

**BIOMECHANICAL AND MUSCLE PERFORMANCE ANALYSIS
DURING FUNCTIONAL ELECTRICAL STIMULATION-
EVOKED CYCLING IN SPINAL CORD INJURY INDIVIDUALS**

PUTERI NUR FARHANA BINTI HAMDAN

**FACULTY OF ENGINEERING
UNIVERSITI MALAYA
KUALA LUMPUR**

2024

**BIOMECHANICAL AND MUSCLE PERFORMANCE ANALYSIS
DURING FUNCTIONAL ELECTRICAL STIMULATION-
EVOKED CYCLING IN SPINAL CORD INJURY INDIVIDUALS**

PUTERI NUR FARHANA BINTI HAMDAN

**THESIS SUBMITTED IN FULFILMENT OF THE
REQUIREMENTS FOR THE DEGREE OF DOCTOR OF
PHILOSOPHY**

**FACULTY OF ENGINEERING
UNIVERSITI MALAYA
KUALA LUMPUR**

2024

UNIVERSITI MALAYA
ORIGINAL LITERARY WORK DECLARATION

Name of Candidate: Puteri Nur Farhana binti Hamdan

Matric No: KVA180015

Name of Degree: Doctor of Philosophy

Title of Thesis (“this Work”): Biomechanical and Muscle Performance Analysis during Functional Electrical Stimulation-Evoked Cycling in Spinal Cord Injury Individuals

Field of Study: Rehabilitation Engineering

I do solemnly and sincerely declare that:

- (1) I am the sole author/writer of this Work;
- (2) This Work is original;
- (3) Any use of any work in which copyright exists was done by way of fair dealing and for permitted purposes and any excerpt or extract from, or reference to or reproduction of any copyright work has been disclosed expressly and sufficiently and the title of the Work and its authorship have been acknowledged in this Work;
- (4) I do not have any actual knowledge nor do I ought reasonably to know that the making of this work constitutes an infringement of any copyright work;
- (5) I hereby assign all and every rights in the copyright to this Work to the Universiti Malaya (“UM”), who henceforth shall be owner of the copyright in this Work and that any reproduction or use in any form or by any means whatsoever is prohibited without the written consent of UM having been first had and obtained;
- (6) I am fully aware that if in the course of making this Work I have infringed any copyright whether intentionally or otherwise, I may be subject to legal action or any other action as may be determined by UM.

Candidate’s Signature

Date: 14/5/2024

Subscribed and solemnly declared before,

Witness’s Signature

Date: 14/5/2024

Name:

Designation:

**BIOMECHANICAL AND MUSCLE PERFORMANCE ANALYSIS DURING
FUNCTIONAL ELECTRICAL STIMULATION-EVOKED CYCLING IN
SPINAL CORD INJURY INDIVIDUALS**

ABSTRACT

Functional electrical stimulation (FES)-evoked cycling has been reported to enhance muscle strength and fatigue resistance after spinal cord injury (SCI). Its goal is to produce the highest possible power to maximize physiological benefits. With the tuning between the foot and pedal contact point to the relative strength of the ankle plantar flexors, power production was simulated to be improved by 14% by releasing the ankle joint from a fixed ankle setup and with the stimulation of the tibialis anterior and triceps surae. FES-evoked cycling however produces very low power and efficiency in individuals with SCI compared to healthy individuals. This is because of the early onset of muscle fatigue among individuals with SCI. To date, muscle fatigue during FES-evoked cycling in individuals with SCI has been quantified in many studies by means of peak torque or pedal power output (PO) decrement. These measures may not be sensitive and do not reflect metabolic markers of fatigue. This study aimed to experimentally determine the effect of releasing the ankle joint on the pedal power production during FES-evoked cycling in individuals with SCI. This study also aimed to examine the relationship between the vibrational performance of electrically-evoked muscles measured through mechanomyography (MMG) and its oxidative metabolism through near-infrared spectroscopy (NIRS) characteristics during FES-evoked cycling in individuals with SCI. This study also sought to quantify muscle fatigue during FES-evoked cycling using MMG and NIRS. Seven individuals with motor complete SCI participated in this study. In achieving the first objective of this study, all participants performed one minute of fixed-ankle and free-ankle FES-evoked cycling with two stimulation modes. In Mode 1, participants performed FES-evoked cycling with the

stimulation of quadriceps and hamstring muscles only (QH stimulation), while Mode 2 had stimulation of quadriceps, hamstring, tibialis anterior, and triceps surae muscles (QHT stimulation). Free-ankle FES-evoked cycling offered greater ankle plantar- and dorsiflexion at specific slices of 20° crank angle intervals compared to fixed-ankle. Fixed-ankle QHT stimulation elevated the peak normalized pedal PO by 14.5% more than free-ankle QH stimulation. Releasing the ankle joint without the stimulation of triceps surae and tibialis anterior reduces PO. The findings of this study suggest that QHT stimulation is necessary during free-ankle FES-evoked cycling to maintain power production as fixed-ankle. For the second and third objectives, all participants performed 30 minutes of FES-evoked cycling with MMG and NIRS sensors on their quadriceps throughout the cycling, and the signals were analyzed. A moderate significant negative correlation was found between MMG root mean square (RMS) and oxyhaemoglobin (O₂Hb) [$r = -0.38$, $p = 0.003$], and RMS and total haemoglobin (tHb) saturation [$r = -0.31$, $p = 0.017$]. There were significant differences in RMS, O₂Hb, and tHb saturation during pre- and post-fatigue of FES-evoked cycling ($p < 0.05$). MMG RMS was negatively associated with O₂Hb and muscle oxygen derived from NIRS. MMG and NIRS sensors showed good inter-correlations with each other, suggesting a promising use of MMG for characterizing metabolic fatigue at the muscle oxygenation level during FES-evoked cycling in individuals with SCI.

Keywords: FES-evoked cycling; Spinal cord injury; Power output; MMG RMS-NIRS; Muscle fatigue.

**ANALISIS BIOMEKANIKAL DAN PRESTASI OTOT SEMASA BERBASIKAL
DENGAN RANGSANGAN ELEKTRIK BERFUNGSI DALAM KALANGAN
INDIVIDU DENGAN KECEDERAAN SARAF TUNJANG**

ABSTRAK

Berbasikal dengan rangsangan elektrik berfungsi (FES) mampu menguatkan kekuatan dan daya tahan otot individu dengan kecederaan saraf tunjang (SCI). Tujuan utamanya adalah untuk menghasilkan kuasa yang tinggi untuk memaksimumkan faedah kesihatan fisiologi. Dengan penalaan titik sentuhan antara kaki dan pedal kepada kekuatan relatif plantar flexor, kajian simulasi berbasikal dengan FES menunjukkan peningkatan kuasa sebanyak 14% apabila pergerakan buku lali dibebaskan berbanding pergerakan buku lali ditetapkan dengan penambahan rangsangan elektrik pada otot tibialis hadapan dan trisep surae. Berbasikal dengan FES menghasilkan kuasa yang sangat rendah dalam kalangan individu dengan SCI berbanding individu sihat. Ini kerana berlakunya keletihan otot yang cepat dalam kalangan individu dengan SCI. Sehingga kini, pengukuran keletihan otot semasa berbasikal dengan FES dalam kalangan individu dengan SCI sebagai penurunan puncak tork atau keluaran kuasa (PO) pedal. Pendekatan ini berkemungkinan tidak sensitif dan tidak menggambarkan petanda keletihan metabolik. Tujuan kajian ini dijalankan adalah untuk membuktikan secara eksperimen kesan pembebasan pergerakan buku lali terhadap PO pedal ketika berbasikal dengan FES dalam kalangan individu dengan SCI. Tujuan kajian ini dijalankan juga adalah untuk memeriksa hubungan antara prestasi getaran ketika rangsangan elektrik di otot melalui mekanomiografi (MMG) dan metabolisme pengoksidaannya melalui ciri-ciri spektroskopi inframerah dekat (NIRS) semasa berbasikal dengan FES dalam kalangan individu dengan SCI. Kajian ini turut dijalankan untuk mengukur keletihan otot ketika berbasikal dengan FES dengan menggunakan MMG dan NIRS. Tujuh individu dengan SCI motor lengkap telah menyertai kajian ini.

Untuk mencapai objektif pertama kajian ini, kesemua peserta telah berbasikal dengan buku lali-tetap dan buku lali-bebas selama satu minit dengan dua mod rangsangan. Semasa mod rangsangan 1, peserta berbasikal dengan FES dengan rangsangan pada otot kuadrisep dan hamstring (rangsangan QH), sementara semasa mod rangsangan 2, peserta berbasikal dengan FES dengan rangsangan pada otot kuadrisep, hamstring, tibialis hadapan, dan trisep surae (rangsangan QHT). Berbasikal dengan FES dengan buku lali-bebas menghasilkan pergerakan dorsifleksi and fleksi plantar yang lebih besar berbanding buku lali-tetap pada setiap 20° sudut engkol tertentu. Buku lali-tetap rangsangan QHT meningkatkan puncak PO pedal yang dinormalkan sebanyak 14.5% daripada buku lali-bebas rangsangan QH. Buku lali-bebas tanpa rangsangan pada tibialis hadapan dan trisep surae mengurangkan PO. Penemuan ini mencadangkan kepentingan rangsangan QHT ketika berbasikal dengan buku lali-bebas untuk mengekalkan penghasilan kuasa seperti berbasikal dengan buku lali-tetap. Untuk objektif kedua dan ketiga, kesemua peserta berbasikal dengan FES selama 30 minit dengan penderia MMG dan NIRS diletakkan pada kuadrisep sepanjang berbasikal, dan isyarat-isyarat daripada penderia tersebut dianalisis. Terdapat korelasi negatif sederhana yang ketara antara MMG punca purata kuasa dua (RMS) dan kepekatan oksihemoglobin (O₂Hb) [$r = -0.38, p = 0.003$], dan RMS dan jumlah kepekatan hemoglobin (tHb) [$r = -0.31, p = 0.017$]. Terdapat juga perbezaan yang ketara antara RMS, dan kepekatan O₂Hb, dan tHb sebelum- dan selepas-keletihan otot ketika berbasikal dengan FES ($p < 0.05$). MMG RMS berkait negatif dengan O₂Hb dan oksigen otot diperolehi daripada NIRS. Penderia MMG dan NIRS telah menunjukkan saling korelasi yang baik antara satu sama lain, mencadangkan penggunaan MMG yang terjamin dalam mencirikan keletihan metabolik pada peringkat pengoksigenan otot semasa berbasikal dengan FES dalam kalangan individu dengan SCI.

Kata kunci: Berbasikal dengan rangsangan elektrik berfungsi; Kecederaan saraf tunjang; Daya kuasa; MMG RMS-NIR; Keletihan otot.

Universiti Malaya

ACKNOWLEDGEMENTS

Firstly, I would like to express my sincere gratitude to my supervisors, Associate Professor Dr. Nur Azah Hamzaid, Professor Dr. Nazirah Hasnan, and Ir. Dr. Nasrul Anuar Abd Razak made this work possible. Their guidance carried me throughout my study. I would also like to thank the Department of Biomedical Engineering of Universiti Malaya for providing me with the facilities and opportunities to complete my study.

A special thanks to Professor Glen M Davis, Dr. Rizal Mohd Razman, and Mrs. Mira Teoh Xiao-Hui for their guidance throughout this study. Many thanks to my fellow research mates for sharing knowledge and enjoyable moments while we were all struggling with our projects. I would also like to give my warmest thanks to the participants who participated in this study consistently. Their commitment to the training and experiment made this study possible to be completed.

I am deeply grateful to my families, Mr. Hamdan Mohamed, Mrs. Raja Zawiah Raja Mohd Noor, Mr. Hizwan Khalid, Miss Puteri Nur Farahin Hamdan, and Mr. Muhammad Fahmi Hamdan for their huge help and endless support throughout my study.

Finally, I thank my husband, Mr. Muhammad Shukri Mohd Sahiban for his moral and financial support throughout my study. And to my children, Muhammad Aariz Muhammad Shukri, Muhammad Idris Muhammad Shukri, and Puteri Nur Airin Muhammad Shukri, this thesis is for you. Bonda loves you guys so much.

This research was supported by the Ministry of Higher Education, Malaysia, and Universiti Malaya through the Fundamental Research Grant Scheme (FRGS) FP099-2018A, FP002-2020, and FRGS/1/2020/SKK0/UM/02/1. This research was also supported by a Postgraduate Research Grant (PPP) PG027-2015A.

TABLE OF CONTENTS

| | |
|--|----------|
| Abstract | iii |
| Abstrak | v |
| Acknowledgements | viii |
| Table of Contents | ix |
| List of Figures | xiv |
| List of Tables..... | xvii |
| List of Symbols and Abbreviations..... | xviii |
| List of Appendices | xxi |
| | |
| CHAPTER 1: INTRODUCTION..... | 1 |
| 1.1 Background..... | 1 |
| 1.1.1 Spinal Cord Injury (SCI): Causes and Effects..... | 1 |
| 1.1.2 Classification of SCI..... | 3 |
| 1.1.2.1 American Spinal Injury Association Impairment Scale (AIS).... | 3 |
| 1.1.2.2 Lesion level | 5 |
| 1.1.3 Recovery After SCI | 6 |
| 1.1.4 Rehabilitation Exercise After SCI..... | 8 |
| 1.1.5 Functional Electrical Stimulation (FES)-Evoked Cycling | 12 |
| 1.1.5.1 The Standard Setup of FES-evoked Cycling..... | 14 |
| 1.1.5.2 Types of FES-evoked Cycling Ergometer | 15 |
| 1.1.5.3 FES-evoked Cycling in the Cybathlon Championship | 18 |
| 1.1.5.4 Benefits of FES-evoked Cycling for Individuals with SCI..... | 19 |
| 1.1.5.5 Limitations of FES-evoked Cycling for Individuals with SCI.. | 20 |
| 1.1.6 Power Output (PO) Production during FES-Evoked Cycling in Individuals with SCI..... | 21 |

| | | |
|--|--|-----------|
| 1.1.7 | Factors Limiting the Production of Mechanical PO during FES-Evoked Cycling in Individuals with SCI..... | 22 |
| 1.1.7.1 | Biomechanical Inefficiency during FES-evoked Cycling..... | 22 |
| 1.1.7.2 | Muscle Fatigue during FES-evoked Cycling..... | 23 |
| 1.2 | Motivation for the Study..... | 26 |
| 1.3 | Problem Statement..... | 27 |
| 1.4 | Objectives of Study..... | 28 |
| 1.5 | Hypothesis of the Study..... | 28 |
| 1.6 | Aim of the Study..... | 29 |
| 1.7 | Significance of the Study..... | 29 |
| 1.8 | Scope of the Study..... | 29 |
| 1.9 | Thesis Organization..... | 30 |
| CHAPTER 2: LITERATURE REVIEW..... | | 32 |
| 2.1 | Low Efficiency and Power Production during FES-Evoked Cycling Exercise in Individuals with SCI..... | 32 |
| 2.2 | Selection of Parameters of Interest from the Teams Participating in the Cybathlon Championship 2016..... | 33 |
| 2.3 | Origins of Power during FES-Evoked Cycling..... | 37 |
| 2.3.1 | Optimization of Stimulation Parameters..... | 37 |
| 2.3.2 | Muscles Stimulation..... | 39 |
| 2.3.3 | Biomechanics of Ankle Joint..... | 42 |
| 2.4 | Muscle Activity Assessment during FES-Evoked Cycling Exercise..... | 45 |
| 2.5 | Summary of Literature Review..... | 48 |
| CHAPTER 3: METHODOLOGY..... | | 49 |
| 3.1 | Participants..... | 50 |

| | | |
|--------------------------------|---|-----------|
| 3.2 | Biomechanical Effects on Power Production during FES-Evoked Cycling in Individuals with SCI (F1) | 51 |
| 3.2.1 | Instrumentation..... | 51 |
| 3.2.2 | Leg Muscles Stimulation Pattern..... | 53 |
| 3.2.3 | Experimental Protocol..... | 54 |
| 3.2.4 | Data Acquisition and Processing..... | 55 |
| 3.2.5 | Statistical Analysis | 56 |
| 3.3 | Muscle Performance at the Muscle Level during FES-Evoked Cycling in Individuals with SCI (F2) | 57 |
| 3.3.1 | Instrumentation..... | 57 |
| 3.3.1.1 | Fatigue measurement..... | 57 |
| 3.3.1.2 | FES-evoked cycling | 57 |
| 3.3.1.3 | Near-Infrared Spectroscopy | 58 |
| 3.3.1.4 | Mechanomyography..... | 59 |
| 3.3.2 | Experimental Protocol..... | 60 |
| 3.3.3 | Data Acquisition and Processing..... | 61 |
| 3.3.3.1 | Mechanomyography..... | 61 |
| 3.3.3.2 | Near-Infrared Spectroscopy | 62 |
| 3.3.3.3 | Power Output..... | 63 |
| 3.3.4 | Statistical Analysis | 63 |
| CHAPTER 4: RESULTS..... | | 65 |
| 4.1 | Analysis of the Biomechanical Effects on Power Production during FES-evoked Cycling in Individuals with SCI | 65 |
| 4.1.1 | Kinetics and Kinematics Change throughout 360° of Crank Angle | 73 |
| 4.2 | Analysis of Muscle Performance at the Muscle Level during FES-Evoked Cycling in Individuals with SCI..... | 77 |

| | | |
|------------------------------------|---|-----------|
| 4.2.1 | Correlation between the MMG and NIRS Signals | 77 |
| 4.2.2 | Correlation between the PO and NIRS signals..... | 80 |
| 4.2.3 | Correlation between the PO and MMG signals..... | 80 |
| 4.2.4 | Effects of 30 Minutes of FES-Evoked Cycling on the MMG, NIRS, and PO Findings | 80 |
| 4.2.5 | Muscle Oxygen Consumption during FES-Evoked Cycling..... | 83 |
| CHAPTER 5: DISCUSSION | | 84 |
| 5.1 | Biomechanical Effects on Pedal Power Production during FES-Evoked Cycling in Individuals with SCI..... | 84 |
| 5.1.1 | The Effects of Releasing the Ankle Joint on the Pedal Power Production 84 | |
| 5.1.2 | The Effects of Releasing Ankle Joint on the Ankle, Knee, and Hip ROMs 87 | |
| 5.2 | Muscle Performance at the Muscle Level during FES-Evoked Cycling in Individuals with SCI..... | 88 |
| 5.2.1 | Relationships between Muscle Performance, Power Output, and Muscle Metabolism during FES-Evoked Cycling in Individuals with SCI..... | 89 |
| 5.2.2 | Muscle Fatigue Assessment using MMG and NIRS..... | 90 |
| 5.3 | Relationship between Biomechanics and Muscle Performance on the Efficiency of FES-Evoked Cycling | 93 |
| CHAPTER 6: CONCLUSION..... | | 96 |
| 6.1 | Limitations of the Study | 96 |
| 6.2 | Future Recommendations | 97 |
| 6.3 | Novelty and Knowledge Contribution..... | 98 |
| | References..... | 99 |

| | |
|---|-----|
| List of Publications and Papers Presented | 123 |
| Appendix | 125 |
| CO-AUTHORS CONSENT..... | 131 |

Universiti Malaya

LIST OF FIGURES

| | |
|--|----|
| Figure 1.1: Types of SCI based on the location of injury (Michaud, 2020). | 5 |
| Figure 1.2: Principle of feedback-controlled FES (Schauer, 2006). | 10 |
| Figure 1.3: Schematic representation of a position of motor point (MP) (Gobbo et al., 2014). | 10 |
| Figure 1.4: FES-evoked cycling system (Tong et al., 2017). | 13 |
| Figure 1.5: Timing of the muscle stimulations during FES-evoked cycling exercise; left quadriceps (LQ), right quadriceps (RQ), left hamstrings (LH), right hamstrings (RH), left gluteus (LG), and right hamstrings (RG) (Johnston et al., 2016). | 14 |
| Figure 1.6: Types of stationary FES-evoked cycling ergometer(a) a traditional ergometer and (b) a hybrid ergometer for home use (Chen et al., 2004). | 16 |
| Figure 1.7: Outdoor recreational FES-evoked cycling ergometer-without hand cycling (Catrike 700 recumbent tricycles) (McDaniel et al., 2017b). | 16 |
| Figure 1.8: Outdoor recreational FES-evoked cycling ergometer-hybrid (with hand cycling) (BerkelBike) (Bakkum et al., 2015). | 17 |
| Figure 1. 1.9: Natural versus artificial muscle activation by FES (Schauer, 2006). | 24 |
| Figure 1.10: An insight into the ways to optimize the efficiency and power production during FES-evoked cycling in individuals with SCI used in this study. | 26 |
| Figure 2.1: Stimulated muscles during FES-evoked cycling in individuals with SCI. | 40 |
| Figure 2.2: Schematic graph for the definition of the power components P1-P4 contributing toward total power during a crank revolution. P1 represents the first power component, P2 represents the second power component, P3 represents the third power component, and P4 represents the fourth power component (Szecsi et al., 2014a). | 41 |
| Figure 2.3: The dead points and the crank position with respect to the hip joint (Abdulla et al., 2014). | 41 |
| Figure 2.4: The ankle is immobilized by Aircast ankle-foot immobilizers to lock the ankle position (McDaniel et al., 2017b). | 43 |
| Figure 3.1: Flow chart of research activities. | 49 |
| Figure 3.2: Setup for fixed-ankle FES-evoked cycling. Shown is the placement of markers over the fifth metatarsophalangeal and ankle joints in the solid AFO. Electrodes | |

were placed on the quadriceps, hamstrings, tibialis anterior, and triceps surae muscles.
 53

Figure 3.3: Two stimulation modes of FES-evoked cycling were used in this study; (a) QH stimulation; (b) QHT stimulation; and (c) stimulation angle. Image adapted from the software 3D Anatomy Learning (Version 3.9, Education Mobile) (open-source project). 54

Figure 3.4: Setup for FES-evoked cycling. Shown is the placement of electrodes over the quadriceps and hamstrings muscle groups. The MMG and NIRS sensors were placed over the muscle belly of the left vastus lateralis. 58

Figure 3.5: Experimental protocol in analyzing the muscle performance at the muscle level during FES-evoked cycling in individuals with SCI. 61

Figure 3.6: The quantification of the initial decrease of the O₂Hb. (a) Muscle oxygen consumption from arterial occlusion can be calculated from (b) the linear decrease in the O₂Hb during occlusion. 63

Figure 4.1: The interaction and boxplot of the effect of fixed- and free-ankle FES-evoked cycling with QH and QHT stimulations across each slice of 20° crank angle intervals on (a) mean normalized pedal PO; (b) peak normalized pedal PO; (c) mean ankle ROM; (d) mean knee ROM; and (e) mean hip ROM. *⁰ Denotes $p < 0.05$ between free-ankle QH stimulation compared to the other settings. 72

Figure 4.2: The PO and ROM generated during fixed- and free-ankle FES-evoked cycling with QH and QHT stimulations by each slice of 20° crank angle position from 0° to 360°. (a) mean normalized pedal PO; (b) peak normalized pedal PO; (c) mean ankle ROM; (d) mean knee ROM; and (e) mean hip ROM. *¹ Denotes $p < 0.05$ between free-ankle QH stimulation and fixed-ankle QHT stimulation, *² denotes $p < 0.05$ between free-ankle QHT stimulation and fixed-ankle QH stimulation, *³ denotes $p < 0.05$ between free-ankle QHT stimulation and free-ankle QH stimulation, *⁴ denotes $p < 0.05$ between free-ankle QHT stimulation and fixed-ankle QHT stimulation, and *⁵ denotes $p < 0.05$ between fixed-ankle QHT stimulation and fixed-ankle QH stimulation. 76

Figure 4.3: Actual data from the NIRS, MMG, and cadence during the experiment. (a) NIRS signals were recorded throughout the experiment, including occlusion; (b) cadence was recorded per minute during exercise only, where epochs were defined; (c) and (d) NIRS and MMG signals were analyzed during exercise, where epochs were defined; (e) and (f) are a closer look at the signals for epoch 3 from NIRS and MMG signals. 78

Figure 4.4: Relationships between the normalized MMG RMS and NIRS parameters, power and NIRS parameters, and normalized MMG RMS and power. (a) RMS-%TSI;

(b) RMS-O₂Hb; (c) RMS-HHb; (d) RMS-tHb; (e) PO-%TSI; (f) PO-O₂Hb; (g) PO-HHb; (h) PO-tHb; and (i) RMS-PO. 79

Figure 4.5: Parameter values from 30 minutes of FES-evoked cycling according to epochs, of (a) MMG RMS; (b) %TSI; (c) O₂Hb; (d) HHb; and (e) tHb. Epochs 1-5 denote pre-defined periods for data collection as described in the data acquisition and processing section. *^a Denotes $p < 0.05$ between epoch 1 compared to the rest of the epochs; *^b denotes $p < 0.05$ between epoch 1 compared to epoch 3, 4, and 5; *^c denotes $p < 0.05$ between epoch 2 and epoch 5; and *^d denotes $p < 0.05$ between epoch 3 and epoch 5. 82

Figure 4.6: Muscle oxygen consumption before and after 30 minutes of FES-evoked cycling. *Denotes $p < 0.05$ (2 tailed) 83

Figure 5.1: An insight into the overall findings of the present study..... 94

Universiti Malaysia

LIST OF TABLES

| | |
|--|----|
| Table 1.1: The classification of SCI based on AIS (Kirshblum et al., 2011)..... | 4 |
| Table 1.2: The classification of SCI based on lesion level (Schauer, 2017)..... | 5 |
| Table 2.1: Modulation of stimulation parameters used during FES-evoked cycling among individuals with SCI in previous studies..... | 39 |
| Table 3.1: Physical characteristics of the SCI participants..... | 51 |
| Table 4.1: The range of raw pedal PO obtained between fixed- and free-ankle FES-evoked cycling with QH and QHT stimulation modes, generated from 0° to 360° crank angle..... | 66 |
| Table 4.2: The normalized pedal PO obtained between fixed- and free-ankle FES-evoked cycling with QH and QHT stimulation modes across each slice of 20° crank angle intervals..... | 72 |

LIST OF SYMBOLS AND ABBREVIATIONS

| | | |
|------------|---|---|
| α | : | Alpha |
| $^{\circ}$ | : | Degree |
| %TSI | : | Percentage of tissue saturation index |
| 3D | : | Three-dimensional |
| ADL | : | Activities of daily living |
| AFO | : | Ankle-foot orthoses |
| AIS | : | American Spinal Injury Association Impairment Scale |
| ANOVA | : | One-way repeated measures analysis of variance |
| C | : | Cervical |
| CNS | : | Central nervous system |
| CVD | : | Cardiovascular disease |
| DM | : | Diabetes mellitus |
| D&B | : | Downs and Black |
| EMG | : | Electromyography |
| F1 | : | Part 1 of the study |
| F2 | : | Part 2 of the study |
| FES | : | Functional electrical stimulation |
| HHb | : | Deoxyhaemoglobin |
| ISNCSCI | : | International Standards for Neurological Classification of Spinal Cord Injury |
| L | : | Lumbar |
| LG | : | Left gluteus |
| LH | : | Left hamstrings |
| LQ | : | Left quadriceps |

| | | |
|--------------------|---|--|
| LSD | : | Least significant difference |
| MMG | : | Mechanomyography |
| mmHg | : | Millimeters of mercury |
| mNIRS | : | Muscle near-infrared spectroscopy |
| MP | : | Motor point |
| mVO ₂ | : | Muscle oxygen consumption |
| N/A | : | Not applicable |
| NIRS | : | Near-infrared spectroscopy |
| NM | : | Not mentioned |
| O ₂ | : | Oxygen |
| O ₂ Hb | : | Oxyhaemoglobin |
| O ₂ Sat | : | Oxygen saturation |
| P1 | : | First power component |
| P2 | : | Second power component |
| P3 | : | Third power component |
| P4 | : | Fourth power component |
| PC | : | Personal computer |
| PO | : | Power output |
| QH | : | Quadriceps and hamstrings |
| QHT | : | Quadriceps, hamstrings, tibialis anterior, and triceps surae |
| QOL | : | Quality of life |
| RG | : | Right gluteus |
| RH | : | Right hamstrings |
| RMS | : | Root mean square |
| ROM | : | Range of movement |
| rpm | : | Revolutions per minute |

| | | |
|------|---|----------------------------------|
| RQ | : | Right quadriceps |
| S | : | Sacral |
| SD | : | Standard deviation |
| sEMG | : | Surface electromyography |
| SCI | : | Spinal cord injury |
| T | : | Thoracic |
| TA | : | Tibialis anterior |
| tHb | : | Total haemoglobin |
| TS | : | Triceps surae |
| TSI | : | Tissue saturation index |
| UMMC | : | Universiti Malaya Medical Centre |

Universiti Malaya

LIST OF APPENDICES

| | |
|--|-----|
| A1: Consent form in English version. | 125 |
| B1: Consent form in Malay version. | 126 |
| C1: The ethics approved by UMMC. | 127 |
| D1: Example of the pedal force captured by the F-scan sensor used in the study. | 128 |
| E1: Example of the hip, knee, ankle joint kinematics captured by the Vicon system used in the study. | 129 |
| F1: Example of the changes in muscle oxygenation captured by the NIRS sensor used in the study. | 130 |

CHAPTER 1: INTRODUCTION

This chapter provides general information related to spinal cord injury (SCI), particularly its causes and effects following the SCI, the classification of the injury, and the recovery plans following the injury types. Besides that, it describes the implementation of functional electrical stimulation (FES) technology in therapy exercises, specifically FES-evoked cycling in individuals with SCI. It also explains the benefits and limitations of FES-evoked cycling and the power output (PO) production during FES-evoked cycling in individuals with SCI.

1.1 Background

1.1.1 Spinal Cord Injury (SCI): Causes and Effects

Spinal cord injury (SCI) is a neuromuscular disease, where an injury happens to the spinal cord that blocks the communications between the central nervous system (CNS) (brain) and peripheral nerves (body) (Ho et al., 2014). The CNS loses the ability to control the intact neuromuscular systems (Fenton et al., 2022; Ho et al., 2014), hence, leading to paralysis, which limits the mobility-producing muscular activation (Dolbow, 2015). Due to paralysis, all areas of life in individuals with SCI change markedly (Kuhn et al., 2014).

The number of SCI cases is growing annually (Arnin et al., 2017). The causes of SCI vary. In general, SCI is a result of physical trauma such as traffic accidents (Schauer, 2017), falls and violent injuries (Singh et al., 2014), or non-traumatic reasons such as tumors (Schauer, 2017). Worldwide, traffic accidents are the major cause of SCI (Singh et al., 2014) and consist of more males, aged younger than 30 (Schauer, 2017).

The effects after SCI depend on the location of the injury level and the severity of the lesion (Fenton et al., 2022). Generally, SCI leads to paralysis below the level of injury

in individuals with SCI (Dolbow, 2015). They lose the ability to walk due to the loss of muscle strength (motor control) and/or sensory control (McKinley et al., 1999). As a result, their abilities to complete functional activities, typical activities of daily living (ADL) (Kasukawa et al., 2022), and independence and mobility have been decreasing (Duenas et al., 2020; Fattal et al., 2021). Hence, they depend on a wheelchair as a medium of mobility for a lifetime (Kasukawa et al., 2022) to improve their quality of life (QOL). However, prolonged immobilization due to muscle inactivity (Pette & Vrbová, 1992) and inactive lifestyle (Bloemen-Vrencken et al., 2007; Manns & Chad, 1999) after SCI can induce muscle atrophy (Rosley et al., 2019), reduce cardiopulmonary function, loss of bone mass (Cardosode Sousa et al., 2019), and other secondary medical complications (Gelenitis et al., 2021).

Muscle atrophy is the most prominent and rapid effect immediately after SCI resulting from prolonged immobilization (Topp et al., 2002). Muscle atrophy is a condition where there is a reduction in muscle mass and the ability of the muscle to contract (Wiesener & Schauer, 2017). Muscle atrophy is more significant in muscles that cross a single joint (Roy et al., 1991; Stein et al., 1992), which are primarily responsible for maintaining posture and bearing weight (Roy et al., 1991). For example, the quadriceps muscles hold the body while standing (Kralj & Bajd, 1989). Following muscle atrophy, the size of quadriceps muscles and the knee joint range of movement (ROM) decrease significantly (Popovic-Maneski et al., 2018). Consequently, it will lead to the development of stiffness in the quadriceps muscles and tendons at the knee joint (Popovic-Maneski et al., 2018). Upon muscle atrophy and limited joint ROM, individuals with SCI have to be bedded or seated in a wheelchair for a lifetime. This inactive lifestyle will lead to the development of blood vessel atrophy (de Groot et al., 2006) and pressure ulcers on the intact body part to the bed or wheelchair. Besides that, the skeletal muscle oxidative capacity is greatly impaired following muscle atrophy

(Gorgey & Dudley, 2007; Talmadge et al., 2002). The muscles transform from type I muscle fibers (slow fiber type) to type II muscle fibers (fast fiber type) within a relatively short period (Wiesener & Schauer, 2017).

Another significant effect of SCI is reducing cardiopulmonary function. Muscle atrophy and increasing fat mass (Gorgey et al., 2014) expose a high risk of cardiovascular disease (CVD) in individuals with SCI (Myers et al., 2007; Phillips et al., 1998). CVD more frequently occurs in individuals with SCI than in other populations (Garshick et al., 2005). Hence, CVD has become the leading cause of mortality in individuals with SCI (Groah et al., 2011) compared to non-disabled individuals (Middleton et al., 2012).

1.1.2 Classification of SCI

As mentioned in section 1.1.1, the effects after SCI depend on the injury level of SCI. In this section, the classification of SCI will be described to provide a further understanding of the effects of SCI associated with the injury level. The classification of SCI has been categorized by different methods, depending on the preserved motor and sensory functions, and the location of the injury. There are two ways of categorizing the SCI; the American Spinal Injury Association Impairment Scale (AIS), and lesion level.

1.1.2.1 American Spinal Injury Association Impairment Scale (AIS)

The AIS is an accurate and specific approach to categorizing both motor and sensory impairment (Dolbow, 2015). This scale identifies the sensory and motor levels as indicated by the most rostral spinal levels with unimpaired function (Kirshblum et al., 2011).

Table 1.1: The classification of SCI based on AIS (Kirshblum et al., 2011).

| AIS | Description |
|------------------------|---|
| A (Complete) | No sensory or motor function is preserved in the sacral segments S4–S5. |
| B (Sensory incomplete) | Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4–S5 (light touch, pin prick at S4–S5, or deep anal pressure), and no motor function is preserved more than three levels below the motor level on either side of the body. |
| C (Motor incomplete) | Motor function is preserved below the neurological level and more than half of key muscle functions below the single neurological level of injury have a muscle grade less than 3. |
| D (Motor incomplete) | Motor function is preserved below the neurological level and at least half of key muscle functions below the neurological level of injury have a muscle grade of 3 or greater. |
| E (Normal) | If sensation and motor function as tested with the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) are graded as normal in all segments, and the patient had prior deficits, then the AIS grade is E. |

Based on **Table 1.1**, AIS A is also known as a complete SCI (Kirshblum et al., 2011). Individuals with complete SCI have no motor or sensory functions below the level of injury (Tong et al., 2017) including the lowest sacral, typically the lower limb. Most of them depend on a wheelchair for a lifetime and have to deal with secondary medical complications (Figoni et al., 2021; Kaur, 2014). They also have greater impairment levels (Dolbow, 2015) and a higher risk of developing CVD, type 2 diabetes mellitus (DM), and osteoporosis compared to individuals with incomplete SCI (Bauman & Spungen, 2008).

On the other hand, incomplete SCI such as AIS B, C, and D are defined when sensation and/or motor activity below the level of injury, including the lowest sacral, is preserved (Kirshblum et al., 2011) (**Table 1.1**). They have fewer impairment levels compared to individuals with complete SCI. In this study, AIS is preferred as it offers a more accurate approach to categorizing SCI.

1.1.2.2 Lesion level

The other way to categorize the SCI is the lesion level. Contrary to AIS classification, lesion level is categorized depending on the location of injury; cervical (C) (vertebra C1–C8), thoracic (T) (vertebra T1–T12), lumbar (L) (vertebra L1–L5), or sacral (S) (vertebra S1–S5) (Schauer, 2017) (**Figure 1.1**). This type of categorization, however, is less precise than AIS (Kirshblum et al., 2011).

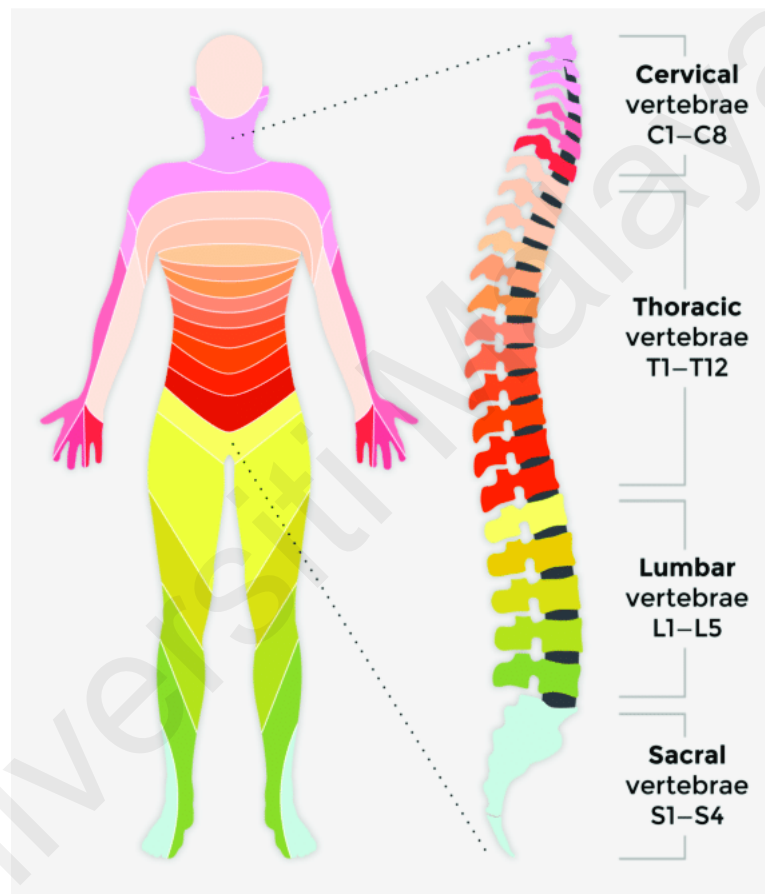


Figure 1.1: Types of SCI based on the location of injury (Michaud, 2020).

