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TITLE: Skeletal Muscle Hypertrophy and Cardiometabolic Benefits after Spinal Cord Injury

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14. ABSTRACT

Spinal cord injury is a devastating medical condition that increases one's risk for reduced aerobic fitness, glucose intolerance and insulin resistance due to increased body fat and relative inactivity. The purpose is to determine the impact of 12+12 weeks of NMES+FES-LEC on oxygen uptake, insulin sensitivity, glucose uptake, anabolic profile(Testosterone and IGF-1), basal metabolic rate (BMR). Four participants have completed the trial so far, two from the 12+12 weeks NMES+FES group and two from the 12+12 weeks control + FES group. Our preliminary data suggests that 12 weeks of NMES-induced resistance training prior to 12 weeks of FES improves metabolic profile, increases muscle size, and prevents an increase in leg fat mass. The NMES+FES group had a 13% increase in basal metabolic rate (BMR), while control+FES had a 13% decrease in BMR. Both groups experienced increased thigh muscle size with 24 weeks of training (~8% for whole thigh and11% for knee extensors). Body composition analysis revealed that NMES +FES prevented the 13% increase in leg fat mass experienced by the control +FES

15. SUBJECT TERMS

RESISTANCE TRAINING, SPINAL CORD INJURY, BODY COMPOSITION AND METABOLISM, FUNCTIONAL ELECTERICAL STIMULATION, IMMUNIOCHEMISTRY, SKELETAL MUSCLES, INFLAMMATORY BIOMARKERS, DUAL ENERGEY X-RAY

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1. **INTRODUCTION:**

Forty eight participants will be randomly assigned into neuromuscular electrical stimulation+ functional electrical stimulation (NMES+FES) or control (passive movement) + FES groups (PM+FES) for 24 weeks (see Appendix 1). The participants will be matched for level of injury and time since injury. Randomization will be conducted prior to the two-day assessment period using n-query computer program (baseline). The NMES+FES group will undergo 12 weeks of supervised unilateral progressive resistance training (RT) twice weekly using surface NMES and ankle weights and followed by 12 weeks twice weekly of progressive FES-LEC **(RT+FES)**. The control + FES group will participate for the first 12 weeks of passive movement without NMES and followed by 12 week twice weekly of progressive FES-LEC **(PM+FES)**. During the 12 week period for the control + FES group, participants will be asked to report to the laboratory twice weekly and will undergo 4 sets of 10 repetitions of passive knee extension and flexion. This will allow balancing the design and account for any interaction between NMES+FES and control + FES groups by having equal study visits and highlighting the significance of muscle hypertrophy on the metabolic health. Following the initial 12 weeks, both groups will undergo a two day assessment period using the same sequence outlined in baseline (post-intervention 1). This will be followed by 12 weeks in which both groups will undergo supervised progressive FES-LEC twice weekly with the goal of 30 minutes of training at the end of each session followed by a two day assessment period using the sequence described for baseline (post-intervention 2). All participants will undergo a physical activity questionnaire at baseline, post-intervention 1 and post-intervention 2.

Study aims:

Aim #1: To determine the impact of 12+12 weeks of NMES+FES-LEC on oxygen uptake, insulin sensitivity and glucose uptake in adults with SCI compared to control + FES-LEC.

Aim 1a: To determine the impact of 12+12 weeks of NMES+ FES-LEC on anabolic profile (Testosterone and IGF-1) and basal metabolic rate (BMR)

Aim 1b: To determine the impact of 12+12 weeks of NMES+ FES-LEC on inflammatory biomarkers (IL-6, CRP, TNF-alpha)

Aim #2: To determine the impact of 12+12 weeks of NMES+FES-LEC on skeletal muscle size, infiltration of intramuscular fat, visceral adiposity as well as fatigue resistance compared to control+ FES-LEC.

Aim 2a To determine the impact of 12+12 weeks of NMES+ FES-LEC on regional, total body composition and anthropometrics measurements compared to control+ FES-LEC.

