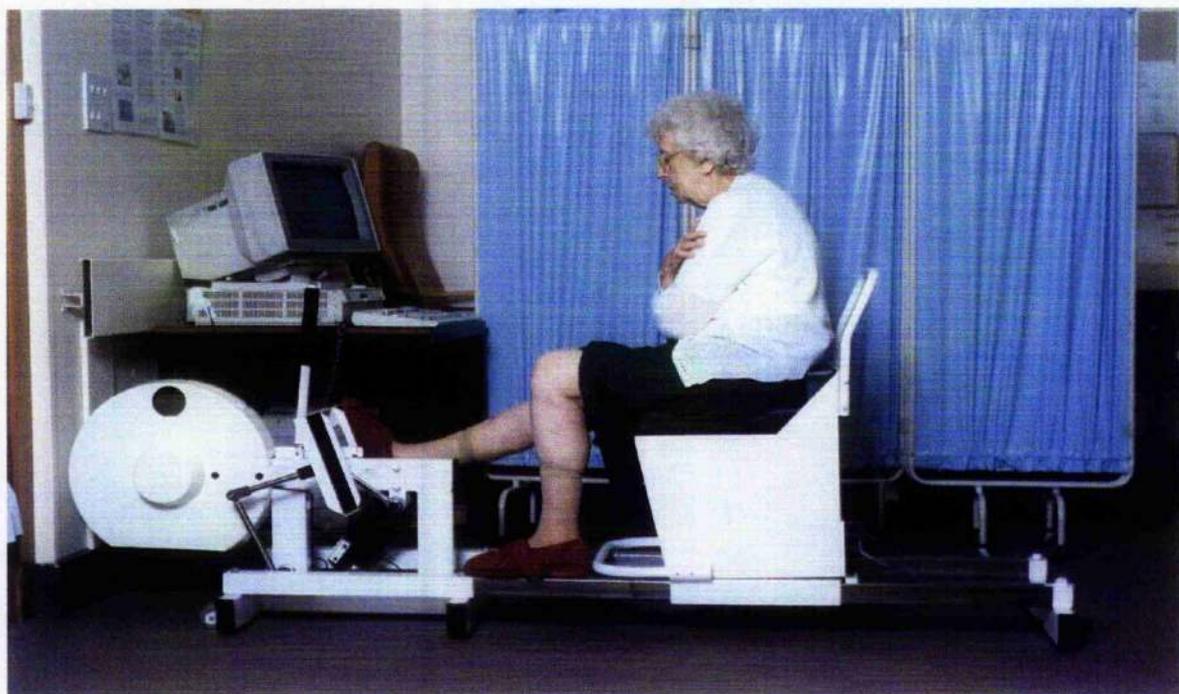
The primary outcome measure was maximal explosive leg extensor power (LEP) measured in watts per kilogram (W/ Kg) using the Nottingham Power Rig (NPR), illustrated in Plate 2. The rig was specifically developed to enable assessment of frail subjects without requiring impacting or unfamiliar manoeuvres, onerous set up or recording protocols or excessive postural demands, but also to be sensitive to ability across the full spectrum (106). Its mode of operation is described in full elsewhere (106). Since each leg thrust lasts no longer than a second, it is possible to record 10 attempts with 30 second rest intervals in under five minutes without causing perceptible fatigue (106). Patient efforts and data recording were undertaken following a protocol for ensuring valid and reliable results which has been developed (106) and refined (5) elsewhere. Leg extensor power of both limbs was recorded over 10 attempts at each session with the minimum 30 seconds of rest between each attempt. The mean of the last 5 attempts was used in the analysis. The reason why muscle power is a more relevant measure than isometric strength has been discussed earlier in 2.2.3. The difference between explosive leg extensor power (a single maximal effort) and maximal short-term power output (normally measured over 15-60 seconds and involving repetitive movements) lies in the additional factors which influence the latter compared to the former, e.g. different metabolic processes and the

**Plate 2. Nottingham Power Rig (a) Start position (b) End position.**

**(a)**



**(b)**



influence of elastic recoil (106). Thus, leg extensor power, as measured by the NPR, is a purer measure of maximal and immediate muscle fibre contractility. Moreover, the angles of ankle, knee and hip during the leg extension effort are similar to those involved in sit to stand and in stair climbing (106).

#### *4.2.4. (ii). Elderly Mobility Scale*

The extensive range of mobility measures for the elderly were outlined earlier in 2.2.2. The Elderly Mobility Scale has been selected for this study for two reasons. Firstly, it was developed as a more specific way of categorising mobility than the Barthel (35). Secondly, there is evidence to suggest that it has both concurrent validity and good inter-rater reliability (35; 107) and is more sensitive to change in mobility performance of elderly adults than both the Barthel and Functional Ambulation Category (108). It is an ordinal scale, scored out of 20, made up of seven items that reflect the key activities required for basic physical independence within the home: lying to sitting; sitting to lying; sitting to standing; standing balance; walking ability; walking speed, and functional reach (Appendix D). Functional reach is also an independent measure of standing balance; its reliability and validity have been reported in several papers (109),(110),(111),(112),(113). Patients who score under 10 on the EMS were more likely to need help with mobility and ADL, whereas a score of 14 or more implied independence of mobility (35). A standard height plinth and chair with armrests and a whiteboard and pen for measuring functional reach were used for the elderly mobility scale tests.

#### *4.2.4. (iii). Modified Barthel Index*

The modified Barthel Index (20-point) was used as a more general measure of disability (Appendix E). It is the physical measure of function recommended by the RCP and BGS assessment package for MDT use in elderly medicine (114). As such it is universally recognised and has been validated and proved robust in use in a variety of settings (115).

#### *4.2.4. (iv) Nottingham Health Profile (Health Related Quality of Life)*

Part 1 of the Nottingham Health Profile (NHP) was selected as an outcome measure for perceived health status. The NHP was constructed to reflect how people feel in various states of ill health. Based on lay perceptions of health status, it is made up of two parts. Part I consists of 38 statements, which, although mixed up together in the questionnaire, can be clearly classified into 6 different domains: sleep, pain, energy, physical mobility, emotional reactions and social isolation, on data processing. A relative weighting system is applied to each statement, so that the total score in any one domain is a minimum of 0 and a maximum of 100. The higher the score the more negative the patient status in that domain. Since all statements relate to limitation

of activity or aspects of distress, the NHP is a severe measure that does not detect minor illness (the sort of health problems that would be affirmed by a large proportion of the population) or minor improvements over time. The focus of Part II is 7 areas of daily living: work, social life, looking after the home, sex life, interests, hobbies and holidays. It is uncertain that all items in Part II apply to some populations, e.g. the elderly or to in-patients, therefore it is not always a useful addition. Moreover, it appears that Part II does not obtain as good a level of reliability as Part I. In terms of face, content and criterion validity, the NHP has proved a satisfactory measure of subjective health status in physical, social and emotional domains; it has been used considerable both in clinical and community settings. It is relatively short and since it is formulated around lay language, using simple yes/no agreement with short statements, it is easily administered and supposedly suitable for self-completion. It is not considered appropriate to calculate an overall health status score across all six domains, therefore totals are only calculated for individual domains (116).

#### **4.2.5. Assessment Protocol, Data Collection and Recording**

Baseline characteristics and outcome measures were assessed in week 0 in one assessment session that lasted approximately 45 minutes and followed a standard sequence that allowed adequate rest time between physical tests. Data for LEP by NPR and MVIC at 60° of knee flexion by Nicholson Hand Held Dynamometer (HHD) were gathered for the fractured and the non-fractured leg. ES set up took place in the afternoon, if baseline assessment took place in the morning, or the next working day. The course of ES treatment commenced the next working day after that. Repeat assessment of outcome measures took place at the end of the intervention period, i.e. in week 6, for both studies. The final assessment for the pilot study took place 10 weeks later, i.e. week 16, following the same time sequence of assessment as the study from which the case controls were to be drawn. The final assessment for the RCT took place slightly earlier at week 14 due to constraints imposed by study funding. If a patient refused or was unable to attend in person, then a telephone or face to face interview took place to gather the Barthel and NHP data. If a patient attended, but was unable or willing to complete the assessment, as much data was gathered as possible. While the original intention was to collect the HHD data as a secondary outcome for muscle function impairment, it was the last measure of the assessment battery and an insufficiently complete data set was gathered. Therefore this measure was subsequently dropped from the analysis. Data were collected on a pro-forma data collection sheet (Appendix G), then entered into a spreadsheet and frequency scanned for anomalies due to data input error. NHP data was converted to numerical values according to the prescribed formula.

## Chapter 5

# PILOT STUDY

### 5.1. Aims

The aims of the pilot study were to evaluate the recruitment rate projections, to establish whether the ES delivery and application protocol were viable for this particular patient group and to undertake a preliminary statistical evaluation of effect by means of a case control comparison.

### 5.2. Methodology

#### 5.2.1. Design and personnel

The pilot study was designed as a case control study aiming to recruit 10 cases which would be frequency matched using a subject: control ratio of 1:2. As the primary research worker, the author undertook the major lead in designing the ES regime design, subject recruitment, treatment application, data input and non-blinded assessment. A second researcher (MB) helped with recruitment and assessment to cover holiday periods and contributed to the NHP data conversion and data analysis. A large part of the methodological detail has been described in the previous chapter.

#### 5.2.2. Recruitment Procedures

##### 5.2.2. (i). *Inclusion/ Exclusion Criteria*

Recruitment into the pilot study was according to the inclusion and exclusion criteria, which were described in Chapter 4.2.2.

##### 5.2.2. (ii). *Sample Size and Recruitment Issues*

The pilot study aimed to recruit 10 subjects into the active treatment group from a single geriatric orthopaedic rehabilitation unit, in Lightburn Hospital, during the months of October 1999 to December 1999 inclusive. However, recruitment rates were lower than anticipated during the first 6 weeks of the study, when a severe flu virus affected Lightburn Hospital (recovery from this illness pushed several otherwise eligible patients beyond the 3 weeks post surgery criteria). Therefore, recruitment was extended to a second site, the male and female acute orthopaedic wards in Hairmyres Hospital and to the end of March 2000. This second site was chosen because it offered access to a second Nottingham Power Rig.

### *5.2.2(iii) Informed consent*

Information sheets were provided and consent gained following the protocol described in Chapter 4.3.2, using the pilot study specific sheets included in Appendix B. The Ethics Committee of Hairmyres Hospital approved the information and consent sheet prior to the start of recruitment at that site.