Table 1.2: The classification of SCI based on lesion level (Schauer, 2017).

| Lesion level | Location of injury |
|--------------------|------------------------------------|
| High (tetraplegia) | Cervical level |
| Low (paraplegia) | Thoracic, lumbar, or sacral levels |

Based on **Table 1.2**, a high lesion level of SCI is defined when the location of injury occurred at the cervical level (Dolbow, 2015). It is also known as tetraplegia (Schauer,

2017) or quadriplegia. Most individuals with SCI are tetraplegia (Schauer, 2017). The impairment of tetraplegics is high (Dolbow, 2015), where all four limbs (Schauer, 2017) and the trunk (Dolbow, 2015) are affected. They have difficulties performing ADLs such as eating and dressing (Dolbow, 2015). Their respiratory function ability is also decreasing (Schauer, 2017), consequently, becoming the primary cause of death in individuals with SCI (Dolbow, 2015).

On the other hand, a low lesion level of SCI is defined when the location of injury occurs at thoracic, lumbar, or sacral levels (Dolbow, 2015) (**Table 1.2**). It is also known as the paraplegia (Schauer, 2017). Typically, the impairment level of paraplegics is low (Dolbow, 2015), and only both legs are affected (Schauer, 2017). However, the trunk is also impaired for paraplegics who have a higher injury level at the thoracic segmental level (T6 and above) (Dolbow, 2015). Some paraplegics can retain their muscle ability to contract and produce a force (Schauer, 2017).

At the end of this section, it can be concluded that the ability to perform ADL with physical and social changes (McDaniel et al., 2017b) is challenging for individuals with SCI. It is also hard for them to keep their body healthy (Dolbow, 2015). With all the effects following the SCI described above, individuals with SCI may have a greater risk for depression (Williams & Murray, 2015) due to their disability and limitations. Therefore, the family, friends, society, and clinical practitioners need to reach, support, and help them to recover, hence, improving their QOL. Section **1.1.3** will describe the goal of recovery after SCI that may be useful to help individuals with SCI regain their QOL, motivation, and independent function through rehabilitation programs.

1.1.3 Recovery After SCI

As mentioned in section **1.1.2**, individuals with SCI lose their motor and/or sensory control, which leads to functional disability and secondary medical complications.

Therefore, recovery after SCI is paramount. The prediction of neurological recovery after SCI has been based on a physical examination of the acute patient using ISNCSCI (Kirshblum et al., 2011). The primary goals of recovery after SCI are to prevent further injury (Maynard et al., 1997) and to achieve optimal independence for a specific injury-level (Harvey, 2008). Therefore, various types of rehabilitation treatments and programs have been implemented by researchers and clinical practitioners to help them recover. Such treatments are prostheses and alternative medications, that may support nerve cell rejuvenation (Schwab, 2002) and improve the function of the nerves that persist after an SCI (Ramon-Cueto et al., 2000).

To prevent a more serious secondary medical condition (Rosley et al., 2019), it is encouraged for individuals with SCI to do regular physical activity (Gorgey et al., 2012; Griffin et al., 2009) and aerobics (Evans et al., 2015) exercises. Exercise can help them to improve their neurologic function (Cup et al., 2007; Daly et al., 2011; Ferrarello et al., 2011; Harness et al., 2008; Haworth et al., 2009; Oncu et al., 2009; Shi et al., 2011), muscle strength (Evans et al., 2015), fitness and psychosocial well-being (Galea et al., 2018), and reverse muscle atrophy (Fenton et al., 2022). Besides that, Evans et al. (2015) recommend individuals with SCI do stretching activities of major joints daily. The stretching exercise will help them to improve the joint ROM and prevent joint contracture following SCI. However, these exercises are limited to the specialized gym and restricted to upper body exercise only (McDaniel et al., 2017b). Due to the functional disability following SCI, the lower body of individuals with complete and sensory incomplete SCI do not get benefits from the exercises. Therefore, researchers have implemented the use of functional electrical stimulation (FES) as a therapeutic exercise (Ho et al., 2014) in the healthcare field (De Carvalho et al., 2022) for individuals with SCI.

FES is used to activate the neuromuscular activation below the lesion level (Behrman et al., 2006) in individuals with SCI to induce involuntary contractions in the skeletal muscle (Fenton et al., 2022) to achieve a motor task (Duenas et al., 2020). Unlike FES, neuromuscular electrical stimulation (NMES) which is also used for therapeutic purposes, may lead to a specific effect that enhances function but does not directly provide function (Sheffler & Chae, 2007). Therefore, FES can restore the function of the trunk, and upper and lower extremities (Ho et al., 2014; Jafari & Erfanian, 2022). Besides that, FES also can prevent secondary medical complications (Kuhn et al., 2014; Rosley et al., 2019). Restoring bladder and respiratory functions, and preventing pressure ulcers may significantly decrease the morbidity and mortality following SCI (Ho et al., 2014). With all the benefits gained from the FES therapeutic exercise, many FES devices have already been commercialized and have been used among clinicians in rehabilitation programs for individuals with SCI (Ho et al., 2014). Despite all the advantages, FES is not able to promote motor control recovery for individuals with complete and sensory incomplete SCI (Galea et al., 2018), thus limiting the functional outcomes of recovery after SCI (Wilson et al., 2012). However, FES therapeutic exercise can reach the primary goals of recovery after SCI; preventing secondary medical complications (Kuhn et al., 2014) and optimizing independent function (Galea et al., 2018), hence, improving the QOL.

It can be concluded that FES implementation offers great benefits in recovery after SCI compared to exercise alone. Therefore, the implementation of FES in rehabilitation exercises after SCI will be further explained in section **1.1.4**.

1.1.4 Rehabilitation Exercise After SCI

As mentioned in section **1.1.3**, physical activity and aerobic exercises promote recovery after SCI (Cash et al., 1997). It shows that exercise is crucial in individuals

with SCI (Fang et al., 2021; Nash, 2005). However, exercise alone is not enough to maximize recovery after SCI, thus may need to be combined with FES technology to achieve neurological recovery (Galea et al., 2018). Due to SCI, the paralyzed legs of individuals with complete and sensory incomplete SCI gain limited benefits from exercises. To involve the lower limbs during exercise among those with SCI, researchers often use FES as a therapeutic exercise tool (Figoni et al., 2021; Ho et al., 2014). FES is implemented to maximize the benefits of exercise. It has been widely used in the neurorehabilitation (Luo et al., 2020) for individuals with neurological disease (Popović, 2014), especially for individuals with SCI (Coelho-Magalhães et al., 2022).

FES is a rehabilitation technique that uses short electrical pulses to the nerves (Luo et al., 2020; Popović, 2014) to produce an artificial muscle contraction (Schauer, 2017) and functional movement (Cousin et al., 2019) of the paralyzed limbs (Ho et al., 2014). Generally, FES is used to replace the blocked signals from the CNS (brain) (Schauer, 2017). Based on **Figure 1.2**, FES is applied to the lower motor neurons (peripheral nerves) (Schauer, 2017) to artificially activate paralyzed muscles (Laubacher et al., 2017), hence producing functional movement (Meng et al., 2017). To date, FES is the only feasible way to activate the paralyzed muscles (Popović et al., 2009).

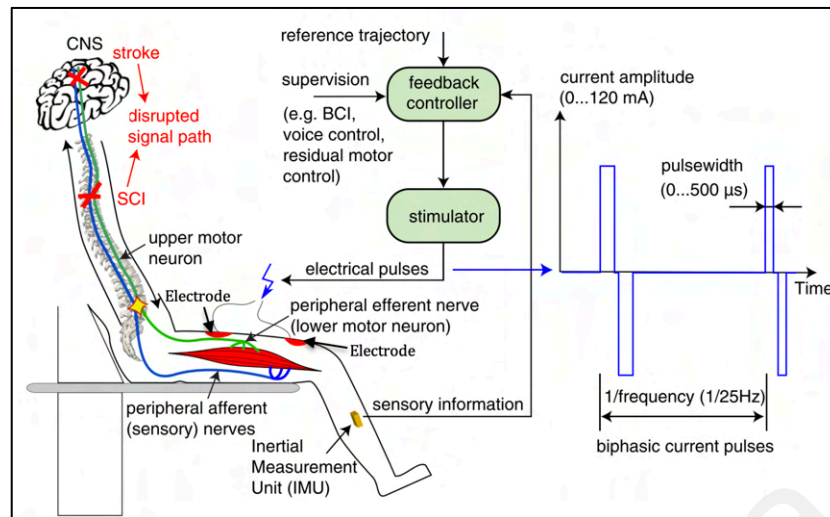


Figure 1.2: Principle of feedback-controlled FES (Schauer, 2006).

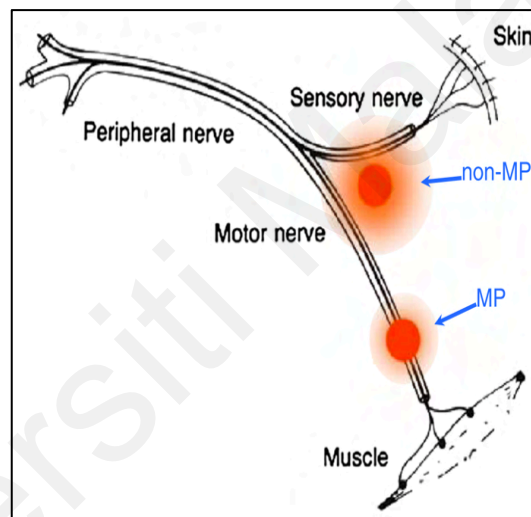


Figure 1.3: Schematic representation of a position of motor point (MP) (Gobbo et al., 2014).

FES signals are applied to the motor point (MP) (**Figure 1.3**) of the designated paralyzed skeletal muscle (Gobbo et al., 2014) via the electrode (Ahmed et al., 2016) (**Figure 1.2**). Based on **Figure 1.3**, MP is located where the motor branch of a nerve enters the muscle belly (Gobbo et al., 2014). The electrodes are placed on the MP of the designated paralyzed skeletal muscles (Gobbo et al., 2014) to maximize the evoked muscular tension (Gobbo et al., 2011) and FES benefits (Gobbo et al., 2014). Therefore, proper electrode positioning is crucial for every desired functional task involving FES to minimize the current intensity injected and hence, minimize the discomfort or pain

(Gobbo et al., 2014) in individuals with SCI. Stimulation on non-MP will require higher current intensity to reach the motor branch, hence, producing discomfort and more pain (Gobbo et al., 2014).

There are two types of electrodes used in FES; surface electrode (also known as an external electrode) (**Figure 1.2**) and implant electrode (also known as an internal electrode) (Braz et al., 2009). The electrode acts as a conductor, delivering electrical charge from a power supply to the tissue (Ho et al., 2014). When a voltage (V) is applied between the two electrodes (active and reference electrodes), an electric field is produced, hence, forcing an electrical charge to flow (Ho et al., 2014). The charge of the applied pulses is usually balanced by using a biphasic stimulation pulses (Schauer, 2017) (**Figure 1.2**). Pulse width and stimulation frequency will then control the muscle force produced by the FES (Schauer, 2017). In other words, the amount of muscle force produced by FES can be varied depending on the modulation of pulse width and stimulation frequency.

In general, FES is used to facilitate the restoration of movement, rehabilitation, and therapy (Ahmed et al., 2016). Due to the technique used and its effectiveness, FES has been widely implemented in rehabilitation exercises after SCI. With advanced sensor technology and appropriate feedback control, FES can restore more complex functional movements relevant to ADL (Schauer, 2017).

Depending on the classification of SCI, different rehabilitation exercise is prescribed. Therefore, the goal of recovery after SCI also varied depending on the impairment level (Dolbow et al., 2015). FES can be applied to various peripheral nerves to produce different functional tasks; such as grasping (Popovic et al., 2001), walking (Calabrò et al., 2021; Chang et al., 2022; Duffell & Donaldson, 2020), standing (Dzulkifli et al., 2018; Zoulias et al., 2019), transferring (Ho et al., 2014), cycling (Duffell & Donaldson,

2020; Islam et al., 2018), and rowing (Lambach et al., 2020). Besides that, FES also has numerous applications including restoration of urine control, and hearing and vision abilities (Ahmed et al., 2016).

Despite all the FES applications mentioned above, cycling with FES getting high attention of many researchers and clinical practitioners due to its safety (Jafari & Erfanian, 2022). Walking and sit-to-stand with FES imposed the risk of falling in individuals with SCI who have lost motor and sensory control of the trunk and limbs (Watanabe & Tadano, 2018). However, cycling with a bicycle ergometer, assisted by FES, minimizes the risk of falling (Coelho-Magalhães et al., 2022; Jafari & Erfanian, 2022; Wiesener & Schauer, 2017), as the exercise is performed in a recumbent position (Coelho-Magalhães et al., 2022).

At the end of this section, it can be concluded that FES implementation in rehabilitation exercises, especially cycling, offers great safety and maximizes health benefits to individuals with SCI from all injury classification fields (Luo et al., 2020). Therefore, section 1.1.5 will further explain how FES works during cycling exercise in individuals with SCI, types of FES-evoked cycling ergometers, benefits gained from FES-evoked cycling, and limitations of FES-evoked cycling for individuals with SCI.

1.1.5 Functional Electrical Stimulation (FES)-Evoked Cycling

Cycling is a popular exercise modality for both healthy individuals and individuals with disabilities, specifically individuals with SCI (Corbin et al., 2021). However, many individuals with disabilities experience limitations in their cycling activities and restrictions in their participation, which often results in difficulty in exercising and being physically active.

Section 1.1.4 has highlighted the advantages of FES-evoked cycling exercises for individuals with SCI from all categories (Galea et al., 2017; Jafari & Erfanian, 2022). Generally, individuals with complete and sensory incomplete SCI gain maximum benefits from FES-evoked cycling exercise (Dolbow et al., 2017). The absence of motor control limits them from other rehabilitation exercise benefits. Unlike them, individuals with motor incomplete SCI have motor control. They can move their joints and walk voluntarily. Therefore, this study focuses on FES-evoked cycling in individuals with complete and sensory incomplete SCI.

Based on **Figure 1.4**, cycling movement is artificially evoked by FES, whereby leg muscles are recruited by electrical pulses delivered on the skin surface via surface electrodes overlying key muscles (Bakkum et al., 2012; Hunt et al., 2012) to provide the force needed to pedal the bike (Davis et al., 2008) at the correct force-producing crank angle. FES applied to the overlying key muscles in continuous sequence depending on the pedal angle would generate pedaling power that could influence the health and fitness of the users' (Davis et al., 2008).

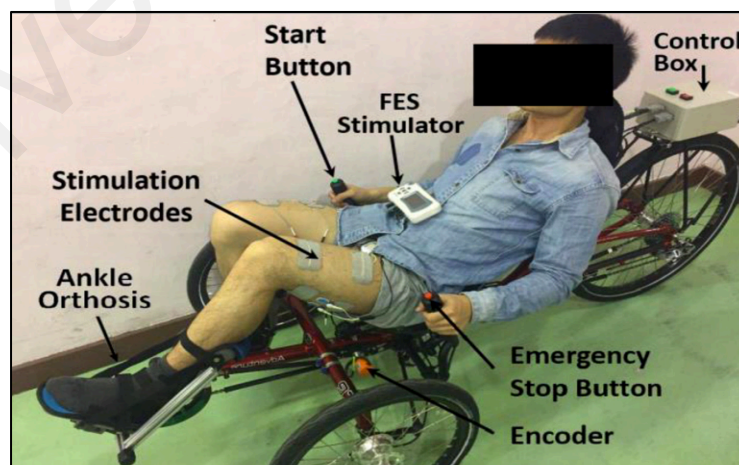


Figure 1.4: FES-evoked cycling system (Tong et al., 2017).

1.1.5.1 The Standard Setup of FES-evoked Cycling

In the standard setup for FES-evoked cycling, the muscles activated are the quadriceps, hamstrings, and gluteus (Tong et al., 2017) using surface electrodes (van Soest et al., 2005), while the ankle joints are immobilized using solid ankle-foot orthoses (AFO) (Bakkum et al., 2012; Hunt et al., 2012) at 90° angle (Wiesener et al., 2016), and the feet fixed to the pedal (Duffell & Donaldson, 2020) (**Figure 1.4**).

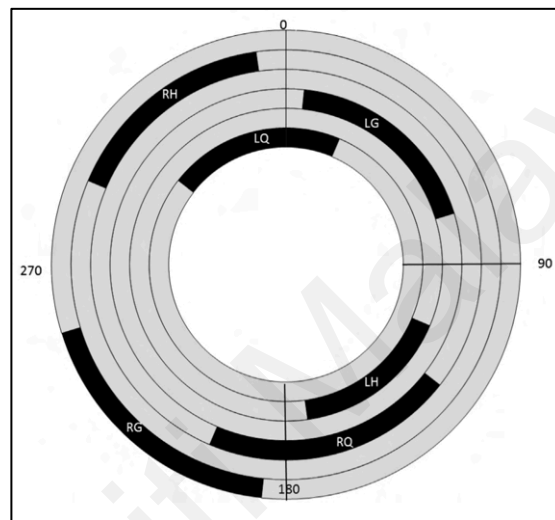


Figure 1.5: Timing of the muscle stimulations during FES-evoked cycling exercise; left quadriceps (LQ), right quadriceps (RQ), left hamstrings (LH), right hamstrings (RH), left gluteus (LG), and right hamstrings (RG) (Johnston et al., 2016).

Generally, different combinations of muscle groups were activated in a sequence manner (Johnston et al., 2016), depending on the crank position (Fattal et al., 2021) (also known as the crank angle) of the bike (**Figure 1.5**). An encoder at the crank (**Figure 1.4**) will measure the position of the crank (Wiesener et al., 2016). The crank position is used to generate the stimulation pattern for inducing a pedaling motion (Hunt et al., 2006; Szecsi et al., 2014a) with a complete 360 degree (°) cycle (Kuhn et al., 2014) (**Figure 1.5**). FES that is applied to overlying key muscles will provide force to pedal the bike (Davis et al., 2008) in respective crank angles.

The primary power source is the knee extensors i.e. the quadriceps, followed by the hamstrings as knee flexors (Szecsi et al., 2014a). However, the power generated from the knee extensors of the quadriceps and knee flexors of the hamstrings were approximately equal in a minority of persons with SCI.

1.1.5.2 Types of FES-evoked Cycling Ergometer

FES-evoked cycling ergometer has become an attractive rehabilitation device for daily and leisure activities in the paraplegics (Perkins et al., 2002). It can be used indoors and outdoors, either for recreation or mobility (Newham & Donaldson, 2007; Perkins et al., 2002). Individuals with SCI can perform cycling for a longer period with minimal risk of injury (Newham & Donaldson, 2007). Besides that, FES-evoked cycling exercise also provides opportunities for individuals with SCI for practicing sports (Fornusek & Davis, 2008). There are two types of FES-evoked cycling ergometers, which are stationary and outdoor recreational.

(a) Stationary FES-evoked cycling ergometer

Stationary FES-evoked cycling ergometer is typically used indoors in clinics (Eser et al., 2003; Pollack et al., 1989) or laboratories for exercise modality (McDaniel et al., 2017b) or experimental purposes (Sijobert et al., 2017). To date, many stationary FES-evoked cycling ergometers have been commercialized (McDaniel et al., 2017b). Typically, the power produced is small; 10-25 Watts (W) (Eser et al., 2003; Pollack et al., 1989). **Figure 1.6** shows an example of a stationary FES-evoked cycling ergometer. It is commonly used by individuals with little or no voluntary leg movement to pedal the bike (van der Scheer et al., 2021).

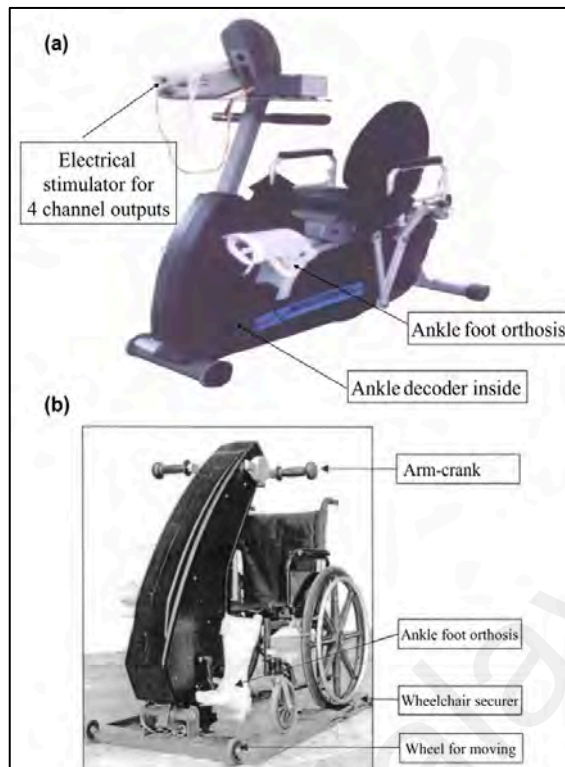


Figure 1.6: Types of stationary FES-evoked cycling ergometer(a) a traditional ergometer and (b) a hybrid ergometer for home use (Chen et al., 2004).

(b) Outdoor recreational FES-evoked cycling ergometer

There are two types of outdoor recreational FES-evoked cycling ergometers, which are without hand cycling (McDaniel et al., 2017b) (**Figure 1.7**) and hybrid (with hand cycling) (Bakkum et al., 2015) (**Figure 1.8**).



Figure 1.7: Outdoor recreational FES-evoked cycling ergometer-without hand cycling (Catrike 700 recumbent tricycles) (McDaniel et al., 2017b).

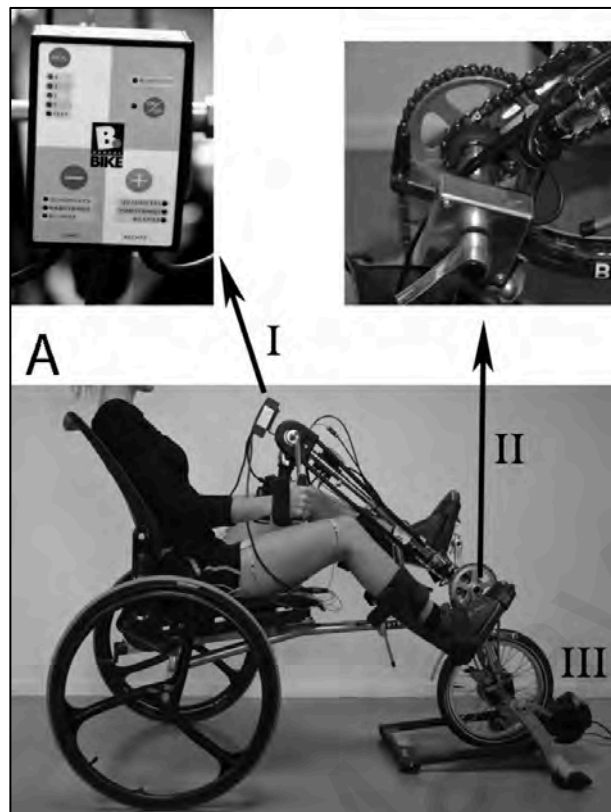


Figure 1.8: Outdoor recreational FES-evoked cycling ergometer-hybrid (with hand cycling) (BerkelBike) (Bakkum et al., 2015).

To date, the prominent mode of outdoor recreational FES-evoked cycling for individuals with SCI is hybrid (with hand cycling) (McDaniel et al., 2017b). The primary goal of outdoor recreational FES-evoked cycling is to enable individuals with SCI to exercise and engage in recreational activities independently in their homes and communities (McDaniel et al., 2017b). They can ride together and with other non-handicapped groups (Metani et al., 2017), hence, encouraging them to be healthy and independent (McDaniel et al., 2017b).

Cycling with an outdoor recreational FES-evoked cycling ergometer without hand cycling makes individuals with SCI forget they were paralyzed from the chest down (McDaniel et al., 2017b). On the other hand, cycling with an outdoor recreational FES-evoked cycling ergometer with hand cycling induces higher metabolic and

cardiorespiratory responses than outdoor recreational FES-evoked cycling ergometer without hand cycling (Bakkum et al., 2014).

However, the technical challenges and efficacy of stimulation-powered over-ground cycling have yet to be fully resolved (McDaniel et al., 2017b). For example, the low peak powers produced with FES-evoked cycling (approximately 25 W) are not enough to overcome rough surfaces, slight inclines, or headwinds that are often encountered during outdoor cycling (McDaniel et al., 2017b).

1.1.5.3 FES-evoked Cycling in the Cybathlon Championship

To further promote the development of a suitable assistance system for daily use among individuals with physical disabilities (Novak et al., 2017; Wolf & Riener, 2018), a platform called Cybathlon was introduced in 2013. While the Paralympics only permit participants to use unpowered assistive technology, Cybathlon promotes the use of powered assistive technology (Novak et al., 2017). The first Cybathlon championship was held in 2016 in Zurich, Switzerland, and featured 6 different disciplines, or races, including an FES bike race (Riener, 2016). In the discipline of FES bike racing at the 2016 event, SCI participants (as “pilots”) competed with each other to promote the potential of technologies in contributing to the exercise and fitness (Coste et al., 2017). Participants cycled at maximum speed within a fixed distance of 750 m for eight minutes (Metani et al., 2017). They were not allowed to use their hands to crank the bike forward; thus, the propelling power could only come from their electrically stimulated leg muscles. The participant who completed five laps around the 750 m track in the fastest time, or who covered the most distance within the shortest time, is declared the winner (Berkelmans & Woods, 2017).

Since its inception in 2013, the Cybathlon championship has been a platform for publicizing the potential of FES-evoked cycling in rehabilitation, exercise, and sports

for individuals with SCI. As it encourages the exchange of information among individuals with disabilities, the general public, researchers, and developers of equipment (Baur et al., 2018), the blending of technology and clinical neurorehabilitation science (Reinkensmeyer, 2019), specifically FES-evoked cycling gained vast attention (Cousin et al., 2019). Such a championship becomes a great interest in motivating individuals with SCI to perform FES-evoked cycling (Taylor et al., 2019).

Overall, FES-evoked cycling serves as an interesting tool for individuals with SCI to exercise like other healthy individuals. The outdoor recreational FES-evoked cycling can attract more of them to exercise, thus promoting healthy lifestyles and improving their QOL. The other benefits gained from FES-evoked cycling will be further described in section **1.1.5.4**.

1.1.5.4 Benefits of FES-evoked Cycling for Individuals with SCI

As mentioned in section **1.1.4**, FES-evoked cycling has been widely implemented in rehabilitation exercise therapy for individuals with neuromuscular disease (Popović, 2014), especially SCI. To date, FES-evoked cycling has become an essential rehabilitation tool to attenuate chronic conditions following SCI (Griffin et al., 2009; Johnston et al., 2011; Skold et al., 2002). In general, FES-evoked cycling helps to improve the cardiopulmonary (Berry et al., 2008; Davis et al., 2014) and musculoskeletal (Duffell et al., 2008; Frotzler et al., 2008, 2009).

FES-evoked cycling has reportedly improved physiological and psychological benefits (Estay et al., 2019; Jafari & Erfanian, 2022), such as muscle strength (de Sousa et al., 2021) and size (Fenton et al., 2022; Griffin et al., 2009; Kahn et al., 2010), ROM of lower limbs (Johnston et al., 2011), muscle fatigue resistance (Decker et al., 2010; Haapala et al., 2008a), cardiovascular (Davis et al., 2008; Mazzoleni et al., 2013) and

cardiopulmonary (Aksöz et al., 2016) function, self-esteem (Figoni et al., 1991), general health and QOL (Rohde et al., 2012), and mechanical power output (PO) (Atkins & Bickel, 2021), skin condition and blood flow in the legs (Bakkum et al., 2012; Hunt et al., 2012; van Soest et al., 2005).

Besides that, FES-evoked cycling has also reportedly reduced bone mass loss (de Sousa et al., 2021), and the incidence of pressure sores (Griffin et al., 2009), offset some of the secondary complications (Bakkum et al., 2012; Farkas et al., 2021; Hunt et al., 2012). Additionally, FES-evoked cycling provides individuals with SCI with an attractive therapy that promotes daily and leisure activities (Perkins et al., 2002) and opportunities for practicing sports (Coste et al., 2017).

Depending on the aim of training, muscle strength training improves bone density but offers fewer benefits on muscular endurance, cardiorespiratory fitness, and muscle PO (Fornusek & Davis, 2004). Muscle power training on the other hand improved muscle PO, cardiorespiratory, and cardiovascular fitness (Fornusek & Davis, 2004). Individuals with a higher impairment level of SCI have no ability to perform voluntary arm cranking, thus, muscle power training will benefit them more, particularly in improving cardiovascular fitness and muscle PO (Fornusek & Davis, 2004). Therefore, this study will focus on muscle power training. Overall, FES-evoked cycling provides maximum physiological and psychological benefits to individuals with SCI.

1.1.5.5 Limitations of FES-evoked Cycling for Individuals with SCI

As mentioned in section 1.1.5.4, FES-evoked cycling offers various health benefits. However, its mechanical PO and efficiency are very low (Berry et al., 2012; Ceroni et al., 2021; Hunt et al., 2012; Hunt et al., 2013; Hunt et al., 2007) compared to volitional cycling (Aksöz et al., 2018). This is because of the limited muscle endurance due to the early onset of muscle fatigue (Aksöz et al., 2016; Bickel et al., 2011). The low

mechanical PO and efficiency prohibited individuals with SCI from maximizing the physiological benefits gained from the FES-evoked cycling exercise (van Soest et al., 2005). These limitations cause a major concern for many researchers and clinical practitioners as FES-evoked cycling is an important rehabilitation tool for recovery after SCI. Section 1.1.6 will further describe the PO produced during FES-evoked cycling.

1.1.6 Power Output (PO) Production during FES-Evoked Cycling in Individuals with SCI

Power output is referred to as the average mechanical power delivered to the crank (van Soest et al., 2005). The magnitude of PO produced strongly reflected the physiological benefits bestowed from FES-evoked cycling in individuals with SCI (Duffell et al., 2009; Duffell et al., 2008; Duffell et al., 2010a; Duffell et al., 2010b). However, as mentioned in section 1.1.5.5, FES-evoked cycling produced very low mechanical PO and efficiency in individuals with SCI (Aksöz et al., 2016). Previous studies have reported that the magnitude of mechanical PO produced during FES-evoked cycling is very low (i.e. 8–35 W) (Duffell et al., 2010) which is lower than the power obtained in volitional cycling of healthy individuals (Szecsi et al., 2014a). The PO is too low for a longer outdoor recreational FES-evoked cycling (Duffell et al., 2009; Duffell et al., 2010; Newham & Donaldson, 2007; Szecsi et al., 2007), thus limiting motivation and enjoyment in individuals with SCI (Szecsi et al., 2014a) during exercise. The limited PO not only constrains the physiological benefits to be obtained from FES-evoked cycling, but it also affects the feasibility of FES-based autonomous tricycle riding (van Soest et al., 2005).

Therefore, it is an important concern in the rehabilitation systems to elicit the possible maximum mechanical PO as it reflects the health advantages bestowed by the FES-evoked cycling (Szecsi et al., 2014a). Prior to this concern, it is important to

understand the factors limiting the production of mechanical PO during FES-evoked cycling in individuals with SCI to maximize the physiological benefits from FES-evoked cycling exercise. Section 1.1.7 will briefly describe the causes of low mechanical PO production during FES-evoked cycling in individuals with SCI.

1.1.7 Factors Limiting the Production of Mechanical PO during FES-Evoked Cycling in Individuals with SCI

Berkelmans (2008), Sinclair et al. (1996), Szecsi et al. (2014a), and Duffel et al. (2010) have reported that the magnitude of mechanical PO produced during FES-evoked cycling exercise in individuals with SCI is very low compared to the PO produced during volitional cycling in healthy individuals. The magnitude of mechanical PO produced is ten times lower than the power produced during volitional cycling in healthy individuals (Metani et al., 2017). Three factors are thought responsible for the lower POs achieved with FES-evoked cycling in individuals with SCI: 1) the inefficiency of artificial muscle activation, 2) the crude control of muscle groups accomplished by stimulation, and 3) muscle atrophy and transformation due to chronic paralysis and disuse (J. Szecsi et al., 2014a). All these causes also lead to an increased fatigue rate, further limiting the health benefits (Dolbow et al., 2014) bestowed by the FES-evoked cycling (Gorgey et al., 2009; Theisen et al., 2002).

1.1.7.1 Biomechanical Inefficiency during FES-evoked Cycling

During FES-evoked cycling, FES only able to artificially stimulate the superficial muscles, and hence produces a lower mechanical PO (Laubacher et al., 2019; Metani et al., 2017). Besides that, the FES applied via the surface electrodes during FES-evoked cycling allows crude control of the muscle group (Szecsi et al., 2014a). Typically, FES employs synchronous stimulation and causes the muscle fibers to contract simultaneously (Deley et al., 2015; Doll et al., 2017; Laughlin, 1987). Unlike

physiological control of the CNS, motor units are activated asynchronously for sharing the workload (Schauer, 2017). The synchronous stimulation of motor units leads to imprecise flexor and extensor coordination and results in a less efficient cycling biomechanics (Szecsi et al., 2014a) and earlier fatigue (Schauer, 2017). This biomechanical inefficiency becomes the most important factor in reducing PO (Duffell et al., 2009).

Ankle positioning during FES-evoked cycling is important for effective pedaling (Gregor et al., 2002), as the overall lower limb biomechanics are affected by the ankle patterns. However, individuals with SCI have weak ankle muscles (Winter, 1991). Therefore, the use of AFO during FES-evoked cycling is crucial to restrict the ankle joint (Bakkum et al., 2012; Hunt et al., 2012) at 90° angle (Wiesener et al., 2016) that may reduce the PO (Ferrante et al., 2005). Releasing the ankle joint with the addition of shank muscle stimulation may improve PO, but this theory has never been proved experimentally (van Soest et al., 2005).

1.1.7.2 Muscle Fatigue during FES-evoked Cycling

The reverse order of muscle fiber recruitment (fast to slow) that occurs during FES-evoked (McDaniel et al., 2017b) leads to the rapid onset of muscle fatigue (Duffell & Donaldson, 2020). Muscle fatigue leads to the reduction of PO over time (Pincivero et al., 2001). In general, muscle fatigue is the incapacitation of muscles to generate enough contraction (Graham et al., 2006). Rapid onset muscle fatigue is characterized by a rapid decline in performance during repetitive activity (Bickel et al., 2004; Gorgey et al., 2009; Gregory et al., 2007). Based on **Figure 1.9**, normal muscles contain a mixed population of slow fatigue-resistant (type 1), fast fatigue-resistant (type 2A), and fast fatigable (type 2B) motor unit types (Schauer, 2017). However, due to muscle atrophy, the disused muscle tends to revert the fiber population to type 2B (Schauer, 2017).

Unlike natural muscle contraction (starting with asynchronous activation of slow then fast twitch muscle fibers), FES-evoked muscle contraction involves mainly type 2 fibers (fast twitch) (Hunt et al., 2012).

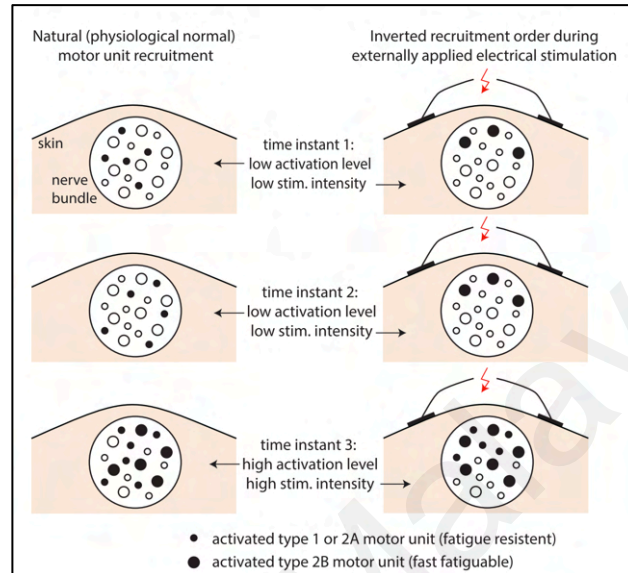


Figure 1. 1.9: Natural versus artificial muscle activation by FES (Schauer, 2006).

Rapid muscle fatigue imposed during FES-evoked cycling in individuals with SCI requires muscle assessment (Faller et al., 2009) to monitor accurate real-time muscle forces generated (Hammell et al., 2009; Hayashibe et al., 2011), and to optimize the exercise efficiency (Matheson et al., 1997) and health benefits (Ng et al., 2014). Muscle fatigue occurrence during FES-evoked cycling in individuals with SCI has been assessed (Pincivero et al., 2001) by quantifying cycling duration or cadence, peak torque, and pedal PO (Fornusek & Davis, 2004). However, these collectively reflect the forces from a group of muscles that are recruited during FES-evoked cycling, and they are influenced by the knee and ankle angular positions (Haapala et al., 2008a; Szecsi et al., 2014a). As such, they do not directly reflect muscle forces associated with the fatigue of individual muscles within a muscle group (Islam et al., 2018). Therefore, physical sensors have been used to assess muscle fatigue by quantifying the signals through software to monitor real-time fatigue at the muscle level (Haapala et al., 2008a).

Such sensors are surface electromyography (sEMG) (Mizrahi et al., 1994), near-infrared spectroscopy (NIRS) (Yoshitake et al., 2001), and mechanomyography (MMG) (Tarata, 2003). However, sEMG is highly susceptible to electrical stimulation artefacts (Islam et al., 2018), making it less appropriate to assess muscle fatigue during FES-evoked cycling (Ibitoye et al., 2014).

At the end of this section, it can be concluded that early muscle fatigue is a significant issue during FES-evoked cycling in individuals with SCI (Uddin & Hamzaid, 2014). Muscle fatigue rapidly occurred during FES-evoked cycling in individuals with SCI (Ibitoye et al., 2014). It leads to the reduction of PO, thus limiting the physiological benefits bestowed by the FES-evoked cycling (Uddin & Hamzaid, 2014). As the main challenge of FES-evoked cycling is to increase PO while delaying fatigue (Baptista et al., 2022), researchers have explored a wide range of approaches to improving biomechanical efficiency and muscle fatigue to maximize the PO and fatigue resistance. However, to date, no study has demonstrated meaningful increases in both power and fatigue (Laubacher et al., 2019). Therefore, **Chapter 2** will discuss the ways to optimize the efficiency and power production, biomechanically (the first part of this study-F1) and at muscle level (the second part of this study-F2) during FES-evoked cycling in individuals with SCI based on the related published literature. This includes improving strategies on pulse modulation and ankle joint biomechanics and measuring muscle fatigue at the muscle level using MMG and NIRS sensors (**Figure 1.10**).