Aim #3 (transitional exploratory aim): To determine the impact of 12+12 weeks of NMES+FES-LEC on determinants of energy metabolism, protein molecules involved in insulin signaling, muscle hypertrophy and oxygen uptake (IRS-1, AMPK, GLUT-4, IGF-1, Akt, mTOR and PGC-1 alpha) and electron transport chain proteins compared to control + FES-LEC only.
Aim 3a: To determine the effect of NMES-RT+FES-LEC on intracellular signaling supporting muscle hypertrophy (phosphorylated of Akt, AMPK, mTOR).

1. **KEYWORDS:** RESISTANCE TRAINING, SPINAL CORD INJURY, BODY COMPOSITION AND METABOLISM, FUNCTIONAL ELECTERICAL STIMULATION, IMMUNIOCHEMISTRY, SKELETAL MUSCLES, INFLAMMATORY BIOMARKERS, DUAL ENERGEY X-RAY ABSORPTIMETRY (DXA), MAGNATIC RESONANCE IMAGING (MRI), NEUROMUSCLUAR ELECTERICAL STIMUALTION

2. **ACCOMPLISHMENTS:**

What were the major goals of the project?

	Timeline (Months)
Major Task 1: Adapt Research Protocol for RICVAMC, VCU, BVAMC	
Subtask 1: Prepare Regulatory Documents and Research Protocol for Study	
Coordinate with Sites for material transfer agreements (MTAs) or clinical trial agreements (CTAs) submission/ Develop a study operating manual for all study procedures	1-4
Coordinate with Sites for nondisclosure agreements (NDAs).	1-4
Refine eligibility criteria, exclusion criteria, screening protocol	1-4
Finalize consent form & human subjects protocol/ Coordinate with Sites for IRB protocol submission	1-4
Submit for Human Research Protection Office (HRPO) Approval	4-6
Coordinate with Sites for annual IRB report for continuing review	Annually
Milestone Achieved: Local IRB approval at RIVAMC, VCU, BVAMC	4
Subtask 2: Refine research protocol and finalize research data collection sheets	4
Coordinate with sites for flow chart for all study steps	5
Major Task 2: Coordinate Study Research Staff and Purchase Equipment	

Subtask1: Hiring and Training of Study Staff	
Coordinate with Sites for job descriptions design	1-2
Advertise and interview for project related staff	2-4
Coordinate for space allocation for new staff	4
Hire 2 Research scientists + 2 Research coordinators + 2 laboratory technicians+1 Research technician	4-5
Training of Research staff using the study operating manual	4-6
Subtask 2: Purchase 3 NMES units+3 FES Bikes and Supplies	
Major Task 3: Participant Recruitment, Therapy, Participant Evaluation	
Subtask 1: Recruitment and Block Randomization of 4 patients per site (n=8)/ (n=8)/(n=8)/(n=8)/(n=8)/(n=8)	6-12 **/**12-18**/** 18-24**/** 24-30/ 30-36 /36-42
Milestone Achieved: screened ,enrolled, trained and test 48 participants	
Major Task 4: Data management, data analysis and final report	
Subtask 1: Data Analysis for Electron Transport Chain (ETC) and molecular protein expression	
Data analysis for the 8 participants/ 8 participants/8 participants/8participants/8 participants/8 Participants	12-15/ 18-21/ 24-27/ 30-33/ 36-39/ 42-45
Milestone Achieved: Data analysis completed for cellular aspects	45
Subtask 2: Coordinate with sites for data collection and database requirements	42-44
Finalize assessment measurements	44-46
Milestone Achieved: Final Report findings from the study	45-46

What was accomplished under these goals?

In the first year of the study, we managed to enroll and retain 7 participants out of total out of the proposed 8 participants (87.5%). The baseline demographics are presented in the following table.

Table 1. Physical characteristics at baseline for participants with motor complete SCI that were assigned to either RT+FES or PM+FES groups.