### *5.2.2. (iv). Control Cases*

Historical controls were selected using a frequency matching procedure from a similarly recruited database gathered during a previous randomized control trial run within the GORU at Lightburn in 1997 and 1998 (5). The study aimed to match 10 cases to 20 controls of the same sex with age within 10 years and to the closest baseline fractured leg extensor power (W/ Kg).

## **5.2.3. Treatment Provision, Outcome Measures and Assessment**

The standard physiotherapy and ES intervention protocols used in the pilot study were described in detail in chapter 4.2.3.

The outcome measures used in the pilot study were leg extensor power (LEP), Elderly Mobility Scale score (EMS), Barthel Score and Nottingham Health profile score (NHP). These measures have been fully described in chapter 4.2.4.

The pilot study assessment schedule and protocol followed the procedures described in 4. 2.5. A synopsis of the timetable is detailed below:

Week 0 (baseline):	Between week 1 and week 3 post surgical fixation of PFF
Week 6:	After completion of the 6 weeks course of ES
Week 16:	10 weeks post cessation of ES

## **5.2.4. Statistical Analysis**

All statistical analysis was performed using SPSS for Windows (version 9.0.0). Comparisons were made using the unpaired student t-test or Mann Whitney U test according to the data distribution. This was checked for normality by visual scanning of the histograms and normality curves produced by SPSS. Statistical significance was accepted as  $p \leq 0.05$ . Data were analyzed according to intention to treat in that where a patient withdrew from ES treatment, but agreed to continue to attend for assessment, their data was included in the ES group analysis. The interval data for LEP was skewed and therefore analysed by means of non-parametric tests. EMS and

Barthel scores are ordinal data, therefore the scores were also analysed using non-parametric tests. As a small pilot study, the sample did not have statistical power for the primary outcome measure of LEP or for the other functional outcomes.

## **5.3. Results**

### **5.3.1. Recruitment**

#### *5.3.1. (i). Intervention Group*

40 PFF patients were admitted to the two rehabilitation units over the period of study, of which 10 met the entry criteria and agreed to participate. Reasons for non-participation for the other 30 were: AMT < 7 (11, 37%), refusal (8, 27%), age less than 65 (5, 17%), previous immobility (2, 7%), profound deafness (1, 3%), severe OA of knees and unable to use power rig (1, 3%), and cardiac pacemaker or too unwell (2, 7%). There were three patients from Lightburn and seven patients from Hairmyres Hospital.

#### *5.3.2. (ii). Control Group*

Case controls were obtained from the database of patients who were randomised to the control group of a previous RCT run within our GORU (5). These patients were recruited in a similar manner as the subjects for the present study and had undergone the same baseline and follow up assessments according to the same schedule. Only one match made a suitable control for one very elderly male, therefore there were a total of only 19 controls. As males were a small minority a male control was matched to a female case to ensure that four male controls were matched to the two male cases.

### **5.3.2. Baseline characteristics & Follow Up**

Table 6 compares the baseline characteristics of the controls (standard group) with the intervention cases (ES group). These were comparable for age, gender, fracture type, days post surgery to baseline, ratio of independent to dependent gait at baseline, EMS and Barthel scores. However, there was a trend for the ES group to be heavier and to have stronger non-fractured leg LEP. Six (60%) of the patients in the treatment group completed the six-week assessment compared to 14 (74%) in the control group. The treatment group maintained this 60% rate of return for the follow up assessment at week 16, by which point the control group return rate had fallen to a similar level (11, 58%).

**Table 6. Pilot Study: Comparison of Baseline Characteristics by Group**

All results are expressed as median (interquartile range) unless otherwise stated.

<b>Characteristic</b>	<b>Standard Group (n = 19)</b>	<b>ES Group (n = 10)</b>
Age (years) <i>Mean (SE)</i>	80 (16)	82 (22)
Male: female ratio	5:14	3:7
BMI (kg/m <sup>2</sup> ) <i>Mean (SE)</i>	20.1 (4.5)	24.3 (9.9)
Intra: extracapsular ratio	8: 11	5:5
Gait ability at baseline Independent: dependent ratio	6:13	3:7
Hairmyres: Lightburn site ratio	0:19	7:3
Days post surgery to baseline <i>Mean (SE)</i>	13 (4)	12 (5.5)
LEP fractured leg (W/kg)	0.28 (0.21, 0.33)	0.35 (0.23, 0.51)
LEP non-fractured leg (W/kg)	0.40 (0.26, 0.63)	0.63 (0.51, 1.27)
Elderly Mobility Scale	11 (9, 13)	10.5 (6, 15)
Barthel Score	13 (13, 15)	13 (10, 15)

### 5.3.3. Treatment Pragmatics

#### 5.3.3. (i). ES Delivery

The median number of ES sessions delivered to the 6 subject in the treatment group who returned for the 6-week assessment was 12.5 (interquartile range 14).

#### 5.3.3. (ii). Initial Contraction Intensity

On initial set up, six (60%) of the ES group tolerated sufficient stimulation intensity to produce only palpable or visible contractions, but no leg movement. Three (30%) of the ES group tolerated sufficient current intensity to produce partial ( $n=1$ ) or full ( $n=2$ ) knee extension. One subject (10%) produced no discernible contraction at all at initial ES set up, nor subsequently.

#### 5.3.3. (iii). Treatment Acceptability

An analysis of the completed comfort questionnaires indicated that of the 36 monitored sessions there were only 3 occasions when patients complained of muscle discomfort during the therapy. The full 6-week programme of ES was tolerated by 7 (70%) of the active treatment group with two (20%) patients withdrawing secondary to new medical problems (not related to treatment) and one (10%) for reasons of personal preference. Two of these withdrawals agreed to return for the 6-week assessment, thus allowing an intention to treat analysis.

### 5.3.4. Outcomes

The results for change in fractured and non-fractured limb LEP and for change in the EMS, Barthel and total domain scores of the Nottingham Health Profile at week 6 and week 16 compared to baseline are summarised in Tables 7 and 8.

#### 5.3.4. (i). Leg Extensor Power (LEP)

At week 6 there was a significant difference in median change in LEP of the fractured limb in the ES group at 0.57 W/Kg (interquartile range 0.33, 0.7) compared to the control group at 0.13 W/Kg (interquartile range 0.04, 0.18), Mann-Whitney U test  $p=0.003$ . At the same time point, there was also a significant difference in median change in LEP of the non-fractured limb (not treated with ES). This difference was 0.53 W/Kg (interquartile range 0.24, 0.98) in the treatment group compared to the control group at 0.08 W/Kg (interquartile range 0.02, 0.19), Mann-Whitney U test  $p=0.005$ . These improvements in fractured limb LEP at week 6 equate to 163% in the treatment group and 46% in the control group, and for the non-fractured limb LEP 84% in the treatment group and to 20% in the controls.

**Table 7. Pilot Study: Improvements in Leg Extensor Power (LEP), Elderly Mobility Scale (EMS) and Barthel Score at Week 6 (End of Intervention) and Week 14, Compared to Baseline.**

All results are expressed as the median (interquartile range).

\*Mann-Whitney U test, P= 0.003.

\*\*Mann-Whitney U test, P= 0.005.

\*\*\*Mann-Whitney U test, P= 0.005.

		<i>LEP</i> Fractured Limb (W/kg)	<i>LEP</i> Non fractured Limb (W/kg)	<i>EMS</i> Score	<i>Barthel</i> Score
<b>Electrical Stimulation</b>	<b>Baseline</b> (n = 10)	0.35 (0.23, 0.51)	0.63 (0.51, 1.27)	10.5 (6, 15)	13.0 (10, 15)
	<b>Change to week 6</b> (n=6)	+0.57* (0.33, 0.70)	+ 0.53 ** (0.24, 0.98)	+ 7 (4, 12)	+ 5 (2, 7)
	<b>Change to week 16</b> (n=5)	+ 0.61 (0.20, 0.93)	+ 0.38*** (0.29, 1.01)	+ 7.5 (4, 12)	+ 5.5 (4, 6)
<b>Control</b>	<b>Baseline</b> (n = 19)	0.28 (0.21, 0.33)	0.40 (0.26, 0.63)	11 (9, 13)	13 (13, 15)
	<b>Change to week 6</b> (n=14)	+ 0.13 (0.04, 0.18)	+ 0.08 (0.02, 0.19)	+5 (3, 6)	+ 4.5 (3, 5)
	<b>Change to week 16</b> (n=11)	+ 0.14 (0.03, 0.29)	+0.05 (-0.03, 0.19)	+ 6 (3, 8)	+ 5 (3, 6)

At week 16 compared to baseline, there was a trend for a greater median change in fractured limb LEP between the treatment group at 0.61 W/Kg (interquartile range 0.2, 0.93) and the control group at 0.14 W/Kg (interquartile range 0.03, 0.29). At week 16 compared to baseline, there was a statistically significant difference in median change in non fractured limb LEP between the treatment group at 0.38 W/Kg (interquartile range 0.29, 1.01) and the control group at 0.05 W/Kg (interquartile range 0.03, 0.19), Mann-Whitney U test  $p=0.005$ .

#### *5.3.4. (ii). EMS and Barthel*

At week 6 there was a non-significant trend towards a greater median improvement in EMS score in the treatment group compared to the control group of 7 points (interquartile range 4, 12) compared to 5 points (interquartile range 3, 6) respectively. The median improvement in the Barthel Index Score was very similar in the treatment group compared to the control group at 5 points (interquartile range 2, 7) and 4.5 points (interquartile range 3, 5) respectively. The non-significant trend towards greater improvement in EMS score was weaker but still evident at week 16 compared to baseline.

#### *5.3.4. (iii). Nottingham Health Profile*

Table 8 presents baseline scores for each domain and the subsequent change values over the assessment schedule. The maximum score in each domain is 100: the higher the score the poorer the perception of status as regards that domain (sleep, energy, pain, physical, emotion and social). Therefore, a reduction in NHP domain score represents improvement. Baseline totals are comparable for all the domains except sleep, wherein the control group had greater perceived problems than the ES group. There were no statistically significant decreases in domain score at week 6 or week 16 compared to baseline between the two groups, except in the domain of pain. At the week 6 assessment point, there was a significant decrease in perceived pain score in the ES group of -23 (interquartile range -38, 6) compared to the controls at 0 (interquartile range -12, 17), Mann-Whitney U,  $p = 0.036$ .

**Table 8. Pilot Study: Changes in Total Domain Scores of the Nottingham Health Profile (NHP) at Week 6 (End of Intervention) and Week 14, Compared to Baseline.**

\*Mann Whitney U test,  $p = 0.036$ .

