

University of Southampton Research Repository
ePrints Soton

Copyright © and Moral Rights for this thesis are retained by the author and/or other copyright owners. A copy can be downloaded for personal non-commercial research or study, without prior permission or charge. This thesis cannot be reproduced or quoted extensively from without first obtaining permission in writing from the copyright holder/s. The content must not be changed in any way or sold commercially in any format or medium without the formal permission of the copyright holders.

When referring to this work, full bibliographic details including the author, title, awarding institution and date of the thesis must be given e.g.

AUTHOR (year of submission) "Full thesis title", University of Southampton, name of the University School or Department, PhD Thesis, pagination

UNIVERSITY OF SOUTHAMPTON
FACULTY OF ENGINEERING, SCIENCE AND MATHEMATICS
School of Electronics and Computer Science

**The Re-education of Upper Limb Movement Post Stroke using Iterative Learning
Control mediated by Electrical Stimulation**

by

Ann-Marie Hughes

Thesis for the degree of Doctor of Philosophy

January 2009

UNIVERSITY OF SOUTHAMPTON

ABSTRACT

FACULTY OF ENGINEERING, SCIENCE AND MATHEMATICS

SCHOOL OF ELECTRONICS AND COMPUTER SCIENCE

Doctor of Philosophy

THE RE-EDUCATION OF UPPER LIMB MOVEMENT POST STROKE USING
ITERATIVE LEARNING CONTROL MEDIATED BY ELECTRICAL STIMULATION

by Ann-Marie Hughes

An inability to perform tasks involving reaching is a common problem following stroke. Evidence supports the use of robotic therapy and electrical stimulation (ES) to reduce upper limb impairments following stroke, but current systems may not encourage maximal voluntary contribution from the participant. This study developed and tested iterative learning control (ILC) algorithms mediated by ES, using a purpose designed robotic workstation, for upper limb rehabilitation post stroke. Surface electromyography (EMG) which may be related to impaired performance and function was used to investigate seven shoulder and elbow muscle activation patterns in eight neurologically intact and five chronic stroke participants during nine tracking tasks. The participants' forearm was supported using a hinged arm-holder, which constrained their hand to move in a two dimensional horizontal plane. Outcome measures taken prior to and after an intervention consisted of the Fugl-Meyer Assessment (FMA) and the Action Research Arm Test (ARAT), isometric force and error tracking. The intervention for stroke participants consisted of eighteen sessions in which a similar range of tracking tasks were performed with the addition of responsive electrical stimulation to their triceps muscle. A question set was developed to understand participants' perceptions of the ILC system. Statistically significant improvements were measured ($p \leq 0.05$) in: FMA motor score, unassisted tracking, and in isometric force. Statistically significant differences in muscle activation patterns were observed between stroke and neurologically intact participants for timing, amplitude and coactivation patterns. After the intervention significant changes were observed in many of these towards neurologically intact ranges. The robot-assisted therapy was well accepted and tolerated by the stroke participants. This study has demonstrated the feasibility of using ILC mediated by ES for upper limb stroke rehabilitation in the treatment of stroke patients with upper limb hemiplegia.

Table of Contents

TABLE OF CONTENTS	II
LIST OF FIGURES	V
LIST OF TABLES	IX
DECLARATION OF AUTHORSHIP	1
ACKNOWLEDGEMENTS	2
GLOSSARY OF ABBREVIATIONS	3
1 INTRODUCTION	4
1.1 Justification	4
1.2 Techniques investigated	5
1.3 Study objective and aims	6
1.4 Experimental research undertaken	7
1.5 Summary of main findings	8
1.6 Structure of thesis	9
1.7 Publications	10
1.8 Summary	11
2 BACKGROUND	12
2.1 Motor learning and control	12
2.1.1 Normal movement	13
2.1.2 Stroke sequelae	14
2.1.3 Motor Learning Theory	15
2.1.4 Motor control	23
2.2 Feedforward control systems - ILC	28
2.2.1 Notation	30
2.2.2 P - type ILC	31
2.3 Review of novel interventions	32
2.3.1 Rehabilitation robots and Electromechanical Devices	32
2.3.2 ES in rehabilitation	42
2.4 Screening tools and evaluation of novel interventions	48
2.4.1 Outcome measures	49
2.4.2 Criteria governing choice of screening and outcome measures	50
2.4.3 Screening tools	52
2.4.4 Clinical outcome measures	53
2.4.5 Non clinical impairment measures	54

2.4.6 EMG	54
2.5 Summary	58
3 METHODOLOGY	60
3.1 Preliminary work	60
3.1.1 Interdisciplinary development of the robot workstation	61
3.1.2 Arm modelling	65
3.1.3 Control scheme	68
3.1.4 Selection of the tasks	69
3.1.5 EMG	70
3.1.6 Electrical stimulation: muscle choice, application and parameters	71
3.2 Neurologically intact participants	73
3.2.1 Study design	73
3.2.2 Participant information	74
3.2.3 Intervention	74
3.2.4 Data processing and analysis	80
3.2.5 Statistical analysis	82
3.3 Stroke participants	83
3.3.1 Study design	83
3.3.2 Participant information	85
3.3.3 Intervention	85
3.3.4 Data processing and analysis for the clinical study	88
3.3.5 Statistical analysis	89
3.3.6 Participant perceptions	89
3.4 Summary	90
4 RESULTS	91
4.1 Neurologically intact participants	92
4.1.1 Tracking error	92
4.1.2 Isometric force	96
4.1.3 Analysis of EMG	97
4.1.4 Summary of results for neurologically intact participants	106
4.2 Stroke participants	107
4.2.1 Clinical outcome measures	109
4.2.2 Tracking error without ES	110
4.2.3 Changes in shoulder and elbow angle resulting from stimulation	112
4.2.4 Isometric force	113
4.2.5 MIVC Data	115
4.2.6 EMG	116
4.2.7 Percentage maximum ES	126
4.2.8 Individual data	128
4.2.9 Participant perceptions	133
4.3 Summary	136
5 DISCUSSION	138
5.1 Summary of the empirical findings	138
5.1.1 Changes in clinical outcome measures	138
5.1.2 Changes in tracking error	140
5.1.3 Directional variation in isometric force	140

5.1.4	Differences in EMG between neurologically intact and stroke participants, and changes in EMG in stroke participants in response to the intervention	141
5.1.5	Changes in percentage maximum ES	146
5.1.6	Participant perceptions	147
5.1.7	Summary	148
5.2	Limitations of the study	149
5.2.1	EMG measurement and muscle activation patterns	149
5.2.2	Participant perceptions	150
5.3	Clinical implications of the study	150
5.4	Future research related to the study	151
5.4.1	Interpretation of results and sample size calculation	152
5.4.2	Motor impairments and activities	153
5.4.3	User requirements and evaluation tools	155
5.5	Summary	156
6	CONCLUSION	158
7	APPENDICES	160
A	Muscles of the shoulder and elbow	161
B	Current neurorehabilitation approaches	162
C	Information sources	163
D	Papers included by Prange (2006), Teasell (2007) Kwakkel (2008) and Mehrholz (2008)	164
E	Differences between the normal physiological system and external stimulation of nerves	166
F	Force sensor calibration data	167
G	Participant perception questionnaire	168
H	Participants' responses to open questions	171
I	Categories for responses to open questions	176
J	EMG and tracking error changes for each participant for each task	180
K	Ethics and insurance forms	181
8	GLOSSARY	207
9	REFERENCES	210

LIST OF FIGURES

Figure 1: Flow diagram of study chronology	8
Figure 2: Stretch reflex (Purves et al., 2001)	24
Figure 3: Voluntary motor control for a) classical and b) current view of motor connections (Lang et al., 2006)	26
Figure 4: Block diagram for the control of muscle length (muscle stretch reflex)	28
Figure 5: ILC concept (Moore & Xu, 2000)	29
Figure 6: Plot of how the variable $y_k(t)$ changes with trial length and iteration (Rogers, 2007)	31
Figure 7: Controller voltage signal (v) vs. pulse width (μ s)	43
Figure 8: Torque (Nm) vs. pulse width (μ s)	44
Figure 9: Twitch response variance with frequency (Kimball, 2008)	45
Figure 10: ICF framework and stroke	49
Figure 11: Linkage arrangement for the robotic arm	62
Figure 12: Close up of a trajectory projected on to the plastic surface	63
Figure 13: Robot workstation schematic showing principal elements and signal requirements	64
Figure 14: Control strategy for the study using a linearising PD controller in the feedback arrangement	69
Figure 15: Control strategy for the study using ILC in addition to the feedback control	69
Figure 16: Pilot work using ES to follow the trajectory	72
Figure 17: Flowchart for neurologically intact participants	73
Figure 18: Participant performing tracking task using the robot workstation showing method of constraint	75
Figure 19: Isometric force measurement directions	75
Figure 20: Description of actual and reference position (red target dot) along a trajectory	76
Figure 21: The reference (black) and actual (blue) tracking error is shown for participant 02 over the T1 LFH trajectory over the a) x and b) y axis. The tracking error magnitude is shown in c)	77
Figure 22: The position of shoulder, elbow and hand at the initial and extended positions on the T3 MMM trajectory (100% reach = 0.658m)	78

Figure 23: Filtered, rectified, smoothed EMG amplitude (µV) against time (s) during maximum voluntary contraction of a) triceps, b) biceps, c) anterior deltoid, d) upper trapezius, e) middle trapezius, f) pectoralis major and g) lower trapezius for participant 01.....	81
Figure 24: Flowchart for the clinical study.....	83
Figure 25: Stroke participant performing a tracking task using the robot showing the method of restraining trunk flexion	86
Figure 26: The position of shoulder, elbow and hand for participant 3 at the initial (dotted) and extended (dashed) positions for the T3LS reference trajectory.....	87
Figure 27: Mean tracking error against iteration number using no stimulation for the T3 MMM trajectory over three iterations for eight participants	94
Figure 28: Mean tracking error (m) against iteration number using ILC mediated by ES for the T3 MMM trajectory over six iterations for five participants.....	95
Figure 29: Trajectory tracking pattern for participant 06 showing three repetitions for T3 tasks.....	96
Figure 30: Raw EMG data for triceps, biceps and the synchronisation pattern for participant 02 over the T1 LFH trajectory	98
Figure 31: Mean amplitude and mean (SD) temporal position of peak EMG during each task across the eight participants. For each task, wedge height and position are given by µEMG and µT ± 0.5 σT. The mean position, µT, of max EMG amplitude is indicated by a line of the same colour orthogonal to the trajectory. T1, 2 and 3 correspond to the orientation of the trajectory. SSL, MMM, and LFH are abbreviations for the length, duration and resistance respectively of the task.....	103
Figure 32: IEMG normalised activation averaged across all participants for a) triceps and b) biceps during the T1 LFH task. Sample mean (indicated by a thicker line), 0.5 and 1 SD envelopes are shown. Maximum reach was at 2.5s. Intervals in which mean EMG exceeds 70 (palest), 80, 90 (darkest) percent of the peak value are also shown	104
Figure 33: IEMG normalised activation averaged across all participants for triceps and biceps (right arm): Intervals in which mean EMG exceeds 70 (palest), 80, 90 (darkest) percent of the peak value are ‘wrapped’ around each trajectory	105
Figure 34: Baseline and Post Treatment FMA scores for stroke participants	110
Figure 35: Baseline and Post Treatment ARAT scores for stroke participants	110

Figure 36: Changes in tracking error data for each participant for each unassisted trajectory performed at the beginning of each treatment session a) T1SS b) T1MS c)T2MS d) T2SS	111
Figure 37: Trajectory tracking pattern for participant 3 showing three repetitions for T3 tasks.....	112
Figure 38: Changes in a) the shoulder and b) elbow angle due to c) stimulation during a T1SS trajectory for participant 3	113
Figure 39: Mean isometric force for each stroke participant: initially, post 18 and post 25 sessions	115
Figure 40: Mean amplitude and mean (SD) temporal position of peak EMG during each task for biceps and triceps for five stroke and eight neurologically intact participants. The mean position, μ T, of max EMG amplitude is indicated by a line of the same colour orthogonal to the trajectory for stroke participants a) pre intervention (solid with circle b) post intervention (dot-dash) and c) neurologically intact (solid). For neurologically intact participants wedge height and position are given by μ EMG and μ T \pm 0.5 σ T for each task. T1, 2 and 3 correspond to the orientation of the trajectory. SSL, MMM and LFH are abbreviations for the length, duration and resistance respectively of the task	121
Figure 41: IEMG normalised activation averaged across stroke participants a) pre intervention b) post intervention and c) for neurologically intact participants for triceps (blue) and biceps (red) during the T1 LFH task. Sample mean (indicated by a thicker line), 0.5 and 1SD envelopes are shown. Maximum reach was at 2.5s. Intervals in which mean EMG exceeds 70 (palest), 80, 90 (darkest) percent of the peak value are also shown by the bar drawn along the x axis.	123
Figure 42: IEMG normalised activation averaged across stroke participants a) pre intervention b) post intervention and c) for neurologically intact participants for triceps (blue) and biceps (red) during the T1, T2 and T3 LFH tasks; Intervals in which mean EMG exceeds 70 (palest), 80, 90 (darkest) percent of the peak value are 'wrapped' around each trajectory	125
Figure 43: Data recorded for all participants during the ES assisted T1SS tracking task showing a) error in tracking b) % max stimulation used	127
Figure 44: Mean error tracking (without ES) for two participants across a short and a medium trajectory.....	128

Figure 45: Isometric force for two participants over the intervention, compared to neurologically intact participants	129
Figure 46: % peak timing data for triceps and biceps for participant 3 pre and post intervention.....	130
Figure 47: % peak timing data for triceps and biceps for participant 4 pre and post intervention.....	131
Figure 48: % peak amplitude data for triceps and biceps for participant 3 pre and post intervention.....	131
Figure 49: % peak amplitude data for triceps and biceps for participant 4 pre and post intervention.....	132
Figure 50: Muscles surrounding the shoulder (Palastanga et al., 1998)	161
Figure 51: % change in peak amplitude towards normal for triceps against change in total error (m) for each participant for each task.....	180
Figure 52: % change in peak timing towards normal for triceps against change in total error (m) for each participant for each task	180

LIST OF TABLES

Table 1: Type, forms and definition of procedural learning.....	16
Table 2: Aspects of motor learning addressed in the ILC study and suggested improvements.....	18
Table 3: Elements for a physiological system.....	27
Table 4: Statements and questions published on user perceptions	41
Table 5: Screening tests criteria	51
Table 6: Upper limb impairment criteria	51
Table 7: Upper limb activity criteria.....	52
Table 8: Length, duration and resistance for each level of task, each of which was performed at three angles: midline and 20% of maximum range to the left and right. Abbreviations used for each task are shown in the right hand column	79
Table 9: Angle, length and duration for each level of task. Abbreviations used for each task are shown in the right hand column	86
Table 10: Demographic characteristics of neurologically intact participants	92
Table 11: Mean tracking error (no stimulation) (m) for all participants over three repetitions of each task.....	93
Table 12: Mean tracking error (m) for participants showing sample mean (SD) over all tasks	94
Table 13: Isometric force (N) generated by neurologically intact participants. Mean (SD) and range [Min-Max] are also shown.....	97
Table 14: Mean (SD) and range [Min-Max] maximum voluntary isometric contraction factor (μ V) generated by neurologically intact participants	99
Table 15: Mean (SD) EMG times of maximum amplitude across orientations and task conditions (expressed as % task duration)	100
Table 16: Mean (SD) EMG maximum amplitude across orientations and task conditions (expressed as % MVIC 'factor').....	101
Table 17: Mean (SD) percentage co-activation of triceps and biceps across orientations and tasks	106
Table 18: Demographic characteristics of study stroke participants with FMA score giving an indication of the level of impairment.....	108

Table 19: Mean (SD) and range [Min-Max] for clinical outcome measures for stroke participants at Baseline and Post Treatment (18 sessions). Mean change (SD) during the 18 intervention sessions, level of significance (Paired t-test) and 95% CI are also shown.....	109
Table 20: Mean and SD of error tracking data generated by all participants for baseline and post 18 sessions	111
Table 21: Mean (SD) and range [Min-Max] isometric force (N) generated by neurologically intact and stroke participants at Baseline and Post Treatment (18 sessions). Mean change (SD), during the 18 treatment sessions, level of statistical significance (Paired t-test) and 95% CI are also shown	114
Table 22: Mean (SD) and range [Min-Max] maximum voluntary isometric contraction factor (μ V) generated by neurologically intact and stroke participants at Baseline and Post Intervention (18 sessions). Mean change (SD) during the 18 intervention sessions, level of statistical significance (Paired t-test) and 95% CI are also shown	116
Table 23: The level of significance for timing of peak activity and amplitude for all muscles across all tasks for i) stroke compared to neurologically intact participants ii) stroke participants pre and post intervention iii) whether the change in the direction for stroke participants is towards that of the neurologically intact participants	119
Table 24: Mean (SD) percentage co-activation of triceps and biceps across each task for neurologically intact and stroke participants pre and post intervention	126
Table 25: Examples of comments collected during the study.....	133
Table 26: Statements and responses from the Likert style questions	134
Table 27: Open responses on system effectiveness	134
Table 28: Open responses on how the system could be improved.....	135
Table 29: Open general questions.....	136
Table 30: Estimated number of participants required for each effect size and SD assumption	153

DECLARATION OF AUTHORSHIP

I, Ann-Marie Hughes, declare that thesis entitled 'The Re-education of Upper Limb Movement Post Stroke using Iterative Learning Control mediated by Electrical Stimulation' and the work presented in this thesis are both my own, and have been generated by me as the result of my own original research. I confirm that:

- this work was done wholly or mainly while in candidature for a research degree at this University;
- where any part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution, this has been clearly stated;
- where I have consulted the published work of others, this is always clearly attributed
- where I have quoted from the work of others, the source is always given. With the exception of such quotations, this thesis is entirely my own work;
- I have acknowledged all main sources of help;
- where the thesis is based on work done by myself jointly with others, I have made clear exactly what was done by others and what I have contributed myself;
- parts of this work have been published as:

Hughes, A. M., Freeman, C., Burridge, J., Chappell, P., Lewin, P. and Rogers, E. (2009) [Upper limb rehabilitation post stroke using Iterative Learning Control mediated by Functional Electrical Stimulation](#). *Journal of Neurorehabilitation and Neural Repair*. DOI: 10.1177/1545968308328718

Hughes, A. M., Burridge, J., Freeman, C., Chappell, P., Lewin, P. and Rogers, E. (2008) [Robotic trajectory tracking for neurological rehabilitation](#). *Progress in Neurology and Psychiatry*, 12 (3). pp. 22-24. ISSN 1367-7543

Hughes, A. M., Freeman, C., Burridge, J., Chappell, P., Lewin, P. and Rogers, E. (2009) [Shoulder and elbow muscle activity during fully supported trajectory tracking in healthy older people](#). *Journal of Electromyography and Kinesiology*. DOI: 10.1016/j.jelekin.2008.09.015 .

Signed:
Date:

ACKNOWLEDGEMENTS

I would like to thank my supervisors, Dr Paul Chappell and Prof Jane Burridge for their wisdom, guidance and encouragement throughout my PhD.

Acknowledgements must also go to Prof Eric Rogers and Dr Paul Lewin. I am indebted to Dr Chris Freeman who has written computer software, designed, built, redesigned and rebuilt the ILC system and for all his engineering solutions to clinical questions. I would also like to thank Dr Ruth Pickering for providing statistical support, and Dr Maggie Donovan-Hall for interviewing the participants for the perception study.

To all the participants who gave freely of their time, tolerated all the assessments and gave helpful suggestions, I am grateful.

I would like to thank my friends and colleagues who have been an enormous support throughout my studies sharing ideas and coffee, particularly Chris, Ruth, Sara, Alda, Maggie, Claudia and Jenny.

My husband, David, I thank him for his love and support, encouragement and proof-reading. Finally I would like to thank my mum and dad, for their enduring guidance, support, joy and love. Without their encouragement, this would not have begun.

GLOSSARY OF ABBREVIATIONS

ADL	Activities of Daily Living
ARAT	Action Research Arm Test
CNS	Central nervous system
DOH	Department of Health
EBRSR	Evidence based review of Stroke Rehabilitation
EMG	Electromyography
ES	Electrical Stimulation
FES	Functional Electrical Stimulation
FIM	Functional Independence Measure
FMA	Fugl-Meyer Assessment
ILC	Iterative Learning Control
LTD	Long term depression
LTP	Long term potentiation
MSR	Muscle stretch reflex
MSS	Motor Status Scale
MVIC	Maximum voluntary isometric contractions
NDT	Neurodevelopmental Treatment
NHS	National Health Service
NT	Neurotransmitter
PD	Proportional + Derivative Control
PEDro	Physiotherapy evidence Database
RCT	Randomised Controlled Trial
sEMG	Surface electromyography
WHO	World Health Organisation

1 Introduction

This chapter presents a justification for the research, introduces the combination of techniques investigated, outlines the specific objective and aims of the study, and summarises the experimental components of the research and the main findings. The thesis structure is summarised and the publications resulting from the study are listed.

1.1 Justification

Strokes affect between 174 and 216 people per 100,000 population in the UK each year (Mant et al., 2004) and account for 11% of all deaths in England and Wales (Intercollegiate Stroke Working Party, 2008). The average stay in hospital for stroke patients is 28 days, resulting in direct costs to the UK's National Health Service (NHS) of £2.8 billion a year, and some £1.8 billion more in lost productivity and disability to the wider economy. Additionally, the annual informal care costs (costs of home nursing and care borne by patients' families) are about £2.4 billion (National Audit Office, 2005).

As stroke is an age-related pathology, the proportion of elderly people in the population is important. Changing demographics within England mean that the percentage of people aged over 65 will increase from 16% in 2003 to 23% in 2031 (National Audit Office, 2005) creating an increased burden on health care and rehabilitation resources (assuming that dependency rates, patterns of care and current funding arrangements remain unchanged). When this effect is added to improved emergency care, many more survivors with increasing levels of disability may be seen.

Approximately two thirds of patients in England will survive their stroke; of the 900,000 stroke survivors fifty percent are disabled and dependent (National Audit Office, 2005). One of the most important factors affecting independence is normal upper limb function as demonstrated in measures of functional independence such as the Barthel ADL Index where the ability to reach is required for over 50% of the activity of daily living tasks (van der Putten et al., 1999) .

About 85% of patients learn to walk again. Although a high number of patients have upper limb impairments initially post stroke (Feys et al., 1998), very few regain useful arm movement (Kwakkel et al., 1999; Wade et al., 1983) despite therapy input in neurorehabilitation. One of the reasons why this is thought to occur is through the learnt disuse theory. Walking forces the use of the patient's hemiplegic leg. For the upper limb, however, patients 'compensate' i.e. they adapt their strategy for accomplishing manual tasks by using their non hemiplegic arm and hand, which does not result in appropriate changes in neuroplasticity.

The rehabilitation of upper limb function, which is regarded as being a very important factor for independence, is a major problem which current approaches including the Bobath concept, Proprioceptive Neuromuscular Facilitation and Motor Re-learning (outlined in Appendix B) have not solved. If the capacity of health and social services is to meet future demand, new approaches to treatment are required. The design of these new approaches needs to be based on improved understanding of the mechanisms underlying motor control and disability as well as patients and healthcare professionals' needs. To examine benefit of the intervention a process of evaluation has to be conducted which must incorporate appropriate measuring tools. To have greatest clinical impact, the intervention has to be acceptable to the users.

1.2 Techniques investigated

Research into conventional therapy and motor learning theory provides evidence that intensity of practice of a task (Inaba et al., 1973; Winstein et al., 2004) variety, feedback and meaningful goals (Magill, 1998) are important. Levels of motivation are also suggested to affect people's views on motor skill learning (Maclean et al., 2000). There is only anecdotal evidence however confirming the link between motivation and rehabilitation outcome post stroke (Maclean et al., 2002).

Rehabilitation robots give people the opportunity to practice movements and systematic reviews of the robot therapy literature for the upper limb suggest that

robot aided therapy improves motor control of the proximal upper limb (Intercollegiate Stroke Working Party, 2008; Kwakkel et al., 2008; Prange et al., 2006) and may also improve functional outcomes (Teasell et al., 2007). Robotic systems have been able to provide assistance based on voluntary movement (e.g through use of active assisted, active resisted, and gravity compensated training programmes). An alternative technique to improve motor control is the application of Electrical Stimulation (ES). There is a body of clinical evidence to support this (De Kroon et al., 2002) and theoretical support from neurophysiology (Burridge & Ladouceur, 2001) and motor learning research (Schmidt & Lee, 1999). A review concluded that the effect of stimulation is enhanced when associated with the person's intention to move (De Kroon et al., 2005). Although systems have been developed in which electrical stimulation is triggered by muscle activity (Francisco et al., 1998), until now, techniques have not allowed feedback to adjust stimulation parameters during tasks. This is a drawback compared with the ability of the training modalities available during robotic assistance to promote voluntary activity. To achieve this using ES, the stimulation must be adjusted in response to the users' performance, in order to provide only the minimum level of stimulation needed to assist the participant in performing the task to a high level of accuracy. However, as far as we know, no systems have been developed that do this. A possible advantage in using ES is that the exercise is conducted through the participant's own muscles rather than via forces applied using a robot. Even if a stroke participant does not contribute voluntary movement, benefits may still be conferred through the reported benefits of ES such as increased muscle strength (Bowman et al., 1979) and cortical excitability (Ridding et al., 2001). This research aims to develop such a system, using a robot workstation and Iterative Learning Control (ILC) mediated by ES. ILC has its origins in the control of processes that repetitively perform a task with a view to improving accuracy from trial to trial by using information from previous executions of the task. The classic example is the area of trajectory following in industrial robot applications.

1.3 Study objective and aims

The primary objective of the study was to test the feasibility of re-educating upper limb movement post stroke, using ILC mediated by ES using a robotic workstation. The design of the intervention was optimised to encourage motor learning within the constraint of the primary objective.

Other aims were to provide answers to the following questions:

- How do isometric force, kinematic measures and muscle activation patterns for upper limb muscles during identified specific reaching tasks using a robot arm differ for neurologically intact subjects and stroke patients?
- For the stroke patients are these affected by undergoing an intervention programme using the robot and ES? If so, how? Are these changes reflected in clinical measures?
- What are the stroke participants' perceptions of the system?

In order to achieve these aims, preliminary work was conducted. Preliminary objectives were:

- To design and develop a ES tool for re-education of upper limb function allowing the practical application of suitable ILC strategies.
- To develop and validate models of the ES system and of the relationship between muscle stimulation and the associated position of the participant's arm and hand.
- To use the developed models to design a range of ILC control algorithms and validate and compare their performance prior to participant based testing.
- To select the task and muscles to record the EMG from, as well as identifying the muscle to be stimulated.

1.4 Experimental research undertaken

The system was tested and refined with eight neurologically intact participants. Normal isometric force was tested in a range of directions and muscle activation patterns were identified during a range of defined movements in the robot workstation. The ability of ILC to correct tracking error via stimulation when no voluntary input was provided by the participant was also tested. Subsequently the system was used by five chronic stroke participants with impaired arm function. Isometric force and muscle activation patterns were again measured. Stroke participants actively tried to track the trajectories using a level of ES to keep them working at the limit of their performance. The stroke participants' surface electromyographic and tracking error performance was contrasted with that of the neurologically normal participants. The study chronology and resulting publications are displayed schematically in Figure 1.

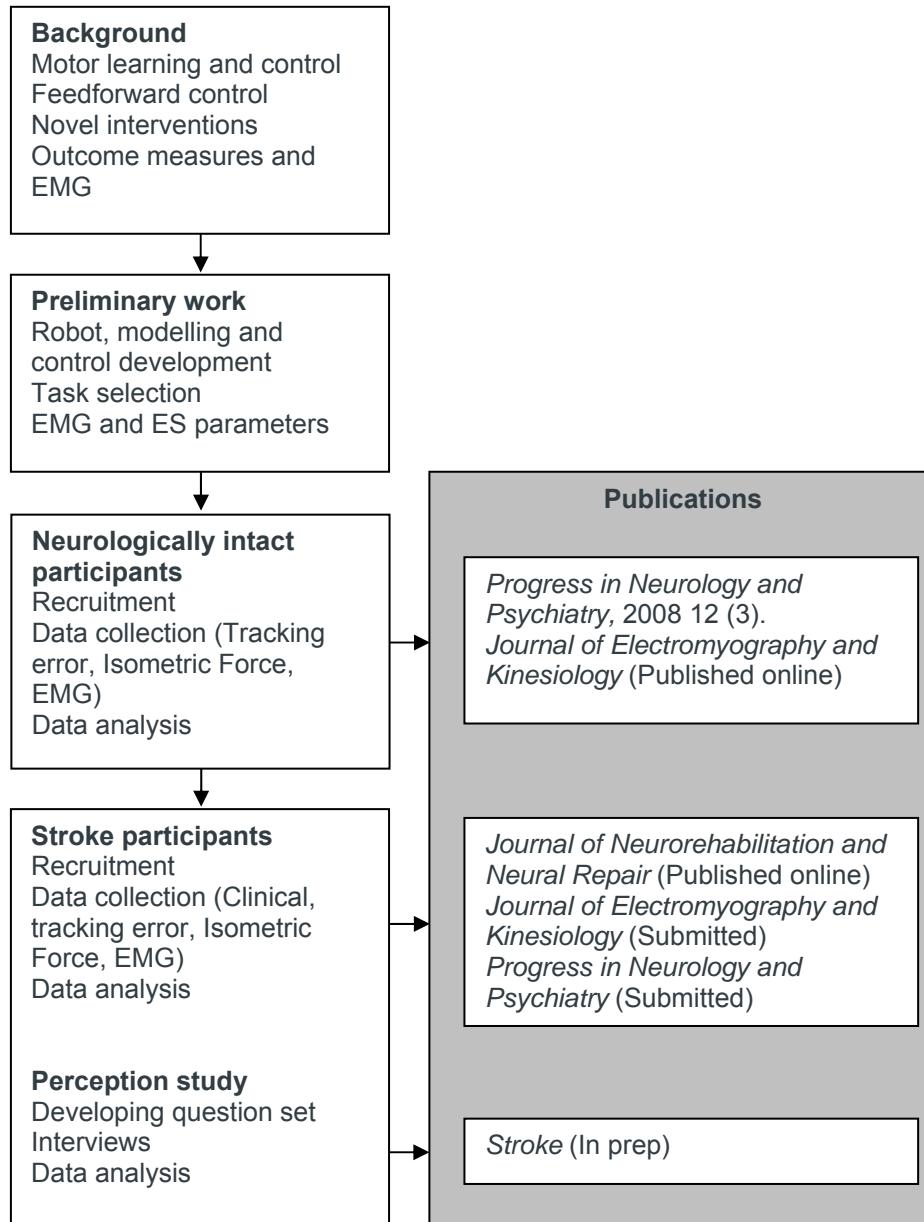


Figure 1: Flow diagram of study chronology

1.5 Summary of main findings

The level of statistical significance accepted in the study was $p \leq 0.05$. Following intervention, statistically significant improvements were measured in: Fugl-Meyer Assessment (FMA) motor score, unassisted tracking (i.e. using the participant's voluntary movement without ES or robot assistance) for three out of four trajectories and in isometric force over five out of six directions for the stroke participants.

Statistically significant differences in muscle activation patterns were observed for stroke compared to neurologically intact participants in: timing (triceps, anterior deltoid, upper trapezius, middle trapezius and pectoralis major); amplitude (biceps, pectoralis major, middle and lower trapezius); and the coactivation patterns of biceps and triceps for four of the nine tasks. After the intervention significant changes were observed towards normal in: timing (triceps, pectoralis major and upper trapezius); amplitude (biceps and middle trapezius); and the coactivation patterns of biceps and triceps for four of the nine tasks. Changes in ARAT were not statistically significant.

The finding from the participant perception study that the ES and robotic workstation system was well accepted and tolerated by the stroke participants was in common with other rehabilitation robot studies (Coote & Stokes, 2003; Doornbosch et al., 2007; Krebs et al., 1998). The time required participating in the intervention and the inconvenience of travelling to the lab, were viewed as the least positive aspects of the study. Stroke participants' comments on the best aspects of the study could be separated into physical and psychological benefits, research interaction, being involved, feedback and enjoyment.

1.6 Structure of thesis

Chapter two reviews the relevant literature informing the research. It considers both normal and impaired movements, as well as theories on motor learning and control and ILC (the control mechanism used in this study). The clinical evidence resulting from interventions using rehabilitation robots and ES is discussed and appraised and includes a discussion of published user perspectives. This is then followed by sections on outcome measures including clinical and robot based measures and EMG. The experimental part of the thesis begins with Chapter three which reports the preliminary work underpinning the research study. This includes the design of the workstation, the arm modelling and algorithm development, as well as the selection of the tasks, muscles for EMG and ES and the parameters used. The chapter continues with the methodology (study design, recruitment of participants, intervention, data processing and statistical analysis) for both the neurologically intact and the stroke participants. In Chapter four the results of the neurologically intact and stroke participants are presented. Tracking error, isometric force and EMG are discussed for both groups. Additionally for the stroke participants, clinical outcome measures, percentage maximum ES, and participant perception question set responses are reported. The analysis of the empirical findings is presented in

Chapter five, together with the limitations and clinical implications of the study and the direction of future work. Chapter six contains the study conclusions.

1.7 Publications

Some of the work in this thesis has already been published or presented at scientific meetings listed below:

Journal Publications

Hughes, A. M., Freeman, C., Burridge, J., Chappell, P., Lewin, P. and Rogers, E. (2008) [Upper limb rehabilitation post stroke using Iterative Learning Control mediated by Functional Electrical Stimulation](#). *Journal of Neurorehabilitation and Neural Repair*. DOI:10.1177/1545968308328718

Hughes, A. M., Burridge, J., Freeman, C., Chappell, P., Lewin, P. and Rogers, E. (2008) [Robotic trajectory tracking for neurological rehabilitation](#). *Progress in Neurology and Psychiatry*, 12 (3). pp. 22-24. ISSN 1367-7543

Hughes, A. M., Freeman, C., Burridge, J., Chappell, P., Lewin, P. and Rogers, E. (2008) [Shoulder and elbow muscle activity during fully supported trajectory tracking in healthy older people](#). *Journal of Electromyography and Kinesiology*. DOI: 10.1016/j.jelekin.2008.09.015 .

Conference Publications

Hughes, A. M., Freeman, C., Burridge, J., Chappell, P., Lewin, P. and Rogers, E. (2009) [Upper Limb Rehabilitation of Stroke Participants using Electrical Stimulation: Changes in Tracking and EMG Timing](#). In: *11th International Conference on Rehabilitation Robotics*, 23-26 June, Kyoto, Japan. (In Press)

Hughes, A. M., Burridge, J., Freeman, C., Chappell, P., Lewin, P. and Rogers, E. (2008) [Changes in upper limb isometric strength and error tracking following training using iterative learning control \(ILC\) mediated by functional electrical stimulation \(FES\)](#). In: Annual Meeting of European Society For Movement Analysis For Adults and Children, 08-13 September 2008, Antalya, Turkey.

Hughes, A. M., Burridge, J., Freeman, C., Chappell, P., Lewin, P. and Rogers, E. (2008) [Re-education of upper limb function post stroke, using Iterative Learning Control \(ILC\) mediated by Functional Electrical Stimulation \(FES\)](#). In: *6th World Stroke Congress*, Sept 24-27, Vienna, Austria.

Hughes, A. M., Freeman, C., Burridge, J., Chappell, P., Lewin, P. and Rogers, E. (2007) [Can Iterative Learning Control \(ILC\) mediated by Functional Electrical Stimulation \(FES\) be used in the re-education of upper limb function post stroke?](#) In: *International Functional Electrical Stimulation Society Conference* , 10-14th November 2007, Philadelphia, USA .

Hughes, A. M., Freeman, C. T., Burridge, J. H., Chappell, P. H., Lewin, P. L. and Rogers, E. (2007) [Can Iterative Learning Control be used in the Re-education of Upper Limb Function, Mediated by Functional Electrical Stimulation \(FES\)?](#) In: *Progress in Motor Control VI*, 9-12 August 2007, Santos, Brazil.

Hughes, A. M., Burridge, J. H., Freeman, C., Chappell, P., Lewin, P. and Rogers, E. (2007) [Can Iterative Learning Control Be Used In The Re-Education of Upper Limb Function, Mediated by Functional Electrical Stimulation \(FES\)?](#) In: *The Future of Restorative Neuroscience in Stroke Rehabilitation*, 24 - 26 September 2007, Windsor, UK.

Hughes, A. M., Burridge, J., Freeman, C., Chappell, P., Lewin, P. and Rogers, E. (2007) [Can Iterative Learning Control be used in the Re-education of upper limb function?](#) In: LSI Forum Conference, 15 March 2007, Southampton.

Hughes, A. M., Burridge, J., Freeman, C., Chappell, P., Lewin, P. and Rogers, E. (2006) [What is the current role of rehabilitation robots in upper limb post stroke therapy?](#) In: 1st UK Stroke Forum Conference, 07 December 2006, Harrogate, UK.

Papers Submitted:

Hughes, A. M., Freeman, C., Burridge, J., Chappell, P., Lewin, P. and Rogers, E. (2009) [Shoulder and elbow muscle activity during fully supported trajectory tracking in people who have had a stroke.](#) *Journal of Electromyography and Kinesiology* . (Submitted)

Hughes, A. M., Freeman, C., Burridge, J., Chappell, P., Lewin, P. and Rogers, E. (2009) [Neurological rehabilitation using Electrical Stimulation mediated by Iterative Learning Control.](#) *Progress in Neurology and Psychiatry* . (Submitted)

Papers Under Development:

Hughes, A.M. MSc, Donovan-Hall, M. PhD, Burridge, J. PhD, Freeman, C. PhD, Chappell, P. PhD Dibb, B. PhD. Stroke participants' perceptions on using a robotic workstation and Iterative Learning Control mediated by FES. Target Journal: Stroke

1.8 Summary

This chapter has presented the justification for the research, the techniques investigated and the study aims and objectives. It has presented the experimental work undertaken and the summary of the main findings. The structure of the thesis has been explained, and the publications resulting from the study listed.

2 Background

The aim of this Chapter is to provide an overview of the background which underpins this research study. To design appropriate interventions which aim to give stroke patients more normal movement, the components of normal movement, as well as stroke sequelae have to be understood. This chapter therefore begins by outlining these topics. It continues with a discussion of the theories of motor learning and control and describes feedback / and feedforward control in order to explain the next section devoted to ILC (the control mechanism being used in the study). The literature relating to the clinical evidence resulting from interventions using rehabilitation robots and ES, as well as user perceptions is evaluated. The final sections discuss and critically review the clinical outcome measures used. Outcome measures produced by the robot (developed in the study) and EMG are also discussed.

2.1 Motor learning and control

This research is based on the principle that similarities may exist between normal motor control development and skill acquisition, and recovery post insult to the central nervous system. The section begins by briefly outlining some of the components of normal motor control and stroke sequelae. In the following section factors influencing learning are outlined and 'plasticity', the mechanism by which learning is believed to occur, is discussed. Knowledge of plasticity could influence how interventions (e.g. the ILC/ES/robotic workstation) are designed, as well as facilitating understanding of how patients' movement might be affected. Theories of motor control are then outlined.

Motor learning has been defined as 'the study of the acquisition and / or modification of movement' (Shumway-Cook & Woollacott, 2001). It is the set of processes

associated with practice (by an individual, of a task within an environment) which leads to relatively permanent changes in capability for movement (Schmidt & Lee, 1999) and can be both adaptive and compensatory. Control theory can be defined as the ability to regulate or direct the mechanisms essential to a system. Motor control has been defined as 'the ability to regulate and direct the mechanisms essential to movement' (Shumway-Cook & Woollacott, 2001).

2.1.1 Normal movement

An understanding of what constitutes 'normal' motor control is essential to be able to identify components outside a normal range of motor impairments and to determine whether people with impaired motor control improve. Possible mechanisms can be postulated and then used as a basis for developing new interventions based on motor learning theory to improve motor control. The intervention developed in this study uses the application of ES to stimulate appropriate nerves to induce muscle activity in the triceps at the same time as the stroke participant is trying to perform a movement. In this section muscles and the factors affecting them, reflexes and physiological nerve conduction have been outlined.

In order to design the intervention, physiological factors which affect normal and impaired movement have to be considered as well as awareness of implications of differences between physiological and electrical stimulation.

The contraction of skeletal muscle and fibrous connective tissues pulling on collagen fibres of tendons and bone matrix is responsible for movement or, through co-activation, the stabilising of the skeleton (for details of muscles responsible for moving and stabilising the shoulder and elbow see Appendix A). The mechanism thought to be responsible for skeletal muscle contraction is the sliding filament theory (Huxley & Hanson, 1954). The slight elasticity of the connective tissues helps to return muscles to their resting lengths, as well as adding to the power and efficiency of the muscles through recoil.

Factors which are known to affect this movement and therefore had to be taken into consideration in the design of the intervention included muscle mechanical factors such as the length tension (at optimum length a muscle contracts more forcefully) and force velocity relationships. Additionally, neural factors such as the capacity of the nervous system to activate muscle through the number and frequency of firing of

motor units affect movement. Structural factors such as the relative proportions of muscle fibre types, muscle size, fascicle arrangement and the size of active motor units (larger units produce stronger contractions) also have important effects.

The implications of differences resulting from normal physiological and ES (summarised in Appendix E) were also considered. Muscle fibre type is dependent on function. Within a single muscle there will be varying proportions of fibre types: slow fatigue resistant which are generally innervated by small alpha motor neurones develop tension slowly and can maintain it for long periods; and fast fatigable, innervated by large alpha motor neurones which develop tension rapidly but fatigue quickly. There are also some fibres that have the ability to morphose from one type to another in response to demand. When using ES to activate muscles, the pattern of recruitment of muscle fibres is different from that achieved during normal muscle activation with the larger motor units nearer the skin surface being activated preferentially, concurrently and repeatedly, exciting fast fatigable muscle fibres. Electrical stimulation therefore causes muscle fibre fatigue more quickly than physiological stimulation.

Another difference between ES and physiological stimulation is seen in the directions in which action potentials travel. Physiological stimulation of nerves throughout the body is based on ionic concentration gradients. These can be slow local potential changes (synaptic potentials) as well as actively propagated potentials (action potentials) for conveying information over distances. For a brief time after the peak of an action potential (the absolute refractory period) another impulse can not be generated. This limits the repetition rate of action potentials and ensures that action potentials under normal physiological conditions occur only in one direction – orthodromically. When a muscle is stimulated using ES however, impulses travel in two directions, ortho and antidromically.

2.1.2 Stroke sequelae

Following stroke many people have a complex and varied pattern of motor and functional impairment in the hemiplegic upper extremity. The aim of rehabilitation is to promote functional recovery through the facilitation of motor control and skill acquisition. Having an understanding of the main neurophysiological changes associated with stroke-related movement variation is essential in designing effective management plans for individuals. This knowledge allows the multidisciplinary team to design interventions to ensure that aggravating and trigger factors for associated

problems (outlined below) are managed appropriately; and facilitate understanding of possible mechanisms for any intervention effects.

Abnormal signs and symptoms (the upper motor neuron syndrome), as well as other problems, depend on the location and size of the brain injury more than the type of stroke, and have to be considered by the developers of any rehabilitation system. Damage to descending motor systems can result in hemiplegia, muscle imbalance, coordination difficulties, altered recruitment patterns, contractures, spasticity, spasms, clonus and a positive Babinski sign. An occlusion of the anterior cerebral artery within the brain for example, will result in contralateral weakness (greater in the leg than the arm) and in cortical sensory loss, aphasia, and apraxia. The upper limb may show involuntary movements, and incontinence and self neglect may also result.

For the purposes of this study, however, only motor control aspects relating to the upper limb are discussed. The importance of upper limb movement to independence is reflected in measures of functional independence such as the Barthel ADL Index (van der Putten et al., 1999) where the ability to reach is required for over 50% of the activity of daily living tasks. Active range of movement at the shoulder and elbow (Cirstea & Levin, 2000) and reach extent (Kamper et al., 2002) have been shown to be reduced for chronic stroke compared to neurologically intact participants.

Following a unilateral stroke affecting areas subserving movement control, individuals have a number of deficits in stabilising arm postures and in producing functional arm movement (Mihaltchev et al., 2005). Some of the possible deficits / impairments which can occur include: muscle weakness (Canning et al., 2000; Nadeau et al., 1999; Patten et al., 2004), timing and magnitude of torque generation in both arms (McCrea et al., 2003), loss of dexterity (Canning et al., 2000), altered spatial and temporal muscle recruitment patterns (Reinkensmeyer et al., 2002), decreased co-ordination (Debaere et al., 2001; Katz et al., 1992), contractures (Patten et al., 2006) and spasticity (Katz et al., 1992).

2.1.3 Motor Learning Theory

A distinction can be drawn between non-associative learning where 'the person is learning about the properties of a stimulus that is repeated' and associative learning where 'a person learns to predict relationships, either relationships of one stimulus to another (classical conditioning) or the relationship of one's behaviour to a

consequence (operant conditioning)' (Shumway-Cook & Woollacott, 2001). This information is presented in Table 1.

Type	Forms	Definition
Associated	Habituation	Gradual waning of a behavioural response to a weak or moderate stimulus.
	Sensitisation	Enhancement of a behavioural response.
	Classical	Benign stimulus (BS) is paired with a stimulus (RS) which evokes a reflexive response. After training, the BS elicits a learned response which often resembles the reflexive response.
	Operant	Behaviours followed by desirable effects will tend to be repeated, whereas behaviours followed by adverse effects will tend to be suppressed.

Table 1: Type, forms and definition of procedural learning

Theories such as Adams's Closed-loop, the motor programming and the schema theory have been developed over the last fifty years to explain motor learning. The central tenet of the Closed-loop theory (Adams, 1971) was the use of closed loop processes (sensory feedback used for the ongoing production of skilled movement) in motor control. It proposed that a sequence of two types of memory are important in movement control: a memory trace used in the selection and initiation of the movement, and a perceptual trace built up over a period of practice (using error feedback) to become the internal reference. Adams suggested that movement is initiated by the memory trace, but is then replaced by the perceptual trace to complete the movement and detect the error (Shumway-Cook & Woollacott, 2001). The main criticisms of the theory come from research, which shows that movements can be made and certain types of learning can occur, without sensory feedback (e.g. central pattern generator), the lack of explanation for performance of novel tasks and the unlikely storage capacity required to maintain a variety of separate perceptual traces.

The motor programming theory (Keele, 1968) evolved including movements in the absence of sensory feedback. It considers that a person learns motor skills through the development and acquisition of open loop motor programmes – sequences of commands - that begin before the movement starts and are not influenced by peripheral feedback. The criticisms of this theory emanate from: different uses of feedback (initial information and feedback from error detection during and after the movement), the unlikely storage capacity required to store the variety of possible

movements, and the ability to explain how motor imagery (no motor training) can result in improved task performance.

The generalised motor program or schema theory (Schmidt, 1988) used schemas defined as 'a rule or set of rules that serves to provide the basis for a decision'. The schema controls a class of actions i.e. a set of different actions having a common but unique set of 'invariant features', such as timing, force and sequence, which are the 'signature' of a schema, forming the basis of what is stored in memory. During movements, data is collected on: initial movement conditions, parameters used in rules controlling the movement, the outcome and the sensory consequences. This information is stored as a recall schema (motor) and recognition schema (sensory), components of the motor response schema. The recall schema is used to select a specific response, whilst the recognition schema is used to evaluate the response. According to this theory, learning consists of the iterative process of updating both schemas with each movement. The criticisms of this theory emanate from its inability to explain how motor programmes exist at birth and to account for the immediate acquisition of novel movement patterns.

The most important common features of all of the theories of motor learning are: the positive correlation between feedback information (both type and frequency) and practice intensity, and improved motor learning and skill acquisition. How these components of motor learning have been addressed in the ILC study are outlined in Table 2, followed by a more detailed discussion of the components and an explanation of the terms used.

Components of motor learning	ILC study	How it could be improved?
Feedback		
Task intrinsic	Natural proprioceptive (may be impaired), visual	
Concurrent augmented	LED circle	
Knowledge of results	Performance curves	
Knowledge of performance	Not addressed	Showing performance on video
Practice Conditions		
Variability	Limited to the 27 two dimensional trajectories	Extending the trajectories to three dimensions
Distribution Amount	At least 24 hours between sessions 18 or 25 * 1hour sessions (For three participants, intervention stopped after 18 sessions – reached point of diminishing returns)	
Whole or part	Not addressed	More applicable to reach and grasp task
Mental practice	Not addressed	Home exercise programme
Context		
Transfer	The practice tracking task is similar to tracking error measure	Gradually being able to 'deweigh' the arm, to provide experience useful in the clinical measures and outside of the research study.
Memory		
Meaningful goal	Tracking task but not a functional goal	Involving the wrist and hand in a grasping action with real or virtual objects

Table 2: Aspects of motor learning addressed in the ILC study and suggested improvements

Feedback

Different types of feedback include: task intrinsic i.e. sensory and perceptual information that is a natural part of performing the movement which is often impaired for stroke participants; and augmented feedback (from a source external to the person) has 2 roles; firstly to facilitate achievement of the goal or of the skill, and secondly to motivate the learner to continue striving towards a goal. It can either be given concurrently whilst they are performing the skill, or after they have finished. A category of augmented feedback that gives information about the outcome of performing a skill or about achieving the goal of the performance is called 'knowledge of results'. Information about the movement characteristics (e.g. shoulder flexion, elbow extension) during or after the performance is termed 'knowledge of performance'.

Practice conditions

These include variability (variety of movement and context characteristics a person experiences while practicing a skill) and distribution (spacing of practice). The amount of rest between practice sessions or trials can either be very short (massed practice) or relatively long (distributed). The latter is thought to encourage motor learning. There is an optimum amount of practice which will deliver the maximum benefits in proportion to the amount of time the practice takes. Beyond this optimum point, diminishing returns will occur. For anything more than a very simple task, it has to be considered whether whole or part practice is preferable (i.e. – whether it is better to have the learner practice the skill in its entirety or in parts). Mental practice, or the cognitive rehearsal of a physical skill in the absence of overt physical movements usually involves imagining oneself performing a skill.

Context

To be useful in real life situations, patients need to be able to transfer their learning i.e. the influence of having previously practiced or performed a skill or skills on the learning of a new skill. The relationship between the practice and test context characteristics and the remembering of movements is given by the encoding specificity principle: the more the test context resembles the practice context the better the retention performance will be (Tulving & Thomson, 1973).

Memory

Memory storage and retrieval influences motor skill learning and performance. A common two component model of human memory (Baddeley, 1995) uses working and long term memory. Working memory is: a short term storage system for recently presented information and for information retrieved from long term memory, and provides essential processing activity needed for the adequate transfer of information into long term memory. The results of studies suggest that the duration (length of time information will remain in working memory) and capacity (amount of information that will reside in working memory at any one time) is similar for word recall and movement information; duration being about 20-30s, capacity is 7 ± 2 items (Adams & Dijkstra, 1966). Long term memory is a more permanent storage repository of information with no apparent limits for duration and capacity. It has been suggested that long term memory is composed of three or more systems (Tulving, 1985), the most relevant of which to this study being procedural memory. This has been described as a subsystem of long term memory that stores and provides knowledge about how to perform a skill or activity (Magill, 2001). This

knowledge can only be acquired for motor skills by physical practice and is stored in procedural memory as a blueprint for future action.

Different factors influence the remembering of motor skill related information including movement characteristics such as location and distance and meaningfulness. Strategies can be used to enhance memory performance and increase meaningfulness including subjective organisation of information into a number of meaningful units (often impaired for stroke patients), and the intention to remember.

Meaningful goal

Motor learning, using a goal oriented task has been demonstrated using natural contexts to facilitate the outcome of motor skill learning. In one study, forty healthy adults were randomly assigned into two groups learning to use chopsticks either in a natural context using cheese, or to a simulated context using erasers (Ma et al., 1999). Each participant practiced 60 trials in an acquisition phase on day 1 and was tested on a transfer task 24 hours after the acquisition phase. The natural context elicited a significantly larger improvement of success rate in the acquisition and transfer phases, although no major differences were found in kinematic variables between the two contexts. In another study, 14 people with stroke and 25 neurologically intact adults under two conditions: reaching forward to scoop real coins off a table into the other hand, and secondly reaching forward to the place where the coins would be placed in the first condition (Wu et al., 2000). The condition of reaching forward for real objects elicited better kinematic performance: shorter movement time, less total displacement, higher peak velocity, greater percentage of reach where peak velocity occurs and fewer movement units.

A subsequent study investigated the addition of repetitive complex movements to 'house typical' occupational therapy for 21 subacute stroke participants and concluded that repetitively training a complex task does not further enhance the function recovery of the affected arm and hand compared with functionally based occupational and physiotherapy (Woldag et al., 2003). However the complex task training was for 20 minutes twice daily for 5 days per week for 4 weeks i.e. 13 hours in total, which might be insufficient intensity to show a difference.

There is some evidence that performance of functional tasks do not always have a beneficial outcome on motor skill learning. Four case studies have been published

of stroke survivors who had been implanted with percutaneous intramuscular electrodes in various muscles of the forearm for hand grasp and release (Chae & Hart, 2003). The results of the study found that a percutaneous hand neuroprosthesis was able to open the hand only when: the arm was supported; participants did not try to assist the stimulation; and when others were controlling the stimulation. When these conditions were not met, the hand opening was significantly reduced due to increased finger flexor hypertonia, even with increased stimulation intensity. In a study investigating reaching using rehabilitation robotics (Krebs et al., 2008) the use of a functional task was shown to lessen elbow extension in reaching (for more detail see section 2.3.1.1).

2.1.3.1 Plasticity

An important model for the encoding of information in the brain postulates that the repetitive activation of a presynaptic neuron together with the simultaneous activation of its postsynaptic counterpart, would lead to a change in one or both neurons so as to produce an increase in the synaptic strength between them (Hebb, 1949). Evidence supporting this theory comes from long lasting alterations in synaptic strength (long term potentiation (LTP) and long term depression (LTD)) at glutamatergic synapses throughout the central nervous system, both at spinal and supraspinal levels (Rushton, 2003).

These synaptic mechanisms combined with neuronal mechanisms (changes in neuronal morphology and electrical properties), influenced by growth factors and associated with gene activation, are involved in neuroplasticity. This is the ability of the nervous system to adapt to changes, for example, a major loss of inputs from a hand or forelimb and is associated with motor learning. Evidence for this comes from animal studies (Jain et al., 1998; Pons et al., 1991).

Evidence for plasticity in healthy animal models has been demonstrated by neuroplastic changes in the functional topography of the primary motor cortex generated in motor skill learning in six neurologically intact adult squirrel monkeys (Nudo et al., 1996). The monkeys were trained in two different tasks, one requiring fine digit control and the other pro and supination of the forelimb. In a later study with neurologically intact adult squirrel monkeys it was concluded that repetitive motor activity alone does not produce functional reorganization of cortical maps (Plautz et al., 2000). Plautz proposed that motor skill acquisition, or motor learning, is a prerequisite factor in driving representational plasticity in the motor cortex. Work

in rat models suggests that reorganisation of the motor cortex and synapse formation do not contribute to the initial acquisition of motor skills but represent the consolidation of motor skill that occurs during late stages of training (Kleim et al., 2004).

Changes in motor evoked potentials from healthy humans (increased corticospinal excitability) resulting from several weeks of skill training, suggest that these changes may be of importance for task acquisition (Jensen et al., 2005). As strength training over the same period was not accompanied by similar changes, it was suggested that different adaptive changes are involved in neural adaptation to strength training.

Evidence for plasticity has also been found in lesioned animal models. A study with rats has indicated that recovery after bilateral forelimb primary motor cortex ablation may be due to the reorganization of specific adjacent areas in the cortex (Castro-Alamancos & Borrell, 1995). This was supported by research with squirrel monkeys, which concluded that substantial functional reorganization occurs in primary motor cortex of adult primates following a focal ischemic infarct. Without post infarct training, the movements formerly represented in the infarcted zone did not reappear in adjacent cortical regions (Nudo & Milliken, 1996).

Evidence for plasticity in stroke patients has also been demonstrated. In one study, focal transcranial magnetic stimulation showed a correlation between motor recovery and size of cortical representation of the hand in 13 chronic stroke patients before and after a 12-day-period of Constraint Induced Movement Therapy (CIMT) (Liepert et al., 2000). Additionally the centre of the output map was shifted, which was suggested to have resulted from recruitment of adjacent areas. Supporting this is work using serial positron emission tomography (Nelles et al., 2001) which has demonstrated that enhanced movement therapy (task oriented) with the hemiplegic arm of recovering stroke patients led to significant regional cerebral blood flow improvements compared with those receiving standard care.

A more recent study has shown evidence for CIMT where intensive practice with the impaired limb has been shown to result in recovery in stroke patients three to nine months post stroke (Wolf et al., 2006). The study follow up showed that these benefits were maintained. (Wolf et al., 2008).

The ILC project is aimed at rehabilitation of the arm. To be successful motor learning is required, and associated plasticity could be expected to result. Understanding the form and mechanisms of neural plasticity induced by injury or during learning may lead to the development of better means of neurological rehabilitation.

2.1.4 Motor control

This section discusses the stretch reflex and theories of motor control.

The most basic form of movement is the monosynaptic reflex loop – in response to being stretched all skeletal muscles have a tendency to contract. All reflexes must involve both a sensory axon arising from muscle spindles (with its cell body in a dorsal root ganglion or other sensory ganglion) and an efferent α motor neuron (with its cell body in the central nervous system). The sensory axons relay information about muscle length changes (amplitude and speed of stretch) to the brain and spinal cord. In the latter they form monosynaptic excitatory connections with the α motor neurones supplying the same muscle in the ventral horns. This results in a muscle contraction which when combined with a simultaneous relaxation (reciprocal inhibition) of the antagonist muscle results in movement.

The stretch reflex is illustrated in Figure 2. The muscle spindle, the sensory receptor that initiates the stretch reflex, muscle and motor neurons are shown in (A). In (B), when a passive stretch is given to biceps (by pouring liquid into a mug) the muscle spindle is stretched, exciting the 1a afferents. Central processes of the 1a afferent synapse directly on the alpha motor neurones within the spinal cord which innervate the biceps muscle causing it to contract. They also excite 1a inhibitory interneurones, which inhibit alpha motor neurones to the antagonist triceps muscle. Diagram (C) shows the stretch reflex operating as a negative feedback loop to control muscle length.

In reality the situation is more complex with modulation occurring via inhibitory circuits within the spinal cord or in the descending pyramidal tracts. The fundamental component of human movement is the reflex, however controlled voluntary movement is achieved by modulation of reflexes and voluntary drive from higher centres, such as the motor cortex. Spasticity, often found in stroke patients, has been defined as a 'motor disorder characterised by a velocity dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks,

resulting from hyperexcitability of the stretch reflex as one component of the upper motor neurone syndrome' (Lance, 1980).