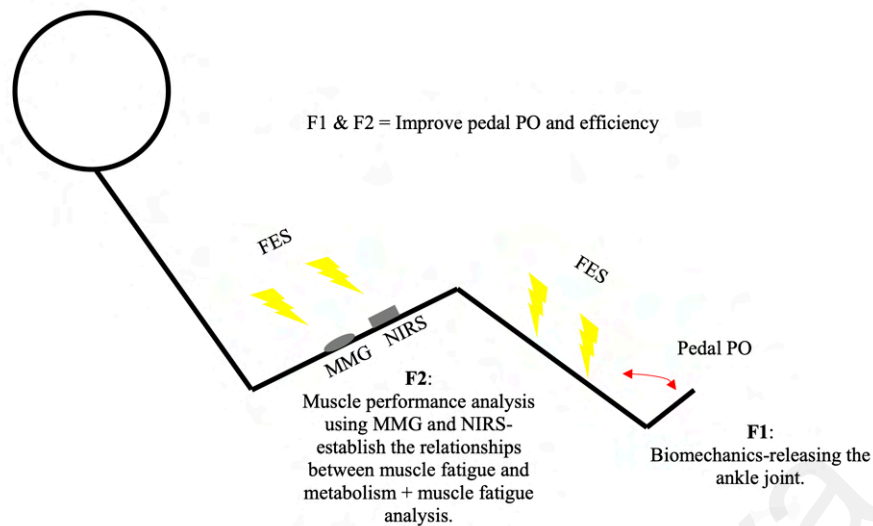


Figure 1.10: An insight into the ways to optimize the efficiency and power production during FES-evoked cycling in individuals with SCI used in this study.

1.2 Motivation for the Study

FES-evoked cycling offers great health and independence benefits to individuals with SCI. It becomes a prominent tool that allows individuals with SCI not to just exercise but also provide mobility independence. Therefore, it is important to maximize the efficiency and PO production during FES-evoked cycling to maximize the merits of physiological and psychological benefits in individuals with SCI. However, the low PO production and efficiency during FES-evoked cycling in individuals with SCI limits the potential benefits gained.

To date, no studies have experimentally investigated the biomechanical effect of releasing the ankle joint on power production during FES-evoked cycling in individuals with SCI. Therefore, this gap will become the strength of the present study as this study measured some interesting variables in FES-evoked cycling, based on predictions from modeling and this particular explanation has not been explored before. It was our goal to encourage more individuals with SCI to exercise, and consequently do sports. Sports are only possible with high PO produced during FES-evoked cycling. The ability to

produce high power during FES-evoked cycling motivates individuals with SCI to be active, and healthier, and thus improve the QOL.

It is also important to understand the muscle responses towards FES-induced during FES-evoked cycling to maximize the efficiency of FES-evoked cycling. Therefore, it is crucial to quantify muscle activities through assessment at the muscle level during FES-evoked cycling in individuals with SCI. It is unclear what the underlying relationships are between muscle performance during FES-evoked cycling, physiological biomarkers of metabolism during fatigue, and MMG outputs derived from skin-surface sensors. NIRS has been widely used to assess muscle oxygen consumption, blood flow, oxygen saturation, and indirectly mitochondria activity within muscles during fatiguing contractions. However, it has never been quantitatively related to the MMG signal as a proxy for muscle force and fatigue during FES-evoked cycling in individuals with SCI. This gap of knowledge motivated the current study to investigate the relationships between muscle performance during FES-evoked cycling, underlying physiological markers derived from NIRS, and skin-surface MMG findings.

1.3 Problem Statement

Despite FES-evoked cycling having been reported to enhance muscle strength and improve fatigue resistance in muscles after SCI, the available literature indicates that FES-evoked cycling produces very low power and efficiency in individuals with SCI when compared to healthy individuals. This is because of the limited muscle endurance due to the early onset of muscle fatigue among SCI-affected individuals. To date, muscle fatigue during FES-evoked cycling in individuals with SCI has been quantified in several studies by means of peak torque or pedal PO decrement. These measures may not be sensitive and do not reflect metabolic markers of fatigue. Hence, optimization of

power production and maximizing efficiency while assessing the muscle performance during FES-evoked cycling in individuals with SCI are crucial in the present study.

1.4 Objectives of Study

- i. To determine the effect of releasing the ankle joint on the power production during FES-evoked cycling in individuals with SCI.
- ii. To examine the relationship between the vibrational performance of electrically-evoked muscles measured through MMG and its oxidative metabolism through NIRS characteristics during FES-evoked cycling in individuals with SCI.
- iii. To quantify muscle fatigue during FES-evoked cycling in individuals with SCI, specifically between pre- and post-fatiguing conditions using MMG and NIRS sensors.

1.5 Hypothesis of the Study

- i. Freeing the ankle joint and adding stimulation of shank muscles in individuals with SCI would elevate the pedal PO by at least 10% compared to fixed-ankle FES-evoked cycling.
- ii. Muscle oxygen derived from NIRS would correlate with the MMG signal, and mirror each other as a proxy for muscle force and fatigue during FES-evoked cycling in individuals with SCI.
- iii. Muscle contraction mechanical (derived from MMG) and physiological behavior association (derived from NIRS) would alter simultaneously following pre- and post-fatiguing conditions during FES-evoked cycling in individuals with SCI.

1.6 Aim of the Study

The study aimed to improve FES-evoked cycling efficiency and power production in individuals with SCI, by means of biomechanical and muscle performance approaches.

1.7 Significance of the Study

- i. The study highlighted the potential of releasing the ankle joint in maximizing the benefits of FES-evoked cycling, mechanically and biomechanically for individuals with SCI.
- ii. The study served as a reference for rehabilitation practitioners in maximizing the benefits of FES-evoked cycling and thus maximizing the physiological benefits of individuals with SCI.
- iii. The study highlighted the potential use of MMG to inform the occurrence of physiological muscle fatigue easily and safely in electrically evoked leg muscles in individuals with SCI undergoing FES-evoked exercises.
- iv. Mechanical muscle signal, i.e., MMG is associated with its muscle oxygenation and oxyhaemoglobin profile during electrically evoked paralyzed leg muscles undergoing cycling-to-fatigue.

1.8 Scope of the Study

The scope of the study was divided into two parts. The first scope was to identify the biomechanical effects on power production during FES-evoked cycling in individuals with SCI. It analyzes which ankle joint biomechanics produce higher power during FES-evoked cycling in individuals with SCI. This scope aimed to compare the biomechanical and power production of FES-evoked cycling under two ankle joint biomechanics conditions, which are fixed and free ankle.

The second scope was to analyze the muscle performance during FES-evoked cycling in individuals with SCI. It establishes the relationships between the outputs from both NIRS and MMG sensors during FES-evoked cycling in individuals with SCI at the muscle level. This scope aimed to identify if the changes in muscle oxygen saturation captured by the NIRS sensor were related to the changes in root mean square (RMS) captured by the MMG sensor. In addition, this scope aimed to identify if the MMG signal was associated with NIRS in pre- and post-fatiguing conditions during FES-evoked cycling in individuals with SCI.

1.9 Thesis Organization

This thesis consists of six chapters, which are Introduction, Literature Review, Methodology, Results, Discussion, and Conclusion.

Chapter 1 is the Introduction. It explains general knowledge related to the SCI, the implementation of FES technology in cycling, PO production during FES-evoked cycling, and the factors limiting PO production in individuals with SCI. This chapter also contains the motivation for the study, the problem statement, and the objectives, hypothesis, aim, significance, and scope of the study.

Chapter 2 is the Literature Review. It mainly addresses the critical analysis of previous relevant studies related to the present study, specifically on the low efficiency and power production during FES-evoked cycling in individuals with SCI. This chapter also describes the ways to optimize the efficiency and PO production of FES-evoked cycling, including the selection of parameters of interest from the participating teams in the Cybathlon, understanding the origin of PO during FES-evoked cycling, and muscle activity assessment during FES-evoked cycling exercise. It also highlights a better approach to minimizing the gap in the study.

Chapter 3 is the Methodology. This chapter describes the scientific protocols and materials that have been used in conducting the current study. It consists of two parts, reflecting the three main objectives of the present study. Part 1 explains the research protocols used for the first part of the study, which is to analyze the biomechanical effect on power production during FES-evoked cycling in individuals with SCI. It reflects the first objective of the study. Part 2 explains the research protocols used for the second part of the study, to analyze the muscle performance at the muscle level during FES-evoked cycling in individuals with SCI. It reflects the second and third objectives of the study.

Chapter 4 is the Results. This chapter contains all the findings of the current study, portraying the objectives of the present study. It consists of two parts. Part 1 explains the findings for the first objective of the study, while part 2 explains the findings for the second and third objectives of the study.

Chapter 5 is the Discussion. It discusses the findings of the current study. This chapter justifies the findings of the current study with the previous studies. It consists of three parts. Part 1 discusses the biomechanical effect on power production during FES-evoked cycling in individuals with SCI. Part 2 discusses the muscle performance at the muscle level during FES-evoked cycling in individuals with SCI. Part 3 discusses the relationship between biomechanics and muscle performance in light of maximizing the efficiency of FES-evoked in individuals with SCI.

Chapter 6 is the Conclusion. It summarizes the findings of the current study. This chapter also provides suggestions and recommendations to develop a better approach to maximizing the biomechanical and muscle performance during FES-evoked cycling in individuals with SCI.

CHAPTER 2: LITERATURE REVIEW

This chapter describes a critical analysis of currently available literature related to the present study. It mainly discusses the ways to optimize the efficiency and PO production of FES-evoked cycling in individuals with SCI. This chapter consists of four sections. The first section discusses the low efficiency and power production during FES-evoked cycling in individuals with SCI. The second section describes the selection of parameters of interest from the participating teams in the Cybathlon to optimize FES-evoked cycling efficiency. The third section explains the origins of power during FES-evoked cycling. The last section discusses muscle activity assessment during FES-evoked cycling exercise.

2.1 Low Efficiency and Power Production during FES-Evoked Cycling Exercise in Individuals with SCI

FES-evoked cycling has one major drawback. The available literature indicates that FES-evoked cycling produces very low power and efficiency (Hunt et al., 2013) in individuals with SCI when compared to healthy individuals (Aksöz et al., 2018). Due to unfavorable biomechanics, weakened or paralyzed muscles, and the fact that FES can partially activate only superficial muscles when using surface electrodes, the mechanical power produced by an individual with SCI is typically ten times lower than that of an average healthy cyclist (Metani et al., 2017). The synchronous stimulation of motor units that are typically employed during FES-evoked cycling using surface electrodes leads to imprecise flexor and extensor coordination and results in a less efficient cycling biomechanics (Szecsi et al., 2014a) and earlier muscle fatigue (Schauer, 2017). Biomechanical inefficiency becomes the most prominent factor in reducing mechanical power (Duffell et al., 2009).

Hence, optimization of power production during the FES-evoked cycling results in increased fatigue resistance (Gibson et al., 1988). It has also been shown that FES-evoked cycling requires a more complex motion, making it difficult to stimulate the muscles accurately (Aksöz et al., 2018). Therefore, optimal stimulation parameters (Gorgey et al., 2009; Kesar et al., 2008) and accurate electrode placement overlying the key muscles are paramount if the muscle response to stimulation is to be maximized (Aksöz et al., 2018).

It is revealed that teams participating in the Cybathlon championship in 2016 also sought to elicit maximum efficiency during FES-evoked cycling to win the race. The Cybathlon has contributed to the selection of parameters of interest that optimized performance in the FES-evoked cycling. Section 2.2 will discuss the parameters of interest that have been used by the teams participating in the Cybathlon championship, specifically in the discipline of the FES bike race.

Consequently, previous researchers have also explored ways to elicit maximum power during FES-evoked cycling to maximize the efficiency of the FES-evoked cycling (Aksöz et al., 2018; Aksöz et al., 2016; Chou et al., 2008; Gibson et al., 1988; Gorgey et al., 2009; Szecsi et al., 2014b). Section 2.3 will discuss the origins of power during FES-evoked cycling.

2.2 Selection of Parameters of Interest from the Teams Participating in the Cybathlon Championship 2016

The first Cybathlon championship was held in 2016, while the following championship was held in 2020. The next Cybathlon championship will be held in 2024. Unlike the first championship, Cybathlon 2020 (global edition) was held globally. Due to the pandemic, pilots from the participating teams compete at their place, not on the same track as the other pilots. The first Cybathlon championship has gained vast

attention worldwide as all pilots compete on the same track. The audience can see the differences in the bike design and technology used by the pilots among the participating teams. Therefore, this section will describe the selection of interest parameters from the teams participating in the first Cybathlon championship.

A bibliometric study has evaluated the contribution of the Cybathlon to the parameters of interest used by teams participating in the Cybathlon championship in 2016 in maximizing the efficiency of FES-evoked cycling to win the race. 13 teams are participating in the FES bike race discipline during the Cybathlon championship 2016. These teams representing their country, university, and manufacturer have focused on specific parameters of interest as a strategy to maximize the efficiency of FES-evoked cycling. Such parameters include the maximization of the power (Berkelmans & Woods, 2017); optimization of stimulation parameters or control systems, which included bike design and biomechanics (Arnin et al., 2017; Schmoll et al., 2022); types of muscle stimulation and electrodes used (McDaniel et al., 2017a; Tong et al., 2017); training protocol (Baptista et al., 2022; Coste et al., 2017; Fattal et al., 2020; McDaniel et al., 2017a); and improvement of muscle strength or endurance (Ceroni et al., 2021; Schauer, 2017). Each team has a similar goal, which is to win the race.

It is reported that most of the participating teams (76.7%) focus on training individuals with SCI in preparation for the Cybathlon championship (Coste et al., 2017). This may be because of the rule that required the Cybathlon participants to cycle at high speed for a longer distance for a longer duration (Metani et al., 2017). The training programs developed by the teams maximize the time they spend producing maximum power (McDaniel et al., 2017a). Therefore, the stamina and consistency of the participants during FES-evoked cycling are paramount in winning the race. It is also revealed that most of the participating teams (63.4%) also focused on the types of

muscles being stimulated and the types of electrodes used (Tong et al., 2017). This may be due to the difficulties in accurately locating and stimulating the muscles needed for the FES-evoked cycling (Aksöz et al., 2018). To maximize the efficiency of FES-evoked cycling during competition, more muscle groups need to be stimulated (Szecsi et al., 2014b). **Section 2.3.2** will further describe the effects of muscle stimulation on FES-evoked cycling efficiency and power production. The types and placement (Aksöz et al., 2018) of electrodes used in individuals with SCI can affect the efficiency of FES-evoked cycling. This is demonstrated by the winning team, i.e., team Cleveland (McDaniel et al., 2017a), whose pilot is the only pilot who uses an implanted stimulation system during the race. All the other teams use surface electrodes. The pilot's cycling pace is also consistent and smooth, thereby ensuring that the muscles are used efficiently and effectively throughout the race.

The bibliometric review revealed that in preparing for the Cybathlon championship, most of the teams (57.8%) focused on maximizing the power of the FES-evoked cycling (Berkelmans & Woods, 2017). Previous researchers have reported that maximizing power production in FES-evoked cycling is important for maximizing efficiency as well (Aksöz et al., 2016). Therefore, most of the participating teams focused on maximizing power to win the race. The review also revealed that instead of focusing on improving muscle strength or endurance, most of the participating teams focused on optimizing their stimulation parameters and control systems, including bike configuration and design (Arnin et al., 2017). These are not surprising as previous studies also showed that optimization of the stimulation parameters maximizes the benefits of FES-evoked cycling (Gorgey et al., 2009) and minimizes fatigue (Chou et al., 2008). Studies have reported that modulation of stimulation parameters, such as frequency, current intensity, and pulse width, affect the muscle response to the stimulation (Aksöz et al., 2018) and the efficiency of the FES-evoked cycling (Hunt et al., 2006). It has also been shown that

adjusting the stimulation parameters can optimize power during the FES-evoked cycling (Janssen & Pringle, 2008). The power produced during FES-evoked cycling can be maximized, and muscle fatigue can be minimized, by using a lower stimulation frequency (less than 50 Hz (Graupe et al., 2000)) and a higher pulse width (350 μ s (Gorgey et al., 2009)). This strategy can be helpful to the participating teams in their efforts to win the race. **Section 2.3.1** will further describe the effect of optimizing stimulation parameters on FES-evoked cycling efficiency and power production.

While the bike's mechanical design is not explicitly reported on in the literature as a parameter of interest for winning the race, it is believed that this is also an important factor for winning. Most of the participating teams reported that the training and "human" characteristics of the pilot were important, just as the FES-related parameters were. A bike's mechanical design may well be a key factor in winning and should be further investigated. Ankle joint fixation, which is reported to have influenced power production, may also be an important factor. It is observed that all bike pilots use a fixed ankle joint configuration, which most likely optimizes force transfer and constrained non-sagittal hip motion (McDaniel et al., 2017a). However, further conclusions cannot be drawn without comparisons with different ankle joint configurations. Body inclination, power, gearing of the bike, and energy transfer from the muscles to the wheels and propulsion, as well as the overall bike weight and weight distribution, are all factors that should be considered when asserting that bike design is a chief contributing factor to winning the race. **Section 2.3.3** will further explain the effect of ankle joint biomechanics on FES-evoked efficiency and power production.

2.3 Origins of Power during FES-Evoked Cycling

Several studies have investigated the origins of cycling PO during the FES-evoked cycling (Duffell et al., 2009; Hunt et al., 2012), including modulation of stimulation parameters, muscle stimulation, and ankle biomechanics.

2.3.1 Optimization of Stimulation Parameters

As mentioned in section 1.1.4, pulse width and stimulation frequency control the muscle force produced by the FES (Schauer, 2017). It is reported that modulation of the stimulation parameters (such as; frequency and pulse width) affects the muscle responses to the stimulation (Aksöz et al., 2018) and the efficiency of the FES-evoked cycling (Hunt et al., 2006) to improve power or fatigue resistance (Laubacher et al., 2019). Generally, researchers and clinical practitioners optimize the stimulation parameters that are commonly used to maximize the benefits of FES-evoked cycling (Binder-Macleod & Guerin, 1990; Gorgey et al., 2009; Gregory et al., 2007) and to minimize fatigue (Chou et al., 2008; Kebaetse et al., 2005) (**Table 2.1**). It is shown that adjusting the stimulation parameters during FES-evoked cycling by means to optimize PO subsequently improves the card-metabolic benefits (Janssen & Pringle, 2008). Besides that, Marsden & Merton (1983) have shown that the degree of muscle fatigue is directly related to the number of pulses received by the muscle.

In the standard setup of FES-evoked cycling in individuals with SCI, rectangular biphasic pulses, at a constant frequency between 25 and 100 Hertz (Hz) (Schauer, 2017) have been deployed. Generally, a higher stimulation frequency leads to a more rapid muscle fatigue (Aksöz et al., 2016) over prolonged stimulation (Schauer, 2017). On the other hand, lower stimulation frequencies (frequencies lower than 25 Hz) produce unfused twitches rather than a smooth muscular contraction (Schauer, 2017). By using a frequency greater than 50 Hz, more muscle fibers are recruited thus, reducing muscle

fatigue (Graupe et al., 2000). Constant stimulation frequencies are usually applied during FES-evoked cycling because it is easy to generate (Schauer, 2017) and showed a significantly higher PO (Aksöz et al., 2018). In addition, randomized stimulation frequency during FES-evoked cycling has no effect in reducing fatigue (Aksöz et al., 2016) and thus, has no effect in elevating PO.

Unlike stimulation frequency, the effect of pulse width on muscle fatigue is not as dominant as the effect of stimulation frequency (Del-Ama et al., 2013). Increasing the pulse width (pulse width greater than 350 microseconds (μs)) can enhance FES-evoked cycling efficiency and increase PO without evoking additional muscle fatigue (Gorgey et al., 2009). However, too high pulse width stimulation (500 μs) is not safe and can elicit a dysreflexia response (Gorgey et al., 2014). On the other hand, randomized pulse width during FES-evoked cycling does not affect the PO generation (Aksöz et al., 2018).

Taken together, it can be concluded that the mechanical PO produced during FES-evoked cycling can be maximized by using a lower stimulation frequency and higher pulse width, where muscle fatigue is minimized. **Table 2.1** shows that most researchers preferred to use the stimulation frequency of 30 Hz and pulse width of 300 μs and 350 μs .

Table 2.1: Modulation of stimulation parameters used during FES-evoked cycling among individuals with SCI in previous studies.

| Study | Pulse width (μ s) | Frequency (Hz) |
|--------------------------------|---|----------------|
| Baptista et al., 2022 | 450 | 50 |
| Jafari & Erfanian, 2022 | 0-500 | 25 |
| Coelho-Magalhães et al., 2022a | 450-600 | 35 |
| Coelho-Magalhães et al., 2022b | 600 | 35 |
| Panisset et al., 2022 | 300-500 | 35 |
| Reid et al., 2022 | 50-500 | 10-60 |
| Schmoll et al., 2022 | 400 | 40 |
| Casabona et al., 2021 | 50-400 | NM |
| Ceroni et al., 2021 | 400 | 30 and 40 |
| Corbin et al., 2021 | 350 | 40 |
| de Sousa et al., 2021 | 500 | 50 |
| Dolbow et al., 2021 | 350 | 50 |
| Everaert et al., 2021 | 300 | 35 |
| Farkas et al., 2021 | NM | 60 |
| Gelenitis et al., 2021 | 255 | 25 |
| Duenas et al., 2020 | 0-400 | 60 |
| Fattal et al., 2020 | 300 | 30 |
| Gill et al., 2020 | 350 | 33.3 |
| Cousin et al., 2019 | 0-400 | 60 |
| Sijobert et al., 2019 | 400 | 30 |
| Duffell et al., 2019 | 200 | 30 |
| Gorgey et al., 2019 | 350 | 33.3 |
| Islam et al., 2018 | 300 | 30 |
| Galea et al., 2018 | Varied according to individual tolerance and capability | NM |
| Watanabe & Tadano, 2018 | 300 | 30 |

*NM in Table 2.1 denotes as not mentioned.

2.3.2 Muscles Stimulation

Three major muscle groups are being stimulated during the standard setup of FES-evoked cycling in individuals with SCI, which are the quadriceps, hamstrings, and gluteus (Fang et al., 2021; Figoni et al., 2021) (**Figure 2.1**). Some systems also utilize the gastrocnemius (Figoni et al., 2021). However, more muscle groups are required to improve the efficiency of FES-evoked cycling in individuals with SCI (Szecsi et al., 2014b). There are four main muscle groups involved in generating a smooth pedal

movement, which are the quadriceps, hamstrings, gluteus, and triceps surae (Szecsi et al., 2014b) (**Figure 2.1**).

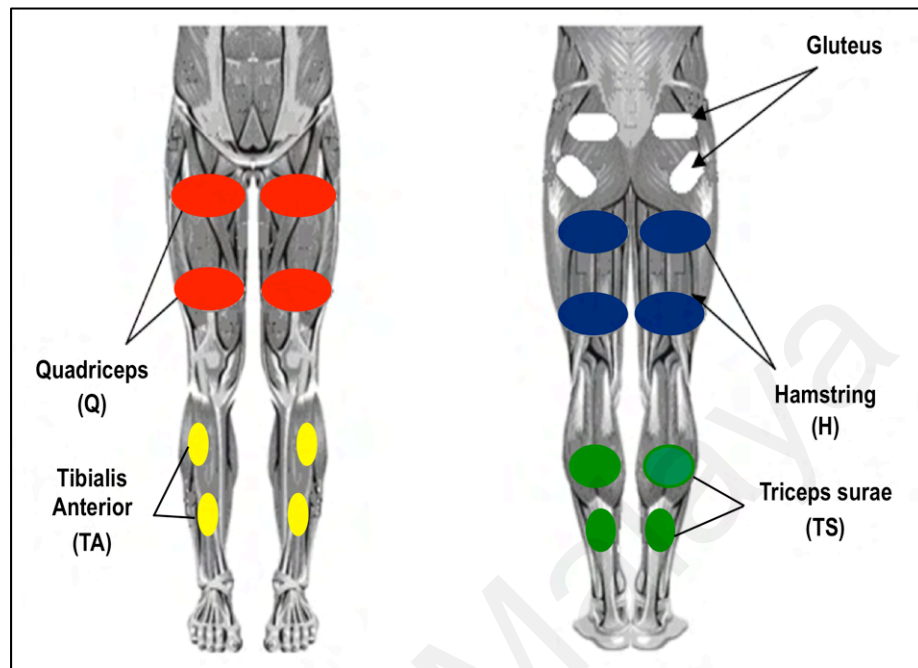


Figure 2.1: Stimulated muscles during FES-evoked cycling in individuals with SCI.

FES-evoked cycling requires a more complex motion, makes it difficult to stimulate the muscles accurately (Aksöz et al., 2018), and hence, makes it difficult to produce a higher force for cycling. As mentioned in section 1.1.8.2, the key muscle groups are stimulated according to the manner, depending on the position of the crank (also known as the crank angle). Therefore, proper electrode placement overlying the key muscles is paramount to maximize the efficiency of FES-evoked cycling and thus maximize the mechanical PO produced (Aksöz et al., 2018).

Several studies have investigated the muscle force generation at the muscle level during FES-evoked cycling in individuals with SCI. Based on **Figure 2.2**, the primary power source is the knee extensors of the quadriceps (Szecsi et al., 2014a), followed by the hip extensors of the gluteus (Franco et al., 1999; Haapala et al., 2008b). The PO produced in the knee extensors of the quadriceps is absorbed by the eccentrically

activated hip flexors of the gluteus (Szecsi et al., 2007). On the other hand, the PO produced from the knee flexors of the hamstrings is lower than the quadriceps (Szecsi et al., 2014a). The PO produced from the hamstrings is crucial to overcome the dead pedal position (**Figure 2.3**), and thus, enhances the FES-evoked cycling efficiency (Laubacher et al., 2017) and maximizes mechanical PO.

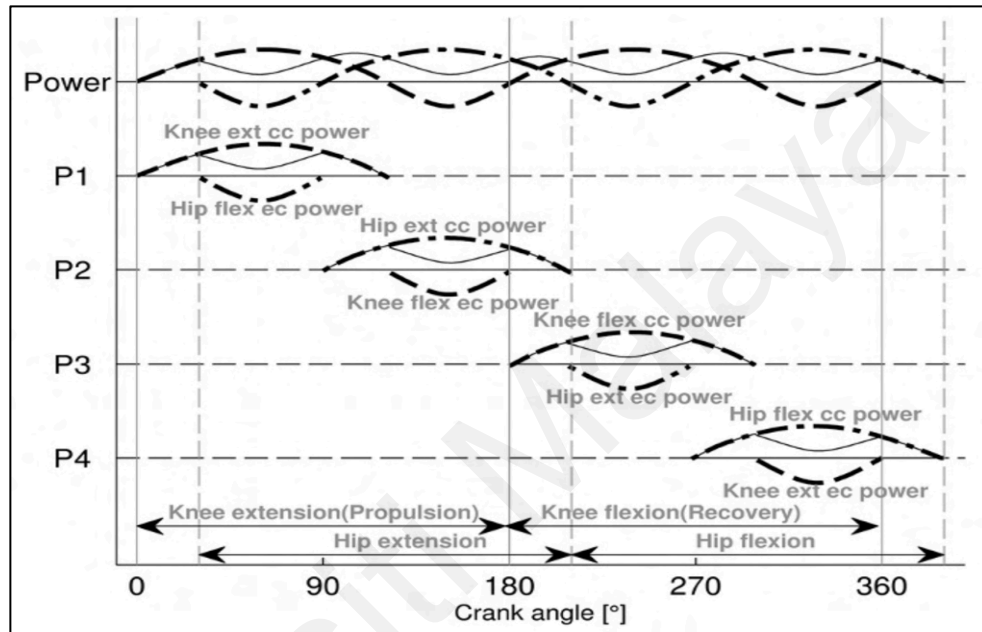


Figure 2.2: Schematic graph for the definition of the power components P1-P4 contributing toward total power during a crank revolution. P1 represents the first power component, P2 represents the second power component, P3 represents the third power component, and P4 represents the fourth power component (Szecsi et al., 2014a).

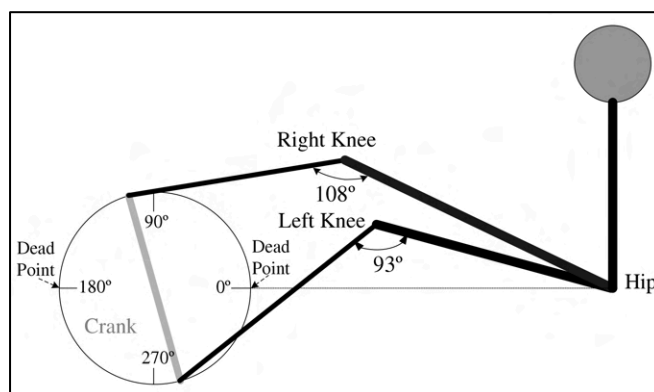


Figure 2.3: The dead points and the crank position with respect to the hip joint (Abdulla et al., 2014).

In another study, however, the gluteal muscles were not stimulated because they produced no measurable crank torques in most individuals with SCI (Szecsi et al., 2014a). It is also reported that in a minority of individuals with SCI, power was generated approximately equally from knee extensors of the quadriceps and knee flexors of the hamstrings (Szecsi et al., 2014a).

Taken together, it can be concluded that, each individual with SCI has a different muscle group strength. Therefore, it is important to know which muscle groups need to be stimulated during FES-evoked cycling for each individual of SCI, to maximize the power produced and cycling efficiency.

2.3.3 Biomechanics of Ankle Joint

Previous research investigated PO produced in FES-evoked cycling from the perspective of knee and hip joint biomechanics. Nevertheless, the ankle joint biomechanics in FES-evoked cycling has received little attention. As mentioned in section 1.1.7.1, ankle positioning during cycling is one of the more important factors for effective pedaling (Gregor et al., 2002; Martin & Brown, 2009), as the overall lower limb biomechanics are affected by ankle patterns (Gregor et al., 1991). Typically, individuals with SCI have weak ankle muscles (Winter, 1991) or no muscle power. They have no ability to control the ankle muscle contractions and movement. Therefore solid AFOs are prescribed to counter muscle weakness at the ankle joint (Chen et al., 2018). AFO is a wearable medical device that is attached to the wearer (Chen et al., 2018) and aligned with the pedal-pushing direction to optimize the forward driving force generated by the contraction of muscles (Tong et al., 2017) (**Figure 2.4**).

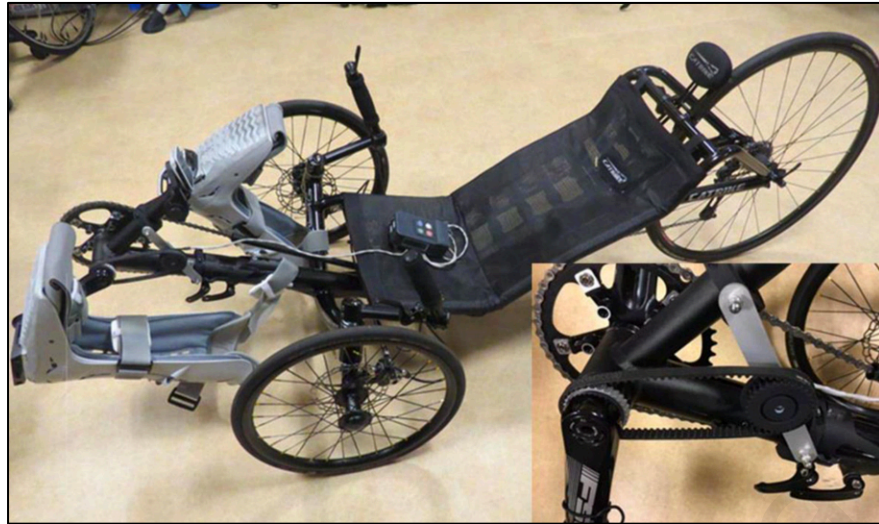


Figure 2.4: The ankle is immobilized by Aircast ankle-foot immobilizers to lock the ankle position (McDaniel et al., 2017b).

In the standard setup for FES-evoked cycling, solid AFOs are often used to limit and control the ankle motion (Watanabe & Tadano, 2018) at 90° angle (Wiesener et al., 2016), and provide shank stability that restricts leg movements in the sagittal plane (Tong et al., 2017) to optimize the force transmission (McDaniel et al., 2017b) to the pedal (Laubacher et al., 2017) for cycling. However, the lack of muscle strength and constraining ankle joint ROM consequently may produce lower PO during FES-evoked cycling. Ferrante et al. (2005) reported that the calf muscles generate limited knee flexion action due to the presence of solid AFO, which might reduce the maximum power during FES-evoked cycling in individuals with SCI.

Koch et al. (2013) reported that there was no significant difference in power production during cycling with and without the use of AFO. On the other hand, Pierson-Carey et al. (1997) reported less power production during cycling with the ankle locked in a neutral position. The inability to plantarflex the ankle joint can reduce the force transmission from the hip and knee to the pedal and, thus, reduces the PO during cycling in healthy individuals (Pierson-carey et al., 1997). On the other hand, releasing the ankle joint during FES-evoked cycling might destroy the direct

kinematical relation between crank angle and joint angles and introduce injury hazards, in that an inadequate muscle stimulation pattern may result in, for example, hyperextension of the knee (van Soest et al., 2005). Therefore, no experimental study has reported the effect of releasing ankle joint during FES-evoked cycling. Extreme care must be taken during experimental validation of the predicted effect of releasing the ankle joint (van Soest et al., 2005).

Theoretically (based on modeling and simulation), the power produced during FES-evoked cycling in released ankle setup (free-ankle joint) and adding the stimulation of shank muscles (triceps surae and tibialis anterior) is 10% lower than fixed-ankle setup (van Soest et al., 2005). The stimulation of the lower leg muscles while fixing the ankle joint during FES-evoked cycling in individuals with SCI produced a non-significant difference in the mechanical work compared to the stimulation of upper leg muscles alone (Hakansson & Hull, 2010), except that it affected only the cardiovascular and circulatory responses (Pierson-carey et al., 1997). This is because the gastrocnemius muscle was the only lower leg muscle that had the potential to generate mechanical work during FES-evoked cycling while fixing the ankle joint. A simulation used to determine the electrical stimulation timing patterns including the lower leg muscles, indicated that the gastrocnemius activity did not result in a net gain in mechanical work to drive the crank (Hakansson & Hull, 2009). Hakansson & Hull (2007) reported a similar finding in able-bodied cyclists despite their ability to flex and extend the ankle joint. Theoretically, the power produced during FES-evoked cycling can be improved by up to 14% by releasing the ankle joint and adding the stimulation of shank muscles (triceps surae and tibialis anterior), only with the tuning of the contact point between the foot and pedal to the relative strength of the ankle plantar flexors of the triceps surae compared to the fixed-ankle joint (van Soest et al., 2005). Taken together, it can be concluded that the free-ankle joint may alter the production of power during FES-

evoked cycling, as the biomechanics are affected by ankle patterns (Gregor et al., 1991). Fornusek et al. (2012) reported that freeing the ankle joint during FES-evoked cycling was found to be safe. The combination of shank muscle stimulation and freeing the ankle joint movement may improve ankle flexibility (Fornusek et al., 2012).

However, to date, no studies have experimentally investigated the effect of releasing the ankle joint on power production during FES-evoked cycling in individuals with SCI. Different ankle joint biomechanics may alter the low power produced during FES-evoked cycling in individuals with SCI. Free-ankle joint setup during FES-evoked cycling may maximize the PO and physiological benefits compared to fixed-ankle joint setup.

2.4 Muscle Activity Assessment during FES-Evoked Cycling Exercise

As mentioned in section 1.1.7.2, FES-related fatigue onsets earlier and more rapidly because human motor units undergo involuntary synchronous firing and their recruitment order is “inverted” with fast-twitch fibers (more fatigue-resistant) being recruited first and slow-twitch fibers (more oxidative and fatigue-resistant) being recruited later, or even not at all (Binder-Macleod et al., 1995). To avoid a decrease in performance caused by muscle fatigue during exercises, sufficient blood supply is required for the muscles to fulfill their metabolic requirements (Raymond et al., 2002). Therefore, this study needs to monitor muscle status and real-time muscle forces during FES-evoked cycling.

Peak torque and pedal PO measures have been used as proxies of muscle fatigue during the FES-evoked cycling (Binder-Macleod et al., 1995; Brown & Jensen, 2003; Fornusek et al., 2007). However, these reflect summated forces from a group of muscles during cycling that can be influenced by knee and ankle angular postures (Szecsi et al., 2014a) (knee and ankle biomechanics). Some studies have utilized reductions in speed

as a surrogate of fatigue (Allison et al., 2016). In addition to allowing the users to titrate the FES stimulus characteristics at an appropriate time to reduce fatigue-related effects, the development of physical sensors and signal quantification software to monitor fatigue in real time would improve the ‘dose-potency’ of the FES exercise (Haapala et al., 2008a). To date, muscle fatigue during FES-evoked cycling in individuals with SCI has been quantified in many studies by means of peak torque or pedal PO decrement. These measures may not be sensitive and do not reflect metabolic markers of fatigue.

Researchers have explored alternative means of muscle fatigue measurement during FES-evoked exercise. Muscle near-infrared spectroscopy (mNIRS) is a popular measurement tool with the advantage of being less affected by motion artefacts than EMG or evoked EMG (Ferrari et al., 2011). It is a non-invasive, real-time approach to quantify muscle metabolism by near-infrared light absorption based on oxygen saturation changes and scattering in biological tissues (Ferrari et al., 2011). The mNIRS allows local differences in muscle oxygen consumption ($m\dot{V}O_2$) and oxygen (O_2) delivery to be estimated, and oxygen saturation kinetics can be used as a proxy of the muscle mitochondrial activity (Ahmadi et al., 2008). It has been widely used to assess muscle oxygen consumption, blood flow, oxygen saturation, and indirectly mitochondria activity within muscles during fatiguing contractions. Sayli et al. (2014) revealed that NIRS oxygenation responses during voluntary handgrip exercise are highly reliable and that certain exercise protocols could be used to gain insight into deoxygenation and oxygen saturation in populations with low exercise tolerance (Celie et al., 2012).

Besides that, MMG has been used for assessing muscle fatigue during voluntary or FES-evoked contractions (Ibitoye et al., 2016; Islam et al., 2013), including FES-evoked cycling (Islam et al., 2018; Naeem et al., 2019). The MMG records and quantifies low-frequency mechanical oscillations produced by dimensional changes in muscle fibers

during contraction. It has been well documented that the amplitude and centre frequency of the MMG signal is associated with the muscle forces (Islam et al., 2018, 2013; Naeem et al., 2019). The RMS amplitude from the MMG signal depends on the muscle fiber activation and it generally increases with increasing muscle force (Faller et al., 2009; Gobbo et al., 2006). It is highly associated with muscle effort and was considered the most reliable parameter in the time domain (Al-Mulla et al., 2011). There are limited prior studies into fatigue assessment using MMG for individuals with SCI during FES-evoked cycling. The MMG-RMS has demonstrated promising findings for quantifying muscle function between pre- and post-fatigue FES-evoked conditions and characterizing muscle fatigue during the FES-evoked cycling (Islam et al., 2018). Since MMG signals are associated with force output (Agarwal et al., 2003) and are immune to electrical interference from FES during exercise (Orizio, 1993), MMG has been considered to be a reliable, reproducible, and valid proxy of muscle fatigue during FES-evoked cycling (Islam et al., 2018). MMG may also hold a known relationship to changes in $m\text{VO}_2$ (and indirectly muscle mitochondrial activity) since the MMG signal is the summation of motor unit recruitment that may also change with the muscle metabolism (Takaishi et al., 1992) - but this fundamental interrelationship has been poorly investigated to date (Praagman et al., 2003).