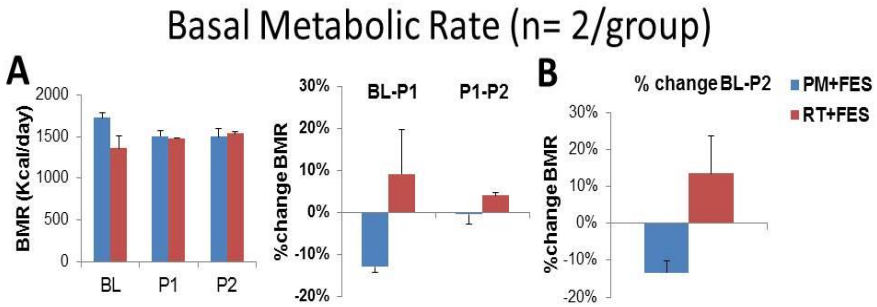
	RT+FES (n=4)					**PM+FES (N=3**)				
ASIA	Age	Weight (kg)	BMI (kg/m 2)	LOI	TSI (yrs)	Age	Weig ht (kg)	BMI (kg/m 2)	LOI	TSI (yrs)
1	34	68.1	20.5	T12	1.5	48	95.2	28.4	T4	17
2	50	73.4	30.0	T3	29	61	75.2	22.6	L1	34
3	53	89.7	28.0	C6	26	25	60.6	19.9	C8	2
4	41	59.3	20.0	T4	25					
Average	44.5	72.6	24.6	1C6 :3T 3-T12	20.4	44.7	77.0	23.6	1C8 :1T4 : 1L1	17.7
SD	8.7	12.8	5.0		12.7	18.2	17.4	4.3		16.0

*LOI: Level of Injury
*TSI: Time Since Injury
*ASIA: American Spinal Injury Association Impairment Scale

Results: We have currently trained and finished data collection on 4 participants. The three other participants are still at different stages of the study. For simplicity purpose, we have decided to present results on 2 individuals who underwent 12 weeks of passive movement followed by 12 weeks of functional electrical stimulation-induced cycling (PM+FES) and 2 individuals who underwent 12 weeks of NMES-induced resistance training (RT) prior to 12 weeks of FES (RT+FES).
It should be noted that these are preliminary results and unlikely to be used to reach a final conclusion.

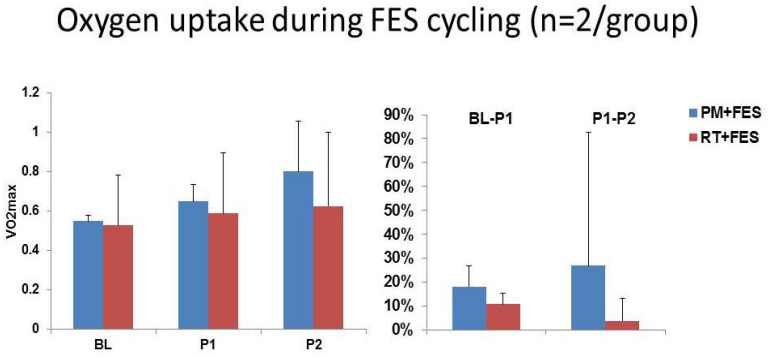
A. Metabolic Profile

1. <u>Basal metabolic rate (BMR)-</u> **Figure 1**



There was 9% increase in BMR after 12 weeks of RT (red bars). In contrast, the average BMR of individuals that received 12 weeks of PM decreased by 13% (blue bars). 12 weeks of FES cycling following 12 weeks of RT resulted in a further 4% increase in BMR, while the PM+FES group had a no change. B) Over the 24 weeks of training the BMR in the RT+FES group increased by 13% while the PM+FES group decreased by 13%. This suggests that RT prior to FES is beneficial to the BMR of individuals with SCI. BL, baseline; P1, post-intervention 1 after 12 weeks of RT or PM; P2, post-intervention 2 after 12 weeks of FES. Values are mean ± SD.