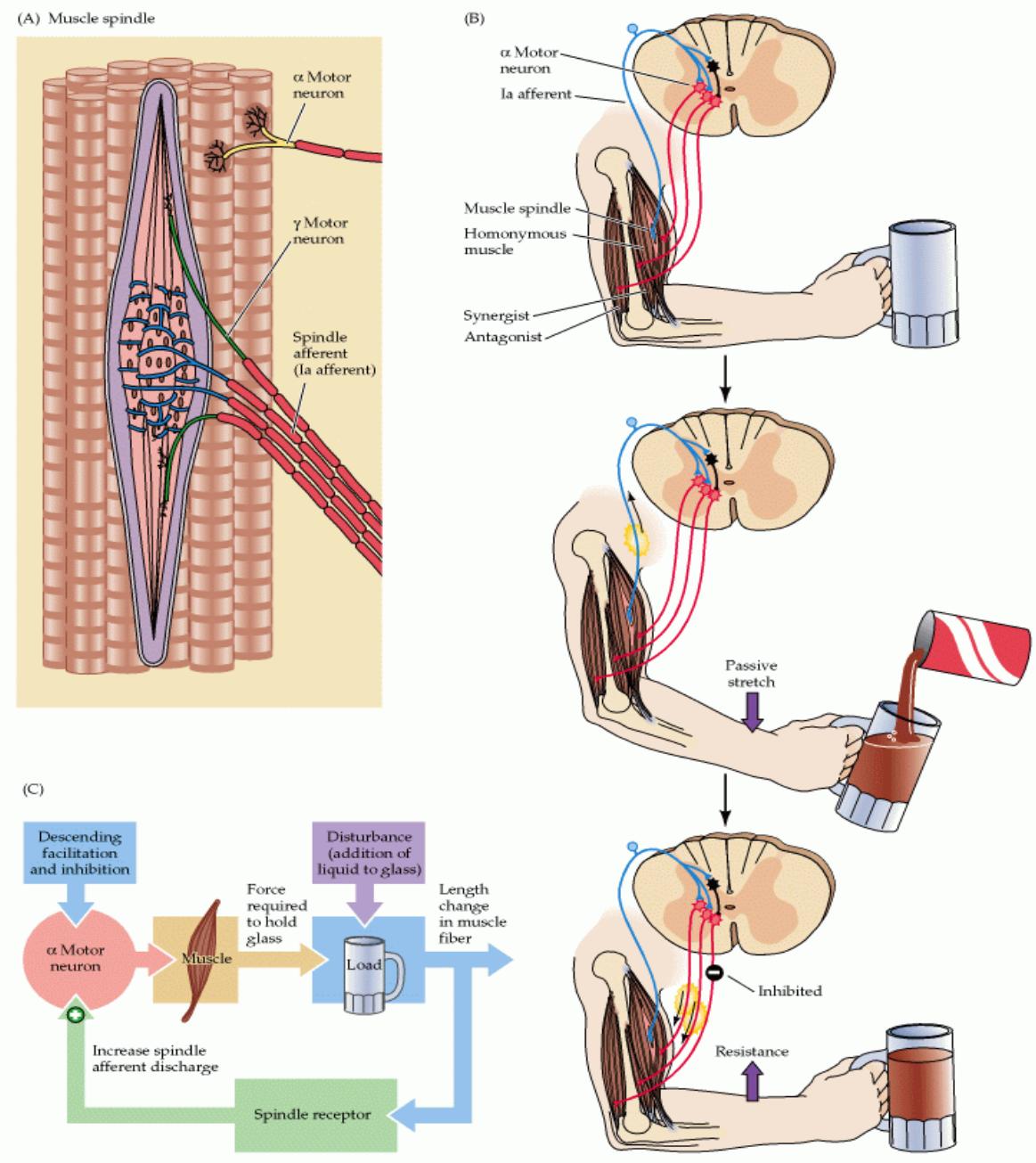


Figure 2: Stretch reflex (Purves et al., 2001)

Copyright of Sinauer Associates, Inc. reproduced with permission

The reflex theory

The reflex theory developed by Sir Charles Sherrington (Sherrington, 1906) stated that reflexes were the building blocks of complex behaviour. He proposed that given an intact nervous system, the reactions due to simple reflexes are combined into the greater actions that constitute the behaviour of the individual. The theory states that reflexes are an important part of normal movement and that abnormal reflexes would be a major reason they are unable to move normally. For example the inability to extend an elbow actively could be attributed primarily to spasticity, defined as a release of the stretch reflex in the elbow flexors. Treatments could then be aimed at reducing elbow flexor spasticity. The criticisms of this theory are that it is unable to explain: movement that occurs in the absence of a sensory stimulus; movements so fast that sensory movement cannot trigger the next movement; how voluntary movement can be achieved when there is no outside stimulus; and how a single stimulus is able to result in varying responses and novel movements.

Hierarchical theory

Hughlings Jackson contended in the hierarchical theory that the control within the CNS is organised in a hierarchical top down model (Jackson, 1882). According to the theory, human movement development is based on the emergence and disappearance of a series of reflexes, whilst CNS damage may be due to re-emergence of primitive reflexes. This led to the neuromaturational theory of development, which was the basis for the treatment approaches including Neurodevelopmental treatment (NDT) clinically known as Bobath as well as Brunnstrom's. The major criticism of this theory is that it is unable to explain the dominance of lower level reflexes in adults in certain situations. More recently this work has been updated with the input of neuroscientists and the shift in understanding is reflected in Figure 3. It is now recognised that each level of the nervous system can influence each other. In addition, the importance of reflexes in the generation and control of movement has diminished. It can be seen that cortical neurons (M1) project to many different spinal neuron pools. Spinal neuron pools receive input from broad overlapping cortical territories and from other spinal neurons. The motor cortex does not map an area to muscle. It is thought that mapping may relate more to patterns of movement, laid down through use. The overlapping and flexible structure underpins the ability of the system to adapt and therefore potentially recover following damage.

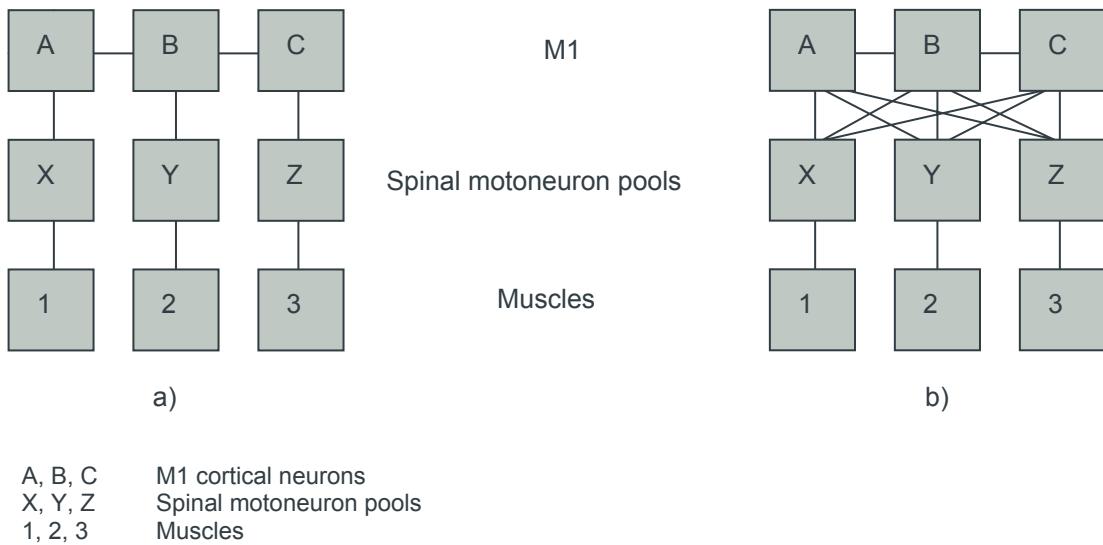


Figure 3: Voluntary motor control for a) classical and b) current view of motor connections (Lang et al., 2006)

Copyright of Cambridge University Press reproduced with permission

In the hierarchy of control, high level control affects structures involved with memory and emotions, and the supplementary motor and pre-motor cortex. It is involved with functions such as intention to initiate / perform / adjust an action, forming complex plans, and communicating with the medium level of control (receives sensory information during movement). The medium level of control affects the sensory motor cortex, cerebellum, basal ganglia and some brainstem nuclei. It is involved with converting complex plans into motor programmes or sub routines to specify posture and perform movements. Programmes are transmitted often via the cerebral cortex, through descending pathways to the lowest level. It also receives sensory information from lower levels enabling adjustments to be made during a movement. Low level control affects the brainstem and spinal cord. It is involved with processing information to determine which motor neurons are activated or inhibited to control muscle activity, moderates reflex activity, receives information from receptors enabling rapid control of movement and conveys this information to the higher centres, controls vital respiratory and cardiovascular function as well as motor control.

Motor programming theory

Although reflexes have been useful in explaining certain stereotypical patterns of movement, it is possible to remove the stimulus and still have a patterned response, such as in a Central Pattern Generator (CPG) for cats (Grillner & Zanger, 1984).

Many authors state that in man there is growing evidence that a CPG exists; afferent feedback has been shown to modulate the locomotor pattern in different ways to adapt it to external demands (Duysens & Van der Crommert, 1998; Verschueren et al., 2003). For proprioceptive afferents, two major roles have been posited. First, afferent input may play an important role in the generation of parts of the muscular activity seen during the step cycle (amplitude effects). Second, the activity from spindles and Golgi tendon organs is thought to be involved in the regulation of phase transitions (timing effects). The term motor program also describes higher level motor programs that represent actions in more abstract terms e.g. a signature maintains an identity when written in different sizes. Rothwell states that it is the 'transformation of an idea into a plan or programme of movement that is the fundamental task of the motor system' (Rothwell, 2004). The criticisms of this theory are: it is unable to explain different resulting movements from similar nervous system commands to muscles depending on starting positions and fatigue, and it fails to consider the environmental and musculoskeletal factors in motor control.

Feedback Control Systems

One of the limitations of rehabilitation systems using ES until now has been the delivery of an appropriate level of stimulation to encourage the participant to work at their maximum level. Within this study, feedforward ILC was used in addition to feedback control to augment damaged motor control systems in stroke patients using ES. This section seeks to outline feedback control and relates it to examples from both mechanical and physiological systems.

A simple model of a feedback control system has six elements: the sensor, set point signal, comparator, effector, controlled variable and error signal (Kingsley, 2000). These are suggested for a physiological system in Table 3.

Elements	Physiological system
Controlled variable	Muscle length
Effector	Muscle
Sensor	Nuclear bag receptors
Comparator / Summator	Spinal cord circuitry
Set point	Supraspinal command signals
Error Signal	Difference in muscle length between the actual and desired

Table 3: Elements for a physiological system

A block diagram illustrating the control of muscle length is shown in Figure 4. Changes in the controlled variable are detected by sensors which send feedback to the summator. The summator evaluates the differences between the feedback and the set point and then alters inputs to the effector. Changes to the effector result in changes in the controlled variable, which is then sent as an error signal.

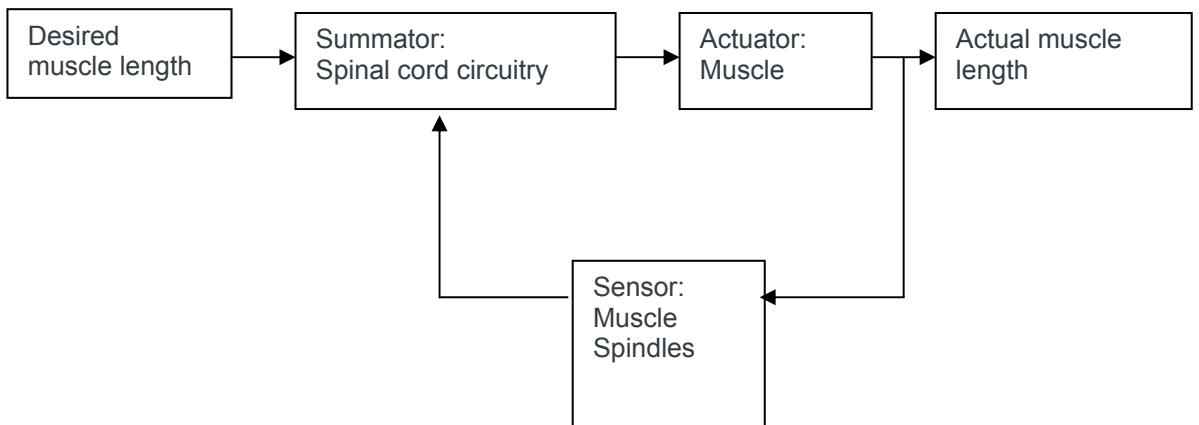


Figure 4: Block diagram for the control of muscle length (muscle stretch reflex)

Forms of feedback control include:

- i) 'On/off' systems - If the controlled variable differs from the set point enough, the summator sends an error signal to the effector to activate it. When the controlled variable reaches the set point, the effector deactivates. A hysteresis or dead zone is usually built in, which ensures the controlled variable is allowed to deviate within a controlled range.
- ii) Proportional control (in which the error signal is proportional to the degree of deviation from the set point and the effector response is also proportional) attempts to perform better than the 'on/off' control example. The responsiveness of the system is described by gain and damping factors.
- iii) Proportional and Derivative Control (PD) in which the inaccuracies of proportional control are mitigated, by adding a term proportional to the time derivative of the error signal (this has the effect of damping oscillations in the system output in order to achieve a critically damped response to changes in the set point).

2.2 Feedforward control systems - ILC

Feedforward control systems are those which select the system input in advance. To achieve the desired performance, this input may be chosen using a model of the process which includes all the appropriate environmental variables. ILC is the novel

application through which, in this study, the application of ES was controlled to allow the stroke participants to actively track a target trajectory over six iterations.

ILC uses feedforward control, but selects the input based on previous trials of the task in order to reduce the error incurred over the subsequent iteration. The concept of ILC was first introduced by Uchiyama, but was not well known until the middle to late 1980s (Uchiyama, 1978). The subject was developed by a Japanese group (Arimoto et al., 1984).

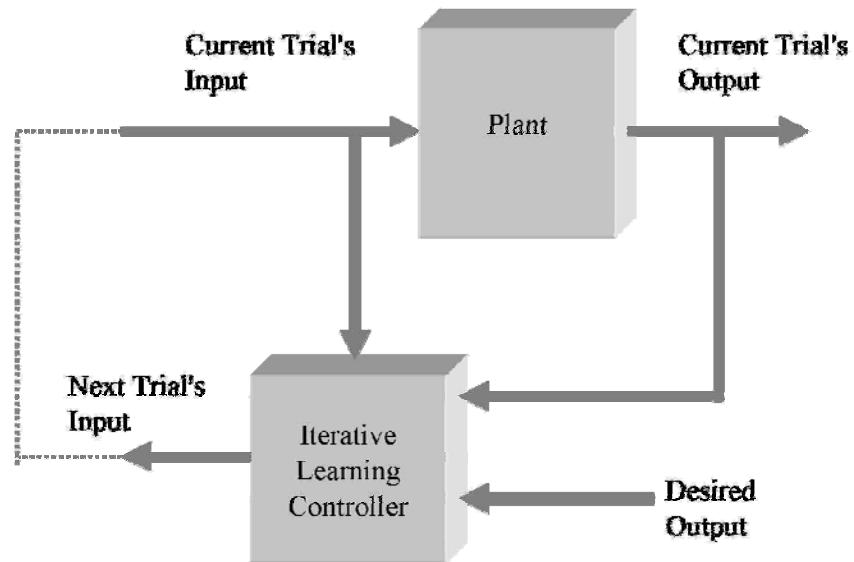


Figure 5: ILC concept (Moore & Xu, 2000)

Copyright of Taylor and Francis reproduced with permission

Early designs were almost entirely theoretically based and used simple control approaches – correcting an error at time t , using the error (or error derivative), at the same time on the previous trial. Problems in control design can be categorised as being either stabilisation or performance based (Moore, 1998). ILC is a technique for overcoming some of the performance based problems. It has been used in the field of robotics, chemical batch processes and reliability testing rigs to improve the transient response and tracking processes of systems which need to repeatedly perform the same action with high precision.

ILC uses information from previous iterations to generate a plant input and reduce the tracking error over the current cycle. If ILC is to be implemented certain conditions and rules must typically apply:

- ILC can be applied to processes which are required to repeat the same operation iteratively over a finite duration
- each complete operation is called a trial and $\alpha < \infty$ is the trial length
- the initial conditions are always reset
- the task (trajectory to be followed) occurs over the finite time interval $0 \leq t \leq \alpha < \infty$. The process then resets to $t=0$ and the operation is repeated.
- there is an undefined time between trials (the trial is performed, then the data is analysed, the control strategy is assessed and refined and then the next trial is commenced).

2.2.1 Notation

To specify a variable two coordinates are required, the trial index or number – subscript k and the position or time along the trial – t .

$$y_k(t), 0 \leq t \leq \alpha < \infty, k \geq 0$$

If the same control law is applied on each trial and the operating conditions remain constant, then the performance (output response errors) will be constant. Once the previous trial (or trials) have been completed, the previous (and current) trial outputs, inputs and errors, recorded during the system operation, can then be used in the modification of the input signal (via algorithms) to help improve performance sequentially from trial to trial. Refinements can be made until the desired performance is achieved. This is a 2D system where information is propagated in two directions – from trial to trial (k) and along the trial (t) (see Figure 6).

Improvements in performance correspond intuitively to reductions in the difference between the desired reference signal and the actual output of the system in a trial. Improving performance is the objective of the control strategy, which can only be achieved using available data in an effective manner. The learning mechanism is iteration. The control input signal is ‘learned’ which ensures that the system’s output is exactly equal to the specified reference trajectory. The updating occurs after each trial.

The desired output $r(t)$ and the current trial error $e_k(t)$ can be written as :

$$r(t), 0 \leq t \leq \alpha < \infty$$

$$e_k(t) = r(t) - y_k(t)$$

A typical control law is:

$$u_{k+1} = u_k + L^* e_k$$

Where u_k = the input to the system during the k th repetition

E_k = the tracking error during the k th repetition and L is a suitable operator

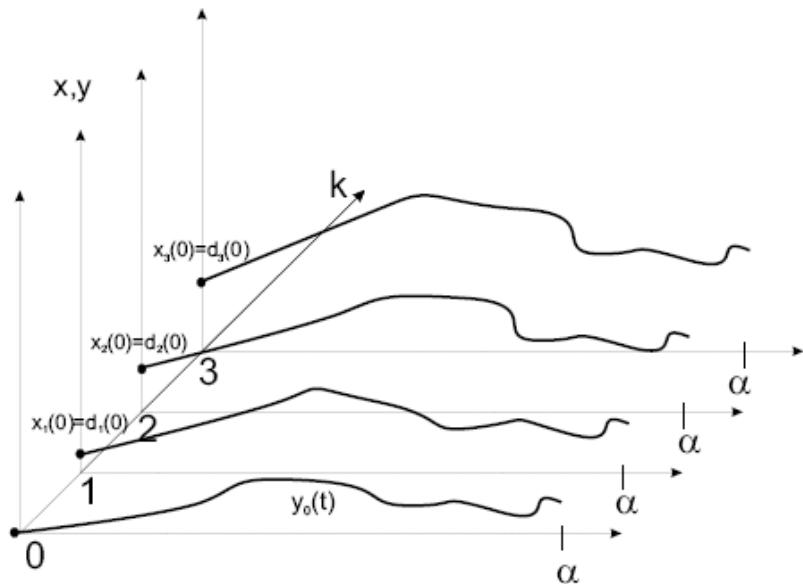


Figure 6: Plot of how the variable $y_k(t)$ changes with trial length and iteration (Rogers, 2007)

Copyright of Rogers reproduced with permission

2.2.2 P - type ILC

Over the past 20 years, significant developments in ILC have been made. The P-type is the simplest form of ILC possible, implemented in a hybrid arrangement with a conventional controller. The input at one point on the current trial is chosen to be equal to the input at the corresponding point on the previous trial plus a proportional component of the error that was recorded at that instant. The P – type law is simple in that it can be implemented without a model of the system. The disadvantages are that it only works well with extremely simple systems, typically needs many trials to converge and the error gained over a trial may increase after a number of trials. The latter effect can be negated by using an aliasing filter. For further information on the practical application of ILC to this study, see section 3.1.3.

2.3 Review of novel interventions

Research into conventional therapy and motor learning theory provides evidence that intensity of practice of a task (Inaba et al., 1973; Winstein et al., 2004) variety and feedback (Magill, 1998) are important. Research into neuroplasticity has shown that the recovery environment may influence plasticity after CNS damage. This knowledge is being applied in novel treatments which provide the opportunity for repetitive movement practice.

First, this chapter examines rehabilitation robots. The evidence is investigated through a series of questions concerning individual studies, and then the results of published systematic reviews are considered. The evidence for user involvement is also investigated. Second, ES is discussed and the evidence reviewed.

2.3.1 Rehabilitation robots and Electromechanical Devices

Robots were originally defined as 'a machine (sometimes resembling a human being in appearance) designed to function in place of a living agent, especially one which carries out a variety of tasks automatically or with a minimum of external impulse' (Capek, 1921). Rehabilitation robots can be classified by: degrees of freedom; structure (end effector or exoskeletal); or location of use (a home or clinic based system). The UK Stroke Guidelines recommend 'Robot-assisted movement therapy should only be used as an adjunct to conventional therapy when the goal is to reduce arm impairment' (Intercollegiate Stroke Working Party, 2008).

Fulfilling the motor learning requirements, robots can provide patients with: intense movement practice; continuous feedback and games (which if not functional tasks, may be motivating or entertaining); a degree of independence during therapy; and a record of progress. The advantages for therapists are that robots are both objective assessment and intervention tools. As with most technologies, there will be a number of barriers to their use which may include: cost; ease of accessibility; location for storage; a limited evidence base; acceptability and usability issues.

In developing new systems, the existing evidence bases have to be explored and used as a platform. At present there are problems with a trade off between design, safety and performance and the difficulty in developing a functional task. Additionally little is known about appropriate patient selection, when the optimal time to begin treatment starts or the length and duration of treatment.

2.3.1.1 Evidence for rehabilitation robots

The number of papers published concerning robots in upper limb therapy has increased rapidly and focuses mainly on shoulder and elbow rehabilitation. A literature search (see Appendix C) resulted in ninety seven upper limb stroke specific papers from 1966-2008, the majority of which were published in the last ten years. These can be categorised into clinical trials, reviews of clinical trials (Kwakkel et al., 2008; Mehrholz et al., 2008; Prange et al., 2006; Teasell et al., 2007), discussion and design papers. Papers addressing questions with implications relevant to the feasibility study have been analysed. One of the main current studies is discussed. The last section discusses the critical reviews in which results of clinical trials were analysed in order to assess the therapeutic effect of robotic therapy on the affected arm in stroke patients.

Question 1: Is robot better than sham robot training and are changes maintained? In one of the first published studies (Aisen et al., 1997) 20 acute stroke patients were randomised to standard rehabilitation supplemented by either robot (MIT-Manus) aided therapy or sham robot therapy to test whether robot manipulation influenced motor recovery. It was found that impairment and disability declined in both groups; the results for the shoulder, elbow and forearm were statistically significant using the Motor Status Scale outcome measure. The paper, however, covered insufficient details on both the nature and number of the tasks practised and over the length of time spent on each. An interesting re-evaluation of 12 of the 20 patients studied by Aisen, was conducted 3 years later (Volpe et al., 1999). It was found that the robot trained group showed significant improvements on the Motor Status Scale (shoulder/elbow) and Motor Power for the period of discharge to follow up. Both groups showed comparable changes in the FMA (shoulder/elbow) and Motor Status Scale (wrist/hand) over the interval.

Question 2: What changes have been identified as stroke participants received robot treatment?

An investigation was conducted to quantify the smoothness of movements made, and to assess changes over the course of recovery for 12 acute inpatients and 19 chronic outpatients using the MIT Manus (Rohrer et al., 2002). Strong trends in reduction of mean speed and duration were found for most subjects. For all (apart from one) there was a significant difference between the groups in the smoothness metrics. The paper presented scant patient information but suggested that kinematic

measures may show changes in recovery which are not reflected in clinical measures.

Question 3: How do robots compare to conventional therapy for chronic stroke participants?

The effect of robot (MIME) assisted movement training compared with conventional neurodevelopmental treatment (see Appendix B) was investigated with 31 chronic stroke patients with baseline characteristics FMA robot 24.8+/-4.5 : control 26.6 +/- 4.7 (Lum et al., 2002). It was found that the group using the robot had larger improvements in the proximal movement portion of the FMA, as well as larger gains in strength and reach extent. At six months the groups did not differ in FMA, but the robot group showed larger improvements in the Functional Independence Measure (FIM).

Question 4: How do muscle activation patterns change during treatment?

A study was conducted with 13 chronic stroke patients (mean FMA 24.8 +/- 16.3) using a robot (MIME) for 24 1 hour sessions over eight weeks (Lum et al., 2004). The interaction force kinematics and EMG (for first and last 2 sessions) were recorded during training of 8 different movement patterns. The results showed no evidence of improved muscle activation patterns in any of the table top movements, with increased activation of antagonists in 2 movement patterns. However there were increased muscle activation patterns for the four movement patterns that started at the table top and ended at shoulder level. Work output significantly increased by week 5 in all eight movement patterns. The low level subjects increased reach, whereas the high level subjects increased speed.

Question 5: How do robots compare with electrical stimulation?

Only two studies compared the use of robots to electrical stimulation. An RCT was conducted with 12 chronic stroke participants (FMA 17-34 initially) randomised to motor learning with either the InMOTION robot or functional neuromuscular stimulation (Daly et al., 2005). The treatment was intensive; 5 hours per day, 5 days per week for 12 weeks. 1.5 hours per session were devoted to shoulder/elbow (robot group) or wrist/hand (ES group). 3.5 hours was devoted to practice of functional tasks. Results provided evidence of training specificity; the robot group produced significant gains in AMAT, AMAT-S/E, FMA upper-limb coordination, target accuracy and movement smoothness, whereas the stimulation group produced significant gains in AMAT-W/H and FMA upper-limb coordination. The

limitations of the study were: the small number of subjects; whether similar gains would have been achieved without the adjunct treatments; and lack of detail regarding the treatment e.g. how many ES repetitions were averaged per subject. The study scored 5 on the EBRSR methodological rating system, but was excluded from their summary of results section.

In another study 44 sub acute patients (FMA <18 initially) were randomly assigned to the Bi Manu Track Arm Trainer (AT) or ES (Hesse et al., 2005). All patients practised 20 mins every work day for six weeks. AT patients performed 800 reps per session, ES 60-80 wrist extensions per session. Results showed the FMA and Motor Power significantly improved for both groups, but the gains were higher in the robot. Possible biases were: a higher level of competence in daily living activities in the AT group; a non-blinded assessment of secondary outcome measures; and that the AT was bilateral and ES unilateral.

Question 6: How does bilateral compare with unilateral training?

Conventional therapy (NDT) was compared with robot therapy (MIME) for 30 subacute subjects assigned to four treatment groups exploring the hypothesis when unilateral and bilateral modes are combined the bilateral enhances the effects of the unilateral (Lum et al., 2006): The treatment groups (with initial proximal and distal FMA) were:

- i) Control group (proximal 21.0+/-4.0 distal 5.0+/-2.5)
- ii) Unilateral passive to active constrained (proximal 23.2+/-3.2 distal 8.4+/-2.2)
- iii) Bilateral reaching and circles (proximal 24.6+/-4.2 distal 14.6+/-4.4)
- iv) 50% bilateral and 50% unilateral (proximal 16.2+/-2.5 distal 5.5+/-2.4)

Although group (iv) had advantages compared with conventional therapy, the gains in all groups were equivalent at six months. Group (iv) yielded functional gains (FIM) that were similar to the gains from group (ii). Lum suggested that the bilateral training may have 'unique benefits in reducing abnormal synergies' based on the results from the MSS scores. The examination of gains in individual subjects suggested robotic treatment was most effective for subjects in a middle range of motor impairment with initial proximal FMA scores between 15 and 23. The limitations of the study were that there were fewer subjects in the control group.

Question 7: Does using robot training reaching to perform a task (real or virtual) have benefits over supported movement without a task?

Robotic therapy was used 3x weekly for six weeks for the paretic upper limb for 47 people split into three groups a) sensorimotor active assistive impairment based exercise during repetitive planar reaching task, or similar to a) but the patient is actively assisted to a series of targets, where it stops to allow the person to interact with b) actual or c) virtual objects (Krebs et al., 2008). The results showed that all three groups improved from pre- to post treatment with the sensorimotor impairment based approach demonstrating the best outcome in terms of FMA. It was speculated the poor result in b) and c) occurred as patients were concentrating on the interaction part of the movement rather than the transport. The limitations of the study were the small number of subjects in groups a (n=32) b (n= 10) and c (n=5) and the discrepancy in the number of reaching movements.

In another study an intervention using a robot neurorehabilitation system (GENTLE/S) was designed with two arms and presented as single case studies of 31 chronic stroke patients (Amirabdollahian et al., 2007). The phases, in ABC or ACB order, comprised 3 weeks each of: Phase A baseline; Phase B robot therapy; and Phase C single plane sling suspension exercises. The FMA results indicated positive, but modest, recovery trends favouring both interventions. Possible gains in the FMA as a result of the interventions may have been limited by time spent in the different phases (4.5 hours per patient).

Question 8: Is the order of specific training important?

Investigation is currently underway to investigate the specificity of robot training using the InMotion2 and InMotion3 in the USA (Krebs et al., 2007a). Chronic stroke patients are being randomly assigned to one of four groups:

- (i) 6 weeks of wrist training followed by six weeks of shoulder/elbow training
- (ii) 6 weeks of shoulder/elbow training followed by six weeks of wrist training
- (iii) 12 weeks of alternating days of shoulder/elbow and wrist training (24 hours between sessions)
- (iv) 12 weeks of mixed of shoulder/elbow and wrist training

All training is for one hour 3 times per week i.e. 36 sessions. It is planned that there will be 40 patients in each group. Preliminary results from 36 patients from groups (i) and (ii) suggest that the order of therapy has no impact on the total FMA score which improves by approximately 10%. However the limb segment trained first improves the most. When generalisation and skill transfer is looked at, the training of the distal segment first leads to twice as much carry over effect compared to the proximal segment, and that improvement in the distal segment continues

significantly even without further training for that limb segment. This leads the authors to conclude that training of the distal limb first may be better as it leads to faster improvement.

Systematic Reviews

Prange considered eight trials all involving only the proximal upper limb (Prange et al., 2006). Six of these used a repeated measures design for robot-aided therapy without a control group. The other two experimental studies using repeated measures of an experimental and control group, of which one was an RCT. The size of the experimental groups varied from 3 to 42, using a total of 12 outcome measures. Qualitative analysis using a structured diagram suggested that 'forward-directed robot aided therapy resulted in improved motor-control in terms of muscle activation patterns, selectivity and speed of movement'. Long term effects of between 3 months to 3 years, were identified for the four groups that measured them. Quantitative meta analysis of the four studies that involved chronic stroke patients supported the positive influence of robot-aided therapy on motor recovery in chronic stroke patients. On the basis of these analyses it was suggested that 'robot aided therapy of the proximal upper limb improves short- and long- term motor control of the paretic shoulder and elbow in subacute and chronic patients; however, we found no consistent influence on functional abilities' (Prange et al., 2006). Factors affecting the conclusions were i) the inclusion of both one sub acute and seven chronic patients groups (both were found to improve in terms of the outcome measures used) ii) difference in treatment intensity iii) use of the upper-limb portion of the FMA for quantitative analysis. Interesting concerns were i) the different response to robot therapy by different patient groups ii) training specificity iii) the role of individual treatment modalities. These findings could be investigated in future trials in order to optimise treatments for patients.

This partially supports the work conducted by Teasell et al. in the Evidence – Based Review of Stroke Rehabilitation (EBSR) which considered 'Robotic Devices for Movement Therapy' (Teasell et al., 2007). A systematic review of the literature was conducted, resulting in 20 studies involving the upper limb. The methodological quality of individual RCTs was assessed using the Physiotherapy Evidence Database (PEDro) tool (Centre of Evidence-Based Physiotherapy, 2008). PEDro was developed for the purpose of accessing bibliographic details and abstracts of randomized-controlled trials (RCT), quasi-randomized studies and systematic reviews in physiotherapy. The size of the experimental groups ranged from 20 to 56

using a range of nine distinct outcome measures. It was concluded that: there was strong evidence that sensorimotor training with robotic devices improves upper extremity functional outcomes, and motor outcomes of the shoulder and elbow; and robotic devices do not improve motor outcomes of the wrist and hand. The difference in opinion between the two studies may be explained by the definition of what constitutes a functional outcome measure as EBRSSR does not qualify its definition.

The Cochrane review (Mehrholz et al., 2008) included randomised controlled trials comparing electromechanical and robot-assisted arm training for recovery of arm function with other rehabilitation interventions or no treatment for patients (sub acute to chronic) after stroke. Eleven trials including 328 participants were identified. The conclusions from the review were that electromechanical and robot assisted training may improve impaired motor function and strength of the paretic arm, but does not improve activities of daily living in people after stroke.

A systematic review into the effects of robot assisted therapy on upper limb recovery (Kwakkel et al., 2008) considered ten RCTs involving the upper limb. Using robot therapy vs: robot exposure (three studies), NDT (two studies), conventional therapy (one study), unassisted reaching (two studies), and ES (two studies). The size of the experimental groups varied from 10 to 56, using a total of 3 outcome measures. A non significant summary effect size in terms of upper limb motor recovery was shown in the metaanalysis. However the subsequent sensitivity analysis of shoulder elbow robotics showed a significant improvement in upper limb motor function after stroke for upper arm robotics, but no significant improvement in ADL function, which was thought to be due to the inadequacy of the FIM and the Barthel to reflect recovery. On the basis of these analyses it was suggested that future research into the effects of robot assisted therapy should therefore distinguish between upper and lower robotics arm training and that kinematic analysis should be used to differentiate between genuine upper limb motor recovery and functional recovery due to compensation strategies by proximal control of the trunk and upper limb.

Trials considered in each of these reviews, along with the first author and robot or electromechanical devices used are listed (see Appendix D). All the reviews acknowledged difficulty in drawing conclusions and suggested that the results must be interpreted with caution due to: the wide variety of outcome measures used and weak methodologies (Prange et al., 2006; Teasell et al., 2007); variations between

the trials in the duration, amount of training and type of treatment and in the patient characteristics (Mehrholz et al., 2008); and the assumptions made in the study: studies used different patients, pooling different outcome measures to get one overall measures and only studies published in English, German and Dutch were included (Kwakkel et al., 2008).

Common themes however, can be drawn. First, the studies agreed that current evidence supports that training with robotic devices improves motor outcomes of the shoulder and elbow (Kwakkel et al., 2008; Mehrholz et al., 2008; Prange et al., 2006; Teasell et al., 2007), but does not show a positive influence on functional activities / activities of daily living (with the exception of Teasell et al., 2007). Second, the proportion of papers published using robots in upper limb post stroke therapy is small in comparison to therapy in general. Third, robots are regarded as having a role in assessment and treatment of patients (however, medium scale trials of one hundred and sixty patients have only just begun in the USA using InMotion 2 robots).

2.3.1.2 User involvement

Despite evidence for therapeutic effectiveness, if a system is not liked by the users (patients or therapists) then it will be employed less frequently. Problems with technology transfer have already been seen with existing systems for example, despite the fact that Functional Electrical Stimulation (FES) techniques have been developed, evaluated and commercialised, FES currently reaches only a small fraction of the appropriate community. To minimise these problems it is important to ensure that future developments (research, technological development, clinical and service provision and commercialisation) in these types of rehabilitation systems fulfil the needs of users. A first step in this is to understand the users' perspectives of an existing system.

At present, there do not appear to be any scales which can be used to assess the user perspectives of different rehabilitation robots. In the corresponding field of assistive technology the Psychosocial Impact of Assistive Devices Scale (PIADS) (Day & Jutai, 1996) is a 26 item self report questionnaire designed to assess the effects of an assistive device on functional independence, well being and quality of life of patients using three subscales: competence, adaptability and self esteem. Thus it addresses a very specific issue but can be used across a range of devices.

Existing research on user perceptions of rehabilitation robotics is limited to a few studies of either patients (Coote & Stokes, 2003; Krebs et al., 1998), or therapists (Lee et al., 2005) or both (Doornbosch et al., 2007). The study by Krebs (Krebs et al., 1998) used six statements / questions (it was unclear from the paper) administered by the therapists to survey the responses of twenty participants during the bi-weekly standard assessments. The statements (which all appeared to be positive, see Table 4) were scored on a 8 point Likert style scale and presented in a Table titled 'Patients' tolerance for the procedure'. The conclusion was that robot-assisted therapy was well accepted and tolerated by the patients.

Coote and Stokes (Coote & Stokes, 2003) formally considered the users' perspectives (8 patients and 6 physical therapists simulating a hemiplegic upper extremity) on using a prototype of the GENTLE/s system. The results of a series of 11 Likert style negative and positive statements addressed issues of safety, comfort, enjoyment, ease of use and interest. Additional closed questions were asked regarding the effect of the time spent in the system on pain, stiffness and functional ability. The results showed that overall the therapists and the patients were positively disposed to the provision of Robot Mediated Therapy (RMT). Patients were found to be more positive than the therapists when asked about the comfort of the arm support, whether RMT was more enjoyable than normal therapy, and the usefulness of computer images in aiding movement.

A questionnaire based study surveyed Canadian physiotherapists' views of robotic devices and the functionality required for effectiveness (Lee et al., 2005). The therapists (only one of whom had experience of a robotic device) were asked to rank items (categorised into eight themes: rehabilitation robotics and biofeedback, patient position and machine movement, patient performance, required information, information distribution, displaying information, power asses control and safety features) as 'must haves', 'preferable' or 'no need'. Comments and suggestions were also encouraged. The researchers concluded therapists: responded positively to the idea of robotic devices in a clinical setting; were interested in using robots; were adamant that systems must be usable.

The experience of 10 sub acute (<2 months) stroke patients and their therapists in using the second prototype of a robotic arm device (ACRE2) were investigated (Doornbosch et al., 2007). Each patient attended 8 sessions of around 20 minutes

twice a week in addition to normal therapy. In sessions 1,4, and 8 the patients were asked to score their experience with ACRE on a 5 point scale. The factors scored were tiredness, painfulness, fun, difficulty, monotonousness, usefulness and duration of the exercises. At regular intervals the therapists filled out a standard observation scores about usefulness, affectivity, efficiency, difficulty and questions about the robotic device. Additional interviews were held with some of the patients and the therapists using seven specific questions concerning the robotic arm and the software outlined in Table 4. The patient results demonstrated that no pain was experienced, the procedure was acceptable, training sessions were pleasant whilst tiredness was scored neutrally. The results from therapists demonstrated that they thought the system was useful, effective and efficient, but scored the arm support as average on size, weight and functionality. Improvements were suggested to increase safety, comfort and self use.

Questions or statements used in participant perception studies (Krebs et al., 1998)	(Doornbosch et al., 2007)
Comfortable with robot therapy	Is the range of motorised support sufficient for reach-to- grasp tasks?
Enjoyed doing robot therapy	Is the patient able to connect himself to the robotic arm?
Believe the robot therapy sessions were beneficial.	Is the fitting of the arm brace comfortable?
Working with the robot helps in ways that nobody else can	Is the gravity compensating mechanism able to create an optimal starting point?
Would like to perform more therapy with robot.	Do the exercises stimulate the patient to complete the whole exercise?
Would rather work with the robot than a therapist	Does the software necessary for the reach-to-grasp exercises help the patient sufficiently? Is the patient able to adjust the exercises by using the touch screen buttons?

Table 4: Statements and questions published on user perceptions

Common limitations with existing surveys include: lack of clarity on question development; questionnaires were often administered by treating therapists; questions or statements used are not always published; psychometric properties of the questionnaires are not established; and frequently no clear tables of results are published.

In view of this, published results of the studies have to be interpreted with caution as the neutrality of unseen questions/statements and treating therapists cannot be

ascertained, so introducing possible bias. Furthermore, the studies are not reproducible and cannot be applied to users of other robotic systems.

2.3.2 ES in rehabilitation

Electrical stimulation has a long history. Galvani in 1791 famously investigated the relationship between electricity and muscle by using metal rods to touch a frog's leg muscles causing them to move. Since then numerous devices have been developed to stimulate nerves and muscles (Geddes, 1994). To date, researchers have been addressing different problems with both surface and implanted electrical stimulation systems. There have been no large randomised control trials, and this may contribute to why they are not routinely used in clinical practices.

2.3.2.1 Definition

Within the context of this study, ES in neurorehabilitation is defined as methods of applying an electrical voltage to drive a limited safe current to stimulate appropriate nerves, in order to activate a damaged or disabled neuromuscular system. There are two categories which are widely used. Functional Electrotherapy was defined by Liberson as providing 'the muscles with electrical stimulation so that at the very time of the stimulation the muscle contraction has a functional purpose either in locomotion or in prehension or in other muscle activity. In other words, functional electrotherapy is a form of replacement therapy where the impulses coming from the central nervous system are lacking' (Liberson et al., 1961). This can be distinguished from Therapeutic Electrical Stimulation (TES) which can be defined as a therapeutic strategy aimed at improving impairments after stimulation (De Kroon et al., 2002) i.e. without the person trying any functional movement at the same time.

2.3.2.2 Stimulation triggering

A review of stimulation triggering was conducted in which several methods of applying stimulation were considered (De Kroon et al., 2005). The first, which did not involve active participation by the user, was by a pre-programmed timed sequence which resulted in repetitive muscle contractions. Those which did involve active participation, included EMG triggered stimulation (when voluntarily controlled EMG signals exceeded a pre-set threshold) and positional feedback stimulation (when voluntary muscle contraction produced joint translation beyond a set threshold).

2.3.2.3 Stimulation parameters

Variations in the response from stimulated muscle tissue will be achieved through manipulation of stimulation parameters. Factors which may be controlled include the stimulus waveform, the current amplitude, the phase duration / pulse width, the frequency and stimulus time modulation (Gorman et al., 2006).

The stimulus waveform can be monophasic, where the current flows in one direction only and cause a net movement of charged ions across the electrode tissue interface such as a rectangular pulse, or, biphasic, in which the current flows alternately in both directions, depolarising and polarising the nerve axon (such as sinusoids or rectangular pulses). Biphasic stimulation is more popular than monophasic as it minimises skin irritation and feels more comfortable (Gorman et al., 2006). Peak current refers to the highest amplitude of each phase. Pulse width refers to the duration of each phase and usually ranges between 5 and 400 μ s.

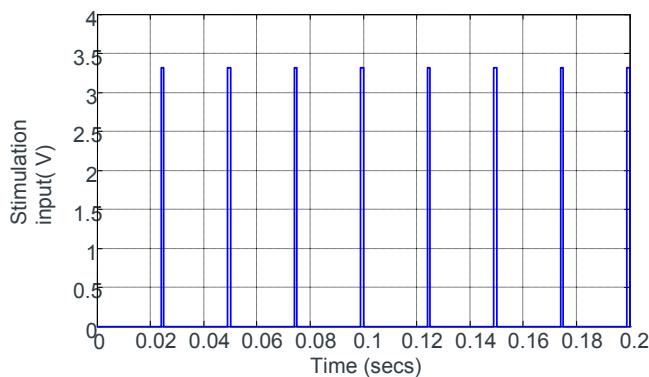


Figure 7: Controller voltage signal (v) vs. pulse width (μ s)

Pilot work for the study is displayed in Figure 7. The voltage signal from the PC to the Odstock controller is approximately 3.3v, the pulse frequency is 40Hz and the pulse width is varied from 0-300 μ s (short durations minimise discomfort). The corresponding stimulation voltage signal is approximately 0-150v, with a peak current of approximately 10mA. As amplitude or duration is increased above threshold, spatial recruitment of additional motor units occurs.

Isometric pulsedwidth input and torque output is represented by a Hammerstein structure involving a static non linearity and linear dynamics. Linear dynamics were calculated using an ES step response in pilot testing. The dynamics were observed

to be relatively similar between people and since the test would not have been comfortable for the stroke participants to experience, the data from the pilot testing were used for all participants. A static non linearity was calculated by first applying a ramp stimulation signal to the participant (in which the pulse width increased from 0 to maximum ES and back), and then calculating the output torque around the elbow. This torque was then deconvolved using the linear activation dynamics in order to remove its effect. The plot of stimulation input versus deconvolved torque around the elbow (see Figure 8) was then produced to provide a good representation of the inverse recruitment curve (the two paths representing the increasing and decreasing stimulation respectively). An average of these 2 lines could be taken however it might not be smooth and could not be used to provide an inverse relationship necessary for the linearising controller. A smooth monotonic function was therefore fitted via non-linear optimization. This relationship between the volt seconds injected and the force output of the muscle being stimulated is important when attempting gradual proportional recruitment of motor strength.

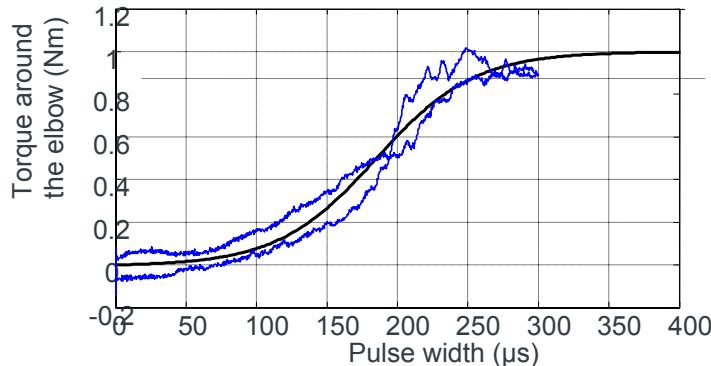


Figure 8: Torque (Nm) vs. pulse width (μs)

The pulse rate / frequency determines the rate of nerve depolarisation. Increasing pulse frequency provides for temporal summation of force output. Pulse rates ranging between 1 and 10 pulses per second (pps) induce twitch contractions of skeletal muscles. Pulse rates between 15 and 25 pps induce incomplete tetanic contractions. Faster than 45-50 pps the fused tetanic contractions generally required for rehabilitation are typically induced (the fibre is maintained in the contracted state as the refractory period is so much shorter than the time needed for contraction and relaxation). There is however, considerable inter-participant variability with regard to fusion frequency. Pulse rate is also associated with stimulation comfort during tetanic contractions. Increasing pulse rate is known to cause a greater degree of

muscle fatigue during tetanic contractions. For ES the trade-off as the stimulating frequency is increased (in order to obtain a smoother contraction) is more rapid muscle fatigue.

This is illustrated in Figure 9. When stimulation pulses are given at 1/sec, the muscle responds with a single twitch. Between 5/sec and 10/sec, the individual twitches begin to fuse together (clonus). At 50 pulses per second, the muscle goes into the smooth, sustained contraction of tetanus.

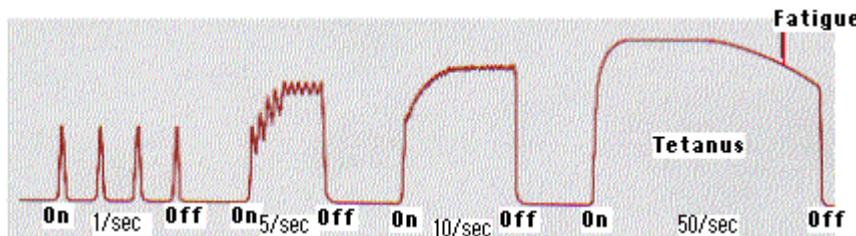


Figure 9: Twitch response variance with frequency (Kimball, 2008)

Copyright of Kimball reproduced with permission

Low frequency stimulation (3Hz) induces prolonged depression of corticospinal excitability, while high frequency (30Hz) stimulation induces prolonged facilitation. These effects persisted for approximately 40–50 min after stimulation ceases (Pitcher et al., 2003). ‘For most stimulation programs, a frequency sufficient to cause tetanisation is desirable since frequencies below tetany result in a ‘tremorous’ contraction, and frequencies markedly higher than this cause increased muscle fatigue’ (Baker et al., 1993). To achieve a smooth muscle contraction with electrical stimulation where motor units are firing synchronously, frequencies of 25-40 Hz are needed (McNeal et al., 1986). More rapid firing means less rest time and in turn more rapid fatigue.

A long rising ramp time of at least two seconds has been recommended to be used clinically wherever spasticity is present (Taylor, 2002). Without the ramp, a sudden contraction will rapidly stretch the antagonist muscle and induce a muscle stretch reflex resulting in a reduced range of movement. Additionally a long ramp has implications for comfort which in itself may reduce tone levels. To achieve movement with minimum discomfort and skin irritation, the peak current and pulse width used will depend on the individual.

2.3.2.4 Evidence for ES

A Cochrane systematic review considered whether ES improved functional ability and ADL after stroke (Pomeroy et al., 2006). Twenty four RCTs with 888 participants (fourteen studies and 434 participants concerning the upper limb) were reviewed in three groups: i) electrostimulation compared with no treatment, ii) electrostimulation compared with placebo and iii) electrostimulation compared with conventional therapy. The majority of benefits were found for group i) which the authors suggested was not surprising as intensity of treatment is thought to be important for outcome (Kwakkel et al., 2004). This Cochrane review, like the systematic review by (De Kroon et al., 2002), included only one upper limb study (Sonde et al., 1998) where elbow extension was included. The remainder focussed on wrist and finger extensors. De Kroon's study considered six Randomised Controlled Trials (RCTs) and concluded that the results suggested a positive effect of ES on motor control. No conclusions could be drawn with regard to the effect on functional abilities.

Electrical stimulation parameters used in nineteen clinical trials (22 patient groups) were investigated in another systematic review (De Kroon et al., 2005). Specific stimulation parameters reviewed included frequency (generally fixed but between 20-50Hz), amplitude (range varied from as wide as 0–100 mA to as narrow as 30–45 mA), and pulse duration (fixed pulse duration of 200 or 300 μ s). Apart from muscle response and patient comfort (one study reported that most participants prefer a symmetrical biphasic over a monophasic or asymmetric biphasic for stimulation of quadriceps femoris (Bowman & Baker, 1985) no fundamental arguments were presented for the specific setting of stimulation parameters. According to the review, there was a wide range in duration of ES treatment: from 30 minutes once a day to 3 times 1 hour per day, for a period of 2 weeks to 3 months. None of the authors substantiated their specific duration of stimulation treatment. The main findings of the review were that a positive effect of ES was reported for thirteen out of twenty two patient groups and that the effect of stimulation is enhanced when associated with the person's intention to move. They also concluded that the specific stimulus parameters may not be crucial in determining the effect of ES.

Systems have been developed in which electrical stimulation is triggered by muscle activity (Francisco et al., 1998). In a study comparing cyclic versus EMG triggered stimulation in twenty two chronic stroke patients, it was theorised that EMG triggered stimulation might be more effective as the participant was actively involved (De

Kroon & IJzerman, 2008). No significant difference was found however between the two methods. A possible reason for this was that active involvement was only required to trigger the stimulation. Once this threshold was reached the stimulation evoked no further cognitive effort until the next muscle contraction.

Two of the main clinical reasons for the use of ES in stroke are for pain relief and attempting to correct shoulder subluxation. Among various factors contributing to the occurrence of shoulder pain in hemiplegia, some are related to the joint, such as lesion of the rotator cuff tendons, reflex sympathetic dystrophy and inferior-anterior subluxation of the head of the humerus; others are related to the neurological lesion, such as central post stroke pain, lack of sensibility, unilateral neglect and spasticity. A systematic review however, stated that the evidence from RCTs so far does not confirm or refute that ES around the shoulder after stroke influences reports of pain, but that there does appear to be benefits for passive humeral lateral rotation, possibly through the reduction of glenohumeral subluxation (Price & Pandyan, 2000).

Other studies have considered fatigue in continuous and intermittent contractions of triceps brachii (Bilodeau, 2006), how shoulder position influences the recruitment efficiency of the corticospinal volleys to motoneurons of intrinsic hand muscles (Dominici et al., 2005) and the effect of triceps stimulation on abnormal torque patterns in the paretic upper limb of participants with hemiparetic stroke (Keller et al., 2005).

2.3.2.5 Theories of mechanisms

A theory regarding the mechanism of ES has been developed (Rushton, 2003). When ES is used, an orthodromic impulse is conveyed to the extrafusal muscle, but an antidromic impulse is sent back up to the anterior horn cell in the spine. It has been seen that after repeated use of ES combined with purposeful activity of patients with neurological impairments, the need for the ES diminishes, and sometimes is no longer required. Rushton postulates that this may be due to Hebbian learning - the repeated antidromic stimulus combined with the stimulus from the intention to move, strengthens the synaptic connection resulting in long term potentiation.

Studies have investigated plasticity at the cortical level (Golaszewski et al., 1999; Wu et al., 2005). Golaszewski used functional magnetic resonance imaging of the

human motor cortex before and after whole hand afferent ES (sub threshold level for sensation) and found that changes occurred in a definite pattern in the regional cerebral blood flow of the brain cortex. Wu applied ES to the median nerve at the wrist (MNS), and found that it elicited a displacement of the centre of gravity for the thumb movement representation towards the other finger representations within the primary somatosensory cortex.

2.3.2.6 Use in this study

The limitations of current ES systems are that they trigger ES but do not vary output in response to performance and hence there exists a theoretical argument that any incentive to use voluntary effort is inhibited. Until now, techniques have not allowed feedback to adjust stimulation parameters during tasks. To our knowledge, no systems have been developed that adjust the stimulation in response to the users' performance in order to provide only the minimum level of stimulation needed to assist the participant in performing the task to a high level of accuracy.

In this study, the purpose of using ES is to stimulate the participant's elbow extensors to move so that the participant can straighten their arm. The controller measures the error between the desired trajectory (which the participant is tasked with following) and the actual trajectory they follow, and changes the ES to minimise the error. The stimulation is then reduced in order to keep the participant working at the limit of their performance. It is believed that ES will facilitate learning through both local and central changes, including long term potential at the anterior horn cell level in the spinal cord, and plastic changes in the brain, resulting in the participant's increased ability to move. Other possible changes include muscle strengthening and possibly a reduction in spasticity through reciprocal inhibition.

2.4 Screening tools and evaluation of novel interventions

Screening tools ensure only participants who fulfil certain criteria are selected to enter a trial. Appropriate activity outcome measures provide a baseline against which any change can be evaluated and can be used to improve interventions. The measures do not, however, offer an explanation of the mechanism. An understanding of the underlying normal and impaired mechanisms is needed for the development of interventions aimed at improving sensory-motor control. Surface electromyography (EMG) is a useful tool with which to identify normal and abnormal muscle activity which may then be related to impaired performance and function. For

example, it is useful to identify whether inability to extend the elbow during reaching is due to weakness in triceps or anterior deltoid, over activity of biceps, or inappropriate co-activation between the agonist and antagonist muscles. The screening tools, impairment and range of activity outcome measures considered for inclusion in this study are discussed.

2.4.1 Outcome measures

The World Health Organisation's International Classification of Functioning, Disability and Health (ICF) is a framework for measuring both health and disability (World Health Organisation, 2001). It consists of domains which are 'health' and 'health related' described in the form of two lists: body functions and structures, and activity and participation. These are illustrated for stroke in Figure 10. Within the classification, impairments are defined as problems in body function or structure such as a significant deviation or loss; activity is the execution of a task or action by an individual and participation is involvement in a life situation (society).

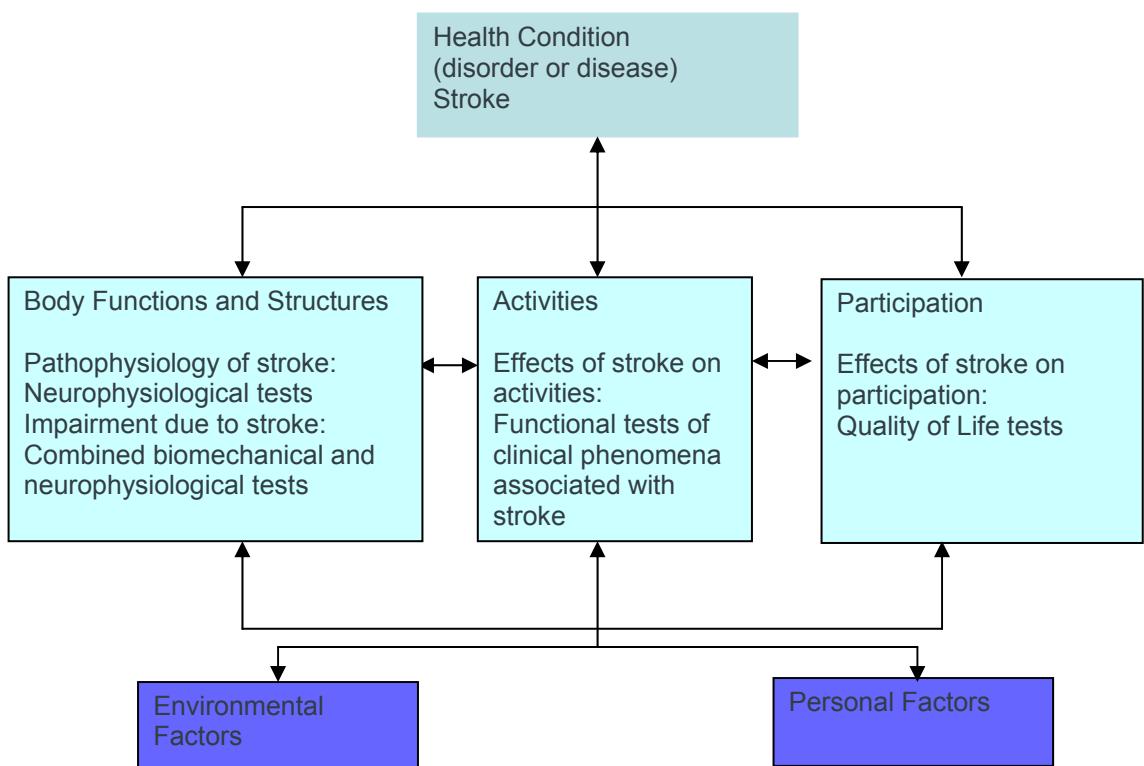


Figure 10: ICF framework and stroke

2.4.2 Criteria governing choice of screening and outcome measures

In considering the criteria for the choice of screening and outcome measures to be used in the study, the following were taken into account: reliability, validity, utility, standardisation and literature area. The forms of reliability considered included internal consistency (whether the test items measure the outcome consistently) and inter-rater reliability. The following forms of validity were considered: content (whether the assessment items reflect the domain they claim to measure); construct (whether the assessment measures the known attributes of the theoretical construct under evaluation); and criterion validity (the agreement between results of the assessment under evaluation and a criterion assessment or gold standard). Utility was also deemed important. For example, whether the rater needed to obtain qualifications in performance of the test, and the time taken to complete the test. It was decided to limit the test time to less than 30 minutes, due to the number of tests that needed to be performed and the possibility of stroke participant fatigue. Standardisation was required in terms of an administration manual / DVD for the test and scoring. The final general consideration was how widely the test was used either in contemporary rehabilitation robotics, electrical stimulation or relevant clinical literature. For the impairment and activities outcome measures, the focus of the test (i.e. who the test was designed for) was considered. Specifically for the activities outcome measures, whether the test was quantitative or qualitative and unilateral was considered.