It is unclear what the underlying relationships are between muscle performance during FES-evoked cycling (i.e., PO or cycling cadence), physiological biomarkers of metabolism (i.e., muscle oxygen saturation and $m\text{VO}_2$) during fatigue, and MMG outputs derived from skin-surface sensors. NIRS is not sensitive to the changes in %MMG-RMS during repetitive electrically-evoked dynamic wrist extension in healthy participants, as these were unrelated (Mohamad Saadon et al., 2019). However, it is reported that sustained FES-evoked dynamic wrist extension exercise in tetraplegia had affected the extensor carpi radialis muscle, both physiologically (percentage of tissue

saturation index (%TSI)) and biomechanically (%MMG-RMS) in a similar manner (Mohamad Saadon et al., 2020), suggesting that MMG and NIRS are related during FES-evoked fatigue. To date, NIRS has never been quantitatively related to the MMG signal as a proxy for muscle force and fatigue during FES-evoked cycling in individuals with SCI. This gap of knowledge motivated the current study to quantify the relationships between the vibrational performance of electrically-evoked muscle measured through MMG and its oxidative metabolism through NIRS characteristics during FES-evoked cycling in fatiguing paralyzed muscles in individuals with SCI, specifically between pre- and post-fatiguing conditions. The goal of this study was to quantify these relationships so that muscle MMG sensors might in the future be deployed as feedback for FES-evoked movements in individuals with SCI and other neurological conditions. It is deemed crucial for the combination of systems to predict and detect fatigue since individuals with ‘complete’ sensorimotor SCI have no sensory feedback from their muscles to predict fatigue failure.

2.5 Summary of Literature Review

At the end of this section, it can be concluded that FES-evoked cycling efficiency could be maximized by using optimal stimulation parameters. The power produced during FES-evoked cycling in individuals with SCI could also be elevated by stimulating more muscle groups, including the addition of lower leg muscles, and by releasing the ankle joint. However, these need to be proved experimentally, which will be described in **Chapter 3**.

The MMG and NIRS have been used to measure muscle fatigue during cycling. Both sensors might correlate with each other. Therefore, the relationship between MMG and NIRS, particularly during FES-evoked cycling in individuals with SCI will be carried out in the next chapter.

CHAPTER 3: METHODOLOGY

This chapter describes the scientific protocols and materials that have been used in conducting the current study. It consists of two parts, reflecting the three main objectives of the present study (**Figure 3.1**). Part 1 explains the research protocols used for the first part of the study (F1) to analyze the biomechanical effects on power production during FES-evoked cycling in individuals with SCI. It reflects the first objective of the study, which is to determine the effect of releasing the ankle joint on power production during FES-evoked cycling in individuals with SCI. Part 2 describes the research protocols used for the second part of the study (F2) to analyze the muscle performance at the muscle level during FES-evoked cycling in individuals with SCI. It reflects the second and third objectives of the study, which are to investigate the relationships between the vibrational performance of electrically-evoked muscles measured through MMG and its oxidative metabolism through NIRS characteristics during FES-evoked cycling in individuals with SCI and to quantify muscle fatigue during FES-evoked cycling in individuals with SCI, specifically between pre- and post-fatiguing conditions using MMG and NIRS sensors.

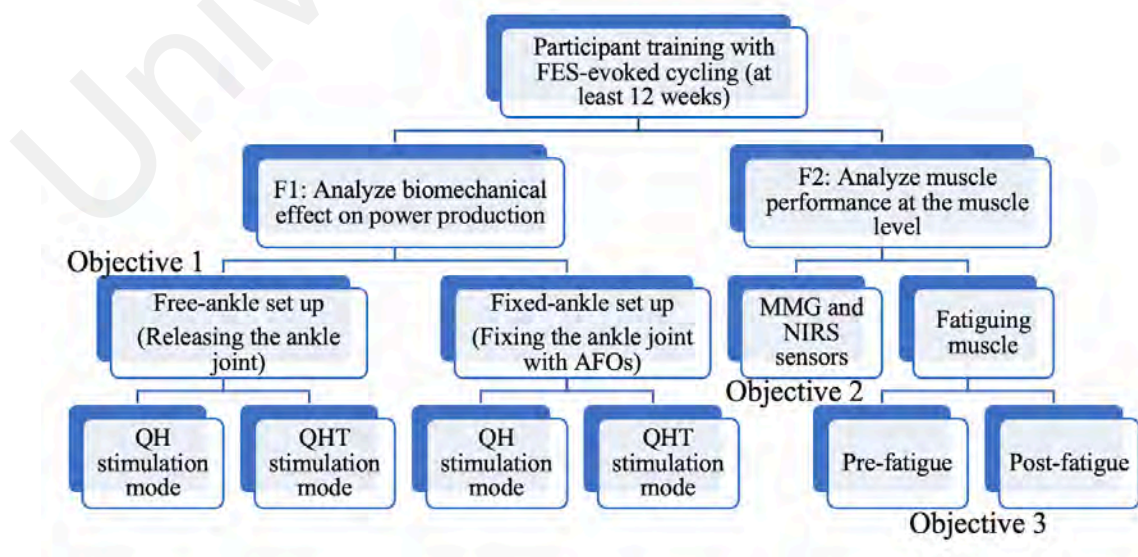


Figure 3.1: Flow chart of research activities.

3.1 Participants

Participants aged 18 years old and above with a SCI traumatic or non-traumatic origin, and motor complete function (AIS A and B) were considered for inclusion. Seven individuals (Casabona et al., 2021; Gelenitis et al., 2022) (six men and one woman (Casabona et al., 2021)) with complete SCI (AIS A and B), lesion levels between C5 to T11 (age 47.4 ± 11.3 years) participated in the study. All participants were recruited from Universiti Malaya Medical Centre (UMMC) (**Table 3.1**). Based on pilot trials, the consistency of biomechanical performance in all tested conditions indicated that the statistical power is sufficient with 7 participants (Dzulkifli et al., 2018), given the highly predictable output due to the mechanical constraints on the legs. Participants were invited as volunteers and were screened according to the AIS assessment by clinicians to meet the inclusion criteria. No participants were excluded from the study. All participants provided their written informed consent before participating in the study (**Appendices A and B**). Participants with no previous or ongoing record of neuromuscular, musculoskeletal, rheumatological, cardiovascular disorder, or orthopedic lower limb injuries were included. Prior to the experiment, all the participants were trained with FES-evoked cycling for at least 12 weeks (Hamzaid et al., 2012). The participants were trained in two sessions per week. To ensure that all the upper and lower leg muscles were equally trained with FES without limiting the ankle joint movement, each training session required the participants to cycle in a free-ankle setup with the stimulation of quadriceps, hamstring, tibialis anterior, and triceps surae muscles; referred to as QHT stimulation at their maximum stimulation intensity for at least 30 minutes. This study was approved by the local Medical Ethics Committee, UMMC, Universiti Malaya, Kuala Lumpur, Malaysia (Ref No.: 1003.14(1); 22/07/2013 (**Appendix C**) and 20166-2552). All methods were performed in accordance with the Declaration of Helsinki.

Table 3.1: Physical characteristics of the SCI participants.

| Participant | Age (years) | Gender | Height (m) | Weight (kg) | Lesion level | AIS | Time since injury (years) | Maximum stimulation intensity (mA) |
|------------------------------------|-----------------|--------|---------------|----------------|--------------|-----|---------------------------|------------------------------------|
| *1 | 49 | F | 1.62 | 82.0 | T4 | B | 26 | 100 |
| 2 | 51 | M | 1.74 | 79.6 | T1 | A | 13 | 100 |
| 3 | 30 | M | 1.71 | 62.4 | C7 | B | 16 | 100 |
| 4 | 36 | M | 1.70 | 75.9 | C6 | A | 19 | 100 |
| 5 | 59 | M | 1.73 | 80.0 | C5-C7 | B | 6 | 60 |
| 6 | 46 | M | 1.79 | 71.6 | C6-C7 | B | 5 | 100 |
| 7 | 61 | M | 1.72 | 60.5 | T10-T11 | A | 15 | 60 |
| Mean \pm standard deviation (SD) | 47.4 \pm 11.3 | | 1.7 \pm 0.1 | 73.1 \pm 8.7 | | | 14.3 \pm 7.3 | 86.7 \pm 20.7 |

*Participant 1 was excluded from the second part of the study due to an unfit rapid inflator thigh cuff.

3.2 Biomechanical Effects on Power Production during FES-Evoked Cycling in Individuals with SCI (F1)

A quasi-experimental research design was adopted whereby participants performed all trials in different conditions (fixed- and free-ankle, with different muscle stimulation), but their order of trials was randomized.

3.2.1 Instrumentation

A MOTomed Viva 2 FES cycle ergometer (RECK-Technik GmbH, Betzenweiler, Germany) was utilized in this study (**Figure 3.2**). Self-adhesive gel-backed surface stimulating electrodes were placed over the belly of the quadriceps, hamstrings, tibialis anterior, and triceps surae muscles that were stimulated. Due to the larger muscle size of the quadriceps and hamstrings, 7.5 x 13 cm rectangular electrodes were used to stimulate the quadriceps and hamstrings. While smaller rectangular electrodes (5 x 9 cm) were used to stimulate the tibialis anterior and triceps surae. For quadriceps, the proximal electrode was placed 1/3 of the distance from the inguinal line to the superior

patellar border and the distal electrode was placed 6-8 cm proximally to the patellar border (Szecsi et al., 2014a). For hamstrings, the proximal electrode was placed 2-4 cm below the gluteal crease and the distal electrode was placed 4-5 cm above the popliteal space (Szecsi et al., 2014a). For tibialis anterior, the proximal electrode was placed 2 cm below the fibula head and the distal electrode was placed 4-5 cm from the ankle joint. For triceps surae, the proximal electrode was placed 4-5 cm below the popliteal space and the distal electrode was placed 4-5 cm from the ankle joint. Stimulating electrode placement was kept consistent between trials. To keep the placement of the stimulating electrodes consistent between trials, only one similar person applied the stimulating electrodes on the participants during training and experimental sessions. In addition, the measurement of the stimulating electrode placement was recorded for each participant. An in-shoe F-scan system (Teckscan Incorporated, Boston, Massachusetts) was placed under the participants' feet and connected to a cuff unit that linked the foot sensors to a computer via a 10 m cable (Kearney et al., 2011). A pair of solid AFOs was used to restrict the ankle joint movement at a neutral position (90°). The lower legs of each participant were placed in the solid AFO that was fixed to the pedal during fixed-ankle FES-evoked cycling. No AFO was used during free-ankle FES-evoked cycling to allow the ankle to move from a neutral position to dorsi-plantarflexion. The pedal spindle was attached to the top middle part of the foot. The seat position from the crank axle was adjusted and recorded for each participant so that the knee extension did not exceed $150\text{-}160^\circ$ at the bottom dead center (Szecsi et al., 2014a) to prevent knee hyperextension. Allowing $20\text{-}30^\circ$ of knee flexion enabled the knee torque to continuously generate at the bottom dead center. The knee extension angle was measured using an analog goniometer. The hip, knee, ankle, pedal, and crank kinematics were recorded using three-dimensional (3D) motion analysis systems

(Qualisys AB, Gothenburg, Sweden, and Vicon, Oxford, UK). During fixed-ankle FES-evoked cycling, the marker placement for the ankle joint was on the AFO.

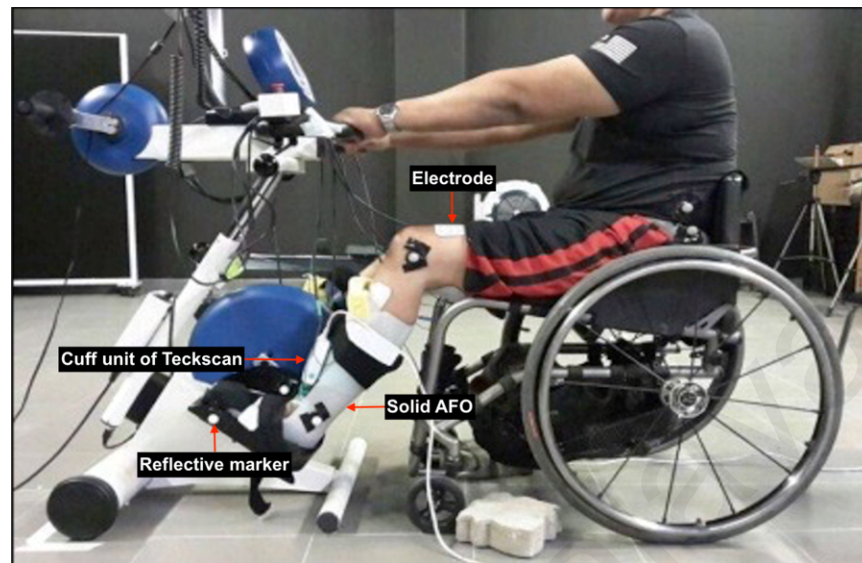


Figure 3.2: Setup for fixed-ankle FES-evoked cycling. Shown is the placement of markers over the fifth metatarsophalangeal and ankle joints in the solid AFO. Electrodes were placed on the quadriceps, hamstrings, tibialis anterior, and triceps surae muscles.

3.2.2 Leg Muscles Stimulation Pattern

Two sets of stimulation modes were determined for comparison. In mode 1, the participants performed FES-evoked cycling with the stimulation of quadriceps and hamstrings muscles, i.e., QH stimulation (**Figure 3.3a**). In mode 2, the participants performed FES-evoked cycling with QHT stimulation (**Figure 3.3b**).

The stimulation angle of each muscle was fixed between the participants and within the cycling modes based on an earlier study (**Figure 3.3c**). The stimulation angle used in the study was derived directly from the MOTomed Viva 2 FES cycle ergometer. The lower leg muscles' stimulation timing, i.e., of the tibialis anterior, and triceps surae, was set to encourage plantar- and dorsiflexion of the ankles (quadriceps: 197° to 337° , hamstring: 17° to 157° , tibialis anterior: 127° to 247° , and triceps surae: 337° to 77°). The gluteal muscles were not stimulated at all in this study as it was reported to produce

no measurable crank torques in most individuals with SCI (Szecsi et al., 2014a), and also due to the limited number of stimulation channels available on the FES cycling device.

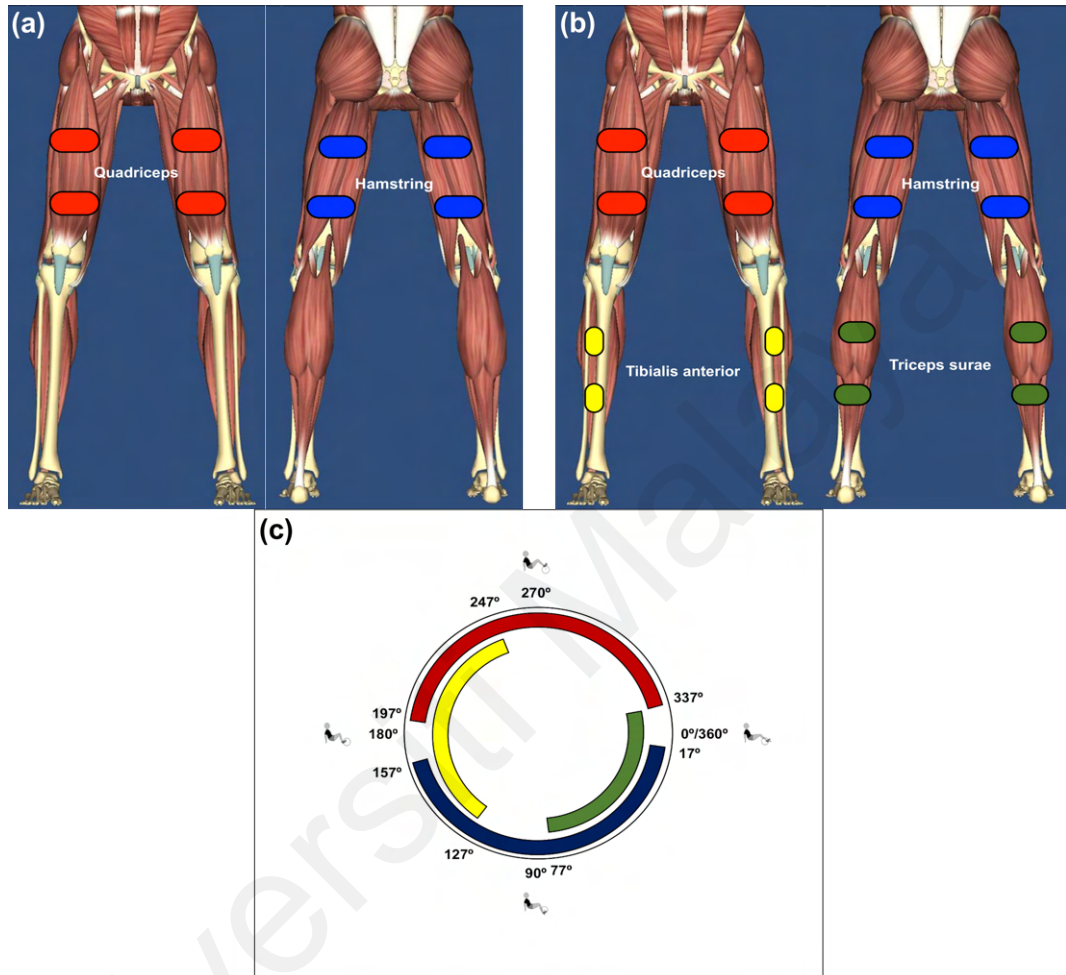


Figure 3.3: Two stimulation modes of FES-evoked cycling were used in this study; (a) QH stimulation; (b) QHT stimulation; and (c) stimulation angle. Image adapted from the software 3D Anatomy Learning (Version 3.9, Education Mobile) (open-source project).

3.2.3 Experimental Protocol

Each participant completed all 2 sets of trials in randomized order. Trial set 1 required the participants to perform fixed-ankle FES-evoked cycling, while trial set 2 required the participants to perform free-ankle FES-evoked cycling. Each trial set required the participants to perform FES-evoked cycling with 2 different stimulation modes, i.e., mode 1 and mode 2. The order of each trial set; fixed-ankle QH stimulation,

free-ankle QH stimulation, fixed-ankle QHT stimulation, and free-ankle QHT stimulation, was randomized for each participant. For each trial set and mode, the participants performed one minute of passive cycling (warm-up), one minute of FES-evoked cycling (Fornusek et al., 2007), one minute of passive cycling (cool-down), and 10 minutes of resting phase. The passive mode was used during FES-evoked cycling, where a motor from the MOTomed assisted the participants to do cycling. Steady-state was identified when the participants reached constant cadence. The participants performed 2 sets of trials in two sessions. Each session was separated by at least 48 hours of recovery period to prevent excessive muscle fatigue effect (Matsunaga et al., 1999). The participants performed FES-evoked cycling at 50 revolutions per minute (rpm). Resistance was set to 1 kg. Fixed stimulation pulse width (300 μ s) and frequency (30 Hz), and the highest tolerance stimulation intensity (up to 120 mA) were applied by an eight-channel stimulator (RehaStim ScienceMode, HASOMED GmbH, Germany) during all trial sets. Prior to the experiment, the highest tolerance stimulation intensity was recorded for each participant at the end of the training periods (**Table 3.1**). The stimulation intensity would be increased gradually from the beginning of the training session. For participants with AIS B, their highest tolerance stimulation intensity was defined when they felt pain or discomfort. For participants with AIS A, their highest tolerance stimulation intensity was defined when there was an initial significant movement induced by the FES.

3.2.4 Data Acquisition and Processing

The pedal force (**Appendix D**) and the hip, knee, and ankle joints kinematics (**Appendix E**) of each trial set were recorded at 120 Hz, displayed in real-time using software (Tekscan Incorporated, Boston, Massachusetts) and 3D motion analysis systems (Qualisys AB, Gothenburg, Sweden and Vicon, Oxford, UK) to store data into a personal computer (PC) for offline analysis. These data were synchronously recorded

and stored for the entire one minute of the FES-evoked cycling period. 10 complete cycles of 0° to 360° crank angle from the last 20 seconds of the data, where the cycling pace was most consistent, were analyzed (Szecsi et al., 2014b, 2014a). The pedal PO was then calculated based on the pedal force captured by the F-scan sensor and the kinematics marker system. The mean and peak pedal POs (W) were normalized (W/W (%)) to the maximum PO of overall performance from 0° to 360° crank angle for each participant. The hip, knee, and ankle angles captured were derived to generate hip, knee, and ankle ROMs. The mean and peak normalized pedal POs, hip, knee, and ankle joints ROMs of each trial set were then averaged for every 20° crank angle for further analyses. The initial crank angle across 20° crank intervals is represented as 20° (the averages of 0° to 20°). The mean and peak normalized pedal POs, hip, knee, and ankle joints' ROMs for each 20° slice from 0° to 360° crank angle were derived for further analyses.

3.2.5 Statistical Analysis

Two-way repeated measures analysis of variance (ANOVA) was performed to analyze the difference in the ankle movement during FES-evoked cycling within the four conditions., i.e., (a) fixed-ankle QH stimulation, (b) free-ankle QH stimulation, (c) fixed-ankle QHT stimulation, and (d) free-ankle QHT stimulation, in terms of its PO and ROM. The two-way ANOVA analyses of each condition were derived from each of the 20° crank angle positions, as 18 segments of 0° to 360° crank angle. In addition, a least significant difference (LSD) post hoc test was conducted to compare all PO and ROM generated by the four conditions of ankle movement during FES-evoked cycling for each 20° slice from 0° to 360° crank angle. All statistical analyses were performed using SPSS software (IBM SPSS Statistics version 20, New York, USA). Statistical significance was determined at an alpha (α) = 0.05 ($p < 0.05$).

3.3 Muscle Performance at the Muscle Level during FES-Evoked Cycling in Individuals with SCI (F2)

3.3.1 Instrumentation

3.3.1.1 Fatigue measurement

Prior to the experiment, fatigue measurement was conducted on the same day as the experiment. A progressive-intensity FES-evoked cycling test was undertaken using a motorized cycle trainer (MOTOmed Viva 2, RECK-Medizintechnik GmbH, Betzenweiler, Germany) to quantify cycle cadence as an indicator of muscle fatigue. Throughout the FES-evoked cycling, the stimulation current intensity was increased progressively to a maximum that the participant could tolerate. This progressive-intensity paradigm was utilized for participants to derive their maximum cycle cadence. Maximum cadence was achieved when the maximum stimulation that the patient could tolerate was achieved. Resistance was set to 1 kg. Fatigue was then quantified post-experiment on the computer using the software Kinovea (0.8.15) (an open-source project). Fatigue was defined as a drop of at least five rpm below the maximum cadence for two consecutive seconds (Allison et al., 2016). The fatigue measurement was repeated on both sessions of exercise.

3.3.1.2 FES-evoked cycling

A six-channel neuromuscular stimulator (Rehastim II, Hasomed GmbH, Magdeburg, Germany) was used to supply FES current to the leg muscles deployed using a MOTOmed. Stimulation was delivered to the quadriceps and hamstrings of each leg using pairs of 7.5 x 13 cm rectangular self-adhesive stimulating electrodes for each muscle group (**Figure 3.4**). Each electrode pair was stimulated independently to avoid co-contractions of other muscle groups. For the quadriceps femoris muscle group, the proximal electrode centre was placed on the skin over the motor point at approximately

1/3 of the distance from the inguinal line to the superior patellar border, and the distal electrode centre was placed 6-8 cm proximal to the patellar border. For the hamstrings muscle group, the proximal electrode centre was placed 2-4 cm below the gluteal crease and the distal electrode centre was placed 4-5 cm above the popliteal space (Szecsi et al., 2014a). The stimulus current amplitude was adjusted accordingly to reach the desired cadence with a maximum amplitude of 120 mA. Controlled muscle contractions were achieved by setting the stimulus pulse width to 300 μ s at a frequency of 35 Hz. The stimulation paradigm was continuous-to-fatigue incremented by 2 mA steps (Szecsi et al., 2014a).

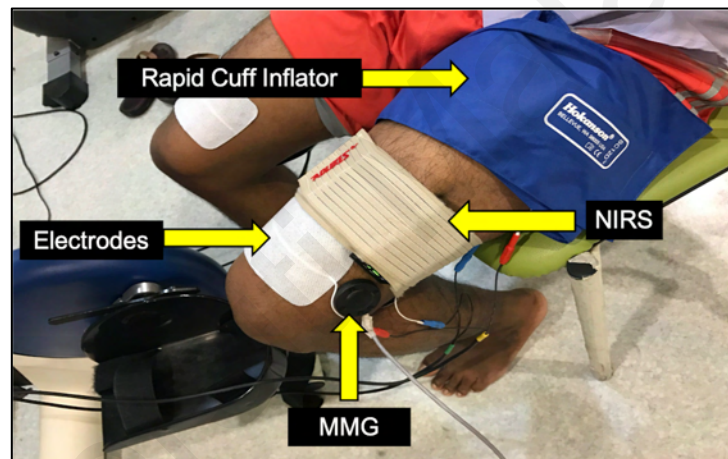


Figure 3.4: Setup for FES-evoked cycling. Shown is the placement of electrodes over the quadriceps and hamstrings muscle groups. The MMG and NIRS sensors were placed over the muscle belly of the left vastus lateralis.

3.3.1.3 Near-Infrared Spectroscopy

An NIRS instrument (PortaMon, Artinis Medical Systems, The Netherlands) was used to continuously record changes in muscle oxygenation from its sub-component signals in real-time in the left legs. Muscle-assessed NIRS emits infrared light at wavelengths of 760 and 850 nm, which is transmitted through the skin, muscle, and adipose tissue. From the amount of light reflected onto the NIRS sensor at their respective wavelengths, these are converted to concentration changes of oxyhaemoglobin (O_2Hb), deoxyhaemoglobin (HHb), and total haemoglobin (tHb) using

a modified Lambert-Beer Law (Delpy et al., 1988). These NIRS signals were used to calculate the %TSI.

Prior to the experiment, the NIRS probe was calibrated according to the manufacturer's instructions. The probe was placed on the left vastus lateralis muscle (on the point between the electrodes placed for electrical stimulation) (**Figure 3.4**). The skin of each participant was cleaned with alcohol wipes to remove any oils on the skin under the probe and to reduce slippage. A light-blocking material was used to wrap the NIRS probe to prevent contamination from ambient light. NIRS measurements were made continuously at rest, throughout FES-evoked cycling exercise, and during two super-systolic arterial occlusions performed before and after exercise. From the basic NIRS signals, derived measurements were used to express the absolute volume and rate of change (kinetics) of %TSI "physiologically calibrated" from the arterial occlusions performed three minutes before and three minutes after exercise.

The super-systolic arterial occlusion (cuff air pressure was inflated to 270 mmHg) was performed to elicit the minimum and maximum oxygen saturation ($O_2\text{Sat}$), the time course of $O_2\text{Sat}$ changes (kinetics) and to calculate $m\text{VO}_2$. Arterial occlusion was continued until the $O_2\text{Sat}$ reached a nadir lasting at least 30 seconds, usually after 5–8 minutes, then the cuff was released immediately, and following a further 3-5 minutes post-occlusion recovery period, participants were prepared for the exercise trials (Ahmadi et al., 2008).

3.3.1.4 Mechanomyography

MMG is a technique to record muscle performance in real-time, elicited by the mechanical activity of muscle contractions using different types of sensors, whereby the instrument's signals quantify the mechanical activity of the muscle, including during muscle fatigue. MMG signals from the left vastus lateralis were obtained using an

accelerometer-based MMG sensor (Sonostics VMG BPS II Transducer Biopac System Inc. USA, operational frequency response = 20-200 Hz, sensitivity 50 V/g, maximum range 2000 g) attached using double-sided tape (3M 157 Center St. Paul, MN, USA) directly on the muscle belly (**Figure 3.4**) to obtain the maximum surface oscillation during contraction-shortening (Ibitoye et al., 2016).

3.3.2 Experimental Protocol

The experiment commenced with 5 minutes of rest followed by an arterial occlusion of the thigh (this 'physiological calibration' procedure took approximately 5-8 minutes). Cuff pressure was then released for a period of post-occlusion recovery until the TSI% reading became stable (usually approximately three minutes). The participant was then prepared for the FES exercise trial.

FES-evoked cycling was initiated with one minute of passive cycling (warm-up) followed by 30 minutes of FES-evoked cycling and one minute of passive cycling (cool-down). The passive mode was used during FES-evoked cycling, where a motor from the MOTomed assisted the participants to do cycling. The second arterial occlusion was then repeated after exercise cessation.

Two sessions of exercise were conducted with 48 hours of recovery in between sessions (Matsunaga et al., 1999). The MMG and NIRS signal data gained from the two sessions of exercise were recorded. The data from each session of exercise were averaged and used for analysis. A schematic diagram of the protocol employed in analyzing the muscle performance at the muscle level during FES-evoked cycling is shown in **Figure 3.5**.

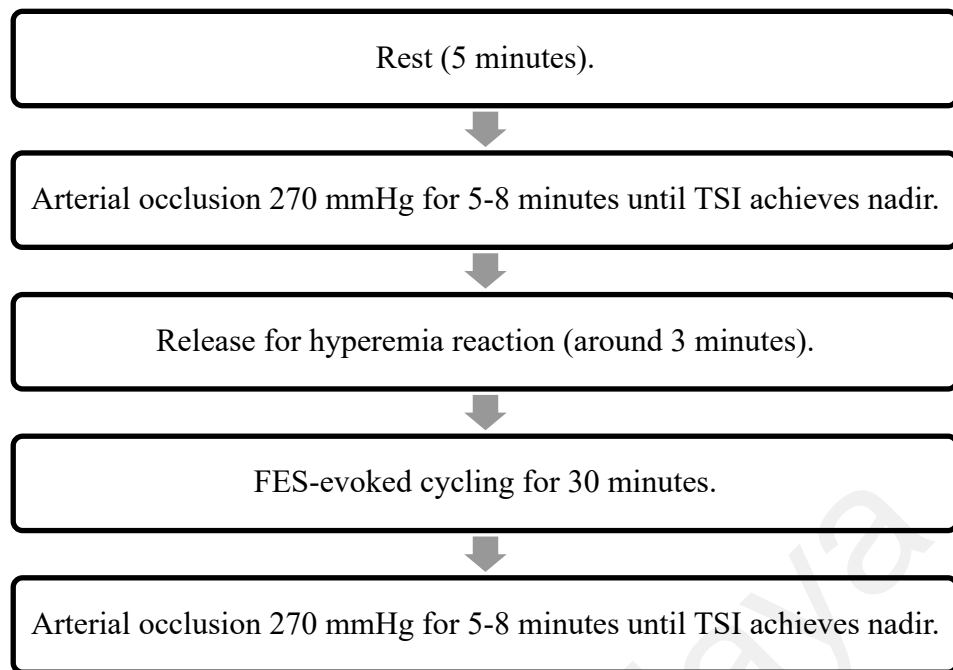


Figure 3.5: Experimental protocol in analyzing the muscle performance at the muscle level during FES-evoked cycling in individuals with SCI.

3.3.3 Data Acquisition and Processing

The raw data of the MMG sensor and NIRS instrument (**Appendix F**) for the entire 30 minutes of cycling were recorded at a sampling rate of 2 kHz and 10 Hz, respectively, displayed in real-time on a PC. These data were synchronously recorded and stored. To determine whether there were any trends of physical performance and physiological responses over 30 minutes of FES-evoked cycling, MMG and NIRS data were separated into pre-defined epochs representing the immediate onset of exercise (Epoch 1 = minute 1 to 2), early steady-state exercise (Epoch 2 = minute 9 to 10), the middle period of exercise (Epoch 3 = minute 10 to 11; Epoch 4 = minute 19 to 20) and just before exercise termination (Epoch 5 = minute 29 to 30).

3.3.3.1 Mechanomyography

Muscle mechanical signals were recorded with the MMG sensor placed over the muscle belly of the left vastus lateralis. Acqknowledge v4.3 data acquisition and analysis software (MP150 and HLT100C, BIOPAC System Inc., USA) was used to

collect data. The signal was then filtered with a bandpass filter (fourth-order Butterworth) at 20-200 Hz. The lower cut-off of the MMG signal was set so that movement and other low-frequency artefacts could be filtered out (De Luca et al., 2010) and the higher cut-off of the MMG signal was set to capture greater ‘signal density’ from fast-firing motor units, which are in much higher proportion in muscles of chronic SCI participants (Higashino et al., 2013). A ‘notch filter’ was used to filter out 50 Hz artefacts due to power line interference from the bike. The dataset processed from the MMG signal was in the time domain, whereby, the amplitude was identified as voltage values to calculate RMS. The MMG RMS is reported as a variable in describing motor unit recruitment during a contraction process (Orizio et al., 2003). The MMG RMS was obtained from MATLAB (R2015a, Mathworks, 2015) at 60 seconds epochs. MMG RMS was extracted from the raw MMG signal (**Equation 3.1**), where x_k is the raw signal from each segment and N is the number of samples. A single peak value from each participant, taken from all the trials conducted on that particular participant across separate days (Ibitoye et al., 2016), was identified from the whole protocol for further normalization. The RMS was then normalized to the respective peak values of each participant (Dzulkifli et al., 2018).

$$RMS = \sqrt{\frac{1}{N} \sum_{k=1}^{N-1} x_k^2}, \text{ for } k = 1, \dots, N,$$

Equation 3.1

3.3.3.2 Near-Infrared Spectroscopy

Instrument-specific software (Oxysoft, Artinis Medical Systems, The Netherlands) was used to analyze the raw NIRS signals offline. The initial decrease of O_2Hb was used to calculate mVO_2 (**Equation 3.2**) (Kooijman et al., 1997; van Beekvelt et al., 2002). **Figure 3.6** shows that muscle oxygen consumption from arterial occlusion can be calculated from the initial linear decrease of the O_2Hb graph that has been plotted

(Praagman et al., 2003). Once the gradient was measured, the mVO_2 was then calculated. The %TSI (**Equation 3.3**) (Millet et al., 2012), O_2Hb , HHb, and tHb were then averaged into 60-second epochs.

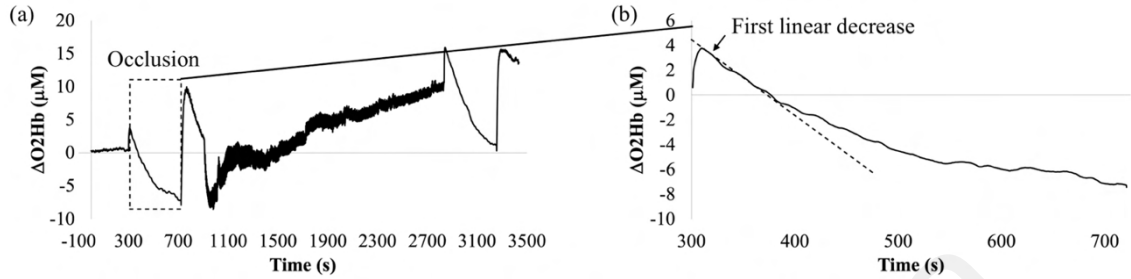


Figure 3.6: The quantification of the initial decrease of the O_2Hb . (a) Muscle oxygen consumption from arterial occlusion can be calculated from (b) the linear decrease in the O_2Hb during occlusion.

$$mVO_2 = Abs \left(\left(\frac{\Delta O_2Hb \times 60}{10 \times 1.04} \right) \times 4 \right) \times \frac{22.4}{1000}$$

Equation 3.2

$$\%TSI = \left(\frac{O_2Hb}{Hb + O_2Hb} \right) \times 100\%$$

Equation 3.3

3.3.3.3 Power Output

The PO was derived from the constant resistance and speed throughout the FES-evoked cycling (**Equation 3.4**). It was then separated into five epochs.

$$Power = Force \times Velocity$$

Equation 3.4

3.3.4 Statistical Analysis

Bivariate correlation analysis was performed to analyze the relationships between (i) normalized RMS from the MMG sensor and %TSI (RMS-%TSI), O_2Hb (RMS- O_2Hb), HHb (RMS-HHb), and tHb (RMS-tHb) from NIRS instrument, (ii) power output and %TSI (PO-%TSI), O_2Hb (PO- O_2Hb), HHb (PO-HHb), and tHb (PO-tHb) from NIRS

instrument in all participants. The interpretation of correlations was based on the criteria, $r > 0.5$ as a strong correlation, $r = 0.3-0.5$ as moderate, $r < 0.3$ as a poor correlation, and $r = 0$ as no correlation (Cohen, 1988). One-way ANOVA with LSD *a posteriori* analyses were performed to analyze the changes of RMS-%TSI, RMS-O₂Hb, RMS-HHb, and RMS-tHb, PO-%TSI, PO-O₂Hb, PO-HHb, PO-tHb at rest and during 30 minutes of FES-evoked cycling. A paired sample *t*-test was performed to compare mVO₂ at rest and after 30 minutes of FES-evoked cycling. All statistical analyses were performed using SPSS software (IBM SPSS Statistics version 20, New York, USA). Statistical significance was determined at an $\alpha = 0.05$ ($p < 0.05$).

CHAPTER 4: RESULTS

This chapter contains all the findings of the current study. It consists of two parts, reflecting the three main objectives of the present study. Part 1 explains the findings for F1, which is to analyze the biomechanical effects on power production during FES-evoked cycling in individuals with SCI. It reflects the first objective of the study, which is to investigate the effect of releasing the ankle joint on power production during FES-evoked cycling in individuals with SCI. Part 2 portrays the findings for F2, which is to analyze the muscle performance at the muscle level during FES-evoked cycling in individuals with SCI. It reflects the second and third objectives of the study, which are to investigate the relationships between the vibrational performance of electrically-evoked muscles measured through MMG and its oxidative metabolism through NIRS characteristics during FES-evoked cycling in individuals with SCI, and to quantify muscle fatigue during FES-evoked cycling in individuals with SCI, specifically between pre- and post-fatiguing conditions using MMG and NIRS sensors.