2. <u>Oxygen uptake during maximal exercise test using FES-cycling –</u> **Figure 2**

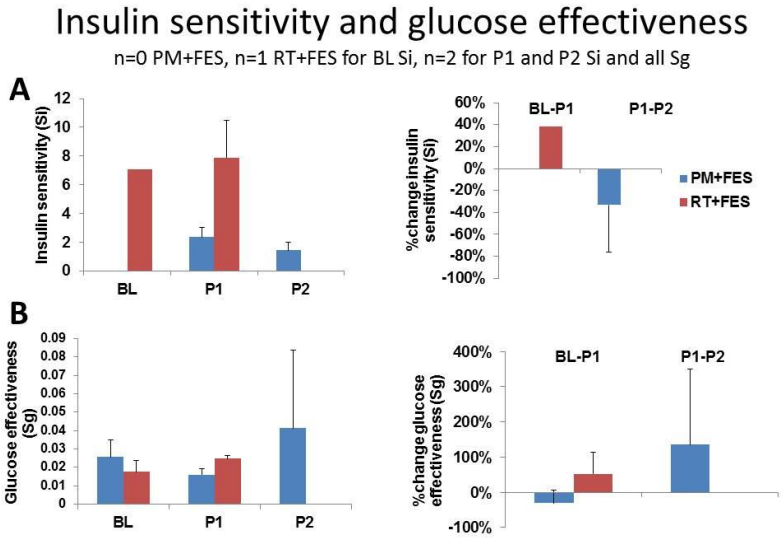


Increasing resistance with the bike motor off resulted in increased VO_2 in individuals with spinal cord injury. After 12 weeks of RT, both participants were able to cycling against higher resistance. However, changes in oxygen uptake with training were highly variable. Table 2 presents the progression in resistance during oxygen uptake measurement using FES-LEC.

Table 2. Progression of resistance of FES-LEC during oxygen uptake measurement in both groups.

Group	Subject	BL	P1	P2
PM+FES	001-10123	7	5	5
	002-10187	3	3	5
RT+FES	003-10122	5	9	13
	004-10006	3	3	5

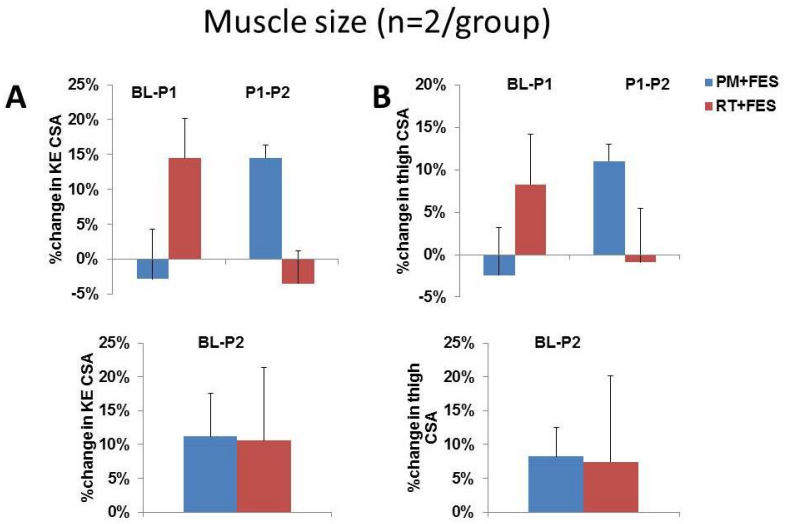
3. <u>Insulin sensitivity and glucose effectiveness –</u> **Figure 3**



For the **RT+FES**, after 12 weeks of RT one participant had a 38% increases in Si. There is also 52% increase after 12 weeks following RT. We are still waiting on P2 data for both participants in the RT+FES group. For the **PM+FES**, after 12 weeks of FES One individual who completed 12 weeks of FES cycling following 12 weeks of PM had no change in Si, while the other had a 37% decrease. There was a 31% decrease in Sg after 12 weeks of PM. Effects of 12 weeks of FES cycling following PM were variable, with a 17% decrease in 1 participant and a 3.87 fold increase in another. Values are average ± SD.