		<b>Energy</b>	<b>Pain</b>	<b>Emotional Reactions</b>	<b>Sleep</b>	<b>Social Isolation</b>	<b>Physical Mobility</b>
<b>Electrical Stimulation</b>	<b>Baseline</b> (n = 10)	61 (24, 100)	29 (16, 79)	27 (0, 76)	22 (0, 78)	23 (0, 64)	68 (46, 87)
	<b>Change to week 6</b> (n=7)	0 (-61, 2)	-23* (-38, 6)	0 (-10, 2)	0 (-4, 29)	0 (-23, 23)	-29 (-35, 11)
	<b>Change to week 16</b> (n=7)	0 (-61, 2)	-16 (-49, 6)	-4 (-36, 5)	+13 (-22, 35)	0 (-20, 23)	-34 (-34, 11)
<b>Control</b>	<b>Baseline</b> (n = 19)	62 (27, 91)	29 (10, 48)	30 (16, 60)	51 (18, 78)	22 (5, 45)	67 (56, 79)
	<b>Change to week 6</b> (n=13)	0 (-37, 37)	0 (-12, 17)	-7 (-23, 8)	0 (-12, 22)	0 (-20, 22)	-1 (-13, 0)
	<b>Change to week 16</b> (n=10)	+12 (-37, 37)	+8 (-9, 18)	-3 (-21, 7)	-8 (-27, 22)	-1.2 (-20, 22)	-13 (-33, 0)

This greater reduction in pain ES versus controls remained as a non-significant trend at week 16 compared to baseline with a reduction of -16 points (interquartile range -49, 6) compared to +8 points (interquartile range -9, 18).

### **5.3.5. Process**

One of the aims of this pilot study was to assess the likely number of patients that could be recruited from the one original site. A lower than anticipated level of recruitment required the extension of patient recruitment to a second site where there was a second Nottingham Power Rig. The second practicality put to the test was how to administer ES post discharge. Transporting patients back into the hospital regularly after discharge, for further ES treatment as outpatients, proved difficult. Therefore it was decided to offer treatment by home visit. The ES administrator undertook these visits for the pilot study. Finally, the pilot study offered the opportunity to investigate further how to optimise patient reaction to ES. The first two patients in the pilot produced strong tetanic contractions achieving full knee extension, but thereafter in some patients ES only produced a tangible flicker of contraction. The pilot provided an opportunity to investigate such patients further with expert advice sought from the Bioengineering Department of Strathclyde University and the Department of Exercise Physiology at Glasgow University. Most options for maximising effect were double-checked: battery power, lead connections, machine integrity, skin preparation and electrode patency. The conclusion appeared to be that the quadriceps of some patients just did not react to stimulation at the maximal level of intensity that they were prepared to tolerate.

## **5.4. Discussion**

### **5.4.1. Principal Findings**

This study had a dual function. It was both a developmental pilot study and a hypothesis testing, case control series design. As a pilot project, its main aim was to highlight problems of study design and logistics. In essence, this meant testing recruitment and ES application procedures and ES acceptability in the target population in preparation for a subsequent RCT. In this respect its principal outcomes were threefold. First, it was realised that the original recruitment site would provide a lower than anticipated recruitment rate and an additional site was identified, prepared and made operational so as to provide additional suitable subjects assessed according to the specified procedures. Second, ES set up procedures were tested and refined in real time with direct patient access in conjunction with expert consultation. It was also realised that modification was required to the ES delivery protocol for subjects discharged from in-patient

care. Finally, phasic style ES treatment proved acceptable in this frail target population, although levels of muscle contraction intensity under ES intensity did not appear to be uniformly high. The full 6-week programme of ES was tolerated by 7 (70%) of the active treatment group with similar assessment drop out rates in the intervention group compared to the control.

As a case control series, the study's principal finding was a strongly positive effect in favour of ES treatment of the fractured limb quadriceps of patients rehabilitating after PFF fixation, as measured by change in both fractured and non-fractured limb LEP at week 6 compared to baseline. Median improvement in fractured limb LEP was 0.57 W/Kg (interquartile range 0.33, 0.7) for the ES group compared to 0.13 W/Kg (interquartile range 0.04, 0.18) for the controls. Median improvement in non-fractured limb LEP was 0.53 W/Kg (interquartile range 0.24, 0.98) for the ES group compared to 0.08 W/Kg (interquartile range 0.02, 0.19) the controls. There were also trends towards greater improvements in functional scores in the treatment group compared to the controls. At week 16, 10 weeks after treatment cessation and compared to baseline, there remained a non-significant trend for greater median change in fractured limb LEP for the ES group compared to the controls. There was also a statistically significant improvement in non fractured limb LEP for the ES group compared to the controls.

#### **5.4.2. Review of Methodology**

The availability of recent historical controls recruited and assessed using the same recruitment criteria and assessment procedures allowed the pilot study to be undertaken in the form of a case control series. The ability to frequency match each pilot case to two such control subjects could be considered a strength of the study, in that it increased numbers and allowed a preliminary statistical comparison of treatment versus no treatment to be made. While encouraging, the strongly positive results of the statistical analysis must be viewed with caution for several reasons. First, although the cases and controls were matched for age and baseline fractured limb LEP, the intervention cases differed to the controls in three important respects, which follow. 1) The majority (70%) of the intervention group cases came from a different recruitment site to the controls. Hairmyres Hospital in East Kilbride may serve a demographically distinct population compared to Lightburn Hospital in Carntyne. Also, the PFF fixation patients in the acute orthopaedic ward of Hairmyres Hospital had not been pre-selected as the type of patient who would require the different rehabilitation offered by a GORU, unlike those of Lightburn. 2) The controls were historical, recruited in 1997 and 1998, compared to the active treatment group in 1999 and 2000. 3) The controls had been assessed by a completely different assessor, which raises the question of inter-observer reliability.

All three of the above factors could potentially lead to systematic bias. With respect to the difference in provenance of the two groups, there was a small difference in fractured limb LEP and larger differences in body mass index and non-fractured limb LEP at initial assessment, ES group to control (Table 6). These might suggest that the ES patients were stronger and fitter than the controls and therefore more likely to improve during rehabilitation. There may have been some systematic bias associated with the patients from the Hairmyres Hospital site that might account for the LEP results.

There are further strengths and weaknesses to this study to consider. First, in historical case control series neither patient nor assessor blinding is feasible, which could be considered both advantageous and disadvantageous. The advantage of no assessor blinding in this particular instance was that it allowed the researcher to practice and refine ES set up and application skills in a relevant clinical environment using appropriate patients and observing their reactions both within and across several treatment sessions. The disadvantage was the potential for introducing both subject and assessor bias. Second, the overall percentage recruitment rate from consecutive patients who underwent PFF fixation across two sites (40, 100%) during the pilot study recruitment period was low (10, 25%). Potentially this limits how far the results can be generalised in the  $\geq 65$  age group. The majority of exclusions were because of cognitive impairment (11, 28%) and refusal to participate (8, 20%). The previous rehabilitation trial in Lightburn GORU, from which the control cases were selected, had a much higher overall recruitment rate of 72% (5). Recruitment from the acute wards of Hairmyres Hospital may have impacted on the percentage of exclusions due to cognitive impairment. Many such patients would not be transferred to a GORU, but rather discharged back to previous nursing home care directly. Finally, what is not completely clear is whether the demonstrated changes in LEP, although statistically significant, have clinical significance.

#### **5.4.3. Review of Findings**

Chapter 3 highlighted the poverty of well designed, relevant clinical studies where quadriceps ES training has been investigated using comparable subjects, in terms of age, pathology and orthopaedic intervention, to this group of frail elderly patients recovering from surgical fixation of recent hip fracture. However, positive studies were identified in each of the four research populations as defined by the structured literature review of Chapter 3. In healthy young volunteers, those randomised, controlled but not blinded trials that used comparable phasic regime parameters have consistently produced quadriceps' force or torque improvement of the same magnitude as voluntary exercise (84),(88),(82),(88),(90). In Caggiano et al's study in

healthy elderly males, low intensity, phasic style ES was as effective as traditional low intensity isometric training in terms of increased isometric quadriceps force (15). In younger clinical populations, ES training has been associated with a significant reduction of quadriceps weakness following anterior cruciate ligament surgery when compared to standard (i.e. voluntary) exercise alone (100),(102),(97). There is some evidence that this effect is strongest where higher intensity stimulation is used (100) and that low intensity may only be as effective as volitional exercise in this situation (100),(99). Higher and lower intensity of treatment in these trials was defined in terms of higher and lower treatment frequencies, high being 2500Hz modulated to a frequency of 75 bursts per second and low being a basic frequency of 50Hz or 55Hz. However, it should be noted that parameters other than frequency were also different. There is weak evidence from a non randomised trial among older clinical populations that ES at 35 bps after total knee replacement for arthritis may increase isometric torque, in addition to conventional therapy such as continuous passive movement (13). Although interesting, it is hard to extrapolate these results to elderly, predominantly female patients with atrophic quadriceps following PFF. Furthermore functional measures have generally not been assessed.

The most appropriate comparison of results appears to be the assessor-blinded, randomised placebo controlled trial by Lamb where a 6 week ES training programme (albeit using a tonic, patterned low frequency and patient applied regime) was compared to standard treatment among 27 elderly women rehabilitating after PFF fixation (18). Lamb does not report overall recruitment rates, or study dropouts by treatment group for comparison, but her overall trial compliance rate was 89%. Since the overall compliance rate for the pilot study was only 70% at the week 6 assessment, this might suggest greater acceptability of a tonic rather than a phasic ES regime. The PNMS regime aimed to elicit only very mild contraction intensity. The counter argument to this is that in the pilot study there was an equal proportion of dropouts from both the ES and the control group, which suggests the nature of the intervention was not the cause of trial withdrawal. In a comparison of treatment effect, this PNMS study appears to endorse the pilot study's median improvement in fractured limb LEP, which was ES group 163% compared to the control group 46%. At the end of a similar 6-week intervention period, the PNMS group showed a mean improvement in fractured limb LEP of 108% compared to the placebo group at 82%. The pilot study showed a trend for greater improvements in mobility score and Barthel score at the end of intervention. Over the same time period, the PNMS study found that a greater number of PNMS patients had recovered independent mobility compared to the placebo control.