Instrument evaluation and selection was informed through reference to a structured review which assesses the evidence for different measures (Rowland & Gustafsson, 2008) and electronic literature searches. Information was not available on all the selection criteria for some of the instruments considered for inclusion in the study questionnaire and consequently evaluation against the selection criteria inevitably involved an element of subjectivity. An outline of the instruments reviewed can be seen in Table 5, Table 6, and Table 7.

Scale	Focus	Reliability	Validity	Utility	Standardisation	Literature
Unilateral Visual Neglect- Behavioural Inattention Test (BIT)	Unilateral visual neglect	✓	✓	✓	✓	Occupational therapy
Mini Mental State Examination	Quantitative assessment of cognitive impairment	✓	✓	✓	✓	Clinical
Modified Ashworth	Assigns a subjective rating to amount of resistance or tone perceived by the examiner as a limb is moved through its full range of motion	?	?	✓	?	Clinical

Table 5: Screening tests criteria

Scale	Focus	Reliability	Validity	Utility	Standardisation	Literature
Fugl-Meyer Assessment	Motor and joint function and sensation. Gross movement	✓	✓	✓	✓	Rehab Robots (Coote et al., 2008; Daly et al., 2005; Hesse et al., 2005; Lum et al., 2002; Volpe et al., 1999)
MRC Muscle Strength	Muscle strength	?	✓	✓	✓	Rehab Robots (Hesse et al., 2005; Volpe et al., 1999)
Motor Status Scale	Evaluating upper limb upper limb isolated movement	✓	✓	?	?	Rehab Robots (Volpe et al., 1999)

Table 6: Upper limb impairment criteria

Scale	Focus	Reliability	Validity	Utility	Standardisation	Quantitative	Qualitative	Unilateral	Literature
Wolf Motor Function Test	mild to moderate	✓	✓	✗	✓	✓	✗	✗	CIMT
Arm Motor Ability Test	mild to moderate	✓	✓	✓	✓	✓	✓	✗	CIMT/rarely Rehab Robots (Daly 05) ES (Mann et al., 2005; Powell et al., 1999)
Action Research Arm Test	Mild to moderate	✓	✓	✓	✓	✓	✗	✓	?
Motor Activity Log	ADL	✓	✓	✓	✓	✗	✓	✗	Rehab Robots (Coote et al., 2008)
Upper Limb-Motor Assessment Scale	Mod	✓	✓	✓	✓	✓	✗	✓	?
ABILHAND	ADL	✓	✓	✗	✗	✗	✓	✗	?
Chedoke Arm and Hand Inventory	ADL	✓	✓	✓	✓	✓	✗	✗	Rarely Rehab Robots Occupational therapy
AMPS	ADL	✓	✓	✗	✓	✓	✗	✗	

Table 7: Upper limb activity criteria

2.4.3 Screening tools

The screening tools chosen were the Unilateral Visual Neglect- Behavioural Inattention Test (BIT) (Wilson et al., 1987), the Mini Mental State Examination (MMSE) (Folstein et al., 1975) and the Modified Ashworth Scale (MAS) (Bohannon & Smith, 1987).

The BIT (Wilson et al., 1987) measures unilateral visual neglect using 6 conventional and 9 behavioural subsets. The two subtests that have been found to be the most sensitive measures are letter and star cancellation, identifying 74% of neglect patients with no false positives (Halligan et al., 1990). This test was chosen, as it was thought that stroke participants with different ranges of visual neglect might respond differently to an intervention focussing on planar reaching tasks in a certain visual field.

The MMSE (Folstein et al., 1975) provides a brief (10 minutes) quantitative assessment of cognitive impairment. A score of 23 or 24 out of the total of 30 is the generally accepted cutoff point indicating the presence of cognitive impairment (Dick

et al., 1984). A limitation of the MMSE is its low reported levels of sensitivity particularly among individuals with mild cognitive impairment. As this was a feasibility study, participants who had a score indicating moderate or severe cognitive impairment were excluded.

The MAS (Bohannon & Smith, 1987) is the current clinical standard (Van Wijck et al., 2001) measuring spasticity using scores rated from 0-4. Reliability of MAS is dependent upon training of testers, standardization of procedures and the muscle being assessed. It may be best suited to assessments of the elbow, wrist and knee flexors (Pandyan et al., 1999). Ambiguity of wording and lack of standardized procedures limit the scales' usefulness for comparison across studies as well as reliability. There are also questions regarding its validity. The test was deemed important for the study as participants with a very high spasticity would have difficulty in maintaining their position in the arm holder with movement.

2.4.4 Clinical outcome measures

There is little consensus in the literature regarding the best motor performance outcome measure for stroke patients (Murphy & Roberts-Warrior, 2003). Most research is on an impairment level basis in rehabilitation robotics with the occasional Activity Level / Motor Function measure included. A recent review on upper limb rehabilitation robotics has suggested 'trials should use valid instruments that measure upper limb skills specifically, such as Action Research Arm Test (ARAT) or Wolf Motor Function Test (WFMT)' to assess improvements in activities of daily living (Kwakkel et al., 2008).

While sometimes used in the robot literature, the Functional Independence Measure and Barthel have been considered unsuitable for measuring upper limb dexterity (Sanford et al., 1993) and it was not expected that an improvement in all aspects of life would result. The primary measure chosen for upper limb function was the ARAT (Carroll, 1965; Lyle, 1981) which was developed to monitor function related to everyday tasks and used a hierarchical measure of grasp, grip, pinch and gross movement. The reaching and grasping movements are rated on quality and speed in three dimensions. The ARAT assesses primarily activity limitations, i.e. a patient's functional loss when interacting with the environment by means of the upper limb. Reliability (Lyle, 1981) and validity (Hsieh et al., 1998; Platz et al., 2005; van der Lee

et al., 2001b) have been established for the ARAT but the measure shows both floor and ceiling effects. The test is widely used in the electrical stimulation literature.

The primary outcome measure chosen to detect changes in upper limb impairment is the FMA (Fugl-Meyer et al., 1975). This test primarily assesses impairment in terms of loss or abnormality of movement, i.e. the ability to perform movements in accordance with specified joint motion pattern. It provides an adequate, reproducible and fairly standardised picture of a patient's sensorimotor and joint characteristics. The FMA is an ordinal scale testing gross movement, coordination and sensation of the upper limb. The motor part of the scale scores a maximum of 66 points: section A (shoulder, elbow and forearm 36 points), B (wrist 10 points), C (hand 14 points) and D (coordination/speed 6 points).

The test is appropriate for severe to mildly affected patients and has high reliability (Duncan, 1983; Sanford et al., 1993) and validity (Fugl-Meyer et al., 1975; Platz et al., 2005). The widespread use of the FMA in research involving rehabilitation robots (Teasell et al., 2007), together with its utility and standardised procedure, meant that it was the obvious choice of impairment outcome measure. In terms of resolution, the FMA could in contrast to the ARAT, detect differences throughout the spectrum of motor dysfunction of the study population and is less affected by floor or ceiling effects.

2.4.5 Non clinical impairment measures

The data the robot produces are positional (tracking error, see section 3.2.3.2) – on line measurement, collecting data anyway – intervention trying to improve tracking, force both isometric (when locked, see section 3.2.3.1) and during movement. Calibration data for the force sensor can be found in Appendix F. Additionally data is produced which demonstrates the relationship between ES and time of the intervention. EMG is covered in the following section.

2.4.6 EMG

Electromyography has been defined as 'the study of muscle function through the inquiry of the electrical signal the muscles emanate' (Basmajian & de Luca, 1985). Surface EMG provides a simple non invasive way to assess general muscle activation during performance of a task. It can aid in determining the intensity and timing of muscular activation and contraction, but is not able to distinguish between concentric or eccentric muscle activity. Owing to its non invasive nature, sEMG is

considered suitable for use with neurological patients (Hesse, 2001). An alternative invasive method, fine wire EMG inserted into the muscles, was not considered due to difficulties with measurement collection (and pain) whilst performing a reaching task, and because it does not present an overview of muscle activity.

2.4.6.1 Definitions and physiology

A motor unit (MU), consisting of a single alpha motor neurone, its muscular junction and the muscle fibres (three to two thousand) it innervates, is the smallest controllable muscular unit. MUs with a high number of muscle fibres, tend to supply the muscle with greater force, but are less controlled and consist of larger diameter alpha neurones which respond more slowly than those with smaller diameter alpha neurones. Finer movement demands fewer fibres per motor unit, and consists of alpha neurones of smaller diameter which respond more quickly. Although all fibres in one MU are activated at the same time, because of the variables of axon lengths and diameters (hence conduction time) and random nature of the neurotransmitter (NT) discharge at the neuromuscular junction, the fibres do not all contract simultaneously. The Henneman size principle states that there is an orderly recruitment of MUs, with smaller MUs being recruited first and with an increase in muscle force more of the larger MUs are recruited (Farina et al., 2004).

A muscle fibre action potential (MAP) is the detected waveform resulting from the depolarisation wave as it propagates in both directions along each muscle fibre from its motor end plate. A motor unit action potential (MUAP) is the spatio-temporal summation of the individual muscle fibre action potentials (MAPs) from muscle fibres in the vicinity of a given electrode. Raw EMG signals represent superimposed motor unit action potentials detectable under electrode sites.

The neuromuscular junction or motor endplate region, where the nerve enters the muscle, is normally near the middle of the muscle fibres (Guyton, 1981) although occasionally there can be two in one muscle. Areas supplied by motor units overlap, so in one region there may be fibres supplied by thirty different motor units. One of the possible reasons for this overlap could be that a smoother, more controlled movement is possible. Typically bipolar electrode configurations and a differential amplifier (which amplifies the difference between the signals, eliminating any background noise e.g. 50Hz from power cables) are used.

2.4.6.2 EMG processing and normalisation

Once raw EMG has been collected, common data processing includes filtering, rectification and smoothing. The main factor influencing EMG signals is muscle activity. Tissue characteristics, physiological cross talk, changes in the geometry between the muscle and electrode site, noise (electrical interference and artefacts) and electrode quality will also affect the signal. To minimise some of these factors the Seniam European Recommendations for Surface Electromyography were published (Hermans et al., 1999). Additionally it is difficult to ensure that the skin impedance or placement of EMG electrodes are identical between participants at the same EMG assessment, and for individual participants over time (between EMG assessments), which could influence the individual values of EMG amplitudes and timings. These can be minimised by ensuring that a standard procedure is followed and by using the same clinician for each EMG collection assessment.

These difficulties mean that a process of normalisation has to be conducted to compare between different individuals' muscles or between the same muscles on different occasions. Different methods of normalisation can be used. In this study the timing and amplitude of peak activity is compared across individual participants' muscles by dividing the processed EMG data by a maximum voluntary isometric contraction factor (individual to each muscle of each participant). The considerable variation in EMG data normalised to MVIC between participants for the same task and muscle prevented direct comparison of muscle activation patterns (strong people performing the same task as weaker people will use a lower percentage of their MVIC). Normalisation was therefore carried out for each EMG recording using the integrated EMG (I EMG) in this case (for further details see section 3.2.4).

2.4.6.3 Evidence base

There has been relatively little research investigating muscle activation patterns whilst reaching in a horizontal plane for neurologically intact as well as stroke participants. A normative data set can act as a template to distinguish between normal and abnormal data and so clarify the effectiveness of treatment (Knutson & Soderburg, 1995).

The temporal relationship between synergistic and antagonistic muscle activity in neurologically intact subjects has been shown to be dependent on direction of movement in supported (Karst & Hasan, 1991; Thoroughman & Shadmehr, 1999) and unsupported reaching (Flanders & Herrmann, 1992) as well as with speed and

distance within the sagittal plane. The effect on EMG signals of varying two components over a reaching task has been examined (Buneo et al., 1994). Varying the length of the trajectory through which the arm moved in a given time resulted in greater EMG amplitude, and varying the length of trajectory while maintaining a constant speed resulted in a decrease in agonist amplitude with distance. In a separate study of muscle activity during both supporting and unsupported reaching in the sagittal plane with healthy older people, changes were identified in EMG amplitude but not timing (Prange et al., 2007).

The EMG activity of shoulder and elbow muscles of neurologically intact subjects was examined during unsupported reaching movements in the horizontal plane in which amplitude speed and direction were varied (Gabriel, 1997). Reaching movements demanding higher angular velocities were associated with increased EMG amplitudes of the shoulder and elbow agonist muscles while temporal parameters between opposing muscle groups at each joint were invariant.

Commonly, studies of chronic stroke participants investigate changes in muscle activation patterns during unassisted movements. Studies have shown that in a single session, reaching movements of the paretic arm of chronic stroke subjects in three dimensions were hindered by inadequate recruitment in the agonist muscles (amplitude rather than timing), not abnormal co-contraction of the agonist and antagonist (Gowland et al., 1992; McCrea et al., 2005). However excess biceps brachii co-contraction limiting performance during voluntary reaching in two dimensions has also been reported (Leonard et al., 2006).

Relatively few studies have examined changes in chronic stroke participants' muscle activation patterns resulting from an intervention consisting of a robot or electrical stimulation. Lum reported increased antagonist EMG amplitudes in two of four table top movement patterns after training patients in the MIME robot for 24 one hour sessions over an eight week period (Lum et al., 2004). By contrast, Hu reported that electromyographic activation levels of the major agonist and antagonist muscle pair of the elbow joint, biceps brachii and triceps brachii, significantly decreased in the first half of the training course, which was associated with an improvement in tracking skill and a decrease in spasticity (Hu et al., 2007).

No studies were identified that examined how muscle activation patterns vary in either neurologically intact or chronic stroke participants during fully supported

reaching across trajectories varying in length, speed and direction with the added variable of resistance. This is despite the fact that resistance training has been shown to reduce musculoskeletal impairments after stroke (Morris et al., 2004).

2.5 Summary

The overall objective of the study was to test the feasibility of re-educating upper limb movement post stroke using ILC mediated by ES using a robotic workstation. This chapter has provided an overview of the research, knowledge and understanding of the topics relevant to this research. Parameters known to influence normal movement, motor learning (such as practice intensity and feedback) and different forms of control theory (motor and engineering) have been discussed and put into context, building on existing knowledge.

Reviews of the clinical evidence from robotic therapy demonstrate that changes to motor control have been identified at an impairment level around the shoulder and elbow. Robots allow a participant to have proportional assistance, which has the disadvantage that if the stroke patient does not contribute voluntary movement, the resultant system provides essentially passive movement. The user perception studies show that stroke participants have a positive view of rehabilitation robotics, but have not used a published question set which can be used across different devices.

Reviews of electrical stimulation suggest that positive effects were enhanced when associated with the person's intention to move, however relatively little work has been done on the shoulder and elbow. Even if a stroke participant does not contribute voluntary movement, benefits are still conferred through the reported benefits of ES such as increased muscle strength (Bowman et al., 1979). Changes in cortical excitability have also been recorded in healthy participants (Ridding et al., 2001) which may apply to stroke participants. The main limitation is that there is little incentive for the participant to work at the limit of their ability which has been reported as being important for motor learning (Schmidt & Lee, 1999). Techniques have not allowed feedback to adjust stimulation parameters during tasks. An ES system which adjusts the ES in response to the users' performance in order to provide only the minimum level of stimulation needed to assist the participant in performing a task to a high level of accuracy is required.

The chapter concludes with a section on evaluation of the intervention. This includes a discussion of measures, including screening measures and the ICF framework. Outcome measures chosen to identify unassisted tracking error, and isometric force for neurologically intact and stroke participants using the workstation are outlined. Additionally for stroke participants, clinical outcome measures, percentage maximum ES and participant perceptions are discussed. Associated changes in muscle activation patterns (using EMG) for neurologically intact and stroke participants during tracking tasks in the workstation are also measured as part of the evaluation of the intervention. The final section discusses EMG and the factors affecting the signals. The types of normalisation used in this study have been outlined. Existing evidence relating to the assessment of upper limb movement using EMG during reaching for both neurologically intact and stroke participants has been discussed. No studies have been identified that have examined how muscle activation patterns vary in neurologically intact older and stroke participants during fully supported reaching across trajectories varying in length, speed and direction with the added variable of resistance. This will be addressed in the present study.

3 Methodology

This chapter discusses preliminary work such as the development of the robot, arm modelling and ILC algorithms, and selection of different parameters that were used in the participant studies. These included: selection of the tracking tasks, EMG (muscle choice, procedure for data recording and analysis, and noise evaluation), ES (muscle choice, placing and parameters) and selection of outcome measures (tracking error definition, screening criteria and clinical measures). The following two sections are structured as 1) design, 2) participant information 3) intervention 4) data processing and analysis and 5) statistical analysis. Section 3.2 outlines the method for answering the question 'What are the isometric force, unassisted tracking error and muscle activation patterns for neurologically intact participants during tracking tasks in the workstation?'. The final section (3.3) addresses the aims of the study by outlining the method for answering the clinical questions: 'what are the isometric force, unassisted tracking error and muscle activation patterns for stroke participants during tracking tasks in the workstation?'; how are these affected by an intervention programme using the robot and ES?'; 'are these changes associated with clinical outcome measures of impairments and activities?' and 'what are the stroke participants' perceptions of the system?' .

3.1 Preliminary work

Protocols were developed for both studies based on clinical knowledge of stroke participants' impairments, advice from stroke participants and preliminary testing by the researchers for: the selection of the tasks, EMG and ES muscle choice and ES parameters.

3.1.1 Interdisciplinary development of the robot workstation

The synergy resulting from the engineer's and physiotherapist's skills and expertise ensured the design of the workstation, as well as the intervention, resulted in a usable system for the therapist and all research participants. The purpose of the robot was to provide the stroke participants with the ability to move successfully, supporting the weight of the arm in much the same way as a therapist would. During tracking trajectories using ES, the action of the robotic arm was i) to make the movement feel 'natural' to the participant, and ii) to provide a minimal level of assistance to ensure the task was achievable, yet allowing the ES to drive its completion.

The therapist's understanding of motor learning at the neurophysiological, biomechanical and behavioural levels, impacted on the design of the workstation, underpinned the intervention in this study as well as the ES. Identification of different constraints on the motor system included looking at possible implications of impairments such as muscle paresis and paralysis, the impact of fatigue, abnormalities of muscle tone and core stability, timing and inter joint co-ordination problems, involuntary movements, the effect of secondary musculoskeletal impairments, sensory impairments, as well as cognitive, perceptual and psychological problems. This knowledge, in addition to the awareness on the theories of the control of reach in normal subjects and stroke patients was important in the design and development of the ILC system.

The skills and expertise brought by the engineer, Dr Freeman included the workstation engineering design, construction and management, and its associated real-time stimulation and image projection systems. In addition, mathematical models of firstly the arms of neurologically intact and stroke participants in response to stimulation, and secondly, of voluntary movement using EMG data were developed and verified. These models have been used to provide a greater understanding of the physical and neurological differences between stroke patients and unimpaired subjects, as well as to design both the task, and controllers used during their treatment using the robotic workstation.

The robot workstation was based on the Massachusetts Institute of Technology's robot MIT-Manus – with a five bar (carbon fibre – for high strength to mass ratio)

linkage arrangement displayed in Figure 11. The link lengths are: $l_1, l_3 = 0.45\text{m}$, $l_2 = 0.2\text{m}$, $l_4 = 0.66\text{m}$ and $l_5 = 0.25\text{m}$.

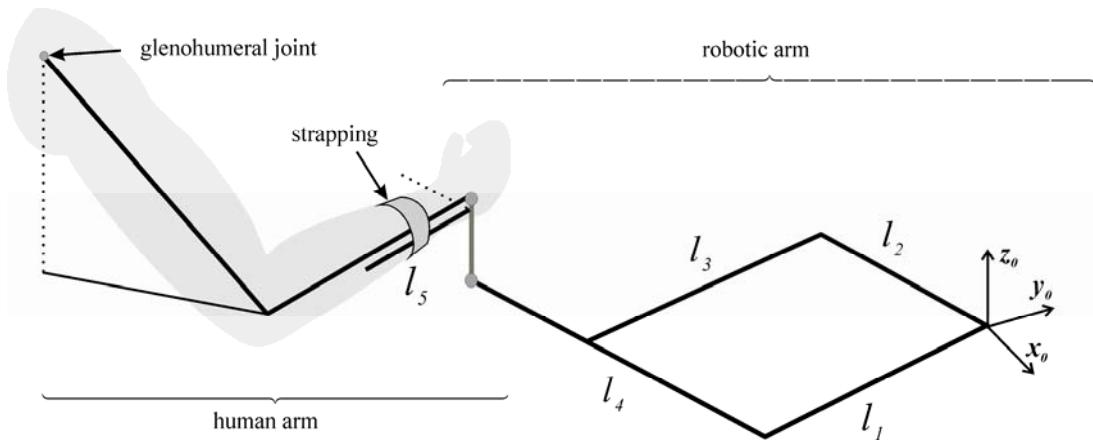


Figure 11: Linkage arrangement for the robotic arm

The arm is constructed from carbon fibre and aluminium, and is actuated using two DC brushless servomotors. These were placed at the origin and were chosen because of the large torques that can be generated at low speeds (sufficient force to keep the participant's arm static against user applied force) and the simplicity of the amplifier stage. Each is capable of producing 5.5Nm continuous output torque with a peak torque capability of 14Nm. A 2:1 ratio gearbox is used on each to increase the available torque so that the robot is capable of continuously applying a force of over 13N (with a peak capability exceeding 33 N) in any direction over the workspace. The subject is strapped to the extreme fifth link, and grips a cushioned handle which is rigidly connected to a 6 axis force/torque sensor which records the force they apply to the robotic end effector. Forces can be measured of up to 200N applied in the horizontal plane with a resolution of 0.0122N.

The joystick was attached by a joint to the torque/force sensor so that it could rotate freely and the change in the angle of the joystick was measured using an encoder. The sensor was chosen by considering the variables of cost, size, resolution and compatibility with the other equipment. To constrain the forearm a plate was designed which screwed into the joystick piece. A thermoplastic arm holder was made to support the elbow and wrist in a neutral position. To ensure the user knew exactly where the joystick should be at any time, the trajectory was shone (from a projector overhead) on to a plastic surface attached to the top of the joystick (see Figure 12). The participant was able to see their hand through a semi transparent section in the plastic whilst the opaque section allowed the trajectory to be

displayed. For clarity, a bull's-eye ring of light emitting diodes allowed the participant to see how far off the target they were.

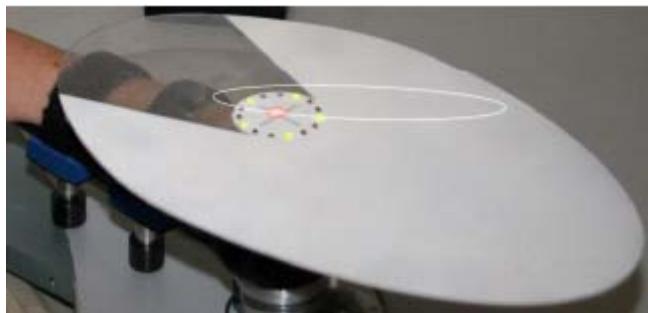


Figure 12: Close up of a trajectory projected on to the plastic surface

The platform for the practical implementation of the control algorithms in real time was chosen by the engineers to be D-SPACE, due to its large selection of control cards, simplicity and ease of programming. The card used had 36 A/D channels (6 for the force/torque sensor, 30 for the goniometer position and EMG data), 8 D/A channels (2 for the control inputs to the motors, 6 to output ES signals), 6 encoder channels (3 to receive the joystick and motor encoder's position, and 3 could be used to receive goniometer position signals) and 50 digital input / output channels (used to produce the ES signals). Data processing and analysis was conducted using Matlab.

Although 6 channels were available for the force/torque sensor, as the robot was a planar system, only 2 force directions (x,y plane) were used. The participant biometrics and the force were used to calculate the torque around the elbow (see Freeman et al. 2008a for full details).

The main elements of the workstation are shown in Figure 13. Neither the workspace of the robotic arm, nor the size of the projected image (1.2m by 0.8m) restricted the participants' movement for the range of trajectories used (see Freeman et al., 2008c for full details related to the design of the workstation, max joint torque, end point force, computational resources, safety precautions used and efficacy of the projection system and robotic arm controller).

The robot used impedance control to ensure a safe interaction with the participant's arm. The robot provided a low level of assistance (60Nm^{-1}) (a "spring" force). The force was proportional to the error in tracking, and effectively only noticeable when

the tracking error was greater than 5cm. Additional information on the ILC algorithms can be found in Freeman et al. 2008a.

The robot mass and damping gains used were $1 \text{ Nm}^{-1}\text{s}^2$ and $15 \text{ Nm}^{-1}\text{s}$ respectively (i.e. the robot produced the effect that the participants were moving a mass of 1Kg with viscous damping of $15 \text{ Nm}^{-1}\text{s}$).

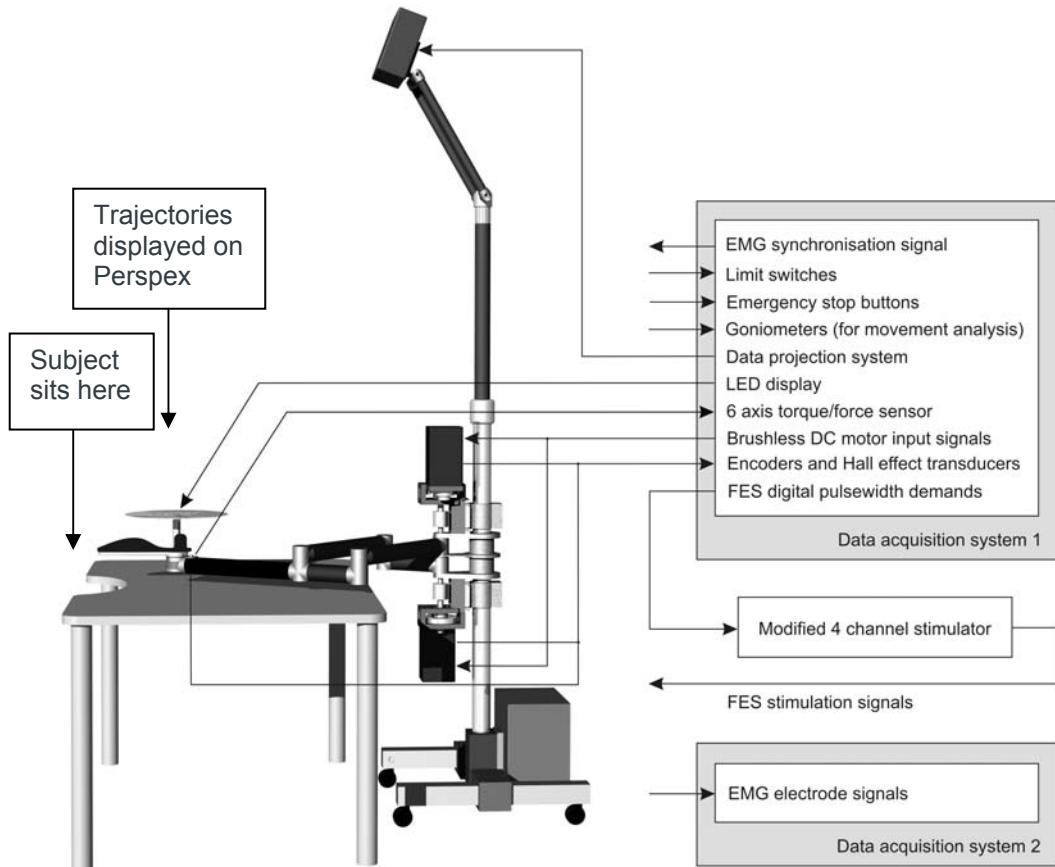


Figure 13: Robot workstation schematic showing principal elements and signal requirements

To ensure the robot's safe interaction with an unknown environment, a form of impedance control (see Colgate & Hogan, 1998, for details) was used to govern the torque demand supplied to the motors. Control measures included the Jelly Bean switch for emergency power cut-off, the Carroll and Meynell Isolation Transformer (1650VA continuous output rating 230V primary voltage) and circuit breakers. The stimulator being used was CE marked and the modifications and safety checking

was done by Salisbury FES who are ISO 13448 approved. Stimuli response tests and maximum stimulation output (limited by discomfort or maximum response) was performed for each participant to ensure that the stimulation was appropriate for that individual.

3.1.2 Arm modelling

The dynamic characteristics of arm movement may be divided into those properties describing its behaviour in the absence of voluntary effort (passive) to which are added the properties determining the response to voluntary control (active). For stroke participants these are compounded by the motor control impairments already discussed (see section 2.1.2).

A dynamic model of the stimulated arm system is required for use in the analysis of treatment, and the design of the stimulation controller. This is used specifically to provide details of participants' passive and active arm properties that are used as outcome measures analyse each participants' performance and to design the advanced control schemes governing the level of stimulation applied to participants over the course of the intervention.

Dynamic models have been produced, firstly for stroke patients with residual voluntary movement to enable analysis of the kinetic and kinematic characteristics of their movements (Beer et al., 2000). These models have incorporated the total torque due to the combined effect of the remaining passive arm properties and voluntary effort. Additionally models have been developed for unimpaired and paralysed limbs (with no voluntary action) that fully incorporate passive arm properties and also include the application of ES (Dou et al., 1999).

Control schemes exist in which EMG from the stimulated muscle is used in order to obtain a direct measure of overall muscle activity, however, the EMG amplitude does not necessarily correlate with either muscle force or limb movement. In addition the EMG signal may often be weak and unreliable and the artefact produced by the stimulation signal may corrupt the natural EMG signal (in which case blanking techniques may be applied).

Little work has been done to produce dynamic models suitable for stroke patients' arms (with residual function) which either explicitly account for all passive arm

properties or include the application of ES. This is partly due to the difficulty associated with measuring or estimating the degree of voluntary effort supplied by the participant.

Model Development

Spasticity and the biarticular nature of triceps were taken into account in developing the model. Evidence has shown that the stretch activation of triceps can produce joint torques at the shoulder (Sangani et al., 2007). Passive properties of stroke patients have been shown to be repeatable intra-session but may vary between sessions (Lum et al., 1999) and can only be assumed to be uncoupled if the level of spasticity is mild. It has been shown that it is possible to model the triceps as uni-articular with respect to applied FES, with careful electrode placement to minimise the degree of biarticular flexion (Lan, 2002).

A mathematical dynamic model was derived incorporating the passive arm properties, and was used to calculate the torque generated by the voluntary effort of stroke participants during reaching movements. The torque generated by triceps in response to ES (represented by the torque generated by an electrically stimulated muscle acting about a single joint) was subsequently added and the model tested in the absence of voluntary effort supplied by the participant.

To estimate the parameters present in the model identification tests were undertaken. The tests were designed to collect the essential data in the minimum time to reduce possible fatigue. They included:

- i) Stimulation parameters – the ES electrode position on the triceps brachii was tested in situ to ensure maximum movement in the given plane of motion, whilst minimising any shoulder torque. The stimulation used was asymmetric biphasic with a fixed amplitude and a period of 40Hz. The pulselwidth was variable from 0 to 300 μ s with a resolution of 1 μ s. The amplitude, which was fixed throughout all subsequent tests, was determined by setting the pulselwidth equal to 300 μ s and slowly increasing the applied voltage until a maximum comfortable limit was reached. This was verified over the full range of elbow extension.
- ii) Biometric data – for each participant the distances from the acromium to the coracoid process of the elbow, and from the coracoid process to the 1st proximal interphalangeal joint were measured. The participant was then seated in the robot

with strapping to restrict trunk flexion. With the dominant (or in the case of a stroke participant, their hemiplegic) arm strapped into the robot arm holder, maximum reach across the workspace was measured. Using the measured lengths, the angle between robot and human arm and an appropriate sampling time, the discrete trajectories were produced.

iii) Passive Dynamics with Applied ES

First an isometric model of the torque produced by the triceps in response to stimulation was produced by the following procedure.

The participant was seated in the robot and was instructed to apply no voluntary effort. The participant's arm was held stationary by the robotic arm and a triangular input was applied to the triceps. The force at the end effector was recorded and the moment about the elbow was calculated. A model of muscle contraction dynamics was then fitted which involved a static non-linearity (the "isometric recruitment curve"), multiplied by a linear model of muscle contraction dynamics (the "linear activation dynamics"). For further details see (Freeman et al., 2008c).

Passive dynamics with no ES were also investigated with neurologically intact and stroke participants. This was done by using the robot to move the human arm through a set of trajectories which excite all the system dynamics of interest and recording the force applied at the end effector. Details of this can be found in (Freeman et al., 2008b). The first test consisted of six trajectories each of 40s duration in which the shoulder angle was held constant and the forearm angle moved between predetermined comfortable limits. The time taken for each movement was slowly reduced from 10s to 1s by increasing the velocity. The second test was similar but involved movement of the shoulder angle between predetermined limits whilst the elbow angle was held constant. For the stroke participants the results from these tests were found to vary significantly over time. To avoid the necessity of repeatedly performing identification tests, standard parameter values were used.

Experimental results have been published (Freeman et al., 2008b) confirming the efficacy of the model and accompanying identification procedures. To further examine the accuracy of the identified models of the electrically stimulated passive arm further tests were conducted. The arm model was then applied to the situations where firstly ES was used in the absence of voluntary action, and then subsequently where voluntary control is present and ES is not applied. Finally a method was

proposed which modelled the effect of applied stimulation while the participant simultaneously exerts voluntary effort.

3.1.3 Control scheme

A substantial amount of work on the practical application of ILC has been conducted at the University of Southampton using test facilities which include a gantry robot (Ratcliffe et al., 2005). To date there has been limited consideration of the application of ILC to problems that are not concerned with industrial processes. Many of the approaches used, however, are also suitable for the model of the stimulated arm that has been developed.

Due to the presence of time varying effects and uncertainty, algorithms are needed which are simple, robust and effective. Using existing expertise and experience in Southampton, ILC linear non causal algorithms of simple structure were considered. In the research study two control strategies have been used (see Figure 14 and Figure 15). The first was a linearising PD controller (needed as the arm model is non linear) (Freeman et al., 2008a) in a standard feedback arrangement. The initial component of which is the isometric recruitment function that is identified for each participant. The second strategy used ILC in addition to the linearising PD controller, as a feedforward signal. Two algorithms were considered: a phaselead (simple structure ILC) and an adjoint (more complex and model-based approach). They both use a non-causal zero-phase filter on the previous error to make the update for the next iteration. The phase lead uses 2 parameters (the amount of phase lead and the gain) but convergence will not occur at high frequencies, which will gradually build up. Effectively a filter is required so it becomes a 3 parameter system. By contrast, the adjoint uses 1 gain parameter, the tuning is easier and it is known to be more robust to disturbances and modelling error, but takes longer to converge at low frequencies. Generally the higher the ILC gain, the faster convergence over all frequencies, however the convergence of the error is limited by non repeatable disturbances in the error. Both laws provided similar results, however the phase lead was used in this study as it converged faster at low frequencies.

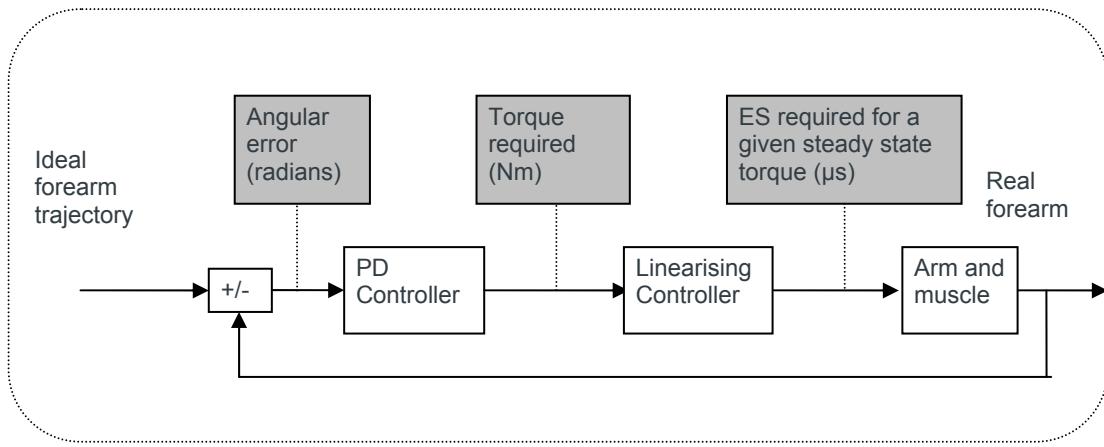


Figure 14: Control strategy for the study using a linearising PD controller in the feedback arrangement

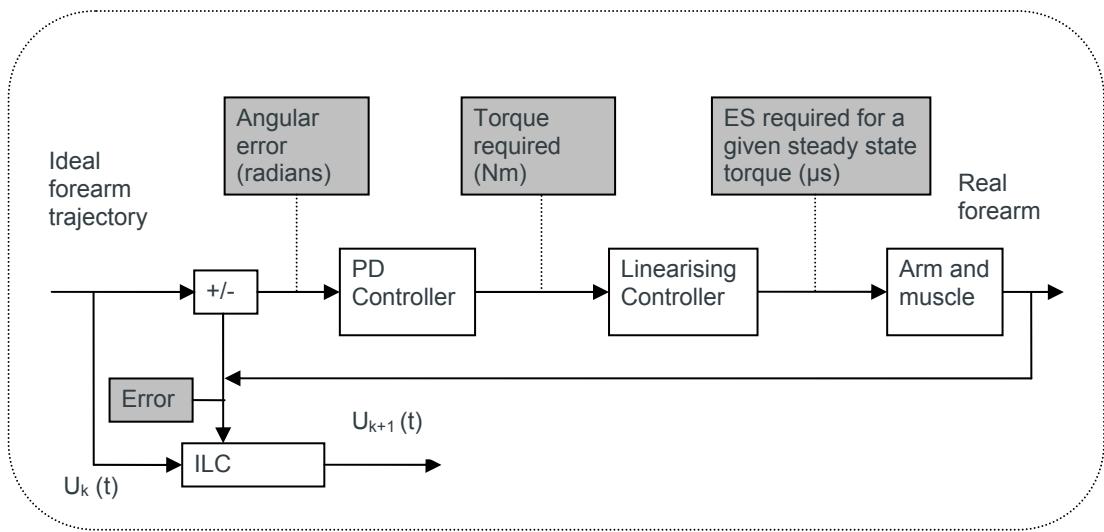


Figure 15: Control strategy for the study using ILC in addition to the feedback control
 The robot moved the participant's arm back to the start position. On the first trial the feedback controller was used as there was no previous data for the ILC algorithm to use. On the second trial the ILC algorithm was used.

3.1.4 Selection of the tasks

Minimal width elliptical trajectories were selected that were comfortably within both the robot's and the participant's workspace. Ellipses were chosen in preference to a straight line as this would have caused the controller to be unable to distinguish between a reach and return. The start and end points were chosen so that they can be reached by a smooth extension of the elbow, and were individually calculated for each participant depending on their maximum reach capability. Different trajectories

ranges were pilot tested and varied in length, speed and resistance until a standard set were obtained.

3.1.5 EMG

The muscles considered for EMG recording were drawn from clinical experience and existing knowledge, published data reporting on EMG in reaching within the horizontal plane and preliminary testing. The muscle needed to be active in the reaching task (for neurologically intact), but not working in the stroke participants. EMG was used to determine which muscle was chosen.

From clinical experience and knowledge it is known that in stroke participants certain muscles, such as the triceps and shoulder stabilisers are weak, and typically elbow extension is difficult. They have difficulty typically in extending their elbow. It is reported (Mottram, 1997) that 'the ability to position and control movements of the scapula is essential for optimal upper limb function'. As there is a lack of ligamentous restraint at the scapulothoracic joint, the muscles that attach the scapula to the thorax (most importantly trapezius and serratus anterior) have a major stabilising role – and hence need appropriate contractile and recruitment properties. Due to difficulties in reliably locating serratus anterior (no standardised SENIAM guidelines) this muscle was excluded.

EMGs from muscles used in previous studies (see section 2.4.6.3), as well as preliminary testing, determined the choice of muscle used in this study (due to the constraint of the forearm and hand by the thermoplastic arm holder, wrist flexors and extensors were automatically excluded).

In preliminary testing, shoulder and upper arm muscle activity were recorded when the testers were using the robot arm holder to track the trajectories. The muscles which demonstrated the highest levels of activity during this action were medial triceps, biceps, anterior deltoid, upper, middle and lower trapezius, and pectoralis major. Testing was conducted under different conditions to investigate noise which might affect the EMG signals. EMG signals were taken with the robot off whilst the participants rested their arm on their lap and then in the arm holder. Subsequently the robot was turned on, and the participants rested their arm in the arm holder initially stationary and then moving in an elliptical path. The noise of the robot was found to be negligible, but having the arm supported in the arm holder did increase the activity seen in upper trapezius.

3.1.6 Electrical stimulation: muscle choice, application and parameters

From the EMG data gathered during preliminary testing, it was established that the triceps, biceps and anterior deltoid most strongly exhibit activation patterns that correspond to when the trajectory was running as opposed to being activated continually. Clinical knowledge suggests that, of these, the triceps and the anterior deltoid are most likely to be weak. The triceps was chosen as it produced greater movement when the arm was strapped to the robot (Freeman et al., 2007).

To ensure that all participants received the same intervention, skin preparation was standardised. The skin surface was cleaned with an alcohol wipe and hypoallergenic blue 1.5 inch 'Pals' self adhesive reusable skin surface electrodes were used. Positioning of the electrodes was approximate (cathode approximately ten centimetres and the anode five centimetres superior to the coracoid process of the elbow). The aim was to elicit the optimal normal pattern of movement whilst the arm was in the robot arm holder. The ES electrode position on the triceps brachii was tested in situ to ensure maximum movement in the given plane of motion, whilst minimising any shoulder torque.

In view of the clinical evidence (see section 2.3.2) and because a commercial CE marked stimulator was being used, stimulation parameters commonly used in the rehabilitation of stroke patients were used. In this system the pc output parallel digital signals of frequency 40Hz, voltage 0-5 V, and pulsewidth 0-300 μ s,. These passed through electronic circuitry to produce a square wave pulse which was fed into the stimulator. This amplified the low voltage pulses, to emerge as the clinically used asymmetric biphasic signal (frequency 40Hz, voltage 0-150V and a varying pulsewidth 0-300 μ s with a resolution of 1 μ s), comfortable to participants. The frequency of 40 Hz ensured a tetanic contraction was produced, whilst the trajectories were kept short (7.5 s) to minimise possible fatigue effects over the six iterations. The pilot work with the ES electrodes positioned on triceps is shown in Figure 16.



Figure 16: Pilot work using ES to follow the trajectory

3.2 Neurologically intact participants

3.2.1 Study design

A repeated measures design was used in which participants attended the laboratory on two occasions. All data collection was performed by a single experienced investigator. The study design and data collected are displayed schematically in Figure 17.

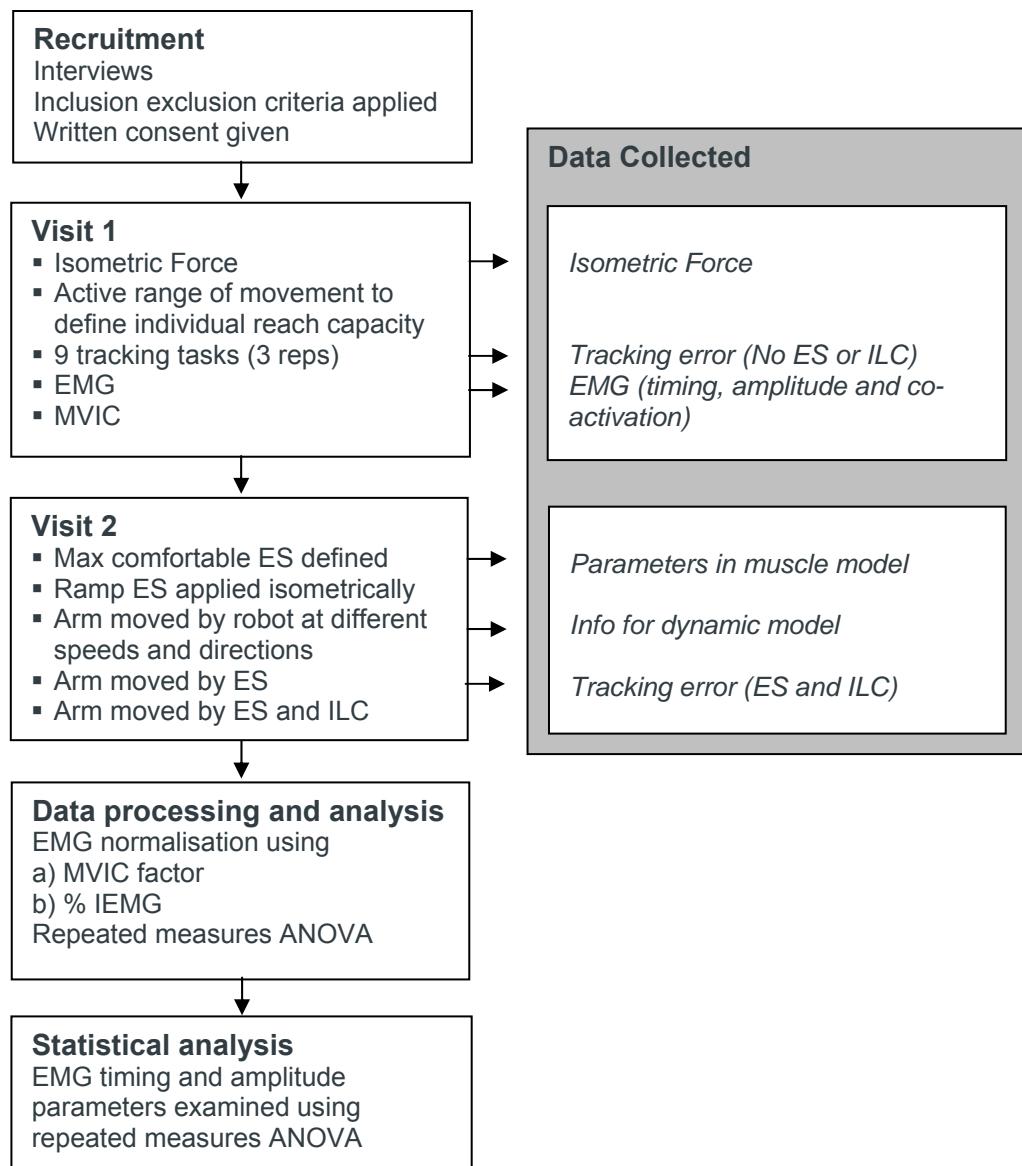


Figure 17: Flowchart for neurologically intact participants

3.2.2 Participant information

As this was a feasibility study no power calculation was performed. The small sample size chosen due to convenience is representative of work conducted in this field. Participants were recruited by word of mouth or by poster invitation. All participants then received an information sheet, and if they were willing to participate, they were asked to sign a consent form.

Neurologically intact participants aged fifty years and over were recruited as representative of stroke patients; strokes are more common in people over 55, and the risk continues to rise with age (Stroke Association, 2006). In addition, the sample reflected other changes occurring in the aging population such as sensory and perceptual, central processing systems, motor systems and arousal and motivational systems which may influence performance of a target tracking task (Welford, 1982).

Participants were excluded from the study if they had uncontrolled epilepsy, required an interpreter, had any active device implant (e.g. pacemaker, implanted cardiac defibrillator, neurostimulator or drug infusion device), an allergy to sticking plaster/tape or alcohol wipes or any serious medical, psychological or cognitive impairment that, in the opinion of the investigators, would compromise the participant's safety or ability to comply with the study. Participants with any orthopaedic or neurological lesions which may affect arm movement were also excluded.

3.2.3 Intervention

Screening was conducted at the recruitment stage. The first visit was used to record isometric muscle force and identify normal muscle activation patterns during different trajectories. All tests were conducted on the participant's dominant arm. Participants were seated in front of the robotic workstation at a height which allowed normal shoulder positioning. Restraining seatbelts were used to prevent compensation by trunk flexion during reaching as shown in Figure 18. Since the strapping lay over 2 electrodes, the anterior deltoid and pectoralis major, it may affect the signal associated with these electrodes. To reduce this possibility, the strapping had soft padding on the underside and was designed to exert minimum pressure on the electrodes. Strapping positions were also standardised to reduce differences across participants.

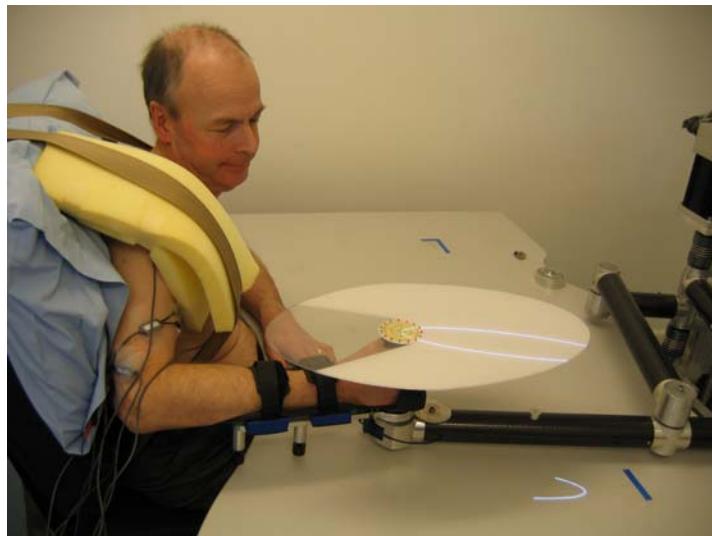


Figure 18: Participant performing tracking task using the robot workstation showing method of constraint

3.2.3.1 Isometric force

Isometric force was assessed by locking the arm holder in a stationary position (18.5cm) directly in front of the participant, who was instructed to exert a force away from themselves in the sagittal plane for five seconds. The participant then moved to the next direction in a clockwise fashion (see Figure 19). Peak values were obtained from three repetitions of each attempt for each direction.

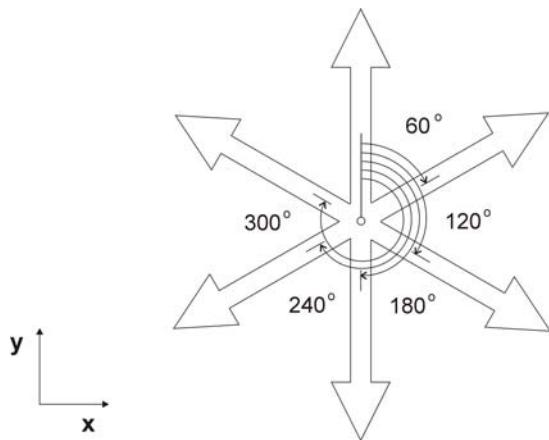


Figure 19: Isometric force measurement directions

3.2.3.2 Error tracking

The participant's arm was placed in the robot arm holder with the hand curled around a padded vertical pillar. The arm holder constrained their hand to move in a

two dimensional plane, but incorporated a hinged mechanism to allow the elbow to lift up at the limit of arm extension. A semi-transparent Perspex elliptical disc was positioned over the hand and forearm and attached to the top of the pillar. A target area (diameter 60mm) defined by a circle of LEDs with a central cross-hair, was marked on the elliptical disc immediately above the hand and pillar. An overhead projector displayed an image of an elliptical trajectory onto the Perspex disc and an illuminated red dot – the tracking signal – moved along the trajectory at constant speed. The participant's arm was moved to the starting position by the robot. A 5 second 'countdown' was visually displayed prior to commencement of the tracking task. To perform the tracking task the participant was instructed to move their hand so that it kept pace with the moving red dot, keeping it within the circle of LEDs and as close as possible to the cross hairs. To reinforce good performance and indicate error, the LEDs changed colour; green when the tracking accuracy was within 25 mm, amber between 25 and 50 mm and red when error exceeded this.

For each trajectory, the error between the cross-hair and the target (shortest straight line between the actual position and the target red dot (see Figure 20) was recorded at every time point using a sampling frequency of 1.6kHz. Trajectory tracking performance was defined as the mean error value over the test duration.

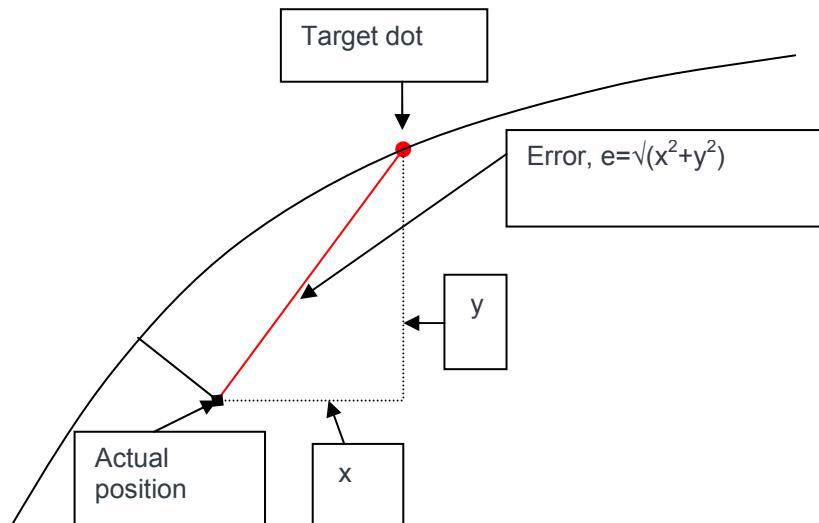


Figure 20: Description of actual and reference position (red target dot) along a trajectory

This tracking error data was represented along the course of the trajectory in Figure 21 (data for participant 02 obtained during one repetition of the T1 LFH trajectory). The top two graphs a) and b) represent the tracking error over the x and y axis respectively. The black line refers to the reference trajectory and the blue line to the displacement by participant 02. The difference between the two is the tracking error. The error magnitude c) was created by $\sqrt{x^2+y^2}$. The mean error, used for displaying the results in Chapter 4, was calculated by summing the error magnitude for each sample timepoint and then by dividing the result by the number of samples (the frequency used was 1.6 KHz). The mean error is shown for this participant broken down into the components of reach and return, given in parentheses. It can be seen that the error in the return phase is greater than in the reach phase.

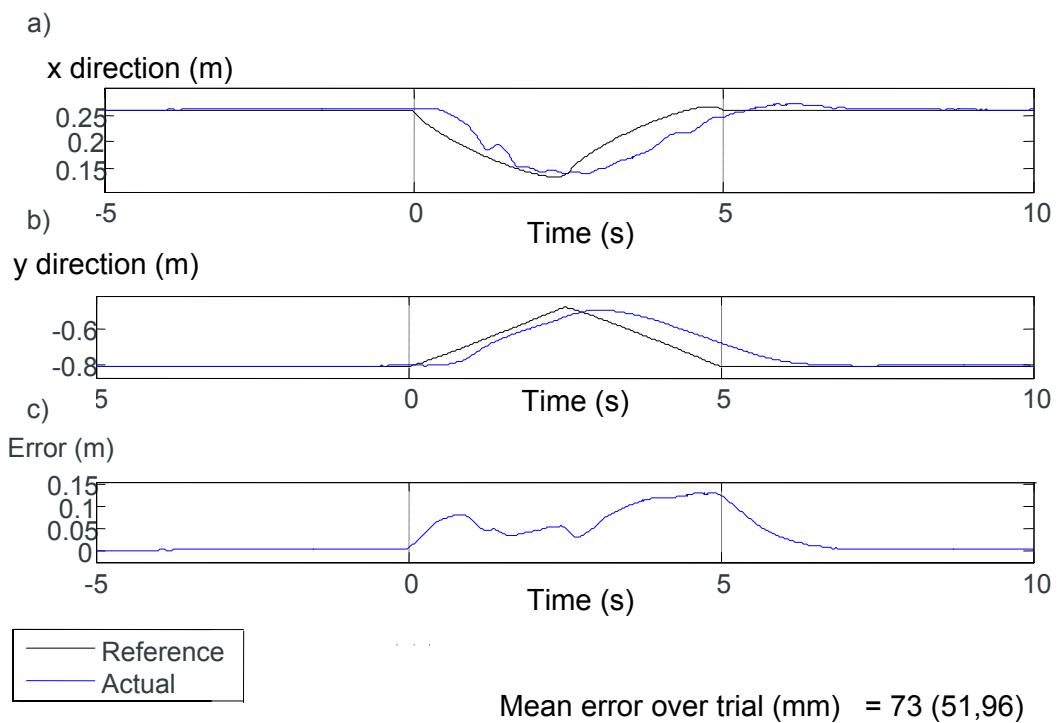


Figure 21: The reference (black) and actual (blue) tracking error is shown for participant 02 over the T1 LFH trajectory over the a) x and b) y axis. The tracking error magnitude is shown in c)

While positioned in the robot, participants were asked to move their arm through their full range of movement to define their individual maximum reach capability. The data collected was also used to calculate the participant's shoulder position together with the elbow position (Freeman et al., 2008b). Participants were then asked to

perform nine different tracking tasks. Tasks were varied in terms of: trajectory (orientation and length), duration, speed and resistance. Length and orientation of trajectory were normalised to each participant's maximum reach. Each trajectory started at a position corresponding to 55% of maximum reach. The ratio of minor to major axis length was 1:5. Three orientations of the major axis were used: mid-line (T2) and 20% of maximum range to left (T1) and to right (T3). For each orientation three levels (1-3) of the task were defined in which length, duration and resistance were adjusted. Tasks are summarised in Table 8 which also gives the abbreviations used throughout the thesis. The participants performed the tasks in the order T1SSL, T1MMM, T1 LFH.....T3LFH and each was performed three times. An example of a T3 MMM tracking task is shown in Figure 22.