4.1 Analysis of the Biomechanical Effects on Power Production during FES-evoked Cycling in Individuals with SCI

In overall cycling performance from 0° to 360° crank angle, fixed- and free-ankle FES-evoked cycling produced mean pedal POs that ranged from 1.2 ± 0.5 W to 27.1 ± 16.8 W (minimum PO \pm SD to maximum PO \pm SD), and from 0.6 ± 0.3 W to 28.4 ± 8.8 W, respectively (**Table 4.1**). These values were derived from two different muscle stimulation settings, i.e., QH and QHT, for each condition. For QH only stimulation, the pedal POs generated during FES-evoked cycling with fixed- and free-ankle ranged between 1.5 ± 0.3 W to 22.4 ± 17.6 W and 0.6 ± 0.3 W to 22.8 ± 16.4 W, respectively. On the other hand, when all QHT were stimulated, the fixed- and free-ankle pedal POs

ranged between 1.2 ± 0.5 W to 27.1 ± 16.8 W and from 1.5 ± 0.8 W to 28.4 ± 8.8 W, respectively.

Table 4.1: The range of raw pedal PO obtained between fixed- and free-ankle FES-evoked cycling with QH and QHT stimulation modes, generated from 0° to 360° crank angle.

| Participant | Pedal PO (W) [mean \pm SD (minimum – maximum)] | | | |
|-------------|--|---------------------------------|---------------------------------|--------------------------------|
| | Fixed-ankle QH stimulation | Free-ankle QH stimulation | Fixed-ankle QHT stimulation | Free-ankle QHT stimulation |
| 1 | 4.8 ± 2.5 (0.3 – 8.7) | 1.5 ± 0.9 (0.2 – 6.2) | 3.1 ± 3.2 (0.1 – 15.1) | 1.5 ± 0.8 (0.1 – 4.3) |
| 2 | 22.4 ± 17.6 (1.7 – 104.9) | 22.8 ± 16.4 (0.6 – 69.2) | 27.1 ± 16.8 (3.5 – 79.8) | 28.4 ± 8.8 (9.4 – 51.7) |
| 3 | 17.9 ± 14.7 (0.9 – 113.5) | 7.6 ± 10.0 (0.2 – 68.0) | 16.1 ± 7.8 (2.3 – 38.2) | 7.3 ± 6.2 (0.6 – 43.9) |
| 4 | 6.1 ± 3.6 (0.6 – 23.7) | 5.1 ± 4.3 (0.03 – 23.8) | 7.0 ± 5.4 (1.5 – 24.6) | 7.2 ± 6.8 (0.2 – 26.7) |
| 5 | 3.1 ± 2.7 (0.3 – 20.1) | 2.5 ± 2.8 (0.1 – 21.6) | 4.1 ± 3.4 (0.3 – 16.1) | 3.3 ± 2.1 (0.04 – 16.1) |
| 6 | 7.6 ± 4.6 (0.2 – 21.6) | 14.2 ± 6.5 (2.3 – 39.1) | 19.2 ± 6.9 (7.0 – 40.3) | 26.6 ± 9.4 (9.1 – 54.9) |
| 7 | 1.5 ± 0.3 (0.6 – 2.5) | 0.6 ± 0.3 (0.04 – 1.3) | 1.2 ± 0.5 (0.4 – 2.9) | 1.7 ± 0.5 (0.8 – 3.6) |

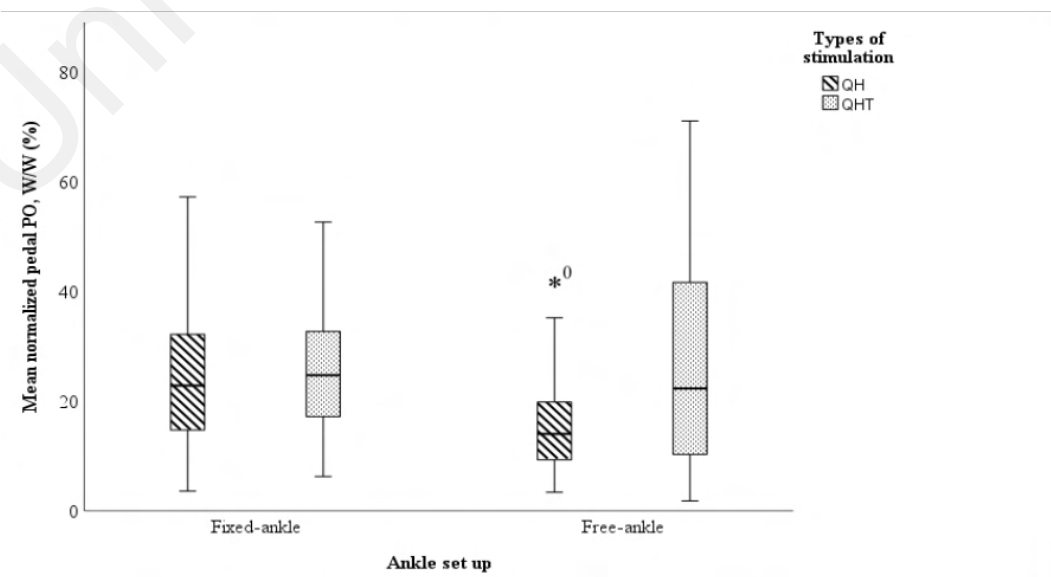
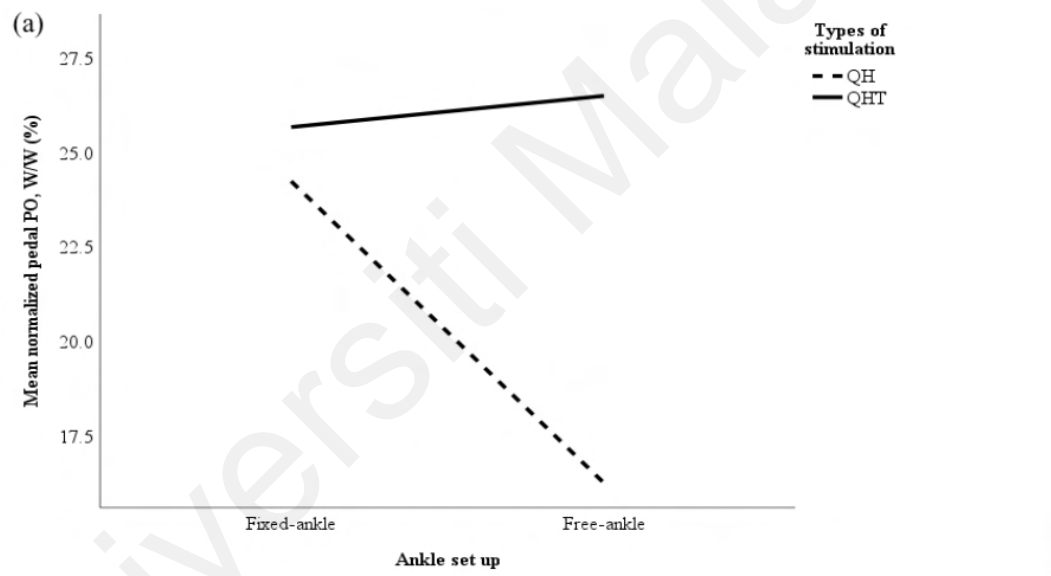
A two-way ANOVA was performed to analyze the effect of fixed- and free-ankle, and QH and QHT stimulations during FES-evoked cycling on the mean and peak normalized pedal POs across 18 segments of 0° to 360° crank angle (**Figure 4.1a** and **4.1b**). The present study revealed that there was a statistically significant interaction between the effect of fixed- and free-ankle, and QH and QHT stimulations during FES-evoked cycling on the mean [$F(1,500) = 14.03$, $p < 0.01$, $\eta_p^2 = 0.027$] and peak normalized pedal POs [$F(1,500) = 7.111$, $p = 0.008$, $\eta_p^2 = 0.014$] for each slice of 20° crank angle intervals. Further analysis showed that the interaction between free-ankle, and QH and QHT stimulations significantly altered the mean and peak pedal POs ($p < 0.01$), but there were no differences between fixed-ankle, and QH ($p = 0.389$) and QHT stimulations ($p = 0.451$). The present study also revealed that there were significantly

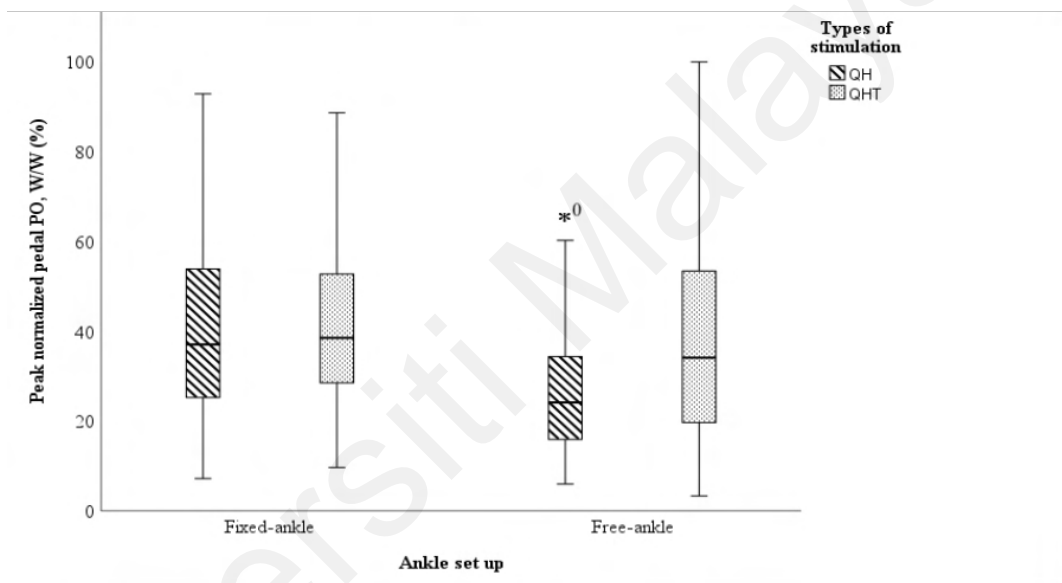
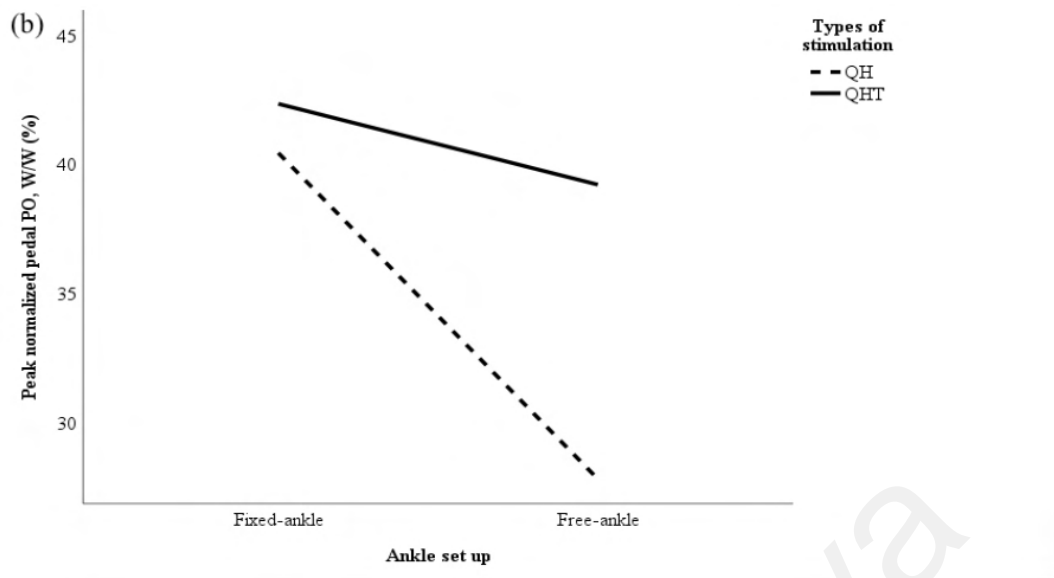
lower mean and peak normalized pedal POs ($16.2 \pm 9.8 \%$ and $27.8 \pm 16.8 \%$, respectively) in the free-ankle QH stimulation compared to the rest of the setting (**Figure 4.1a** and **4.1b**) for each slice of 20° crank angle intervals. Free-ankle QHT stimulation elevated the mean normalized pedal PO by 0.8% than the fixed-ankle QHT stimulation (**Table 4.2**). Fixed-ankle QHT stimulation elevated the peak normalized pedal PO by 14.5% more than free-ankle QH stimulation.

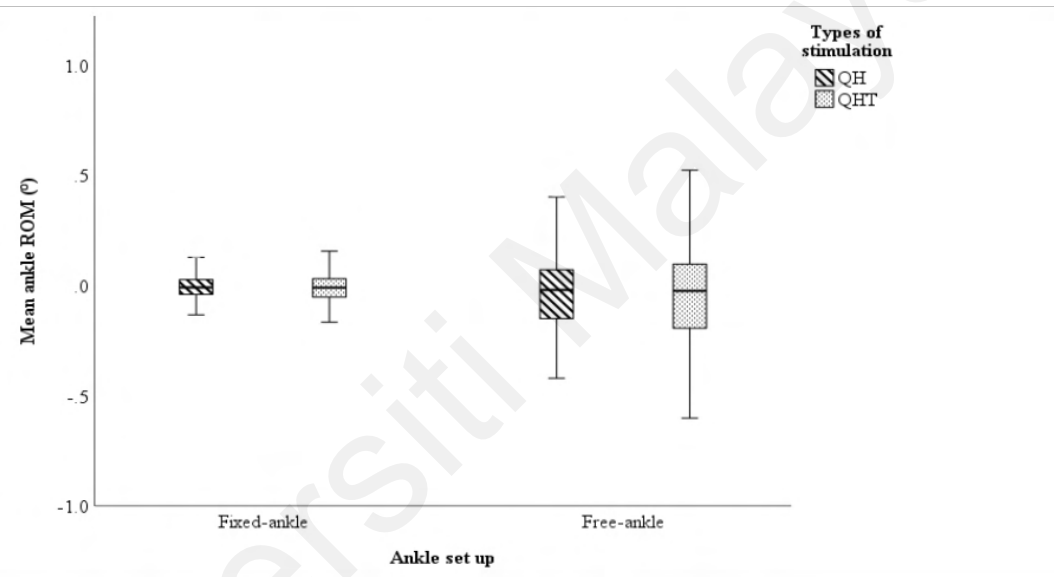
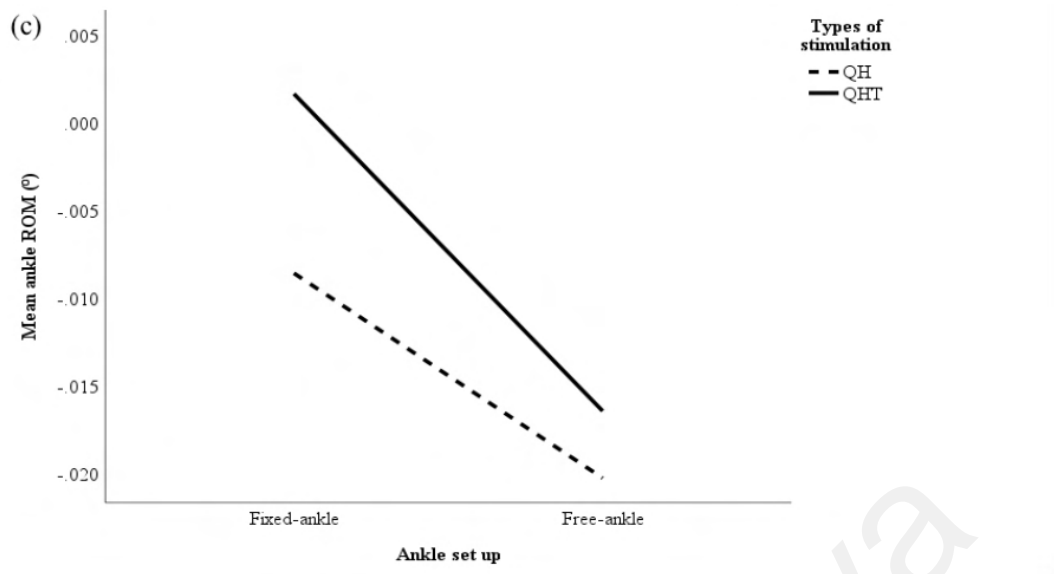
In overall cycling performance across 18 segments of 0° to 360° crank angle, fixed- and free-ankle FES-evoked cycling generated ankle ROM that ranged from $-0.007 \pm 0.1^\circ$ to $0.1 \pm 0.6^\circ$, and from $-0.001 \pm 0.4^\circ$ to $0.02 \pm 0.3^\circ$, respectively. The ankle ROM during fixed- and free-ankle QH stimulations ranged from $-0.004 \pm 0.02^\circ$ to $0.002 \pm 0.04^\circ$ and $-0.04 \pm 0.3^\circ$ to $0.03 \pm 0.2^\circ$, respectively. On the other hand, the ankle ROM generated during fixed- and free-ankle QHT stimulations ranged between $-0.007 \pm 0.1^\circ$ to $0.1 \pm 0.6^\circ$ and $-0.001 \pm 0.4^\circ$ to $0.01 \pm 0.1^\circ$, respectively. The present study revealed that free-ankle setting allowed not significantly greater ankle variations for both QH ($-0.020 \pm 0.3^\circ$) and QHT stimulations ($-0.016 \pm 0.3^\circ$), compared to fixed-ankle QH ($-0.009 \pm 0.1^\circ$) and QHT stimulations ($0.002 \pm 0.3^\circ$) across each slice of 20° crank angle intervals (**Figure 4.1c**). On the other hand, the knee ROM produced during fixed- and free-ankle FES-evoked cycling ranged from $-0.01 \pm 0.8^\circ$ to $0.1 \pm 0.6^\circ$ and $0.001 \pm 0.1^\circ$ to $0.1 \pm 0.6^\circ$, respectively. Whereas the hip ROM obtained during fixed- and free-ankle FES-evoked cycling ranged from $-0.05 \pm 0.5^\circ$ to $0.01 \pm 0.3^\circ$ and $-0.005 \pm 0.1^\circ$ to $0.03 \pm 0.2^\circ$, respectively.

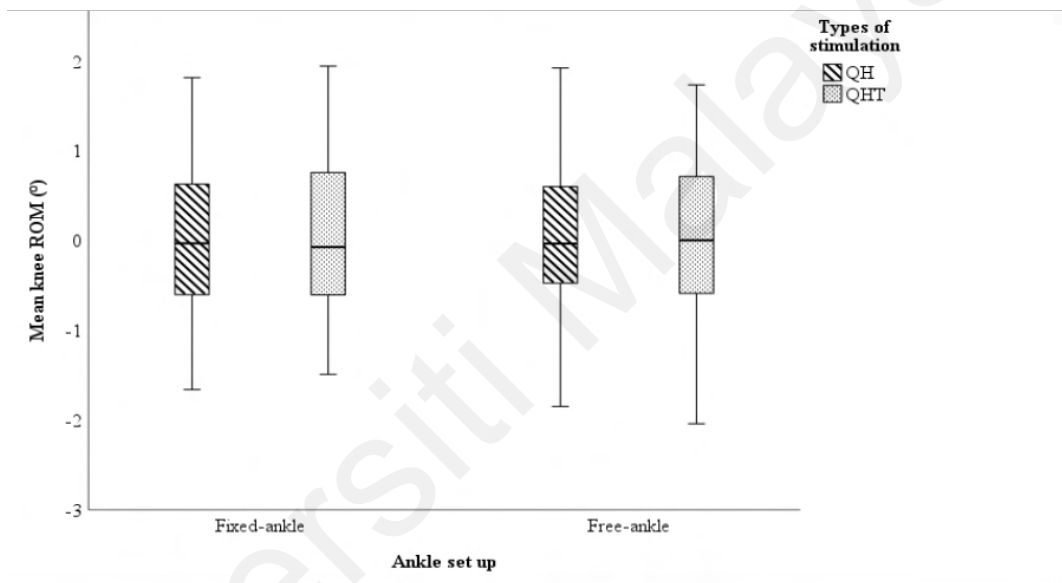
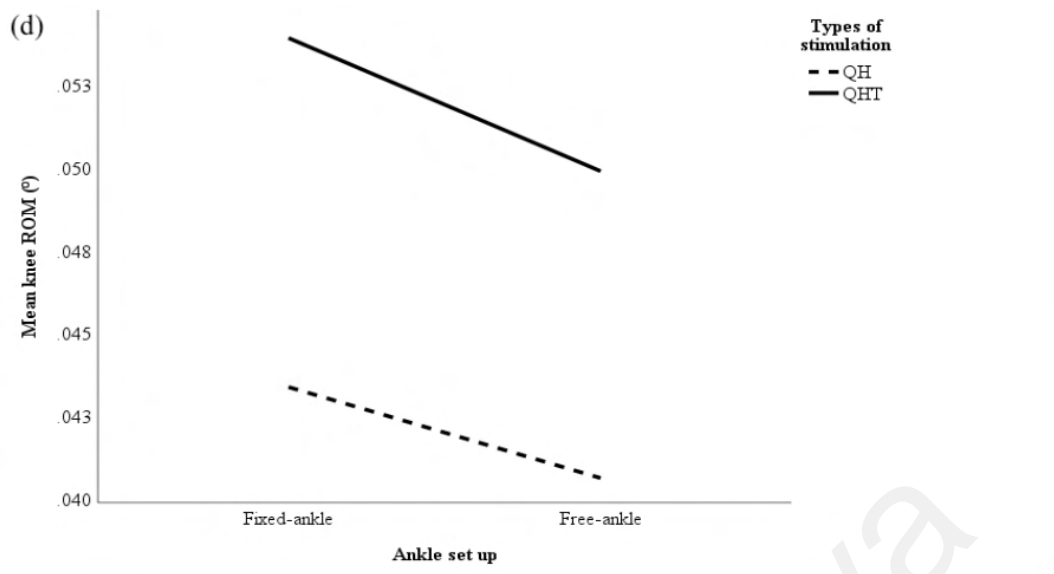
A two-way ANOVA was also performed to analyze the effect of fixed- and free-ankle, and QH and QHT stimulations during FES-evoked cycling on the mean ankle, knee, and hip ROMs for each slice of 20° crank angle intervals (**Figure 4.1c**, **4.1d**, and

4.1e). The present study revealed that there was no statistically significant interaction between the effect of fixed- and free-ankle, and QH and QHT stimulations during FES-evoked cycling on the ankle [$F(1,500) = 0.020$, $p = 0.888$, $\eta_p^2 < 0.001$], knee [$F(1,500) = 0.00$, $p = 0.993$, $\eta_p^2 < 0.001$], and hip ROMs [$F(1,500) = 0.043$, $p = 0.836$, $\eta_p^2 < 0.001$] for each slice of 20° crank angle intervals. Further analysis showed that the interaction between fixed-ankle and free-ankle, and QH and QHT stimulations did not significantly alter the mean ankle ($p = 0.751$ and $p = 0.905$, respectively), knee ($p = 0.979$ and $p = 0.969$, respectively), and hip ROMs ($p = 0.777$ and $p = 0.993$, respectively).









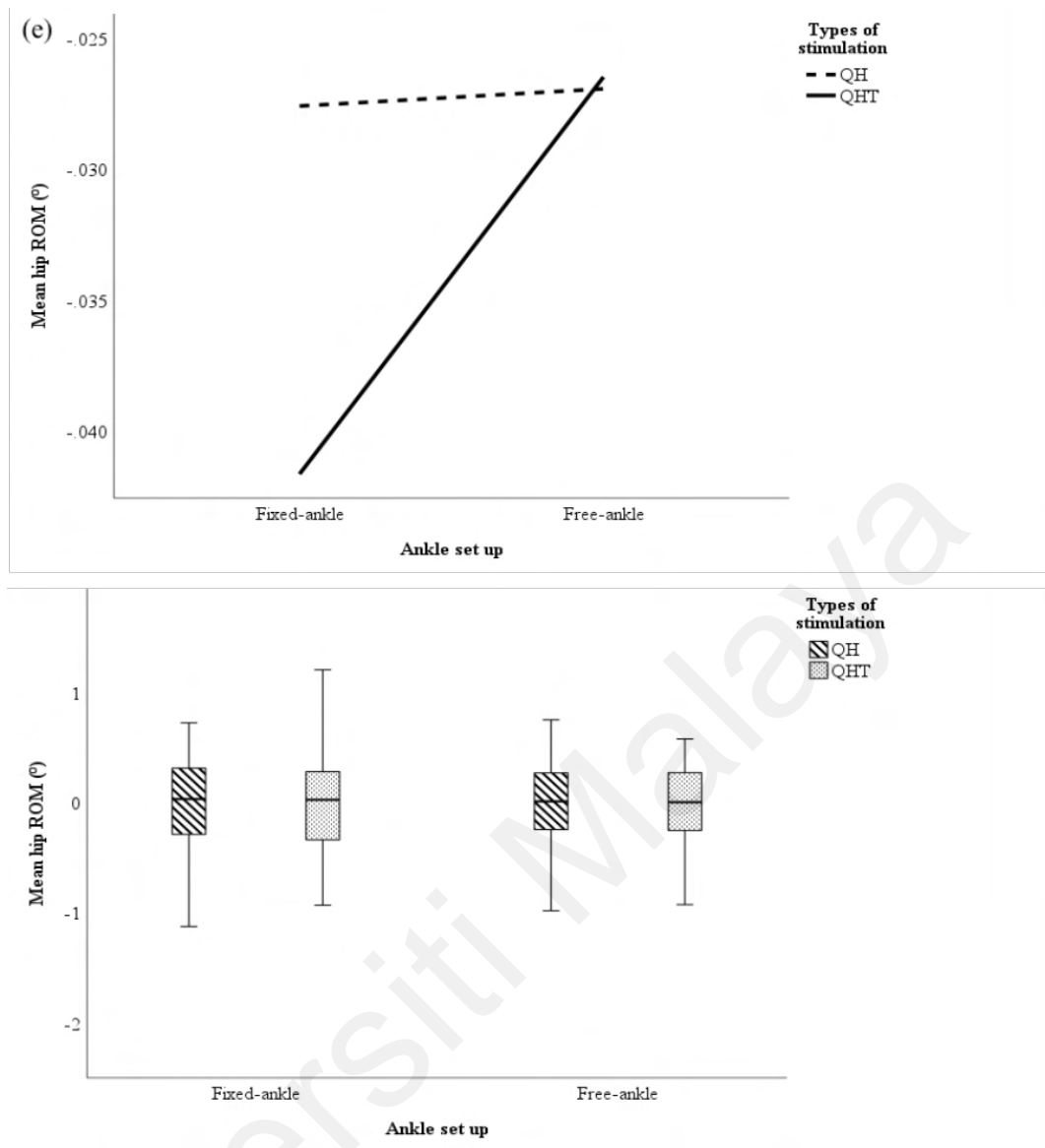


Figure 4.1: The interaction and boxplot of the effect of fixed- and free-ankle FES-evoked cycling with QH and QHT stimulations across each slice of 20° crank angle intervals on (a) mean normalized pedal PO; (b) peak normalized pedal PO; (c) mean ankle ROM; (d) mean knee ROM; and (e) mean hip ROM. *⁰ Denotes $p < 0.05$ between free-ankle QH stimulation compared to the other settings.

Table 4.2: The normalized pedal PO obtained between fixed- and free-ankle FES-evoked cycling with QH and QHT stimulation modes across each slice of 20° crank angle intervals.

| Stimulation modes | Fixed-ankle FES-evoked cycling | | Free-ankle FES-evoked cycling | |
|-------------------|--|--|--|--|
| | Mean normalized pedal PO (%) (mean \pm SD) | Peak normalized pedal PO (%) (mean \pm SD) | Mean normalized pedal PO (%) (mean \pm SD) | Peak normalized pedal PO (%) (mean \pm SD) |
| QH | 24.2 \pm 12.3 | 40.4 \pm 20.5 | *16.2 \pm 9.8 | *27.8 \pm 16.8 |
| QHT | 25.7 \pm 11.6 | 42.3 \pm 18.3 | 26.5 \pm 17.8 | 39.2 \pm 23.6 |

*Only free-ankle FES-evoked cycling with QH stimulation mode is significantly lower

different than the other 3 settings, $p < 0.01$.

4.1.1 Kinetics and Kinematics Change throughout 360° of Crank Angle

The mean and peak normalized pedal POs generated during FES-evoked cycling with fixed- and free-ankle QH stimulation, and fixed- and free-ankle QHT stimulation for each slice of 20° crank angle intervals are presented in **Figure 4.2a** and **4.2b**. Simple main effects analysis showed that all FES-evoked cycling conditions i.e., between fixed- and free-ankle, and QH and QHT stimulations, have a statistically significant effect on mean and peak pedal POs ($p < 0.001$) for each slice of 20° crank angle intervals. The present study revealed that there was a significant difference in the mean normalized pedal PO generated between free-ankle QH stimulation and fixed-ankle QHT stimulation ($p = 0.037$) at the crank angle of 80° (**Figure 4.2a**).

There was also a significant difference in the peak normalized pedal PO generated between free-ankle QH stimulation and fixed-ankle QHT stimulation ($p = 0.033$) at the crank angle of 140° (**Figure 4.2b**).

The mean ankle, knee, and hip ROMs generated during FES-evoked cycling with fixed- and free-ankle QH stimulation, and fixed- and free-ankle QHT stimulation for each slice of 20° crank angle intervals are presented in **Figure 4.2c**, **4.2d**, and **4.2e**. Simple main effects analysis revealed that there were significant differences in the mean ankle ROM generated at the crank angle of 20° and 160° between fixed-ankle QH stimulation and free-ankle QHT stimulation ($p < 0.001$ and $p = 0.001$, respectively), free-ankle QH stimulation and free-ankle QHT stimulation ($p = 0.018$ and $p = 0.021$, respectively), and fixed- and free-ankle QHT stimulation ($p = 0.002$ and $p = 0.025$, respectively) (**Figure 4.2c**). There were also significant differences in the mean ankle ROM at the crank angle of 140° and 180° generated between fixed-ankle QH stimulation and free-ankle QHT stimulation ($p = 0.033$ and $p = 0.004$, respectively). At

the crank angle of 320°, there were significant differences in the mean ankle ROM generated between fixed-ankle QHT stimulation and fixed-ankle QH stimulation ($p = 0.014$), and fixed- and free-ankle QH stimulation ($p = 0.048$). Meanwhile, at the crank angle of 360°, there were significant differences in the mean ankle ROM generated between fixed- and free-ankle QH stimulation ($p = 0.015$), fixed-ankle QH stimulation, and free-ankle QHT stimulation ($p < 0.001$), free-ankle QH stimulation and fixed-ankle QHT stimulation ($p = 0.007$), and fixed- and free-ankle QHT stimulation ($p < 0.001$).

The present study also revealed that there were significant differences in the mean knee ROM generated between free-ankle QH stimulation and fixed-ankle QHT stimulation ($p = 0.016$), and fixed- and free-ankle QHT stimulation ($p = 0.05$) at the crank angle of 340° (**Figure 4.2b**).

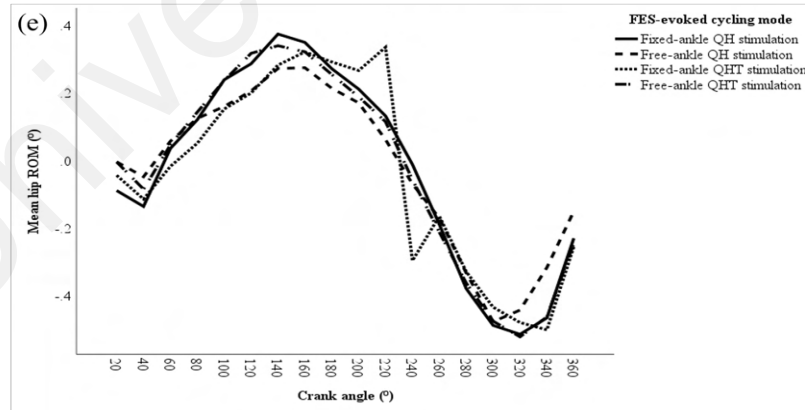
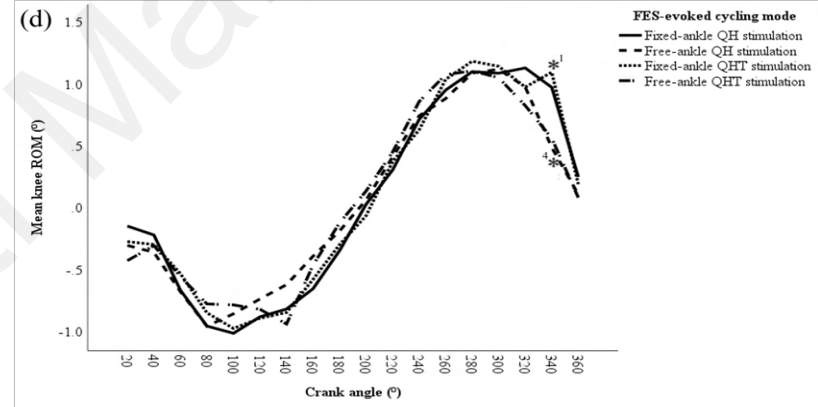
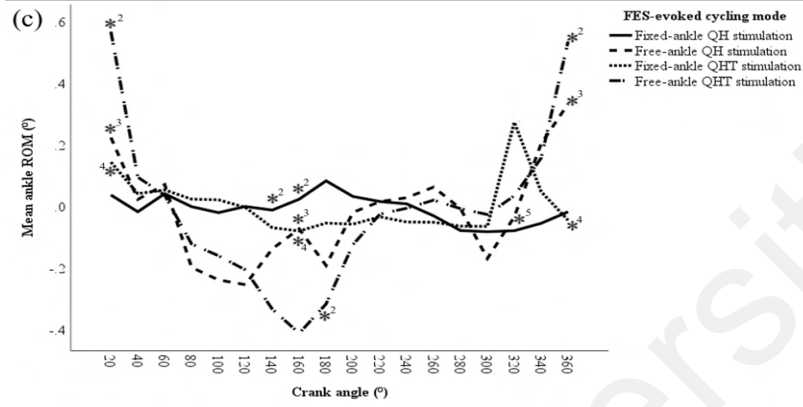
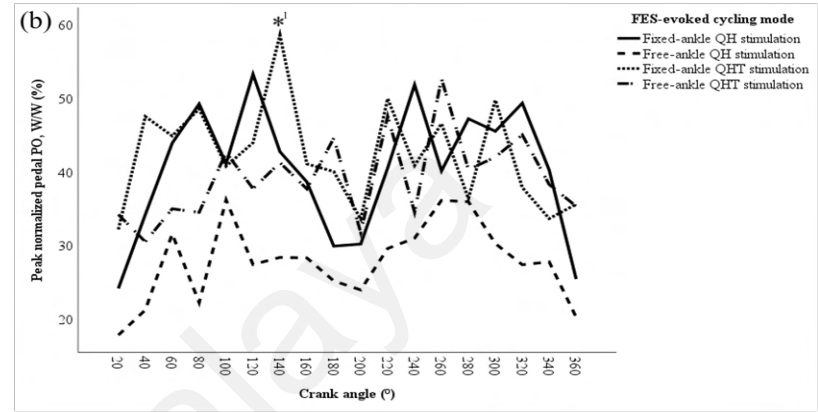
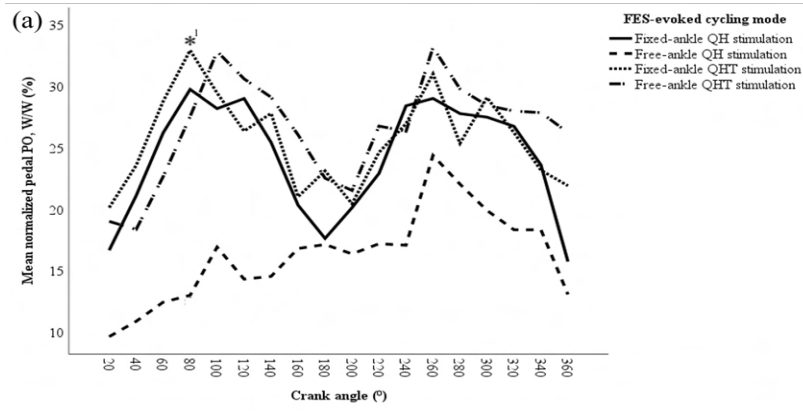


Figure 4.2: The PO and ROM generated during fixed- and free-ankle FES-evoked cycling with QH and QHT stimulations by each slice of 20° crank angle position from 0° to 360°. (a) mean normalized pedal PO; (b) peak normalized pedal PO; (c) mean ankle ROM; (d) mean knee ROM; and (e) mean hip ROM. *¹ Denotes $p < 0.05$ between free-ankle QH stimulation and fixed-ankle QHT stimulation, *² denotes $p < 0.05$ between free-ankle QHT stimulation and fixed-ankle QH stimulation, *³ denotes $p < 0.05$ between free-ankle QHT stimulation and free-ankle QH stimulation, *⁴ denotes $p < 0.05$ between free-ankle QHT stimulation and fixed-ankle QHT stimulation, and *⁵ denotes $p < 0.05$ between fixed-ankle QHT stimulation and fixed-ankle QH stimulation.

Universiti Malaysia

4.2 Analysis of Muscle Performance at the Muscle Level during FES-Evoked Cycling in Individuals with SCI

4.2.1 Correlation between the MMG and NIRS Signals

Figure 4.3 presents sample data from the experiment where cadence and both NIRS and MMG signals were shown. NIRS data was recorded throughout the experiment while MMG and cadence data were only recorded during cycling exercise. The present study revealed that there was a moderate significant negative correlation between normalized RMS-O₂Hb [$r = -0.38$, $p = 0.003$] (**Figure 4.4b**) and RMS-tHb [$r = -0.31$, $p = 0.017$] (**Figure 4.4d**). One of the participants was excluded from the RMS-%TSI correlation analysis because there were no changes in %TSI throughout 30 minutes of FES-evoked cycling. There were poor or non-existent correlations between the normalized RMS-%TSI [$r = 0.12$, $p = 0.397$], and RMS-HHb [$r = 0.06$, $p = 0.674$] (**Figure 4.4**).