Some specific differences between the tonic and phasic regimes are interesting to note. First, Lamb's tonic regime used a patterned, low frequency of mean 10Hz of prolonged duration. In

animal studies at least, Type II glycolytic motor units transform into oxidative motor units when subjected to chronic (i.e. prolonged) low frequency ES typical of a oxidative motor neuron discharge and thus such stimulation increases endurance but reduce strength (82). Second, use of the stimulators was in the control of each subject and compliance rates were not reported, although the aim was for prolonged periods each day summing as 84 hours of total 'on-time'. This compares with the phasic regime offered to the pilot study patients, characterised by flexible treatment frequencies within the higher ' phasic' range from 40 to 100Hz and shorter, therapist controlled sessions with a median total 'on-time' of 52.5 minutes. Allowing for the design limitation caveats discussed above (5.4.2.), there is thus the possibility that a phasic regime (i.e. one that aims for sustained tetanic contraction at as high a contraction intensity as possible) might produce greater improvement in fractured limb LEP for less treatment time than a tonic regime.

One particularly interesting pilot study result was that there was also a significant median improvement in non-fractured limb LEP in ES group (84%) compared to the control (20%). This limb did not receive ES and these contra-lateral improvements were not mirrored in the study by Lamb where mean improvements of non-fractured limb LEP in the PNMS group were lower than in the placebo (9% compared to 22% respectively). There is some research evidence to support a potential crossover effect from ES such that improvements may occur in the untreated limb (82), (9), (117).

#### **5.4.4. Potential Mechanism of Effect**

Various mechanisms of effect have been proposed to explain the potential efficacy of ES as a muscle training modality (see earlier Chapter 2. 3.6). First, pain or joint capsule distension may produce reflex inhibition that results in decreased stimuli from the central nervous system post-operatively and thus poorer voluntary muscle contraction ability (8). This theory has been used to explain the positive effects of involuntary muscle contraction via ES training compared to traditional exercise in some studies post knee surgery. Second, there is the theory that ES selectively targets Type II muscle fibres. Provided the stimulation is of a nature to stress the muscle fibres through sufficiently high contraction intensity and thus produce hypertrophy, this should in theory produce fibre hypertrophy and enhanced function. Given the lower than anticipated contraction levels, unless subsequent contraction intensity increased as acute post surgical effects subsided, neither of these two mechanism is likely to explain the pilot results. Observation of progressive ES sessions suggests that there was no subsequent improvement in contraction intensity. The third potential mechanism of effect has been proposed as a result of

studies that have demonstrated enhanced performance without concurrent fibre hypertrophy - the neuronal potentiation proposition. This suggests that ES might produce muscle performance gains via increased activation of anterior horn cells (also accounting for the cross transfer effect), increased synapse sensitivity and greater synchronisation of motor unit firing patterns. Fourth, ES may also reduce pain in the affected limb either by means of its stimulation of cutaneous nerves in the manner of a TENS machine (18) or by helping to dissipate post-operative odema. While the pilot findings of greater improvements in the pain domain of the Nottingham Health Profile in the ES group mirror the findings reported by Lamb, they should be interpreted with caution since the values only just reach statistical significance and involve repeated analysis of multiple variables. However, subjective improvements in pain sensation have also been described in subjects undergoing ES following total knee arthroplasty although the method of assessing these changes was not made clear [23]. Finally, if a cross-over effect does exist, it may be explained by neuronal activity either at a cortical or a spinal level. An alternative explanation is that improvements in LEP in the fractured leg allow improvements in mobility such that LEP in the non-treated leg also improves.

#### **5.4.5. Conclusion**

Although it is interesting to consider potential physiological mechanisms of effect, it would be not only premature, but also inappropriate to make any statement in support of the ES as a supplement to standard therapy, based on the results of this pilot study. As a case control series it was small, under-powered and open to potential methodological bias from various sources. Despite its limitations, however, this pilot study was a primarily a pragmatic study designed to assess whether and how phasic style ES might have a place in the rehabilitation of frail elderly individuals following surgical fixation of PFF and to prepare the way for the subsequent RCT. Even when interpreted with caution, the results appeared promising and warranted further study using the similar, but modified protocol.

## Chapter 6

# A RANDOMISED CONTROLLED TRIAL OF ELECTRICAL STIMULATION OF QUADRICEPS IN PATIENTS REHABILITATING AFTER SURGICAL FIXATION OF PFF

### 6.1. Aims

The primary aim of this trial was to test the hypothesis that a 6 weeks course of ES of quadriceps of the fractured leg, supplementary to standard physiotherapy, will result in a significantly greater change in fractured limb LEP at the end of treatment period, than standard physiotherapy alone. Secondary aims were to test whether any effect would persist beyond this time period and whether ES treatment would also produce changes in mobility performance, basic activities of daily living and perceived health related quality of life.

### 6.2 Methodology

#### 6.2.1. Design and personnel

The study design was a pragmatic, parallel group, randomised, controlled trial using a blind assessor. As the primary researcher, the author was responsible for recruitment, ES prescription (which occurred for all subjects prior to group allocation) and blinded assessment. A research assistant was employed to supervise the in-patient, out-patient and domiciliary ES treatment sessions. Randomisation was effected by means of computer generated random numbers, with codes held in sealed envelopes by an administrator independent from the study. The first site received 30 envelopes. The second site received 10 envelopes, which had been selected to contain an equal number of control and ES allocations. Patients underwent baseline assessment and ES set up before being randomised into either the control or intervention group. The target sample size was 40 patients.

#### 6.2.2. Recruitment Procedures

##### 6.2.2. (i). Inclusion/ Exclusion Criteria

Recruitment for the RCT was undertaken according to the inclusion and exclusion criteria as described in chapter 4.2.2.

### *6.2.2. (ii). Sample Size, Recruitment Issues*

The RCT study aimed to recruit a sample size of 40 subjects from a single geriatric orthopaedic rehabilitation unit, in Lightburn Hospital, in the 7-month period from November 1999 to May 2000. However, the average recruitment rate for the first 3 months was only 2 consented patients per month, therefore recruitment was extended to include patients from the acute orthopaedic wards at Hairmyres Hospital (as per the pilot study) and the recruitment period was extended to July 2000. This allowed for the final follow up assessment to take place within the funded period of the study, before the end of November 2000.

### *6.2.2. (iii). Informed consent*

Information sheets were provided and consent gained following the protocol described in chapter 4.3.2, using the RCT specific sheets included in Appendix B. The Ethics Committee of Hairmyres Hospital approved the information and consent sheets prior to the start of recruitment at that site.

## **6.2.3. Treatment Provision**

### *6.2.3. (i) Therapy Provision*

Standard therapy at both sites was provided to both groups as described in chapter 4.2.3. Electrical stimulation was provided only to the quadriceps of the fractured leg of the patients randomised to the ES group as described in chapter 4.2.3. Since the researcher was the blinded assessor and also responsible for the initial ES set up process and parameter prescription, all recruited subjects underwent ES set up prior to randomisation. A research assistant was employed to provide subsequent ES treatment and to record session data (i.e. how many sessions took place and the comfort questionnaire completion). This assistant was instructed to increase the ES intensity according to patient tolerance as sessions progressed.

## **6.2.4. Outcome Measures & Assessment**

The outcome measures employed were leg extensor power (LEP), elderly mobility scale score (EMS), Barthel score and Nottingham health profile score (NHP). They have been fully described in chapter 4.2.4.

Measurement, data collection and spreadsheet entry took place as detailed in 4.2.5. A summary of the assessment schedule for the RCT is provided below:

- Week 0 (baseline): Between 7 and 21 days following surgical fixation of PFF
- Week 6: 6 weeks + one day after randomisation (allows for ES completion)
- Week 16: 10 weeks post cessation of ES

### 6.2.5. Statistical Analysis

All statistical analysis was performed using SPSS for Windows (version 9.0.0) as per the pilot study. Statistical significance was accepted as  $p \leq 0.05$ . The target sample size was set at 40 according to the formula by Lehr, cited by Campbell et al (118) for estimating sample sizes for continuous outcomes in two group comparisons, see Figure 6. This sample size gave the study more than 80% power to detect a clinically significant difference in change in LEP of 0.12 W/kg, ES group compared to control. The estimate of the standard deviation of the population was taken as 0.11 W/ Kg, and the effect size as 0.12 W/ Kg. These were based on the descriptive statistics for change in control group fractured limb LEP from a prior rehabilitation trial where LEP was the primary outcome and which used Lightburn hospital GORU patients following PFF in a comparison of progressive strengthening exercises with standard treatment (5). Much larger sample sizes are required to demonstrate clinically significant differences in functional scales, therefore the sample size of 40 patients made this study slightly under powered for change in EMS and Barthel. Data were analysed according to intention to treat, i.e. where patients withdrew from the ES intervention, but agreed to continue with assessment, their outcomes were included in the ES group for the purpose of statistical analysis.

**Figure 6. Sample size calculation according to Lehr, cited (118)**

Where  $m$  = group size (assuming equal size groups),  $d = \delta/\sigma$ ,  $\delta$  = effect size, and  $\sigma$  = estimate of the population standard deviation, for a two-sided significance level of 5% and a power of 80%, the number required in each group is given approximately by the formula:  
 $m = 16/d^2$

Therefore, for values of  $\delta = 0.12$  W/Kg and  $\sigma = 0.11$  W/ Kg:

$$\begin{aligned} m &= 16 / (0.12/0.11)^2 \\ \therefore m &= 16(1.21) \\ \therefore m &= 13.2 \text{ subjects per group} \end{aligned}$$

## 6.3. Results

### 6.3.1. Recruitment and Follow up

A flow chart of how the patients progressed through the study is shown in Figure 7. There were 100 consecutive admissions from which 61 patients were excluded, 26 patients were recruited and 13 refused to participate. Reasons for exclusion were poor cognition (n=36), longer than 21 days post surgery (n=6), medical instability (n=6), pacemaker (n=2), systematic atypical rehabilitation requirement (n=7), previous immobility (n=2) and regional transfer (2). The sample was randomised into the control group (n=11) or the ES group (n=15). Loss to follow up was evenly spread between the groups. At week 6 there was a 90% (n = 10) rate of return for the control group compared to an 86% rate of return in the ES group (n = 13). The 3 patients who did not return for physical assessment agreed to a telephone assessment for the questionnaire elements. By the final assessment at week 14 there had been 2 deaths, one in each group respectively and there were 6 refusals to attend assessment (control group n=1, ES group n=5). Of these refusals to attend 4 agreed to telephone assessment (control group n=1, ES group n=4).