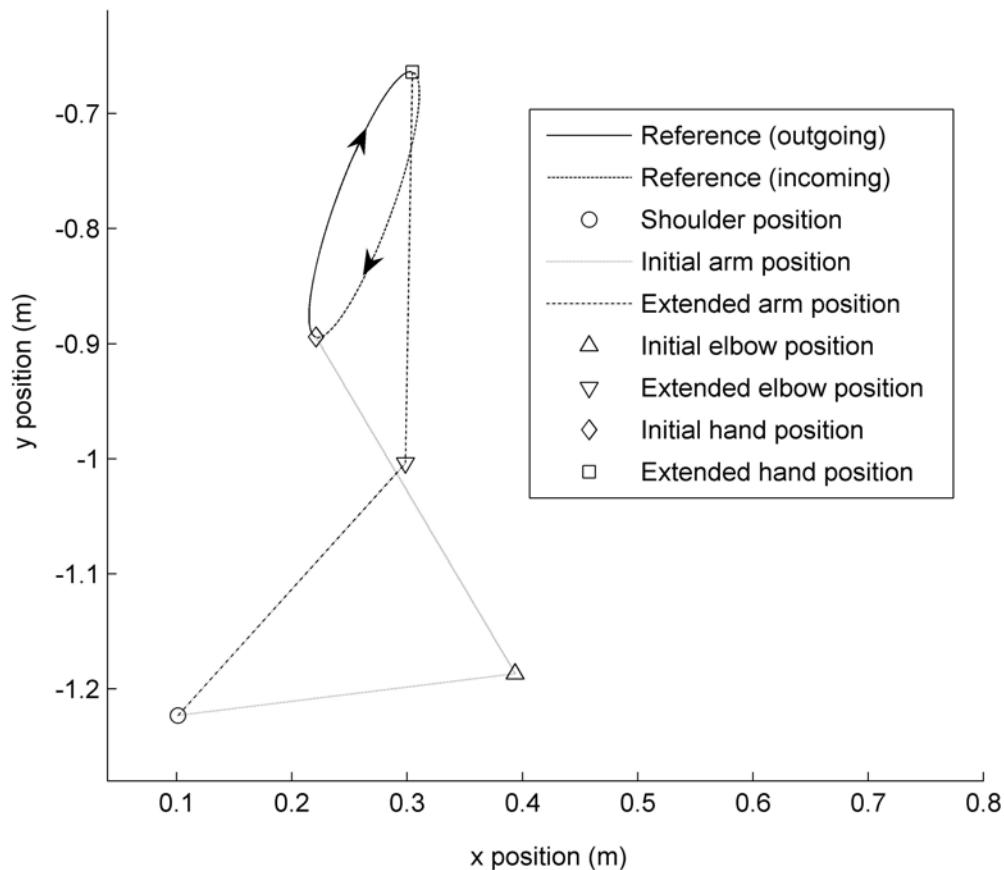


Figure 22: The position of shoulder, elbow and hand at the initial and extended positions on the T3 MMM trajectory (100% reach = 0.658m)

The intention is to repeat the study with stroke participants using trajectories tailored to 80, 90 and 99% of passive reach (i.e. their arm will be moved to maximum available range by a clinician) so that the trajectories will pose a significant

challenge. Based on clinical experience tasks were conducted in an order of increasing difficulty, to maximise stroke participants' performance. To facilitate comparison between stroke and neurologically intact participants, the same test order was used in both cases. Participants were allowed to see a demonstration of the trajectory but were not allowed to practice the trajectories prior to the assessment.

Length	Duration (s)	Resistance(Nm ⁻¹ s)	Abbreviations
Short (80% of reach)	Slow (15)	Low (10)	SSL
Medium (90% of reach)	Medium (10)	Medium (20)	MMM
Long (99% of reach)	Fast (5)	High (40)	LFH

Table 8: Length, duration and resistance for each level of task, each of which was performed at three angles: midline and 20% of maximum range to the left and right. Abbreviations used for each task are shown in the right hand column

3.2.3.3 EMG recording, processing and analysis

EMG recordings from triceps, biceps, anterior deltoid, upper, middle and lower trapezius and pectoralis major were made during all tracking tests. A standard procedure, described in the Seniam guidelines (Hermans et al., 1999), was used for skin preparation and electrode placement for all muscles except the medial head of triceps and pectoralis major for which electrodes were positioned to detect the greatest amplitude during maximum voluntary isometric contraction (MVIC). The reference electrode was placed over the electrically neutral lateral epicondyle where it interfered least with the movement and other electrode sites. Signals were recorded using Noraxon Dual Ag-AgCl snap electrodes (product # 272) with an inter-electrode spacing of 2cm. Skin impedance was measured, and for all recordings was below 10 kilo ohms (Cools et al., 2002). EMG electrodes were connected to a hub and transmitted wirelessly to the Noraxon data acquisition system, to enable unimpeded movement. EMG signals were sampled at 1500Hz. Raw signals were amplified x2 at the electrodes to reduce the signal to noise ratio. Further EMG signal processing was performed using Matlab (7.2.0.232). Data was zero phase bandpass filtered (fourth order Butterworth 10-500Hz), full wave rectified and smoothed (moving average 0.1s window). Using standard limb positions (Kendall et al., 1993), EMG was recorded during three five second MVICs, during which strong verbal encouragement was given with participants asked to push or pull as hard as they could. Prior to performance of the tracking tests all EMG

channels were checked to ensure that strong signals were recorded with minimal noise. If signals were considered unsatisfactory electrodes were removed and re-positioned.

The second visit was used for the arm modelling and the application of ILC. Participants were positioned as in the first visit and were asked to relax. To provide data for the dynamic model, the arm was moved by the robot in different directions at varying speeds. The maximum comfortable level of stimulation was then identified and used as an upper limit. The sequence of movements was then repeated whilst using stimulation (asymmetric, biphasic, 40Hz fixed amplitude, variable pulse width 0-300 μ s with a resolution of 1 μ s) to identify parameters in a model of the triceps muscle. Finally, the participant was again asked to relax their arm and to shut their eyes, so they did not anticipate movement. ILC mediated by ES was then used to control the movement of their arm over six iterations of selected trajectories.

3.2.4 Data processing and analysis

Two methods of normalisation were used to compare a) timing and amplitude of peak activity b) EMG amplitude as a percentage of the integrated EMG for that muscle during each task.

a) For each participant an MVIC factor was calculated as follows: peak amplitude for three consecutive MVICs was recorded (shown by the symbol '+' in Figure 23). Their mean was found (dotted horizontal line in Figure 23) and all data points >60% of the mean were averaged to give the MVIC 'factor' which was used to normalise EMG amplitude recorded for each muscle during subsequent tests. This was above background levels between contractions and within a region where changing the threshold did not lead to large differences in the resulting MVIC factor. Following the completion of all tests the three EMG recordings corresponding to each muscle, task and participant were replaced with a single trace whose value at each time-point was the mean of the three traces at the same time-point. Then the peak amplitude of each EMG trace was identified, together with the time-point at which it occurred. The values of peak amplitude corresponding to the same task and muscle were averaged to give μ_{EMG} (which therefore represented the mean across all participants). Similarly the mean and standard deviation (SD) were identified for all the time-points corresponding to the same task and muscle to provide μ_T , σ_T respectively. The amplitude and time-points of maximum EMG are presented in Figure 31 as wedges on size standardised representations of each trajectory. On

each representation, a wedge is drawn for each muscle. The height of each wedge is proportional to the mean peak amplitude, μ_{EMG} and the wedge width is drawn between $\mu_T - \sigma_T / 2$ and $\mu_T + \sigma_T / 2$. If a point travels along the ellipse at constant velocity, arriving at the finish point at the time of test duration, it will encounter the wedge between times $\mu_T - \sigma_T / 2$ and $\mu_T + \sigma_T / 2$ seconds. The wedge location therefore corresponds to the period in which the muscle is most active over the course of the trajectory tracking task.

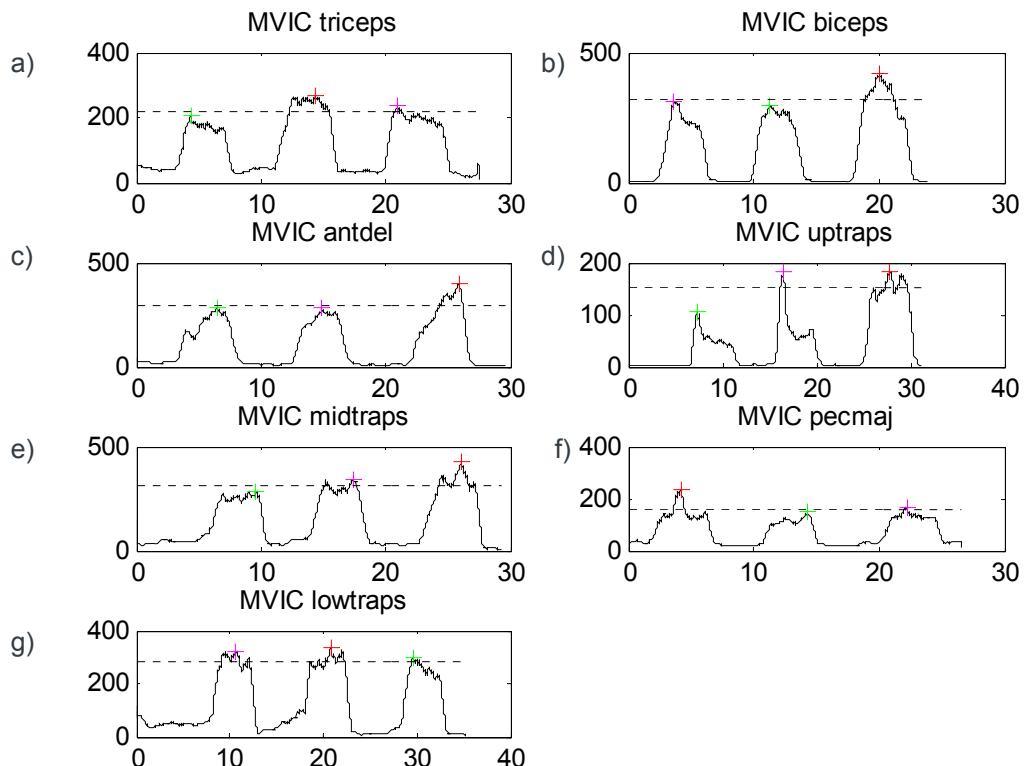


Figure 23: Filtered, rectified, smoothed EMG amplitude (µV) against time (s) during maximum voluntary contraction of a) triceps, b) biceps, c) anterior deltoid, d) upper trapezius, e) middle trapezius, f) pectoralis major and g) lower trapezius for participant 01

b) The considerable variation in EMG data normalised to MVIC between participants for the same task and muscle prevented direct comparison of muscle activation patterns. Normalisation was therefore carried out for each EMG recording using the integrated EMG (I EMG). The three EMG traces corresponding to each muscle, task and participant were replaced with a single trace whose value at each time-point

was the mean of the three traces at the same time-point. For each trajectory the total activation of the muscle, I , was then found by summing the data points over the trajectory. Each point was then multiplied by $100/I$ so that the total activation equalled 100. By compensating for the total muscle activity in each task, periods of relatively high or low muscle activation could be compared between participants, and focus directed towards timing and co-activation between muscles.

For each task, all the data related to each muscle was collected and the mean and SD calculated at each time-point. The mean and envelopes corresponding to 0.5 and 1 SD are shown for the triceps and biceps brachii using the T1 LFH task in Figure 32. Similar plots were produced for each task and the intervals in which mean activation exceeded 70, 80 and 90% of the peak value noted. These are shown in Figure 32 represented by shading: 70% (palest) to 90% (darkest). To facilitate comparison between trajectories, in Figure 33 these intervals have been drawn around each trajectory. This allows relative activity, in terms of timing and co-activation between biceps and triceps across all participants during different trajectories, to be compared.

3.2.5 Statistical analysis

The time and amplitude parameters extracted from each EMG trace were examined using repeated measures ANOVA (using the command SAS PROC MIXED in SAS Version 9.1). Participants were included as random effects, and the 2×2 factors (T1, T2, T3 and SSL, MMM, LFH) and their interaction as fixed within participant effects, tested using the Kenward Roger option (Kenward & Roger, 1997). This was performed for each muscle and each parameter.

3.3 Stroke participants

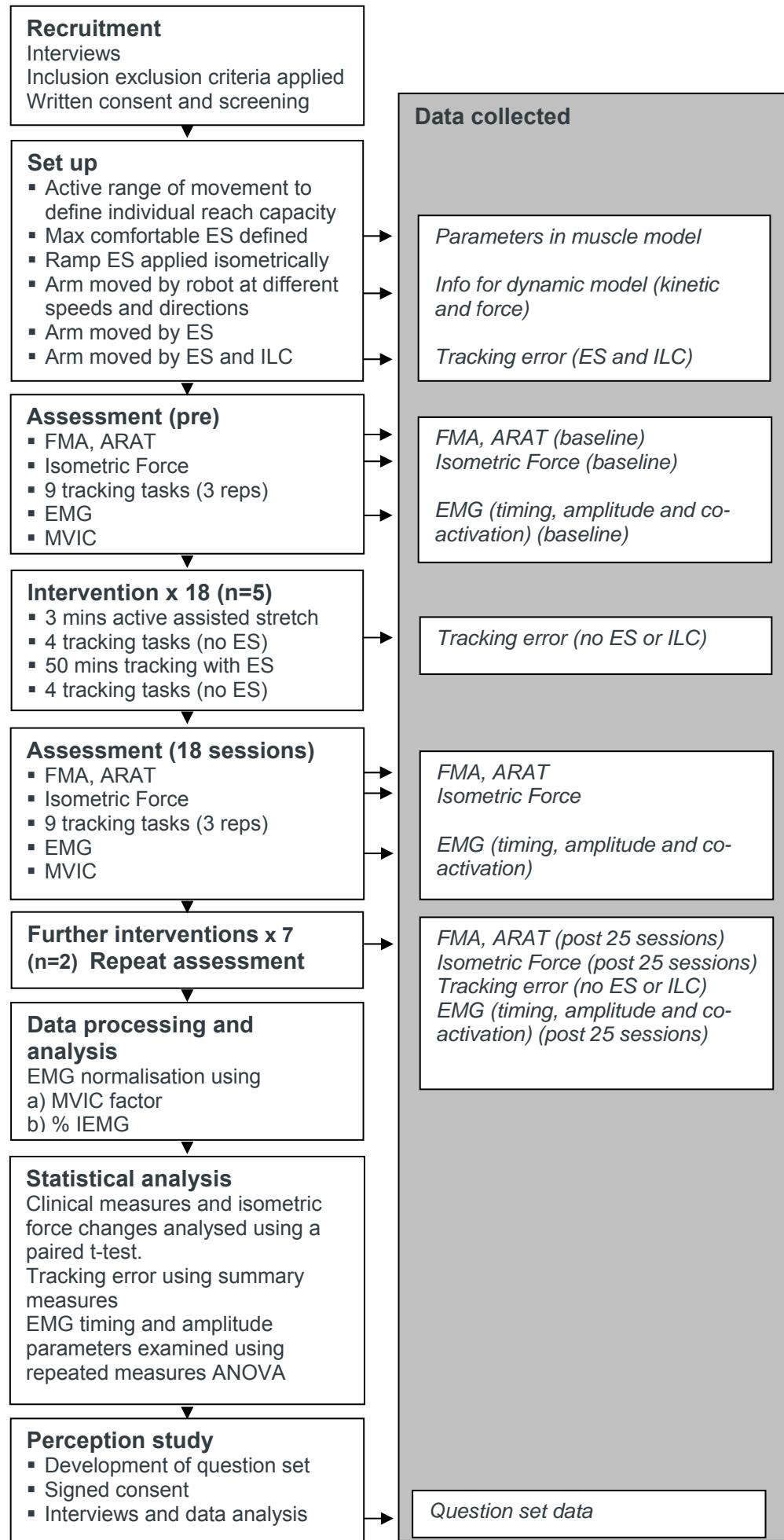
This section describes the methodology for the primary objective of the study, testing the feasibility of re-educating upper limb movement post stroke, using ILC mediated by ES using a robotic workstation. From the study with neurologically intact participants, the feasibility of using ILC with participants contributing no voluntary action was established. This part of the study involves an intervention with stroke participants contributing voluntary movement to the task at the same time as using ILC mediated by ES. Changes in activity and impairment measures resulting from the intervention were established using the clinical outcome measures, Fugl-Meyer and ARAT, as well as isometric force, tracking error and EMG.

3.3.1 Study design

A repeated measures design was used. All participants attended the laboratory on eighteen occasions. At the end of this period it was clear that three participants had reached a high level of tracking ability over the tasks used. Two participants were still showing improvements and were therefore offered an additional seven sessions. All data collection was carried out by a single experienced investigator.

See the next page for the flowchart for the clinical study.

Figure 24: Flowchart for the clinical study



3.3.2 Participant information

A convenience sample of participants was recruited from the community through local television publicity. The criteria for inclusion were: adults over 18 years who were more than six months post stroke, with a hemiparesis resulting in weakness of elbow extension, but with perceivable voluntary control of finger flexors, upper arm and shoulder muscles. In addition, when positioned in the robot they also needed to respond to surface ES applied to triceps brachii, resulting in elbow extension.

Participants were excluded from the study if they had uncontrolled epilepsy, required an interpreter, had any active device implant (e.g. pacemaker, implanted cardiac defibrillator, neurostimulator or drug infusion device), an allergy to sticking plaster/tape or alcohol wipes or any serious medical, psychological or cognitive impairment that, in the opinion of the investigators would compromise the participant's safety or ability to comply with the study. Participants with any orthopaedic or neurological lesions which may affect arm movement were also excluded. Anyone expressing interest by contacting the research team by phone, post or e-mail was telephoned to assess whether they met the basic criteria. If they did, they were sent a participant information sheet and then asked to complete a reply slip to confirm their interest in participating. Potential participants were then invited to meet with the research team.

3.3.3 Intervention

The participant's hemiplegic arm was placed in the robot arm holder with the hand curled around a padded vertical pillar.



Figure 25: Stroke participant performing a tracking task using the robot showing the method of restraining trunk flexion

To create personalised trajectories, participants were positioned in the robot and manually assisted to move their arm over their full available range of movement. Parameters extracted from the data collected were then used to define length of trajectories for each participant. Each trajectory extended from 55% to 80% (short), 90% (medium), or 99% (long) of maximum reach. Trajectories were orientated in one of three directions (mid-line and 20% of maximum range to either side), and were performed at three speeds (5, 10 and 15 second duration). Trajectory details are summarised in Table 9, and the abbreviations for angle, length and duration used throughout the thesis are defined.

Angle	Length	Duration (s)	Abbreviations
T1 (20% internal rotation)	S (short – 80% of reach)	Slow (15)	SS
T2 (midline)	M (medium 90% of reach)	Medium (10)	MM
T3 (20% external rotation)	L (long 99% of reach)	Fast (5)	LF

Table 9: Angle, length and duration for each level of task. Abbreviations used for each task are shown in the right hand column

An example of a T3LS trajectory is shown in Figure 26 for a right hemiplegic case, in which the co-ordinate reference frame is aligned with the robot origin.

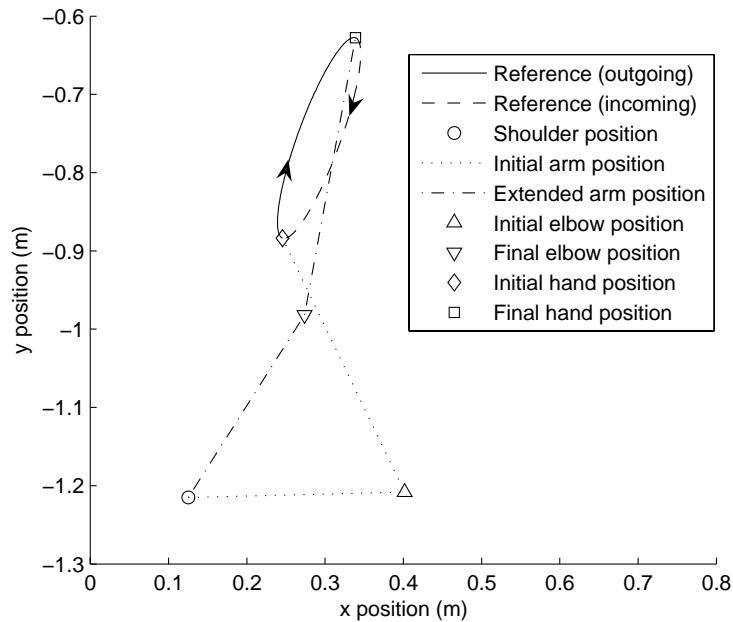


Figure 26: The position of shoulder, elbow and hand for participant 3 at the initial (dotted) and extended (dashed) positions for the T3LS reference trajectory

Following this, the level of comfortable maximum stimulation was identified for each participant and used as an upper limit in subsequent tests. A full mathematical biomechanical model of the arm was then produced in order to describe movement in response to stimulation (Freeman et al., 2008b). The model parameters were identified using a series of tests in which the robot moved their arm (no voluntary action) about the workspace whilst low levels of ES were applied (asymmetric, biphasic, 40Hz fixed amplitude variable pulse width 0-300 μ s with a resolution of 1 μ s) through a CE marked commercially available stimulator. The biomechanical model was then used by the ES controller during all treatment sessions (Freeman et al., 2008a).

Intervention Sessions

All participants attended eighteen one hour intervention sessions, and two attended an additional seven sessions (for reasons previously described in section 3.3.1). Three minutes of active assisted stretches were performed prior to and immediately after placing the arm in the robot. The instructions given to the participants prior to

the tracking tasks were “Try and keep the crosshair on the moving target”. During sessions, electrical stimulation was applied to the participant’s triceps brachii muscle to assist them in completing tracking tasks. A task consisted of tracking one of a selection of twenty-seven different trajectories, 6 times (one participant could only manage 4) with a rest period of 15 seconds between each iteration. The error tracking was similar to that of neurologically intact participants (see section 3.2.3.2) except that movement was clockwise for right and anticlockwise for left hemiplegics to ensure that the easier movement was associated with reaching. The number of tracking tasks practised during each session was limited only by fatigue. During each iteration, ILC used kinematic and force data recorded during the previous iteration, in conjunction with the biomechanical model of the arm, to update the stimulation applied during the next iteration of the trajectory. Isometric force (see section 3.2.3.1) and EMG data (see section 3.2.3.3) were collected in the same way as for neurologically intact subjects.

Outcome measures

Outcome measures were applied by the same assessor. Clinical outcome measures, the ARAT and FMA, isometric force and EMG data were collected pre intervention (2 time-points, immediately beforehand and one month prior to ensure no natural changes were occurring for the ARAT and FMA), after session 18, and, for 2 participants, after 25 sessions.

The primary robotic workstation based impairment measure was the ability to perform tracking tests (motor control). Participants were asked to perform four different tracking trajectories at the beginning and end of the treatment session using only voluntary action (no robotic assistance or ES), so any change in unassisted tracking ability could be measured. The trajectories, chosen to be easy enough for all participants to attempt, were T1SS, T1MS, T2MS and T2SS conducted in the order given.

For further details of the outcome measures used and other outcome measures considered can be found in Section 2.4.2.

3.3.4 Data processing and analysis for the clinical study

EMG analysis, tracking error and isometric force data processing was carried out using the same method as for neurologically intact participants.

3.3.5 Statistical analysis

Statistical analysis was performed using SPSS v14.0. Descriptive statistics are presented for all outcome measures. Where statistics are calculated across the sample, only data from the first 18 sessions are used to ensure the tests are unbiased (see Table 19, Table 20 and Table 21). Full individual tracking and isometric force results, however, are provided elsewhere (Figure 36, Figure 39 and Figure 43). Baseline for clinical measures is taken as the mean of the 2 measurements pre intervention (immediately beforehand and one month prior). Statistically significant changes in clinical measures and isometric force between baseline and session 18 were estimated using a Paired t-test. Changes in tracking error were estimated using summary measures, considered appropriate for a small sample (Matthews et al., 1990). Statistical significance of changes in tracking error was estimated using a one sample t-test applied to the linear regression of error against session.

3.3.6 Participant perceptions

At the beginning of every intervention session stroke participants were asked to give any comments on aspects that arose following the last session. Following the clinical study, a purpose designed set of questions was developed to survey stroke participants' perceptions of the ILC system and intervention. This was developed, based on those reported in a user perception study of an FES system (Turk et al., 2008). It consisted of four basic sections i) the effectiveness of the system to enable participants to exercise and recover their arm function (5 Likert style, 3 open questions) ii) the usability of the system (7 Likert style) and iii) participants' ideas on how the system could be improved upon (2 Likert style and 4 open questions) and iv) general questions (2 Likert style and 2 open questions). Questions were formulated to address the study objectives outlined above.

The question set was developed and piloted on therapists and a health psychologist. The Likert answers were comprised of both negative and positive statements. Participants were invited to a face to face interview (with a health psychologist researcher independent of the ILC study) conducted either at the University of Southampton or at their home. The Likert choices were written on to cards, so that moderately aphasic participants could point to their intended responses. All responses were anonymised to ensure all participants were as open as possible.

Data analysis

Continuous quantitative data collected from the Likert scale items was analysed using descriptive statistics. The open-ended questions resulted in qualitative data which was analysed using content analysis. The anonymised data were analysed by the clinical researcher.

3.4 Summary

This chapter has discussed the preliminary work carried out as well as the methodologies for both the neurologically intact and stroke participants. The interdisciplinary nature of the intervention ensured the system was developed based on neurophysiological principles and the usability of the system for stroke participants based on their likely movement impairments. The arm modelling and control scheme developed by the engineers has been outlined and the selection of tasks, and EMG and ES parameters and muscle choice discussed. Procedures were established for: skin preparation for both the EMG and ES electrodes; EMG electrode recording; electrode placement; and EMG analysis were developed. Tracking error calculation was standardised and outcome measures for the stroke participant study were selected.

For the neurologically intact participants, tracking error, isometric force and EMG data were collected over two sessions. All stroke participants attended eighteen treatment sessions (two attended a further 7 sessions). Clinical outcome measures, isometric force and EMG data were taken pre and post intervention. EMG data was normalised using two methods to compare a) timing and amplitude of peak activity, and b) periods of high and low levels of muscle activity relative to their use within each task. Unassisted tracking error was recorded at the beginning of each session.

After the clinical study a question set was developed to assess stroke participants' perceptions of the intervention. This was administered by a health psychologist independent of the clinical study.

4 Results

The study was performed to test the feasibility of re-educating upper limb movement post stroke, using ILC mediated by ES using a robotic workstation. Other aims were to provide answers to the following questions:

- How do isometric force, kinematic measures and muscle activation patterns for upper limb muscles during identified specific reaching tasks using a robot arm differ for neurologically intact subjects and stroke patients?
- For the stroke patients are these affected by undergoing an intervention programme using the robot and ES? If so, how? Are these changes reflected in clinical measures?
- What are the stroke participants' perceptions of the system?

To provide answers to these questions the study was first done with neurologically intact participants and then with stroke participants.

The many limitations to the results, including the lack of blinding of outcome measures and several factors that could not be controlled for in the study, make it unwise to attribute all responses to the intervention. Limitations are further discussed in section 5.2.

For the neurologically intact participants the following data are presented: demographic; tracking error (with and without ES); isometric force; and EMG (MVIC, timing and amplitude and co-activation data). For clarity, all neurologically intact participants' identification numbers will be prefixed with '0'. For the stroke participants, the following are presented as descriptive data: demographic; clinical outcomes; tracking error (both with and without ES); changes in shoulder and elbow angle with ES; isometric force; percentage maximum ES; and EMG (timing and amplitude and co-activation data). Individual data illustrating differences in response

to the intervention between participants with a higher and lower initial FMA score are presented for tracking error (both with and without stimulation), isometric force and EMG.. Participant comments collected during the study, and data collected from the question set at the end of the study are reported.

4.1 Neurologically intact participants

Following University of Southampton ethical approval (SO5-12/1) eight right-handed participants (four male and four female) were recruited and gave written informed consent. Their demographic characteristics are shown in Table 10. Participant ages ranged from 51-67 with a mean age of 58 years.

Participant ID	Age (years)	Gender
01	67	Male
02	59	Male
03	53	Female
04	61	Male
05	58	Female
06	64	Male
07	51	Female
08	54	Female

Table 10: Demographic characteristics of neurologically intact participants

4.1.1 Tracking error

Voluntary tracking (without ES) was compared with tracking using movement generated solely by ILC mediated by ES, to assess the feasibility of using ILC mediated by ES with stroke participants. For details of how the tracking error was calculated see section 3.2.3.2.

Tracking error data from movement generated solely by ILC mediated by ES were only collected from five participants. This is because one participant was unable to tolerate surface ES applied to triceps brachii at a level required for elbow extension when positioned in the robot, and two participants were able to tolerate the stimulation at a suitable level, but the ILC algorithms were not able to be used successfully with them.

4.1.1.1 Tracking error (without ES)

Mean tracking error (as defined in section 3.2.3.2) without ES data for all participants over three iterations for all tasks are reported in Table 11. It can be observed that errors generally decrease from the first to the third repetition of the task, however this is only significant for four trajectories T1MMM, T2LFH, T3MMM and T3LFH.

Task	01	02	03	04	05	06	07	08
T1 SSL	0.0074	0.0072	0.006	0.0084	0.0105	0.0097	0.0124	0.0065
T1 SSL	0.0067	0.0043	0.0075	0.0066	0.0102	0.0084	0.0096	0.0059
T1 SSL	0.0079	0.0048	0.0074	0.0072	0.0092	0.0112	0.0091	0.0064
T1MMM	0.0139	0.0104	0.0235	0.0121	0.0134	0.024	0.0152	0.0151
T1MMM	0.0104	0.0079	0.0158	0.0108	0.0114	0.0133	0.0114	0.0099
T1MMM	0.008	0.0094	0.0158	0.0109	0.0124	0.013	0.0121	0.0088
T1LFH	0.0238	0.016	0.0485	0.0185	0.0233	0.0318	0.0261	0.0148
T1LFH	0.0247	0.0172	0.0262	0.0204	0.0223	0.0191	0.0128	0.0129
T1LFH	0.0186	0.0147	0.031	0.0206	0.0172	0.016	0.0165	0.0129
T2SSL	0.007	0.0048	0.0104	0.0065	0.0064	0.008	0.004	0.0037
T2SSL	0.0069	0.0041	0.006	0.0057	0.0076	0.0081	0.0059	0.0041
T2SSL	0.0063	0.004	0.0065	0.0052	0.0075	0.007	0.0076	0.003
T2MMM	0.0092	0.0093	0.0126	0.0101	0.0131	0.015	0.0123	0.013
T2MMM	0.0104	0.0089	0.0143	0.0084	0.0105	0.0119	0.0078	0.0132
T2MMM	0.0099	0.008	0.0131	0.0084	0.0141	0.01	0.0109	0.0122
T2LFH	0.0184	0.0141	0.0292	0.0156	0.0175	0.0186	0.0145	0.0145
T2LFH	0.018	0.0143	0.0178	0.0156	0.0166	0.0235	0.0113	0.0227
T2LFH	0.0161	0.0137	0.0183	0.0144	0.0166	0.0151	0.0151	0.0151
T3 SSL	0.0055	0.0045	0.0086	0.0066	0.0055	0.0122	0.0029	0.0035
T3 SSL	0.0056	0.0039	0.0061	0.0058	0.0062	0.0061	0.0032	0.0071
T3 SSL	0.0071	0.0048	0.0051	0.006	0.0057	0.0064	0.0056	0.0069
T3MMM	0.0107	0.0087	0.0117	0.0102	0.0121	0.0115	0.0084	0.0099
T3MMM	0.0094	0.007	0.0122	0.0101	0.0134	0.0107	0.0087	0.0099
T3MMM	0.0102	0.0073	0.0104	0.0099	0.0123	0.0099	0.0078	0.0075
T3LFH	0.0275	0.0122	0.0187	0.0145	0.0158	0.0151	0.0165	0.0153
T3LFH	0.0231	0.0136	0.0161	0.0138	0.0177	0.015	0.0109	0.017
T3LFH	0.0228	0.0112	0.0182	0.0149	0.0168	0.0131	0.0075	0.012

Table 11: Mean tracking error (no stimulation) (m) for all participants over three repetitions of each task

This data is presented as summary data (see Table 12). Tracking (without ES) accuracy for the neurologically intact participants was high in all cases, typically with a mean error of less than 15mm over each trajectory.

Task	Mean	SD	[Min-Max]
T1SSL	0.008	0.002	0.005-0.010
T1MMM	0.013	0.003	0.009-0.018
T1LFH	0.022	0.006	0.016-0.035
T2SSL	0.006	0.002	0.004-0.008
T2MMM	0.011	0.002	0.009-0.013
T2LFH	0.017	0.003	0.014-0.022
T3SSL	0.006	0.001	0.004-0.008
T3MMM	0.010	0.002	0.008-0.013
T3LFH	0.016	0.004	0.012-0.024

Table 12: Mean tracking error (m) for participants showing sample mean (SD) over all tasks

The data from the three iterations of T3 MMM are illustrated in Figure 27. It can be seen that for most participants motor learning occurs over the three attempts to track the trajectory, making a smaller error by the third attempt (ranging between 0.0073m and 0.0123m) compared with the first (0.0084m to 0.0121m).

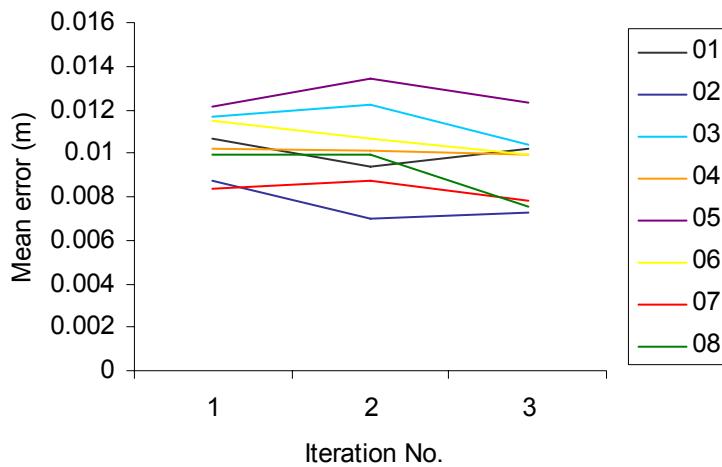


Figure 27: Mean tracking error against iteration number using no stimulation for the T3 MMM trajectory over three iterations for eight participants

4.1.1.2 Tracking error (with ES)

The mean tracking error over each trajectory for five participants (for reasons explained in 4.1) was calculated for movement generated solely by ILC mediated by ES applied to the triceps (without the person contributing any voluntary movement) over six iterations. This is represented graphically for the T3MMM trajectory in Figure 28. Compared to Figure 27 initial errors are much higher (ranging between 0.01m and 0.048m) but falls quickly by the fourth iteration (ranging between 0.006m and 0.16m) to values comparable with normal tracking.

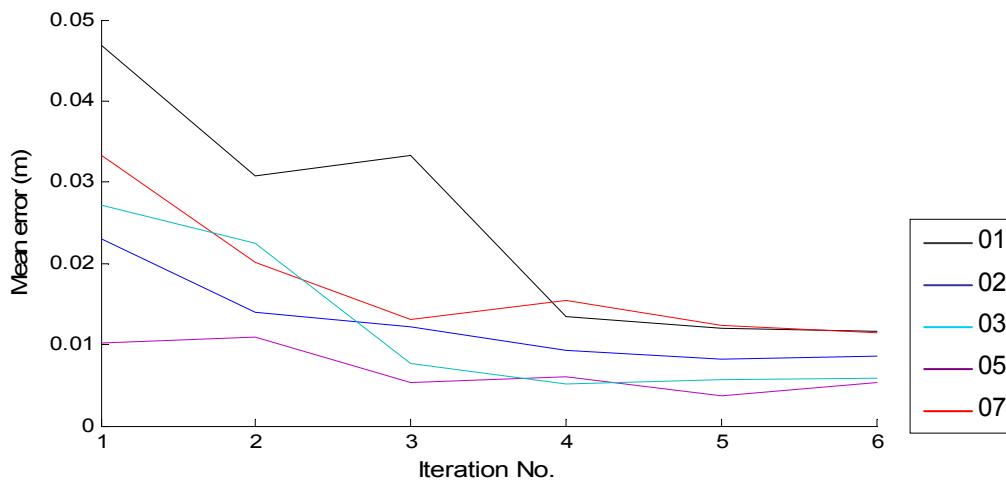


Figure 28: Mean tracking error (m) against iteration number using ILC mediated by ES for the T3 MMM trajectory over six iterations for five participants

4.1.1.3 Tracking error pattern

The overall tracking pattern for participant 06 over the T3 SSL, MMM and LFH trajectories is shown in Figure 29, showing the point on the trajectory where the errors occur. The pattern of error appears to be similar over the three repetitions, which may not be the case for stroke participants. Note that the origin for the figure is in the top left, outside the display.

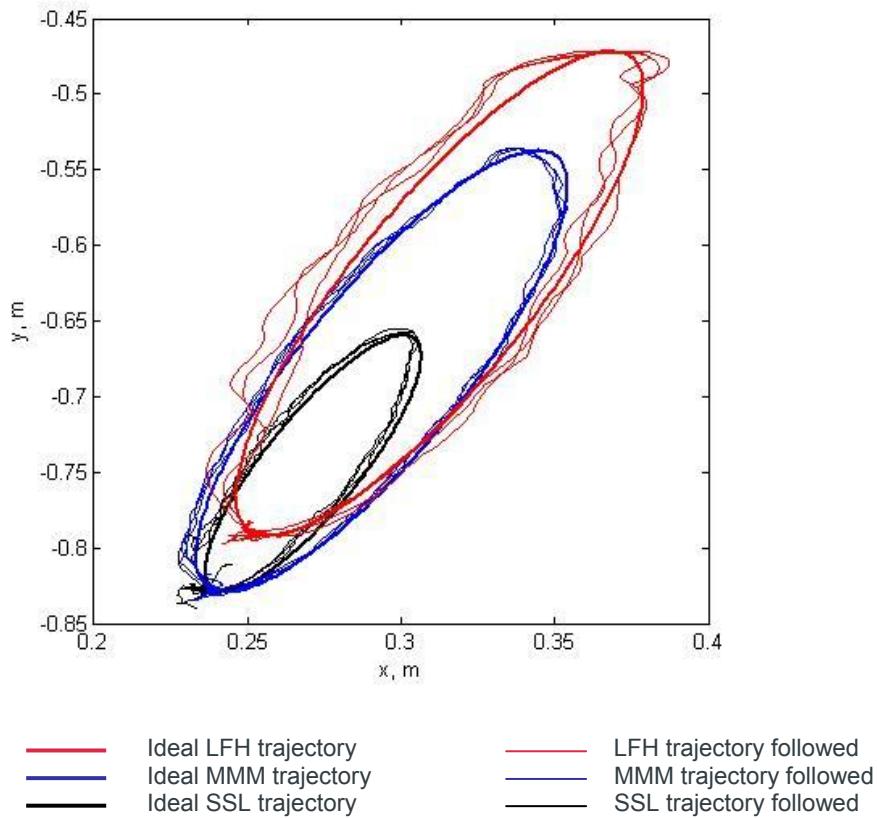


Figure 29: Trajectory tracking pattern for participant 06 showing three repetitions for T3 tasks

4.1.2 Isometric force

Isometric force was measured to show the difference between neurologically intact and stroke participants. Isometric force data for the neurologically intact participants is displayed in Table 13. It can be seen that the direction in which the participants can exert the most force is at 0° and the direction they are weakest in is 60°.

Angle	Participants								Mean (SD) [Min-Max]
	01	02	03	04	05	06	07	08	
0°	91.81	92.48	75.96	90.11	77.32	79.53	75.58	71.22	81.75 (08.39) [71.22-92.48]
60°	81.38	58.71	20.13	59.80	54.36	48.95	44.39	31.28	49.88 (18.71) [20.13-81.38]
120°	79.94	91.66	31.60	93.24	72.20	71.06	78.00	67.85	73.19 (19.18) [31.60-93.24]
180°	65.67	89.52	54.10	95.78	66.05	65.88	66.15	74.52	72.21 (13.87) [54.10-95.78]
240°	79.75	93.69	40.52	91.68	82.61	60.74	72.81	49.86	71.46 (19.41) [40.52-93.69]
300°	58.35	84.93	33.79	88.68	70.93	54.62	53.97	46.01	61.41 (18.89) [33.79-88.68]

Table 13: Isometric force (N) generated by neurologically intact participants. Mean (SD) and range [Min-Max] are also shown

4.1.3 Analysis of EMG

To identify how muscle activation patterns (peak timing and amplitude) factors for upper limb muscles during identified specific reaching tasks using a robot arm differ for neurologically intact subjects and stroke patients, and how they might change during the process of an intervention, EMGs were first collected from seven muscles (triceps, biceps, anterior deltoid, upper, middle and lower trapezius and pectoralis major) from neurologically intact participants.

The raw EMG signals from biceps and triceps along with the synchronisation signal can be seen in Figure 30. The lowest graph shows the synchronisation signal moving from -3 to 0 as the countdown to the start of the trajectory began. During this period there was minimal activation of triceps and biceps. Triceps activity was greatest from 0.2s to 3s, and biceps activity greatest from 0.5s through the trajectory. Both muscles' activity remained higher than baseline for the two seconds (5s-7s) after the task had finished.

Results – Neurologically intact

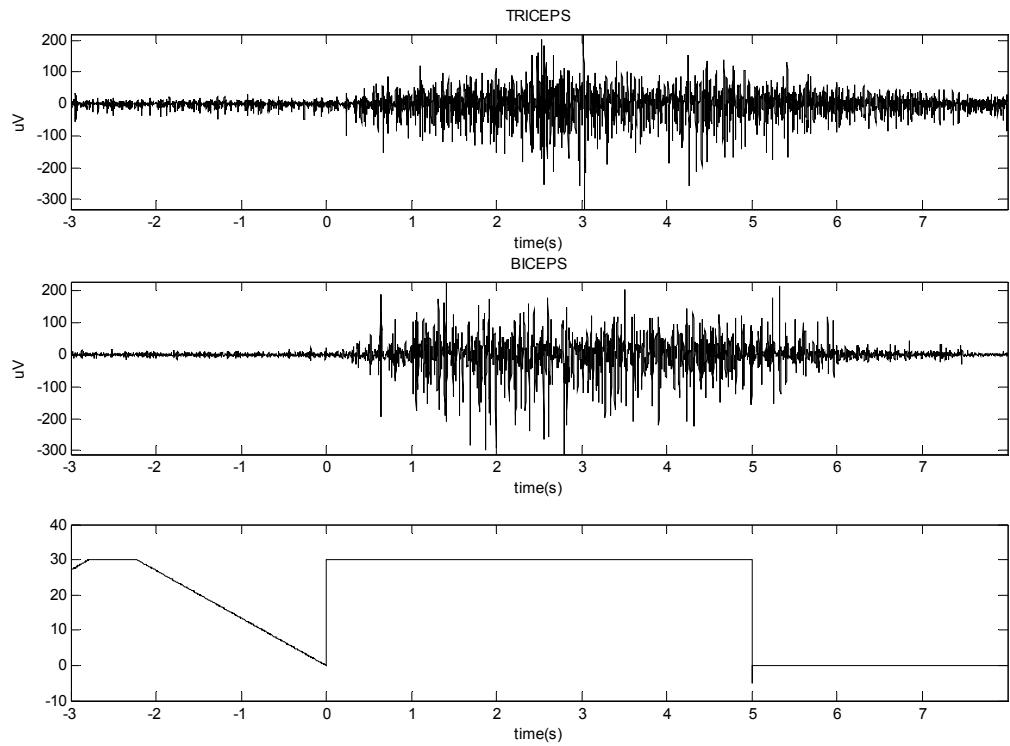


Figure 30: Raw EMG data for triceps, biceps and the synchronisation pattern for participant 02 over the T1 LFH trajectory

MVIC factors

MVIC factors were used in the normalisation of the timing and amplitude data and were used to identify differences between stroke and neurologically intact participants. The MVIC factors generated by each of the neurologically intact participants for each of the muscles under consideration are shown in Table 14. A wide variation between individuals can be observed for each muscle.

Muscle	Participants								Mean (SD) [Min-Max]
	01	02	03	04	05	06	07	08	
Triceps	217.42	152.21	176.96	213.95	101.65	229.70	110.19	21.34	152.91 (71.83) [21.34-229.71]
Biceps	322.80	200.92	196.79	386.96	250.39	86.71	68.40	33.48	193.31 (125.42) [33.48-386.96]
Anterior Deltoid	291.25	86.29	198.39	388.32	230.21	224.29	116.32	76.98	201.51 (107.13) [76.98-388.32]
Upper Traps	155.06	130.94	228.20	323.71	48.70	67.88	169.35	107.55	153.92 (89.23) [48.70-323.71]
Mid Traps	317.71	127.14	333.56	97.54	75.10	135.59	111.72	90.11	161.06 (103.50) [75.10-333.56]
Pec Maj	164.78	122.02	170.88	340.73	77.28	265.36	113.41	63.37	164.73 (95.26) [63.37-340.73]
Low Traps	283.27	179.22	245.94	242.34	145.39	180.61	253.48	179.74	213.75 (48.38) [145.39-283.27]

Table 14: Mean (SD) and range [Min-Max] maximum voluntary isometric contraction factor (µV) generated by neurologically intact participants

Timing of peak EMG amplitude

The temporal positions for the mean maximum amplitude for each muscle and task were identified for the neurologically intact participants, so that the data could be compared with stroke participants. Mean EMG times of maximum amplitude across all orientations and task conditions are given in Table 15. The results of the statistical analysis (see section 3.2.5) confirms that:

- 1) Biceps varied predominantly with task conditions
- 2) Upper trapezius, pectoralis major and lower trapezius varied with trajectory orientation
- 3) Triceps and middle trapezius varied with both task conditions and trajectory orientation
- 4) Anterior deltoid was neither task condition nor orientation dependent.

Muscle		Mean (SD) % TASK			Mean	P ¹		
		SSL	MMM	LFH				
Triceps	T1	39.8 (10.4)	53.5 (7.8)	50.2 (10.5)	47.8	<0.001 (orientation)		
	T2	40.1 (6.5)	45.5 (5.1)	49.0 (4.6)	44.9			
	T3	35.7 (7.6)	38.0 (9.2)	43.7 (7.9)	39.1			
	mean	38.6	45.6	47.6		<0.001 (task)		
Biceps	T1	68.9 (15.0)	60.7 (14.2)	61.4 (12.9)	63.7	0.128 (orientation)		
	T2	75.7 (12.9)	59.7 (12.1)	63.1 (14.1)	66.2			
	T3	80.9 (11.4)	66.4 (15.4)	63.1 (12.9)	70.1			
	mean	75.2	62.2	62.5		<0.001 (task)		
Ant del	T1	45.8 (2.7)	47.9 (5.0)	51.0 (10.3)	48.2	0.056 (orientation)		
	T2	46.0 (11.5)	44.0 (6.1)	49.2 (11.9)	46.4			
	T3	46.8 (9.7)	42.2 (2.6)	41.5 (4.1)	43.5			
	mean	46.2	44.7	47.1		0.420 (task)		
Upper traps	T1	72.5 (15.3)	81.2 (11.4)	79.5 (10.7)	77.7	0.014 (orientation)		
	T2	83.7 (8.0)	83.3 (7.1)	86.8 (4.8)	84.6			
	T3	84.0 (4.4)	80.2 (6.8)	82.6 (7.6)	82.3			
	mean	80.1	81.6	83.0		0.464 (task)		
Mid traps	T1	86.6 (4.3)	78.5 (11.1)	82.9 (5.5)	82.7	<0.001 (orientation)		
	T2	84.2 (8.0)	76.0 (13.0)	73.6 (10.1)	77.9			
	T3	73.4 (19.8)	72.7 (19.8)	66.7 (14.4)	70.9			
	mean	81.4	75.7	74.4		0.034 (task)		
Pec maj	T1	38.0 (4.9)	32.4 (9.9)	32.1 (8.3)	34.1	<0.001 (orientation)		
	T2	42.8 (14.7)	37.5 (13.6)	33.0 (11.8)	37.8			
	T3	41.6 (20.1)	51.6 (15.3)	65.3 (15.4)	52.8			
	mean	40.8	40.5	43.5		0.691 (task)		
Lower traps	T1	72.9 (11.6)	66.4 (8.2)	76.4 (9.1)	71.9	<0.001 (orientation)		
	T2	68.1 (10.6)	63.4 (9.3)	63.8 (7.3)	65.1			
	T3	62.4 (15.2)	55.9 (17.7)	53.6 (12.4)	57.3			
	mean	67.8	61.9	64.6		0.080 (task)		

¹ Kenward-Roger tests for differences between levels in a mixed model including orientation and task as fixed factors, and participant as a random effect.

Table 15: Mean (SD) EMG times of maximum amplitude across orientations and task conditions (expressed as % task duration)

The mean maximum amplitude values across all orientations and tasks are given in Table 16. In this case the statistical results indicate that the amplitude increase which is seen as the task condition changes from SSL to MMM to LFH, is significant for all muscles except anterior deltoid. The amplitude value also varies significantly depending on the orientation for the anterior deltoid, middle and lower trapezius and pectoralis major.

Muscle		Mean (SD)			Mean	P ¹		
		TASK						
		SSL	MMM	LFH				
Triceps	T1	9.7 (4.4)	15.6 (4.8)	25.5 (7.3)	16.9	0.393 (orientation)		
	T2	9.8 (4.3)	15.4 (7.2)	27.2 (8.2)	17.5			
	T3	9.6 (4.4)	15.6 (6.1)	29.1 (7.7)	18.1			
	mean	9.7	15.5	27.3	17.5	<0.001 (task)		
Biceps	T1	7.1 (5.4)	12.7 (11.7)	23.1 (18.8)	14.3	0.148 (orientation)		
	T2	8.4 (10.0)	13.8 (18.8)	24.5 (28.8)	15.6			
	T3	6.3 (6.1)	11.6 (15.0)	16.0 (14.5)	11.3			
	mean	7.3	12.7	21.2	13.7	<0.001 (task)		
Ant del	T1	20.1 (12.9)	38.3 (37.8)	56.6 (64.5)	38.4	<0.001 (orientation)		
	T2	17.3 (14.1)	30.3 (31.8)	46.8 (42.1)	31.5			
	T3	20.1 (13.4)	27.2 (19.3)	37.4 (32.4)	38.4			
	mean	18.9	31.9	47.0	32.6	0.156 (task)		
Upper traps	T1	32.0 (8.5)	47.9 (18.4)	65.5 (35.1)	48.5	0.974 (orientation)		
	T2	37.9 (16.2)	50.2 (19.4)	60.3 (33.1)	49.5			
	T3	32.6 (17.3)	52.1 (20.6)	65.5 (36.0)	49.1			
	mean	34.2	50.1	62.8	49.0	<0.001 (task)		
Mid traps	T1	14.8 (5.6)	19.0 (7.7)	27.9 (14.5)	27.9	<0.001 (orientation)		
	T2	15.0 (6.8)	16.4 (6.8)	27.0 (10.6)	19.4			
	T3	11.2 (5.8)	19.0 (6.9)	20.9 (9.1)	15.6			
	mean	13.7	16.7	25.2	18.5	<0.001 (task)		
Pec maj	T1	10.3 (3.5)	14.7 (5.2)	26.4 (9.9)	17.1	<0.001 (orientation)		
	T2	6.5 (2.2)	10.6 (3.1)	18.4 (5.7)	11.8			
	T3	4.7 (1.1)	6.8 (1.8)	12.4 (3.1)	7.9			
	mean	7.2	10.7	19.0	12.3	<0.001 (task)		
Lower traps	T1	8.5 (4.0)	11.8 (4.7)	19.7 (9.5)	13.3	<0.001 (orientation)		
	T2	6.7 (3.3)	7.9 (4.0)	17.0 (7.4)	10.5			
	T3	6.1 (3.0)	7.1 (3.5)	13.1 (8.2)	8.8			
	mean	7.1	8.9	16.6	10.9	<0.001 (task)		

¹Kenward-Roger tests for differences between levels in a mixed model including orientation and task as fixed factors, and participant as a random effect.

Table 16: Mean (SD) EMG maximum amplitude across orientations and task conditions (expressed as % MVIC ‘factor’)

For each task the mean maximum amplitude μ_{EMG} and corresponding variation in temporal position for each muscle is shown in Figure 31 and illustrates how peak muscle activity varied with task. As a point moves along the ellipse at constant velocity, it will encounter each wedge during the time period in which the corresponding muscle is most active (e.g. between 12.34s and 13.63s for the middle trapezius in T1SSL (duration 15s)). Peak EMG amplitude increased with resistance,

Results – Neurologically intact

duration and speed at which the task was performed and length of trajectory. For each wedge the position of the line (in the same colour as the wedge) orthogonal to the trajectory indicates timing of mean peak EMG activity and the wedge width indicates variability (SD) of time of peak activity across the sample. Peak activity of the triceps, anterior deltoid and pectoralis major muscles generally occurred during the reaching component of the task, whereas peak activity for all other muscles occurred during the return component of the task.

Temporal locations of peak EMG amplitudes can be broadly classified as: 1) varying with task conditions – length, duration and resistance (moving vertically in Figure 31), 2) varying with trajectory orientation (moving horizontally in Figure 31), 3) varying with both task conditions and trajectory orientation or 4) being largely invariant.

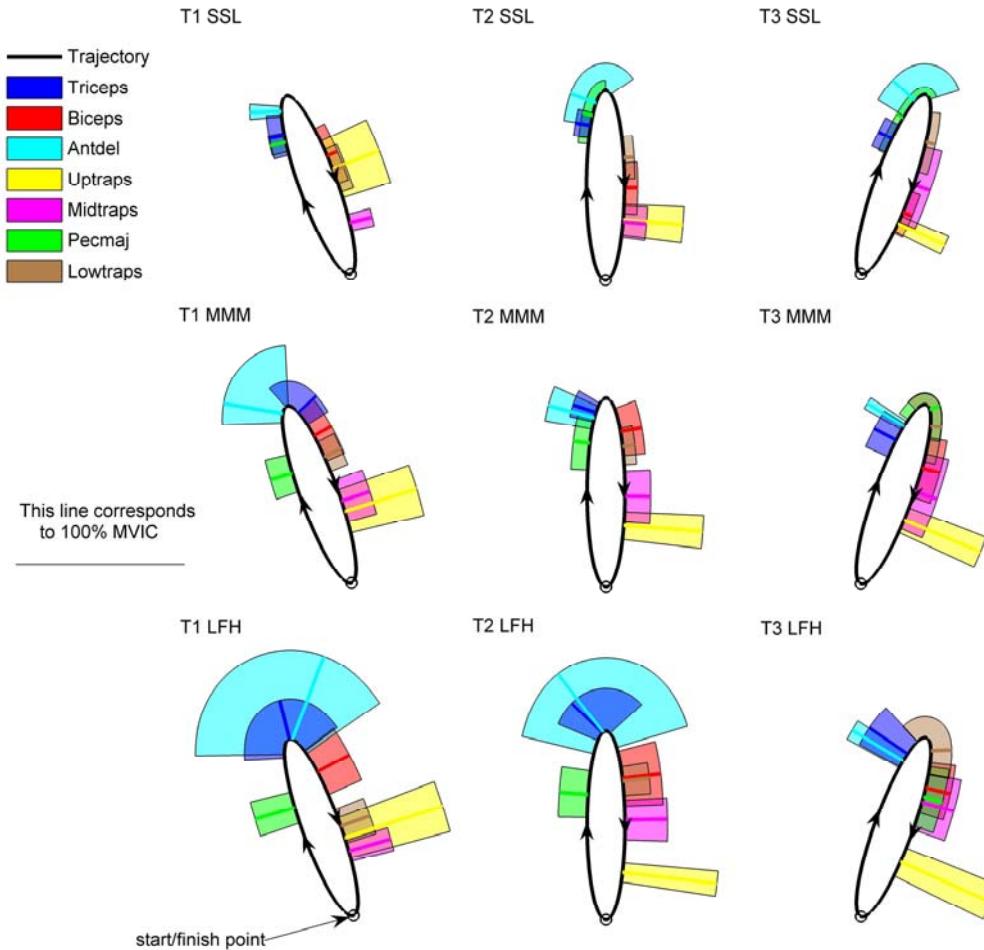


Figure 31: Mean amplitude and mean (SD) temporal position of peak EMG during each task across the eight participants. For each task, wedge height and position are given by μEMG and $\mu\text{T} \pm 0.5 \sigma\text{T}$. The mean position, μT , of max EMG amplitude is indicated by a line of the same colour orthogonal to the trajectory. T1, 2 and 3 correspond to the orientation of the trajectory. SSL, MMM, and LFH are abbreviations for the length, duration and resistance respectively of the task

Triceps and biceps activation patterns during T1 LFH

Figure 32 shows the I EMG normalised activity for triceps and biceps for T1 LFH. Envelopes corresponding to 0.5SD and 1SD are shown to illustrate variability across the sample. The 5s task begins at 0s, and maximum reach occurs at 2.5s. Activity increases in both muscles during the extension phase with a steeper gradient during the first second in triceps than biceps. Activity in triceps declines rapidly during the first 1.5s after maximum reach, while biceps remains constant at approximately 25% IEMG. Peak activity is observed in both muscles at maximum reach. Co-activation is therefore observed. There is greater variation in activity across the sample in biceps than in triceps.

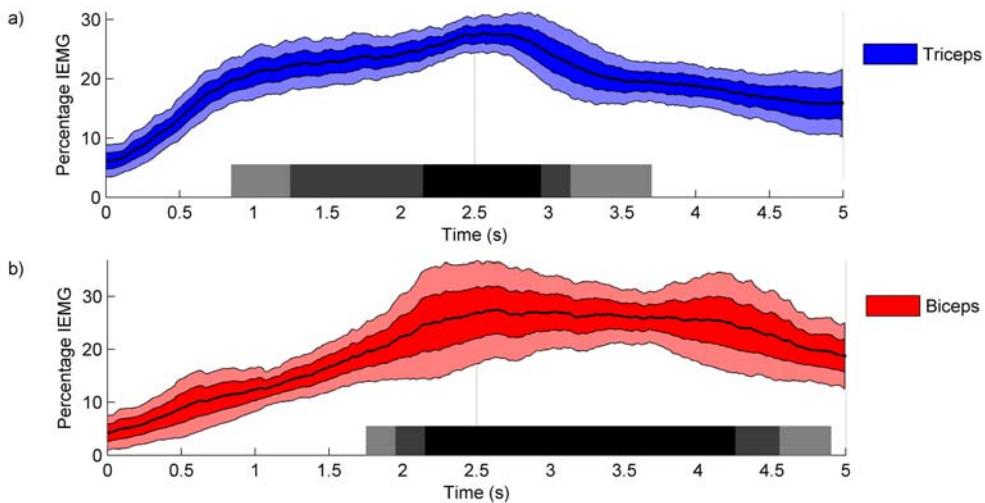


Figure 32: IEMG normalised activation averaged across all participants for a) triceps and b) biceps during the T1 LFH task. Sample mean (indicated by a thicker line), 0.5 and 1 SD envelopes are shown. Maximum reach was at 2.5s. Intervals in which mean EMG exceeds 70 (palest), 80, 90 (darkest) percent of the peak value are also shown

Triceps and biceps activation patterns during all tasks

The time periods during which biceps and triceps EMG exceeded 70, 80 and 90% of maximum amplitude for that task are shown in Figure 33. The duration and intensity of muscle activity is compared across all tasks and is displayed using a range of threshold levels. 70% (palest shade) is regarded as the threshold for the muscle being 'on'. This was chosen as it is above a level of intermittent activation for the tasks used, but is within a region in which changes in the exact value do not lead to large differences in the overall activation trends observed. For all trajectories triceps activity precedes biceps and biceps remains active to the end of the task. As the trajectory orientation varied from across the body to away from the body (moving horizontally from T1 to T3 in Figure 33) triceps activity turned 'off' earlier, and the biceps activity came 'on' at a later point. Less co-activation between biceps and triceps activity occurred as a result. As task conditions became more demanding (moving vertically from SSL to LFH in Figure 33) triceps came 'on' at a later point. Similar plots and statistical analysis can be conducted for the remaining 20 muscle combinations.