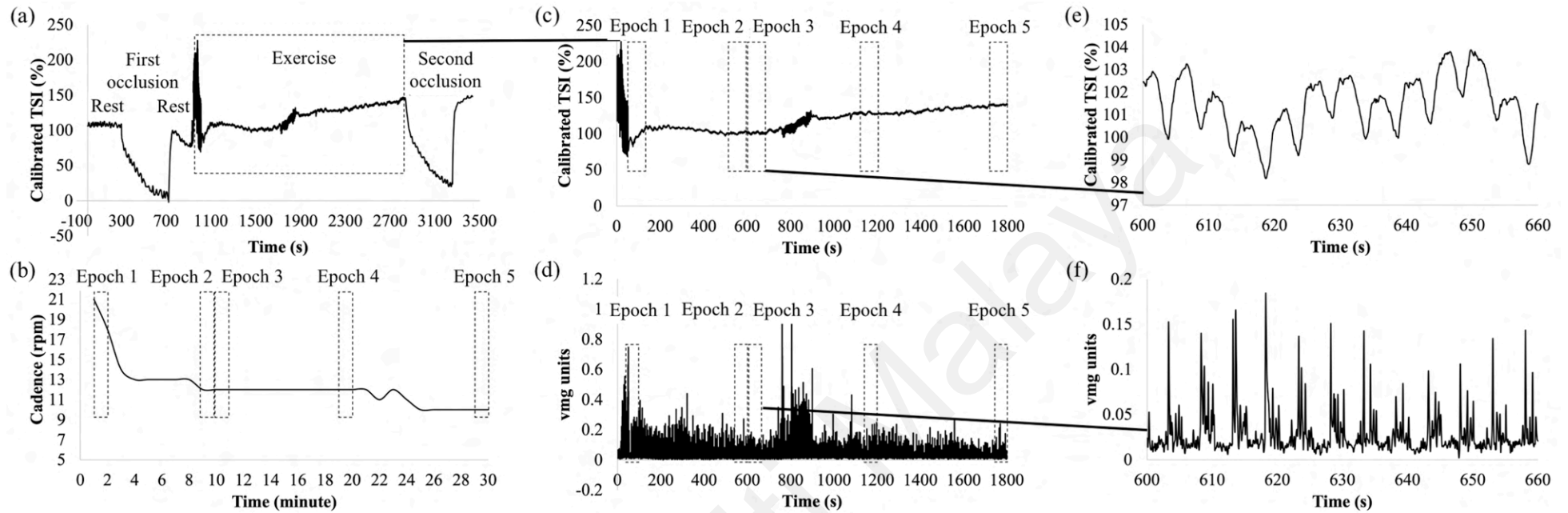


Figure 4.3: Actual data from the NIRS, MMG, and cadence during the experiment. (a) NIRS signals were recorded throughout the experiment, including occlusion; (b) cadence was recorded per minute during exercise only, where epochs were defined; (c) and (d) NIRS and MMG signals were analyzed during exercise, where epochs were defined; (e) and (f) are a closer look at the signals for epoch 3 from NIRS and MMG signals.

***vmg is a non-standard abbreviation for vibromyography, a parameter measured by the accelerometer-based MMG sensor, Sonostic VMG BPS II Transducer (Biopac System, Inc., Goleta, CA, USA) that describes the vibrational acceleration of the muscles when it contracts.**

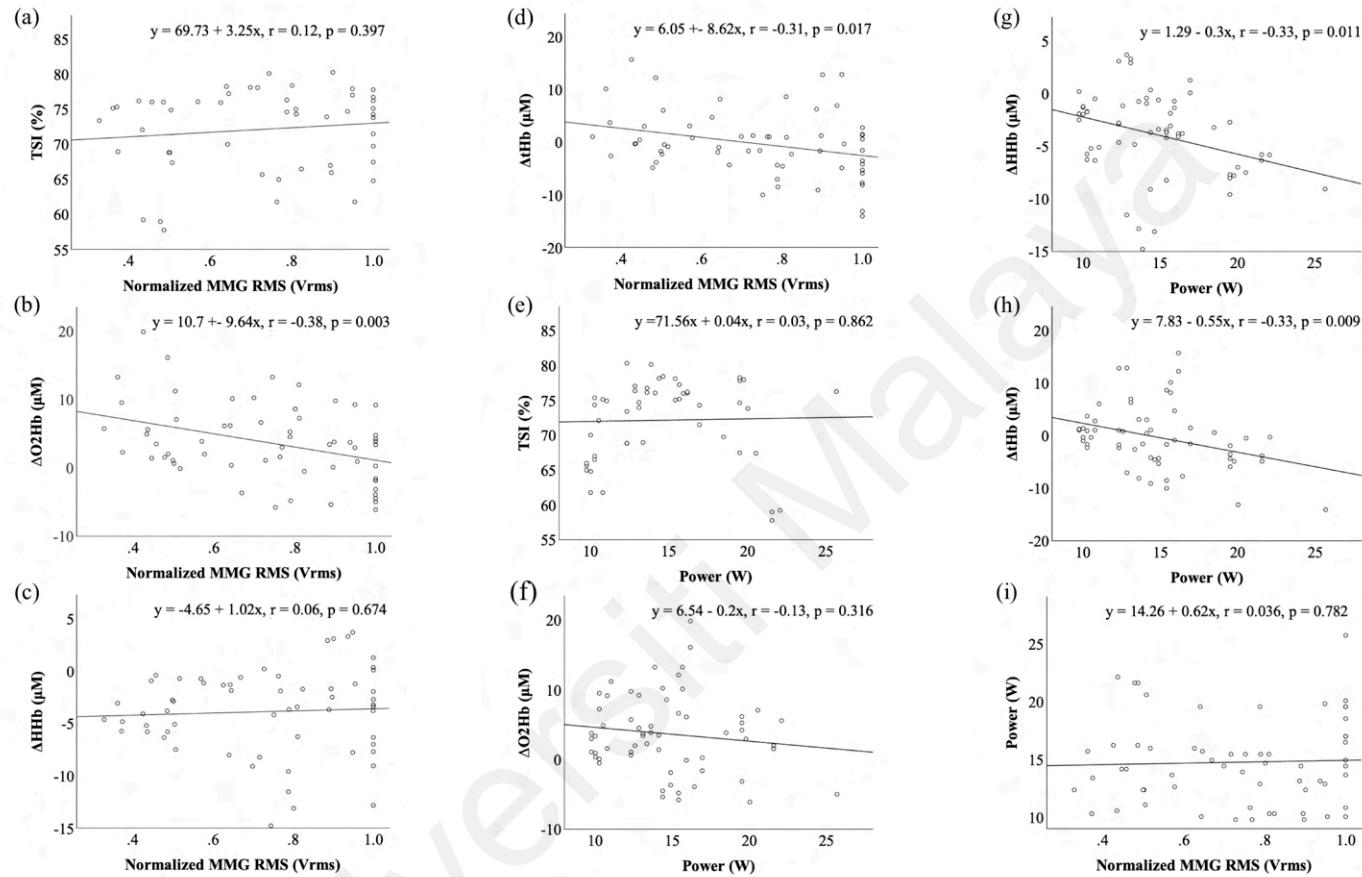


Figure 4.4: Relationships between the normalized MMG RMS and NIRS parameters, power and NIRS parameters, and normalized MMG RMS and power. (a) RMS-%TSI; (b) RMS- ΔO_2Hb ; (c) RMS- ΔHHb ; (d) RMS- ΔtHb ; (e) PO-%TSI; (f) PO- ΔO_2Hb ; (g) PO- ΔHHb ; (h) PO- ΔtHb ; and (i) RMS-PO.

4.2.2 Correlation between the PO and NIRS signals

The present study revealed that there was a moderate significant negative correlation between PO-HHb [$r = -0.33$, $p = 0.011$] (**Figure 4.4g**) and PO-tHb [$r = -0.33$, $p = 0.009$] (**Figure 4.4h**). There were poor or non-existent correlations between PO-%TSI [$r = 0.03$, $p = 0.862$], and PO-O₂Hb [$r = -0.13$, $p = 0.316$] (**Figure 4.4**). One of the participants was excluded from the PO-%TSI correlation analysis because there were no changes in %TSI throughout 30 minutes of FES-evoked cycling.

4.2.3 Correlation between the PO and MMG signals

The present study revealed that there were poor correlations between PO-MMG [$r = 0.04$, $p = 0.782$] (**Figure 4.4i**).

4.2.4 Effects of 30 Minutes of FES-Evoked Cycling on the MMG, NIRS, and PO Findings

The present study revealed that there was a significant main effect for time with differences between exercise epochs for cadence during 30 minutes of FES-evoked cycling [$F(4,55) = 2.56$, $p = 0.049$] (**Figure 4.5a**), power [$F(4,55) = 2.56$, $p = 0.049$] (**Figure 4.5b**), O₂Hb [$F(4,55) = 5.29$, $p = 0.001$] (**Figure 4.5e**), and for tHb [$F(4,55) = 3.47$, $p = 0.014$] (**Figure 4.5g**). In contrast, there were no differences in the normalized RMS [$F(4,55) = 2.19$, $p = 0.082$], %TSI [$F(4,45) = 0.60$, $p = 0.665$], and HHb [$F(4,55) = 0.12$, $p = 0.973$] over 30 minutes of cycling (**Figure 4.5**).

A posteriori analysis of the epochs representing different “phases” of the steady-state exercise test revealed that there were significant differences in the normalized MMG RMS during 30 minutes of FES-evoked cycling between epochs 1 and 3 ($p = 0.009$), epochs 1 and 4 ($p = 0.029$), and epoch 1 and 5 ($p = 0.036$), representing a fall of muscle power from the first minute of FES-evoked cycling exercise to the later minutes (**Figure**

4.5c). On the other hand, there were no significant differences in the normalized MMG RMS between epochs 2 and 3, epochs 3 and 4, and epochs 4 and 5.

There were significant differences in the O₂Hb between epochs 1 and 3 ($p = 0.031$), epochs 1 and 4 ($p = 0.002$), epochs 1 and 5 ($p < 0.01$), epoch 2 and 5 ($p = 0.008$), and epoch 3 and 5 ($p = 0.043$), denoting a small increase of oxygenated haemoglobin during leg exercise compared to the first minute (**Figure 4.5e**). The tHb also showed significant differences between epochs 1 and 3 ($p = 0.045$), epochs 1 and 4 ($p = 0.007$), and epochs 1 and 5 ($p = 0.001$) (**Figure 4.5g**). In contrast, there were no other significant differences in the %TSI and HHb between epochs from early to late exercise in the 30-minute FES-evoked cycling bout.

There were significant differences in the cadence and PO between epochs 1 and 2 ($p = 0.019$), epochs 1 and 3 ($p = 0.028$), epochs 1 and 4 ($p = 0.022$), and epochs 1 and 5 ($p = 0.006$), representing a reduction of cadence caused the fall of PO from the first minute of FES-evoked cycling exercise to the later minutes (**Figure 4.5a and 4.5b**).

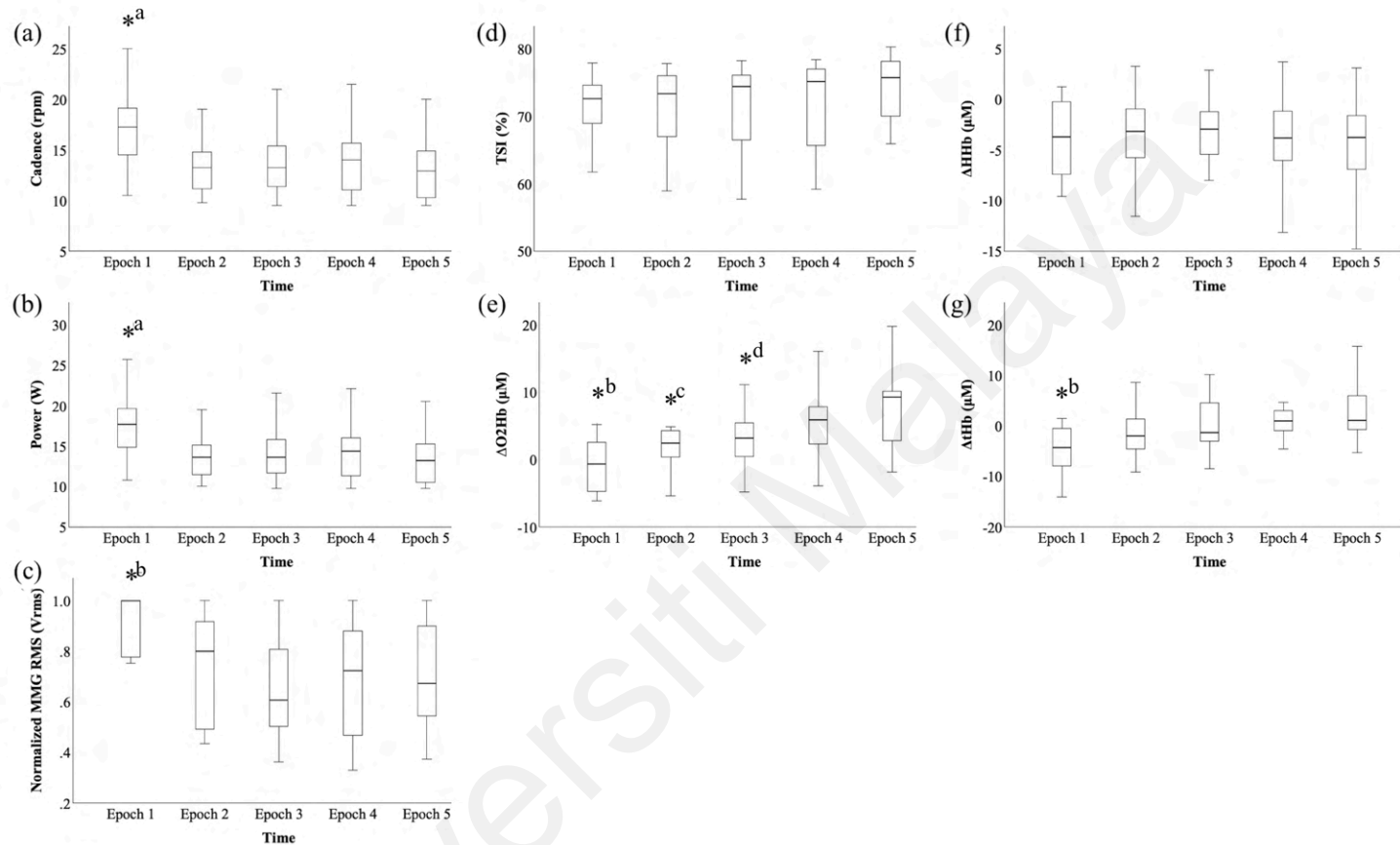


Figure 4.5: Parameter values from 30 minutes of FES-evoked cycling according to epochs, of (a) MMG RMS; (b) %TSI; (c) O_2Hb ; (d) HHb ; and (e) tHb . Epochs 1-5 denote pre-defined periods for data collection as described in the data acquisition and processing section. *^a Denotes $p < 0.05$ between epoch 1 compared to the rest of the epochs; *^b denotes $p < 0.05$ between epoch 1 compared to epoch 3, 4, and 5; *^c denotes $p < 0.05$ between epoch 2 and epoch 5; and *^d denotes $p < 0.05$ between epoch 3 and epoch 5.

4.2.5 Muscle Oxygen Consumption during FES-Evoked Cycling

The present study observed that there were no significant differences in the mVO_2 after 30 minutes of FES-evoked cycling [$t(11) = -1.10$, $p = 0.148$] compared to the rest (Figure 4.6).

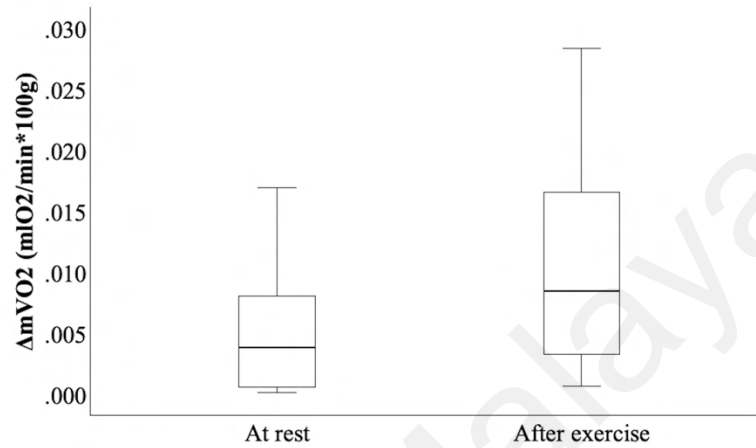


Figure 4.6: Muscle oxygen consumption before and after 30 minutes of FES-evoked cycling. *Denotes $p < 0.05$ (2-tailed).

CHAPTER 5: DISCUSSION

This chapter discusses the findings of the current study and evaluates them with the previous studies. It consists of three parts. The first part discusses the biomechanical effect on power production during FES-evoked cycling in individuals with SCI. The second part discusses the muscle performance at the muscle level during FES-evoked cycling in individuals with SCI. The third part discusses the relationship between biomechanics and muscle performance in light of maximizing the efficiency of FES-evoked cycling in individuals with SCI.

5.1 Biomechanical Effects on Pedal Power Production during FES-Evoked Cycling in Individuals with SCI

5.1.1 The Effects of Releasing the Ankle Joint on the Pedal Power Production

The present study sought to investigate the possible differences in mean and peak pedal POs, and hip, knee, and ankle joint ROMs during FES-evoked cycling with fixed- and free-ankle setup in individuals with SCI. The mean pedal POs generated from 0° to 360° crank angle during fixed- and free-ankle FES-evoked cycling in the current study were 1.2 W - 27.1 W, and from 0.6 W - 28.4 W, respectively (**Table 4.1**). To date, no studies have as yet investigated the effect of fixed- and free-ankle on the pedal PO during FES-evoked cycling in individuals with SCI, experimentally. However, it was reported that the mean and peak pedal POs achieved by healthy individuals during voluntary recumbent cycling with AFO-constrained movement were 17.2 ± 9.0 W (range 2 – 36 W) and 27.2 ± 12.0 W (range 6 – 60 W), respectively. Duffell et al. (2010) reported that the magnitude of mechanical power produced by individuals with SCI during FES-evoked cycling was 8–35 W. The mean pedal PO revealed in the current study was similar to the previous studies. This finding suggested that free-ankle FES-evoked cycling did not significantly elevate the maximum mechanical PO in individuals

with SCI from the established PO in the previous studies. This might be due to the muscles of each individual with SCI having their maximum power production capacity. One-to-one comparison may not provide an accurate conclusion; thus, a comparison was made on their normalized power production. However, the findings should be interpreted with caution due to low subject numbers.

There was a statistically significant interaction between the effect of fixed- and free-ankle, and QH and QHT stimulations during FES-evoked cycling on the mean and peak normalized pedal POs across each slice of 20° crank angle intervals, particularly between free-ankle, and QH and QHT stimulations (**Figure 4.1**). These findings suggested that both ankle setup and stimulation modes influence power production during FES-evoked cycling in individuals with SCI. There were also significant differences in the mean and peak normalized pedal POs between free-ankle QH stimulation, fixed-ankle QH stimulation, fixed-ankle QHT stimulation, and free-ankle QHT stimulation across each slice of 20° crank angle intervals. This was not the case in healthy individuals, as reported by a previous study where different ankle constraint movements do not influence altering power production during voluntary recumbent cycling in healthy individuals. Koch et al. (2013) also reported that there was no significant difference in power production during cycling with and without the use of AFO. This finding suggested that fixed- and free-ankle setups only affected the pedal PO produced during FES-evoked cycling. Unlike individuals with SCI, the leg muscles of healthy individuals have the ability to adapt to different ankle positioning during voluntary cycling. Overall, free-ankle QH stimulation produced the lowest mean and peak normalized pedal POs (**Table 4.2**). Free-ankle QHT stimulation produced the highest mean normalized pedal PO, while fixed-ankle QHT stimulation produced the highest peak normalized pedal PO. A significant interaction between free-ankle, and QH and QHT stimulations suggests that releasing the ankle joint without the stimulation

of tibialis anterior and triceps surae limits the power transmission to the pedal during FES-evoked cycling in persons with SCI. Mean and peak pedal POs generated by free-ankle QH stimulation were shifted down across each slice of 20° crank angle intervals compared to the other settings. There was a significant loss of mean and peak power at the crank angle of 80° and 140°, respectively during free-ankle QH stimulation. The transmission of power produced by the hamstring muscles to the pedal to overcome the dead pedal position (0°/360° and 180° crank angle) (Laubacher et al., 2017) lost at the ankle joint during free-ankle QH stimulation. Fixed-ankle QH stimulation was shown to produce higher pedal PO than free-ankle QH stimulation. This is because solid AFO maintained the legs in the sagittal plane (Tong et al., 2017) to optimize the power transmission (McDaniel et al., 2017b) to the pedal (Laubacher et al., 2017) during FES-evoked cycling in these individuals. The addition of stimulating tibialis anterior and triceps surae during free-ankle FES-evoked cycling, with pedal spindle attached to the top middle part of the foot was shown to significantly elevate the mean normalized pedal PO by 10.3% more than without the stimulation of shank muscles during free-ankle FES-evoked cycling. The addition of stimulating tibialis anterior and triceps surae during fixed-ankle FES-evoked cycling was shown to significantly elevate the peak normalized pedal PO by 14.5% more than without the stimulation of shank muscles during free-ankle FES-evoked cycling. The present study also revealed that the addition of stimulating tibialis anterior and triceps surae during free-ankle FES-evoked cycling was shown to only elevate the mean normalized pedal PO by 0.8% more than fixed-ankle. This finding did not support the theory developed using simulation models whereby the power could be improved by 14% by releasing the ankle joint and stimulating the triceps surae and tibialis anterior, with the tuning of the contact point between the foot and pedal to the relative strength of the ankle plantar flexors of the triceps surae compared to the fixed-ankle joint (van Soest et al., 2005). However, it was

expected that releasing the ankle joint would not lead to a large increase in PO upheld in reality (van Soest et al., 2005). The pedal POs generated by fixed-ankle QH stimulation and fixed-ankle QHT stimulation showed no significant differences. This finding suggested that the stimulation of the tibialis anterior and triceps surae contributed to no significant increment of pedal PO during fixed-ankle FES-evoked cycling. The present study reported a similar finding to the previous studies, where gastrocnemius produced no significant difference in mechanical work (Hakansson & Hull, 2010; Hakansson & Hull, 2009; Hakansson & Hull, 2007). A non-statistically significant interaction between fixed-ankle, and QH and QHT stimulations found in this study proves that tibialis anterior and triceps surae are a small muscle group that might produce lower power than the quadriceps. This further justifies that the primary power source of FES-evoked cycling was the knee extensors of the quadriceps, followed by the knee flexors of the hamstring (Szecsi et al., 2014a). However, the lower leg muscles need to be stimulated for muscle health, with or without power output production at the beginning of training. With more training sessions, there is potential for lower leg muscles to produce power, but physiologically this cannot be gained immediately or with only a few sessions as the muscles have been passive for a very long time.

5.1.2 The Effects of Releasing Ankle Joint on the Ankle, Knee, and Hip ROMs

There was no statistically significant interaction between the effect of fixed- and free-ankle, and QH and QHT stimulations during FES-evoked cycling on the ankle, knee, and hip ROMs across each slice of 20° crank angle intervals (**Figure 4.1**). These findings suggested that ankle setup and stimulation modes do not influence altering ankle, knee, and hip ROMs during FES-evoked cycling in individuals with SCI. The present study also suggested that free-ankle FES-evoked cycling resulted in no knee hyperextension. There were also no significant differences in the ankle, knee, and hip

joints ROMs during FES-evoked cycling between fixed-ankle QH stimulation, free-ankle QH stimulation, fixed-ankle QHT stimulation, and free-ankle QHT stimulation across each slice of 20° crank angle intervals. However, further analysis showed that there were significant differences in the ankle joint ROM across each slice of 20° crank angle intervals, particularly at the crank angle of 20°, 140°, 160°, 180°, 320°, and 360° (**Figure 4.2**). During free-ankle FES-evoked cycling, a significant ankle dorsi- and plantarflexion movement was generated between 140° to 180° and 0°/360° to 20° crank angle, respectively compared to fixed-ankle FES-evoked cycling. These findings suggested that free-ankle FES-evoked cycling produced greater ankle joint ROM than fixed-ankle joint ROM across each slice of 20° crank angle intervals, with the pedal spindle attached to the top middle part of the foot. The combination of shank muscle stimulation and freeing the ankle joint movement was reported to potentially improve the ankle flexibility (Fornusek et al., 2012), for therapeutic benefits and hopefully provide a competitive FES-evoked cycling advantage through the PO increment. Even though the use of AFO in the present study has been proved to limit the ankle dorsi- and plantarflexion movement during fixed-ankle FES-evoked cycling, it was however useful to provide shank stability to individuals with SCI that restricts leg movements in the sagittal plane (Trumbower et al., 2005). Unfortunately, the present study did not analyze the ankle, knee, and hip ROMs in the sagittal plane. Future studies could investigate the effects of free- and fixed-ankle FES-evoked cycling on the ankle, knee, and hip ROMs in the sagittal plane.

5.2 Muscle Performance at the Muscle Level during FES-Evoked Cycling in Individuals with SCI

The present study sought to investigate the relationships between (i) muscle performance (MMG RMS) and metabolism (%TSI, O₂Hb, HHb, and tHb), quantified by MMG and NIRS, as well as (ii) power output and muscle metabolism during FES-

evoked cycling in individuals with SCI, specifically between pre- and post-fatiguing conditions. To the best knowledge, this is the first study that has explored these MMG RMS-NIRS and PO-NIRS inter-relationships simultaneously during FES-evoked cycling in this population. However, the findings should be interpreted with caution due to low subject numbers.

5.2.1 Relationships between Muscle Performance, Power Output, and Muscle Metabolism during FES-Evoked Cycling in Individuals with SCI

Overall, RMS-O₂Hb, RMS-tHb, PO-HHb, and PO-tHb revealed moderate associations between these variables, while RMS-%TSI, RMS-HHb, PO-%TSI, PO-O₂Hb, and RMS-PO revealed poor associations (**Figure 4.4**). This response was not reflected in non-disabled individuals, as reported by a previous study wherein MMG RMS and NIRS did not together mirror muscle performance during repetitive electrically-evoked wrist extension (Mohamad Saadon et al., 2019). The correlation between %RMS-%TSI reported by Mohamad Saadon et al. (2019) in healthy individuals performing repetitive FES wrist extension was $r = 0.05$ (pre-fatiguing) (weak) and $r = 0.36$ (post-fatiguing) (moderate). Unlike individuals with SCI, the muscles of non-disabled individuals can immediately adapt to prolonged functioning activities, such as extending the wrist joint, walking, or cycling, with or without being electrically stimulated. On the other hand, the poor correlations of PO-%TSI and RMS-PO observed in the present study were similar to Saadon et al.'s findings. It was reported that there were weak correlations between %PO-%TSI [$r = -0.16$ (post-fatiguing)] and %PO-%RMS [$r = 0.26$ and -0.23 (post-fatiguing)] (Mohamad Saadon et al., 2019). The study, however, did not identify the correlation between RMS-O₂Hb, RMS-HHb, RMS-tHb, PO-O₂Hb, PO-HHb, and PO-tHb. Taken together, the findings of the current study revealed that MMG RMS-NIRS and PO-NIRS data demonstrated a

moderate relationship with specific NIRS parameters during FES-evoked cycling in individuals with SCI.

5.2.2 Muscle Fatigue Assessment using MMG and NIRS

There were significant differences at various time points in the normalized MMG RMS over 30 minutes of cycling in all participants (**Figure 4.5a**). When FES-evoked cycling was subdivided into time epochs representing exercise onset, early steady-state, mid-exercise, and just before cessation phases, noticeable differences in MMG RMS responses were observed between the first minute and those epochs following. A *posteriori* analysis revealed that there was a significant decrease in normalized MMG RMS between epochs 1 and 3, epochs 1 and 4, and epochs 1 and 5, representing a general decline of muscle performance after the initial period of FES-evoked cycling. An earlier study by Islam et al. (2018) reported that the normalized MMG RMS for vastus lateralis was altered significantly between the pre and post-conditions during FES-evoked cycling in SCI participants. Their findings agreed with the outcome of the present study where the normalized MMG RMS showed significant differences between the pre (epoch 1) and post (epoch 3, 4, and 5) FES-evoked cycling. Both Islam et al. (2018) and the current studies reported a reduction of MMG RMS amplitude post-FES-evoked cycling. The decline of MMG amplitude can be attributed to physiological changes concomitant with early muscle fatigue, such as reduced tissue oxygenation that might have altered the muscle's mechanical performance as seen through its MMG RMS responses, also reflecting the dimensional changes of muscle fibers (Hogan et al., 1994). It has also been reported that MMG RMS demonstrated good potential for characterizing muscle function between pre- and post-fatigue FES-evoked conditions and portraying muscle fatigue during the FES-evoked cycling (Islam et al., 2018). These findings suggested that the vastus lateralis began to fatigue quickly after the first minute

(epoch 1), with differences in muscle performance apparent by 10 minutes (epoch 3) onwards.

The changes in MMG RMS, cadence (**Figure 4.5a**), and PO (**Figure 4.5b**) appeared to similarly reduce only during epoch 1 (pre-fatiguing). However, this behavior was not similar after epoch 2 through epoch 5 (post-fatiguing). MMG RMS initially showed a reduction from epoch 2, and a slight increment from epoch 4 onwards. In contrast, cadence and PO showed a small increment from epoch 2 onwards, followed by a reduction in epoch 5. An earlier study by Saadon et al. (2019) reported similar findings where a clearer pattern of increasing %RMS MMG was observed along with declining %PO during post-fatiguing. These observations suggested that the reduction in the MMG RMS was not related to cycling cadence and PO during post-fatiguing contraction. The MMG RMS however was mirrored by a significant rise of O₂Hb from the onset of exercise to the following minutes and a trend for an increase in %TSI over time during FES-evoked cycling (**Figure 4.5**). The increase of O₂Hb and %TSI reported herein has also been described in a previous investigation of electrically-evoked wrist extension to fatigue (Muraki et al., 2004). Similar to the findings of the current study, during voluntary arm exercise, tissue oxygen saturation in triceps brachii was observed to increase along with O₂Hb and %TSI (Muraki et al., 2004). The current finding was also similar to those where it was reported that %TSI was observed to increase during repetitive electrically-evoked wrist extension in tetraplegia participants (Mohamad Saadon et al., 2022). A plausible physiological explanation is that during a repetitive task such as FES-evoked exercise, muscle blood flow is enhanced due to increased cardiac output and arteriolar vasodilation, with the amount of blood supply (and oxygen saturation) exceeding the oxidative demands of low-intensity muscle metabolism (mVO₂) during cycling (van Dieën et al., 2009). After SCI, there is a reduction of vessel diameter and alteration of resting muscle blood flow due to the musculoskeletal atrophy

(Boot et al., 2002), limiting the ability of leg muscles to take up oxygen even when there is a surfeit oxygen supply during fatigue (Mohamad Saadon et al., 2019). In the current study, vastus lateralis began to display fatigue after about 10 minutes (epoch 3), thus giving rise to O_2Hb and %TSI during the latter 20 minutes of FES-evoked leg cycling. In contrast, the present study revealed that there was an increment in the MMG RMS after epoch 3, indicating muscle fatigue recovery occurred during epochs 4 and 5 (post FES-evoked cycling). The findings of the present study were similar to those where it was reported there was an increment in %RMS-MMG during the post-fatigue part of the FES-evoked exercise in healthy muscles (Mohamad Saadon et al., 2019).

In other words, MMG RMS showcased a decline followed by an increasing trend, as reflected in the FES-evoked healthy muscle repetitive contraction (Mohamad Saadon et al., 2019) unlike the behavior in SCI participants that showed consistent decline throughout the training (Mohamad Saadon et al., 2020). The findings of this study proposed that MMG RMS, PO, and NIRS-derived O_2Hb and %TSI exhibited good potential for characterizing muscle fatigue during FES-evoked cycling. The present study also suggested that the normalized MMG RMS was negatively associated with O_2Hb and %TSI, while PO was negatively associated with HHb and tHb during such exercise in individuals with SCI.

Finally, the present study observed a small increase of mVO_2 after 30 minutes of FES-evoked cycling (i.e., post-fatigue) compared to before exercise (i.e., at rest) – a relatively small increase of metabolism during this modality of leg exercise (**Figure 4.6**). The post-fatigue mVO_2 was slightly greater than the pre-fatigue mVO_2 , while the normalized MMG RMS demonstrated a significant decrement over 30 minutes of FES-evoked cycling. It has been reported that MMG may hold a known relationship to changes in mVO_2 since the MMG signal is a summation of motor unit recruitment that

may also titrate the mVO_2 (Takaishi et al., 1992). However, the fundamental relationship between MMG RMS and NIRS-derived mVO_2 may require further investigation based on the findings of this study, which has shown that MMG RMS is negatively associated with muscle metabolism during repetitive FES-induced muscle contractions, such as during cycling.

5.3 Relationship between Biomechanics and Muscle Performance on the Efficiency of FES-Evoked Cycling

Overall, the present study sought to analyze the biomechanics (ankle joint biomechanics) and muscle performance (using MMG and NIRS) during FES-evoked cycling in individuals with SCI. The first part of the study sought to improve the pedal PO and efficiency of FES-evoked cycling by freeing the ankle joint of individuals with SCI. The second part of the study sought to investigate muscle performance during FES-evoked cycling in individuals with SCI by establishing the relationships between muscle fatigue and its metabolism quantified by MMG and NIRS sensors. Hence, this section aims to establish the relationship between biomechanics and muscle performance in light of maximizing the efficiency of FES-evoked cycling in individuals with SCI (**Figure 5.1**).

During one minute of FES-evoked cycling, it was observed that free-ankle FES-evoked cycling with QHT stimulation significantly elevated the normalized pedal POs (**Table 4.2**). Consequently, MMG RMS and O_2Hb derived from NIRS observed that muscle began to fatigue after epoch 1 (minutes 1-2) during 30 minutes of FES-evoked cycling (**Figure 4.5**). These findings suggested that the first minute of FES-evoked cycling is sufficient if the goal is to get maximum PO, as muscle power begins to fall from the first minute of FES-evoked cycling. However, one minute of FES-evoked cycling is insufficient for training purposes, as individuals with SCI usually cycle for 30

minutes (Astorino et al., 2008; Zbogar et al., 2008) or more. Previous studies reported that the benefits of FES-evoked cycling can be achieved with 30 minutes of cycling (Wilder et al., 2002). In the present study, MMG RMS and O₂Hb derived from NIRS have shown that muscle fatigue took place in later minutes of 30 minutes of FES-evoked cycling, suggesting that free-ankle QHT stimulation might maximize power production during 30 minutes of FES-evoked cycling. However, further investigation on the effects of free-ankle QHT stimulation on pedal power production and muscle fatigue, quantified by MMG and NIRS during 30 minutes of FES-evoked cycling is needed.

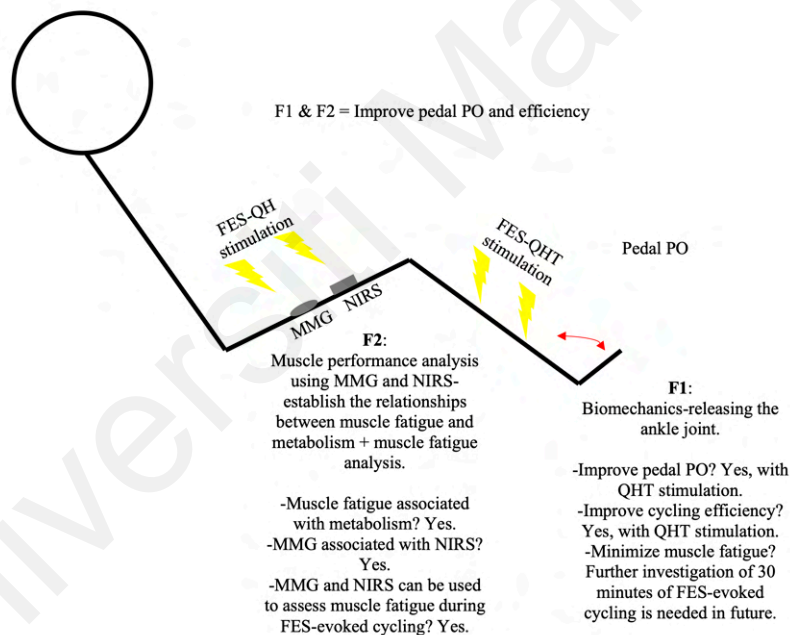


Figure 5.1: An insight into the overall findings of the present study.

It can be concluded that altering the ankle joint biomechanics by releasing the ankle joint and assessing muscle performance, specifically quantifying muscle fatigue using MMG and NIRS are equally important and needed in maximizing FES-evoked cycling power production and efficiency in individuals with SCI. As they mirrored each other, muscle fatigue assessment using MMG and NIRS could help provide information on the

muscle level and its metabolism while aiming to maximize the efficiency of FES-evoked cycling in individuals with SCI.

Universiti Malaya

CHAPTER 6: CONCLUSION

The present study suggests that QHT stimulation is necessary during free-ankle FES-evoked cycling to maintain power production as fixed-ankle. Releasing the ankle joint and stimulating the triceps surae and tibialis anterior during FES-evoked cycling improves mean normalized pedal PO by 0.8% more than fixing the ankle joint. Even though there is no large mechanical PO increment shown, the findings of the present study might be useful for rehabilitation practitioners in maximizing the physiological benefits of FES-evoked cycling, especially the lower leg muscles and ankle joint flexibility of individuals with SCI as it was found to be safe. Free-ankle AFO with stops to limit the ankle joint ROM could also be implemented in rehabilitation programs to prevent knee hyperextension during FES-evoked cycling.

Besides that, MMG RMS was negatively associated with O₂Hb and muscle oxygen derived from NIRS, suggesting that MMG and NIRS sensors showed good inter-correlations with each other. The present study also suggests that MMG could be used for characterizing metabolic fatigue at the muscle oxygenation level during FES-evoked cycling in individuals with SCI.

6.1 Limitations of the Study

The present study's findings might be useful for rehab practitioners in maximizing the benefits of FES-evoked cycling, thus maximizing the health of individuals with SCI. However, the findings should be interpreted with caution due to low participant numbers and small effect sizes. The limitation of this study is in the aspect of gathering more participants. Due to disability and mobility limitations, our potential participants could not be recruited. They could not commit to a longer duration of training sessions (at least three months) prior to the experiments. They have no proper transport and caretaker that could help them to come to our laboratory for training with FES-evoked

cycling. With that, the gathering of potential participants will only be conducted through the in-patients from UMMC that would commit to the three-months training session. Those who could not commit will be eliminated from the experiment session.

Besides that, a short duration of power production during fixed- and free-ankle with QH and QHT stimulations cycling in the present study might be insufficient to maximize the cycling benefits when compared to a longer duration of cycling. A long cycling duration which is commonly practiced by rehabilitation practitioners in individuals with SCI was more likely to maximize muscle strength and endurance.

6.2 Future Recommendations

The general purpose of the present study was to establish the interaction between different ankle setups and stimulation modes on power production during FES-evoked, without muscle fatigue consideration. Therefore, one minute of cycling in the present study is crucial to justify that the significant changes in power production were solely due to either fixed- and free-ankle, or QH and QHT stimulations, or both, not because of other factors such as muscle fatigue. Muscle fatigue might take place in a longer duration of FES-evoked cycling. Therefore, further studies are recommended to understand the effects of releasing the ankle joint during 30 minutes of FES-evoked cycling on power production among higher SCI participant numbers. It is also recommended to determine the effects of releasing the ankle joint during 30 minutes of FES-evoked cycling on cardiovascular output.