### 6.3.2. Baseline Characteristics

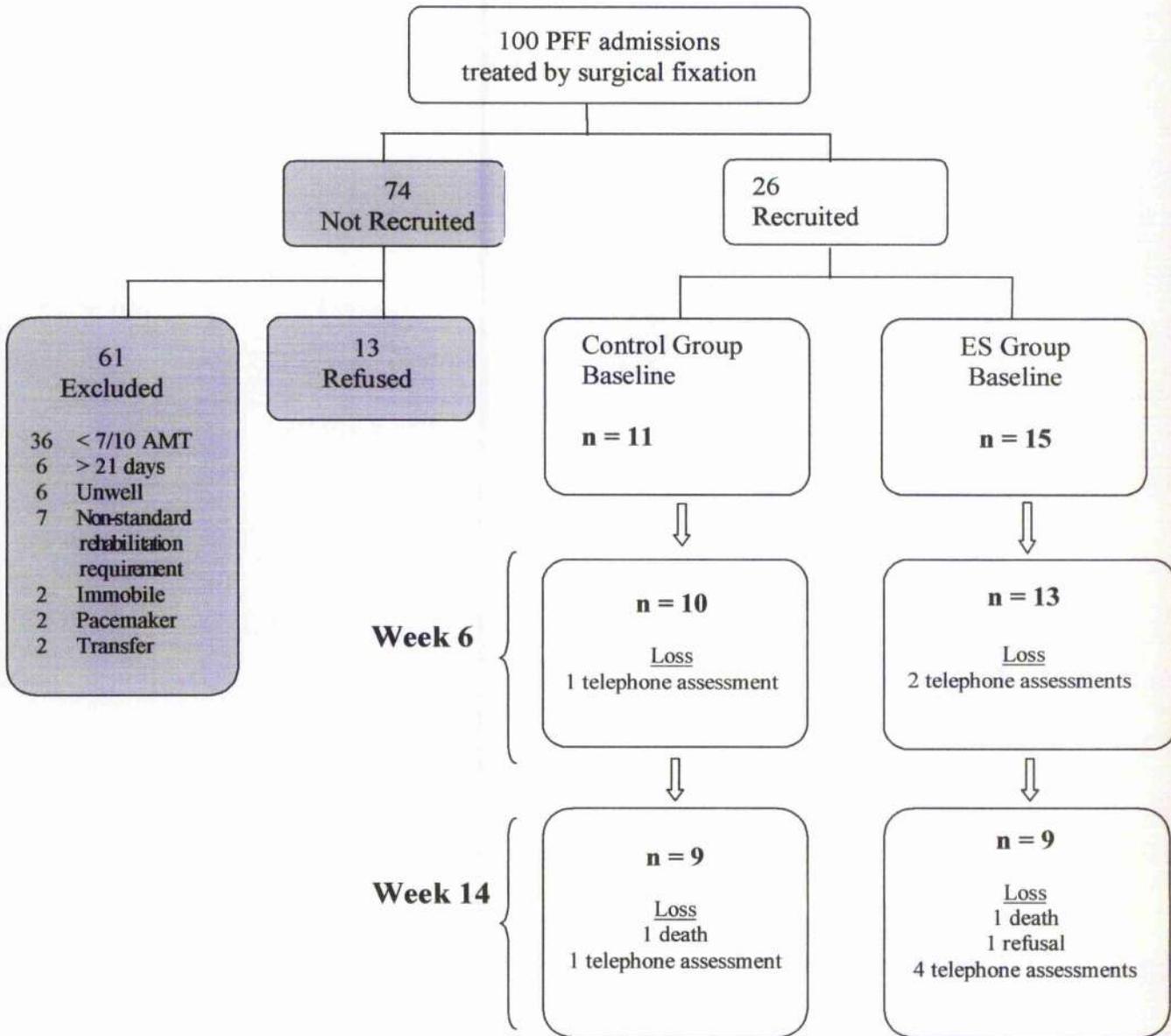
Baseline characteristics of the two groups are summarised in Table 9. The ES group and the control group had similar baseline characteristics in terms of age, gender, days post surgery, and non-fractured limb LEP. However, there was a trend for the control group to have greater fractured limb LEP, higher Barthel scores and for more of them to be independent walkers at baseline assessment.

### 6.3.3. Treatment pragmatics

#### 6.3.3. (i). ES Delivery

A median of 10 (interquartile range 6, 17) sessions of ES were given to the 13 (87%) subjects in this group who returned for the week 6 LEP assessment. Several ES sessions were lost due to staffing problems (early retirement, illness, road accident) and the repeated replacement of ES assistants which sometimes resulted in a gap where there was no person able to deliver treatment.

**Figure 7. RCT: Patient Flow Through the Study.**



**Table 9. RCT: Comparison of Baseline Characteristics by Group**

All results are expressed as median (interquartile range) unless otherwise stated.

<b>Characteristic</b>	<b>Standard Group (n = 11)</b>	<b>ES Group (n = 15)</b>
Age (years) <i>Mean (SE)</i>	80 (2)	81 (2)
Male: female ratio	0:11	2:13
BMI (kg/m <sup>2</sup> ) <i>Mean (SE)</i>	23 (2)	23 (1)
Intra: extracapsular ratio	5:6	5:9
Gait ability at baseline Independent: dependent ratio	6:5	4:11
Site 1: site 2 ratio	4:7	4:11
Days post surgery to baseline <i>Mean (SE)</i>	10 (1)	11 (1)
LEP fractured limb (W/kg)	0.32 (0.30, 0.44)	0.27 (0.16, 0.62)
LEP non-fractured limb (W/kg)	0.67 (0.54, 1.2)	0.69 (0.49, 0.92)
Elderly Mobility Scale	9 (6, 17)	9 (4, 13)
Barthel Score	14 (10, 17)	12 (9, 15)

### 6.3.3. (ii). Initial Contraction Intensity

Eleven (73%) of the ES group patients tolerated sufficient stimulation intensity on initial set up to produce only palpable or visible contractions, but no leg movement. Three (20%) produced some knee extension and 1 (6%) produced no contraction at all.

### 6.3.3. (iii). Treatment Acceptability

Treatment acceptability did not appear to be a major problem. Three patients withdrew. An analysis of the completed comfort questionnaires indicated that in 63 monitored sessions there were only 2 (3%) reports of being unhappy or very unhappy about having treatment on that day. These two patients withdrew from treatment at the time of the first session. There was only one complaint of pain during ES treatment. One (6%) patient had 10 treatment sessions as an in-patient, then withdrew from ES treatment after discharge.

## 6.3.4. Outcomes

Revised power calculations for the smaller than anticipated sample size indicated 80% power to demonstrate a significant difference in change in LEP of 0.14 W/ Kg, illustrated in Figure 8. The change values for all measures at week 6 and week 14, except Nottingham Health Profile results (NHP), are compared to absolute baseline values in Table 10. The NHP data are summarised for the same time points in Table 11.

### Figure 8. Revised Power Calculations for sample size at Week 6 Assessment

\*Lehr's formula is based on an assumption of two equal groups (118).

For a two-sided significance level of 5% and a power of 80%, the number required in each group is given approximately by the formula,  $m = 16/d^2$ . Therefore, by derivation, it is possible to estimate that for given values of  $m$  and  $\sigma$ , a study will have the same power to detect an effect size ( $\delta$ ) as follows:

$$m = 16/(\delta/\sigma)^2$$

$$m \times (\delta/\sigma)^2 = 16$$

$$(\delta/\sigma)^2 = 16/m$$

$$\delta/\sigma = \sqrt{(16/m)}$$

$$\delta = \sqrt{(16/m)} \times \sigma$$

Therefore, where  $m = 11^*$  (the number in the smaller of the two groups in the RCT) and where  $\sigma$  is 0.12 W/ Kg, the study will have a power of 80% at a two tailed significance level of 5% to detect an effect size  $\delta = \sqrt{(16/m)} \times \sigma$ :

$$\delta = \sqrt{(16/11)} \times 0.12$$

$$\delta = \sqrt{1.45} \times 0.12$$

$$\delta = 1.21 \times 0.12$$

$$\delta = 0.14 \text{ W/ Kg}$$

#### *6.3.4. (i). Leg Extensor Power*

There was an increase in median LEP compared to baseline for both the fractured and the non-fractured limbs in the ES group and the control group at both points of assessment. However, at neither point was there a statistically significant difference in improvement of median fractured or non-fractured limb LEP in the ES group, compared to the control. At the week 6 assessment (end of treatment) fractured limb LEP median improvement was 0.20 W/kg (interquartile range 0.14, 0.32) for the ES group compared to 0.22 W/kg (interquartile range 0.1, 0.43) for the control group. At the same point, mean improvement in non-fractured limb LEP was 0.18 W/kg (interquartile range 0.08, 0.38) for the ES group compared to 0.13 W/kg (interquartile range 0.03, 0.22) for the controls.

At the week 14 assessment (8 weeks after the end of treatment) fractured limb LEP mean improvement compared to baseline was 0.29 W/Kg (interquartile range SE) for the ES group, compared to 0.33 W/Kg (interquartile range 0.18, 0.79) for the control group. At the same point mean improvement on baseline in non-fractured limb LEP was 0.27 W/kg (interquartile range 0.09, 0.52) for the ES group compared to 0.25w/kg (interquartile range 0.09, 0.42) for the controls.

#### *6.3.4. (ii). Elderly Mobility Scale*

There was an improvement in EMS score for both the ES and standard group at week 6 and 14, but there was no statistically significant difference in change in EMS between the groups at either point. At the week 6 assessment (end of treatment) median improvement in EMS score was 7 (interquartile range 4, 10) for the ES group compared with 7 (interquartile range 2, 9) for the control group. At the week 14 assessment (end of treatment) there was a trend for greater median improvement in EMS score compared to baseline, which was 8 (interquartile range 5, 11) for the ES group compared 4 (interquartile range 2, 9) for the control group.

#### *6.3.4. (iii). Barthel Index*

There was an improvement in Barthel score for both the ES and standard group at week 6 and 14, but there was no statistically significant difference in change in Barthel score between the groups at either point. At the week 6 assessment (end of treatment) median improvement in Barthel score was 5 (interquartile range 4, 7) for the ES group compared with 4 (interquartile range 2, 7) for the control group. At the week 14 assessment (end of treatment) median improvement in Barthel score compared to baseline was 6 (interquartile range 3, 7) for the ES group compared with 3 (interquartile range 2, 5) for the control group.

**Table 10. RCT: Improvements in Leg Extensor Power (LEP), Elderly Mobility Scale (EMS) and Barthel score at Week 6 (End of Intervention) and Week 14, Compared to Baseline.**

All results are expressed as median (interquartile range).

Valid count variance is due to some patients only being available for telephone follow up.