Results – Neurologically intact

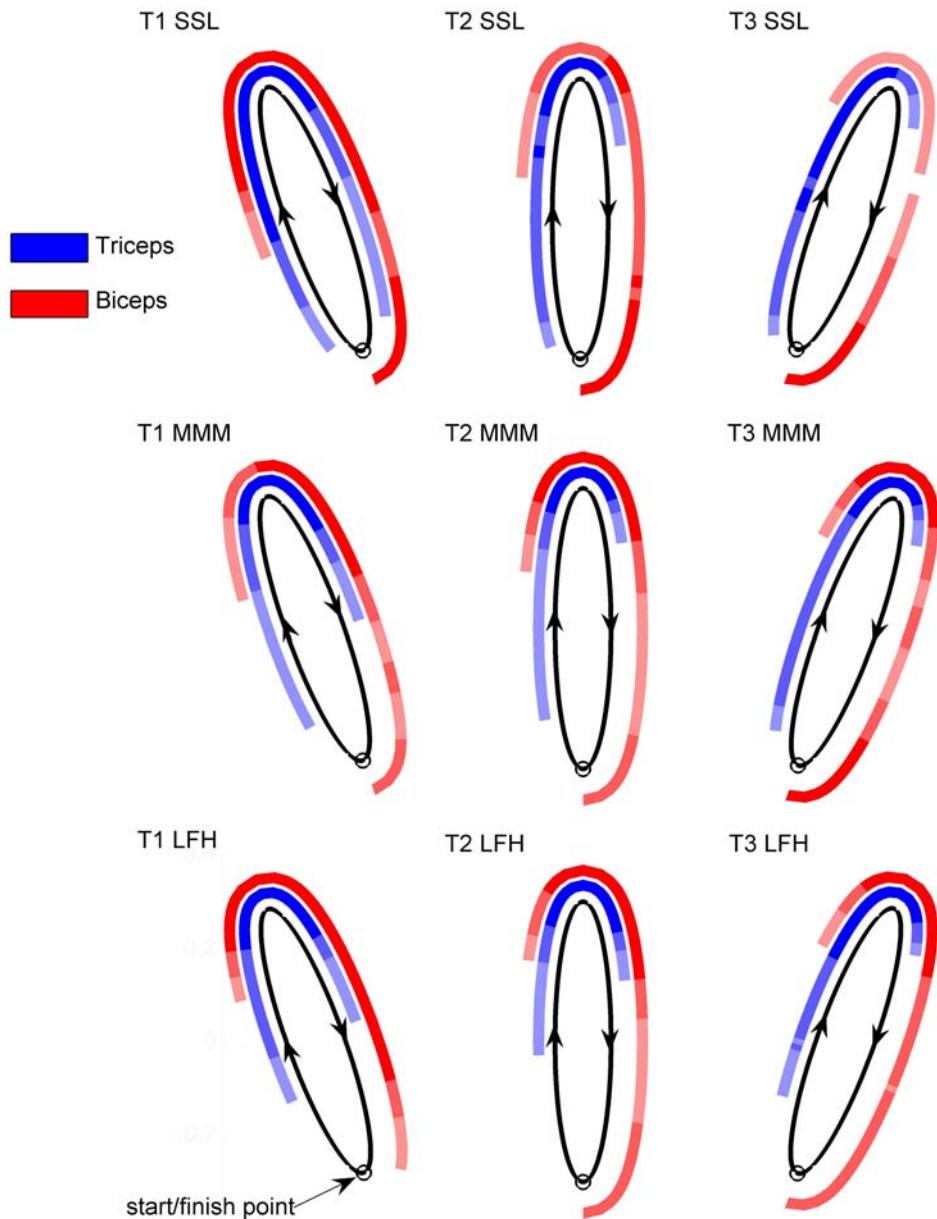


Figure 33: IEMG normalised activation averaged across all participants for triceps and biceps (right arm): Intervals in which mean EMG exceeds 70 (palest), 80, 90 (darkest) percent of the peak value are ‘wrapped’ around each trajectory

Data for the duration of biceps / triceps co-activation (percentage of task duration when both muscle are ‘on’) are shown in Table 17. Duration of co-activation has been calculated for each participant individually, and the table shows the mean (SD) co-activation across orientations and tasks. The statistical analysis confirms that the level of co-activation depends significantly on both orientation and task condition. It can be seen that the percentage co-activation increase from T3 to T2 to T1 is more pronounced for SSL than for MMM and LFH.

	Mean(SD) % co-activated *			P ¹
	SSL	MMM	LFH	
T1	58.2 (19.7)	34.2 (6.6)	33.0 (14.8)	41.8
T2	32.1 (10.2)	24.2 (5.9)	21.5 (8.9)	25.9
T3	14.8 (6.8)	14.9 (8.9)	16.6 (7.7)	15.4
mean	35.0	24.4	23.7	27.7
				0.001 (task)

¹ Kenward-Roger tests for differences between levels in a mixed model including orientation and task as fixed factors, and participant as a random effect.

* Percentage of task duration when both muscles are 'on'

Table 17: Mean (SD) percentage co-activation of triceps and biceps across orientations and tasks

4.1.4 Summary of results for neurologically intact participants

The outputs from the work with neurologically intact participants were used to inform the clinical study in the following ways:

- Triceps was chosen to be stimulated in the stroke participant study
- The screening process for stroke participants was adapted following the study with neurologically intact participants. At the screening stage stroke participants' arms were placed in the robot arm holder and ES was applied to triceps brachii. The ES had to produce elbow extension for the participants to be accepted on to the study.
- It was identified that tracking error (without ES) over four repetitions was similar to that produced by movement generated solely by ILC mediated by ES (no voluntary movement). These results demonstrated the feasibility of using ILC mediated by ES with stroke participants. The next stage was to determine whether the ILC could be combined with the stroke participants' own movements to provide only the minimum level of assistance
- The identification of isometric force, kinematic measures and muscle activation patterns for upper limb muscles during specific reaching tasks provided data to be used in a comparison with stroke participants, both pre and post intervention, to identify whether any changes which occurred following the intervention were towards normal
- Additionally the efficiency of the set up and data collection was refined for the clinical study.

4.2 Stroke participants

The aim of this part of the study was to provide answers to the following questions:

- How do isometric force, kinematic measures and muscle activation patterns for upper limb muscles during identified specific reaching tasks using a robot arm differ for neurologically intact subjects and stroke patients?
- For the stroke patients are these affected by undergoing an intervention programme using the robot and ES? If so, how? Are these changes reflected in clinical measures?
- What are the stroke participants' perceptions of the system?

Following University of Southampton ethical approval (SO7/04-01), participant screening began. Of the 60 original enquiries, two people left insufficient details for us to contact them. Fifty-eight participants were contacted by telephone to establish whether they met the basic inclusion and exclusion criteria and were informed of the travel commitments involved in attending the study (12 did not meet the criteria, and 10 either lived too far away or would not have been able to travel frequently enough for the study). Thirty-six were sent the participant information sheet (12 did not reply). Twenty-four were invited to an interview: one did not attend, six participants were discounted before using the ES (four participants movement was too good, and two had poor skin condition), and 17 participants tried the ES. Seven had a good response (10 had either no response to ES or the ES could not move their arm when in the robot). Five participants were selected to take part in the study, and two participants were reserves.

The five participants (three men and two women) were recruited and gave written informed consent. Their demographic characteristics are shown in Table 18. Participant ages ranged from 38 to 77 with a mean age of 52 years. Participants had suffered haemorrhagic or ischemic strokes ranging from 8 months to 8.4 years, mean 4 years, prior to recruitment to the study; three had a hemiparesis of the right side and two of the left.

The participants' baseline FMA scores ranged from 8.5 to 16.5 with a mean of 12.9 (normal score 66). These FMA scores have been classified as 'severe' (Daly et al., 2005; Lum et al., 2002).

ID	Age (years)	Gender	Time from stroke (years)	Stroke Type	Side of hemiparesis	Previous dominant side	Baseline* FMA score
1	38	Male	2.8	Infarction	L	L	13.5
2	77	Female	8.4	Haemorrhage	L	R	16.5
3	41	Male	4.8	Infarction	R	R	8.5
4	55	Female	3.6	Haemorrhage	R	R	15.5
5	51	Male	0.7	Unknown	R	L	10.5

* Baseline is the mean of the two pre-treatment evaluations.

Table 18: Demographic characteristics of study stroke participants with FMA score giving an indication of the level of impairment

Participant 1 was a 38 year old previously left handed male with a left hemiplegia, who attended the study 33 months after his stroke. Participant 1 reported that he had tried several different types of 'new' treatments including Botox (in toes), and the Saeboflex and had used ES on his lower limb. He presented with limited active proximal movement, and very limited active distal movement. To keep his wrist in neutral and fingers only slightly flexed he wore a plastic moulded night time splint. He walked with a pronounced limp but with no aids.

Participant 2 was a 77 year old right handed female with a left hemiplegia, who attended the study 101 months after her stroke. She had no prior experience of ES. Proximal movement was limited and distal movement was very limited with tightness in finger and wrist flexors; she had a moulded night time splint but did not use it. She walked with a pronounced limp and used a stick.

Participant 3 was a moderately aphasic (with good understanding) 41 year old previously right handed male with a right hemiplegia (resulting from an infarction in the left internal carotid artery), who attended the study 57 months after his stroke. Participant 3 had no prior experience of ES. Proximal movement was limited, and distal movement was very limited. He was not using a splint. He walked with a pronounced limp and used an ankle brace, but no stick.

Participant 4 was a 55 year old previously right handed female with a right hemiplegia (resulting from a haemorrhage) who attended the study 43 months after her stroke. She had no prior experience of ES. Proximal movement was limited and distal movement was very limited. She did not wear a splint. She walked with a slight limp, but no aids.

Participant 5 was a moderately aphasic (with good understanding) 51 year old left handed male with a right hemiplegia, who attended the study 8 months after his stroke. Participant 5 had no prior experience of ES. Proximal movement was limited and distal movement was very limited. He wore a night time moulded splint. He walked with a pronounced limp and a stick.

4.2.1 Clinical outcome measures

Mean clinical outcomes at baseline and after 18 sessions are shown in Table 19. The results show a statistically significant improvement was only identified for the impairment outcome measure after 18 sessions. Pre and post intervention, the mean activity limitation ARAT and FMA scores are very low. The extra sessions for participants 3 and 5 showed no significant improvement on either clinical scale.

Outcome Measure (n=5)	Baseline Mean* (SD) [Min-Max]	Post Treatment Mean (SD) [Min-Max]	PT-B (SD) P-value [95% CI]
Normal score			
ARAT 57 FMA (motor) 66	4.00 (1.46) [3.0-6.5]	3.40 (0.55) [3.0-4.0]	0.60 (1.19) 0.32 [-0.88, 2.08]
	12.90 (3.36) [8.5-16.5]	15.40 (4.28) [9-19]	-2.50 (1.58) 0.02 [-4.46,-0.54]

* Baseline is the mean of the two pre-treatment evaluations.

Table 19: Mean (SD) and range [Min-Max] for clinical outcome measures for stroke participants at Baseline and Post Treatment (18 sessions). Mean change (SD) during the 18 intervention sessions, level of significance (Paired t-test) and 95% CI are also shown.

A comparison between the baseline and the post treatment for the FMA and the ARAT for the stroke participants can be seen in Figure 34 and Figure 35 respectively. All participants post treatment FMA scores improved. The percentage increases for FMA for participants 1-5 are: 33.3%, 9.1%, 5.9%, 22.3% and 24%. Changes in the ARAT were minimal and showed a variable response to the intervention. For participants 1-5 are: 0%, -38%, 0%, 14% and -25%.

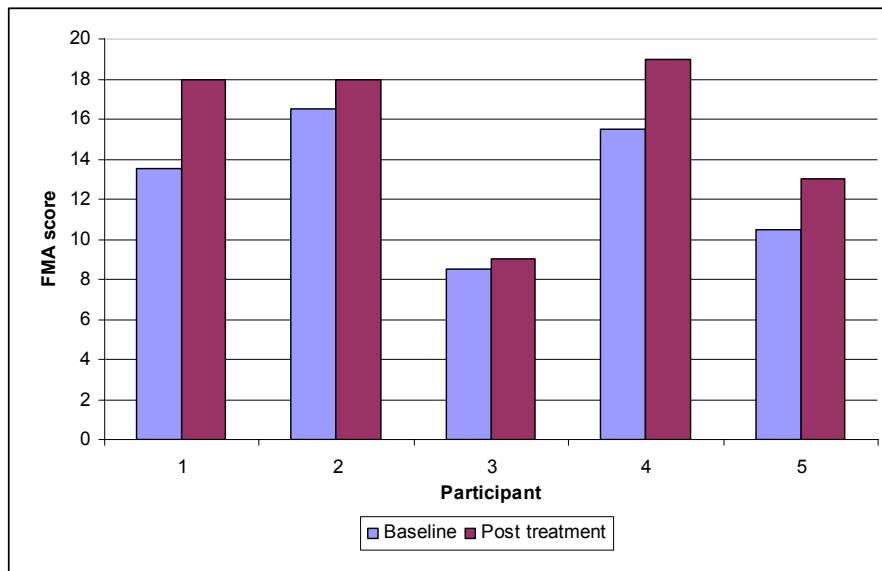


Figure 34: Baseline and Post Treatment FMA scores for stroke participants

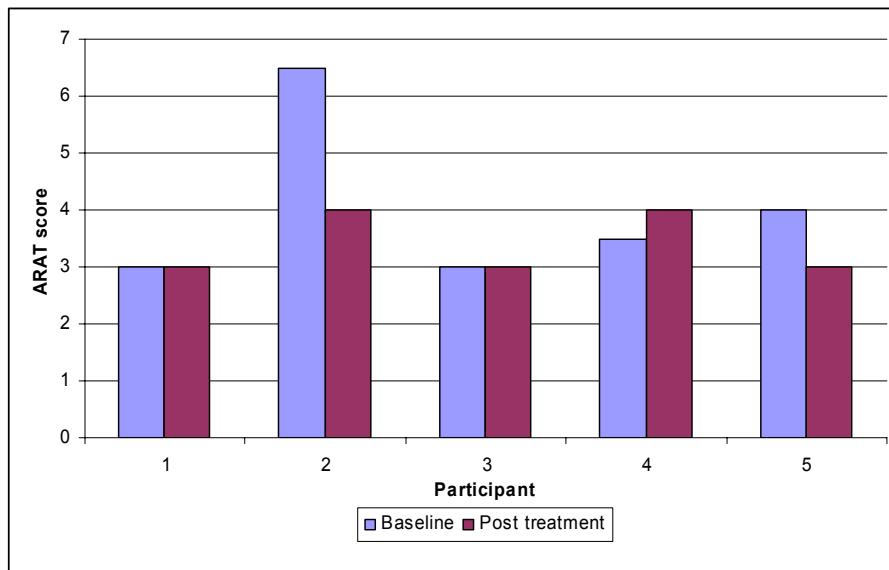


Figure 35: Baseline and Post Treatment ARAT scores for stroke participants

4.2.2 Tracking error without ES

For each participant the change in tracking error data over the four different unassisted tracking (No ES) trajectories performed at the beginning of each treatment session is shown in Figure 36 (for details of how the tracking error was calculated see section 3.2.3.2.). Although the trend for participants is a decrease in tracking error over time, the change is not monotonic i.e. adjacent values may increase. The tracking error decreased most for participants 3 and 5 across all trajectories over the intervention.

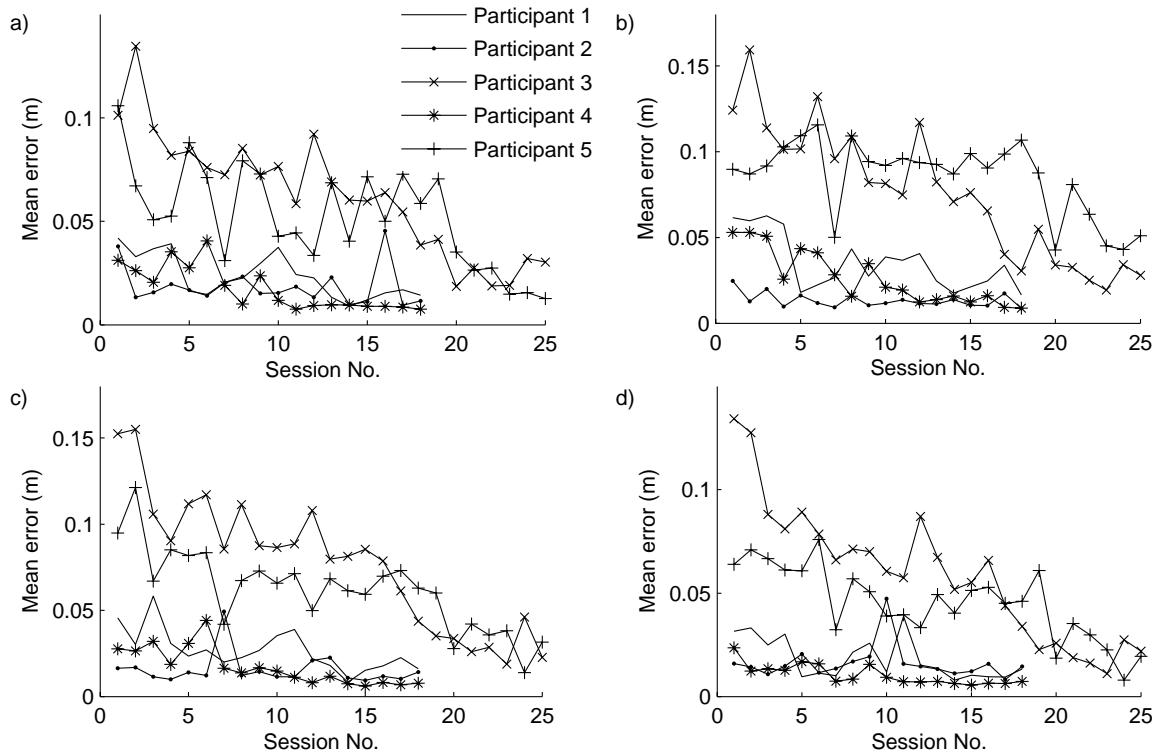


Figure 36: Changes in tracking error data for each participant for each unassisted trajectory performed at the beginning of each treatment session a) T1SS b) T1MS
c) T2MS d) T2SS

The data in Table 20 shows the reduction in tracking error is significant for three out of the four tested trajectories: T1SS, T1MS and T2MS trajectories.

Trajectory (n=5)	Mean Difference	Standard Deviation	P value
T1SS	-0.0018080	0.001224528	0.030
T1MS	-0.0023180	0.001637515	0.034
T2MS	-0.0021420	0.001697756	0.048
T2SS	-0.0015628	0.001539635	0.086

T1SS 20° internal rotation 80% reach 15 s, T1MS 20° internal rotation 90% reach 10s
T2MS midline 90% reach 10s, T2SS midline 80% reach 15s

Table 20: Mean and SD of error tracking data generated by all participants for baseline and post 18 sessions

4.2.2.1 Tracking error pattern

The overall tracking pattern for participant 3 over the T3 SSL, MMM and LFH trajectories is shown in Figure 37, showing the point on the trajectory where the errors occur. As might be expected, the pattern of error is more varied than the neurologically intact participant; a large initial error could be seen in reaching, return was more consistent.

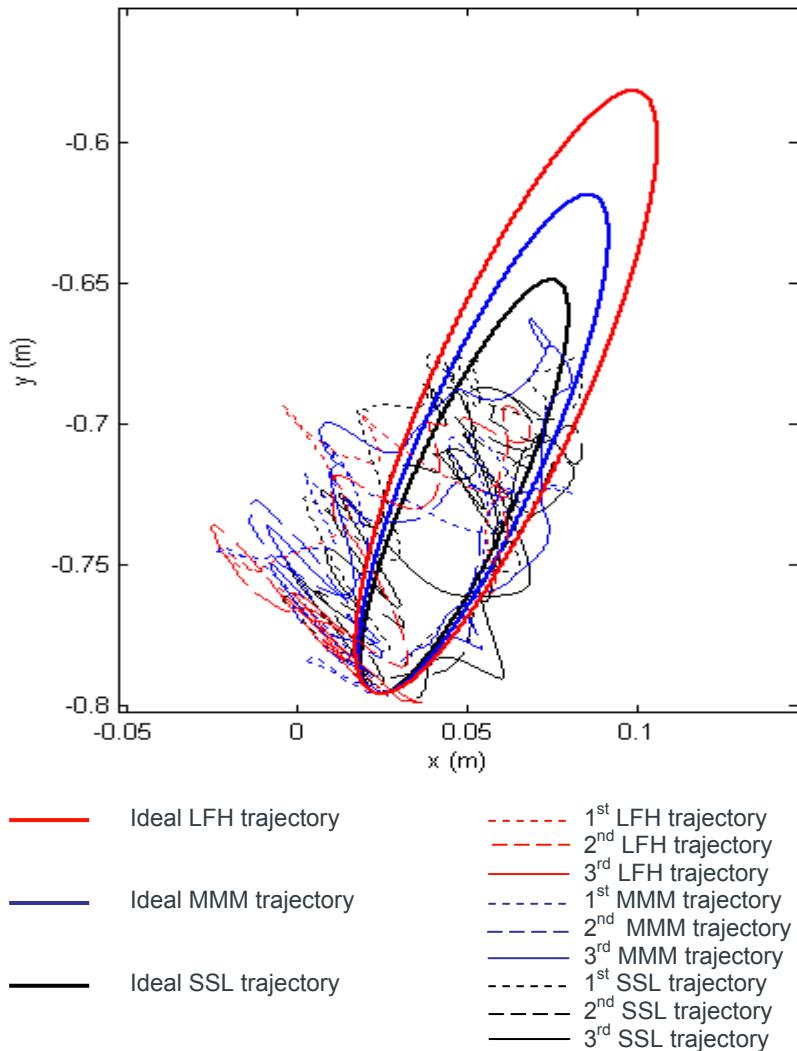


Figure 37: Trajectory tracking pattern for participant 3 showing three repetitions for T3 tasks

4.2.3 Changes in shoulder and elbow angle resulting from stimulation

To illustrate the effect of the stimulation in assisting tracking, Figure 38 a) and b) show typical changes in the angle of the shoulder and elbow over the duration of a T1SS trajectory. The solid line shows the ideal movements which would be required

to complete the trajectory successfully; the dotted line represents unassisted movement, and the dashed line shows movement assisted by ES. Figure 38 c) shows the ES pulse-width that is applied using ILC in order to produce these assisted movements. During the 5s ‘countdown’ period, before the target movement starts, there is minimal stimulation. On the reach component of the trajectory (5–12.5s) stimulation increases rapidly. There is a delay period of approximately 2s between the stimulation peak and the peak shoulder and elbow angle, associated with the biomechanical response to stimulation. The robot provided a low level of assistance (60Nm^{-1}) which was effectively only noticeable when the tracking error was greater than 5cm.

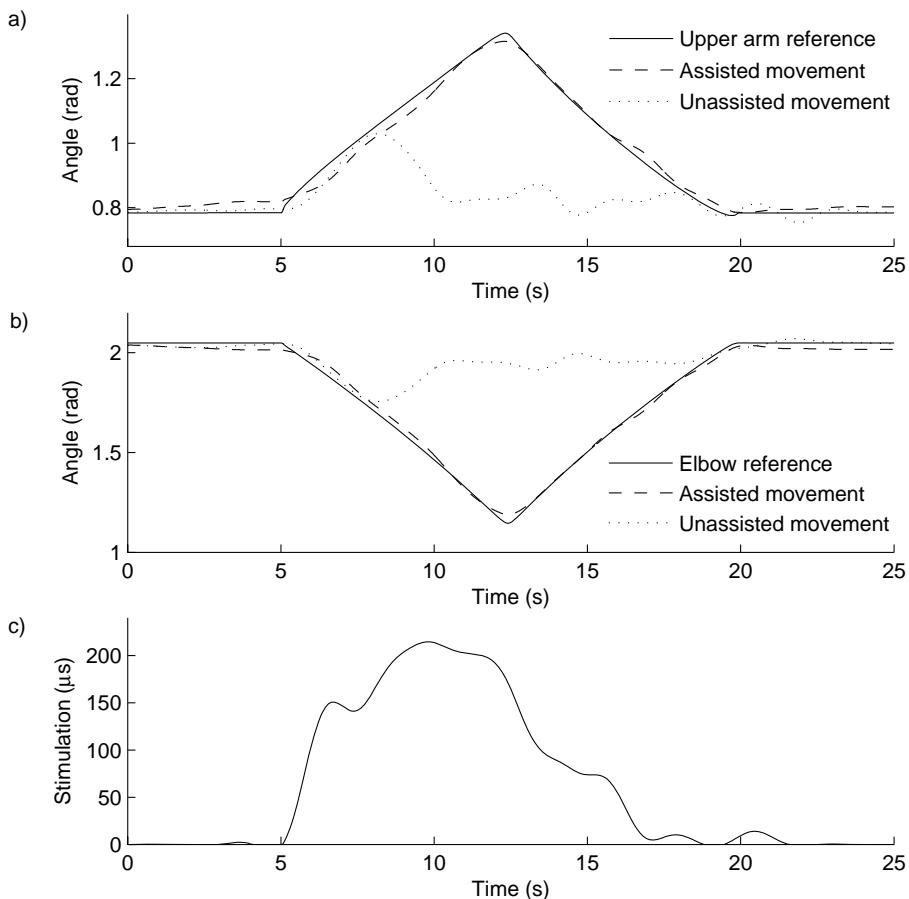


Figure 38: Changes in a) the shoulder and b) elbow angle due to c) stimulation during a T1SS trajectory for participant 3

4.2.4 Isometric force

The mean and maximum isometric force generated in six different directions (0° , 60° , 120° , 180° , 240° , 300°) recorded for i) the sample of eight neurologically unimpaired right handed participants and ii) the five stroke participants’ mean (SD)

isometric force values at baseline and after 18 sessions is shown in Table 21. Note that the direction in which the angle is measured is reversed depending on the side of hemiplegia to allow comparison across all participants. Mean (SD) change of isometric force, level of significance (Paired t-test) and 95% CI is also shown. For normal subjects the isometric force varied with direction: it was strongest at 0° and 120° and weakest in the 60° and 300° directions. For stroke participants the isometric force also varied with direction; for both the pre and post intervention the strongest was at 120° and 180° and weakest in the 60° and 0° directions. The largest gains in force were made in the 300° and 180° directions and the smallest in the 60° and 240° directions; changes in force data across the group are significant in all but one direction (180°).

Angle	Neurologically intact Mean (SD) [Min-Max]	Stroke Baseline Mean (SD) [Min-Max]	Stroke Post Treatment Mean (SD) [Min-Max]	Stroke PT– B (SD) P-value [95% CI]
0°	81.75 (8.39) [71.22-92.48]	35.58 (12.41) [24.06-54.83]	48.41 (18.41) [26.96-68.33]	12.82 (9.70) 0.04 [24.87,0.78]
60°	49.88 (18.71) [20.13-81.38]	33.35 (12.40) [25.67-54.86]	37.93 (12.68) [27.53-59.92]	4.58 (2.77) 0.02 [8.02,1.13]
120°	73.19 (19.18) [31.60-93.24]	57.28 (18.40) [34.56-79.70]	68.41 (24.21) [40.61-97.75]	11.13 (6.69) 0.02 [19.44,2.81]
180°	72.21 (13.87) [54.10-95.78]	53.21 (6.60) [43.71-60.53]	66.42 (6.23) [61.33-74.86]	13.21 (12.22) 0.07 [28.39,-1.96]
240°	71.46 (19.41) [40.52-93.69]	40.61 (8.64) [31.13-52.66]	51.66 (10.46) [38.82-67.88]	11.05 (6.18) 0.02 [18.73,3.37]
300°	61.41 (18.89) [33.79-88.68]	38.08 (12.74) [24.35-53.84]	56.20 (11.69) [42.05-71.65]	18.11 (3.36) <0.01 [22.28,13.94]

Table 21: Mean (SD) and range [Min-Max] isometric force (N) generated by neurologically intact and stroke participants at Baseline and Post Treatment (18 sessions). Mean change (SD), during the 18 treatment sessions, level of statistical significance (Paired t-test) and 95% CI are also shown

For each participant the mean isometric force results for each assessment are shown in Figure 39. Each of the stroke participants' data are superimposed on results from the neurologically intact sample; the mean of eight participants (dark) and the strongest individual (light grey). In most cases the axis along which the principal changes in isometric force occurred was associated with the side of hemiplegia; in left hemiplegics (participants 1 and 2) this was from bottom left to top right, for right hemiplegics (participants 3, 4 and 5) from top left to bottom right. It can be observed that further force changes were evident after 25 sessions, but in a reduced number of directions compared to session 18; the improvements were seen

in 3 directions (as opposed to all 6) for participant 3, and 4 directions (as opposed to 6) for participant 5.

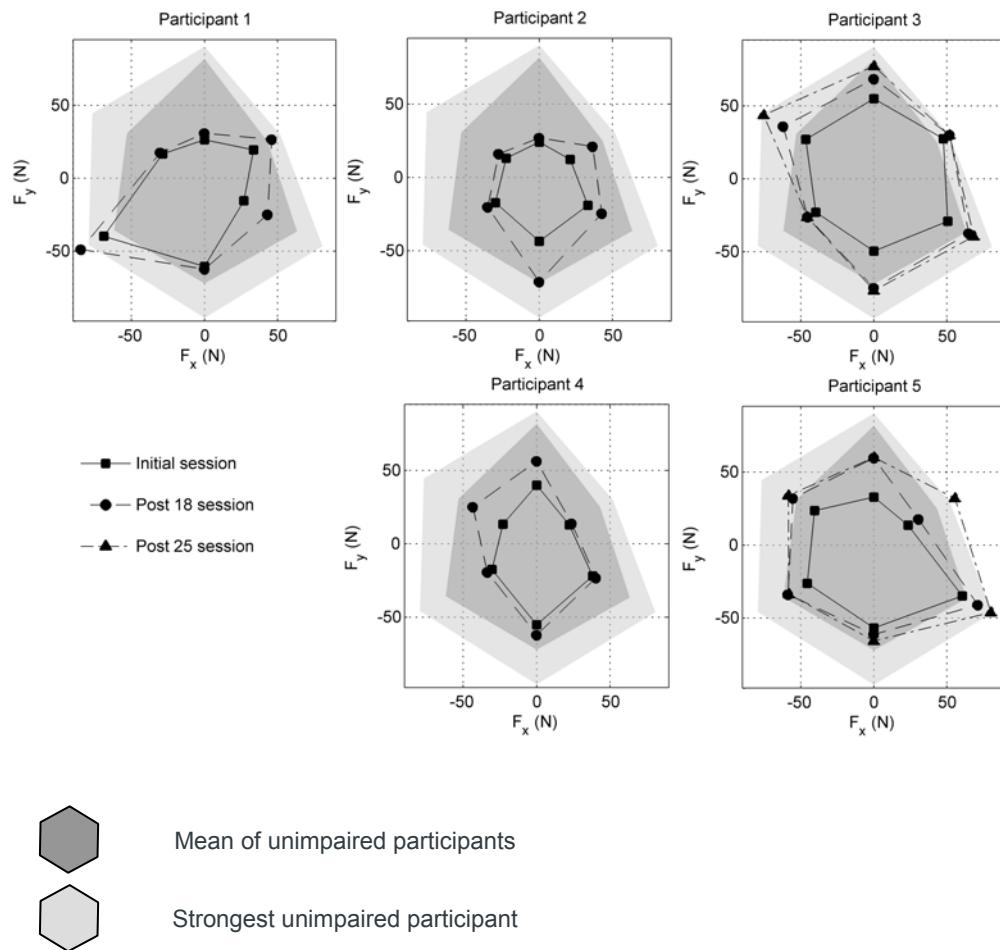


Figure 39: Mean isometric force for each stroke participant: initially, post 18 and post 25 sessions

4.2.5 MIVC Data

The mean (SD) MVIC factor generated from seven muscles of a) neurologically intact and b) stroke participants are shown in Table 22. For stroke participants: Mean (SD) at baseline and post 18 sessions; Mean (SD) change of MVIC during the intervention (Post intervention – Baseline [PI-B]); level of significance (Paired t-test) and 95% CI are shown. Pre intervention the highest MVIC factor was generated for upper trapezius and the lowest for middle trapezius. Post intervention all muscles with the exception of anterior deltoid showed an increase in the MVIC factor, which for triceps was statistically significant ($p=0.05$). For the neurologically intact

participants the highest MVIC factor was recorded from lower trapezius and the lowest from triceps.

Muscle	Normal Mean (SD) [Min-Max]	Baseline Mean (SD) [Min-Max]	Post Intervention Mean (SD) [Min-Max]	PI-B (SD) P-Value [95%CI]
Triceps	152.91 (71.83) [21.34-229.71]	58.63 (49.46) [27.99-145.27]	130.18 (76.66) [45.16-216.85]	-71.55 0.047 [-141.58, -1.53]
Biceps	193.31 (125.42) [33.48-386.96]	37.96 (24.08) [7.50-64.33]	80.75 (50.66) [39.14-155.72]	-42.79 0.078 [-93.25, 7.67]
Anterior	201.51 (107.13) [76.98-388.32]	54.84 (30.08) [28.56-87.92]	53.76 (31.74) [21.11-97.32]	1.08 0.946 [-40.96, 43.12]
Deltoid	153.92 (89.23) [48.70-323.71]	92.14 (76.10) [32.71-203.63]	98.55 (52.93) [52.87-175.11]	-6.41 0.877 [-114.24, 101.42]
Upper	161.06 (103.50) [75.10-333.56]	15.07 (6.98) [5.17-22.11]	34.07 (14.71) [16.36-53.07]	-18.99 0.061 [-39.44, 1.45]
Traps	164.73 (95.26) [63.37-340.73]	37.02 (20.54) [13.68-61.07]	66.00 (45.82) [26.04-140.47]	-28.98 0.087 [-64.65, 6.7]
Mid Traps	213.75 (48.38) [145.39-283.27]	25.79 (16.84) [2.94-40.97]	26.67 (8.86) [18.77- 41.86]	-0.89 0.912 [-21.74, 19.97]
Low				
Traps				

statistically significant

Table 22: Mean (SD) and range [Min-Max] maximum voluntary isometric contraction factor (μ V) generated by neurologically intact and stroke participants at Baseline and Post Intervention (18 sessions). Mean change (SD) during the 18 intervention sessions, level of statistical significance (Paired t-test) and 95% CI are also shown

4.2.6 EMG

Data are presented in tables for all muscles: the timing and amplitude of peak EMG (Table 23) and mean (SD) MVIC factor (Table 22), and for the case of triceps and biceps: mean (SD) percentage co-activation across all tasks (Table 24). Graphical representations are used to illustrate changes occurring as a result of the intervention, assisting in the interpretation of principal features, focussing on the triceps and biceps; mean amplitude and mean temporal position of peak EMG (Figure 40), IEMG normalised activation (Figure 41), and activation patterns during the LFH tasks (Figure 42).

Timing and amplitude of peak EMG

The statistical results of significance levels for timing of peak activity and amplitude for all muscles across all tasks for i) stroke compared to neurologically intact participants, ii) stroke participants pre and post intervention, and iii) whether the change in the direction for stroke participants is towards that of the neurologically

intact participants are presented in Table 23. The muscle timing of peak activity and amplitude can be roughly categorised using these significance levels for the majority of the trajectories:

Pre intervention stroke compared to neurologically intact participants

None of the stroke participants' muscles studied showed both timing of peak activity and amplitude to be similar to the neurologically intact participants. The trend was for nearly all EMG amplitudes to be higher for stroke participants. This can be seen for biceps and triceps in Figure 40. Significant differences were found in the timing for triceps, anterior deltoid, and upper trapezius; the amplitude for biceps and lower trapezius; for both for middle trapezius and pectoralis major.

Stroke participants pre and post intervention

The trend was for nearly all amplitudes to decrease post intervention. Significant differences were found in the timing for triceps and pectoralis major; the amplitude for biceps and middle trapezius; for both for upper trapezius. Neither the timings nor the amplitudes were significantly different for anterior deltoid and lower trapezius.

These changes were significantly towards normal in timing for triceps, upper trapezius and pectoralis major; in amplitude for biceps and middle trapezius. For anterior deltoid and lower trapezius neither the timing nor the amplitude were significantly towards normal.

MUSCLE	TASK	ANGLE	Timing of peak activity p values			Amplitude p values		
			Normal- Stroke pre *	Stroke pre- post **	Towards normal ***	Normal- Stroke pre *	Stroke pre- post **	Towards normal***
			*	**	***	*	**	***
TRICEPS	SSL	T1	0.02	0.08	0.04	0.16	0.86	0.28
		T2	0.05	0.08	0.23	0.10	0.20	0.11
		T3	0.01	0.03	0.09	0.13	0.27	0.07
	MMM	T1	0.64	0.48	0.11	0.05	0.14	0.05
		T2	0.01	0.04	0.04	0.19	0.30	0.08
		T3	<0.01	0.02	0.05	0.19	0.19	0.02
	LFH	T1	0.01	0.01	0.01	0.59	0.38	0.26
		T2	<0.01	0.01	0.02	0.88	0.69	0.11
		T3	<0.01	0.02	0.01	0.87	0.56	0.21
BICEPS	SSL	T1	0.14	0.71	0.10	<0.01	0.01	0.01
		T2	<0.01	0.04	<0.01	<0.01	0.01	0.01
		T3	<0.01	0.11	0.05	<0.01	0.08	0.04
	MMM	T1	0.22	0.70	0.49	<0.01	0.02	0.01
		T2	0.53	0.29	0.37	0.01	0.01	0.01
		T3	0.87	0.08	0.65	<0.01	0.01	0.01
	LFH	T1	0.76	0.29	0.88	0.03	0.30	0.23
		T2	0.65	0.22	0.88	0.15	0.79	0.32
		T3	0.52	0.04	0.43	0.01	0.60	0.30
ANTDEL	SSL	T1	<0.01	0.03	0.01	0.17	0.66	0.29
		T2	0.40	0.18	0.30	0.01	0.08	0.05
		T3	0.51	0.20	0.30	0.02	0.03	0.07
	MMM	T1	0.01	0.07	0.30	0.43	0.12	0.14
		T2	0.03	0.13	0.13	0.35	0.14	0.12
		T3	0.01	0.11	0.29	0.03	0.08	0.04
	LFH	T1	0.01	0.01	0.01	0.92	0.11	0.38
		T2	0.22	0.16	0.12	0.96	0.58	0.08
		T3	<0.01	0.01	0.01	0.43	0.33	0.48
UPTRAPS	SSL	T1	0.70	0.06	0.46	0.13	0.08	0.31
		T2	0.01	0.03	0.03	0.79	0.07	0.86
		T3	<0.01	0.22	0.11	0.24	0.02	0.95
	MMM	T1	0.03	0.04	0.04	0.64	0.03	0.90
		T2	0.01	0.05	0.05	0.53	0.02	0.98
		T3	0.01	0.01	0.07	0.71	0.01	0.98
	LFH	T1	0.05	0.12	0.09	0.68	0.04	0.99
		T2	<0.01	0.08	0.05	0.37	0.05	0.96
		T3	<0.01	0.01	0.02	0.59	<0.01	1.00
MIDTRAPS	SSL	T1	<0.01	0.04	0.04	<0.01	<0.01	<0.01
		T2	<0.01	0.11	0.06	<0.01	<0.01	<0.01
		T3	0.02	0.15	0.16	<0.01	<0.01	<0.01
	MMM	T1	0.22	0.75	0.79	<0.01	<0.01	0.01

MUSCLE	TASK	ANGLE	Timing of peak activity p values			Amplitude p values		
			Normal-Stroke pre	Stroke pre-post	Towards normal ***	Normal-Stroke pre	Stroke pre-post	Towards normal***
			*	**		*	**	
PECMAJ	SSL	T2	0.03	0.06	0.05	<0.01	<0.01	0.01
		T3	0.52	0.75	0.90	<0.01	<0.01	<0.01
		LFH	T1	0.02	0.03	0.08	0.09	0.05
		T2	0.18	0.12	0.24	0.13	0.02	0.26
		T3	0.02	<0.01	<0.01	0.01	0.01	0.03
		MMM	T1	<0.01	0.01	0.02	0.03	0.24
		T2	0.03	0.01	0.06	0.02	0.20	0.15
		T3	0.66	0.18	0.15	0.01	0.05	0.03
		LFH	T1	<0.01	<0.01	<0.01	0.73	0.36
		T2	<0.01	<0.01	<0.01	0.13	0.38	0.27
		T3	0.50	0.05	0.62	0.02	0.04	0.05
LOWTRAPS	SSL	SSL	T1	0.38	0.41	0.95	<0.01	0.82
		T2	0.05	0.63	0.56	0.01	0.63	0.32
		T3	0.24	0.95	0.36	0.01	0.73	0.37
		MMM	T1	0.18	0.72	0.19	0.02	0.54
		T2	0.31	0.72	0.42	0.01	0.68	0.34
		T3	0.89	0.05	0.19	0.01	0.40	0.20
		LFH	T1	0.17	0.05	0.20	0.10	0.84
		T2	0.59	0.56	0.44	0.08	0.54	0.23
		T3	0.71	0.52	0.02	0.04	0.75	0.38

statistically significant

*Normal – Stroke used a two tailed unpaired t- test

**Stroke pre post used a paired T test

***Trend towards normal used a Right-tailed t-test

Table 23: The level of significance for timing of peak activity and amplitude for all muscles across all tasks for i) stroke compared to neurologically intact participants ii) stroke participants pre and post intervention iii) whether the change in the direction for stroke participants is towards that of the neurologically intact participants

For ease of interpretation, data for biceps and triceps are displayed in more detail in Figure 40 which shows the mean maximum amplitude μ_{EMG} and corresponding variation in temporal position for biceps and triceps for each task and illustrates how timing and amplitude of peak muscle activity varied with task. Each wedge representing neurologically intact participants is bisected by a solid line of the same colour. The position of the line on the ellipse indicates timing of mean peak EMG activity and the wedge width indicates variability (SD) of time of peak activity across the sample. Peak activity of triceps occurred towards the end of reach for eight out of the nine tasks and biceps always on the return. For stroke participants the position of the dotted line indicates timing of mean peak EMG activity pre intervention and the dot-dash line post intervention. In all cases pre intervention the timing of mean peak EMG activity was on the return consistently for triceps and for eight out of the nine trajectories for biceps. The amplitude for biceps was significantly greater than for normal for all but one trajectory. Post intervention this had changed so that the timing for triceps was towards the end of reach for the same trajectories as the neurologically intact participants and the biceps on the return for eight out of the nine trajectories. The amplitude for biceps significantly reduced for all task excluding the LFH.

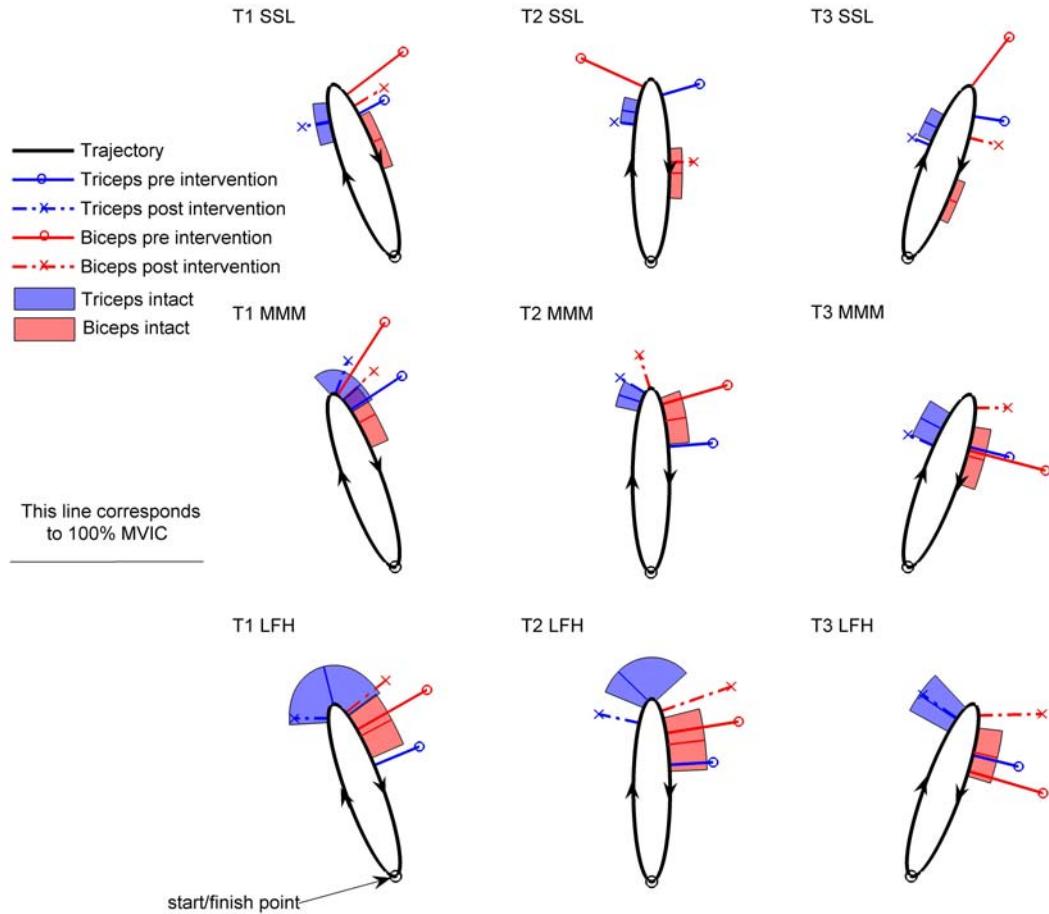


Figure 40: Mean amplitude and mean (SD) temporal position of peak EMG during each task for biceps and triceps for five stroke and eight neurologically intact participants. The mean position, μT , of max EMG amplitude is indicated by a line of the same colour orthogonal to the trajectory for stroke participants a) pre intervention (solid with circle b) post intervention (dot-dash) and c) neurologically intact (solid). For neurologically intact participants wedge height and position are given by μEMG and $\mu T \pm 0.5 \sigma T$ for each task. T1, 2 and 3 correspond to the orientation of the trajectory. SSL, MMM and LFH are abbreviations for the length, duration and resistance respectively of the task

Variability of triceps and biceps activation patterns

The IEMG normalised activity for triceps and biceps for T1 LFH is shown for stroke participants at baseline and post intervention (Figure 41a and b respectively) and for neurologically intact participants (Figure 41c). Envelopes corresponding to 0.5SD and 1SD are shown to illustrate variability across the sample. The 5s task begins at 0s and maximum reach occurs at 2.5s.

Pre intervention stroke compared to neurologically intact participants

There was a greater variability in triceps activity in stroke compared to neurologically intact participants for all tasks. The extension phase had a marked reduction in gradient in the first 1s, increased during the remainder of the extension phase and remained consistently high during the return phase. For biceps, the muscle activation patterns (SD, activity gradient in the first 1s, and during return) were similar for pre intervention stroke and neurologically intact participants. The period during which 70% max activity threshold began and ended can be seen using the bar drawn along the x axis. Pre intervention triceps 70% max activity began and ended later (1.9s vs 0.9s and 5 vs 3.7s) respectively. Pre intervention biceps began slightly later but ended slightly earlier (1.9s vs 1.8 s and 4.8s vs 4.9 s) respectively.

Stroke participants pre and post intervention

Changes between pre and post intervention were observed in the temporal activity patterns of both biceps and triceps muscles. Post intervention, triceps SD was reduced, and a steeper gradient during the first 1s of the extension phase was observed. Triceps activity during the return was reduced, and the period during which 70% max activity threshold began and ended shifted to earlier in the task . This can be seen using the bar drawn along the x axis. (1.2 s vs 1.9s) and (4.2s vs 5s) respectively. Biceps 70% threshold also shifted to earlier in the task but ended slightly later (1.6s vs 1.9s) and (5s vs 4.8s) respectively.

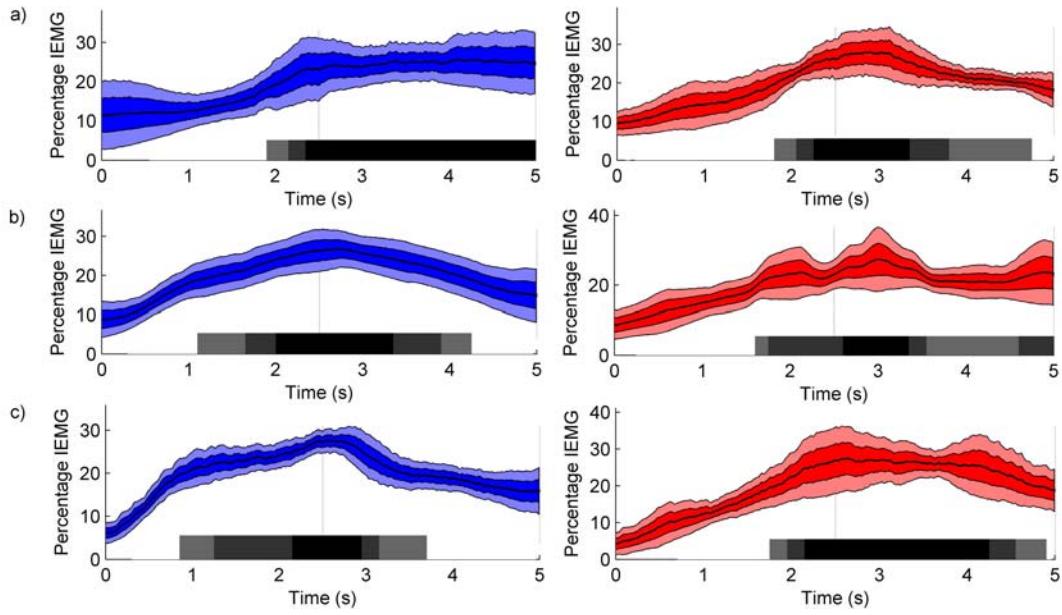


Figure 41: IEMG normalised activation averaged across stroke participants a) pre intervention b) post intervention and c) for neurologically intact participants for triceps (blue) and biceps (red) during the T1 LFH task. Sample mean (indicated by a thicker line), 0.5 and 1SD envelopes are shown. Maximum reach was at 2.5s. Intervals in which mean EMG exceeds 70 (palest), 80, 90 (darkest) percent of the peak value are also shown by the bar drawn along the x axis.

Triceps and biceps co-activation during the LFH tasks

The time periods during which biceps and triceps EMG exceeded 70, 80 and 90% of maximum amplitude for the LFH tasks are illustrated in Figure 42. The duration and intensity of muscle activity is compared across all tasks and is displayed using a range of threshold levels. 70% (palest shade) is regarded as the threshold for the muscle being 'on'. This was chosen as it is above a level of intermittent activation for the tasks used, but is within a region in which changes in the exact value do not lead to large differences in the overall activation trends observed.

For the stroke participants, triceps activity preceded biceps for two out of the three trajectories pre intervention (T2 and T3), but all three post intervention; biceps is active until the end of the task for one trajectory (T2) pre intervention and for two trajectories (T1 and T3) post intervention. For the neurologically intact participants, in all trajectories triceps activity precedes biceps and biceps remains active to the end of the task.

For stroke participants pre intervention, triceps remained active until the end of the task, and biceps came 'on' at an earlier point. Following intervention, triceps turned 'off' earlier for T2 and T3 than T1; biceps activity did not appear to change greatly. For the neurologically intact participants, as the trajectory orientation varied from across the body to away from the body (moving horizontally from T1 to T3 in Figure 42) triceps activity turned 'off' earlier, and the biceps activity came 'on' at a later point. The consequence for stroke participants post intervention and neurologically intact participants was that less co-activation between biceps and triceps activity occurred as a result of moving from T1 to T3 trajectories. Similar plots and statistical analysis can be conducted for the remaining 20 muscle combinations.

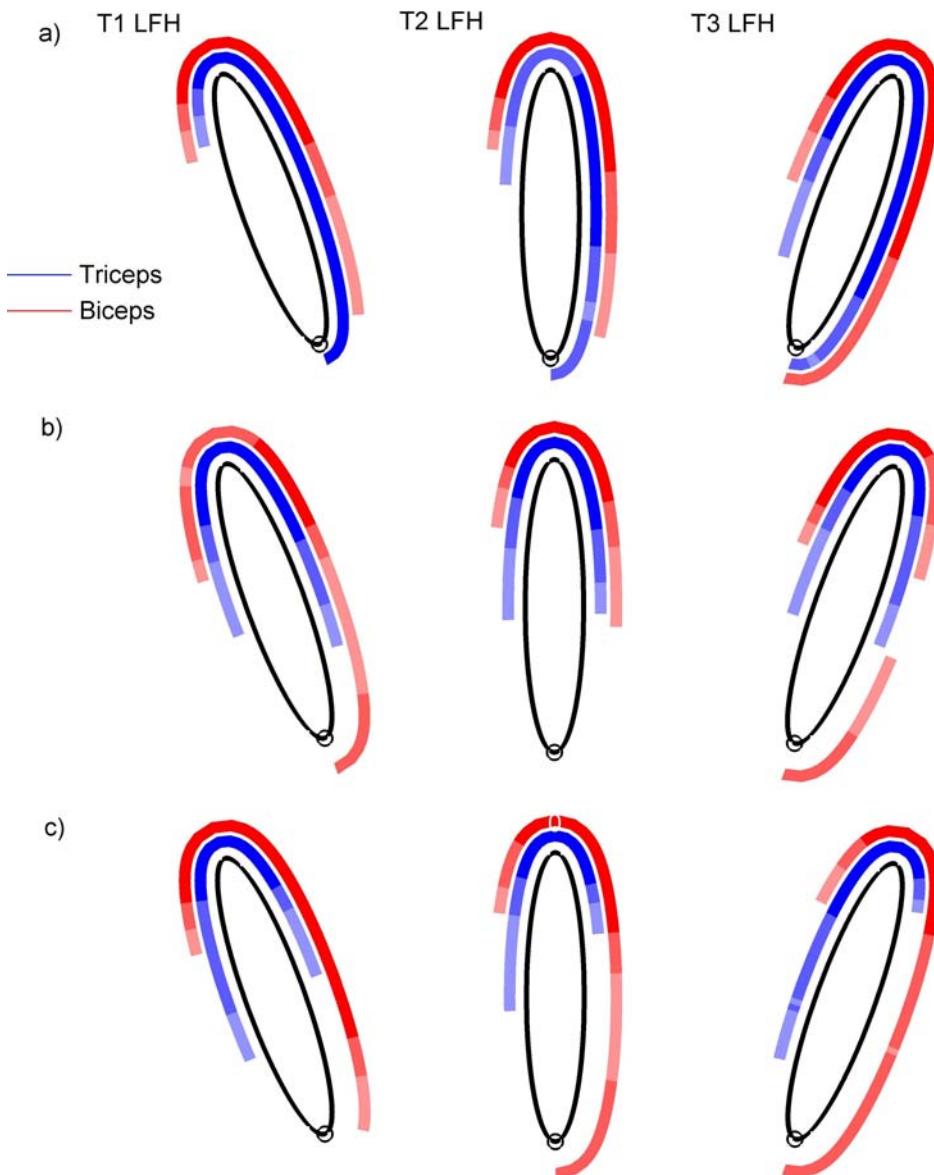


Figure 42: IEMG normalised activation averaged across stroke participants a) pre intervention b) post intervention and c) for neurologically intact participants for triceps (blue) and biceps (red) during the T1, T2 and T3 LFH tasks; Intervals in which mean EMG exceeds 70 (palest), 80, 90 (darkest) percent of the peak value are ‘wrapped’ around each trajectory

Summary data for biceps and triceps co-activation (percentage of task duration when both muscles are ‘on’) are shown in Table 24. The co-activation has been calculated for each participant individually and the table shows the mean (SD). The statistical analysis confirms that the level of co-activation was significantly different between stroke and neurologically intact participants for T3 SSL, T3 MMM, T2 and T3 LFH. Change between pre and post- intervention for the stroke participants was only significant for T3 MMM and T3 LFH. The swing towards normal co-activation

was significant for T3 SSL, T3 MMM and T3 LFH. The percentage co-activation increased from T3 to T2 to T1 for neurologically intact participants. This pattern is not observed for the stroke participants pre intervention, but can be observed post intervention.

Task	Co-activation Mean (SD)		Stroke post	Unpaired T test Normal – Stroke	Paired T Test Stroke Pre-post	One Sided T test Swing towards normal
	Neurologically intact	Stroke pre				
T1SSL	58.2 (19.7)	40.9 (23.6)	40.0 (15.9)	0.1821	0.9565	0.3467
T2SSL	32.1 (10.2)	33 (19.7)	38.7 (7.2)	0.917	0.5097	0.0873
T3SSL	14.8 (6.8)	46.9 (26.3)	17.7 (7.9)	0.0064	0.0934	0.0364
T1MMM	34.2 (6.6)	43.9 (9.45)	43.1 (7.0)	0.0514	0.8625	0.4313
T2MMM	24.2 (5.9)	29.1 (14.6)	37 (8.8)	0.4024	0.3068	0.6554
T3MMM	14.9 (8.9)	44.3 (17.2)	30.4 (14.3)	0.0017	0.0234	0.0493
T1LFH	33.0 (14.8)	43.1 (19.5)	41.2 (17.4)	0.31	0.8836	0.0605
T2LFH	21.5 (8.9)	55.3 (20.8)	38.6 (5.4)	0.0017	0.1374	0.0687
T3LFH	16.6 (7.7)	57.0 (20.5)	30.8 (7.87)	0.0003	0.0344	0.0172

statistically significant

Table 24: Mean (SD) percentage co-activation of triceps and biceps across each task for neurologically intact and stroke participants pre and post intervention

4.2.7 Percentage maximum ES

The assisted trajectory tracking tasks used during the intervention were selected based on clinical need. As such they were not necessarily used in every session, but could also have been used more than once. Figure 43 shows data recorded during the assisted T1SS task for all participants when used. Where the task was repeated in the same session, data from the first performance is shown. For each iteration the mean error was calculated, and the minimum over all iterations is displayed in Figure 43 a). It can be seen that the mean error over the sessions is between 15mm and 8mm, and does not decrease over time. Figure 43 b) shows the corresponding percentage of maximum stimulation required to correct the tracking

error in the most accurate iteration. For all participants the ES required decreased over the 18 sessions.