The MMG and NIRS could be used to investigate the effects of releasing ankle joint on muscle fatigue during 30 minutes of FES-evoked cycling in individuals with SCI. This is because biomechanics and muscle performance are equally important and much needed in maximizing the efficiency of FES-evoked cycling in this population.

6.3 Novelty and Knowledge Contribution

To the best knowledge, the effects of releasing the ankle joint on pedal power production during FES-evoked cycling in individuals with SCI have never been experimentally investigated. Therefore, this gap will become the strength of the present study as this study measured some interesting variables in FES-evoked cycling, based on predictions from modeling. Consequently, the present study proves the potential of releasing the ankle joint in maximizing power production during FES-evoked cycling in individuals with SCI.

In addition, NIRS has never been quantitatively related to the MMG signal as a proxy for muscle force and fatigue during FES-evoked cycling in individuals with SCI. This gap of knowledge motivated the current study to investigate the relationships between muscle performance during FES-evoked cycling, underlying physiological markers derived from NIRS, and skin-surface MMG findings. This study establishes the relationships between MMG and NIRS during FES-evoked cycling in individuals with SCI. This study also contributes to the potential use of MMG to inform the occurrence of physiological muscle fatigue easily and safely in electrically evoked leg muscles in individuals with SCI undergoing FES-evoked exercises.

REFERENCES

- Agarwal, S., Kobetic, R., Nandurkar, S., & Marsolais, E. B. (2003). Functional electrical stimulation for walking in paraplegia: 17-year follow-up of 2 cases. *The Journal of Spinal Cord Medicine*, 26(1), 86–91. <https://doi.org/10.1080/10790268.2003.11753666>
- Ahmadi, S., Sinclair, P. J., & Davis, G. M. (2008). Muscle oxygenation after downhill walking-induced muscle damage. *Clinical Physiology and Functional Imaging*, 28(1), 55–63. <https://doi.org/10.1111/j.1475-097X.2007.00777.x>
- Ahmed, M., Huq, M. S., Ibrahim, B. S. K. K., Ahmed, A., & Ahmed, Z. (2016). New concept for FES-induced movements. In *International Engineering Research and Innovation Symposium (IRIS)* (Vol. 160). Malacca: IOP. <https://doi.org/10.1088/1757-899X/160/1/012104>
- Aksöz, E. A., Luder, M. A., Laubacher, M., Riener, R., Binder-Macleod, S. A., & Hunt, K. J. (2018). Stochastically modulated inter-pulse intervals to increase the efficiency of functional electrical stimulation cycling. *Journal of Rehabilitation and Assistive Technologies Engineering*, 5, 1–6. <https://doi.org/10.1177/2055668318767364>
- Aksöz, E. A., Laubacher, M., Binder-Macleod, S., & Hunt, K. J. (2016). Effect of stochastic modulation of inter-pulse interval during stimulated isokinetic leg extension. *European Journal of Translational Myology*, 26(3), 229–234. <https://doi.org/10.4081/EJTM.2016.6160>
- Al-Mulla, M. R., Francisco, S., & Colley, M. (2011). A review of non-invasive techniques to detect and predict localised muscle fatigue. *Sensors*, 11(4), 3545–3594. <https://doi.org/10.3390/s110403545>
- Allison, D. J., Chapman, B., Wolfe, D., Sequeira, K., Hayes, K., & Ditor, D. S. (2016). Effects of a functional electrical stimulation-assisted cycling program on immune and cardiovascular health in persons with spinal cord injury. *Topics in Spinal Cord Injury Rehabilitation*, 22(1), 71–78. <https://doi.org/10.1310/sci2201-71>
- Arnin, J., Yamsa-ard, T., Triponywasin, P., & Wongsawat, Y. (2017). Development of practical functional electrical stimulation cycling systems based on an electromyography study of the Cybathlon 2016. *European Journal of Translational Myology*, 27(4), 295–301. <https://doi.org/10.4081/ejtm.2017.7111>
- Astorino, T. A., Tyerman, N., Wong, K., & Harness, E. (2008). Efficacy of a new rehabilitative device for individuals with spinal cord injury. *Journal of Science and Medicine in Sport*, 31(5), 586–591. <https://doi.org/10.1080/10790268.2008.11754606>
- Atkins, K. D., & Bickel, C. S. (2021). Effects of functional electrical stimulation on muscle health after spinal cord injury. *Current Opinion in Pharmacology*, 60, 226–231. <https://doi.org/10.1016/j.coph.2021.07.025>
- Bakkum, A. J. T., de Groot, S., Onderwater, M. Q., de Jong, J., & Janssen, T. W. J.

- (2014). Metabolic rate and cardiorespiratory response during hybrid cycling versus handcycling at equal subjective exercise intensity levels in people with spinal cord injury. *Journal of Spinal Cord Medicine*, 37(6), 758–764. <https://doi.org/10.1179/2045772313Y.0000000164>
- Bakkum, A. J. T., de Groot, S., van der Woude, L. H. V., & Janssen, T. W. J. (2012). The effects of hybrid cycle training in inactive people with long-term spinal cord injury: Design of a multicenter randomized controlled trial. *Disability & Rehabilitation*, 1–6. <https://doi.org/10.3109/09638288.2012.715719>
- Bakkum, A. J. T., Paulson, T. A. W., Bishop, N. C., Goosey-Tolfrey, V. L., Stolwijk-Swüste, J. M., Van Kuppevelt, D. J., ... Janssen, T. W. J. (2015). Effects of hybrid cycle and handcycle exercise on cardiovascular disease risk factors in people with spinal cord injury: A randomized controlled trial. *Journal of Rehabilitation Medicine*, 47, 523–530.
- Baptista, R. S., Moreira, M. C. C., Pinheiro, L. D. M., Pereira, T. R., Carmona, G. G., Freire, J. P. D. F., ... Bo, A. P. L. B. (2022). User-centered design and spatially-distributed sequential electrical stimulation in cycling for individuals with paraplegia. *Journal of NeuroEngineering and Rehabilitation*, 19(1). <https://doi.org/10.1186/s12984-022-01014-6>
- Bauman, W. A., & Spungen, A. M. (2008). Coronary heart disease in individuals with spinal cord injury: Assessment of risk factors. *Spinal Cord*, 46(7), 466–476. <https://doi.org/10.1038/sj.sc.3102161>
- Baur, K., Haufe, F. L., Sigrist, R., Dorfschmid, K., & Riener, R. (2018). The CYBATHLON - Bionic Olympics to Benchmark Assistive Technologies. In *International Conference on Inclusive Robotics for A Better Society, INBOTS 2018* (pp. 175–179). Springer, Cham. https://doi.org/10.1007/978-3-030-24074-5_29
- Behrman, A. L., Bowden, M. G., & Nair, P. M. (2006). Neuroplasticity after spinal cord injury and training: An emerging paradigm shift in rehabilitation and walking recovery. *Physical Therapy*, 86(10), 1406–1425. <https://doi.org/10.2522/ptj.20050212>
- Berkelmans, R. (2008). FES cycling. In *Journal of Automatic Control* (Vol. 18, pp. 73–76). <https://doi.org/10.2298/JAC0802073B>
- Berkelmans, R., & Woods, B. (2017). Strategies and performances of functional electrical stimulation cycling using the BerkelBike with spinal cord injury in a competition context (CYBATHLON). *European Journal of Translational Myology*, 27(4), 255–258. <https://doi.org/10.4081/ejtm.2017.7189>
- Berry, H., Kakebeeke, T. H., Donaldson, N., Perret, C., & Hunt, K. J. (2012). Energetics of paraplegic cycling: Adaptations to 12 months of high volume training. *Technology and Health Care*, 20, 73–84.
- Berry, H. R., Perret, C., Saunders, B. A., Kakebeeke, T. H., Donaldson, N. de N., Allan, D. B., & Hunt, K. J. (2008). Cardiorespiratory and power adaptations to stimulated cycle training in paraplegia. *Medicine and Science in Sports and Exercise*, 40(9), 1573–1580. <https://doi.org/10.1249/MSS.0b013e318176b2f4>

- Bickel, C. S., Gregory, C. M., & Dean, J. C. (2011). Motor unit recruitment during neuromuscular electrical stimulation: A critical appraisal. *European Journal of Applied Physiology*, *111*(10), 2399–2407. <https://doi.org/10.1007/s00421-011-2128-4>
- Bickel, C. S., Slade, J. M., & Dudley, G. A. (2004). Long-term spinal cord injury increases susceptibility to isometric contraction-induced muscle injury. *European Journal of Applied Physiology*, *91*, 308–313. <https://doi.org/10.1007/s00421-003-0973-5>
- Binder-Macleod, S. A., & Guerin, T. (1990). Preservation of force output through progressive reduction of stimulation frequency in human quadriceps femoris muscle. *Physical Therapy*, *70*(10), 619–625. Retrieved from <http://www.ncbi.nlm.nih.gov/htbin-post/Entrez/query?db=m&form=6&dopt=r&uid=0002217541>
- Binder-Macleod, S., Halden, E., & Jungles, K. (1995). Effects of stimulation intensity on the physiological responses of human motor units. *Medicine & Science in Sports & Exercise*, *27*(4), 556–565.
- Bloemen-Vrencken, J. H. A., de Witte, L. P., Post, M. W. M., & van den Heuvel, W. J. A. (2007). Health behaviour of persons with spinal cord injury. *Spinal Cord*, *45*, 243–249. <https://doi.org/10.1038/sj.sc.3101967>
- Boot, C. R. L., Groothuis, J. T., van Langen, H., & Hopman, M. T. E. (2002). Shear stress levels in paralyzed legs of spinal cord-injured individuals with and without nerve degeneration. *Journal of Applied Physiology*, *92*(6), 2335–2340. <https://doi.org/10.1152/jappphysiol.00340.2001>
- Braz, G. P., Russold, M., & Davis, G. M. (2009). Functional electrical stimulation control of standing and stepping after spinal cord injury: A review of technical characteristics. *Neuromodulation*, *12*(3), 180–190. <https://doi.org/10.1111/j.1525-1403.2009.00213.x>
- Brown, N. A. T., & Jensen, J. L. (2003). The development of contact force construction in the dynamic-contact task of cycling. *Journal of Biomechanics*, *36*(1), 1–8. [https://doi.org/10.1016/S0021-9290\(02\)00329-9](https://doi.org/10.1016/S0021-9290(02)00329-9)
- Calabrò, R. S., Filoni, S., Billeri, L., Balletta, T., Cannavò, A., Militi, A., ... Naro, A. (2021). Robotic rehabilitation in spinal cord injury: A pilot study on end-effectors and neurophysiological outcomes. *Annals of Biomedical Engineering*, *49*(2), 732–745. <https://doi.org/10.1007/s10439-020-02611-z>
- Cardosode Sousa, A. C., Cascás Sousa, F. S., & Lanari Bó, A. P. (2019). Simulation of the assistance of passive knee orthoses in FES cycling. In *2019 41st Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBS)* (pp. 3811–3814). Berlin, GERMANY. <https://doi.org/10.1109/EMBC.2019.8857912>
- Casabona, A., Valle, M. S., Dominante, C., Laudani, L., Onesta, M. P., & Cioni, M. (2021). Effects of functional electrical stimulation cycling of different duration on viscoelastic and electromyographic properties of the knee in patients with spinal

cord injury. *Brain Sciences*, 11(1). <https://doi.org/10.3390/brainsci11010007>

- Cash, M. S., Jacobs, P. L., Montalvo, B. M., Klose, K. J., Guest, R. S., & Needham-Shropshire, B. M. (1997). Evaluation of a training program for persons with SCI paraplegia using the Parastep®1 ambulation system :Part 5. Lower extremity blood flow and hyperemic responses to occlusion are augmented by ambulation training. *Archives of Physical Medicine and Rehabilitation*, 78, 808–814. <https://doi.org/0003-9993/97/7808-423>
- Celie, B., van Coster, R., & Bourgois, J. (2012). Reliability of near infrared spectroscopy (NIRS) for measuring forearm oxygenation during incremental handgrip exercise. *European Journal of Applied Physiology*, 112(6), 2369–2374. <https://doi.org/10.1007/s00421-011-2183-x>
- Ceroni, I., Ferrante, S., Conti, F., No, S. J., Dalla Gasperina, S., Dell’eva, F., ... Ambrosini, E. (2021). Comparing fatigue reducing stimulation strategies during cycling induced by functional electrical stimulation: A case study with one spinal cord injured subject. In *2021 43rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)* (pp. 6394–6397). ELECTRONETWORK: IEEE. <https://doi.org/10.1109/EMBC46164.2021.9630197>
- Chang, C. H., Casas, J., Brose, S. W., & Duenas, V. H. (2022). Closed-loop torque and kinematic control of a hybrid lower-limb exoskeleton for treadmill walking. *Frontiers in Robotics and AI*, 8(January), 1–19. <https://doi.org/10.3389/frobt.2021.702860>
- Chen, B., Zi, B., Zeng, Y., Qin, L., & Liao, W.-H. (2018). Ankle-foot orthoses for rehabilitation and reducing metabolic cost of walking: Possibilities and challenges. *Mechatronics*, 53, 241–250. <https://doi.org/10.1016/j.mechatronics.2018.06.014>
- Chou, L., Kesar, T. M., & Binder-Macleod, S. A. (2008). Using customized rate-coding and recruitment strategies to maintain forces during repetitive activation of human muscles. *Physical Therapy*, 88(3), 363–375.
- Coelho-Magalhães, T., Azevedo Coste, C., & Resende-Martins, H. (2022). A novel functional electrical stimulation-induced cycling controller using reinforcement learning to optimize online muscle activation pattern. *Sensors*, 22(23). <https://doi.org/10.3390/s22239126>
- Coelho-Magalhães, T., Fachin-Martins, E., Silva, A., Azevedo Coste, C., & Resende-Martins, H. (2022). Development of a high-power capacity open source electrical stimulation system to enhance research into FES-assisted devices: Validation of FES cycling. *Sensors*, 22(2). <https://doi.org/10.3390/s22020531>
- Cohen, J. (1988). *Statistical power analysis for the behavioral sciences*. Lawrence Erlbaum Associates Inc (2nd ed., Vol. 13). Hillsdale, New Jersey.
- Corbin, G. N., Weaver, K., Dolbow, D. R., Credeur, D., Pattanaik, S., & Stokic, D. S. (2021). Safety and preliminary efficacy of functional electrical stimulation cycling in an individual with cervical cord injury, autonomic dysreflexia, and a pacemaker: Case report. *Journal of Spinal Cord Medicine*, 44(4), 613–616. <https://doi.org/10.1080/10790268.2019.1692180>

- Coste, C. A., Bergeron, V., Berkelmans, R., Martins, E. F., Fornusek, C., Jetsada, A., ... Wolf, P. (2017). Comparison of strategies and performance of functional electrical stimulation cycling in spinal cord injury pilots for competition in the first ever Cyathlon. *European Journal of Translational Myology*, 27(4), 251–254. <https://doi.org/10.4081/ejtm.2017.7219>
- Cousin, C. A., Rouse, C. A., Duenas, V. H., & Dixon, W. E. (2019). Controlling the cadence and admittance of a functional electrical stimulation cycle. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, 27(6), 1181–1192. <https://doi.org/10.1109/TNSRE.2019.2914579>
- Cup, E. H., Pieterse, A. J., ten Broek-Pastoor, J. M., Munneke, M., van Engelen, B. G., Hendricks, H. T., ... Oostendorp, R. A. (2007). Exercise therapy and other types of physical therapy for patients with neuromuscular diseases: A systematic review. *Archives of Physical Medicine and Rehabilitation*, 88(11), 1452–1464. <https://doi.org/10.1016/j.apmr.2007.07.024>
- Daly, J. J., Zimbelman, J., Roenigk, K. L., McCabe, J. P., Rogers, J. M., Butler, K., ... Ruff, R. L. (2011). Recovery of coordinated gait: Randomized controlled stroke trial of functional electrical stimulation (FES) versus no FES, with weight-supported treadmill and over-ground training. *Neurorehabilitation and Neural Repair*, 25(7), 588–596. <https://doi.org/10.1177/1545968311400092>
- Davis, G. M., Nur Azah Hamzaid, N. A., & Fornusek, C. (2008). Cardiorespiratory, metabolic, and biomechanical responses during functional electrical stimulation leg exercise: Health and fitness benefits. *Artificial Organs*, 32(8), 625–629. <https://doi.org/10.1111/j.1525-1594.2008.00622.x>
- Davis, G. M., Nur Azah Hamzaid, & Nazirah Hasnan. (2014). Functional electrical stimulation in clinical applications: Fitness and cardiovascular health. In *2014 IEEE 19th International Functional Electrical Stimulation Society Annual Conference (IFESS)*. Kuala Lumpur: IEEE.
- De Carvalho, I. D. G., Kurchchoff, R. R., Neto, G. N. N., & Nohama, P. W. (2022). A LabVIEW™-developed Biphasic Functional Multichannel Electrical Stimulator. *Pan American Health Care Exchanges, PAHCE*. <https://doi.org/10.1109/GMEPE/PAHCE55115.2022.9757732>
- de Groot, P. C., Bleeker, M. W., van Kuppevelt, D. H., van der Woude, L. H., & Hopman, M. T. (2006). Rapid and extensive arterial adaptations after spinal cord injury. *Archives of Physical Medicine and Rehabilitation*, 87(5), 688–696. <https://doi.org/10.1016/j.apmr.2006.01.022>
- De Luca, C. J., Donald Gilmore, L., Kuznetsov, M., & Roy, S. H. (2010). Filtering the surface EMG signal: Movement artifact and baseline noise contamination. *Journal of Biomechanics*, 43(8), 1573–1579. <https://doi.org/10.1016/j.jbiomech.2010.01.027>
- de Sousa, A. C. C., Sousa, F. S. C., de S. Baptista, R., & Bo, A. P. L. (2021). Passive knee orthoses assistance in functional electrical stimulation cycling in an individual with spinal cord injury. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, 29, 690–698. <https://doi.org/10.1109/TNSRE.2021.3070468>

- Decker, M. J., Griffin, L., Abraham, L. D., & Brandt, L. (2010). Alternating stimulation of synergistic muscles during functional electrical stimulation cycling improves endurance in persons with spinal cord injury. *Journal of Electromyography and Kinesiology*, 20(6), 1163–1169. <https://doi.org/10.1016/j.jelekin.2010.07.015>
- Del-Ama, A. J., Koutsou, A. D., Bravo-Esteban, E., Gómez-Soriano, J., Piazza, S., Gil-Agudo, Á., ... Juan, M. (2013). A comparison of customized strategies to manage muscle fatigue in isometric artificially elicited muscle contractions for incomplete SCI subjects. *Journal of Automatic Control*, 21, 19–25. <https://doi.org/10.2298/JAC1301019A>
- Deley, G., Denuziller, J., Babault, N., & Taylor, J. A. (2015). Effects of electrical stimulation pattern on quadriceps isometric force and fatigue in individuals with spinal cord injury. *Muscle & Nerve*, 52(2), 260–264. <https://doi.org/10.1002/mus.24530>
- Delpy, D. T., Cope, M., van der Zee, P., Arridge, S., Wray, S., & Wyatt, J. (1988). Estimation of optical pathlength through tissue from direct time of flight measurement. *Physics in Medicine and Biology*, 33(12), 1433–1442. <https://doi.org/10.1088/0031-9155/33/12/008>
- Dolbow, D. R. (2015). Exercise following spinal cord injury: Physiology to therapy. *Journal of Neurorestoratology*, 3, 133–139. <https://doi.org/http://dx.doi.org/10.2147/JN.S61828>
- Dolbow, D. R., Credeur, D. P., Lemacks, J. L., Stokic, D. S., Pattanaik, S., Corbin, G. N., & Courtner, A. S. (2021). Electrically induced cycling and nutritional counseling for counteracting obesity after spinal cord injury: A pilot study. *Journal of Spinal Cord Medicine*, 44(4), 533–540. <https://doi.org/10.1080/10790268.2019.1710939>
- Dolbow, D. R., Gorgey, A. S., Gater, D. R., & Moore, J. R. Body composition changes after 12 months of FES cycling: Case report of a 60-year-old female with paraplegia, 52 Spinal Cord S3–S4 (2014). Nature Publishing Group. <https://doi.org/10.1038/sc.2014.40>
- Dolbow, D. R., Gorgey, A. S., Khalil, R. K., & Gater, D. R. (2017). Effects of a fifty-six month electrical stimulation cycling program after tetraplegia: Case report. *Journal of Spinal Cord Medicine*, 40(4), 485–488. <https://doi.org/10.1080/10790268.2016.1234750>
- Dolbow, D. R., Gorgey, A. S., Recio, A. C., Stiens, S. A., Curry, A. C., Sadowsky, C. L., ... McDonald, J. W. (2015). Activity-based restorative therapies after spinal cord injury: Inter-institutional conceptions and perceptions. *Aging and Disease*, 6(4), 254–261. <https://doi.org/10.14336/AD.2014.1105>
- Doll, B. D., Kirsch, N. A., Bao, X., Dicianno, B. E., & Sharma, N. (2017). Dynamic optimization of stimulation frequency to reduce isometric muscle fatigue using a modified Hill-Huxley model. *Muscle & Nerve*, 57(4), 634–641. <https://doi.org/10.1002/mus.25777>
- Duenas, V. H., Cousin, C. A., Rouse, C., Fox, E. J., & Dixon, W. E. (2020). Distributed

- repetitive learning control for cooperative cadence tracking in functional electrical stimulation cycling. *IEEE Transactions on Cybernetics*, 50(3), 1084–1095. <https://doi.org/10.1109/TCYB.2018.2882755>
- Duffell, L. D., & Donaldson, N. D. N. (2020). A comparison of FES and SCS for neuroplastic recovery after SCI: Historical perspectives and future directions. *Frontiers in Neurology*, 11. <https://doi.org/10.3389/fneur.2020.00607>
- Duffell, L. D., Donaldson, N. D. N., & Newham, D. J. (2009). Why is the metabolic efficiency of FES cycling low? *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, 17(3), 263–269. <https://doi.org/10.1109/TNSRE.2009.2016199>
- Duffell, L. D., Donaldson, N. D. N., & Newham, D. J. (2010). Power output during functional electrically stimulated cycling in trained spinal cord injured people. *Neuromodulation*, 13(1), 50–57. <https://doi.org/10.1111/j.1525-1403.2009.00245.x>
- Duffell, L. D., Donaldson, N. D. N., Perkins, T. A., Rushton, D. N., Hunt, K. J., Kakebeeke, T. H., & Newham, D. J. (2008). Long-term intensive electrically stimulated cycling by spinal cord-injured people: Effect on muscle properties and their relation to power output. *Muscle & Nerve*, 38(4), 1304–1311. <https://doi.org/10.1002/mus.21060>
- Duffell, L. D., Paddison, S., Alahmary, A. F., Donaldson, N., & Burridge, J. (2019). The effects of FES cycling combined with virtual reality racing biofeedback on voluntary function after incomplete SCI: A pilot study. *Journal of NeuroEngineering and Rehabilitation*, 16(1). <https://doi.org/10.1186/s12984-019-0619-4>
- Duffell, L. D., Rowlerson, A. M., Donaldson, N. D. N., Harridge, S. D. R., & Newham, D. J. (2010). Effects of endurance and strength-directed electrical stimulation training on the performance and histological properties of paralyzed human muscle: A pilot study. *Muscle & Nerve*, 42(5), 756–763. <https://doi.org/10.1002/mus.21746>
- Eser, P. C., Donaldson, N. D. N., Knecht, H., & Stüssi, E. (2003). Influence of different stimulation frequencies on power output and fatigue during FES-Cycling in recently injured SCI people. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, 11(3), 236–240. <https://doi.org/10.1109/TNSRE.2003.817677>
- Estay, F. I. E., Rouse, C. A., Cohen, M. H., Cousin, C. A., & Dixon, W. E. (2019). Cadence and position tracking for decoupled legs during switched split-crank motorized FES-cycling. In *Proceedings of the American Control Conference* (pp. 854–859). Philadelphia, PA. <https://doi.org/10.23919/acc.2019.8814365>
- Evans, N., Wingo, B., Sasso, E., Hicks, A., Gorgey, A. S., & Harness, E. (2015). Exercise recommendations and considerations for persons with spinal cord injury. <https://doi.org/10.1016/j.apmr.2015.02.005>
- Everaert, D. G., Okuma, Y., Abdollah, V., & Ho, C. (2021). Timing and dosage of FES cycling early after acute spinal cord injury: A case series report. *Journal of Spinal*

- Faller, L., Nogueira Neto, G. N., Button, V. L. S. N., & Nohama, P. (2009). Muscle fatigue assessment by mechanomyography during application of NMES protocol. *Revista Brasileira De Fisioterapia*, 13(5), 422–429. <https://doi.org/10.1590/S1413-35552009005000057>
- Fang, C.-Y., Lien, A. S.-Y., Tsai, J.-L., Yang, H.-C., Chan, H.-L., Chen, R.-S., & Chang, Y.-J. (2021). The effect and dose-response of functional electrical stimulation cycling training on spasticity in individuals with spinal cord injury: A systematic review with meta-analysis. *Frontiers in Physiology*, 12. <https://doi.org/10.3389/fphys.2021.756200>
- Farkas, G. J., Gorgey, A. S., Dolbow, D. R., Berg, A. S., & Gater, D. R. (2021). Energy expenditure, cardiorespiratory fitness, and body composition following arm cycling or functional electrical stimulation exercises in spinal cord injury: A 16-week randomized controlled trial. *Topics in Spinal Cord Injury Rehabilitation*, 27(1), 121–134. <https://doi.org/10.46292/sci20-00065>
- Fattal, C., Schmoll, M., Le Guillou, R., Raoult, B., Frey, A., Carlier, R., & Azevedo-Coste, C. (2021). Benefits of 1-yr home training with functional electrical stimulation cycling in paraplegia during COVID-19 crisis. *American Journal of Physical Medicine & Rehabilitation*, 100(12), 1148–1151. <https://doi.org/10.1097/PHM.0000000000001898>
- Fattal, C., Sijobert, B., Daubigny, A., Fachin-Martins, E., Lucas, B., Casillas, J. M., & Azevedo, C. (2020). Training with FES-assisted cycling in a subject with spinal cord injury: Psychological, physical and physiological considerations. *Journal of Spinal Cord Medicine*, 43(3), 402–413. <https://doi.org/10.1080/10790268.2018.1490098>
- Fenton, J. M., King, J. A., Hoekstra, S. P., Valentino, S. E., Phillips, S. M., & Goosey-Tolfrey, V. L. (2022). Protocols aiming to increase muscle mass in persons with motor complete spinal cord injury: A systematic review. *Disability and Rehabilitation*, 1–11. <https://doi.org/10.1080/09638288.2022.2063420>
- Ferrante, S., Saunders, B., Duffell, L., Pedrocchi, A., Hunt, K., Perkins, T., & Donaldson, N. (2005). Quantitative evaluation of stimulation patterns for FES cycling. In *10th Annual Conference of the International FES Society* (pp. 2–4). Montreal, Canada.
- Ferrarello, F., Baccini, M., Rinaldi, L. A., Chiara, M., Mossello, E., Masotti, G., ... Mossello, E. (2010). Efficacy of physiotherapy interventions late after stroke: A meta analysis. *Journal of Neurology, Neurosurgery and Psychiatry*, 82(2), 136. <https://doi.org/10.1136/jnnp.2009.196428>
- Ferrari, M., Muthalib, M., & Quaresima, V. (2011). The use of near-infrared spectroscopy in understanding skeletal muscle physiology: Recent developments. *Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences*, 369(1955), 4577–4590. <https://doi.org/10.1098/rsta.2011.0230>

- Figoni, S. F., Dolbow, D. R., Crawford, E. C., White, M. L., & Pattanaik, S. (2021). Does aerobic exercise benefit persons with tetraplegia from spinal cord injury? A systematic review. *Journal of Spinal Cord Medicine*, *44*(5), 690–703. <https://doi.org/10.1080/10790268.2020.1722935>
- Figoni, S. F., Roger, G. M., Rodger, M. M., Hooker, S. P., Ezenwa, B. N., Collins, S. R., ... Gupta, S. C. (1991). Acute hemodynamic responses of spinal cord injured individuals to functional neuromuscular stimulation-induced knee extension exercise. *The Journal of Rehabilitation Research and Development*, *28*(4), 9–18. <https://doi.org/10.1682/JRRD.1991.10.0019>
- Fornusek, C., & Davis, G. M. (2004). Maximizing muscle force via low-cadence functional electrical stimulation cycling. *Journal of Rehabilitation Medicine*, *36*(5), 232–237. <https://doi.org/10.1080/16501970410029843>
- Fornusek, C., & Davis, G. M. (2008). Cardiovascular and metabolic responses during functional electric stimulation cycling at different cadences. *Archives of Physical Medicine and Rehabilitation*, *89*(4), 719–725. <https://doi.org/10.1016/j.apmr.2007.09.035>
- Fornusek, C., Davis, G. M., & Baek, I. (2012). Stimulation of shank muscles during functional electrical stimulation cycling increases ankle excursion in individuals with spinal cord injury. *Archives of Physical Medicine and Rehabilitation*, *93*(11), 1930–1936. <https://doi.org/10.1016/j.apmr.2012.05.012>
- Fornusek, C., Sinclair, P. J., & Davis, G. M. (2007). The force-velocity relationship of paralyzed quadriceps muscles during functional electrical stimulation cycling. *Neuromodulation*, *10*(1), 68–75. <https://doi.org/10.1111/j.1525-1403.2007.00089.x>
- Franco, J. C., Perell, K. L., Gregor, R. J., & Scremin, A. M. E. (1999). Knee kinetics during functional electrical stimulation induced cycling in subjects with spinal cord injury: A preliminary study. *Journal Of Rehabilitation Research And Development*, *36*(3), 207–216. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/10659804>
- Frotzler, A., Coupaud, S., Perret, C., Kakebeeke, T. H., Hunt, K. J., Donaldson, N. D. N., & Eser, P. (2008). High-volume FES-cycling partially reverses bone loss in people with chronic spinal cord injury. *Bone*, *43*(1), 169–176. <https://doi.org/10.1016/j.bone.2008.03.004>
- Frotzler, A., Coupaud, S., Perret, C., Kakebeeke, T. H., Hunt, K. J., & Eser, P. (2009). Effect of detraining on bone and muscle tissue in subjects with chronic spinal cord injury after a period of electrically-stimulated cycling: A small cohort study. *Journal of Rehabilitation Medicine*, *41*(4), 282–285. <https://doi.org/10.2340/16501977-0321>
- Galea, M. P., Dunlop, S. A., Geraghty, T., Davis, G. M., Nunn, A., Olenko, L., & Collaborator, S. S.-O. T. (2018). SCIPA Full-On: A randomized controlled trial comparing intensive whole-body exercise and upper body exercise after spinal cord injury. *Neurorehabilitation and Neural Repair*, *32*(6–7), 557–567. <https://doi.org/10.1177/1545968318771213>
- Galea, M. P., Panisset, M. G., El-Ansary, D., Dunlop, S. A., Marshall, R., Clark, J. M.,

- ... Collaborators, S. S.-O. T. (2017). SCIPA Switch-on: A randomized controlled trial investigating the efficacy and safety of functional electrical stimulation-assisted cycling and passive cycling initiated early after traumatic spinal cord injury. *Neurorehabilitation and Neural Repair*, 31(6), 540–551. <https://doi.org/10.1177/1545968317697035>
- Garshick, E., Kelley, A., Cohen, S. A., Garrison, A., Tun, C. G., Gagnon, D., & Brown, R. (2005). A prospective assessment of mortality in chronic spinal cord injury. *Spinal Cord*, 43, 408–416. <https://doi.org/10.1038/sj.sc.3101729>
- Gelenitis, K., Foglyano, K., Lombardo, L., McDaniel, J., & Triolo, R. (2022). Motorless cadence control of standard and low duty cycle-patterned neural stimulation intensity extends muscle-driven cycling output after paralysis. *Journal of NeuroEngineering and Rehabilitation*, 19(1). <https://doi.org/10.1186/s12984-022-01064-w>
- Gelenitis, K., Foglyano, K., Lombardo, L., & Triolo, R. (2021). Selective neural stimulation methods improve cycling exercise performance after spinal cord injury: A case series. *Journal of NeuroEngineering and Rehabilitation*, 18(1). <https://doi.org/10.1186/s12984-021-00912-5>
- Gibson, H., Cooper, R. G., Stokes, M. J., & Edwards, R. H. T. (1988). Mechanisms resisting fatigue in isometrically contracting human skeletal muscle. *Quarterly Journal of Experimental Physiology*, 73(6), 903–914.
- Gill, S., Adler, J., Khalil, R. E., & Gorgey, A. S. (2020). Attenuation of autonomic dysreflexia during functional electrical stimulation cycling by neuromuscular electrical stimulation training: Case reports. *Spinal Cord Series and Cases*, 6(1). <https://doi.org/10.1038/s41394-020-0262-0>
- Gobbo, M., Gaffurini, P., Bissolotti, L., Esposito, F., & Orizio, C. (2011). Transcutaneous neuromuscular electrical stimulation: Influence of electrode positioning and stimulus amplitude settings on muscle response. *European Journal of Applied Physiology*, 111(10), 2451–2459. <https://doi.org/10.1007/s00421-011-2047-4>
- Gobbo, M., Ce, E., Diemont, B., Esposito, F., & Orizio, C. (2006). Torque and surface mechanomyogram parallel reduction during fatiguing stimulation in human muscles. *European Journal of Applied Physiology*, 97(1), 9–15. <https://doi.org/10.1007/s00421-006-0134-8>
- Gobbo, M., Maffioletti, N. A., Orizio, C., & Minetto, M. A. (2014). Muscle motor point identification is essential for optimizing neuromuscular electrical stimulation use. *Journal of NeuroEngineering and Rehabilitation*, 11(1), 1–6. <https://doi.org/10.1186/1743-0003-11-17>
- Gorgey, A. S., Black, C. D., Elder, C. P., & Dudley, G. A. (2009). Effects of electrical stimulation parameters on fatigue in skeletal muscle. *Journal of Orthopaedic & Sports Physical Therapy*, 39(9), 684–692. <https://doi.org/10.2519/jospt.2009.3045>
- Gorgey, A. S., Dolbow, D. R., Dolbow, J. D., Khalil, R. K., Castillo, C., & Gater, D. R. (2014). Effects of spinal cord injury on body composition and metabolic profile -

part I. *The Journal of Spinal Cord Medicine*, 37(6), 693–702.
<https://doi.org/10.1179/2045772314Y.0000000245>

Gorgey, A. S., & Dudley, G. A. (2007). Original Article Skeletal muscle atrophy and increased intramuscular fat after incomplete spinal cord injury, 304–309.
<https://doi.org/10.1038/sj.sc.3101968>

Gorgey, A. S., Khalil, R. E., Davis, J. C., Carter, W., Gill, R., Rivers, J., ... Adler, R. A. (2019). Skeletal muscle hypertrophy and attenuation of cardio-metabolic risk factors (SHARC) using functional electrical stimulation-lower extremity cycling in persons with spinal cord injury: Study protocol for a randomized clinical trial. *Trials*, 20(1). <https://doi.org/10.1186/s13063-019-3560-8>

Gorgey, A. S., Mather, K. J., Cupp, H. R., & Gater, D. R. (2012). Effects of resistance training on adiposity and metabolism after spinal cord injury. *Medicine and Science in Sports and Exercise*, 44(1), 165–174.
<https://doi.org/10.1249/MSS.0b013e31822672aa>

Gorgey, A. S., Poarch, H. J., Dolbow, D. R., Castillo, T., & Gater, D. R. (2014). Effect of adjusting pulse durations of functional electrical stimulation cycling on energy expenditure and fatigue after spinal cord injury. *Journal of Rehabilitation Research & Development*, 51(9), 1455–1468. <https://doi.org/10.1682/JRRD.2014.02.0054>

Graham, G. M., Thrasher, T. A., & Popovic, M. R. (2006). The effect of random modulation of functional electrical stimulation parameters on muscle fatigue. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, 14(1), 38–45.
<https://doi.org/10.1109/TNSRE.2006.870490>

Graupe, D., Suliga, P., Prudiant, C., & Kohn, K. H. (2000). Stochastically-modulated stimulation to slow down muscle fatigue at stimulated sites in paraplegics using functional electrical stimulation for leg extension. *Neurological Research*, 22(7), 703–704.

Gregor, R. J., Broker, J. P., & Ryan, M. M. (1991). The biomechanics of cycling. *Exercise and Sport Sciences Reviews*. Retrieved from <http://www.scopus.com/inward/record.url?eid=2-s2.0-0025996365&partnerID=tZOtx3y1>

Gregor, S. M., Perell, K. L., Rushatakankovit, S., Miyamoto, E., Muffoletto, R., & Gregor, R. J. (2002). Lower extremity general muscle moment patterns in healthy individuals during recumbent cycling. *Clinical Biomechanics*, 17, 123–129.
[https://doi.org/10.1016/S0268-0033\(01\)00112-7](https://doi.org/10.1016/S0268-0033(01)00112-7)

Gregory, C. M., & Bickel, C. S. (2005). Recruitment patterns in human skeletal muscle during electrical stimulation. *Physical Therapy*, 85(4), 358–364.
<https://doi.org/10.1093/ptj/85.4.358>

Gregory, C. M., Dixon, W., & Bickel, C. S. (2007). Impact of varying pulse frequency and duration on muscle torque production and fatigue. *Muscle & Nerve*, 35, 504–509. <https://doi.org/10.1002/mus.20710>

Griffin, L., Decker, M. J., Hwang, J. Y., Wang, B., Kitchen, K., Ding, Z., & Ivy, J. L.