		<i>LEP</i> Fractured Limb (W/kg)	<i>LEP</i> Non fractured Limb (W/kg)	<i>EMS</i> Score	<i>Barthel</i> Score
<b>Electrical Stimulation</b>	<b>Baseline</b> (n = 15)	0.27 (0.16, 0.62)	0.69 (0.49, 0.92)	9 (4, 13)	12 (9, 15)
	<b>Change to week 6</b> (n=13 unless stated)	+0.20 (0.14, 0.32)	+0.18 (0.08, 0.38)	+7 (4, 10)	+5 (4, 7) <b>n=15</b>
	<b>Change to week 14</b> (n=9 unless stated)	+0.29 (0.27, 0.35)	+0.27 (0.09, 0.52)	+8 (5, 11)	+6 (3, 7) <b>n=13</b>
<b>Control</b>	<b>Baseline</b> (n = 11)	0.32 (0.30, 0.44)	0.67 (0.54, 1.2)	9 (6,17)	14 (10,17)
	<b>Change to week 6</b> (n=10)	+0.22 (0.1, 0.43)	+0.13 (0.03, 0.22)	+7 (2, 9)	+4 (2, 7)
	<b>Change to week 14</b> (n=9 unless stated)	+0.33 (0.18, 0.79)	+0.25 (0.09, 0.42)	+4 (2, 9)	+3 (2, 5) <b>n=10</b>

#### *6.3.4. (iv). Nottingham Health Profile*

As outlined in 5.3.4(iii), a reduction in NHP domain score represents improvement in terms of perceived health status in that particular domain. The results of the RCT data show that there was no statistically significant difference in reduction in any domain score, ES group compared to control group at either re-assessment point, with the exception of social isolation. Change in perceived social isolation score at week 6 and 14 was statistically significant, with an apparent greater reduction in score in the ES group compared to the control group. However, this appears to be of little clinical note since the median for the control group suggested there were no perceived problems in this area for this group to begin with. Unlike in the case control pilot study, there was no significant difference in change in pain perception between the two groups at any point.

**Table 11. RCT: Changes in Total Domain Scores of the Nottingham Health Profile at Week 6 (End of Intervention) and Week 14, Compared to Baseline.**

Reduction in score reflects reduced perceived difficulties in that domain.

All scores are median (interquartile range).

\* Mann Whitney U test,  $p < 0.05$

		<b>Energy</b>	<b>Pain</b>	<b>Emotional Reactions</b>	<b>Sleep</b>	<b>Social Isolation</b>	<b>Physical Mobility</b>
<b>Electrical Stimulation</b>	<b>Baseline</b> (n = 15)	24 (0, 61)	27 (6, 49)	21 (7, 30)	22 (13, 34)	22 (19, 23)	68 (47, 79)
	<b>Change to week 6</b> (n= 14)	-12 (-61, 0)	-24 (-36, -16)	-17 (-21, 0)	0 (-22, 0)	-22* (-23, 0)	-21 (-32, -11)
	<b>Change to week 14</b> (n=13)	-24 (-37, 0)	-16 (-27, 8)	-9 (-21,0)	0 (-23, 3)	-22* (-23, 0)	-23 (-35, -10)
<b>Control</b>	<b>Baseline</b> (n = 11)	39 (0, 100)	35 (0, 49)	7 (0, 38)	12.6 (0, 78)	0 (0, 22)	57 (35, 79)
	<b>Change to week 6</b> (n=11)	0 (-37, 0)	-10 (-37, 0)	0 (-18, 19)	0 (0, 0)	0 (-20, 22)	-22 (-34, 34)
	<b>Change to week 14</b> (n=10)	0 (-24, 0)	-24 (-49, 0)	-4 (-18, 0)	-20 (-35, 27)	0 (0, 2)	-35 (-44, 9)

## **6.4. Discussion**

### **6.4.1. Principal Findings**

This study found that a median of 10 sessions over 6 weeks of supplementary ES of quadriceps to the fractured leg did not produce greater improvements in fractured limb leg extensor power (LEP), mobility or disability in elderly patients rehabilitating after surgical fixation of PFF. Each ES session consisted of 36 repetitions of a duty cycle of 7: 23 seconds aiming for as strong a contraction as possible with the affected leg in a position of free knee flexion. The current used was an asymmetrical balanced square wave delivered by a portable 9V stimulation unit. A uniform frequency from the range 40 to 100Hz was selected to optimise comfort and contraction intensity for individual patients. The sample size had 80% power at a 2 tailed significance of 5% to detect a clinically significant difference of LEP of 0.14 W/Kg. Despite a flexible, individually tailored approach to frequency selection and electrode placement, low stimulation tolerance levels were associated with poor ES-induced contractions. The majority of the ES group patients tolerated sufficient stimulation intensity on initial set up to produce only palpable or visible contractions, but no leg movement. One fifth of patients produced some knee extension and a single patient produced no contraction at all.

### **6.4.2. Review of Methodology**

This study followed robust design and reporting procedures. It took the form of a randomised, controlled and single blinded design, which is the closest most rehabilitation trials using physical agents that produce a visible effect ever come to the 'gold standard' for clinical medical research. Recruitment criteria were kept as wide as possible within safety and ethical reasons, in order to include as many as possible of this frail, elderly, multi-pathology patient group that might potentially benefit from the treatment. Recruitment exclusions and patient flow through the study were reported in full. The outcome measures used were valid, reliable and comprehensive. They covered impairment and mobility, disability and perceived health status. The statistical analysis for the primary outcome variable was supported by power calculations and was undertaken on an intention to treat basis (all subjects who consented to assessment were included in the analysis regardless of their adherence to the ES treatment regime). The study was also designed to build on previous research into this population by the Glasgow University Academic Section of Geriatric Medicine, by using comparable outcome measures and recruitment procedures.

Nevertheless, there were also limitations to the study design and methodology, which will be expanded below:

The first important limitation is the potential for a Type II error. The numbers recruited ( $n = 26$ ) fell short of the initial target ( $n = 40$ ) and the power calculations were reworked to give some indication of the size of treatment effect that would be detected at the set level of 80% power and 0.05 level of probability. Since the original sample size was somewhat overpowered for LEP, the revised 'clinical effect' of 0.14W/ Kg was only slightly higher than the original 0.12 W/ Kg. Nevertheless, this may have meant that a smaller but still clinically significant effect was missed. Projected recruitment level was based on the 72% rate achieved in the trial of progressive quadriceps resistance training completed in 1998 from which the pilot study controls were drawn. The lower than anticipated recruitment rates were largely due to the high percentage of cognitively impaired individuals undergoing PFF fixation and refusals to participate. It is possible that the very notion of electrical stimulation was frightening to this particular population of elderly patients.

The second limitation to consider is the trend for the control group to have stronger fractured limb LEP and to be less disabled in terms of independence of gait and Barthel score at study entry, which could have been a cause of bias. A block randomisation process whereby 10 envelopes were sent to Hairmyres, balanced for control and intervention allocation, was only partially adequate in ensuring equal allocation by site: the control group was smaller and more dominated by Hairmyres patients than the intervention group.

Third, it was logistically impossible to measure in any objective detail the quantity and content of other rehabilitation provision, i.e. standard treatment. Local, non research physiotherapy staff had been requested to complete daily schedules of time and gross content of treatment, but due to staff pressures this were not consistently completed. Also, this attempt to gauge equality of other treatment did not include occupational therapy input and therefore might have been invalid even had the physiotherapy data been adequate. Lightburn rehabilitation may have differed in content to the acute wards of Hairmyres partly with respect to its status as a GORU and partly as a result of the influence of a previous positive trial of progressive resisted quadriceps training, which may have had an influence on physiotherapy approach.

The fourth limitation was lack of patient blinding. This is notoriously difficult to achieve where an intervention is intended to produce an immediate physical and visually obvious effect and where treatment provision is dependent on an external operator. It is not impossible but creates

difficulty and added expense in design and implementation, particularly where phasic regimes that seek tetanic rather than merely 5% of MVIC are on trial. The issue of patient blinding has received some discussion in papers on ES (81) and has been attempted in some tonic studies (14; 18). As a feature of experimental design, patient blinding is primarily intended to counteract the placebo effect of receiving a new (and therefore potentially 'better') treatment. Thus, where a trial intervention has produced no differential effect, lack of patient blinding may be less critical.

Finally, the number of ES sessions delivered was lower than anticipated in the original study plan and also lower than in the pilot study. Subsequent refusal by consented patients did not appear to be the major issue. An unexpectedly high turnover of research assistants may have been an important contributing factor. There was unforeseen staff turnover involved in the ES delivery process for several reasons. At the planning stage of the research, it was not anticipated that recruitment would have to be extended to a second site, nor that so many of the subjects would be reluctant to return for out-patient treatment. Thus there was little extra funding for additional research assistants to deliver the ES at Hairmyres Hospital and for domiciliary visits, which could not, in contrast to the pilot study, be undertaken by the primary researcher in her role as blinded assessor. Therefore, ES delivery became dependent in part on staff members who were either academically ambitious volunteers or assistants paid pro-rata. An unfortunate set of coincidences compounded this problem through the early loss of two key ES delivery personnel due to unforeseen circumstances.

#### **6.4.3. Review of Findings**

The nil differential effect of supplementary ES in the RCT contrasts with the statistically significant benefit, demonstrated in the pilot. In the latter, there was a significantly greater improvement of both fractured and non-fractured limb LEP, despite a similar range of initial ES evoked quadriceps contraction intensity in both studies, according to the same simple observational scale. The weaknesses of the pilot study design have been discussed in full earlier (5.4.2), but the primary ones were a historic control, non-blinded assessment and site imbalance between groups.

There are no other trials where phasic style ES has been tested as a quadriceps training modality in frail elderly adults, or in frail elderly PFF patients rehabilitating after surgical fixation. Therefore it is not known whether under different conditions of application (to be expanded below in section 6.4.5.) it is possible to produce greater contraction intensities within comfort limits. Although phasic regimes have proved effective in healthy young adults, perhaps these

subjects can tolerate higher stimulation intensities. There is some evidence that similar current intensities produce a higher force of contraction in young compared to elderly males (10).

The results of the RCT also contrast with the trend for greater improvements in LEP associated with patterned neuromuscular electrical stimulation (PNMS) in elderly females during the early stages of rehabilitation after PFF fixation as studied by Lamb (18). In this PNMS trial, patterned low frequency stimulation (mean 10 Hz) was applied for prolonged periods at a low level that allowed a patient to carry on with her normal ADL. The advantage of such tonic style regimes is that they are not dependent on high levels of current intensity and therefore do not cause any discomfort in terms of muscle contraction 'cramp' or skin sensation. In animal studies at least, however, Type II glycolytic motor units transform into oxidative motor units when subjected to chronic (i.e. prolonged) low frequency ES typical of a oxidative motor neuron discharge. Type II fibres are the most important for maximal short burst leg extensor power, such as that required for efficient sit to stand and stair climbing. Therefore, it seemed preferable in this research project to attempt a form of ES training more likely, at least in theory, to target these fibres. Although low frequency, the current used by Lamb et al (18) was delivered using a variable frequency discharge the pattern of which replicated the pattern of fatigued motor unit. This may produce different effects than the uniform low frequencies used in animal models.