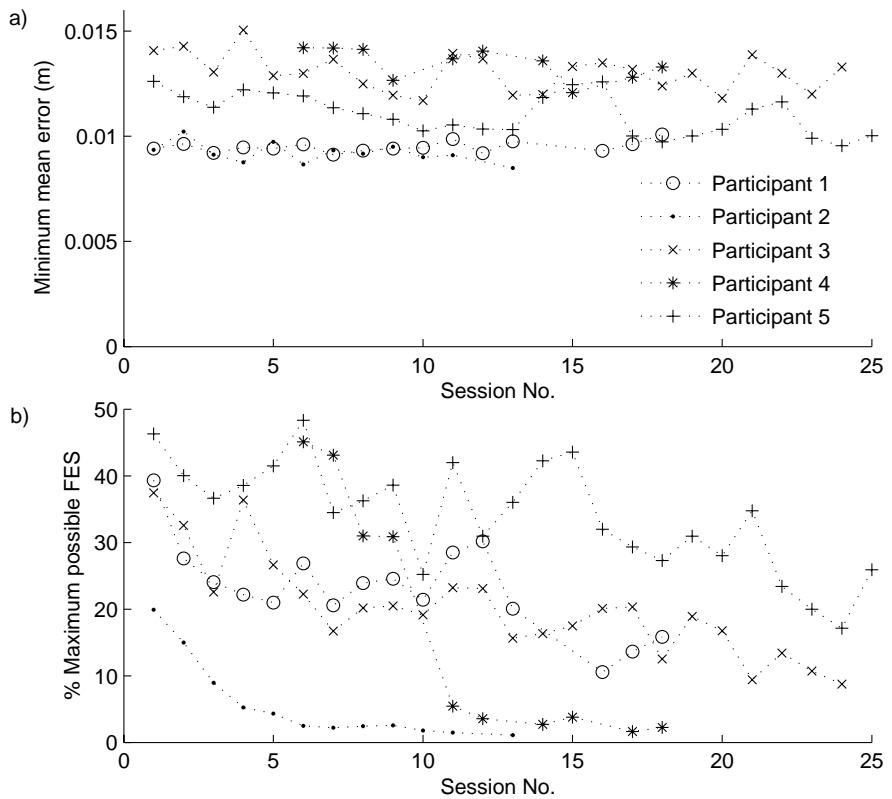


Figure 43: Data recorded for all participants during the ES assisted T1SS tracking task showing a) error in tracking b) % max stimulation used

4.2.8 Individual data

To identify whether initial FMA can be used to predict good and poor responders to the intervention, data from two participants are presented in greater detail.

Participants 3 and 4 were selected as they were both previously right handed, with a right hemiparesis, had no prior experience of ES and did not use splints. Participant 3 was younger than participant 4 (41 vs 55 years) and time from stroke was longer (4.8 vs 3.6 years). Initially ARAT scores were 3 and 3.5; FMA scores were 8.5 and 15.5. Post intervention ARAT scores were 3 and 4; FMA scores were 9 and 19. Note that participant 2 who had the highest initial FMA was excluded due to her difficulties with attention and fatigue levels, only able to tolerate four iterations of ILC in a single tracking task.

4.2.8.1 Tracking error (without ES)

The mean tracking error (see results for participants 3 and 4 over a short and medium trajectory are presented in Figure 44 (for details of how the tracking error was calculated see section 3.2.3.2). It can be observed that participant 3 has a high initial error on each trajectory which decreases through the first 20 sessions.

Participant 4 has an initial error of 0.03m which decreases rapidly over the first 10 sessions and then remains fairly constant at a level of error reflecting that of neurologically intact participants (mean error 0.015m).

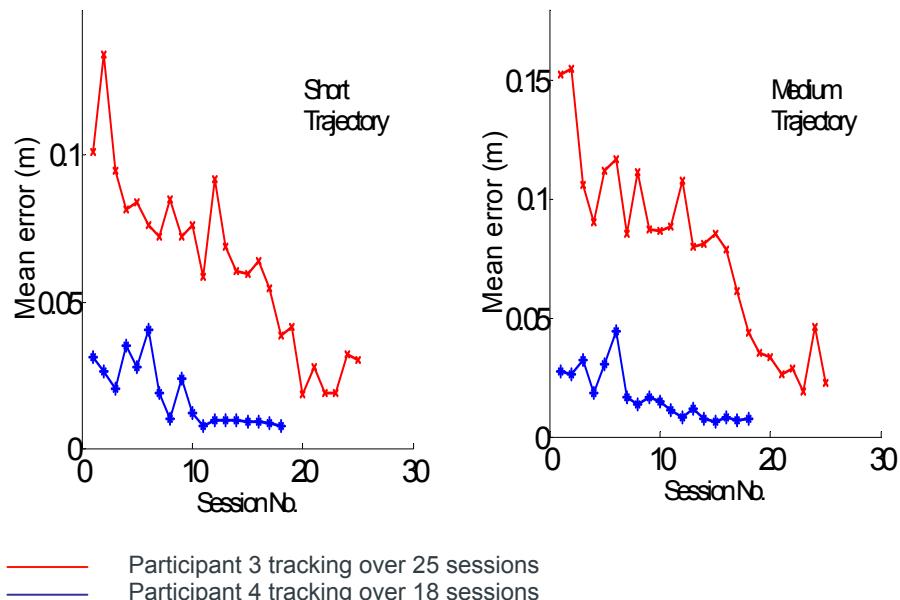


Figure 44: Mean error tracking (without ES) for two participants across a short and a medium trajectory

4.2.8.2 Isometric force

The changes in isometric force for participants 3 and 4 (both right hemiplegic) compared with the neurologically intact participants are illustrated in Figure 45. Initially participant 3 (male aged 41 years) exhibited a symmetrical pattern of isometric force; the force in the 60° direction was greater than that seen with the neurologically intact participants. After 18 intervention sessions this pattern became less symmetrical with improvements seen in the 0° , 120° , 180° and 300° directions. With the further 7 intervention sessions, further increases in isometric force were seen but only in the 300° and 0° directions. Participant 4 (female aged 55 years) initially exhibited less isometric force in all directions compared to the neurologically intact participants and over the course of the intervention the improvements in isometric force were recorded in the 300° and 0° direction.

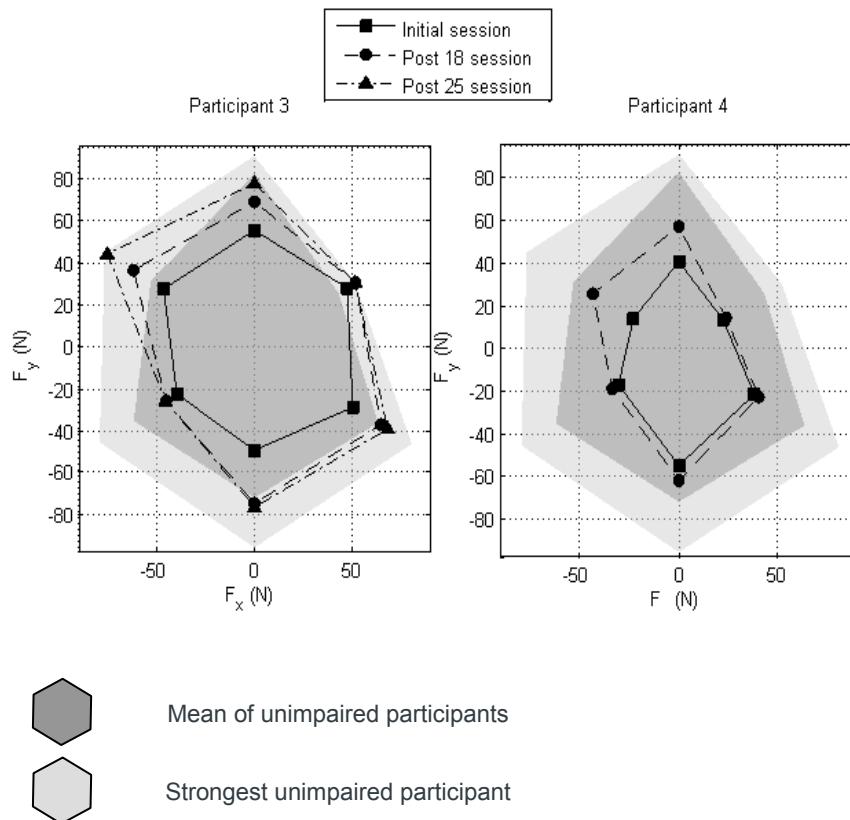


Figure 45: Isometric force for two participants over the intervention, compared to neurologically intact participants

4.2.8.3 EMG

The peak timing data for biceps and triceps for participant 3 are shown in Figure 46. The timing of peak triceps activity for participants 3 and 4 was different pre intervention, and changed as a result of the intervention. Figure 46 illustrates that pre intervention for participant 3, triceps peak activity was consistently in the return part of the trajectory (over 50%), whereas after the intervention it occurred during reach for eight out of the nine trajectories. This post intervention data was more consistent with the neurologically intact data. For participant 3 it can be seen that biceps pre intervention consistently came on either at almost full reach or during return (ranging from 50-87%). After the intervention, biceps peak activity was later in five cases (T1SSL, T2SSL, T3SSL, T1 MMM and T1 LFH) and earlier in the remaining four cases.

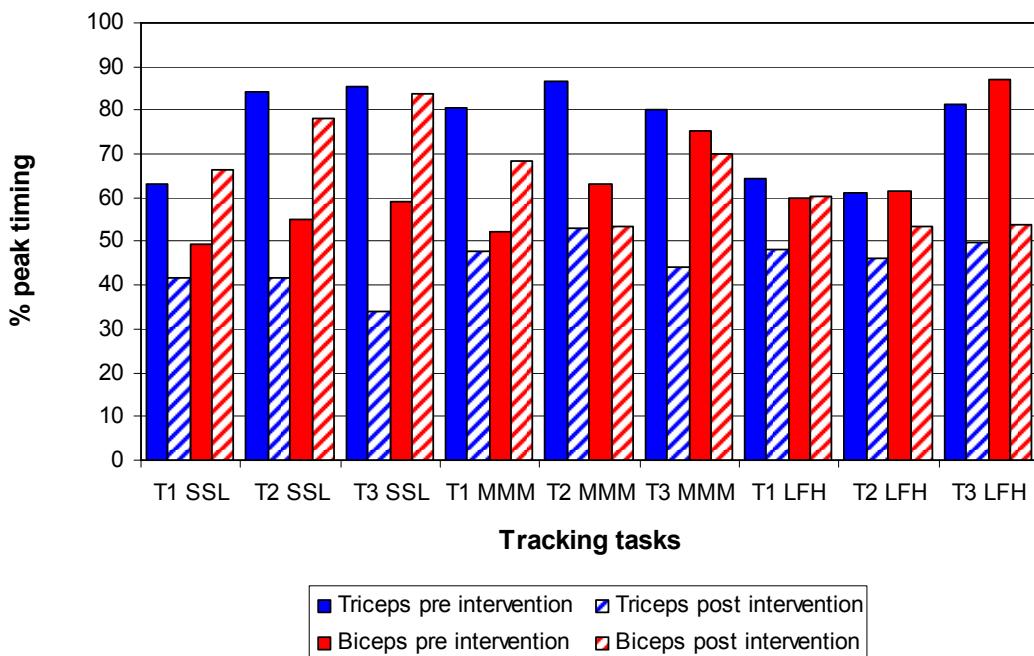


Figure 46: % peak timing data for triceps and biceps for participant 3 pre and post intervention

The peak timing data for biceps and triceps for participant 4 are shown in Figure 47. Pre intervention, the peak triceps activity was during reach for six out of the nine trajectories; post intervention, it was consistently during reach. For participant 4 the range of peak biceps activity pre intervention was lower than for participant 3, (41% to 58%) peak biceps activity occurred during reach for two tasks (T2 and T3 SSL). Post intervention peak biceps activity occurred during reach for only one task, T3

SSL. This post intervention data was more consistent with the neurologically intact data.

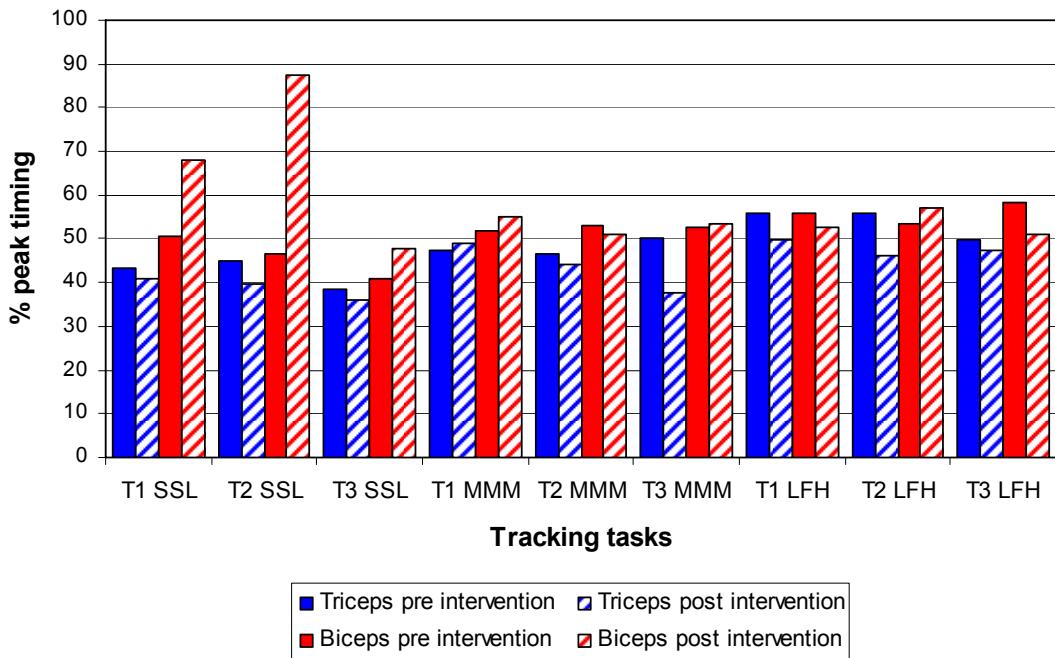


Figure 47: % peak timing data for triceps and biceps for participant 4 pre and post intervention

Figure 48 illustrates that for participant 3 the amplitude of both triceps and biceps decreased after the intervention, with the exceptions of T1SSL for triceps and T2 LFH and T3 LFH for biceps.

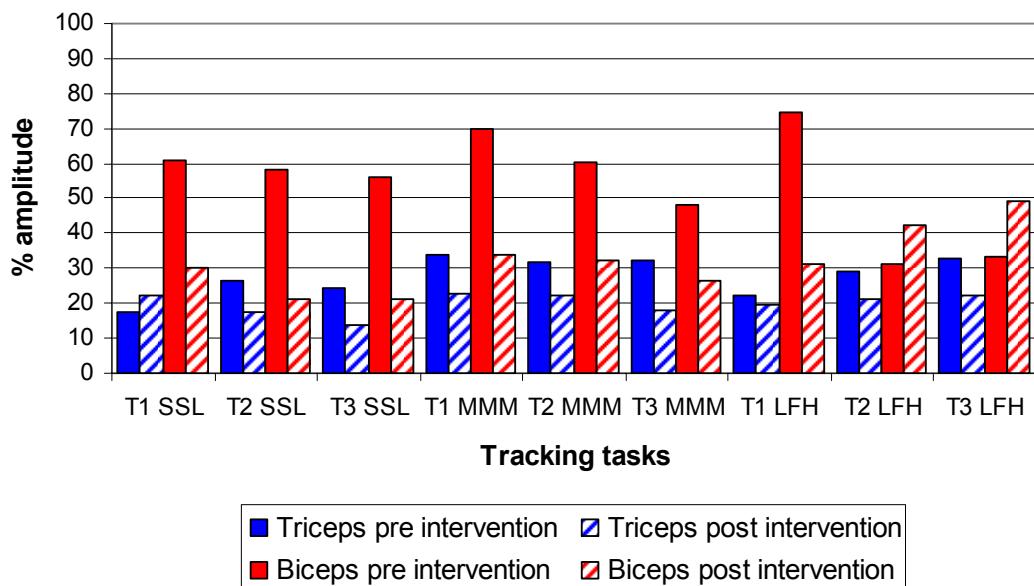


Figure 48: % peak amplitude data for triceps and biceps for participant 3 pre and post intervention

Figure 49 illustrates that for participant 4 the amplitude of both triceps and biceps decreased after the intervention, with the exceptions of T1 LFH and T3 LFH for triceps and T3SSL, and T1 LFH for biceps.

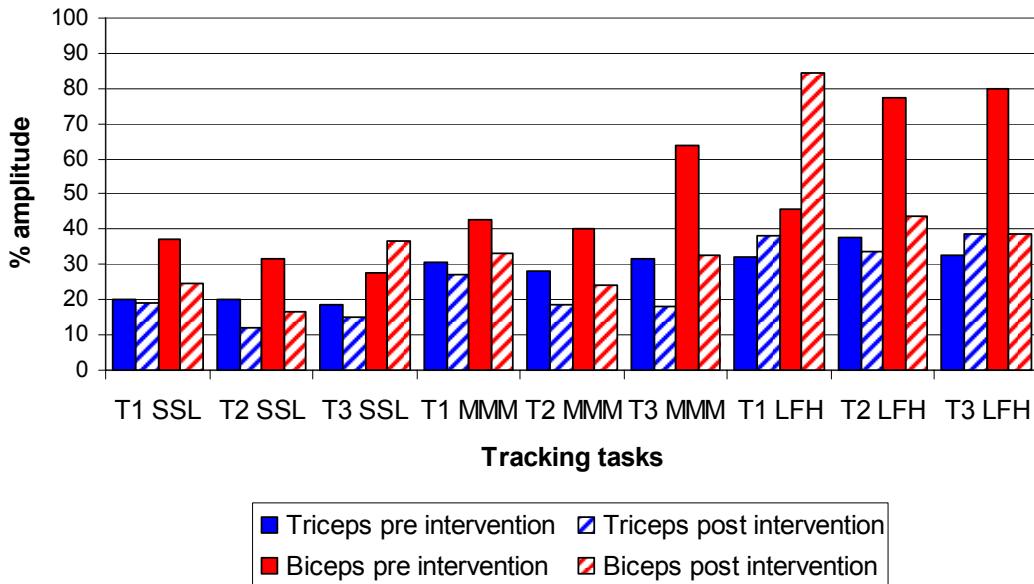


Figure 49: % peak amplitude data for triceps and biceps for participant 4 pre and post intervention

4.2.8.4 Summary of individual stroke participant data

This section presented the results of two different participants for tracking error, isometric force and EMG timing and amplitude data. Although participants had similar initial and final ARAT scores, differences in initial impairment levels were shown by the FMA scores of 8.5 for participant 3 and 15.5 for participant 4.

Participant 4 showed a larger change in the FMA post intervention 19, compared to 9 for participant 3. This was unexpected. Compared to participant 4, participant 3 demonstrated a greater change in unassisted tracking error in response to the intervention; more symmetrical initial isometric force and a gain in force in more directions post intervention. These changes were associated with changes in the EMG data. The peak timing of triceps was initially delayed for both participants occurring during return for all nine tasks for participant 3, and for six tasks for participant 4. For both participants this shifted earlier in the trajectory to the reach phase after the intervention. The timing of biceps occurred for both participants primarily in the return phase, which did not change greatly post intervention. The amplitude for both participants for triceps and biceps reduced post intervention.

4.2.9 Participant perceptions

This part of the study addresses the aim “What are the stroke participants’ perceptions of the system?” which is important to be able to ensure usability of future similar systems. Data were collected from all five of the participants both during and after the ILC study and were analysed using descriptive statistics. Examples of comments provided at the beginning of each of the sessions over which the intervention was trialled are presented in quotes in Table 25.

Participant	Session No	Comment
01	3	‘When lying down could straighten elbow for the first time last night’
	5	‘Itching in hand’ (no visible irritation / redness)
	16	‘Using arm more e.g. holding up trousers when dressing’
02	14	‘Arm not feeling so floppy’
	17	‘Hand relaxing more when I am not noticing’
03	12	‘Something happening with shoulder – not pain – thinks it is good’
	19	‘Has been using arm a little over Christmas’
04	04	‘Finding arm more relaxed when sitting, standing or in bed’
	06	‘Able to put arm around dog – does not normally do this’
	11	‘Feels shoulder is better positioned and is helping walking’
	1	‘Arm a bit tired after last visit’ (assessment)
	13	‘Arm movement difficult – no pain’
05	18	‘Felt funny sensations over all of arm – not pain’
	21	‘Arm aching’ (no focal point tenderness)

Table 25: Examples of comments collected during the study

Responses from the Likert statements are reported in Table 26. These have been summarised into three categories as follows:

Effectiveness: The participants expressed mixed views on whether: they were now more aware of their arm, their arm felt tighter and they could reach out more easily. Most participants either disagreed or strongly disagreed with the statements that their arm felt weaker (1 undecided), they could now pick up objects (1 agreed) and that they did not find the treatment enjoyable.

Usability: Participants expressed mixed views of whether it was difficult to put their arm in the arm holder and that they did not understand the graphs showing their performance. Most participants either disagreed or strongly disagreed that they did not find the treatment enjoyable and that the stimulation was uncomfortable. Most participants either agreed or strongly agreed that it was easy to understand what they had to do, the arm holder was comfortable and that the target was easy to see.

Ideas for future development: Participants expressed mixed views on whether adding games would add to motivation and enjoyment. Most participants either

disagreed or strongly disagreed that they would not recommend the treatment to others who have had a stroke (1 undecided) and they would not like to have more muscles stimulated (1 undecided and 1 agreed). Most participants either agreed or strongly agreed that they would have liked to have continued longer with the treatment.

Statement	Strongly disagree	Disagree	Undecided	Agree	Strongly agree
I am now more aware of my affected arm	2	1	1	1	1
My arm feels weaker	3	1	1		
My arm feels tighter	1	2	1		1
I can reach out with my arm more easily	1	2	1	1	
I can now pick up objects	3	1		1	
I did not find the treatment enjoyable	4	1			
It was easy to understand what I had to do				1	4
It was difficult to put my arm in the arm holder		2		1	2
The arm holder was comfortable					5
The stimulation was uncomfortable	1	4			
The target was easy to see				3	2
I did not understand the graphs showing my performance	1	2		1	1
Adding games would add to my motivation and enjoyment of the treatment		2	1	1	1
I would not like to have more arm muscles stimulated	3		1	1	
I would not recommend the treatment to other people who have had a stroke	4		1		
I would have liked to have continued longer with the treatment				2	3

Table 26: Statements and responses from the Likert style questions

Open Questions:

The results of the participants' perceptions on the effectiveness of the intervention (questions 6-8) are presented in Table 24, divided into two categories: physical and functional effects.

Qn6: Are you now able to do things you could not do before? Please give examples		
Qn7: Are you able to do things better than you could before? Please give examples		
Qn8: Can you perform any two handed tasks more easily? Please give examples		
Category	Number of Responses	Example
Physical	7	'Hold arm above head when stretching'
Functional	9	'Open a bottle of wine'

Table 27: Open responses on system effectiveness

The results investigating how the participants think the system could be improved are presented in Table 28. To improve the task, the participants' responses were grouped into: more joints, motivational factors; differences to the treatment protocol; home exercises; and functional tasks. Suggested improvements to the system design were grouped into: more joints, modifications to the equipment and mobile systems. One participant wanted a more attractive system and one person found it difficult to be specific about any improvements. The most popular movements requested were those involving the hand and wrist.

Qn18: How do you think the task could be improved?		
Category	Number of Responses	Example
More Joints	4	'Hand and wrist with forearm'
Motivate	1	'Group work'
Treatments	2	'More treatments'
Home Exercises	2	'Would have liked something to do at home'
Function	2	'To pick up a cup would be major'
Qn22: If we could design the ideal system describe five features it should have		
Category	Number of Responses	Example
More Joints	3	'Help with fingers at the same time (if fingers don't work you can't use your arm)'
Equipment	2	'Better adjustments for a tall person (chair, arm adjustments)'
System	3	'Mobile equipment that could be used every day'
Aesthetics	1	'Look more attractive (looks off-putting)'
General	1	'It is difficult to be specific when there is little movement at the moment'
Qn23: If we could stimulate more muscles which movements would you like?		
Category	Number of Responses	Example
Hand / Wrist	5	'More hand movement'
Combined	2	'Gripping and lifting'
Shoulder	1	'Front of shoulder to be able to lift arm up'

Table 28: Open responses on how the system could be improved

The results from the general questions are presented in Table 29. Issues surrounding travel and time were viewed as the worst aspects of the study. The best aspects of the study were physical, psychological, being involved, researcher interaction, feedback and enjoyment. Fear of communication difficulties was an issue for one participant, however four out of five participants felt the questionnaire was easy to understand and answer.

Qn21a: What were the worst aspects of the study?		
Category	Number of Responses	Example
Travel	3	'Transport was difficult'
Time	4	'Having to come in every other day (very busy)'
Qn21b: What were the best aspects of the study?		
Qn24: Is there anything else you would like to add?		
Category	Number of Responses	Example
Physical Benefits	7	'Helped walking because arm moves back better, this has helped the gait, most important improvement.'
Psychological benefits	9	'The system gave you an example with your own arm to give you the feeling of it working properly'
Being involved	4	'Felt like they were taking part and not having things done to them' (comment by carer)
Researcher interaction	3	'Researchers were fun to be with and patient and friendly'
Feedback	2	'Could see and understand results'
Enjoyment	6	'Really enjoyed it'
Qn25: Can you comment on how easy this questionnaire was to understand and answer?		
Category	Number of Responses	Example
Communication	2	'Was worried about communication'
Ease	4	'Fine'

Table 29: Open general questions

4.3 Summary

This chapter has presented results from neurologically intact and stroke participants.

Key findings are summarised below.

For neurologically intact participants:

- Tracking error with voluntary movement (no ES) after three repetitions was shown to be similar to that produced by the ES (no voluntary movement) over four iterations.
- Isometric force was strongest in the 0° and weakest in the 60° directions
- EMG – A wide variation in muscle activation patterns, in terms of timing and amplitude, was observed between participants performing the same task. EMG amplitude increased significantly with length, duration and resistance of the task for all muscles except anterior deltoid. Co-activation between biceps and triceps was significantly dependent on both task and trajectory orientation. Activation pattern of pectoralis major was dependent on trajectory. Normal ranges of timing and amplitude of muscle activity during the tasks were identified.

For stroke participants:

- statistically significant changes were measured in FMA, unassisted tracking for three out of four trajectories and in isometric force over five out of six directions

(except 180). Changes in the ARAT were not demonstrated for stroke participants.

- Isometric force pre and post intervention was strongest in the 120° and weakest in the 60° directions. Largest gains were made in the 300° direction.
- Tracking error remained in a limited range (<15mm) whilst the ES required reduced over the intervention.
- EMG – Statistically significant differences were observed in the timing of peak muscle activity between stroke and neurologically intact participants (triceps, anterior deltoid, upper trapezius, middle trapezius and pectoralis major). Following the intervention a statistically significant change towards normal was observed in timing (triceps, pectoralis major and upper trapezius). Statistically significant differences were also observed in amplitude (biceps, pectoralis major, middle and lower trapezius) between stroke and neurologically intact participants. Following the intervention a statistically significant change towards normal was observed in amplitude (biceps and middle trapezius).
- Robot-assisted therapy was well accepted and tolerated by the patients. Patients' comments on the best aspects of the study could be separated into physical and psychological benefits, research interaction, being involved, feedback and enjoyment.

5 Discussion

This thesis reports an investigation into the feasibility of re-educating upper limb movement post stroke in a robotic workstation using ILC mediated by ES. The development of the intervention utilised certain motor learning principles: feedback (concurrent augmented and knowledge of results); practice conditions (variability, distribution, amount); and a goal oriented task. Other motor principles, such as knowledge of performance, whole or part practice, mental practice, and a functional goal oriented task, were not addressed. The empirical findings of this study provide answers to the study questions (outlined in Section 1.3) and in this chapter are interpreted within the context of existing literature. Limitations of the study, within which the results must be viewed, are outlined and the clinical implications of the findings are discussed. Additionally, future work based on motor learning principles is proposed.

5.1 Summary of the empirical findings

This study has identified changes in: clinical outcome measures, error tracking, isometric muscle force, percentage maximum level of stimulation required to correct error and muscle activation patterns in five chronic stroke participants as a result of an intervention using ILC mediated by ES. The intervention consisted of either 18 or 25 sessions during which participants practiced planar reaching tasks augmented by responsive ES of the triceps brachii muscle. After the intervention, participant perceptions of the ILC system and intervention were sought.

5.1.1 Changes in clinical outcome measures

The choice of the clinical measures in the study (FMA and ARAT) was validated by a recent review published subsequent to the study design (Kwakkel et al., 2008). A comparison between the baseline and post treatment for the FMA and the ARAT

showed that for all participants post treatment FMA scores improved, however, changes in the ARAT were minimal.

A statistically significant change was observed in the mean FMA (impairment), but not in the mean ARAT (activity) in Table 16. As the minimally clinically important difference (MCID) has been suggested to be 10% of the value of both scales (van der Lee et al., 2001a), neither showed a clinically relevant change. If impairment measures from an intervention show changes which do not have functional clinical relevance it could be posited that the intervention is not worthwhile. However it has been suggested in a review article covering 2000 hours of robot therapy with 76 stroke patients, that the coarse nature of clinical outcome measures fail to show details important for optimising therapy (Krebs et al., 2000). This view may of course reflect vested interests in commercial robots, but it is the opinion of the author (AMH) that changes in impairment measures illustrate changes occurring in the underlying neurophysiology and plasticity which demonstrate potential for change in clinical measures. The ILC intervention involved only stimulation of the triceps brachii muscle, during 2D tracking tasks requiring elbow and shoulder repetitive movement during which the forearm was supported. The clinical outcome measures used assessed unsupported shoulder and elbow movement and included hand tasks (especially in the ARAT) which were unlikely to be affected by the intervention.

Many of the existing studies have related variability in response to an intervention, to participants' initial FMA scores, with the aim of identifying future good and bad responders. With the limited number of participants in this study, there appears to be little relation between FMA percentage improvement post intervention (see Figure 34) and initial scores, with participant 1 showing the greatest FMA percentage improvement with the third highest initial score. However results (see 4.2.8) show that the participant with the lowest initial FMA showed substantial reductions in tracking error, isometric force and changes in timing of peak triceps activity. These findings are in contrast to results from previous studies (Ferraro et al., 2003; Stein et al., 2004) which identified a clear relationship between FMA improvement post intervention and initial scores; greatest improvements being seen in groups with initial mean FMA of 26 and over 20 respectively. Despite this, Stein suggested that rehabilitation robots are the only practical technique for providing exercise for patients with severe paresis because techniques such as constraint-induced movement therapy are not feasible for these individuals.

5.1.2 Changes in tracking error

The change in unassisted error tracking for all participants over all trajectories was not monotonic (reflecting individual variations in day to day motor control), but was significant for three out of the four trajectories (T1SS, T1MS, T2MS). When individual performance was observed, the participant with the lowest initial FMA score (participant 3) improved most in tracking across all trajectories (see Figure 36); this improvement in tracking was not reflected in either the FMA or ARAT outcome measures. Improved performance on the unassisted tracking tests was expected as the context between this and the assisted tracking practised during the intervention was very close and therefore the transfer of motor learning was good. A ceiling effect was observed for some participants and so these results may have implications for future stroke participant selection. The existing tasks have been demonstrated to be suitable for participants with an initial FMA of 12 or less, and more challenging tasks need to be developed for participants with an initial FMA higher than 12.

5.1.3 Directional variation in isometric force

Mean isometric force data were lower in all directions for stroke than neurologically intact participants (Table 21). The directional variation in stroke participants' isometric data (both baseline and post treatment) closely reflects the pattern of variation occurring in neurologically intact participants. This is true for all directions except for 0°, which was the second weakest direction for stroke participants and the strongest for neurologically intact participants. This might have been because triceps is activated more in the 0° direction. When other directions are considered, similarities emerge; the next strongest directions include 120°, 180° and 240°, then 300°. The weakest direction for all participants is 60°, which requires a degree of shoulder lateral rotation (known to be difficult for stroke patients). Differences in orientation appear therefore to have a large effect on the ability to generate isometric force in both groups.

All the participants' isometric force data increased (significantly for five out of six directions tested as shown in Table 21) over the 18 sessions and improved further over the extra 7 sessions as illustrated in Figure 39. The gain in force over the intervention might be predicted to be greatest in the 0° direction i.e. directly away from the body as triceps brachii was stimulated in the intervention; however, this

was not the case. The mean isometric force increased most in the direction of 300°, surprisingly then in 180° and then in the 0° direction; the gains were smallest in the direction in which participants were weakest (60°). Improvements in force reflected individual impairments including the side of hemiplegia.

This would imply that for the hemiplegic participants the gains in isometric force were most marked in directions requiring the use of pectoralis major, a powerful shoulder adductor as well as triceps brachii and biceps brachii. A change in triceps brachii force would be expected (either from the ES or from the repetitive practice), but the reason for a change in biceps brachii force is less clear. Co-activation, observed during motor learning, may increase joint stiffness and stability to improve performance. A future study could investigate whether increased activation of biceps brachii resulting from co-activation in the practice of new tasks leads to an increase in isometric muscle force.

5.1.4 Differences in EMG between neurologically intact and stroke participants, and changes in EMG in stroke participants in response to the intervention

Muscle activity can be described in terms of isometric, concentric or eccentric activity and examination of signals from multiple muscles can be used to identify co-activation; either between agonists and antagonists to increase joint stiffness and stability, or synergic activation where two or more muscles are active together to steer or reinforce a movement.

This study examined muscle activation patterns in terms of timing and amplitude in stroke and neurologically intact older participants. Differences between groups and pre and post an intervention, variability across the sample and differences due to trajectory orientation and task conditions were observed.

The difficulties in measuring EMG signals (for example in ensuring that skin impedance or placement of EMG electrodes is identical between participants at the same EMG assessment, and for individual participants between EMG assessments) mean that a process of normalisation has to be conducted to compare between different individuals' muscles or between the same muscles on different occasions. Different methods of normalisation can be used. In this study the timing and

amplitude of peak activity was compared across individual participants' muscles by dividing the processed EMG data by a maximum voluntary isometric contraction factor (individual to each muscle of each participant). The considerable variation in EMG data normalised to MVIC between participants for the same task and muscle prevented direct comparison of muscle activation patterns (strong people performing the same task as weaker people will use a lower percentage of their MVIC). Normalisation was therefore carried out for each EMG recording using the integrated EMG (I EMG) in this case (for further details see section 3.2.4) for coactivation data.

Significant increases in isometric force were only reflected in a significant increase in MVIC factor amplitude for triceps post intervention (reported in Table 22). During the trajectory reaching tasks post intervention, it might be expected that the normalised triceps amplitude would be significantly reduced (due to the significant increase in MVIC factor). This was not the case.

When individual participant's change in triceps amplitude was investigated, no clear relationship could be established between % change in peak amplitude towards normal and change in total error (m) when comparing across tasks (see Appendix J).

It might be expected that there would be no other significant reductions in amplitude. Changes in MVIC for biceps and middle trapezius, did not reach significance (during the MVIC). In the reaching tasks, tracking error was decreasing, and normalised amplitudes for biceps and middle trapezius were significantly reduced. These results might suggest that post intervention, the participants were more economical with their muscle activity in performing the same trajectory tracking task.

5.1.4.1 Amplitude of peak EMG

Statistically significant reductions in amplitude were observed between stroke and neurologically intact participants for: biceps, pectoralis major, middle and lower trapezius. Following the intervention a statistically significant change towards normal was observed in amplitude for biceps and middle trapezius.

In previous work, increased agonist EMG amplitudes were regarded as providing positive evidence for improved muscle activation patterns (Lum et al., 2004).

Following a rehabilitation robotic intervention no evidence was found of improved

muscle activation patterns in any of the table top movements, however increased activation of antagonists in two movement patterns (posterior deltoid and pectoralis major) was observed. It was not reported whether there were any significant decreases in antagonist EMGs.

The findings relating to amplitude from this ILC study, are similar to a study of seven chronic stroke participants (Hu et al., 2007). Hu reported a significant decrease in normalised EMG amplitudes of biceps brachii, triceps brachii and anterior deltoid after 20 robot assisted rehabilitation (which was associated with an improvement in tracking skill). Over activation of muscles during the initial period of motor learning for a skillful task, and / or spasticity were suggested by Hu as possible explanations for the initially higher amplitudes.

The authors of the above studies appear to disagree on whether improved muscle activation patterns post intervention are defined by an increase or decrease in amplitude (Hu et al., 2007; Lum et al., 2004). The EMG findings from the ILC study investigated both amplitude and timing. Amplitude at the wrong time (i.e. of triceps during the return) appears to be important. It is hypothesised that the demonstrated shift in the period during which 70% max activity threshold of triceps began and ended to earlier in the task (Figure 41), would lead to a reduction in amplitude of biceps during the return phase of movement, lowering the biceps amplitude level over the entire trajectory.

5.1.4.2 Timing of peak EMG

Statistically significant differences were observed in the timing of peak muscle activity between stroke and neurologically intact participants for: triceps, anterior deltoid, upper trapezius, middle trapezius and pectoralis major (see Table 23). Following the intervention a statistically significant change towards normal was observed in timing for triceps, pectoralis major and upper trapezius.

Triceps activity was investigated in greater depth as it was the muscle stimulated in the intervention. Stroke participants were found to have delays in initiation and termination of triceps activity compared to neurologically intact participants. This is illustrated for the T1 LFH task in Figure 41. After the intervention, the delay in initiation and termination can be seen to have reduced, so that the muscle activity more closely resembled that of the neurologically intact participants. Delays in initiation and termination of wrist flexors and extensors have been reported in

chronic stroke participants (Chae et al., 2002; Hammond et al., 1988). Chae reported a significant difference in delay of initiation and termination of flexor carpi radialis and extensor carpi radialis contraction between the paretic and nonparetic upper limbs of stroke survivors. In addition, a significant difference in delay of initiation and termination of those muscles was correlated significantly with upper limb motor impairment. Hammond investigated flexor carpi radialis and extensor carpi radialis longus (ECRL) and found that: i) both agonist and antagonist recruitment times were slower in paretic compared to healthy control forearms; and ii) the paretic ECRL showed the greatest impairment with a very long latency to contract.

The difference in delay in the flexor reflex response between paretic and nonparetic limbs have been reported to range between 10 and 40 ms in upper limb muscles including the biceps and triceps (Dewald et al., 1999). As a result of this, Chae suggested that the mechanism behind the delay in initiation was likely to be due to impairments in motor processing rather than efferent response (Chae et al., 2002). If this is applicable to triceps in this study, where the delay in initiation reduced as a result of the intervention, this would suggest that motor processing has become more efficient, possibly as a result of synaptic changes or increased cortical drive. This is supported by a study which used electroencephalography to identify prolonged cognitive planning time and elevated cognitive effort in stroke compared to neurologically intact participants during a 2D reaching task (Daly et al., 2006). Following a period of intense neurorehabilitation with three of the stroke participants there was a significant reduction towards normal in the cognitive planning time and effort. This might also have similar implications for rehabilitation of the hand.

When individual participant's change in triceps timing was investigated, no clear relationship could be established between % change in peak timing towards normal and change in total error (m) when comparing across tasks (see Appendix J).

5.1.4.3 Task dependent changes in muscle activation patterns for neurologically intact and stroke participants

An illustration showing how amplitude and temporal location of peak activity for the seven muscles under investigation varies with the task for neurologically intact participants is seen in Figure 31. As might be expected EMG amplitude is greater during the faster, longer tasks where there was greater resistance to the movement. This is especially obvious in the concentric activity of anterior deltoid and triceps during reaching. Temporal location of peak activity varied less with task conditions

but considerably with trajectory orientation and is most marked in pectoralis major, a powerful adductor of the humerus at the shoulder, where the muscle is active in the reaching component of T1 and T2, but not until maximum reach or the return component in T3. Comparison between T1 LFH and T3 LFH shows how temporal location of peak activity of pectoralis major is entirely trajectory orientation dependent (confirmed in Table 15). For the trajectories used, changing the orientation does not lead to a large change in joint movements required to perform the task. Relatively subtle differences in movements appear therefore to have a large effect on muscle activity and demonstrate the complexity of control even in a two dimensional supported task.

For neurologically intact participants for all tasks the reaching component is initiated by triceps and the return component completed by biceps, illustrated in Figure 33. T3 SSL illustrates in particular what was expected: triceps active on the reaching component, biceps on the return. The triceps and biceps activation patterns during the LFH tasks are examined in more detail for the stroke participants as these were the hardest tasks for them to perform. Figure 42 illustrates that pre intervention the reaching component is initiated by triceps (T2 LFH and T3 LFH) and completed by biceps for T3 LFH. Post intervention, the muscle activation patterns change to more closely reflect those seen by neurologically intact participants; the reaching component is initiated by triceps and the return component completed by biceps for T1, 2 and 3 LFH trajectory orientations. For all tasks co-activation is observed at maximum reach, where the direction of movement changed, and may provide stability and joint stiffness. When the elbow is extending, eccentric activity in biceps may also act as a brake to the extension movement (Saladin, 2004) however EMG alone is not able to distinguish between concentric, eccentric and co-activation.

5.1.4.4 Co-activation between biceps and triceps for neurologically intact and stroke participants

For pre intervention stroke compared to neurologically intact participants, co-activation was increased for eight out of the nine tasks (see Table 24). This increase in co-activation may have interfered with performance of the task. Data presented in tracking over four trajectories (T3SSL, T3 MMM, T2LFH and T3LFH), showed a significant increase in the percentage co-activation compared to the neurologically intact participants, with the T3 trajectory angle consistently showing more co-activation (which could be because the task was more difficult and so more effort was applied). For the SSL and MMM trajectories the minimum co-activation was for

the T2 trajectory angle. Post intervention the period during which co-activation is observed is related to the trajectory orientation (longest for T1 and shortest for T3), similar to the neurologically intact participants. It is possible that the T1 trajectory required more control, however, T1 was the first trajectory to be performed by all participants and what we observed may have been a consequence of motor learning and is discussed in section 5.2 (limitations of the study) and is a subject of further investigation. Although the trend was for a reduction in mean percentage co-activation between pre and post intervention, there were only two trajectories (T3MMM and T3LFH) where the reduction was significant.

Co-activation may increase joint stiffness and stability to improve performance, act as a brake to movement, or to fine tune movement. During motor learning co-activation has been shown to decrease with skill acquisition in neurologically intact participants during target reaching movements (Osu et al., 2002; Thoroughman & Shadmehr, 1999). Osu observed shoulder and elbow movement in the horizontal plane at the shoulder level and Thoroughman used a manipulandum which created systematic forces.

The results of the ILC study support work conducted with stroke participants (Hu et al., 2007) which found significant decreases in the co-activation of muscle pairs (triceps and posterior deltoid, biceps and triceps, biceps and anterior deltoid, anterior and posterior deltoid, triceps and anterior deltoid, and biceps and posterior deltoid) in all participants after a robot intervention.

5.1.5 Changes in percentage maximum ES

The ILC system was developed taking into account that the effect of ES is enhanced when associated with the participant's intention to move (De Kroon et al., 2005) and that to maximise plasticity, stroke participants need to work at their maximum effort in planning and executing tasks during rehabilitation interventions. Although systems have been developed in which electrical stimulation is triggered by muscle activity (Francisco et al., 1998), until now, techniques have not allowed feedback to adjust stimulation parameters during tasks. This is a drawback compared with the ability of the training modalities available during robotic assistance to promote voluntary activity. The ILC system adjusted the level of ES in response to the users' performance, in order to provide only the minimum level of stimulation needed to assist the participant in performing the task to a high level of accuracy. During the intervention, the error tracking remained within a limited range (<15mm) whilst the

ES required to achieve it reduced over the course of the intervention (see Figure 43). Thus, the balance of ES and voluntary effort required to perform the reaching task changed, with the participants proportionally contributing greater voluntary movement, indicating motor learning had occurred.

It has been suggested that mechanisms for the recovery of voluntary power after using ES are due to effects on peripheral muscle such as: strength, fitness, length and spasticity or central mechanisms: cortical or segmental reorganisation and modification of Hebb synapses (Rushton, 2003). Cortical reorganisation includes: expansion of movement representations within the motor cortex; more synapses per neuron; and increased synaptic density within the motor cortex. Neuroscience supports the importance of coinciding voluntary activation times with ES as modifications of the synaptic strengths in horizontal connections in the motor cortex and synaptogenesis have been shown to underlie functional modifications in the motor cortex of animals during skill learning and may apply to stroke patients.

Hebb's rule states that synapses between two neurons become stronger if both of the neurons are activated at the same time. It is also likely that the proximity of the synapses will also have an effect. The cellular substrates of learning are the mechanisms which bring about synaptic modification either increasing (LTP) or decreasing (LTD) synaptic strength. LTP (Hebbian) is the coincidence of pre synaptic NT (glutamate) release and postsynaptic neuron depolarisation. An increase in the sensitivity of NT receptors, and release of NTs occurs resulting in subsequent stimuli eliciting a larger response for a few hours. Longer term changes in synaptic modification require the synthesis of proteins (Longstaff, 2005). Changes in NTs and responses therefore, are not fixed, but dependent on those which have occurred previously. Towards the end of the study, as a participant tried to track a trajectory, a weak activation of a synapse would have generated a greater release of NTs and a larger response than at the beginning of the study.

5.1.6 Participant perceptions

The aim of this study was to provide an insight into the participant perspectives of the ILC system (an evaluation) and also their ideas on how the system could be improved (addressing user requirements). There is at present, however, no generic evaluation tool available to be used across different rehabilitation robot systems. In view of this participant comments were recorded during the intervention sessions and then a question set was developed to explore effectiveness, acceptability and

usability of the ILC system. The question set was administered by a health psychologist to the five stroke participants, and was found to be easy to interpret.

The findings from this study using a robotic workstation and ES were congruent with other studies (Coote & Stokes, 2003; Doornbosch et al., 2007; Krebs et al., 1998); robot-assisted therapy was well accepted and tolerated by the patients. Patients' comments on the best aspects of the study could be separated into physical and psychological benefits, research interaction, being involved, feedback and enjoyment.

Although neither of the clinical measures used showed a clinically relevant change, the questions during the intervention and the structured interview provided evidence (from both the Likert style questions and open questions) that some of the stroke participants observed changes in impairments and function which were meaningful to them in their lives. Reasons for this could include: that the clinical measures are not sensitive enough to detect change, or that people are more likely to feel better and present a positive view as they are taking part in an exciting research study (see section 5.2.2). This demonstrates the importance of assessing benefits from the users' perspectives as well as using objective, applied outcome measures.

It is recognised that there are two direct end users of rehabilitation robotics (patients and therapists), as well as indirect users e.g. rehabilitation managers, consultants and budget holders. It is salient to investigate stakeholders' (both direct and indirect) perceptions of rehabilitation robots to ensure effective technology transfer. This is discussed under future work.

5.1.7 Summary

A discussion of the empirical findings of the ILC study has put the results into the context of the extant literature. Whilst there was no significant improvement for the stroke participants in the activity measure (ARAT) post intervention, it was found that improvements in impairment measures (isometric force, tracking error) were associated with a change towards more normal EMG patterns. When individual participant's results were viewed it was evident that the relationship is complex. Evidence from other studies suggest improvements in impairments could result from effects on peripheral muscles and / or central mechanisms.

5.2 Limitations of the study

The results obtained from this feasibility study have to be interpreted whilst acknowledging the limitations of the study. The limitations were minimised where possible by using standardised procedures, or where this was not possible, were identified as topics to be addressed in future work.

The small number of participants resulted in limited strength of the clinical and statistical findings and, as there was no control group, the degree to which the observed changes were related to movement practice or to ILC mediated by ES cannot be separated. Future trials would address this limitation by having a control group using the robot without electrical stimulation and increasing the robotic assistance to provide similar levels of tracking accuracy.

5.2.1 EMG measurement and muscle activation patterns

It is difficult to ensure that the placement of EMG electrodes is identical between participants at the same EMG assessment, and for individual participants over time (between EMG assessments), which could influence the individual values of muscle amplitudes and timings. This was minimised by ensuring that a standard procedure was followed and using the same clinician for each EMG collection assessment.

Muscle activity may vary not only with task, but also with practice and consequent motor learning or fatigue. The results of this study show that overlap between biceps and triceps decreased from T1 to T2 to T3 for neurologically intact and stroke participants post intervention. Since each participant performed the same three tracking tasks three times in each of the three positions in the same order, the degree to which the observed reduction in co-activation was related to task or to motor learning cannot be separated. The lack of randomization means that it is not possible to determine what is an order effect and what is a condition effect. Fatigue may also have influenced performance and EMG amplitude or timing but was minimised by allowing participants to rest between trajectories. Both these potential sources of bias would be addressed by performing the trajectories in a random order. A further limitation of the study is the possibility that contralateral muscle activity influenced muscle activity in the dominant, tested arm. Although this potential confounding variable was addressed by asking the participants to relax, and to position the contralateral arm in a resting position, because EMG signals

were not recorded from the contralateral arm, absence of contralateral activity could not be confirmed.

5.2.2 Participant perceptions

The purpose designed set of questions was developed to gain an insight into users' perceptions of the system. The results of the perception study have to be interpreted with caution due to the possible influence of social desirability bias, defined as a tendency to overestimate desirable traits and underestimate undesirable traits when using self report measures (Nederhof, 1985). This was minimised by including Likert scale items in the question set and the independence of the interviewer (a health psychologist experienced in conducting interviews) from the clinical study. There were some problems with the questions that were asked, for example, some participants found it confusing when the statement was read out in the first person, negative statements were difficult for some of the participants to understand, and sometimes carers would try and answer for the participant. The researcher in this study ensured that it was primarily participants' views that were recorded.

5.3 Clinical implications of the study

Active assisted or partially facilitated exercises are recommended clinically in the UK for stroke patients who are unable to move by themselves (Edwards, 2002; Jackson, 2004). To measure the effectiveness of such techniques, physiotherapists are more likely to use activity or participant based outcome measures, which explain how effective an intervention has been (which may be more relevant to the patient). Impairment based measures, however, which normally require more equipment, explain why these changes are being seen.

The impairment based results of this study may provide insights into changes in isometric force and muscle activation patterns which are occurring during active assisted upper limb exercises during rehabilitation. In post-stroke hemiplegia abnormal EMG patterns were observed in timing, amplitude and co-activation during supported reaching. In this group of participants, difficulty in elbow extension during supported reaching was associated with significantly increased (but not premature) peak activity in biceps and a delay in the peak activation of triceps (not low peak triceps EMG amplitude) which both became significantly more normal over the course of the intervention. The return component was characterised by changes towards normal in the timing of upper trapezius and pectoralis major and an amplitude changes of biceps and middle trapezius towards normal.

These changes were detected over a relatively short period of intervention and may have potential as a useful sensitive outcome measure revealing an individual's rehabilitation potential before clinical changes are observed. If a strong association is found between latency changes and improved performance, future research could focus on interventions which most effectively target and lead to changes in the latency.

Additionally the stroke participants' responses to the question set developed in this study are suggestive of how other people with a stroke may perceive combinations of ES and rehabilitation robots in rehabilitation. The question set could be used as a starting point for clinicians and researchers to assess patient (and other users) responses to different types of technology.

This research would suggest that stroke participants with a severe FMA score will benefit from this treatment in terms of error tracking and improved isometric force, with associated changes in timing and amplitude of triceps and biceps respectively. It is not clear who would benefit most in terms of FMA but it is suggested that participants with some hand function would show greater gains on the ARAT from this treatment.

The results of this feasibility study demonstrated significant improvements in unassisted error tracking, isometric force and reduction of impairments as measured on the upper limb FMA motor scale as well as a wide variation in EMG activity across participants. Additionally the stroke participants accepted and tolerated the intervention well. The results add weight to the growing body of evidence that suggests that robotic or ES interventions can be used both to provide objective assessments (before, during and after an intervention), as well as being an accepted and well tolerated treatment which results in changes in impairment levels.

5.4 Future research related to the study

The findings of the ILC study have demonstrated benefits in using qualitative, in addition to quantitative methods of study design. To develop effective usable novel rehabilitation systems to be used in patients' homes and clinics, as well as in laboratories, future research needs to integrate both quantitative and qualitative methods.

5.4.1 Interpretation of results and sample size calculation

The number of tests of significance used on the stroke participants was 138 of which 62 were significant to a level of 0.05. This suggests that 7 results may have occurred due to chance alone.

As the data were reused for testing several hypotheses, the Bonferroni correction could have been applied to adjust p-values to reduce the risk of Type 1 error.

However, after applying this methodology interpretation of a finding depends on the number of other tests performed, and the likelihood of type II errors is increased, so that truly important differences are deemed non-significant. In view of these weaknesses is it suggested that by “simply describing what tests of significance have been performed, and why, is generally the best way of dealing with multiple comparisons” (Perneger 1998). The primary objective of this study was to test the feasibility of using iterative learning control in upper limb stroke rehabilitation. The design of the intervention was optimised to encourage motor learning within the constraint of the primary objective. The analyses of the results of this exploratory study were performed to provide a basis on which future studies could be designed. If the Bonferroni corrections had been applied there would have been a risk that truly important differences would have been found to be non significant, and so would not have been investigated in a follow up study.

In calculating the required sample size for a follow on study, the three key outcome measures considered were the ARAT and FMA (motor) scores and tracking error. There was no improvement in ARAT score ($p=0.60$). The ARAT outcome measure requires hand function, and it is considered that as the intervention focused on shoulder and elbow movement it would not be a suitable outcome measure to assess the intervention in a subsequent study, so a power calculation was not performed. The present study ($n=5$) was adequately powered to demonstrate a statistically significant improvement in FMA (motor) score ($p=0.02$) (Table 19). Sample size calculations were computed (using PS Program Power and Sample Size Calculation) for FMA and unassisted tracking error using effect size and standard deviation results from the present study.

The calculations were repeated using a conservative model which included the assumptions that the effect size would be halved, the standard deviation doubled, and allowing for a 10% drop out rate. All sample size calculations were based on

80% power and alpha=0.05. The number of participants required in each scenario is displayed in Table 30. Using the conservative model (figures in shaded rows), it is estimated that 136 participants should be recruited into a subsequent study when unassisted tracking error is used as the primary outcome measure.

Values	Effect size	SD	Estimated number of participants
FMA	2.5	1.58	5
FMA	1.25	3.16	17
Unassisted tracking error	-0.0016	0.0015	10
Unassisted tracking error	-0.0008	0.0030	136

Shaded rows denote conservative model

Table 30: Estimated number of participants required for each effect size and SD assumption

5.4.2 Motor impairments and activities

In the light of findings from the participant perception study, the first changes will be to make it easier to place stroke participants' arms in the arm holder and to clarify the graphical display of performance. As this was a feasibility study, data were collected from only a few neurologically intact and stroke participants. To provide a more precise characterisation of reaching and to verify the impairment results the intervention would clearly need to be applied to a larger sample of participants.

To be able to assess the degree to which the observed changes were related to movement practice or to ILC mediated by ES, a trial would include a control group using the robot without electrical stimulation and increasing the robotic assistance to provide similar levels of tracking accuracy. In order to explore further the relationship between muscle activity in response to trajectory orientation and task condition, EMG electrodes will be used to measure muscle activation patterns whilst the participant tries to track the moving target. This time however the order in which the tasks are attempted will be randomized to eliminate any learning effects.

Further investigations need to use a larger sample size to increase understanding of the relationships of muscle activation patterns (and how they differ after a stroke and post intervention). This will require investigations into the mechanisms behind latent initiation of agonists. Additionally the relationships between changes in muscle

activation and other impairments (such as isometric force) and clinical measures of improved performance need to be clarified. Future work will investigate the extent to which the change in the performance of the task is due to changing muscle activation patterns, or whether more accurate performance led to more normal muscle activation or whether there is any correlation between the two.

Muscle weakness has been found to be the main contributor to activity limitation in other studies (Ada et al., 2006). The improvements in isometric force and reductions in other impairments have not however translated into clinically relevant improvements as measured by the ARAT and the FMA in this feasibility study. Long term extensions to this research will involve broadening the movement range further, increasing the number of stimulated muscles including the anterior deltoid and, in particular, incorporating wrist and hand function in accordance with the wishes most requested by the stroke participants. This will require relaxing the horizontal forearm constraint to allow a greater range of movement. Stimulating more muscles will present considerable ILC challenges, due to the complex interaction between muscles and different rates at which muscles will fatigue. Furthermore, functional tasks will involve point to point trajectories possibly with no predefined trajectories, and the added complexity of adapting to different natural movement speeds. It will present the problem of how to choose the most efficient way to assist a participant in performing a task, stimulating just the right number of muscles.

For severely affected stroke participants an improvement in shoulder and elbow activity without the hand is not likely to result in significant improvements in activities of daily living. If the opportunity for recovery is limited i.e. the competition for real estate (Krebs et al., 2007b) is happening, it is the opinion of the author (AMH) that better function can be obtained firstly by improving movement of the hand to be able to grasp and release using functional goal oriented tasks. This would enable the complicated tasks of reaching and grasping to be practiced in isolation.

Robots are now being developed for hand therapy (Kawasaki et al., 2007; Masia et al., 2006), however few studies are reporting clinical results, possibly due to the complexity of human hand movement (15 joints and 22 degrees of freedom). Recent work reporting robot based hand motor therapy with 13 chronic stroke patients using HWARD, a 3 degree of freedom, pneumatically actuated device that assists the hand in grasp and release movements resulted in significant gains in the ARAT and

FMA (Takahashi et al., 2008). The grasping task practised during robotic therapy, when performed during fMRI, showed increased sensorimotor cortex activation, while a non practised task did not.

Evidence suggests that movements which are practised the most, improve the most. It is the opinion of the author (AMH) that the next stage of arm rehabilitation should focus on hand function during supported reaching, with the patient receiving the minimum amount of assistance to enable them to complete the task. This would facilitate maximum sensory input via the muscle spindles and golgi tendon organs before the participant also has to support the arm. This is currently being trialled in an A-B B-A blinded cross over study (Loureiro & Harwin, 2007) using Gentle/G. Reach, grasp, transfer and release movement sequences are used; phase A comprised 16 hours of robot therapy in addition to their normal therapy; and phase B comprised normal therapy. Early results showed a positive result from the robot therapy (Harwin, 2008).

Finally, it is the opinion of the author that this training should then be followed by a further 18 hours progressively decreasing upper limb support during reaching with hand function during goal oriented tasks. It has been shown that the amount of elbow extension would decrease (Beer et al., 2004). Mechanical devices such as the ARMEO (Housman et al., 2007) provide opportunities for this to occur, but at present the level of support has to be manually adjusted and there is no component for practising release of grasp.

Ideally these would be longitudinal studies using repeated measures to understand how movement patterns change during and after robotic assisted therapies as well as imaging techniques to assess whether changes associated with the intervention are occurring at a central level (cortical or spinal level or both) or a peripheral level or both (e.g. using TMS to measure motor evoked potentials).

5.4.3 User requirements and evaluation tools

The findings from the question set in this study reported participant evaluations of the ILC system (well accepted and tolerated) as well as participant perceptions of what they wanted from a system (more therapy, mobile system and home exercises).

Accurate user requirements and evaluations will lead to improved quality and functionality of new rehabilitation robots and robot training programmes, thereby making the rehabilitation of stroke patients with hemiplegia easier and more comfortable for both the patient and the therapist. That users need to contribute to design has long been recognised in the field of human computer interaction (Nielsen, 1993). Some benefits of user involvement have been summarised as being: improved quality of the system arising from more accurate user requirements, avoiding costly system features that the user did not want or cannot use, improved levels of acceptance of the system and a greater understanding of the system by the user resulting in more effective use (Damodaran, 1996). It has been suggested that technical advances have up until now dominated the published literature and that the fundamentals of robotic design need also to consider psychological and social factors (Kiesler & Hinds, 2004).