- (2009). Functional electrical stimulation cycling improves body composition, metabolic and neural factors in persons with spinal cord injury. *Journal of Electromyography and Kinesiology*, 19(4), 614–622. <https://doi.org/10.1016/j.jelekin.2008.03.002>
- Groah, S. L., Nash, M. S., Ward, E. A., Libin, A., Mendez, A. J., Burns, P., ... Hamm, L. F. (2011). Cardiometabolic risk in community-dwelling persons with chronic spinal cord injury. *Journal of Cardiopulmonary Rehabilitation and Prevention*, 31(2), 73–80. <https://doi.org/10.1097/HCR.0b013e3181f68aba>
- Haapala, S. A., Faghri, P. D., & Adams, D. J. (2008a). Leg joint power output during progressive resistance FES-LCE cycling in SCI subjects: Developing an index of fatigue. *Journal of Neuroengineering and Rehabilitation*, 5(14). <https://doi.org/10.1186/1743-0003-5-14>
- Haapala, S. A., Faghri, P. D., & Adams, D. J. (2008b). Leg joint power output during progressive resistance FES-LCE cycling in SCI subjects: Developing an index of fatigue. *Journal of NeuroEngineering and Rehabilitation*, 5(1), 14. <https://doi.org/10.1186/1743-0003-5-14>
- Hakansson, N. A. & Hull, M. L. (2007). Influence of pedaling rate on muscle mechanical energy in low power recumbent pedaling using forward dynamic simulations. *IEEE Transaction on Neural Systems and Rehabilitation Engineering*, 15, 509–516. <https://doi.org/10.1109/TNSRE.2007.906959>
- Hakansson, N. A. & Hull, M. L. (2009). Muscle stimulation waveform timing patterns for upper and lower leg muscle groups to increase muscular endurance in functional electrical stimulation pedaling using a forward dynamic model. *IEEE Transaction on Biomedical Engineering*, 56, 2263–2270. <https://doi.org/10.1109/TBME.2009.2020175>
- Hakansson, N. A. & Hull, M. L. (2010). The effects of stimulating lower leg muscles on the mechanical work and metabolic response in functional electrically stimulated pedaling. *IEEE Transaction on Neural Systems and Rehabilitation Engineering*, 18, 498–504. <https://doi.org/10.1109/TNSRE.2010.2052132>
- Hammell, K. W., Miller, W. C., Forwell, S. J., Forman, B. E., & Jacobsen, B. A. (2009). Managing fatigue following spinal cord injury: A qualitative exploration. *Disability and Rehabilitation*, 31(17), 1437–1445. <https://doi.org/10.1080/09638280802627694>
- Harness, E. T., Yozbatiran, N., & Cramer, S. C. (2008). Effects of intense exercise in chronic spinal cord injury. *Spinal Cord*, 46(11), 733–737. <https://doi.org/10.1038/sc.2008.56>
- Harvey, L. (2008). *Management of spinal cord injuries: A guide for physiotherapists*. (Butterworth-Heinemann, Ed.). Edinburgh: Elsevier Health Sciences.
- Haworth, J., Young, C., & Thornton, E. (2009). The effects of an “exercise and education” programme on exercise self-efficacy and levels of independent activity in adults with acquired neurological pathologies: An exploratory, randomized study. *Clinical Rehabilitation*, 23(4), 371–383.

<https://doi.org/10.1177/0269215508101728>

- Hayashibe, M., Zhang, Q., Guiraud, D., & Fattal, C. (2011). Evoked EMG-based torque prediction under muscle fatigue in implanted neural stimulation. *Journal of Neural Engineering*, 8(6), 064001. <https://doi.org/10.1088/1741-2560/8/6/064001>
- Higashino, K., Matsuura, T., Suganuma, K., Yukata, K., Nishisho, T., & Yasui, N. (2013). Early changes in muscle atrophy and muscle fiber type conversion after spinal cord transection and peripheral nerve transection in rats. *Journal of NeuroEngineering and Rehabilitation*, 10(46). <https://doi.org/10.1186/1743-0003-10-46>
- Ho, C. H., Triolo, R. J., Elias, A. L., Kilgore, K. L., DiMarco, A. F., Bogie, K., ... Mushahwar, V. K. (2014). Functional electrical stimulation and spinal cord injury. *Physical Medicine and Rehabilitation Clinics*, 25(3), 631–654. <https://doi.org/10.1016/j.pmr.2014.05.001>
- Hogan, M. C., Richardson, R. S., & Kurdak, S. S. (1994). Initial fall in skeletal muscle force development during ischemia is related to oxygen availability. *Journal of Applied Physiology*, 77(5), 2380–2384. <https://doi.org/10.1152/jappl.1994.77.5.2380>
- Hunt, K. J., Fang, J., Saengsuwan, J., Grob, M., & Laubacher, M. (2012). On the efficiency of FES cycling: A framework and systematic review. *Technology and Health Care*, 20, 395–422. <https://doi.org/10.3233/THC-2012-0689>
- Hunt, K. J., Ferrario, C., Grant, S., Stone, B., McLean, A. N., Fraser, M. H., & Allan, D. B. (2006). Comparison of stimulation patterns for FES-cycling using measures of oxygen cost and stimulation cost. *Medical Engineering & Physics*, 28(7), 710–718. <https://doi.org/10.1016/j.medengphy.2005.10.006>
- Hunt, K. J., Hosmann, D., Grob, M., & Saengsuwan, J. (2013). Metabolic efficiency of volitional and electrically stimulated cycling in able-bodied subjects. *Medical Engineering & Physics*, 35(7), 919–925. <https://doi.org/10.1016/j.medengphy.2012.08.023>
- Hunt, K. J., Saunders, B. A., Perret, C., Berry, H., Allan, D. B., Donaldson, N., & Kakebeeke, T. H. (2007). Energetics of paraplegic cycling: A new theoretical framework and efficiency characterisation for untrained subjects. *European Journal of Applied Physiology*, 101, 277–285. <https://doi.org/10.1007/s00421-007-0497-5>
- Ibitoye, M. O., Estigoni, E. H., Nur Azah Hamzaid, Ahmad Khairi Abdul Wahab, & Davis, G. M. (2014). The effectiveness of FES-evoked EMG potentials to assess muscle force and fatigue in individuals with spinal cord injury. *Sensors*, 14(7), 12598–12622. <https://doi.org/10.3390/s140712598>
- Ibitoye, M. O., Nur Azah Hamzaid, Nazirah Hasnan, Ahmad Khairi Abdul Wahab, Islam, M. A., Kean, V. S. P., & Davis, G. M. (2016). Torque and mechanomyogram relationships during electrically-evoked isometric quadriceps contractions in persons with spinal cord injury. *Medical Engineering and Physics*, 38(8), 767–775. <https://doi.org/10.1016/j.medengphy.2016.05.012>

- Islam, M. A., Nur Azah Hamzaid, Ibitoye, M. O., Nazirah Hasnan, Ahmad Khairi Abdul Wahab, & Davis, G. M. (2018). Mechanomyography responses characterize altered muscle function during electrical stimulation-evoked cycling in individuals with spinal cord injury. *Clinical Biomechanics*, *58*, 21–27. <https://doi.org/10.1016/j.clinbiomech.2018.06.020>
- Islam, M. A., Sundaraj, K., Ahmad, R. B., & Ahamed, N. U. (2013). Mechanomyogram for muscle function assessment: A review. *PLoS ONE*, *8*(3), e58902. <https://doi.org/10.1371/journal.pone.0058902>
- Jafari, E., & Erfanian, A. (2022). A distributed automatic control framework for simultaneous control of torque and cadence in functional electrical stimulation cycling. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, *30*, 1908–1919. <https://doi.org/10.1109/TNSRE.2022.3188735>
- Janssen, T. W. J., & Pringle, D. D. (2008). Effects of modified electrical stimulation-induced leg cycle ergometer training for individuals with spinal cord injury. *Journal of Rehabilitation Research & Development*, *45*(6), 819–830. <https://doi.org/10.1682/JRRD.2007.09.0153>
- Johnston, T. E., Marino, R. J., Oleson, C. V., Schmidt-Read, M., Leiby, B. E., Sendeki, J., ... Modlesky, C. M. (2016). Musculoskeletal effects of 2 functional electrical stimulation cycling paradigms conducted at different cadences for people with spinal cord injury: A pilot study. *Archives of Physical Medicine and Rehabilitation*, *97*(9), 1413–1422. <https://doi.org/10.1016/j.apmr.2015.11.014>
- Johnston, T. E., Modlesky, C. M., Betz, R. R., & Lauer, R. T. (2011). Muscle changes following cycling and/or electrical stimulation in pediatric spinal cord injury. *Archives of Physical Medicine and Rehabilitation*, *92*(12), 1937–1943. <https://doi.org/10.1016/j.apmr.2011.06.031>
- Kahn, N. N., Feldman, S. P., & Bauman, W. A. (2010). Lower-extremity functional electrical stimulation decreases platelet aggregation and blood coagulation in persons with chronic spinal cord injury: A pilot study. *Journal of Spinal Cord Medicine*, *33*(2), 150–158. <https://doi.org/10.1080/10790268.2010.11689690>
- Kasukawa, Y., Shimada, Y., Kudo, D., Saito, K., Kimura, R., Chida, S., ... Miyakoshi, N. (2022). Advanced equipment development and clinical application in neurorehabilitation for spinal cord injury: Historical perspectives and future directions. *Applied Sciences-BASEL*, *12*(9). <https://doi.org/10.3390/app12094532>
- Kaur, J. (2014). A comprehensive review on metabolic syndrome. *Cardiology Research and Practice*, *2014*, 1–21. <https://doi.org/10.1155/2014/943162>
- Kearney, R. S., Lamb, S. E., Achten, J., Parsons, N. R., & Costa, M. L. (2011). In-shoe plantar pressures within ankle-foot orthoses: Implications for the management of achilles tendon ruptures. *The American Journal of Sports Medicine*, *39*, 2679–2685. <https://doi.org/10.1177/0363546511420809>
- Kebaetse, M. B., Lee, S. C., Johnston, T. E., & Binder-Macleod, S. A. (2005). Strategies that improve paralyzed human quadriceps femoris muscle performance during repetitive, nonisometric contractions. *Archives of Physical Medicine and Rehabilitation*, *86*(12), 2311–2318. <https://doi.org/10.1016/j.apmr.2005.09.011>

- Kesar, T., Chou, L.-W., & Binder-Macleod, S. A. (2008). Effects of stimulation frequency versus pulse duration modulation on muscle fatigue. *Journal of Electromyography and Kinesiology*, 18, 662–671. <https://doi.org/10.1016/j.jelekin.2007.01.001>
- Kirshblum, S. C., Burns, S. P., Biering-Sørensen, F., Donovan, W., Graves, D. E., Jha, A., ... Waring, W. (2011). International standards for neurological classification of spinal cord injury (Revised 2011). *Journal of Spinal Cord Medicine*, 34(6), 535–546. <https://doi.org/10.1179/204577211X13207446293695>
- Koch, M., Fröhlich, M., Emrich, E., & Urhausen, A. (2013). The impact of carbon insoles in cycling on performance in the Wingate Anaerobic Test. *Journal of Science and Cycling*, 2(2), 2–5.
- Kooijman HM, Hopman MTE, Colier WNJM, Van Der Vliet JA, Oeseburg B. (1997). Near infrared spectroscopy for noninvasive assessment of claudication. *Journal of Surgical Research*, 72(1), 1–7. <https://doi.org/10.1006/jsre.1997.5164>
- Kralj, A. R., & Bajd, T. (1989). *Functional electrical stimulation: Standing and walking after spinal cord injury*. CRC Press.
- Kuhn, D., Leichtfried, V., & Schobersberger, W. (2014). Four weeks of functional electrical stimulated cycling after spinal cord injury: A clinical cohort study. *International Journal of Rehabilitation Research*, 37(3), 243–250. <https://doi.org/10.1097/MRR.0000000000000062>
- Lambach, R. L., Stafford, N. E., Kolesar, J. A., Kiratli, B. J., Creasey, G. H., Gibbons, R. S., ... Beaupre, G. S. (2020). Bone changes in the lower limbs from participation in an FES rowing exercise program implemented within two years after traumatic spinal cord injury. *Journal of Spinal Cord Medicine*, 43(3), 306–314. <https://doi.org/10.1080/10790268.2018.1544879>
- Laubacher, M., Aksöz, E. A., Bersch, I., & Hunt, K. J. (2017). The road to Cybathlon 2016-Functional electrical stimulation cycling Team IRPT SPZ. *European Journal of Translational Myology*, 27(4), 259–264. <https://doi.org/10.4081/ejtm.2017.7086>
- Laubacher, M., Aksoz, E. A., Brust, A. K., Baumberger, M., Riener, R., Binder-Macleod, S., & Hunt, K. J. (2019). Stimulation of paralysed quadriceps muscles with sequentially and spatially distributed electrodes during dynamic knee extension. *Journal of NeuroEngineering and Rehabilitation*, 16(1), 1–12. <https://doi.org/10.1186/s12984-018-0471-y>
- Laughlin, M. H. (1987). Skeletal muscle blood flow capacity: Role of muscle pump in exercise hyperemia. *American Journal of Physiology*, 253(5), H993–H1004.
- Luo, S., Xu, H., Zuo, Y., Liu, X., & All, A. H. (2020). A review of functional electrical stimulation treatment in spinal cord injury. *NeuroMolecular Medicine*, 22(4), 447–463. <https://doi.org/10.1007/s12017-019-08589-9>
- Manns, P. J., & Chad, K. E. (1999). Determining the relation between quality of life,

handicap, fitness, and physical activity for persons with spinal cord injury. *Archives of Physical Medicine and Rehabilitation*, 80, 1566–1571.

Marsden, C. D., & Merton, P. A. (1983). “Muscular wisdom” that minimizes fatigue during prolonged effort in man: Peaks rates of motoneuron discharge and slowing of discharge during fatigue. *Motor Control Mechanisms in Health and Disease*, 39, 169–211.

Martin, J. C., & Brown, N. A. T. (2009). Joint-specific power production and fatigue during maximal cycling. *Journal of Biomechanics*, 42, 474–479. <https://doi.org/10.1016/j.jbiomech.2008.11.015>

Matheson, G. O., MaffeyWard, L., Mooney, M., Ladly, K., Fung, T., & Zhang, Y. T. (1997). Vibromyography as a quantitative measure of muscle force production. *Scandinavian Journal of Rehabilitation Medicine*, 29(1), 29–35.

Matsunaga, T., Shimada, Y., & Sato, K. (1999). Muscle fatigue from intermittent stimulation with low and high frequency electrical pulses. *Archives of Physical Medicine and Rehabilitation*, 80, 48–53. [https://doi.org/10.1016/S0003-9993\(99\)90306-4](https://doi.org/10.1016/S0003-9993(99)90306-4)

Maynard, F. M., Bracken, M. B., Creasey, G., Ditunno, J. F., Donovan, W. H., Ducker, T. B., ... Young, W. (1997). International standards for neurological and functional classification of spinal cord injury. *Spinal Cord*, 35, 266–274. <https://doi.org/10.1038/sj.sc.3100432>

Mazzoleni, S., Stampacchia, G., Gerini, A., Tombini, T., & Carrozza, M. C. (2013). FES-cycling training in spinal cord injured patients. In *2013 35th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)* (pp. 5339–5341). Osaka.

McDaniel, J., Lombardo, L. M., Foglyano, K. M., Marasco, P. D., & Triolo, R. J. (2017a). Cycle training using implanted neural prostheses: Team Cleveland. *European Journal of Translational Myology*, 27(4), 289–294. <https://doi.org/10.4081/ejtm.2017.7087>

McDaniel, J., Lombardo, L. M., Foglyano, K. M., Marasco, P. D., & Triolo, R. J. (2017b). Setting the pace: Insights and advancements gained while preparing for an FES bike race. *Journal of NeuroEngineering and Rehabilitation*, 14(118). <https://doi.org/10.1186/s12984-017-0326-y>

McKinley, W. O., Jackson, A. B., Cardenas, D. D., & DeVivo, M. J. (1999). Long-term medical complications after traumatic spinal cord injury: A Regional Model Systems Analysis. *Archives of Physical Medicine and Rehabilitation*, 80(11), 1402–1410. [https://doi.org/10.1016/S0003-9993\(99\)90251-4](https://doi.org/10.1016/S0003-9993(99)90251-4)

Meng, L., Porr, B., Macleod, C. A., & Gollee, H. (2017). A functional electrical stimulation system for human walking inspired by reflexive control principles. *Proceedings of the Institution of Mechanical Engineers, Part H: Journal of Engineering in Medicine*, 231(4), 315–325. <https://doi.org/10.1177/0954411917693879>

- Metani, A., Popović-Maneski, L., Mateo, S., Lemahieu, L., & Bergeron, V. (2017). Functional electrical stimulation cycling strategies tested during preparation for the first Cyathlon competition: A practical report from team ENS de Lyon. *European Journal of Translational Myology*, 27(4), 279–288. <https://doi.org/10.4081/ejtm.2017.7110>
- Michaud, F. (2020). *Neuromusculoskeletal human multibody models for the gait of healthy and spinal-cord-injured subjects* [Doctoral thesis, University of A Coruna]. Research Gate.
- Middleton, J. W., Dayton, A., Walsh, J., Rutkowski, S. B., Leong, G., & Duong, S. (2012). Life expectancy after spinal cord injury: A 50-year study. *Spinal Cord*, 50(11), 803–811. <https://doi.org/10.1038/sc.2012.55>
- Millet GY, Muthalib M, Jubeau M, Laursen PB, Nosaka K. (2012) Severe hypoxia affects exercise performance independently of afferent feedback and peripheral fatigue. *Journal of Applied Physiology*, 112(8), 1335–44. <https://doi.org/10.1152/jappphysiol.00804.2011>
- Mizrahi, J., Levy, M., Ring, H., Isakov, E., & Liberson, A. (1994). EMG as an indicator of fatigue in isometrically FES-activated paralyzed muscles. *IEEE Transactions on Rehabilitation Engineering*, 2(2), 57–65. <https://doi.org/10.1109/86.313147>
- Muhammad Afiq Dzulkifli, Nur Azah Hamzaid, Davis, G. M., & Nazirah Hasnan. (2018). Neural network-based muscle torque estimation using mechanomyography during electrically-evoked knee extension and standing in spinal cord injury. *Frontiers in Neurorobotics*, 12. <https://doi.org/10.3389/fnbot.2018.00050>
- Muraki, S., Tsunawake, N., & Yamasaki, M. (2004). Limitation of muscle deoxygenation in the triceps during incremental arm cranking in women. *European Journal of Applied Physiology*, 91(2), 246–252. <https://doi.org/10.1007/s00421-003-0962-8>
- Myers, J., Lee, M., & Kiratli, J. (2007). Cardiovascular disease in spinal cord injury: An Overview of prevalence, risk, evaluation, and management. *American Journal of Physical Medicine & Rehabilitation*, 86(2), 142–152. <https://doi.org/10.1097/PHM.0b013e31802f0247>
- Naeem, J., Nur Azah Hamzaid, Islam, M. A., Azman, A. W., & Bijak, M. (2019). Mechanomyography-based muscle fatigue detection during electrically elicited cycling in patients with spinal cord injury. *Medical & Biological Engineering & Computing*, 57(6), 1199–1211. <https://doi.org/10.1007/s11517-019-01949-4>
- Nash, M. S. (2005). Exercise as a health-promoting activity following spinal cord injury. *Journal of Neurologic Physical Therapy*, 29(2), 87–103. <https://doi.org/10.1097/01.NPT.0000282514.94093.c6>
- Newham, D. J., & Donaldson, N. D. N. (2007). FES cycling. In D. E. Sakas, B. A. Simpson, & E. S. Krames (Eds.), *Operative Neuromodulation: Volume 1: Functional Neuroprosthetic Surgery. An Introduction* (pp. 395–402). Vienna: Springer Vienna. <https://doi.org/10.1007/978-3-211-33079-1-52>

- Ng, M. Y., Pourmajidian, M., & Nur Azah Hamzaid. (2014). Mechanomyography sensors for detection of muscle activities and fatigue during Fes-evoked contraction. *2014 IEEE 19th International Functional Electrical Stimulation Society Annual Conference, IFESS 2014 - Conference Proceedings*, 0–2. <https://doi.org/10.1109/IFESS.2014.7036759>
- Novak, D., Wolf, P., & Guglielmelli, E. (2017). Cybathlon 2016: Showcasing advances in assistive technologies through competition. *IEEE Robotics and Automation Magazine*, 24(4), 24–25, 122. <https://doi.org/10.1109/MRA.2017.2757721>
- Nur Azah Hamzaid, Pithon, K. R., Smith, R. M., & Davis, G. M. (2012). Functional electrical stimulation elliptical stepping versus cycling in spinal cord-injured individuals. *Clinical Biomechanics*, 27(7), 731–737. <https://doi.org/10.1016/j.clinbiomech.2012.03.005>
- Nurhaida Rosley, Nur Azah Hamzaid, Nazirah Hasnan, Davis, G. M., & Haidzir Manaf. (2019). Muscle size and strength benefits of functional electrical stimulation-evoked cycling dosage in spinal cord injury: A narrative review. *Sains Malaysiana*, 48(3), 607–612. <https://doi.org/10.17576/jsm-2019-4803-13>
- Nurul Salwani Mohamad Saadon, Nur Azah Hamzaid, Nazirah Hasnan, Muhammad Afiq Dzulkifli, & Davis, G. M. (2019). Electrically evoked wrist extensor muscle fatigue throughout repetitive motion as measured by mechanomyography and near-infrared spectroscopy. *Biomedical Engineering-Biomedizinische Technik*, 64(4), 439–448. <https://doi.org/10.1515/bmt-2018-0058>
- Nurul Salwani Mohamad Saadon, Nur Azah Hamzaid, Nazirah Hasnan, Muhammad Afiq Dzulkifli, Teoh, M. & Davis, G. M. (2022). Mechanomyography and tissue oxygen saturation during electrically-evoked wrist extensor fatigue in people with tetraplegia. *Artificial Organs*, 46(10), 1998–2008. <https://doi.org/10.1111/aor.14329>
- Oncu, J., Durmaz, B., & Karapolat, H. (2009). Short-term effects of aerobic exercise on functional capacity, fatigue, and quality of life in patients with post-polio syndrome. *Clinical Rehabilitation*, 23(2), 155–163. <https://doi.org/10.1177/0269215508098893>
- Orizio, C. (1993). Muscle sound: Bases for the introduction of a mechanomyographic signal in muscle studies. *Critical Reviews in Biomedical Engineering*, 21(3), 210–243.
- Orizio, C., Gobbo, M., Diemont, B., Esposito, F., & Veicsteinas, A. (2003). The surface mechanomyogram as a tool to describe the influence of fatigue on biceps brachii motor unit activation strategy. Historical basis and novel evidence. *European Journal of Applied Physiology*, 90(3–4), 326–336. <https://doi.org/https://doi.org/10.1007/s00421-003-0924-1>
- Panisset, M. G., El-Ansary, D., Dunlop, S. A., Marshall, R., Clark, J., Churilov, L., & Galea, M. P. (2022). Factors influencing thigh muscle volume change with cycling exercises in acute spinal cord injury—a secondary analysis of a randomized controlled trial. *Journal of Spinal Cord Medicine*, 45(4), 510–521. <https://doi.org/10.1080/10790268.2020.1815480>

- Perkins, T. A., Donaldson, N. D. N., Hatcher, N. A. C., Swain, I. D., & Wood, D. E. (2002). Control of leg-powered paraplegic cycling using stimulation of the lumbosacral anterior spinal nerve roots. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, *10*(3), 158–164. <https://doi.org/10.1109/TNSRE.2002.802860>
- Pette, D., & Vrbová, G. (1992). Adaptation of mammalian skeletal muscle fibers to chronic electrical stimulation. *Reviews of Physiology, Biochemistry and Pharmacology*, *120*(May), 115–202. <https://doi.org/10.1007/BFb0036123>
- Phillips, W. T., Kiratli, B. J., Sarkarati, M., Weraarchakul, G., Myers, J., Franklin, B. A., ... Froelicher, V. (1998). Effect of spinal cord injury on the heart and cardiovascular fitness. *Current Problems in Cardiology*, *23*(11), 649–716. [https://doi.org/10.1016/S0146-2806\(98\)80003-0](https://doi.org/10.1016/S0146-2806(98)80003-0)
- Pierson-carey, C. D., Brown, D. A., & Dairaghi, C. A. (1997). Changes in resultant pedal reaction forces due to ankle immobilization during pedaling. *Journal of Applied Biomechanics*, *13*, 334–346.
- Pincivero, D. M., Gear, W. S., & Sterner, R. L. (2001). Assessment of the reliability of high-intensity quadriceps femoris muscle fatigue. *Medicine and Science in Sports and Exercise*, *33*(2), 334–338. <https://doi.org/10.1097/00005768-200102000-00025>
- Pollack, S. F., Axen, K., Spielholz, N., Levin, N., Haas, F., & Ragnarsson, K. T. (1989). Aerobic training effects of electrically induced lower extremity exercises in spinal cord injured people. *Archives of Physical Medicine and Rehabilitation*, *70*, 214–219.
- Popovic-Maneski, L., Aleksic, A., Metani, A., Bergeron, V., Cobeljic, R., & Popovic, D. B. (2018). Assessment of spasticity by a pendulum test in SCI patients who exercise FES cycling or receive only conventional therapy. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, *26*(1), 181–187. <https://doi.org/10.1109/TNSRE.2017.2771466>
- Popović, D. B. (2014). Advances in functional electrical stimulation (FES). *Journal of Electromyography and Kinesiology*, *24*(6), 795–802. <https://doi.org/10.1016/J.JELEKIN.2014.09.008>
- Popović, D. B., Sinkjær, T., & Popović, M. B. (2009). Electrical stimulation as a means for achieving recovery of function in stroke patients. *NeuroRehabilitation*, *25*(1), 45–58. <https://doi.org/10.3233/NRE-2009-0498>
- Popovic, M. R., Curt, A., Keller, T., & Dietz, V. (2001). Functional electrical stimulation for grasping and walking: Indications and limitations. *Spinal Cord*, *39*, 403–412. <https://doi.org/10.1038/sj.sc.3101191>
- Praagman, M., Veeger, H. E. J., Chadwick, E. K. J., Colier, W. N. J. M., & van der Helm, F. C. T. (2003). Muscle oxygen consumption, determined by NIRS, in relation to external force and EMG. *Journal of Biomechanics*, *36*(7), 905–912. [https://doi.org/10.1016/S0021-9290\(03\)00081-2](https://doi.org/10.1016/S0021-9290(03)00081-2)

- Ramon-Cueto, A., Cordero, M. I., Santos-Benito, F. F., & Avila, J. (2000). Functional recovery of paraplegic rats and motor axon regeneration in their spinal cords by olfactory ensheathing glia. *Neuron*, 25, 425–435. <https://doi.org/10.1016/j.ridd.2010.07.022>
- Raymond, J., Davis, G. M., & van der Plas, M. (2002). Cardiovascular responses during submaximal electrical stimulation-induced leg cycling in individuals with paraplegia. *Clinical Physiology and Functional Imaging*, 22(2), 92–98. <https://doi.org/10.1046/j.1365-2281.2002.00386.x>
- Reid, K. F., Storer, T. W., Pencina, K. M., Valderrabano, R., Latham, N. K., Wilson, L., ... Bhasin, S. (2022). A multimodality intervention to improve musculoskeletal health, function, metabolism, and well-being in spinal cord injury: Study protocol for the FIT-SCI randomized controlled trial. *BMC Musculoskeletal Disorders*, 23(1). <https://doi.org/10.1186/s12891-022-05441-3>
- Reinkensmeyer, D. J. (2019). JNER at 15 years: Analysis of the state of neuroengineering and rehabilitation. *Journal of NeuroEngineering and Rehabilitation*, 16, 144. <https://doi.org/10.1186/s12984-019-0610-0>
- Riener, R. (2016). The Cybathlon promotes the development of assistive technology for people with physical disabilities. *Journal of NeuroEngineering and Rehabilitation*, 13(49). <https://doi.org/10.1186/s12984-016-0157-2>
- Rohde, L. M., Bonder, B. R., & Triolo, R. J. (2012). Exploratory study of perceived quality of life with implanted standing neuroprostheses. *Journal of Rehabilitation Research and Development*, 49(2), 265–278. <https://doi.org/10.1038/ncomms7768>. Prion-like
- Roy, R. R., Baldwin, K. M., & Edgerton, V. R. (1991). The plasticity of skeletal muscle: Effects of neuromuscular activity. *Exercise and Sport Sciences Reviews*, 19(1), 269–312.
- Sayli, O., Akin, A., & Cotuk, H. B. (2014). Correlation analysis between surface electromyography and continuous-wave near-infrared spectroscopy parameters during isometric exercise to volitional. *Turkish Journal of Electrical Engineering & Computer Sciences*, 22(3), 780–793. <https://doi.org/10.3906/elk-1210-51>
- Schauer, T. (2006). *Feedback control of cycling in spinal cord injury using functional electrical stimulation* [Doctoral dissertation, Glasgow University]. Research Gate.
- Schauer, T. (2017). Sensing motion and muscle activity for feedback control of functional electrical stimulation: Ten years of experience in Berlin. *Annual Reviews in Control*, 44, 355–374. <https://doi.org/10.1016/j.arcontrol.2017.09.014>
- Schmoll, M., Le Guillou, R., Fattal, C., & Coste, C. A. (2022). OIDA: An optimal interval detection algorithm for automatized determination of stimulation patterns for FES-Cycling in individuals with SCI. *Journal of NeuroEngineering and Rehabilitation*, 19(1). <https://doi.org/10.1186/s12984-022-01018-2>
- Schwab, M. E. (2002). Repairing the injured spinal cord. *Science*, 295, 1029–1031. <https://doi.org/10.1126/science.1067840>

- Sheffler L. R. & Chae J. (2007). Neuromuscular electrical stimulation in neurorehabilitation. *Muscle Nerve*, 35(5), 562-90. doi: 10.1002/mus.20758.
- Shi, Y. X., Tian, J. H., Yang, K. H., & Zhao, Y. (2011). Modified constraint-induced movement therapy versus traditional rehabilitation in patients with upper-extremity dysfunction after stroke: A systematic review and meta-analysis. *Archives of Physical Medicine and Rehabilitation*, 92(6), 972–982. <https://doi.org/10.1016/j.apmr.2010.12.036>
- Sijobert, B., Fattal, C., Daubigney, A., & Azevedo-Coste, C. (2017). Participation to the first Cybathlon: An overview of the FREEWHEELS team FES-cycling solution. *European Journal of Translational Myology*, 27(4), 265–271. <https://doi.org/10.4081/ejtm.2017.7120>
- Sijobert, B., Le Guillou, R., Fattal, C., & Azevedo Coste, C. (2019). FES-induced cycling in complete SCI: A simpler control method based on inertial sensors. *Sensors (Switzerland)*, 19, 4268. <https://doi.org/10.3390/s19194268>
- Sinclair, P. J., Davis, G. M., Smith, R. M., Cheam, B. S., & Sutton, J. R. (1996). Pedal forces produced during neuromuscular electrical stimulation cycling in paraplegics. *Clinical Biomechanics*, 11(1), 51–57. [https://doi.org/10.1016/0268-0033\(95\)00030-5](https://doi.org/10.1016/0268-0033(95)00030-5)
- Singh, A., Tetreault, L., Kalsi-Ryan, S., Nouri, A., & Fehlings, M. G. (2014). Global prevalence and incidence of traumatic spinal cord injury, 309–331.
- Skold, C., Lonn, L., Harms-Ringdahl, K., Hultling, C., Levi, R., Nash, M., & Seiger, A. (2002). Effects of functional electrical stimulation training for six months on body composition and spasticity in motor complete tetraplegic spinal cord-injured individuals. *Journal of Rehabilitation Medicine*, 34(1), 25–32. <https://doi.org/10.1080/165019702317242677>
- Stein, R. B., Gordon, T., Jefferson, J., Sharfenberger, A., Yang, J. F., De Zepetnek, J. T., & Belanger, M. (1992). Optimal stimulation of paralyzed muscle after human spinal cord injury. *Journal of Applied Physiology*, 72(4), 1393–1400.
- Szecszi, J., Krause, P., Krafczyk, S., Brandt, T., & Straube, A. (2007). Functional output improvement in FES cycling by means of forced smooth pedaling. *Medicine and Science in Sports and Exercise*, 39(5), 764–780. <https://doi.org/10.1249/mss.0b013e3180334966>
- Szecszi, J., Straube, A., & Fornusek, C. (2014a). A biomechanical cause of low power production during FES cycling of subjects with SCI. *Journal of Neuroengineering and Rehabilitation*, 11(1), 123. <https://doi.org/10.1186/1743-0003-11-123>
- Szecszi, J., Straube, A., & Fornusek, C. (2014b). Leg general muscle moment and power patterns in able-bodied subjects during recumbent cycle ergometry with ankle immobilization. *Medical Engineering & Physics*, 36(11), 1421–1427. <https://doi.org/10.1016/j.medengphy.2014.05.010>
- Takaishi, T., Ono, T., & Yasuda, Y. (1992). Relationship between muscle fatigue and oxygen uptake during cycle ergometer exercise with different ramp slope

- increments. *European Journal of Applied Physiology and Occupational Physiology*, 65(4), 335–339. <https://doi.org/10.1007/BF00868137>
- Talmadge, R. J., Castro, M. J., Apple, D. F. J., & Dudley, G. A. (2002). Phenotypic adaptations in human muscle fibers 6 and 24 wk after spinal cord injury. *Journal of Applied Physiology*, 92(1), 147–154. <https://doi.org/10.1152/jappphysiol.000247.2001>
- Tarata, M. T. (2003). Mechanomyography versus electromyography, in monitoring the muscular fatigue. *BioMedical Engineering OnLine*, 2(3). <https://doi.org/10.1016/j.archoralbio.2016.03.002>
- Taylor, M. J., Schils, S., & Ruys, A. J. (2019). Home FES: An Exploratory Review. *European Journal of Translational Myology*, 29(4), 283–292. <https://doi.org/10.4081/ejtm.2019.8285>
- Theisen, D., Fornusek, C., Raymond, J., & Davis, G. M. (2002). External power output changes during prolonged cycling with electrical stimulation. *Journal of Rehabilitation Medicine*, 34, 171–175. <https://doi.org/10.1080/16501970213238>
- Tong, R. K. Y., Wang, X., Leung, K. W. C., Lee, G. T. Y., Lau, C. C. Y., Wai, H. W., ... Leung, H. C. (2017). How to prepare a person with complete spinal cord injury to use surface electrodes for FES trike cycling. In *2017 International Conference on Rehabilitation Robotics (ICORR)* (pp. 801–805). London: IEEE. <https://doi.org/10.1109/ICORR.2017.8009346>
- Topp, R., Ditmyer, M., King, K., Doherty, K., & Hornyak, J. (2002). The effect of bed rest and potential of prehabilitation on patients in the intensive care unit. *AACN Clinical Issues*, 13(2), 263–276. <https://doi.org/10.1097/00044067-200205000-00011>
- Trumbower, R. D. & Faghri, P. D. (2005). Kinematic analyses of semireclined leg cycling in able-bodied and spinal cord injured individuals. *Spinal Cord* 43, 543–549. <https://doi.org/10.1038/sj.sc.3101756>
- Uddin, R., & Nur Azah Hamzaid. (2014). A study protocol to compare between two configurations of multi-pad electrode array for functional electrical stimulation-evoked cycling among paraplegics. In *2014 IEEE 19th International Functional Electrical Stimulation Society Annual Conference (IFESS)*. Kuala Lumpur. <https://doi.org/10.1109/IFESS.2014.7036756>
- van Beekvelt MCP, van Engelen BG, Wevers RA, Colier WNJM. (2002). In vivo quantitative near-infrared spectroscopy in skeletal muscle and bone during rest and isometric exercise. *Clinical Physiology and Functional Imaging*, 22(3), 210–7. <https://doi.org/10.1117/12.499818>
- van der Scheer, J. W., Goosey-Tolfrey, V. L., Valentino, S. E., Davis, G. M., & Ho, C. H. (2021). Functional electrical stimulation cycling exercise after spinal cord injury: A systematic review of health and fitness-related outcomes. *Journal of NeuroEngineering and Rehabilitation*, 18(1). <https://doi.org/10.1186/s12984-021-00882-8>

- van Dieën, J. H., Westebring-van der Putten, E. P., Kingma, I., & de Looze, M. P. (2009). Low-level activity of the trunk extensor muscles causes electromyographic manifestations of fatigue in absence of decreased oxygenation. *Journal of Electromyography and Kinesiology*, 19(3), 398–406. <https://doi.org/10.1016/j.jelekin.2007.11.010>
- van Soest, A. J., Gföhler, M., & Richard Casius, L. J. (2005). Consequences of ankle joint fixation on FES cycling power output: A simulation study. *Medicine & Science in Sports & Exercise*, 37(5), 797–806. <https://doi.org/10.1249/01.MSS.0000161802.52243.95>
- Watanabe, T., & Tadano, T. (2018). Experimental tests of a prototype of IMU-based closed-loop fuzzy control system for mobile FES cycling with pedaling wheelchair. *IEICE Transactions on Information and Systems*, E101D(7), 1906–1914. <https://doi.org/10.1587/transinf.2017EDP7299>
- Wiesener, C., Ruppin, S., & Schauer, T. (2016). Robust discrimination of flexion and extension phases for mobile functional electrical stimulation (FES) induced cycling in paraplegics. *International Federation of Automatic Control (IFAC)-PapersOnLine*, 49(32), 210–215. <https://doi.org/10.1016/j.ifacol.2016.12.216>
- Wiesener, C., & Schauer, T. (2017). The Cybathlon RehaBike inertial-sensor-driven functional electrical stimulation cycling by team Hasomed. *IEEE Robotics & Automation Magazine*, 24(4), 49–57. <https://doi.org/10.1109/MRA.2017.2749318>
- Wilder, R. P., Jones, E. V., Wind, T. C., & Edlich, R. F. (2002). Functional electrical stimulation cycle ergometer exercise for spinal cord injured patients. *Journal of Long-Term Effects of Medical Implants*, 12(3), 161–174.
- Williams, R., & Murray, A. (2015). Prevalence of depression after spinal cord injury: A meta-analysis. *Archives of Physical Medicine and Rehabilitation*, 96(1), 133–140. <https://doi.org/10.1016/j.apmr.2014.08.016>
- Wilson, J. R., Cadotte, D. W., & Fehlings, M. G. (2012). Clinical predictors of neurological outcome, functional status, and survival after traumatic spinal cord injury: A systematic review. *Journal of Neurosurgery: Spine*, 17(1), 11–26. <https://doi.org/10.3171/2012.4.AOSPINE1245>
- Winter, D. A. (1991). *Biomechanics and motor control of human gait: Normal, elderly and pathological*. Ontario: University of Waterloo Press.
- Wolf, P., & Riener, R. (2018). Cybathlon: How to promote the development of assistive technologies. *Science Robotics*, 3(17), eaat7174. <https://doi.org/10.1126/scirobotics.aat7174>
- Yoshitake, Y., Ue, H., Miyazaki, M., & Moritani, T. (2001). Assessment of lower-back muscle fatigue using electromyography, mechanomyography, and near-infrared spectroscopy. *European Journal of Applied Physiology*, 84(3), 174–179. <https://doi.org/10.1007/s004210170001>
- Zbogar, D., Eng, J. J., Krassioukov, A. V., Scott, J. M., Esch, B. T. A., & Warburton, D. E. R. (2008). The effects of functional electrical stimulation leg cycle ergometry

training on arterial compliance in individuals with spinal cord injury. *Spinal Cord*, 46(11), 722–726. <https://doi.org/10.1038/sc.2008.34>

Zoulias, I. D., Armengol, M., Poulton, A., Andrews, B., Gibbons, R., Harwin, W. S., & Holderbaum, W. (2019). Novel instrumented frame for standing exercising of users with complete spinal cord injuries. *Scientific Reports*, 9. <https://doi.org/10.1038/s41598-019-49237-3>

Universiti Malaya