#### **6.4.4. Consideration of Mechanism of Lack of Effect**

Objective measures of the intensity of ES evoked muscle contraction were beyond the scope of this study. Elsewhere ES training intensity has been quantified by isodynamic dynamometer, a piece of assessment equipment quite unsuited to this frail elderly group. Nevertheless a crude observational scale judged the initial contraction effect to be disappointing. It was also beyond the scope of this study to establish whether contraction intensity increased over time. However, observation during the pilot study and informal discussion with the RCT treatment assistants suggested this was not the case. The most likely reason for the lack of intensity of electrically induced muscle contraction appears to be due to low tolerance of the skin sensation produced by increasing stimulation intensity. No subjects reached a strong, possibly supramaximal tetanic contraction that would produce the muscle cramp discomfort sometimes associated with strong electrically induced contraction. It is not possible to compare the ES training intensity of the RCT group to that of the healthy elderly males investigated by Hakkinen et al (10) and Caggiano et al (15). However, while such subjects tolerated sufficient current to produce an average of 36% of their maximal voluntary isometric contraction force (15), it does seem that most of our

frail, hospitalized elderly, who had the additional burden of a recent surgical wound in their thigh, had lower tolerance.

Notwithstanding lower than ideal apparent training intensities, the number of treatment sessions may also have been insufficient to promote improved muscle function. The median number of 10 sessions delivered per patient was lower than the predicted minimum of 18 and even lower than in the pilot study. Practical issues with ES delivery staff may have been more of a problem than treatment acceptability in this respect. Provided current intensity was restricted to individual comfort levels, ES acceptability did not appear to be a major problem since 13 (80%) of the ES group completed the 6-week course. It could also be argued that although the median number of treatment sessions was lower than planned, each patient underwent 36 repetitions per session, which is a much higher number than the standard 10 repetitions per session featured in phasic style ES training regimes with healthy adults (64). Thus, had ES delivered a sufficient intensity of contraction, the 'dose' received might have been expected to have shown some beneficial effect.

There are also potential physiological explanations for lack of ES effect in this frail elderly group. First, phasic style ES may target Type II fibres preferentially and there is evidence to suggest that elderly adults have fewer discrete Type II fibres and more hybrid ones (48). Second, elderly adults may tend to have more fat and connective tissue in their motor unit cross sectional area, which would increase impedance (51). Linked to this theory, it has been suggested that ES is less effective in females per se (who predominate in our study) because of increased electrical impedance associated with adipose tissue around the thigh (8). Finally, post-operative tissue oedema of the thigh may also have contributed to increased impedance.

#### **6.4.5. Future Research**

In retrospect there may be a variety of ways that phasic ES might be made more effective. Initial use of a hand held electrode to explore optimal siting of electrodes might facilitate greater muscle stimulation without causing excess discomfort (15). A third electrode (15), or selecting from a range of different sizes, shapes and alignment of electrodes (119), might optimise the current delivery to quadriceps allowing greater stimulation at a lower intensity. It has been shown that skin temperature affects current transmission and also, conversely that icing the skin over quadriceps prior to ES application increases contraction effect (120). There is also some evidence that using a TENS like level of ES for a 10 minute 'warm-up' to get the patient used to the particular skin sensation associated with ES delivery results in toleration of higher

stimulation intensities (121). Finally, it could be argued that many of the phasic style ES currents tested among young healthy adults were produced by 2,500Hz current modulated down to a 50Hz frequency using a mains unit and therefore not replicated in these study parameters. A previous review has stated that the practical difference between alternating currents produced by 'low' frequency versus modulated 'medium' frequency generators is negligible (62), but concedes that the shorter waveform may be more comfortable. There is mixed evidence as to the effectiveness, consistency and relative comfort of portable, battery powered ES units compared to mains operated machines (122).

#### **6.4. Conclusion**

In this randomised, controlled and single blinded study, a 6-week course of ES of the fractured limb quadriceps, supplementary to standard treatment, did not increase fractured leg LEP or reduce disability in elderly patients rehabilitating following surgical fixation of PFF. Poor ES-induced contractions associated with low stimulation tolerance levels may best explain the lack of effect. However, due to unexpectedly low recruitment rates, this was a small study and it is possible to have missed a modest beneficial outcome. As ES failed to enhance LEP, it was to be expected that there would not be any changes in the functional scores. It is interesting to note that a large proportion of admissions following PFF fixation were excluded from the study on the grounds of cognitive impairment.

## Chapter 7

### FINAL SUMMARY

The broad aim of this research project was to evaluate the effects of a supplementary programme of electrical stimulation to the quadriceps of the affected leg of patients rehabilitating after proximal femoral fracture.

A review of the background to this subject outlined the importance of research into disability after PFF, examined the links between quadriceps function, leg extensor power and mobility impairment in this frail patient group and provided an overview of electrical stimulation protocol specification and potential mechanism of effect. The literature that informed this ES overview was drawn from review articles and experimental studies in normally innervated quadriceps. It is possible that some useful information might have been missed from ES studies of other normally innervated muscle groups, or from the literature concerning ES use in stroke or spinal cord injury patients.

A systematic search of the literature on quadriceps training studies using ES in healthy and clinical populations was undertaken. This followed a robust methodology that was similar to the search process used in by Cochrane reviewers, although necessarily more restricted in the extent of searching by hand and personal communication. A structured review of the results of this search highlighted major methodological concerns in many of the existing studies, which do not tend to feature in existing review articles. Variation in ES and training regime parameters between studies introduces added complexity and further limits cross study comparison. Thus, there appears to be continuing uncertainty of ES effect, particularly in clinical groups. The low number of studies of ES quadriceps training in older clinical populations suggests that it is a relatively novel area of research.

Nevertheless, from the training literature, it appeared that two broadly different types of ES regimes have been evaluated in the past. The first, labeled by this author as a 'phasic' style regime, seeks to produce a muscle training effect via the traditional muscle overload principle using relatively few repetitions with relatively long rest intervals and aiming for high muscle contraction intensity with frequencies (base or pulse) between 30 and 100 Hz. The second, labeled by this author as a 'tonic' style regime, seeks to produce a muscle training effect via neural modulation using high and frequent repetitions. It aims to produce only low muscle contraction intensity and uses considerably lower frequencies, i.e. <30Hz which are sometimes varied within the session. Only one study was identified that investigated ES in PFF patients in the first months after fixation. This study was also one of the more robust in terms of design quality and tested a 'tonic' regime of patterned neuromuscular

stimulation (PNMS) that allowed patients to carry on their activities of daily living while undergoing treatment. The results suggested a potential benefit in terms of a trend towards increased LEP and improved recovery of independent indoor mobility and gait speed. A previous study in our unit had shown that traditional, progressive, high intensity resistance training improves LEP and mobility outcomes in the same type of patient. A hypothesis was generated that a supplementary course of ES using the traditional 'phasic' approach might also offer benefits, with the advantage of negating the need for patient volition.

A case controlled pilot study was undertaken which produced positive results in a limited sample using recent historic controls. This led to a parallel group randomised controlled and assessor blinded trial, in which supplementary ES produced no beneficial effect. While the trial of PNMS by Lamb excluded patients with certain co-morbidities that might affect mobility performance, both the pilot and the RCT were pragmatically designed, clinical training studies that sought to include as many PFF patients as possible. It could be argued that they sought to test effectiveness of supplementary phasic style ES (i.e. does it work?) before the case for efficacy (i.e. can it work?) had been fully established. Project timing had dictated that only a few of the pilot study cases had completed by the time the RCT had to start. It happened that the initial recruits into the pilot showed a very positive reaction to ES of their quadriceps, however subsequent subjects in the pilot and the RCT did not. Use of historic controls and an unforeseen site imbalance in pilot cases may explain the very positive differential in change in LEP achieved by ES in the pilot study. In the more robust design of the RCT, low tolerance of ES intensity associated with poor ES induced quadriceps contractions may explain the lack of any beneficial effect of ES.

The question arises whether further study using phasic style ES in this patient group would be worthwhile. It would be interesting to refine the application parameters and techniques in an effort to produce a better muscle contraction in these subjects. Alternatively, the phasic style regime could be used as a prompt to action as a part of a voluntary programme, negating the need for a physiotherapy assistant to supervise the repetition count. Patterned neuromuscular stimulation has yet to be widely tested and is dependent on elderly subjects being able to treat themselves over prolonged periods of time. Nevertheless it may provide benefits and is worth further investigation.

## **APPENDICES**

## APPENDIX A

A randomised controlled trial of electrical stimulation of the quadriceps of patients rehabilitating after a proximal femoral fracture (PFF).

### PATIENT INFORMATION

**You are being 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 and relatives and your doctor 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.**

**Consumer 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.**

**What does the title really mean?** A study looking at two groups of patients recovering after a broken leg using electrical stimulation on the thigh muscle of one group, and not on the other.

**What is the study's purpose?**

This study aims to measure the effects of electrical stimulation on thigh muscle strength and overall functional ability during recovery from a broken leg.

**Why have I been asked to join?**

All patients who come to Lightburn for rehabilitation after surgery for a broken leg are being approached to take part, except where other illness disallows.

**Do I have to take part? What if I want to stop after joining?**

If you do not wish to take part in the Research project or, if at any time, you wish to stop taking part in the strength training section you may do so. The care that you are presently receiving will not be affected in any way. You will continue to receive standard physiotherapy.

**What will happen if I agree?**

If you agree to take part, you will randomly allocated to one of two groups: the treatment group or the control group. The control group will receive standard physiotherapy. The treatment group will receive standard physiotherapy plus the electrical stimulation therapy. Then the results of the two groups will be compared. 'Randomly allocated' means that the groups are selected by a computer which has no information about the individual - i.e. by chance. So, even if you agree to take part, you may not receive electrical stimulation.

Before the treatment, at three weeks, at six weeks and at 2 months after the treatment is finished, we will measure the strength, or power, of your leg muscles, observe how you are walking, and ask you to complete a questionnaire on how you are feeling.