5.4.3.1 Development of user requirements and evaluation tools

As there has been very little research investigating and reporting people's views of rehabilitation robots a qualitative study is called for, to provide an in-depth level of insight through directly exploring people's beliefs and opinions (Flick, 2002). This could investigate perspectives of potential users of upper limb robotic devices. In the future, as the number of people who have used novel systems increase, another qualitative study could be used to investigate users' beliefs and opinions of the novel systems, allowing comparisons to be made across devices. It is acknowledged that with a qualitative study there is a possibility that people with communication problems would be disadvantaged. Views would have to be sought from people who could express themselves and these could then be developed into user requirement and user evaluation questionnaires.

The end result of such investigations would be clear guidance for researchers, research funders, healthcare professionals and providers, and commercial organisations, based on the opinions of users. This would inform the future research and development of these devices and increase uptake through service provision and clinical adherence.

5.5 Summary

This section has discussed the empirical findings which provide answers to the original study objective and questions. The changes in the clinical outcome

measures section (FMA) demonstrated the feasibility of re-educating upper limb movement post stroke using ILC mediated by ES using a robotic workstation. Differences between stroke and neurologically intact participants have been identified in isometric force, kinematic measures and muscle activation patterns for upper limb muscles during identified specific reaching tasks using a robot arm. Changes in these measures for stroke participants in response to the intervention have been discussed, with possible mechanisms. The stroke participants' perceptions of the system have been outlined along with the limitations of the study.

The relevance of the work to physiotherapeutic practice of active assisted movements, and the use of the ILC system as both an assessment and treatment tool have been discussed. The possibility of changes in EMG, isometric force and tracking being used as outcome measures which are more sensitive than existing clinical measures at demonstrating possible rehabilitation potential has been suggested. The future research section outlined both quantitative and qualitative short and long term work directly related to motor learning principles and this study.

6 Conclusion

A novel rehabilitation method using ILC mediated by ES, has been tested with chronic stroke participants during supported planar tracking tasks. The level of ES used was adjusted in response to the user's performance at tracking trajectories, and was found to decrease over the course of the intervention. ILC produced an input which used all the previous errors made by the participants, in order to compensate for the error expected during the subsequent trial. Compliance with the intervention was excellent. The results of the study demonstrated significant improvements in unassisted error tracking for three out of four trajectories: T1SS, T1MS, T2M2 and T2SS (p values = 0.03, 0.03, 0.05, 0.08 respectively); significant mean improvements of isometric force for five out of six directions: 0° (12.82N, p=0.04) , 60° (4.58N, p=0.02), 120° (11.13N, p=0.02), 180° (13.21N, p=0.07), 240° (11.05N, p=0.02) and 300 (18.11N, p <0.01); significant reduction of impairments as measured on the upper limb FMA (p=0.02). Greatest improvements in tracking were seen in participants with the lowest initial FM score. The study results also demonstrated that the level of FES used by each participant when performing the tracking tasks decreased over time, whilst similar levels of tracking accuracy were maintained, indicating that the participants were increasing their voluntary input over the intervention. Neither clinical outcome measure (FMA and ARAT) however, showed a clinically relevant change. Despite this, participants' comments both during intervention sessions and in the semi structured interview subsequent to the study, revealed that they had experienced some functional benefits from participating. This may reflect a lack of sensitivity in the clinical outcome measures used.

Novel methods of characterizing muscle activation patterns have been presented and shown the following for neurologically intact participants: triceps and anterior

deltoid were most active during the reaching component of all tasks; pectoralis major was active during reaching when the trajectory demanded shoulder adduction and in the return component when it demanded shoulder adduction; biceps, upper, middle and lower trapezius were most active during the return component on all tasks. The variation in activity in response to trajectory orientation and task condition has been determined for each muscle tested. Co-activation between biceps and triceps was found to be task and trajectory orientation dependent, but the effect of learning cannot be ignored. Stroke participants differed significantly from neurologically intact participants in terms of both the timings of peak muscle activity (triceps, anterior deltoid, upper and middle trapezius and pectoralis major) and amplitude (biceps, middle and lower trapezius and pectoralis major). After the intervention timings of peak muscle activity (triceps, upper trapezius and pectoralis major) and amplitude (biceps and middle trapezius) significantly changed towards normal. Co-activation between biceps and triceps was also found to be trajectory orientation dependent. After intervention the stroke participants' coactivation patterns more closely reflected those of neurologically intact participants, but again the effect of learning cannot be ignored.

This research has demonstrated the efficacy of the processing and analysis techniques used, the practicality of the data collection procedures and the clarity of the methods used to represent the results. Statistical analysis has confirmed that significant patterns exist in the muscle activation data which can form a basis for comparison between those of neurologically intact and those of stroke participants.

7 Appendices

A Muscles of the shoulder and elbow

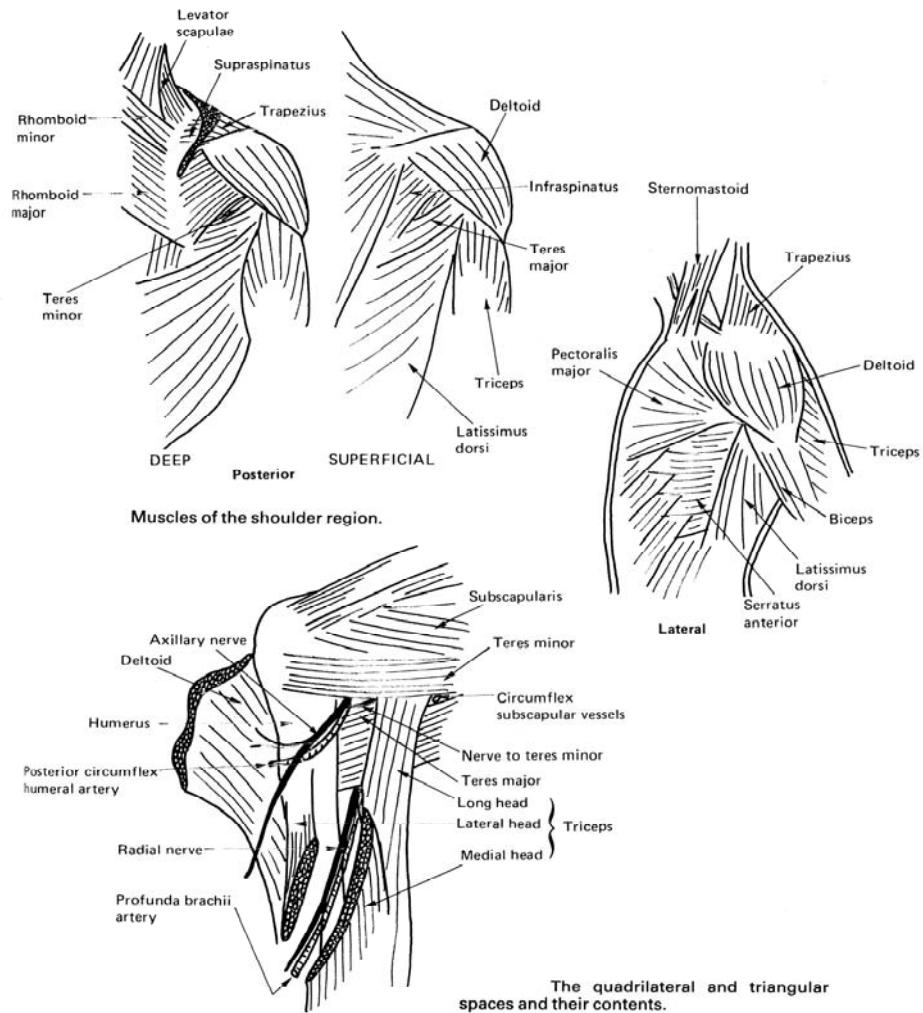


Figure 50: Muscles surrounding the shoulder (Palastanga et al., 1998)

Copyright of Elsevier reproduced with permission

B Current neurorehabilitation approaches

- The Bobath concept, also known as neurodevelopmental treatment (NDT) within the USA, was developed by Karel and Bertha Bobath. It is one of the most widely used approaches in stroke rehabilitation within Europe (Lennon et al, 2001). It aims to improve recovery of the hemiplegic side by focusing on normalising both tone and movement patterns using specialist handling techniques, preferably within real life situations.
- Proprioceptive Neuromuscular Facilitation was developed by Knott and Voss between 1946 and 1951. The aim is to facilitate a motor response by using maximum resistance, normal patterns of movement, using maximum proprioceptive and tactile sensory input and progressing activities in a developmental sequence.
- Motor Re-learning was developed by Carr and Shepherd in the 1980s. They shifted away from exercise and facilitation towards controlling movement using information from fields such as neurophysiology, psychology of learning, biomechanics and movement science. The emphasis of the technique is on elimination of unnecessary movement, feedback, repetition and the link between postural adjustment and movement.

C Information sources

Searches were conducted across the OVID databases: Amed (1985-2005), Cinahl (1982-2005), Embase (1980-2005) and Medline (1966 – 2005). Additional information was found by searching PEDRO, and COCHRANE and liaising with companies and teams involved in research in the UK, Ireland, and the Massachusetts Institute of Technology in the US (a world leader in the field).

D Papers included by Prange (2006), Teasell (2007) Kwakkel (2008) and Mehrholz (2008)

Authors *	Robot / Mechanical Device	Year	(Prange et al, 2006)	(Teasell et al, 2007)	Kwakkel et al 2008	Mehrholz et al 2008
Aisen et al.	MIT -Manus	1997			x	
Volpe et al.	MIT -Manus	1999		x		
Burgar et al.	MIME	2000		x	x	
Kahn et al.	ARM	2000			x	
Volpe et al	MIT -Manus	2000		x	x	x
Krebs et al.	MIT -Manus	2000	x			
Reinkensmeyer et al.	ARM	2000	x			
Lum et al.	MIME	2002	x	x	x	x
Fasoli et al.	MIT -Manus	2003		x		x
Ferraro et al.	MIT -Manus	2003	x	x		
Hesse et al.	Bi-Manu-Track	2003		x		
Fasoli et al.	MIT -Manus	2004	x	x	x	
Krebs et al.	MIT -Manus	2004	x			
Lum et al.	MIME	2004	x			
Stein et al.	MIT -Manus	2004	x	x		
Volpe et al.	CPM device	2004		x		
Daly et al.	InMOTION	2005		x	x	x
Finley et al.	MIT -Manus	2005		x		
Hesse et al.	Bi-Manu-Track	2005		x	x	x
MacClellan et al.	MIT -Manus	2005		x		
Kahn et al.	ARM	2006		x	x	x
Lum et al.	MIME	2006		x	x	x
Masiero et al.	Ne-Re-Bot	2006		x		
Amirabdollahian et al.	GENTLE/s	2007				x

Authors *	Robot / Mechanical Device	Year	(Prange et al, 2006)	(Teasell et al, 2007)	Kwakkel et al 2008	Mehrholz et al 2008
Fazekas et al.	REHA-ROB	2007				x
Masiero et al.	Ne-Re-Bot	2007		x		x
Patel et al.	MIME	2007		x		
Volpe et al.	InMOTION2	2008				x
Coote et al	GENTLE/s	2008		x		
Total			8	20	10	11

* References not included in Chapter 8, may be found in the referenced reviews

E Differences between the normal physiological system and external stimulation of nerves

Type of Stimulation	Direction of impulse	Recruitment of motor neurones	Fibre type recruitment	Frequency to achieve smooth muscle contraction	Variables	Fibre Changes
Physiological	Orthodromic	Small diameter fire first then larger	Type 1 oxidative – Slow	3-25 Hz nerve frequency	Frequency and timing of impulse No of units stimulated The synaptic connections made by the nerve units	Type II glycolytic convert to Type 1 oxidative over months
Electrical	Orthodromic Antidromic	All motor units supplied by the nerve fibres will fire concurrently but large diameter recruited first due to proximity	Type II glycolytic – Fast fatiguable	25-40Hz external stimulation frequency	Current Voltage Pulse Width Frequency Wave form	Type II glycolytic convert to Type 1 oxidative over months

F Force sensor calibration data

JR3
Multi-Axis Load Cell Technologies

**FORCE-MOMENT SENSOR SYSTEM
SPECIFICATION SHEET**

JR3, Inc.
22 Harter Avenue
Woodland, CA 95776
(530) 661-3677
Fax (530) 661-3701
e-mail: jr3@jr3.com

1dec05

200N Analog calibration.

JR3 Sensor Model No. 67M25A3-I40S-A 200N12 Ser. No. 3090

Electrical Load Settings	Sensor Load Ratings	Calibration Loads used
Fx 200 N	222 N	50.0 lbs
Fy 200 N	222 N	50.0 lbs
Fz 400 N	445 N	100.0 lbs
Mx 12 NM	14.86 NM	110.0 in-lbs
My 12 NM	14.86 NM	110.0 in-lbs
Mz 12 NM	14.86 NM	110.0 in-lbs

Calibration Matrix: Multiply the calibration matrix and the sensor Voltage vector to determine the loads (N and NM).

X Axis through screw hole

84.302	4.405	3.679	1.188	4.546	-2.386
-0.824	81.362	-2.856	4.032	-6.521	-1.812
-13.199	11.844	167.838	2.055	-1.216	-27.699
0.142	-0.077	-0.003	5.567	0.611	0.485
-0.209	0.489	0.040	-0.437	5.555	-0.572
-0.018	-0.087	0.104	-0.239	0.055	5.643

Fx Volts
Fy Volts
Fz Volts
Mx Volts
My Volts
Mz Volts

Connector Contact Layout (face view)

1 2 3 4 5
6 7 8 9
DE9P

Pin 1 Fx	Final Inspection:	Calibration Date	<u>28 Nov 05</u>
Pin 2 Fy		Calibration Matrix	/
Pin 3 Fz		Axis Orientation	/
Pin 4 Mx		Units N & NM	/
Pin 5 My		Hardware Correct	/
Pin 6 Mz		Label Correct	/
Pin 7 +8V (+7V to +15V)		Functional Test	/
Pin 8 -8V (-7V to -15V)		Inspection Date	<u>2 Dec 05</u>
Pin 9 Common		Inspector Initial	<u>JR</u>

G Participant perception questionnaire

Participant Perceptions Questionnaire for the Iterative Learning Control (ILC) System

Introduction: Thank you for agreeing to participate in this interview. We want to find out your views on the ILC system so please answer as openly and fully as possible, as it will help us to improve systems for the future. Remember that the person interviewing you is not personally involved in the project and that your name will not be put on the interview sheet so your responses will remain anonymous.

Please indicate the extent to which you agree or disagree with the following statements.

Please note that these statements and questions ask about the effect of the course of the treatment not individual sessions

A. System Effectiveness

I am now more aware of my affected arm

Strongly disagree Disagree Undecided Agree Strongly agree

My arm feels weaker

Strongly disagree Disagree Undecided Agree Strongly agree

My arm feels tighter

Strongly disagree Disagree Undecided Agree Strongly agree

I can reach out with my arm more easily

Strongly disagree Disagree Undecided Agree Strongly agree

I can now pick up objects

Strongly disagree Disagree Undecided Agree Strongly agree

Are you now able to do things that you could not do before?

YES / NO

Please give examples

Are you now able to do things better than you could before?

YES / NO

Please give examples

Can you now perform any two handed tasks more easily?

YES / NO

Please give examples

B. System Usability

I did not find the treatment enjoyable

Strongly disagree Disagree Undecided Agree Strongly agree

It was easy to understand what I had to do

Strongly disagree Disagree Undecided Agree Strongly agree

It was difficult to put my arm in the arm holder

Strongly disagree Disagree Undecided Agree Strongly agree

The arm holder was comfortable

Strongly disagree Disagree Undecided Agree Strongly agree

The stimulation was uncomfortable

Strongly disagree Disagree Undecided Agree Strongly agree

The target was easy to see

Strongly disagree Disagree Undecided Agree Strongly agree

I did not understand the graphs showing my performance

Strongly disagree Disagree Undecided Agree Strongly agree

C. Questions about how the system could be improved

Adding games would add to my motivation and enjoyment of the treatment

Strongly disagree Disagree Undecided Agree Strongly agree

I would not like to have more arm muscles stimulated

Strongly disagree Disagree Undecided Agree Strongly agree

How do you think the task could be improved?

D. General Questions

I would not recommend the treatment to other people who have had a stroke

Strongly disagree Disagree Undecided Agree Strongly agree

I would have liked to have continued longer with the treatment

Strongly disagree Disagree Undecided Agree Strongly agree

Looking back on it, was taking part in this study worthwhile for you?

YES / NO

What were the worst aspects of it?

What were the best aspects of it?

E. Dreamtime

If we could design the ideal system describe five features it should have:

If we could stimulate more muscles which movements would you like?

Is there anything else you would like to add?

Can you comment on how easy this questionnaire was to understand and answer?

Please thank the participant

H Participants' responses to open questions

SYSTEM EFFECTIVENESS

Question 6: Are you able to do things now that you could not do before? Please give examples

P#	Response 1	Response 2	Response 3	Response 4
01	Can move arm back-less painful and feels stronger			
03	Stronger muscles so able to lift	Able to grip things – hold on to bottles (as long as no fingers required)		
04	Hold arm out to get T shirt on	Keep arm straight to open a bottle of wine	Hold arm above head when stretching	
05	Leaning back	Movement upwards	Pushing forward	Reaching out

Question 7: Are you able to do things better than you could before? Please give examples

P#	Response 1	Response 2	Response 3	Response 4
04	Putting on a T shirt			

Question 8: Can you perform any two handed task more easily? Please give examples

P#	Response 1	Response 2	Response 3	Response 4
01	Can cuddle			
04	Opening a bottle of wine	Hold things e.g zip on trousers		

HOW THE SYSTEM COULD BE IMPROVED

Question 18: How do you think the task could be improved?

P#	Response 1	Response 2	Response 3	Response 4
02	More manipulation with wrist	Making hand work	Group work to motivate	
03	Hand and wrist together with forearm	Complete arm		
05	Longer treatments	More treatments		

GENERAL QUESTIONS

Question 21: What were the worst aspects of the study?

P#	Response 1	Response 2	Response 3	Response 4
01	Nothing about study	Transport was difficult		
02	Finding the travel	Problems finding someone to drive		
03	Time	Having to come in every other day (very busy)	Would have liked to do something at home	Stimulation at home whilst in armchair (Personal ES)
04	Being the first patients- the researchers were a little unprepared. Towards the end it was better as they knew the system (guesswork to start)	Couple of wasted journeys as Chris was needed and they needed to wait for him	Not too bad as they didn't have far to come	

Question 22: What were the best aspects of the study?

P#	Response 1	Response 2	Response 3	Response 4	Response 5	Response 6
01	The researchers help and motivation	The science – finding out and being part of research that may help others (even if this wasn't himself)	Knowing that equipment he finds useful is being tested by others	When nobody was helping or felt no more improvement, it was good that people still thought they could help	The arm has come back to being part of his body and has increased awareness (not just about function) Made him more in touch and caring about his arm	Gave him confidence to do something by himself
02	Meeting other people in the same situation (but didn't mix much – weekly meeting would be nice). Only met in corridor	The researchers were helpful and patient				
03	Found it effective	Helped walking because arm moves back better, this has helped the gait, most important improvement.				
04	Seeing the results	Researchers were fun to be with and patient and friendly				
05	Really enjoyed it	Liked AM and that someone was taking an interest	Range of tests gave an accurate assessment of what arm could do (very interesting)	Could see and understand results	Could see improvement	

DREAMTIME

Question 22: If we could design the ideal system describe five features it should have:

P#	Response 1	Response 2	Response 3	Response 4
01	Look at the problems with arm and leg together	Any improvement in function would help	It is difficult to be specific when there is little movement at the moment	To pick a cup up would be major
02	The system made your arm work and showed you how far to go	System gave you an example with your own arm to give you the feeling of it working properly	Better chair that didn't wobble	
03	Help with fingers at the same time (if fingers don't work can't use your arm)	Help with wrist	Likes the thought of games	Perhaps music
04	Look more attractive (looks off putting)			
05	Better adjustments for a tall person (chair, arm adjustments)	Mobile equipment that could be used everyday	Equipment helps motivate	Equipment increases commitment

Question 23: If we could stimulate more muscles which movements would you like:

P#	Response 1	Response 2	Response 3	Response 4	Response 5
01	Any				
02	Holding	Gripping and lifting	More hand movement	Grasping and lifting	
03	To be able to put (reach) elbow	Move fingers and wrist			
04	Front of shoulder to be able to lift arm up				
05	Hand grip movement	Stiff fingers – would help with being more open / relaxed			

Question 24: Is there anything else you would like to add?

P#	Response 1	Response 2	Response 3	Response 4	Response 5	Response 6	Response 7
01	Any help						
02	Enjoyed whole experience	It was not hurried	It was a pleasant experience				
05	Enjoyed it	Sorry when it stopped	Got very positive results	Very positive experience	Good for them as being proactive as difficult to get NHS	Nice to know taking part in something that would help others	Feels like they were taking part and not having things done to them

Question 25: Can you comment on how easy this questionnaire was to understand and answer?

P#	Response 1	Response 2	Response 3	Response 4	Response 5	Response 6	Response 7
01	Was worried about communication	Was also worried this would stop him being in the study					
02	Fine						
03	Easy						
04	Fine						
05	Fine						

I Categories for responses to open questions

Question 6: Are you able to do things you could not do before? Please give examples

Physical

Move arm back (01)
Feels stronger (01)
Leaning back (05)
Keep arm straight (04)
Hold arm above head when stretching (04)
Movement upwards (05)

Pain

Less painful (01)

Functional

Able to lift (03)
Hold arm out to get T-shirt on (04)
Able to grip things (03)
Hold on to bottles (as long as no fingers required) (03)
Open a bottle of wine (04)
Pushing forwards (05)
Reaching out (05)

Question 7: Are you able to do things better than you could before? Please give examples

Functional

Putting on a T-shirt (04)

Question 8: Can you perform any two handed task more easily? Please give examples

Functional

Can cuddle (01)
Opening bottle of wine (04)
Hold things e.g. zip on trousers (04)

Question 18 How do you think the task could be improved?

More joints

More manipulation with wrist (02)
Making hand work (02)
Hand and wrist with forearm (03)
Complete arm (03)

Motivate

Group work (02)

Treatments

Longer treatments (05)
More treatments (05)

Question 21 What were the worst aspects of the study?

Travel

Transport was difficult (01)
Problems finding someone to drive (02)
Not too bad as they did not have far to come (04)

Time

Time (03)

Having to come in every other day (very busy) (03)

Couple of wasted journeys as Chris was needed and they needed to wait for him (04)

Home ex

Would have liked something to do at home (03)

Stimulation at home whilst in arm chair (personal ES) (03)

Frustration

Being the first patients – the researchers were a little unprepared. Towards the end it was better as they knew the system (guesswork to start) (04)

Question 22: What were the best aspects of the study?

Physical benefits

The arm has come back to being part of his body and has increased awareness (not just about function). Made him more in touch and caring about his arm (01)

Found it effective (03)

Helped walking because arm moves back better, this has helped the gait, most important improvement. (03)

Could see improvements (05)

Psychological benefits

The researchers help aid motivation (01)

Knowing that the equipment he finds useful is being tested by others (01)

When nobody was helping or felt no more improvement, it was good that people still thought they could help (01)

Being involved

The science - finding out and being part of research that may help others (even if this wasn't himself) (01)

Meeting other people in the same situation (but didn't mix much- weekly meeting would be nice). Only met in corridor (02)

The researchers were helpful and patient (02)

Researchers were fun to be with and patient and friendly (04)

Liked AM and that someone was taking an interest (05)

Feedback

Seeing the results (04)

Could see and understand results (05)

Enjoyment

Really enjoyed it (05)

Assessment

Range of tests gave an accurate assessment of what arm could do (very interesting) (05)

Question 22: If we could design the ideal system describe five features it should have

More joints

Look at the problems of arm and leg together (01)

Help with fingers at the same time (if fingers don't work you can't use your arm) (03)

Help with wrist (03)

Function

Any improvement in function would help (01)

To pick up a cup would be major (01)

General

It is difficult to be specific when there is little movement at the moment (01)

The system made your arm work and showed you how far to go (02)

Equipment

Better chair that didn't wobble (02)

Better adjustments for a tall person (chair, arm adjustments)

System

Likes the thought of games (03)

Perhaps music (03)

Mobile equipment that could be used every day (05)

Aesthetics

Look more attractive (looks off-putting) (04)

Psychological

The system gave you an example with your own arm to give you the feeling of it working properly (02)

Equipment helps motivate (05)

Equipment increases commitment (05)

Question 23: If we could stimulate more muscles which movements would you like?

General

Any (01)

Hand/Wrist

Holding (02)

More hand movement (02)

Move fingers and wrist (03)

Hand grip movement (05)

Stiff fingers – would help with being more open / relaxed (05)

Combined

Gripping and lifting (02)

Grasping and lifting (02)

Elbow

To be able to put elbow (03)

Shoulder

Front of shoulder to be able to lift arm up (04)

Question 24: Is there anything else you would like to add?

General

It was not hurried (02)

Enjoy

Enjoyed whole experience (02)

It was a pleasant experience (02)

Enjoyed it (05)

Psychological

Very positive experience (05)

Sorry when it stopped (05)

Good for them as being proactive as difficult to get NHS (05)

Involved

Feels like they were taking part and not having things done to them (05)

Nice to know taking part in something that would help others (05)

Physical

Got very positive results (05)

Question 25: Can you comment on how easy this questionnaire was to understand and answer?

Communication

Was worried about communication (01)

Was also worried this would stop him being in the study (01)

Ease

Fine (02) (04) (05)

Easy (03)

J EMG and tracking error changes for each participant for each task

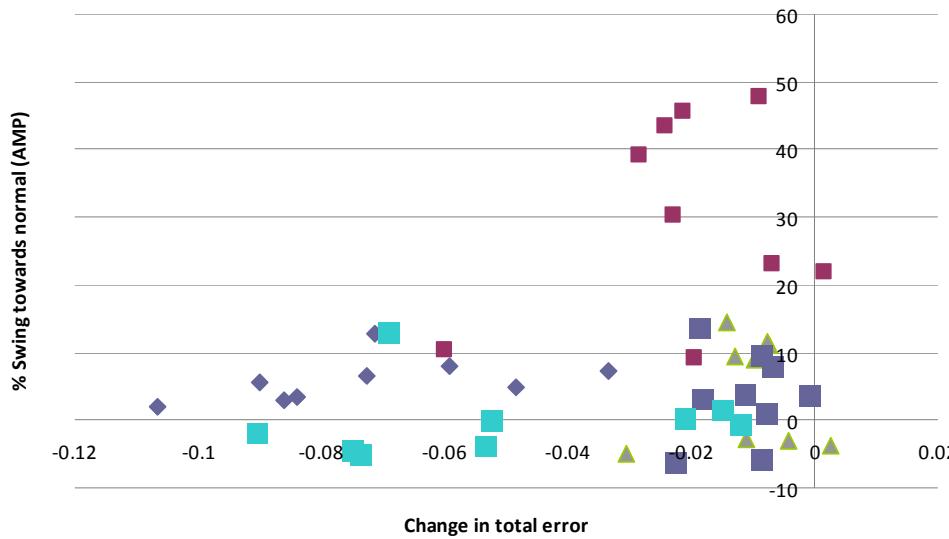


Figure 51: % change in peak amplitude towards normal for triceps against change in total error (m) for each participant for each task

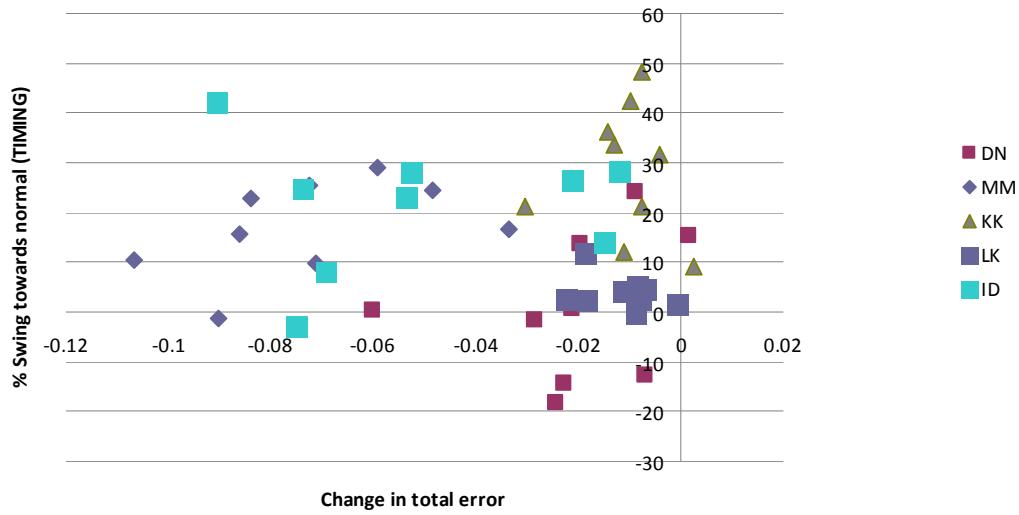


Figure 52: % change in peak timing towards normal for triceps against change in total error (m) for each participant for each task

K Ethics and insurance forms

Neurologically intact study: participant information sheet, consent form, final approval for ethics and insurance

Stroke participants: participant information sheet, consent form, final approval for ethics, amended ethics approval (for extra 7 sessions) and insurance and insurance to cover amendments

Participant perception study: participant information sheet, consent form, final approval for ethics and insurance

PARTICIPANT INFORMATION SHEET

A project measuring arm movement in people without impairment, to provide information for the design of a system to control electrical stimulation in the treatment of people who have had a stroke

**Dr J. Burridge¹, Professor E. Rogers², Dr P. Lewin², Dr P. Chappell²,
Dr C. Freeman², A. Hughes¹**

¹School of Health Professions and Rehabilitation Sciences

²School of Electronics and Computer Science

University of Southampton

Highfield

Southampton

SO17 1BJ

1. Introduction

I am a Research Fellow at the University of Southampton and I would like to invite you to participate in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and your GP if you wish. If something is not clear, or you would like more information, please do not hesitate to contact me. Take time to decide whether or not you wish to take part.

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

Thank you for reading this.

2. What is the purpose of this study?

All movements are dependant on the correct muscles being used in a specific pattern at the correct time. After a stroke these movement patterns are altered, so many people have problems in regaining the use of their arm. It is essential that treatment for them is as effective as possible. Research has shown that using robots or electrical stimulation as therapy can be more beneficial than conventional treatment alone. No work has yet been done on combining the 2 approaches, to see if they could have a cumulative effect on recovery of function.

The anticipated total duration of this study is for 6 months. The main purpose is to provide information that can be used in the study with people who have had a stroke. The first visit will generate information on which muscles will need to be stimulated and in what way, with both the elbow movement unrestricted by tape, and then restricted by tape. The second and third visits will be used to create a mathematical model of your arm being controlled by electrical stimulation (ES) again both with and without tape. The fourth visit will provide information on how effective the robot can be at controlling movement in a reaching task using electrical stimulation whilst the elbow movement is unrestricted by tape and then restricted by tape.

3. Why have I been chosen?

In this research project we have chosen 10 people to be studied. You have been chosen because you are a healthy adult over 50 years old. Please note that you will not be able to take part if you have an allergy to sticking plasters/tape or alcohol cleansing wipes, or have any implanted devices.

4. Do I have to take part?

It is up to you to decide whether or not to participate. If you decide to participate, you will be given this information sheet to keep and asked to sign a consent form. You will be given a copy of the information sheet and a signed consent form to keep. You are still free to withdraw at any time and without giving a reason.

5. What will happen to me if I take part?

If you return the attached form saying you are interested in taking part then you will be contacted by Ann-Marie Hughes, who will answer any questions you may have. A visit to Laboratory 1 in the School of Health Professions and Rehabilitation Sciences (Building 45) at the University of Southampton will be arranged at a time to suit you. You will be asked to attend the Laboratory a further two times within 2 weeks and then about 1 month later. The visits should last no longer than 2 hours.

For all the visits you will need to wear a top with straps over the shoulder, so that the equipment to be used can be appropriately placed on your skin. During the visits you will be offered opportunities to rest between the different tests.

We intend to use a cross sectional observational research method. This means that we will repeat the same procedure and gather the same information on each participant.

Visit 1

On arrival, you will be shown the equipment and the procedures will be explained to you again. If you are happy to continue, you will be asked to sign a consent form and some basic measurements of your body will be taken.

You will then be asked to sit keeping your back against the chair, in front of a table as in Figure 1. You will place your arm in the robot arm. A light will be shining from above the table. There will be a target disc located on the hand grip. The aim will be for you to move your arm forward in different directions, at different speeds, trying to keep the light shining on the centre of the target disc. In between each reaching movement you will be required to rest. You can stop at any time if you become tired. The researcher will then apply tape over your elbow to make movement a little more difficult. The reaching movements will then be repeated.

Visits 2 and 3

In these visits you will be asked to place your arm into the robot arm and to relax. Your arm will be moved by the robot through different directions and speeds. Measurements will then be taken to choose the appropriate electrical stimulation for 2 of your muscles in turn. Your arm will then be moved in the robot arm through different directions and speeds, whilst using the stimulation. Following this, the researcher will apply tape over your elbow to make movement a little more difficult. The reaching movements will then be repeated.

Visit 4

On the fourth visit, you will again be asked to place your arm into the robot arm and to relax. Your arm will be moved by electrical stimulation alone over a number of different directions. The researcher will then apply tape over your elbow to make straightening your elbow more difficult. The reaching movements will be repeated.

Please see Fig 1 for the set up of the robot.

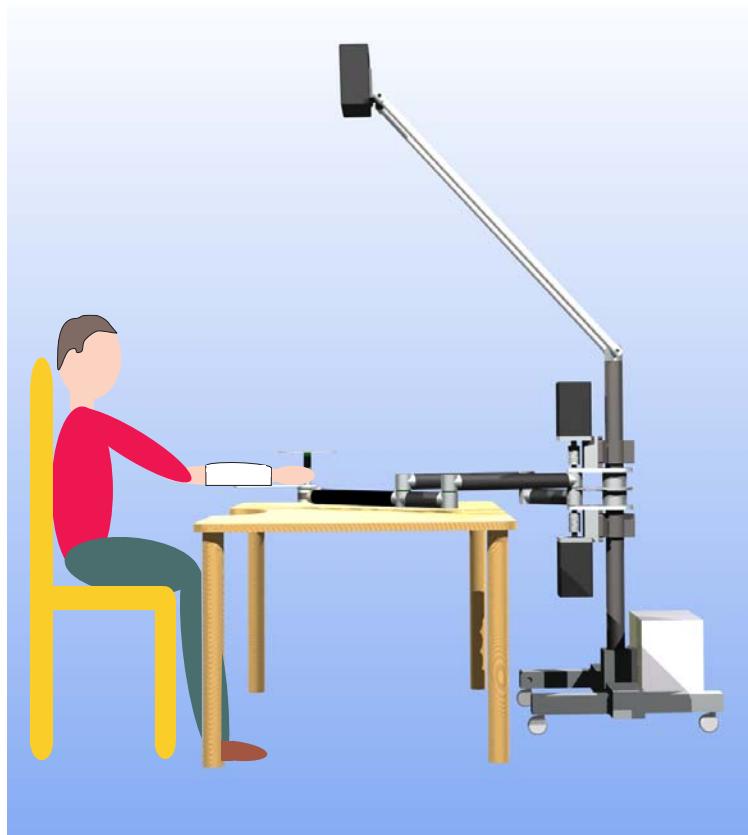


Figure 1 – Participant sitting using the robot

6. What do I have to do?

There are no lifestyle restrictions involved in taking part in this study.

7. What is The Procedure being Tested?

The procedure being tested is to assess whether the electrical stimulation of nerves can be automatically adjusted to optimise improvement in the way a person performs a task.

8. What are the side effects, disadvantages or risks of taking part?

There are unlikely to be any side effects. You may find that there is a slightly uncomfortable pins and needle sensation during the electrical stimulation (second and third visits). There are no disadvantages or risks involved in taking part.

9. What are the possible benefits of taking part?

There will be no direct benefit to you from taking part in the study. However the data collected will be fundamental to our research with people who have had a stroke, and it is hoped that this will lead to future improvements in their rehabilitation.

10. What if something goes wrong?

If you become uncomfortable or distressed during the session you will be offered assistance there and then by the research team.

In the unlikely event that you are harmed by taking part in this research, or if you have any concerns about any aspect of the way you have been approached or treated during the course of this study, the University of Southampton complaints procedures are open to you. If you wish to make a complaint please contact Dr Jane Burridge on 023 8059 8885 at the University of Southampton.

11. Will my taking part in this study be kept confidential?

Information collected about you during the course of this research will be kept strictly confidential. Any information about you which is used in research reports or publications will have your name and contact details removed so that you cannot be recognised from it.

12. What will happen to the results of the research?

On completion of the research the data collected will be securely stored at the University of Southampton for 15 years according to the University policy. The results will be used to inform research with people who have had a stroke. These results will be presented at conferences and may be published in research papers for scientific journals. If you would like a copy of the published results at the end of the study please let us know.

13. Who is organising the research and funding the study?

The study is organised through the University of Southampton and is a joint venture between the Schools of Health Professions and Rehabilitation Sciences and Electronics and Computer Science. It is being funded by the Engineering and Physical Sciences Research Council.

14. Who has reviewed the study?

The project is being submitted to the School of Health Professions and Rehabilitation Sciences Ethics Committee.

15. Contact for further information:

If you would like any further information, please contact:

Ann-Marie Hughes: Research Fellow, School of Health Professions and Rehabilitation Sciences, University of Southampton, SO17 1BJ

Telephone: 023 8059 5191

Email: A.Hughes@soton.ac.uk

Thank you again for taking the time to read this information



**University
of Southampton**

Email: jhb1.ac.uk
Secretary: 023 8059 8927

School of Health Professions & Rehabilitation

Dr Jane Burridge
University of Southampton
Highfield
Southampton
SO17 1BJ
United Kingdom
Tel +44 (0)23 8059 2142
Admissions +44 (0)23 8059 5260
Fax +44 (0)23 8059 5301
Email sotpadm@soton.ac.uk
Web www.sohp.soton.ac.uk/sohp/

Participant Identification Number:

Participant Consent Form

**Iterative learning control for re-education of upper limb function
mediated by Functional Electrical Stimulation in Healthy Adults**

Principal Investigator: Dr Jane Burridge
Research Fellow: Ann-Marie Hughes
School of Health Profession
and Rehabilitation Sciences
University of Southampton
Highfield
SOUTHAMPTON
Tel: 023 8059 8885
Tel: 023 8059 5191

Please initial box

1. I confirm that I have read and understand the information sheet dated 06/01/06 for the above study and have had the opportunity to ask questions.
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
3. I confirm that I have no known allergies to alcohol or sticking plaster
4. I confirm that I do not have any implanted devices
5. I agree to the storing and processing of my information for the purposes of the research.
6. I agree to take part in the above study

Name of Participant _____

Date _____

Signature _____

Researcher _____

Date _____

Signature _____



13 January 2006

Anne-Marie Hughes
 School of Health Professions
 University of Southampton

Dear Anne-Marie

Submission No: SO5-12/1

Title: Identification of activation patterns in reaching

I am pleased to confirm **full approval** for your study has now been given. The approval has been granted by the School of Health Professions and Rehabilitation Sciences Ethics Committee.

You are required to complete a University Research Governance Form (enclosed) in order to receive insurance clearance before you begin data collection. You need to submit the following documentation in a plastic wallet to Dr Martina Dorward in the Research Support Office (RSO, University of Southampton, Highfield Campus, Bldg. 37, Southampton SO17 1BJ):

- Completed Research Governance form (**signed by both student and supervisor**)
- Copy of your research protocol (final and approved version)
- Copy of participant information sheet
- Copy of SoHPRS Risk Assessment form, **signed by yourself and supervisor** (original should be with Zena Galbraith)
- Copy of your information sheet and consent form
- Copy of this SoHPRS Ethical approval letter

Your project will be registered at the RSO, and then automatically transferred to the Finance Department for insurance cover. **You can not commence data collection until you have received a letter stating that you have received insurance clearance.**

Please note that you have ethics approval only for the project described in your submission. If you want to change any aspect of your project (e.g., recruitment or data collection) you must discuss this with your supervisor and you may need to request permission from the Ethics Committee.

Yours sincerely

Dr Emma Stack
 Chair, SHPRS Ethics Committee
 Enc.



**University
of Southampton** | **Finance
Department**

Memorandum

From: Ruth McFadyen

To: Dr Jane Burridge

Ext: 22417

Dept: School of Health Professions and
Rehabilitation Sciences

E-mail: hrm@soton.ac.uk

Date: 15 December 2005

Reference: HRM/GFT

Professional Indemnity Insurance

Project No: TBA

Iterative Learning Control for Re-Education of Upper Limb Function Mediated by Functional Electrical Stimulation in Healthy Adults

Thank you for forwarding the completed insurance questionnaire for this project.

Having taken note of the information provided, I can confirm that this project will be covered under the terms and conditions of the above policy, subject to written consent being obtained from the participating volunteers and the project receiving Ethics Committee approval.

Please forward a copy of the Ethics Committee approval letter as soon as it is to hand to complete the insurance placement. Receipt of the letter will activate the insurance and the project may not commence prior to this.

Ruth M. Miller

Ruth McFadyen
Insurance Services Manager

PARTICIPANT INFORMATION SHEET

A project measuring arm movement using a system to control electrical stimulation in the treatment of people who have had a stroke

**Dr J. Burridge¹, Professor E. Rogers², Dr P. Lewin², Dr P. Chappell²,
Dr C. Freeman², A. Hughes¹**

¹School of Health Professions and Rehabilitation Sciences

²School of Electronics and Computer Science

University of Southampton

Highfield

Southampton

SO17 1BJ

1. Introduction

I am a Research Fellow at the University of Southampton and I would like to invite you to participate in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and your GP if you wish. If something is not clear, or you would like more information, please do not hesitate to contact me. Take time to decide whether or not you wish to take part.

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

Thank you for reading this.

2. What is the purpose of this study?

Movements are dependant on appropriate muscles being used in a specific pattern at the right time. After a stroke these movement patterns are altered, so many people have problems in regaining the use of their arm. Research has shown that using robots or electrical stimulation as therapy can be more beneficial than conventional treatment alone. No work has yet been done on combining the 2 approaches, to see if they could have a cumulative effect on recovery of function. The anticipated total duration of this study is 6 months. A previous study has provided us with information on which muscles will need to be stimulated and in what way, created a mathematical model of arms being controlled by electrical stimulation (ES), and looked at the effectiveness of the robot at controlling movement in a reaching task using electrical stimulation. The purpose of this study is see how effectively this information can be used in the treatment of people with a stroke.

3. Why have I been invited to take part?

In this research project we have chosen between 5 and 10 people to be studied. You have been invited to take part because you have had a stroke which has resulted in you having difficulty using your arm. Please note that you will not be able to take part if you have an allergy to sticking plasters/tape or alcohol cleansing wipes, or have any implanted devices, such as pacemakers.

4. Do I have to take part?

It is up to you to decide whether or not to participate. If you decide to participate, you will be given this information sheet to keep and asked to sign a consent form. You will be given a copy of the information sheet and a signed consent form to keep. You are still free to withdraw at any time and without giving a reason.

5. What will happen to me if I take part?

If you return the attached form saying you are interested in taking part, you will be contacted by Ann-Marie Hughes, who will answer any questions you may have, and invite you to attend a discussion meeting at the University of Southampton. If you are willing to be involved in the project you will be asked to sign a consent sheet. Screening tests will also be carried out at this stage. You will then be invited back for up to five preliminary test sessions at Laboratory 1 in the School of Health Professions and Rehabilitation Sciences (Building 45) at the University of

Southampton. These will be arranged at a time to suit you. The results of these tests will be looked at, and then if appropriate, you will be asked to attend the Laboratory for two clinical assessments one month apart. This will then be followed by three treatment sessions of 1 hour each week for 6 weeks. At the end of this time a further two assessment tests will be conducted. The preliminary tests and assessment sessions should last no longer than 3 hours. For all the sessions you will need to wear a top with straps over the shoulder, so that the equipment to be used can be appropriately placed on your skin. During the sessions you will be offered opportunities to rest between the different tests.

We intend to use a cross sectional observational research method. This means that we will repeat the same procedure and gather the same information on each participant.

We may be contacted by the media, who may wish to interview you and take photographs or video recordings for publication or transmission via the media. This will be entirely voluntary, will not affect your participation in the study and you can withdraw from this at any time. If you decide to be involved with the media, you can choose if you wish to be identified by your real name or by an alternative name.

5.1 Preliminary Tests

On arrival, you will be shown the equipment and the procedures will be explained to you again. Some basic measurements of your shoulder and arm will be taken. In this session you will be asked to place your arm into the robot arm and to relax. Your arm will be moved by the robot through different directions and speeds. Measurements will then be taken to choose the appropriate electrical stimulation for up to 2 of your muscles in turn. Your arm will then be moved in the robot arm through different directions and speeds, whilst using the stimulation. Your arm will then be moved by electrical stimulation alone over a number of different directions and the reaching movements will be repeated.

In the next test we will put some electromyographic electrodes on some muscles around your back, shoulder and arm (these are rather like the sticky pads used to measure your heart beat). We will then ask you to make some movements, and we will take some readings from your muscles. You will then be asked to sit keeping your back against the chair, in front of a table as in Figure 1. You will place your affected arm in the robot arm. A light will be shining from above the table. There will be a target disc located on the hand grip. The aim will be for you to move your arm forward in different directions, at different speeds, trying to keep the light shining on the centre of the target disc. In between each reaching movement you will be required to rest. You can stop at any time if you become tired. The reaching movements will then be repeated.

The following tests will be as before, but you will also be asked to try and track the trajectory yourself, whilst the robot arm assists you using the electrical stimulation.

5.2 Assessments

These will take place twice before the treatment sessions, one month apart and then after the treatment sessions again, along with the electromyographic electrode measurement. Two different tests will be conducted to assess your ability to perform different tasks. While undertaking these tests we would like to record your movements using video and photographs. This will enable us to check our scoring of the tests at a later date, and may be used for educational or scientific purposes, in which case your identity will be obscured. You will be fully clothed during the filming or photographs, which will be taken by either the research fellows or a technician in Laboratory 1. The recording of video and photographs is optional.

5.3 Treatment Sessions 1-18

In the treatment sessions 1-18 you will be asked to come in to Lab 1 to use the robot for one hour. You will be asked to place your affected arm into the robot arm. Two electrodes will then be attached to the back of your arm. The aim will be for you to move your arm forward in different directions, at different speeds, trying to keep the light shining on the centre of the target disc. You will be assisted by the stimulation. As you repeat the task, the stimulation will be reduced. In between each reaching movement you will be required to rest. You can stop at any time if you become tired.

Please see Fig 1 for the set up of the robot.

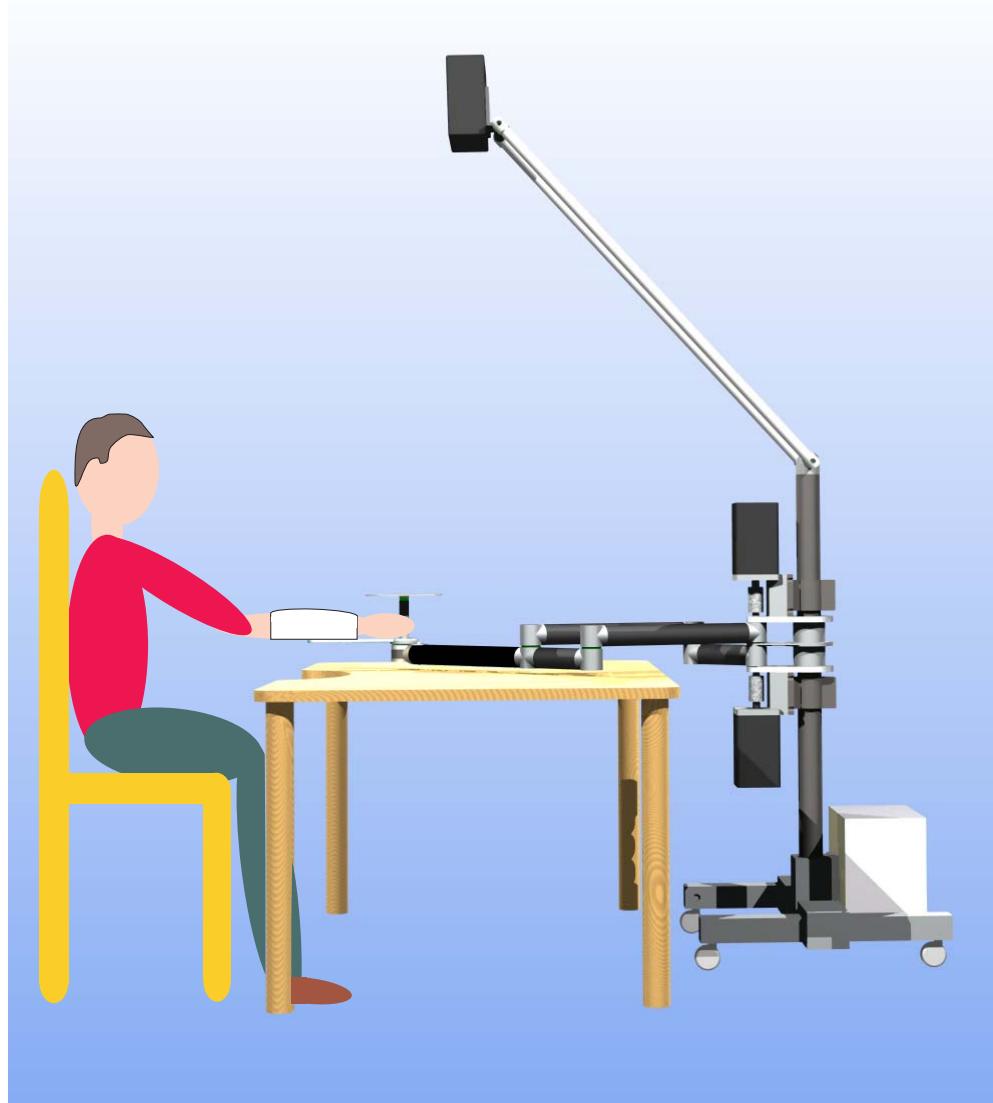


Figure 1 – Participant sitting using the robot

6. What do I have to do?

There are no lifestyle restrictions involved in taking part in this study.

7. What is The Procedure being Tested?

The procedure being tested is to assess whether the electrical stimulation of nerves can be automatically adjusted to optimise improvement in the way a person who has had a stroke performs a task and to see if there is a clinical benefit to the treatment.

8. What are the side effects, disadvantages or risks of taking part?

There are unlikely to be any side effects. You may find that there is a slightly uncomfortable pins and needle sensation during the electrical stimulation. There are no disadvantages or risks involved in taking part.

9. What are the possible benefits of taking part?

This is a preliminary study and we do not know whether there will be direct benefit to you from taking part in the study. However the data collected will be fundamental to our research with people who have had a stroke, and it is hoped that this will lead to future improvements in rehabilitation.

10. What if something goes wrong?

If you become uncomfortable or distressed during the session you will be offered assistance there and then by the research team.

In the unlikely event that you are harmed by taking part in this research, or if you have any concerns about any aspect of the way you have been approached or treated during the course of this study, the University of Southampton complaints procedures are open to you. If you wish to make a complaint please contact Dr Jane Burridge on 023 8059 8885 at the University of Southampton.

11. Will my taking part in this study be kept confidential?

Information collected about you during the course of this research will be kept strictly confidential. Any information about you which is used in research reports or publications will have your name and contact details removed so that you cannot be recognised from it.

12. What will happen to the results of the research?

On completion of the research the data collected will be securely stored at the University of Southampton for 15 years according to the University policy. The results will be used to inform research with people who have had a stroke. These results will be presented at conferences and may be published in research papers for scientific journals. If you would like a copy of the published results at the end of the study please let us know.

13. Who is organising the research and funding the study?

The study is organised through the University of Southampton and is a joint venture between the Schools of Health Professions and Rehabilitation Sciences and Electronics and Computer Science. It is being funded by the Engineering and Physical Sciences Research Council.

14. Who has reviewed the study?

The project is being submitted to the School of Health Professions and Rehabilitation Sciences Ethics Committee.

15. Contact for further information:

If you would like any further information, please contact:

Ann-Marie Hughes: Research Fellow, School of Health Professions and
Rehabilitation Sciences, University of Southampton, SO17 1BJ

Telephone: 023 8059 5191

Email: A.Hughes@soton.ac.uk

Thank you again for taking the time to read this
information



University
of Southampton

Email: jhb1.ac.uk
Secretary: 023 8059 8927

School of Health Professions & Rehabilitation

Dr Jane Burridge
University of Southampton
Highfield
Southampton
SO17 1BJ
United Kingdom

Tel +44 (0)23 8059 2142
Admissions +44 (0)23 8059 5260
Fax +44 (0)23 8059 5301
Email sotpadm@soton.ac.uk
Web www.sohp.soton.ac.uk/sohp/

Participant Consent Form

Iterative learning control for re-education of upper limb function mediated by Functional Electrical Stimulation in people who have had a stroke

Principal Investigator: Dr Jane Burridge Tel: 023 8059 8885
Research Fellow: Ann-Marie Hughes Tel: 023 8059 5191
Address: School of Health Profession and Rehabilitation Sciences,
University of Southampton, Highfield, SOUTHAMPTON

Please initial box

1. I confirm that I have read and understand the information sheet dated 13/09/07 for the above study and have had the opportunity to ask questions.
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
3. I confirm that I have no known allergies to alcohol wipes or sticking plaster
4. I confirm that I do not have any implanted devices, such as a pacemaker
5. I agree to the storing and processing of my information for the purposes of the research.
6. I agree to being recorded on video and photographs being taken for research purposes
7. I agree to being recorded on video and photographs being taken for teaching / presentation purposes.
8. I agree to take part in the above study
9. I agree to being filmed during an interview, recorded on video and photographs being taken for publicity purposes.
10. I choose to be identified in the publicity material by my first name / by a false name (please underline your choice)

Name of Participant

Date

Signature

Researcher

Date

Signature

Participant consent form v 6 12/09/07
ILC Project - Ethics Number: SO7/04-01

1 for participant; 1 for researcher



18 June 2007

Anne-Marie Hughes
 School of Health Professions and Rehabilitation Sciences
 University of Southampton

Dear Anne-Marie

Submission No: SO7/04-01

Title: Robotic training for Stroke patients' arms

I am pleased to confirm **full approval** for your study has now been given. The approval has been granted by the School of Health Professions and Rehabilitation Sciences Ethics Committee

You are required to complete a University Research Governance Form (enclosed) in order to receive insurance clearance before you begin data collection. You need to submit the following documentation in a plastic wallet to Dr Martina Dorward in the Research Support Office (RSO, University of Southampton, Highfield Campus, Bldg. 37, Southampton SO17 1BJ):

- Completed Research Governance form
- Copy of your research protocol (final and approved version)
- Copy of participant information sheet
- Copy of SoHPRS Risk Assessment form, (original should be with Zena Galbraith)
- Copy of your information sheet and consent form
- Copy of this SoHPRS Ethical approval letter

Your project will be registered at the RSO, and then automatically transferred to the Finance Department for insurance cover. **You can not commence data collection until you have received a letter stating that you have received insurance clearance.**

Please note that you have ethics approval only for the project described in your submission. If you want to change any aspect of your project (e.g., recruitment or data collection) you must discuss this with your supervisor and you may need to request permission from the Ethics Committee.

Yours sincerely

Dr Emma Stack
 Chair, SHPRS Ethics Committee
 Enc.



**University
of Southampton**

School of Health Professions and Rehabilitation Sciences

Dr Paula Kersten, Head of School

University of Southampton Tel +44 (0)23 8059 2142
Highfield Fax +44 (0)23 8059 5301
Southampton Web www.sohp.soton.ac.uk/shprs/
SO17 1BJ
United Kingdom

8 January 2008

Anne-Marie Hughes
School of Health Professions and Rehabilitation Sciences
University of Southampton

Dear Anne-Marie

Submission No: SO7/04-01

**Title: Iterative Learning Control for the re-education of upper limb
function mediated by functional electrical stimulation in stroke
patients**

Short title: Robotic training for Stroke patients' arms

Thank you for requesting an amendment to the above research project. The rationale for extending the number of treatment sessions, followed by final assessment to determine whether improvements continue, is justified. The new consent form and the amendments to the information sheet are appropriate.

The extension to this study is therefore approved. Please now request an extension for the insurance cover.

**Please note that you have ethics approval only for the project described in
your submission. If you want to change any aspect of your project (e.g.,
recruitment or data collection) you must discuss this with your supervisor and
you may need to request permission from the Ethics Committee.**

Yours sincerely

A handwritten signature in black ink, appearing to read 'Maria Stokes'.

Professor Maria Stokes
Acting Chair, SHPRS Ethics Committee



Legal Services - Research Governance Office

University of Southampton	Tel	+44 (0)23 8059 8848/9
Highfield	Fax	+44 (0)23 8059 5781
Southampton	Email	mad4@soton.ac.uk
SO17 1BJ United Kingdom		ld7@soton.ac.uk

RGO REF: 5260

Ms Ann Marie Hughes
 School of Health Professions and Rehabilitation Sciences
 Building 45
 University of Southampton
 University Road
 Highfield
 Southampton
 SO17 1BJ

19 July 2007

Dear Ms Hughes

Project Title: Robot Training for Stroke Patients' Arms

I am writing to confirm that the University of Southampton is prepared to act as sponsor for this study under the terms of the Department of Health Research Governance Framework for Health and Social Care (2nd edition 2005).

The University of Southampton fulfils the role of Research Sponsor in ensuring management, monitoring and reporting arrangements for research. I understand that you will be acting as the Principal Investigator responsible for the daily management for this study, and that you will be providing regular reports on the progress of the study to the Research Governance Office on this basis.

I would like to take this opportunity to remind you of your responsibilities under the terms of the Research Governance Framework, and the EU Clinical Trials Directive (Medicines for Human Use Act) if conducting a clinical trial. We encourage you to become fully conversant with the terms of the Research Governance Framework by referring to the Department of Health document which can be accessed at:

<http://www.dh.gov.uk/assetRoot/04/12/24/27/04122427.pdf>

In this regard if your project involves NHS patients or resources please send us a copy of your NHS REC and Trust approval letters when available.

Please do not hesitate to contact me should you require any additional information or support. May I also take this opportunity to wish you every success with your research.

Yours sincerely



Dr Martina Doward
 Research Governance Manager

cc: File

Dear Ann Marie

Re: Robot training for stroke patients' arms

Thank you for information regarding an extension to the above-mentioned study. It is our understanding that this extension involves a revised end date but does not involve any change in the number of participants.

On this basis I can confirm that the sponsorship and insurance cover put in place for this study (letters dated 18/07/07 & 19/07/07) remain valid for the duration of the research.

Kind regards
Lindy

Dr Lindy Dalen
Research Governance Administrator
Legal Services B37, 4009
University of Southampton
Highfield
Southampton SO17 1BJ

Tel: +44 (0)23 8059 8849
Fax: +44 (0)23 8059 5781
Email: Ld7@soton.ac.uk



Participant Information Sheet

Project Title: **Participant Perceptions on using the Iterative Learning Control (ILC) system**

Ethics Submission No:

Introduction

Please take time to read the following information carefully and discuss it with others, including your GP if you wish.

Part 1 tells you the purpose of this study and what will happen to you if you take part. Part 2 gives you more detailed information about the conduct of the study.

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. Thank you for reading this.

Part 1

What is the purpose of the study?

Over the last six months you have been a participant on the ILC project. You have been using an electrical stimulation system with a robot to help your arm muscles to contract to allow you to track a target. We would now like to find out your views on the ILC system and your experience of using it. This will help us to improve the system and how it is used with participants in the future.

Why have I been chosen?

You are one of five people who have been involved in the ILC project.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the normal care you receive.

What will happen to me if I take part?

After reading this information sheet, if you are interested in taking part in the questionnaire, you should let the Research Therapist know either by phone or by e-mail. The Research Therapist will discuss the questionnaire with you and you will have an opportunity to ask questions. If, after this, you decide you do want to take part, the Research Therapist will arrange the date with you when this will take place and you will be asked to sign a consent form.

The interview, where structured questions will be asked, is expected to take 30 minutes and will either take place at the university (travel expenses will be refunded) or over the phone (the researcher will phone you).

The questions will be asked by an interviewer so that you do not have to write anything yourself, but you will be given a copy of the questionnaire to look at. This will be sent to you prior to the interview if you choose to be interviewed over the phone. It is important to us that your answers are as open and full as possible, so we have chosen an interviewer who is not involved in the project. In addition your name or any identification details will not be put on the answer sheet, so that your answers remain anonymous.

What if there is a problem?

Any complaint about the conduct of the interview will be addressed. The detailed information on this is given in Part 2.

Will my taking part in the study be kept confidential?

Yes. It is important that all the information about your participation in this study will be kept confidential. The details are included in Part 2.

Contact Details

Dr Jane Burridge, Principal Investigator, School of Health Professions and Rehabilitation Sciences, University of Southampton, Southampton SO17 1BJ Tel: 023 8059 8885

Ann-Marie Hughes, Research Fellow, School of Health Professions and Rehabilitation Sciences, University of Southampton, Southampton SO17 1BJ Tel: 023 8059 5191

This completes Part 1 of the Information Sheet. If the information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision.

Part 2**Complaints:**

If you have a concern about any aspect of this study, you should ask to speak with the Principal Investigator Jane Burridge who will do her best to answer your questions (023 8059 8885). If you remain unhappy and wish to complain formally, you can do this through the Research Governance Office at the University of Southampton (Dr Martina Dorward, 023 8059 8848).

Will my taking part in this study be kept confidential?

Your name will not appear on the research documents. Your answers will be identified by unique subject number for the purposes of analysis but will not be connected to you. The data recorded, for the purpose of the research project, will be held on a password protected computer or as paper records kept in a locked filing cabinet. Under Data Protection Legislation you have the right of access to, and if needed the right of correction of, the data. You can request this through your research therapist.

Who has reviewed the study?

The questionnaire design and this document has been reviewed and approved by the research ethics committee who approved the original study.

You will be given a copy of this information leaflet and a signed and dated copy of the consent form to keep if you agree to participate in this study.

Thank you for considering taking part or taking time to read this sheet.

A.M. Hughes
Research Fellow
Direct tel: +44 (0)23 80 595191
Ah10@soton.ac.uk

Dr Jane Burridge
Principal Investigator



Consent Form

Participant perceptions on using the Iterative Learning Control (ILC) system

Name of Researchers: Dr Jane Burridge, Ann-Marie Hughes

Please initial box

1. I confirm that I have read and understand the information sheet dated 03/06/08 (version 2) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
3. I understand that my name or other identifying details will not appear on the questionnaire answer sheet and that my responses will remain anonymous.
4. I agree to take part in the questionnaire

Name of Patient

Date

Signature

Researcher

Date

Signature

When completed, 1 for patient; 1 for researcher site file; 1 (original) to be kept in medical notes



Ann-Marie Hughes
School of Health Professions and Rehabilitation Sciences
University of Southampton

09 June 2008

Dear Ann-Marie

Ethics Submission No: SHPRS-ETHICS 08-023
Title: Participant Perceptions on using the iterative learning control (ILC) system

I am pleased to confirm **full approval** for your study has now been given. The approval has been granted by the School of Health Professions and Rehabilitation Sciences Ethics Committee.

You are required to complete a University Insurance and Research Governance Research Governance Application Form (IRGA) in order to receive insurance clearance before you begin data collection. The blank form can be found via the SUSSED portal under Research Governance Office

<http://www.resource1.soton.ac.uk/corporateservices/rgo/regprois/whatdocs.html>

You need to submit the following documentation in a plastic wallet to Dr Martina Prude in the Research Governance Office (RGO, University of Southampton, Highfield Campus, Bldg. 37, Southampton SO17 1BJ):

- Completed IRGA Research Governance form
- Copy of your research protocol/School Ethics Form (final and approved version)
- Copy of participant information sheet
- Copy of SoHPRS Risk Assessment form, **signed** (original should be with Zena Galbraith)
- Copy of your information sheet and consent form
- Copy of this SoHPRS Ethical approval letter

Continued overleaf

School of Health Professions and Rehabilitation Sciences, University of Southampton, Highfield Campus,
Southampton SO17 1BJ United Kingdom
Tel: +44 (0)23 8059 2142 Fax: +44 (0)23 8059 5301 www.sohp.soton.ac.uk

Your project will be registered at the RGO, and then automatically transferred to the Finance Department for insurance cover. You can not begin recruiting until you have received a letter stating that you have received insurance clearance.

Please note that you have ethics approval only for the project described in your submission. If you want to change any aspect of your project (e.g. recruitment or data collection) you must request permission from the Ethics Committee and RGO (students should discuss changes with their supervisor before submitting the request to the Ethics Committee).

Yours sincerely



Maggie Donovan-Hall
Chair, SHPRS Ethics Committee

Direct tel: +44 (0)23 8059 8880
Direct fax: +44 (0)23 8059 4792
email: mh699@soton.ac.uk

Secretary SoHPRS Ethics Committee: Zena Galbraith
Direct tel: +44 (0)23 8059 4791
email: Z.Galbraith@soton.ac.uk



Ms Ann Marie Hughes
School of Health Professions and Rehabilitation Sciences
Building 45
University of Southampton
University Road
Highfield
Southampton
SO17 1BJ

26 June 2008

Dear Ms Hughes

RCO Ref: 5880

Project Title Participant perceptions on using Iterative Learning Control (ILC) System.

I am writing to confirm that the University of Southampton is prepared to act as sponsor for this study under the terms of the Department of Health Research Governance Framework for Health and Social Care (2nd edition 2005).

The University of Southampton fulfils the role of Research Sponsor in ensuring management, monitoring and reporting arrangements for research. I understand that you will be acting as the Principal Investigator responsible for the daily management for this study, and that you will be providing regular reports on the progress of the study to the Research Governance Office on this basis.

I would like to take this opportunity to remind you of your responsibilities under the terms of the Research Governance Framework, and the EU Clinical Trials Directive (Medicines for Human Use Act) if conducting a clinical trial. We encourage you to become fully conversant with the terms of the Research Governance Framework by referring to the Department of Health document which can be accessed at:

<http://www.dh.gov.uk/assetRoot/04/12/24/27/041224>

In this regard if your project involves NHS patients or resources please send us a copy of your NHS REC and Trust approval letters when available.

Please do not hesitate to contact me should you require any additional information or support. May I also take this opportunity to wish you every success with your research.

Yours sincerely

A handwritten signature in black ink, appearing to read "M. Prude".

Dr Martina Prude
Head of Research Governance
Tel: 023 8059 5058
email: rgoinfo@soton.ac.uk

Corporate Services, University of Southampton, Highfield Campus, Southampton SO17 1BJ United Kingdom
Tel: +44 (0) 23 8059 4684 Fax: +44 (0) 23 8059 5781 www.southampton.ac.uk

8 Glossary

Afferent – A neuron or pathway that sends signals to the CNS or a higher processing centre.

Assymmetric Biphasic Waveform – an electrical pulse which deviates first in one direction from the zero current baseline and then in the opposite direction from the baseline. One or more attributes of the waveform (i.e. amplitude and/or duration) is unequal for the two phases. Assymmetric biphasic waveforms may be balanced (equal current flow in both directions) or unbalanced (unequal current flow) (Baker et al, 1993).

Babinski sign – a reflex that can identify diseases of the spinal cord and brain.

Backdrivable - low intrinsic endpoint mechanical impedance (Krebs et al, 2000).

Causal feedback ILC - current trial error data.

Clonus – a cyclic movement of central origin most often elicited in response to a quick stretch of the muscle; generally used to refer to a lower frequency and higher amplitude oscillatory movement than that called tremor (Baker et al, 1993).

Concentric muscle activity – muscle shortening under tension

Contracture – a limitation of mechanical joint movement due to fibrosis of muscle or other soft tissues surrounding the joint.

Damping –

underdamped - the controlled variable follows a series of oscillations before reaching the set point

critically damped - the system reaches the set point in the minimal time without oscillating

overdamped - takes longer to reach the set point

Eccentric muscle activity – muscle lengthening under tension

Efferent – indicates that a neuron or pathway sends signals from the CNS to the periphery or to a lower processing centre

Electromyogram (EMG) - the electrical activity recorded from an active muscle.

Feedback systems - measure the controlled variable (output) and compare it with a desired variable. Any error is corrected by applying a change to the input variable AFTER the error has been detected.

Feedforward systems - effects of environmental disturbances on a system are anticipated and corrective action is applied IN ADVANCE of a measured error in the output.

Functional Abilities – the abilities required to carry out activities of everyday life

Fused tetanic contraction – a contraction when the force fluctuations to each individual impulse can no longer be distinguished.

Gain - determines the speed with which a proportional control system corrects an error in the controlled variable, i.e. the higher the gain the more responsive a system is.

Hysteresis - is a property of systems that do not instantly react to the forces applied to them, but react slowly, or do not return completely to their original state.

Kinematics - the description of motion without regard to force or mass. It generally uses the descriptors displacement, velocity and acceleration. Kinematic measures are 'performance production measures that are based on recording the movement of specific body segments while a person is performing a skill'. (Magill, 1998)

Kinetics - the description of forces involved in producing body movements.

Length Tension effect – the force delivered by a muscle contraction is dependent on the length of the muscle; the region of greatest force production approximates the length the relaxed muscle assumes in the body in the normal anatomical position. In general the shorter the muscle, the lower the maximal tension, while the lengthened muscle increases in maximal force delivered (Baker et al, 1993).

Lower motor neuron – a neuron whose cell body is in the anterior (ventral) horns of the spinal cord and whose axon ends in muscle tissue; these neurons comprise the motor component of the peripheral nerves.

Motoneuron – (motor nerve) an anterior horn cell of the spinal cord which directly innervates skeletal muscle fibres.

Motor Adaptation Studies have demonstrated that when people are repeatedly exposed to a force field that systematically disturbs arm motion, subjects learn to anticipate and cancel out the forces and recover their original kinematic patterns. After the disturbing force field is unexpectedly removed, the subjects make erroneous movements in directions opposite the perturbing forces. (Patton 2006)

Motor Fibre Action Potential (MAP) – The detected waveform resulting from the depolarisation wave as it propagates in both directions along each muscle fibre from its motor end plate

Motor Unit – this is a basic 'quantal' unit of muscular contraction and represents the smallest number of fibres that can be activated by the CNS at any one time.

Motor Unit Action Potential (MUAP) – The spatio-temporal summation of the individual muscle fibre action potentials (MAPs) from all the fibres of a single motor unit.

Motor Unit Action Potential Train (MUAPT) – the repetitive sequence of MUAPs from a given motor unit.

Muscle fatigue - a decreased force-generating capacity or inability to maintain movement performance (Jaric et al, 1997)

Neural repair - describes the range of interventions by which neuronal circuits lost to injury or disease can be restored. Included in this term are means to enhance

axonal regeneration, the transplantation of a variety of tissues and cells to replace lost neurons and the use of prosthetic neuronal circuits to bridge parts of the nervous system that have become functionally separated by injury or disease (processes that do not occur spontaneously in humans to a degree sufficient to result in functional recovery).

Neurorehabilitation - the clinical subspeciality that is devoted to the restoration and maximisation of functions that have been lost due to impairments caused by injury or disease of the nervous system

Skeletal muscle - 'voluntary striated muscle that is usually attached to one or more bones' (Saladin, 2004)

Spasticity – the state in which muscles show an increased resistance to passive quick stretch as a result of increased responsiveness of the stretch reflex. This hyperreflexia is often reflected by the presence of clonus.

Stroke – a focal (or at times global) neurological impairment of sudden onset, and lasting more than 24 hours (or leading to death), and of presumed vascular origin' (World Health Organisation, 2005)

Subluxation – an incomplete or partial dislocation of a joint.

Tetanic Stimulation – repetitive stimulation to a nerve or muscle delivered at a rate sufficient to produce a fused contraction in the muscle

Transfer of learning - 'the influence of previous experience on performing a skill in a new context or on learning a new skill' (Magill, 1998)

Twitch contraction – The response of skeletal muscle to a single nervous impulse.

Upper motor neuron syndrome - Signs and symptoms that result from damage to descending motor systems; these include paralysis, spasticity, and a positive Babinski sign.

Voluntary muscle – Muscle that is usually under conscious control i.e. skeletal muscle

9 References

Ada, L., O'Dwyer, N., and O'Neill, E. (2006) Relation between spasticity, weakness and contracture of the elbow flexors and upper limb activity after stroke: an observational study, *Disability and Rehabilitation*, 28 (13-14), pp. 891-897

Adams, J. A. (1971) A closed loop theory of motor learning, *Journal of Motor Behavior*, 3, pp. 111-150

Adams, J. A. and Dijkstra, S. J. (1966) Short term memory for motor responses, *Journal of Experimental Psychology*, 71, pp. 314-318

Aisen, M. L., Krebs H.I., Hogan, N., McDowell, F., and Volpe, B. T. (1997) The effect of robot-assisted therapy and rehabilitative training on motor recovery following stroke, *Archives of Neurology*, 54, pp. 443-446

Amirabdollahian, F., Loureiro, R., Gradwell, E., Collin, C., Harwin, W, and Johnson, G. (2007) Multivariate analysis of the Fugl-Meyer outcome measures assessing the effectiveness of GENTLE/S robot-mediated stroke therapy, *Journal of NeuroEngineering and Rehabilitation*.5, DOI:10.1186/1743-0003-4-4

Arimoto, S., Kawamura, S., and Miyazaki, F. (1984) Bettering operations of robots by learning, *Journal of Robotic Systems*, 1 (2), pp. 123-140

Baddeley, A. D. (1995) 'Working memory', in Gazzaniga, M. S. (ed.) *The cognitive neurosciences*. Cambridge, MA: MIT Press, pp.

Baker, L. L., McNeal, D. R., Benton, L. A., Bowman, B. R., and Waters, R. L. (1993) *Neuromuscular Electrical Stimulation - A practical guide*. 3rd edn. Los Amigos Research and Education Institute.

Basmajian, J. V. and de Luca, C. J. (1985) *Muscles Alive*. 5th edn. Baltimore: Williams and Wilkins.

Beer, R. F., Dewald, J. P., Dawson, M. L., and Rymer, W. Z. (2004) Target-dependent differences between free and constrained arm movements in chronic hemiparesis, *Experimental Brain Research*, 156 (4), pp. 458-470

Beer, R. F., Dewald, J. P., and Rymer, W. Z. (2000) Deficits in the coordination of multijoint arm movements in patients with hemiparesis: evidence for disturbed control of limb dynamics, *Experimental Brain Research*, 131 (3), pp. 305-319

Bilodeau, M. (2006) Central fatigue in continuous and intermittent contractions of triceps brachii, *Muscle and Nerve*, 34 (2), pp. 205-213

Bohannon, R. W. and Smith, M. B. (1987) Interrater reliability of a modified Ashworth scale of muscle spasticity, *Physical Therapy*, 67 (2), pp. 206-7

Bowman, B. R. and Baker, L. L. (1985) Effects of waveform parameters on comfort during transcutaneous neuromuscular electrical stimulation, *Annals of Biomedical Engineering*, 13 (1), pp. 59-74

Bowman, B. R., Baker, L. L., and Walker, R. L. (1979) Positional feedback and electrical stimulation: an automated treatment for the hemiplegic wrist, *Archives of Physical Medicine*, 60, pp. 497-501

Buneo, C. A., Soechting, J. F., and Flanders, M. (1994) Muscle activation patterns for reaching: the representation of distance and time, *Journal of Neurophysiology*, 71 (4), pp. 1546-1558

Burridge, J. H. and Ladouceur, M. (2001) Clinical and therapeutic applications of neuromuscular stimulation: A review of current use and speculation into future developments, *Neuromodulation*, 4 (4), pp. 147-154

Canning, C. G., Ada, L., and O'Dwyer, N. J. (2000) Abnormal muscle activation characteristics associated with loss of dexterity after stroke, *Journal of the Neurological Sciences*, 176 (1), pp. 45-56

Rossum's Universal Robots by Capek, K. (1921). Prague National Theatre.

Carroll, D. (1965) A quantitative test for upper extremity function, *Journal of Chronic Disability*, 18, pp. 479-491

Castro-Alamancos, M. A. and Borrell, J. (1995) Functional recovery of forelimb response capacity after forelimb primary motor cortex damage in the rat is due to the reorganisation of adjacent areas of cortex, *Neuroscience*, 68 (3), pp. 793-805

Centre of Evidence-Based Physiotherapy (2008) *PEDro* available at: http://www.pedro.fhs.usyd.edu.au/scale_item.html (Accessed 20-01-09)

Chae, J. and Hart, R. (2003) Intramuscular hand neuroprosthesis for chronic stroke survivors, *Neurorehabilitation and Neural Repair*, 17 (2), pp. 109-117

Chae, J., Yang, G., Park, B. K., and Labatia, I. (2002) Delay in initiation and termination of muscle contraction, motor impairment, and physical disability in upper limb hemiparesis, *Muscle and Nerve*, 25 (4), pp. 568-575

Cirstea, M. C. and Levin, M. F. (2000) Compensation strategies for reaching in stroke, *Brain*, 123, pp. 940-953

Colgate, J.E. and Hogan, N. (1988) Robust control of dynamically interacting systems, *International Journal of Control* 48 (1) pp. 65-88.

Cools, A. M., Witvrouw, E. E., De Clercq, G. A., Danneels, L. A., Willems, T. M., Cambier, D. C., and Voight, M. L. (2002) Scapular muscle recruitment pattern: electromyographic response of the trapezius muscle to sudden shoulder movement before and after a fatiguing exercise, *Journal of Orthopaedic and Sports Physical Therapy*, 32 (5), pp. 221-229

Coote, S., Murphy, B., Harwin, W., and Stokes, E. K. (2008) The effect of the GENTLE/s robot-mediated therapy system on arm function after stroke, *Clinical Rehabilitation*, 22 (5), pp. 395-405

Coote, S. and Stokes, E. K. (2003) Robot mediated therapy: Attitudes of patients and therapists towards the first prototype of the GENTLE/s system, *Technology and Disability*, 15 (1), pp. 27-34

Daly, J. J., Fang, Y., Perepezko, E. M., Siemionow, V., and Yue, G. H. (2006) Prolonged cognitive planning time, elevated cognitive effort, and relationship to coordination and motor control following stroke, *IEEE Transactions on Neural Systems & Rehabilitation Engineering*, 14 (2), pp. 168-171

Daly, J. J., Hogan, N., Perepezko, E. M., Krebs, H. I., Rogers, J. M., Goyal, K. S., Dohring, M. E., Fredrickson, E., Nethery, J., and Ruff, R. L. (2005) Response to upper-limb robotics and functional neuromuscular stimulation following stroke, *Journal of Rehabilitation Research and Development*, (6), pp. 723-736

Damodaran, L. (1996) User involvement in the systems design process - a practical guide for users, *Behaviour & Information Technology*, 15 (6), pp. 363-377

Day, H. I. and Jutai, J. J. (1996) Measuring the psychosocial impact of assistive Devices: The PIADS, *Canadian Journal of Rehabilitation*, 9, pp. 159-168

De Kroon, J. R and IJzerman, M. J. (2008) Electrical stimulation of the upper extremity in stroke: Cyclic versus EMG-triggered stimulation, *Clinical Rehabilitation*, 22 (8), pp. 690-697

De Kroon, J. R, IJzerman, M. J., Chae, J., Lankhorst, G. J., and Zilvold, G. (2005) Relation between stimulation characteristics and clinical outcome in studies using electrical stimulation to improve motor control of the upper extremity in stroke., *Journal of Rehabilitation Medicine*, 37 (2), pp. 65-74

De Kroon, J. R, van der Lee, J. H, IJzerman, M. J, and Lankhorst, G. J. (2002) Therapeutic electrical stimulation to improve motor control and functional abilities of the upper extremity after stroke: a systematic review, *Clinical Rehabilitation*, 16, pp. 350-360

Debaere, F., Van Assche, D., Kiekens, C., Verschueren, S., and Swinnen, S. (2001) Coordination of upper and lower limb segments: deficits on the ipsilesional side after unilateral stroke, *Experimental Brain Research*, 141 (4), pp. 519-529

Dewald, J. P., Beer, R. F., Given, J. D., McGuire, J. R., and Rymer, W. Z. (1999) Reorganisation of flexion reflexes in the upper extremity of hemiparetic subjects, *Muscle and Nerve*, 22 (9), pp. 1209-1221

Dick, J. P. R., Guillot, R. J., and Stewart, A. (1984) Mini-Mental State Examination in neurological patients, *Journal of Neurology, Neurosurgery and Psychiatry*, 47, pp. 496-499

Dominici, F., Popa, F. T., Ginanneschi, R., Mazzocchio, R., and Rossi, A. (2005) Cortico-motoneuronal output to intrinsic hand muscles is differentially influenced by static changes in shoulder positions, *Experimental Brain Research*, 164 (4), pp. 500-504

Doornbosch, A. J., Cools, H. J. M., Slee-Turkenburg, M. E. C., van Elk, M. G., and Schoone-Harmsen, M. (2007) Robot-mediated ACtive REhabilitation (ACRE2) for the hemiplegic upper limb after a stroke: A pilot study, *Technology & Disability*, 19 (4), pp. 199-203

Dou, Huifang, Tan, Kok Kiong, Lee, Tong Heng, and Zhou, Zhaoying. (1999) Iterative learning feedback control of human limbs via functional electrical stimulation, *Control Engineering Practice*, 7 (3), pp. 315-325

Duncan, P. W. (1983) Reliability of the Fugl-Meyer assessment of sensorimotor recovery following cerebrovascular accident, *Physical Therapy*, 63 (10), pp. 1606-1610

Duysens, J. and Van der Crommert, H. W. (1998) Neural control of locomotion; part 1: the central pattern generator from cats to humans, *Gait and Posture*, 7, pp. 131-141

Edwards, S. (2002) *Neurological physiotherapy: a problem-solving approach*. Elsevier Health Sciences.

Farina, D., Merletti R, and Stegeman D. (2004) 'Biophysics of the generation of EMG signals', in Merletti R and Parker, P (ed.) *Electromyography: Physiology, Engineering and Non-Invasive Applications*. Hoboken: John Wiley & Sons, pp. 81-102.

Ferraro, M., Palazzolo, J. J., Krol, J., Krebs, H. I., Hogan, N., and Volpe, B. T. (2003) Robot-aided sensorimotor arm training improves outcome in patients with chronic stroke, *Neurology*, 61 (11), pp. 1604-1607

Feys, H. M., De Weerd, W. J., Selz, B. E., Cox Steck, G. A., Spichiger, R., Vereeck, L. E., Putman, K. D., and Van Hoydonck, G. A. (1998) Effect of a therapeutic intervention for the hemiplegic upper limb in the acute phase after stroke: a single-blind, randomized, controlled multicenter trial, *Stroke*, 29 (4), pp. 785-792

Flanders, M. and Herrmann, U. (1992) Two components of muscle activation: scaling with the speed of arm movement, *Journal of Neurophysiology*, 67 (4), pp. 931-943

Flick, U. (2002) Qualitative research - state of the art, *Social Science Information*, 41 (1), pp. 5-24

Folstein, M. F., Folstein, S. E., and McHugh, P. R. (1975) "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician, *Journal of Psychiatric Research*, 12 (3), pp. 189-198

Francisco, G., Chae, J., Chawla, H., Kirshblum, S., Zorowitz, R., Lewis, G., and Pang, S. (1998) Electromyogram-triggered neuromuscular stimulation for improving the arm function of acute stroke survivors: a randomized pilot study, *Archives of Physical Medicine & Rehabilitation*, 79 (5), pp. 570-575

Freeman, C. T., Hughes A.M., Burridge J.H., Chappell, P. H, Lewin, P. L., and Rogers, E. (2007) 'An experimental facility using functional electrical stimulation for stroke rehabilitation of the upper limb', *10th International conference on rehabilitation robotics (ICORR'07)*. Noordwijk aan Zee, The Netherlands 12-6-2007.

Freeman, C. T., Hughes, A. M., Burridge, J. H., Chappell, P. H, Lewin, P. L, and Rogers, E. (2008a) Iterative Learning Control of FES applied to the upper extremity for rehabilitation, *Control Engineering Practice*, DOI: 10.1016/j.conengprac.2008.08.003

Freeman, C. T., Hughes, A. M., Burridge, J. H., Chappell, P. H, Lewin, P. L, and Rogers, E. (2008b) A model of the upper extremity using FES for stroke rehabilitation, *ASME Journal of Biomechanical Engineering*, DOI: 10.1115/1.3005332

Freeman, C. T., Hughes, A. M., Burridge, J. H., Chappell, P. H., Lewin, P. L., and Rogers, E. (2008c) A robotic workstation for stroke rehabilitation of the upper extremity using FES, *Medical Engineering and Physics*, (DOI: 10.1016/j.medengphy.2008.05.008)

Fugl-Meyer, A. R., Jaasko, L., Leyman, I., Olsson, S., and Steglind, S. (1975) The post-stroke hemiplegic patient. 1. a method for evaluation of physical performance, *Scandinavian Journal of Rehabilitation Medicine*, 7 (1), pp. 13-31

Gabriel, D. A. (1997) Shoulder and elbow muscle activity in goal-directed arm movements, *Experimental Brain Research*, 116 (2), pp. 359-366

Geddes, L. A. (1994) The First Stimulators, *IEEE Engineering in Medicine & Biology Magazine*, Aug/Sept, pp. 532-542

Golaszewski, S., Kremser, C., Wagner, M., Felber, S., Aichner, F., and Dimitrijevic, M. (1999) Functional magnetic resonance imaging of the human motor cortex before and after whole-hand afferent electrical stimulation, *Scandinavian Journal of Rehabilitation Medicine*, 31 (3), pp. 165-173

Gorman, P., Alon, G., and Peckham, P. (2006) 'Functional electrical stimulation in neurorehabilitation', in Selzer, M., Clarke, S., Cohen, L., Duncan, P., and Gage, F. (ed.) *Textbook of Neural Repair and Rehabilitation*. Cambridge, pp. 119-135.

Gowland, C., deBruin, H., Basmajian, J. V., Plews, N., and Burcea, I. (1992) Agonist and antagonist activity during voluntary upper-limb movement in patients with stroke, *Physical Therapy*, 72 (9), pp. 624-633

Grillner, S. and Zangger, P. (1984) The effect of dorsal root transection on the efferent motor pattern in the cat's hindlimb during locomotion., *Acta Physiol Scand*, 120, pp. 393-405

Guyton, A. C. (1981) *Textbook of medical physiology*. 6th edn. W.B. Saunders Company.

Halligan, P., Wilson, B., and Cockburn, J. (1990) A short screening test for visual neglect in stroke patients, *International Disability Studies*, 12 (3), pp. 95-99

Hammond, M. C., Kraft, G. H., and Fitts, S. S. (1988) Recruitment and termination of electromyographic activity in the hemiparetic forearm, *Archives of Physical Medicine & Rehabilitation*, 69 (2), pp. 106-110

Harwin, W. (2008) 'Virtual and tele-rehabilitation rehabilitation', *Euron Winter Meeting in Rehabilitation Robotics*. 30-3-0008.

Hebb, D. O. (1949) *The Organization of Behavior*. New York: John Wiley.

Hermans, H. J., Freriks B, Merletti R, Stegeman D, Blok J, Rau G, Disselhorst-Klug C, and Hagg G. (1999) *European Recommendations for surface Electromyography, results of the SENIAM project*. Rossingh Research and Development b.v.

Hesse, S. (2001) Locomotor therapy in neurorehabilitation, *Neurorehabilitation*, 16 (3), pp. 133-139

Hesse, S., Werner, C., Pohl, M., Rueckriem, S., Mehrholz, J., and Lingnau, M. L. (2005) Computerized arm training improves the motor control of the severely

affected arm after stroke: a single-blinded randomized trial in two centers, *Stroke*, 36 (9), pp. 1960-1966

Housman, S. J., Le, V., Rahman, T., Sanchez, R. J., and Reinkensmeyer, D. J. (2007) 'Arm-training with T-WREX after chronic stroke: preliminary results of a randomized controlled trial', *IEEE 10th International Conference on Rehabilitation Robotics*. Noordwijk aan Zee, The Netherlands 12-6-2007.

Hsieh, C. L., Hsueh, I. P., Chiang, F. M., and Lin, P. H. (1998) Inter-rater reliability and validity of the action research arm test in stroke patients, *Age and Ageing*, 27 (2), pp. 107-13

Hu, X., Tong, K. Y., Song, R., Tsang, V. S., Leung, P. O., and Li, L. (2007) Variation of muscle coactivation patterns in chronic stroke during robot-assisted elbow training, *Archives of Physical Medicine and Rehabilitation*, 88 (8), pp. 1022-1029

Huxley, H. E. and Hanson, J. (1954) Changes in the cross-striations of muscle during contraction and stretch and their structural interpretation, *Nature*, 173, pp. 973-976

Inaba, M., Edberg, E., Montgomery, J., and Gillis, M. K. (1973) Effectiveness of functional training, active exercise, and resistive exercise for patients with hemiplegia, *Physical Therapy*, 53 (1), pp. 28-35

Intercollegiate Stroke Working Party. (2008) *National Clinical Guidelines for Stroke (3rd Edition)*. London: Royal College of Physicians.

Jackson, J. (2004) 'Specific treatment techniques', in Stokes, M (ed.) *Physical Management in Neurological Rehabilitation*. Elsevier Mosby, pp. 393-413.

Jackson, J. H. (1882) On some implications of dissolution of the nervous system, *Medical Press and Circular*, 2, pp. 411-426

Jain, N., Florence, S. L., and Kaas, J. H. (1998) Reorganization of Somatosensory Cortex After Nerve and Spinal Cord Injury, *News in Physiological Sciences*, 13 (3), pp. 143-149

Jaric, S., Radovanovic, S., Milanovic, S., Ljubisavljevic, M, and Anastasijevic, R. (1997) A comparison of the effects of agonist and antagonist muscle fatigue on performance of rapid movements, *European Journal of Applied Physiology*, 76, pp. 41-47

Jensen, J. L., Marstrand, P. C. D., and Nielsen, J. B. (2005) Motor skill training and strength training are associated with different plastic changes in the central nervous system, *Journal of Applied Physiology*, 99 (4), pp. 1558-1568

Kamper, D. G., Kenna-Cole, A. N., Kahn, L. E., and Reinkensmeyer, D. J. (2002) Alterations in reaching after stroke and their relation to movement direction and impairment severity, *Archives of Physical Medicine and Rehabilitation*, 83 (5), pp. 702-707

Karst, G. M. and Hasan, Z. (1991) Initiation rules for planar, two-joint arm movements: agonist selection for movements throughout the work space, *Journal of Neurophysiology*, 66 (5), pp. 1579-1593

Katz, R. T., Rovai, G. P., Brait, C., and Rymer, W. Z. (1992) Objective quantification of spastic hypertonia - correlation with clinical findings, *Archives of Physical Medicine and Rehabilitation*, 73 (4), pp. 339-347

Kawasaki, H, Ito, S., Ishigure, Y., Nishimoto, T., Aoki, T., Mouri, T., Sakaeda, H., and Abe, M. (2007) 'Development of a hand motion assist robot for rehabilitation therapy by patient self motion control', *IEEE 10th International Conference on Rehabilitation Robotics*. Noordwijk aan Zee, The Netherlands 12-6-2007.

Keele, S.W. (1968) Movement control in skilled motor performance, *Psychological Bulletin*, 70, pp 387-403

Keller, T., Ellis, M. D., and Dewald, J. P. (2005) Overcoming abnormal joint torque patterns in paretic upper extremities using triceps stimulation, *Artificial Organs*, 29 (3), pp. 229-232

Kendall, F. P., Mc Creary, E. K., and Provance, P. G. (1993) *Muscles - Testing and Function*. 4th edn. Baltimore: Williams & Wilkins.

Kenward, M. G. and Roger, J. H. (1997) Small sample inference for fixed effects from restricted maximum likelihood, *Biometrics*, 53 (3), pp. 983-997

Kiesler, S and Hinds, P. (2004) Human robot interaction, *Human Computer Interaction*, 19 (Numbers 1 & 2), pp. 1-8

Kimball, J. W. (2008) *Kimball's Biology Pages*. Available at: <http://users.rcn.com/jkimball.ma.ultranet/BiologyPages/M/Muscles.html#filaments> (Accessed: 9-1-2009).

Kingsley, R. F. (2000) *Concise Text of Neuroscience*. 2nd edn. Lippincott Williams and Wilkins.

Kleim, J. A., Hogg, T. M., VandenBerg, P. M., Cooper, N. R., Bruneau, R., and Remple, M. (2004) Cortical synaptogenesis and motor map reorganization occur during late, but not early, phase of motor skill learning, *Journal of Neuroscience*, 24 (3), pp. 628-633

Knutson, M. L. and Soderburg, G. L. (1995) 'EMG: use and interpretation in gait', in Craik, R. L. and Oatis, C. A. (ed.) *Gait Analysis Theory and Application*. Mosby Publishing, pp.

Krebs, H. I., Dipietro, L., Volpe, B., and Hogan, N. (2007a) An investigation of the specificity of robotic training, *Critical Reviews in Physical and Rehabilitation Medicine*, 19 (2), pp. 141-152

Krebs, H. I., Hogan, N., Aisen, M. L., and Volpe, B. T. (1998) Robot-aided neurorehabilitation, *IEEE Transactions on Rehabilitation Engineering*, 6 (1), pp. 75-87

Krebs, H. I., Mernoff, S., Fasoli, S. E., Hughes, R., Stein, J., and Hogan, N. (2008) A comparison of functional and impairment-based robotic training in severe to moderate chronic stroke: A pilot study, *Neurorehabilitation*, 23 (1), pp. 81-87

Krebs, H. I., Volpe, B. T., Aisen, M. L., and Hogan, N. (2000) Increasing productivity and quality of care: robot-aided neuro-rehabilitation, *Journal of Rehabilitation Research & Development*, (6), pp. 639-652

Krebs, H. I., Volpe, B. T., Williams, D., Celestino, J., Charles, S. K., Lynch, D., and Hogan, N. (2007b) Robot-aided neurorehabilitation: a robot for wrist rehabilitation, *IEEE Transactions on Neural Systems & Rehabilitation Engineering*, 15 (3), pp. 327-335

Kwakkel, G., Kollen, B. J., and Krebs H.I. (2008) Effects of robot-assisted therapy on upper limb recovery after stroke: a systematic review, *Neurorehabilitation and Neural Repair*, 22, pp. 111-121

Kwakkel, G., Kollen, B. J., and Wagenaar, R. C. (1999) Therapy impact on functional recovery in stroke rehabilitation: a critical review of the literature, *Physiotherapy*, 85 (7), pp. 377-391

Kwakkel, G., van Peppen, R., Wagenaar, R., Dauphinee, S., Richards, C., and Ashburn, A. (2004) Effects of augmented exercise therapy time after stroke., *Stroke*, 35, pp. 2529-2536

Lan, N. (2002) Stability analysis for postural control in a two-joint limb system, *IEEE Transactions on Neural Systems & Rehabilitation Engineering*, 10 (4), pp. 249-259

Lance, J. W. (1980) 'Pathophysiology of spasticity and clinical experience with Baclofen', in Lance, J. W., Feldman, R, Young, R. R., and Koella, W. P. (ed.) *Spasticity: Disordered Motor Control*. Chicago: Year Book Medical, pp. 185-204.

Lang, C. E., Reilly, K. T., and Schieber, M. H. (2006) 'Human voluntary motor control and dysfunction', in Selzer, M., Clarke, S., Cohen, C., Duncan, P., and Gage, F. (ed.) *Textbook of Neural Repair and Rehabilitation*. Cambridge: Cambridge University Press, pp. 24-36.

Lee, M., Rittenhouse, M., and Abdullah, H. A. (2005) Design issues for therapeutic robot systems: results from a survey of physiotherapists, *Journal of Intelligent Robotic Systems*, 42, pp. 239-252

Lennon, S., Baxter, D., and Ashburn, A. (2001) Physiotherapy based on the Bobath Concept: a survey within the UK, *Disability & Rehabilitation*, 23 (6), pp. 254-262

Leonard, C. T., Gardipee, K. A., Koontz, J. R., Anderson, J., and Wilkins, S. A. (2006) Correlation between impairment and motor performance during reaching tasks in subjects with spastic hemiparesis, *Journal of Rehabilitation Medicine*, 38 (4), pp. 243-249

Liberson, W. T, Holmquest, H. J, Scott, M. E. D, and DOW, M. (1961) Functional electrotherapy: stimulation of the peroneal nerve synchronized with the swing phase of the gait of hemiplegic patients, *Archives of Physical Medicine and Rehabilitation*, 42, pp. 101-105

Liepert, J., Bauder, H., Wolfgang, H. R., Miltner, W. H., Taub, E., and Weiller, C. (2000) Treatment-induced cortical reorganization after stroke in humans, *Stroke*, 31 (6), pp. 1210-1216

Longstaff, A. (2005) *Neuroscience*. 2nd edn. Abingdon, Oxon: Taylor and Francis.

Loureiro, R. C. V. and Harwin, W. S. (2007) 'Reach and grasp therapy: design and control of a 9-DOF robotic neurorehabilitation system', *IEEE 10th International Conference of Rehabilitation Robotics (ICORR 2007)*. Noordwijk aan Zee, The Netherlands 12-6-2007.

Lum, P. S., Burgar, C. G., Kenney, D. E., and Van der Loos, H. F. (1999) Quantification of force abnormalities during passive and active-assisted upper-limb reaching movements in post-stroke hemiparesis, *IEEE Transactions on Biomedical Engineering*, 46 (6), pp. 652-662

Lum, P. S., Burgar, C. G., and Shor, P. C. (2004) Evidence for improved muscle activation patterns after retraining of reaching movements with the MIME robotic system in subjects with post-stroke hemiparesis, *IEEE Transactions on Neural Systems & Rehabilitation Engineering*, 12 (2), pp. 186-194

Lum, P. S., Burgar, C. G., Shor, P. C., Majmundar, M., and Van der Loos M. (2002) Robot-assisted movement training compared with conventional therapy techniques for the rehabilitation of upper-limb motor function after stroke, *Archives of Physical Medicine and Rehabilitation*, 83 (7), pp. 952-959

Lum, P. S., Burgar, C. G., Van der Loos M., Shor, P. C., Majmundar, M., and Yap, R. (2006) MIME robotic device for upper-limb neurorehabilitation in subacute stroke subjects: A follow-up study, *Journal of Rehabilitation Research & Development*, 43 (5), pp. 631-642

Lyle, R. C. (1981) A performance test for assessment of upper limb function in physical rehabilitation treatment and research, *International Journal of Rehabilitation Research*, 4 (4), pp. 483-492

Ma, H., Trombly, C. A., and Robinson-Podolski. (1999) The effect of context on skill acquisition and transfer, *American Journal of Occupational Therapy*, 53, pp. 138-144

Maclean, N., Pound, P., Wolfe, C., and Rudd, A. (2002) The concept of patient motivation: a qualitative analysis of stroke professionals' attitudes, *Stroke*, 33 (2), pp. 444-448

Maclean, Niall, Pound, Pandora, Wolfe, Charles, and Rudd, Anthony. (2000) Qualitative analysis of stroke patients' motivation for rehabilitation, *BMJ*, 321 (7268), pp. 1051-1054

Magill, R. A. (1998) *Motor Learning - Concepts and Applications*. 5th edn. McGraw-Hill International Editions.

Magill, R. A. (2001) *Motor Learning: Concepts and Applications*. 6th edn. McGraw-Hill International Editions.

Mann, G. E., Burridge, J. H., Malone, L. J., and Strike, P. W. (2005) A pilot study to investigate the effects of electrical stimulation on recovery of hand function and sensation in subacute stroke patients, *Neuromodulation*, (3), pp. 193-202

Mant, J, Wade, D, and Winner, S. (2004) 'Health care needs assessment:stroke', in Stevens, A, Raferty, J, Mant, J, and Simpson, S (ed.) *Health care needs assessment: the epidemiologically based needs assessment reviews*. Oxford: Radcliffe Medical Press

Masia, L., Krebs, H. I., Cappa, P., and Hogan, N. (2006) 'Whole-arm rehabilitation following stroke: hand module', *Biomedical Robotics and Biomechatronics, 2006. BioRob 2006*. Pisa, Italy 20-2-2006.

Matthews, J. N. S., Altman, D., Campbell, M. J., and Royston, P. (1990) Analysis of serial measurements in medical research, *British Medical Journal (Clinical Research Ed.)*, 300 (6719), pp. 230-235

McCrea, P. H., Eng, J. J., and Hodgeson, A. J. (2003) Time and magnitude of torque generation is impaired in both arms following stroke, *Muscle and Nerve*, 28 (1), pp. 46-53

McCrea, P. H., Eng, J. J., and Hodgeson, A. J. (2005) Saturated muscle activation contributes to compensatory reaching strategies after stroke, *Journal of Neurophysiology*, 94 (5), pp. 2999-3008

McNeal, D., Baker, L. L., McCaffrey, S., and Lopez, J. (1986) 'Subject preference for pulse frequency with cutaneous stimulation of the quadriceps', *9th Annual conference of the rehabilitation engineering society of north America*. Minneapolis, Minnesota 23-6-1986.

Mehrholz, J., Platz, T., Kugler, J., and Pohl, M. (2008) *Electromechanical and robot-assisted arm training for improving arm function and activities of daily living after stroke*. Cochrane Database of Systematic Reviews, Issue: 4. Art. No.: CD006876. DOI: 10.1002/14651858.CD006876.pub2

Mihaltchev, P., Archambault, P. S., Feldman, A. G., and Levin, M. F. (2005) Control of double-joint arm posture in adults with unilateral brain damage, *Experimental Brain Research*, 163 (4), pp. 468-486

Moore, K. L. (1998) 'Iterative Learning Control: An expository overview', *Iterative Learning Control for deterministic systems*. Springer-Verlag, pp. 151-214.

Moore, K. L. and Xu, J. X. (2000) Special issue on iterative learning control, *International Journal of Control*, 73 (10), pp. 819-823

Morris, S., Dodd, K. J., and Morris, M. E. (2004) Outcomes of progressive resistance strength training following stroke: a systematic review, *Clinical Rehabilitation*, 18, pp. 27-39

Mottram, S. L. (1997) Dynamic stability of the scapula, *Manual Therapy*, 2 (3), pp. 123-131

Murphy, M. A and Roberts-Warrior, D. (2003) A review of motor performance measures and treatment interventions for patients with stroke, *Topics in Geriatric Rehabilitation*, 19 (1), pp. 3-42

Nadeau, S., Arsenault, B., Gravel, D., and Bourbonnais, D. (1999) Analysis of the clinical factors determining natural and maximal gait speeds in adults with a stroke, *American Journal of Physical Medicine and Rehabilitation*, 78 (2), pp. 123-130

National Audit Office. (2005) *Reducing Brain Damage: Faster access to better stroke care*. London: Department of Health.

Nederhof, A. J. (1985) Methods of coping with social desirability bias: A review, *European Journal of Social Psychology*, 15 (3), pp. 263-280

Nelles, G., Jentzen, W., Jueptner, M., Muller, S., and Diener, H. C. (2001) Arm training induced brain plasticity in stroke studied with serial positron emission tomography, *Neuroimage*, 13 (6), pp. 1146-1154

Nielsen, J. (1993) *Usability Engineering*. Boston, MA: Academic Press.

Nudo, R. J. and Milliken, G. W. (1996) Reorganization of movement representations in primary motor cortex following focal ischemic infarcts in adult squirrel monkeys, *Journal of Neurophysiology*, 75 (5), pp. 2144-2149

Nudo, R. J., Milliken, G. W., Jenkins, W. M., and Merzenich, M. M. (1996) Use-dependent alterations of movement representations in primary motor cortex of adult squirrel monkeys, *Journal of Neuroscience*, 16 (2), pp. 785-807

Osu, R., Franklin, D. W., Kato, H., Gomi, H., Domen, K., Yoshioka, T., and Kawato, M. (2002) Short and long-term changes in joint co-contraction associated with motor learning as revealed from surface EMG, *Journal of Neurophysiology*, 88 (2), pp. 991-1004

Palastanga, N., Soames, R. W., and Field, D. (1998) *Anatomy and Human Movement: Structure and Function*. 3rd edn. Oxford: Butterworth-Heinemann.

Pandyan, A. D., Johnson, G. R., Price, C. I., Curless, R. H., Barnes, M. P., and Rodgers, H. (1999) A review of the properties and limitations of the Ashworth and modified Ashworth Scales as measures of spasticity, *Clinical Rehabilitation*, 13 (5), pp. 373-383

Patten, C., Dozono, J., Schmidt, S., Jue, M. E., and Lum, P. S. (2006) Combined functional task practice and dynamic high intensity resistance training promotes recovery of upper-extremity motor function in post-stroke hemiparesis: a case study, *Journal of Neurologic Physical Therapy*, 30 (3), pp. 99-115

Patten, C., Lexell, J., and Brown, H. E. (2004) Weakness and strength training in persons with poststroke hemiplegia rationale, method, and efficacy, *Journal of Rehabilitation Research and Development*, 41 (3), pp. 293-312

Perneger, T.V. (1998) Education and debate: What's wrong with Bonferroni adjustments, *British Medical Journal*, 316:1236-1238

Pitcher, J. B., Ridding, M. C., and Miles, T. S. (2003) Frequency-dependent, bi-directional plasticity in motor cortex of human adults, *Clinical Neurophysiology*, 114 (7), pp. 1265-1271

Platz, T., Pinkowski, C., van Wijck, F., Kim, I. H., Di Bella, P., and Johnson, G. (2005) Reliability and validity of arm function assessment with standardized guidelines for the Fugl-Meyer Test, Action Research Arm Test and Box and Block Test: a multicentre study, *Clinical Rehabilitation*, 19 (4), pp. 404-411

Plautz, E. J., Milliken, G. W., and Nudo, R. J. (2000) Effects of repetitive motor training on movement representations in adult squirrel monkeys: role of use versus learning, *Neurobiology of Learning and Memory*, 74 (1), pp. 27-55

Pomeroy, V. M., King, L., Pollock, A., Baily-Hallam, A., and Langhorne, P. (2006) *Electrostimulation for promoting recovery of movement or functional ability after stroke*. Cochrane Database of Systematic Reviews, Issue: 2. Art. No.: CD003241. DOI: 10.1002/14651858.CD003241.pub2

Pons, T. P., Garraghty, P. E., Ommaya, A. K., Kaas, J. H., Taub, E., and Mishkin, M. (1991) Massive cortical reorganization after sensory deafferentation in adult macaques, *Science*, 252 (5014), pp. 1857-1860

Powell, J., Pandyan, A. D., Granat, M., Cameron, M., and Stott, D. J. (1999) Electrical stimulation of wrist extensors in poststroke hemiplegia, *Stroke*, 30 (7), pp. 1384-1389

Prange, G. B., Jannink, M. A., Groothuis-Oudshoorn, C. G. M, Hermens, H., and IJzerman, M. J. (2006) Systematic review of the effect of robot-aided therapy on recovery of the hemiparetic arm after stroke, *Journal of Rehabilitation Research and Development*, 43 (2), pp. 171-184

Prange, G. B., Kallenberg, L. A. C., Jannink, M. J. A., Stienen, A. H. A., van der Kooij, H., IJzerman, M. J., and Hermens, H. J. (2007) Influence of gravity compensation on muscle activity during reach and retrieval in healthy elderly, *Journal of Electromyography and Kinesiology*, DOI: 10.1016/j.jelekin.2007.08.001

Price, C. I. and Pandyan, A. (2000) *Electrical stimulation for preventing and treating post-stroke shoulder pain*. Cochrane Database of Systematic Reviews, Issue: 4. Art. No.: CD001698. DOI: 10.1002/14651858.CD001698

PS Program Power and Sample Size Calculation Version 3.0.2. Available at: <http://biostat.mc.vanderbilt.edu/twiki/bin/view/Main/PowerSampleSize> (Accessed: 25-04-2009)

Purves, D., Augustine, G.J., Fitzpatrick, D., Hall, W.C., Lamantia, A.S., McNamara, J.O., Williams, S.M. (2001) *Neuroscience*. Available at: <http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=.0|EyAAH-ZoGjuUKDcmQOcer5rv-KCEYHQC1usUAB> (Accessed: 28-08-2008)

Ratcliffe, C. M., Hatonen, J. J., Lewin, P. L., Rogers, E., Harte, T. J., and Owens, D. H. (2005) P-type iterative learning control for systems that contain resonance, *International Journal of Adaptive Control and Signal Processing*, 19, pp. 769-796

Reinkensmeyer, D., Kenna, C. A., Kahn, L., and Kamper, D. (2002) Directional control of reaching is preserved following mild/moderate stroke and stochastically constrained following severe stroke, *Experimental Brain Research*, 143 (4), pp. 525-530

Ridding, M. C., McKay, D. R., Thompson, P. D., and Miles, T. S. (2001) Changes in corticomotor representations induced by prolonged peripheral nerve stimulation in humans, *Clinical Neurophysiology*, 112 (8), pp. 1461-1469

Rogers, E. (2007) *Iterative Learning Control - from Hilbert Spaces to Robotics to Healthcare Engineering*. [United Kingdom Automatic Control Council Seminar]. 15-3-2007.

Rohrer, B., Fasoli, S., Krebs, H. I., Hughes, R., Volpe, B., Frontera, W. R., Stein, J., and Hogan, N. (2002) Movement smoothness changes during stroke recovery, *Journal of Neuroscience*, 22 (18), pp. 8297-8304

Rothwell, J. (2004) 'Motor Control', in Stokes, M. (ed.) *Physical Management in Neurological Rehabilitation*. Elsevier Mosby, pp. 3-19.

Rowland, T. J. and Gustafsson, L. (2008) Assessments of upper limb ability following stroke: a review, *British Journal of Occupational Therapy*, 71 (10), pp. 427-437

Rushton, D. N. (2003) Functional electrical stimulation and rehabilitation - an hypothesis, *Medical Engineering & Physics*, 25 (1), pp. 75-78

Saladin, K. S. (2004) *Anatomy and Physiology: The unity of form and function*. 3rd edn. New York, NY: McGraw-Hill.

Sanford, J., Moreland, J., and Swanson, L. R. (1993) Reliability of the Fugl-Meyer assessment for testing motor performance in patients following stroke, *Physical Therapy*, 73 (7), pp. 447-454

Sangani, S. G., Starsky, A. J., McGuire, J. R., and Schmit, B. (2007) Multijoint reflexes of the stroke arm: neural coupling of the elbow and shoulder., *Muscle & Nerve*, 36 (5), pp. 694-703

Schmidt, R. A. (1988) 'Motor and action perspectives on motor behaviour', in Meijer, O. G. and Roth, K. (ed.) *Complex Motor Behaviour: 'The' motor-action controversy*. Amsterdam: Elsevier, pp. 3-44.

Schmidt, R. A. and Lee, T. D. (1999) *Motor control and learning a behavioural emphasis*. 3rd Edition. Human Kinetics Part 3 Motor Learning.

Sherrington, C. S. (1906) *The integrative action of the nervous system*. New York: C Scribner and Sons.

Shumway-Cook, A and Woollacott, M. H. (2001) *Motor Control : Theory and practical applications*. Lippincott Williams and Wilkins.

Sonde, L., Gip, C., Fernaeus, S. E., Nilsson, C. G., and Viitanen, M. (1998) Stimulation with low frequency (1.7 Hz) transcutaneous electric nerve stimulation (low-TENS) increases motor function of the post-stroke paretic arm, *Scandinavian Journal of Rehabilitation Medicine*, 30, pp. 95-99

Stein, J., Krebs, H. I., Frontera, W. R., Fasoli, S. E., Hughes, R., and Hogan, N. (2004) Comparison of two techniques of robot-aided upper limb exercise training after stroke, *American Journal of Physical Medicine and Rehabilitation*, 83 (9), pp. 720-728

Stroke Association. Stroke Statistics Fact Sheet. 2006.

Takahashi, C. D., Der-Yeghaian, L., Le, V., Motiwala, R. R., and Cramer, S. C. (2008) Robot-based hand motor therapy after stroke, *Brain*, 131 (Pt:2), pp. 2-37

Taylor, P. N. (2002) *Functional Electrical Stimulation Newsletter*. Jan. 2002. Salisbury, UK.

Teasell, R, Foley, N, Salter, K, Bhogal, R. S, Bayona, N, Jutai, J, and Speechley, M. (2007) *Evidence Based Review of Stroke Rehabilitation*. Available at: <http://www.ebsr.com> (Accessed: 11-1-2009).

Thoroughman, K. A. and Shadmehr, R. (1999) Electromyographic Correlates of Learning an Internal Model of Reaching Movements, *Journal of Neuroscience*, 19 (19), pp. 8573-8588

Tulving, E. (1985) How many memory systems are there?, *American Psychologist*, 40, pp. 385-398

Tulving, E. and Thomson, D. M. (1973) Encoding specificity and retrieval processes in episodic memory, *Psychological Review*, 80, pp. 352-373

Turk, R, Burridge J.H., Merrill, D. R., Hughes A.M., Cosendai, G., and Schulman, J. (2008) 'Clinical effectiveness and participant perceptions of an implanted closed-loop neurostimulator-sensor system for arm rehabilitation post-stroke', *13th Annual Conference of the International Functional Electrical Stimulation Society "From movement to mind"*. Freiburg, Germany 21-9-2008. Berlin - New York: Walter de Gruyter

Uchiyama, M. (1978) Formation of high speed motion pattern of mechanical arm by trial, *Transactions of the Society of Instrumentation and Control Engineers*, 19 (5), pp. 706-712

van der Lee, J. H., Beckerman, H., Lankhorst, G. J., and Bouter, L. M. (2001a) The responsiveness of the Action Research Arm test and the Fugl-Meyer Assessment scale in chronic stroke patients, *Journal of Rehabilitation Medicine*, 33 (3), pp. 110-113

van der Lee, J. H., De Groot, V., Beckerman, H., Wagenaar, R. C., Lankhorst, G. J., and Bouter, L. M. (2001b) The intra- and interrater reliability of the action research arm test: a practical test of upper extremity function in patients with stroke, *Archives of Physical Medicine and Rehabilitation*, 82 (1), pp. 14-19

van der Putten, J. J. M. F., Hobart, J. C., Freeman J.A, and Thompson, A. J. (1999) Measuring change in disability after inpatient rehabilitation: comparison of the responsiveness of the Barthel Index and the Functional Independence Measure, *Journal of Neurology, Neurosurgery and Psychiatry*, 66 (4), pp. 480-484

Van Wijck, F. M. J., Pandyan, A. D., Johnson, G. R., and Barnes, M. P. (2001) Assessing motor deficits in neurological rehabilitation: patterns of instrument usage, *Neurorehabilitation and Neural Repair*, 15 (1), pp. 23-30

Verschueren, S. M. P., Swinnen, S. P., Desloovere, K., and Duyssens, J. (2003) Vibration-induced changes in EMG during human locomotion, *Journal of Neurophysiology*, 89 (3), pp. 1299-1307

Volpe, B. T., Krebs, H. I., Hogan, N., Edelstein, L., Diels, C. M., and Aisen, M. L. (1999) Robot training enhanced motor outcome in patients with stroke maintained over 3 years, *Neurology*, 53 (8), pp. 1874-1876

Wade, D. T., Langton-Hewer, R., Wood, V. A., Skilbeck, C. E., and Ismail, H. M. (1983) The hemiplegic arm after stroke: measurement and recovery, *Journal of Neurology, Neurosurgery and Psychiatry*, 46 (6), pp. 521-524

Welford, A. T. (1982) 'Motor skills and aging', in Mortimer, J., Pirozzolo, F. J., and Maletta, G. (ed.) *The Aging Motor System*. New York: Praeger, pp. 152-187.

Wilson, B. A., Cockburn, J., and Halligan, P. (1987) *Behavioural Inattention Test*. Titchfield, Hants: Thames Valley Test Company.

Winstein, C. J., Rose, D. K., Tan, S. M., Lewthwaite, R., Chui, H. C., and Azen, S. P. (2004) A randomized controlled comparison of upper-extremity rehabilitation strategies in acute stroke: a pilot study of immediate and long-term outcomes., *Archives of Physical Medicine and Rehabilitation*, 85 (4), pp. 620-628

Woldag, H., Waldmann, G., Heuschkel, G., and Hummelsheim, H. (2003) Is the repetitive training of complex hand and arm movements beneficial for motor recovery in stroke patients?, *Clinical Rehabilitation*, 17 (7), pp. 723-730

Wolf, S. L., Winstein, C. J., Miller, J. P., Taub, E., Uswatte, G., Morris, D., Giuliani, C., Light, K. E., and Nichols-Larsen, D. (2006) Effect of constraint-induced movement therapy on upper extremity function 3 to 9 months after stroke: the EXCITE randomized clinical trial., *Journal of the American Medical Association*, 296 (17), pp. 2095-2104

Wolf, S. L., Winstein, C. J., Miller, J. P., Thompson, P. A., Taub, E., Uswatte, G., Morris, D., Blanton, S., Nichols-Larsen, D., and Clark, P. C. (2008) Retention of upper limb function in stroke survivors who have received constraint-induced movement therapy: the EXCITE randomised trial, *Lancet Neurology*, 7 (1), pp. 33-40

World Health Organisation. (2001) *International Classification of Functioning, Disability and Health (ICF)*.

World Health Organisation. (2005) *The WHO STEPwise approach to stroke surveillance*.

Wu, C-Y., Trombly, C. A., Lin, K-C., and Tickle-Degnen, L. (2000) A kinematic study of contextual effects on reaching performance in persons with and without stroke: Influences of object availability, *Archives of Physical Medicine and Rehabilitation*, 81 (1), pp. 95-101

Wu, C., van Gelderen, P., Hanakawa, T., Yaseen, Z., and Cohen, L. G. (2005) Enduring representational plasticity after somatosensory stimulation, *Neuroimage*, 27 (4), pp. 872-884