**What does electrical stimulation involve?**

Two patches will be put on the thigh muscle of your broken leg and a small electrical current, sufficient to make the muscle contract, will be applied. Treatment will be given for approximately 20 minutes daily, 5 days per week for 6 weeks. If you are discharged from hospital within this time, you will continue to receive the electrical stimulation therapy twice a week as an out-patient in Lightburn day hospital.

**What are the alternatives for treatment?**

All patients will continue to undergo standard physiotherapy. The electric stimulation is offered in addition to the normal rehabilitation programme.

**What are the side effects of taking part?**

Occasionally electric stimulation causes minor local discomfort, however this can easily be prevented by changing the position of the patches or by reducing the strength of the electrical current. You may be left with a little skin reddening after the patch is removed, but this soon disappears.

**What are the possible disadvantages? What if something goes wrong?**

Electrical muscle stimulation treatment is safe. It has been widely used on people who have lost control of their muscles after spinal cord injury, and in some countries it is standard treatment after certain orthopaedic surgical procedures. The possibility of minor local discomfort has been pointed out above under side effects.

**What are the possible benefits?**

After a broken leg, the thigh muscles become very weak. This results in problems in walking and other physical activities. Electrical stimulation of the thigh muscles has been claimed to be a simple, convenient method of improving strength, thus helping people to regain their mobility. Please note that if you agree to take part, this research project may be of little benefit to you but the results may help other patients in the future.

**Will my taking part in this study be kept confidential?**

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

**Who is in charge of the study? Will my GP hear about it?**

The people running the study are research doctors and physiotherapists who work for the Glasgow Royal Infirmary. The study is being paid for by GRI Trust Research & Development Endowment Funding and there are no other financial interests involved. If you decide to take part, your local GP will be notified.

**Who has reviewed the study?**

The study has been reviewed and approved by the GRI Ethics Committee.

**What will happen to the results of this study?**

The study report should be completed by Sept 2000. Our aim is to secure its publication in leading national and international rehabilitation journals. You can obtain a copy of the published results from the contact below.

**Who do I contact for more information?**

If you have any queries regarding taking part, or about your treatment, or about getting the results of the study, please ask to speak to **Dr Mark Barber** through the hospital SWITCHBOARD.

**What now?**

You will be given a copy of this information sheet and a consent form to sign and keep if you agree to take part.

Thank you for reading this.

**APPENDIX B**

A randomised controlled trial of electrical stimulation of the quadriceps of patients  
rehabilitating after a proximal femoral fracture (PFF).

**CONSENT FORM**

After a broken leg, the thigh muscles become very weak. This results in problems in walking and other physical activities. Electrical stimulation of the thigh muscles has been claimed to be a simple, convenient method of improving strength, or power, thus helping people regain their mobility. This research project aims to measure the effects of electrical stimulation on recovery of leg strength and functional ability during recovery after a broken leg.

If you agree to take part in this project, you will be randomly allocated to one of two groups: the treatment group or the control group. The control group will receive standard physiotherapy. The treatment group will receive standard physiotherapy plus the electrical stimulation therapy.

Before the treatment, at three weeks, at six weeks and at 2 months after the treatment is finished, we will measure the strength, or power, of your leg muscles, observe how you are walking, and ask you to complete a questionnaire on how you are feeling.

Please note that if you agree to take part, this research project may be of little benefit to you but the results may help other patients in the future.

Your participation in this research project is voluntary and if at any time you wish to stop taking part in the electrical stimulation section you may do so. The care that you are presently receiving will not be affected in any way.

I, (Name) ..... of (Address) .....  
.....

agrec to take part in the research project/study described above.

Dr/Mr ..... has explained to me what I have to do, how it might affect me and the purpose of the research project. I also confirm that I have read and understood the information sheet for this study.

Signed ..... Date .....

Witness ..... Date .....

PLEASE CONTACT **Dr Mark Barber** THROUGH SWITCHBOARD IF YOU HAVE ANY QUERIES REGARDING YOUR TREATMENT.

-----  
Study number:

Patient information number for this trial:

## APPENDIX C

### Elderly Mobility Scale

<u>Lying to Sitting</u>	
Independent	2
Needs help of 1 (verbal/ physical)	1
Needs help of 2 or more people	0
 <u>Sitting to Lying</u>	
Independent	2
Needs help of 1 (verbal/ physical)	1
Needs help of 2 or more people	0
 <u>Sit to Stand</u>	
Independent in under 3 seconds	3
Independent in over 3 seconds	2
Needs help of 1 (verbal/ physical)	1
Needs help of 2 or more people	0
 <u>Stand</u>	
Stand without support and able to reach arms forwards and sideways while remaining steady and safe.	3
Stands without support but needs support to reach	2
Stands but needs support (frame, stick or furniture)	1
Stands only with physical help	0
 <u>Gait</u>	
Independent or safe with stick	3
Safe with frame	2
Mobile with stick or frame but erratic/ unsafe turning	1
Needs physical help to walk/ needs constant supervision	0
 <u>Timed walk</u>	
Under 15 seconds	3
15 - 30 seconds	2
Over 30 seconds	1
Unable	0
 <u>Functional Reach</u>	
Over 16 cm	4
8 to 16 cm	2
Under 8cm or unable	0
Total _____ / 20	



APPENDIX E: DATA RECORDING FORM

TEST 1 2 3

DATE \_\_\_\_\_

NAME \_\_\_\_\_

AGE \_\_\_\_\_

SEX \_\_\_\_\_

TEL NO: \_\_\_\_\_

DATE OF FRACTURE \_\_\_\_\_

AFFECTED SIDE L / R

TYPE OF FRACTURE \_\_\_\_\_

TYPE OF OP \_\_\_\_\_

<i>ES Settings</i>
--------------------

<b>Diagnoses</b>		<b>Medication</b>	
1)	6)	1)	6)
2)	7)	2)	7)
3)	8)	3)	8)
4)	9)	4)	9)
5)	10)	5)	10)

HEIGHT \_\_\_\_\_

WEIGHT \_\_\_\_\_

BMI \_\_\_\_\_

PREVIOUS MOBILITY - Independent / Stick / Frame

BARTHEL	
---------	--

NOTTINGHAM HEALTH PROFILE	
---------------------------	--

ELDERLY MOBILITY SCALE	
------------------------	--

**LEP SET UP - DISTANCE MEASURED WITH LEG EXTENDED:**

POWER (Watts)	
Left	Right
6	
7	
8	
9	
10	
Mean	

Left - _____ Watts/Kg
-----------------------

Right - _____ Watts/Kg
------------------------

Date of Discharge \_\_\_\_\_

Place of Discharge \_\_\_\_\_

## APPENDIX F: GUIDELINES FOR ES APPLICATION

**Remember:** if a patient shows discomfort or distress at any time during treatment, switch the ES unit off and seek further assistance. Never leave a patient alone while the machine is switched on, unless they have an alarm buzzer close to hand or there is someone else in the gym/ward aware of the situation, who knows how to switch off the machine.

**IMPORTANT:** Never adjust the positioning of the electrodes without first switching off the unit. Never switch the machine on unless the electrodes are already in their correct position.

1. **Ward check:** for no medical change overnight/week-end prohibiting treatment for EACH patient before EVERY session. Also, make sure the patient is dressed appropriately (shorts/skirt). Check toileting requirements first.
2. **Patient set up:** 1) Sit patient right back in chair with legs resting on 60 degree angle foam wedge. Make sure they are least likely to slide forward in the chair and that their foot is clear of the floor.
3. **Patient comfort questionnaire** THIS IS ONLY REQUIRED FOR THE FIRST 5 ES SESSIONS AND THE LAST ONE. Ask the patient to fill in the pre ES questions. Help them to do so if required. (The blanks are ready in patient's plastic envelope in blue ward file).
4. **Apply the electrodes:** 1) Clean skin with an alcowipe and check for hairs (you may need to clip some). 2) Wet the sticky side of the electrodes slightly, then apply to affected leg by centering them on the indelible ink marks on the patient's skin (if these marks are fading, re-apply!). 3) Connect the black lead to the electrode nearest the hip and the red one to the electrode nearest the knee. 4) Check uniform adhesion.
5. **Check the ES unit.** The unit number and setting switches need to be correct for your patient. These settings are noted at the top of the patient tick sheet. Switch the ES unit on **before connecting to the patient** (in case of current surge) and check that the battery indicator light is strong. If not, change the battery in the unit (note this in the battery monitor sheet).
6. **Start the session:** 1) Ask the patient if he/she is ready. 2) Remind him/her not to touch the electrodes at any time. 3) Switch the unit on and turn the intensity dial up to the prescribed initial setting. 3) Start the stopwatch or note the time ES is started and note when the session is due to end (24 minutes later).
7. **First 5 bursts of ES:** 1) Turn the intensity up as high as the patient can comfortably tolerate over the course of the first 5 bursts. 2) Ask or help the patient to fill out the remaining comfort questions 3) Rest one or two pillows on the patient's lap and give them the tick sheet to fill out before leaving to distant supervision by yourself or by ward staff.
8. **End session:** After 36 contractions (24 minutes), switch the machine off and gently remove the electrodes. Check the patient's skin, and if required massage a little E45 on to the electrode site. Reassure the patient that any reddening will settle down. Fill in the session details on patient tracker sheet and use comments box to explain if session shortened.

### **HELP?**

If the patient felt any undue discomfort during ES, or if you, or they, have any queries about proceeding, please contact DR MARK BARBER. (Dial 1000 and ask switchboard to radio page him) OR Sarah Mitchell on page 1671 or ext 0546. See ES Guidelines Folder for key application points and trouble shooting!

## APPENDIX G

### KEY POINTS FOR ES APPLICATION FOR RESEARCH ASSISTANTS

1. Make sure that the patient's leg is clear of the ground.
2. Alcohol wipe leg.
3. Change machine settings?
4. Ankle weight?
5. Set stopwatch as well as giving patient the tick sheet.
6. Comfort questionnaire (SESSIONS 1 - 5 AND LAST ONE).
7. Check leg movement matches initial setting description.
8. Increase intensity to maximum tolerable during first 5 'contractions'.
9. Refresh indelible ink marks.
10. Fill in tracker sheet at the end of each session.
11. On patient discharge, transfer patient documentation from blue ward folder to the ES reference folder.

### TROUBLE SHOOTING - NO CONTRACTION?

- Check setting sheet comment about patient reaction to stimulation.
- Check battery.
- Check electrodes (try new set).
- Check leads (try different set).
- Try a different machine. The initial setting may be different, so go cautiously!
- Report to defective machine to Virginia (without mentioning patient name). If you can, transfer patient to a different machine pending repair.

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