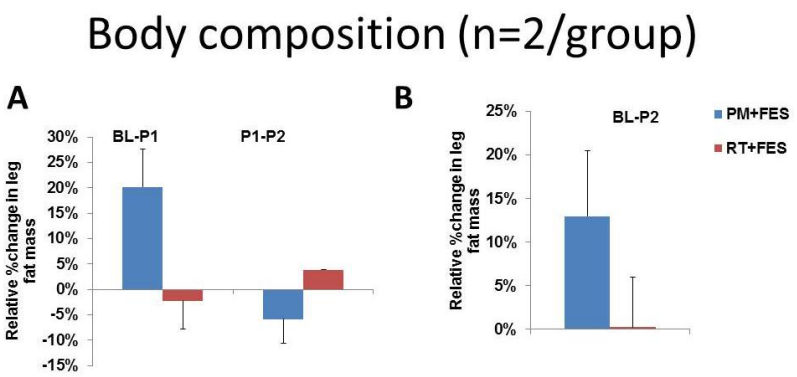
B. Body Composition

4. Muscle size – **Figure 4**



Twelve weeks of PM had little effect on muscle size. In contrast, 12 weeks of RT resulted in a 14% increase in knee extensor (KE) cross sectional area (CSA). 12 weeks of FES cycling following 12 weeks of PM increased KE CSA by 15%, however there was no change in KE CSA in the RT+FES group. Interestingly, over 24 weeks, the PM+FES group had similar overall KE CSA increases as the RT+FES group and similar results were found with whole thigh CSA.

5. Body composition – **Figure 5**



Twelve weeks of RT prevented the increase in leg FM experienced by the PM group. There was little effect of FES on leg FM. Over the 24 weeks, the PM+FES group had a 13% increase in leg FM while the RT+FES group experienced no change.

ii. **Major activities:**

a. Coordinated with Virginia Commonwealth University and Bronx VA Medical Center for clinical trial agreement (CTAs). **20-07-2015**

b. Coordinated with Virginia Commonwealth University and Bronx VA Medical Center for nondisclosure agreements (NDAs). **11-08-2015**

c. Refined study protocol including inclusion/exclusion criteria, research data collection sheet **-10-07-2015**

d. Finalized consent form and human subject protocol: RICVAMC: **25-11-2015**,
VCU: **22-12-2015**.

e. Coordinate with sites for flow chart for all study steps: **20-07-2015**

f. Submitted for Human Research Protection Office (HRPO) Approval. **31-10-2015**.

g. Local IRB Approvals for the three sites had be issued as follows: RICVAMC: **17-09-2015**, VCU: **27-10-2015**, BVAMC: **29-10-2015**.

h. Developing study operating manual and forms for all study procedures. **Completed by: 30-11-2015.**

i. Coordinated with sites for job descriptions for hiring and training study staff. **12-10-2015**

j. Advertised for the study related opening position. **19-10-2015**.

k. Interviewed study related staff:
-Research Scientist: **06-11-2015**
-Research Technician: **30-10-2015**

l. Coordinated space allocation for the new staff. **01-11-2015**.

m. Hired:
   a) 1 Research Scientist, Laura O'Brien, PhD: **04-01-2016**.

b) 2 Research Coordinators, Refka Khalil, DC: RICVAMC Research Coordinator: **05-10-2015**.
Alison Molitor: VCU Research Coordinator: **17-11- 2015**.

c) 1 Research Technician, Rodney Wade, BS: **11-01-2016**.

n. Training Research staff using the study operating manual:
1. Trained VCU Research Coordinator, Alison Molitor: **14-12-2015** and **11-01-2016**.
2. Trained Research Scientist, Laura O'Brien, PhD: **04-01-2016-08-01-2016** and **13-01-2016**.
3. Trained RICVAMC Research Coordinator, Refka Khalil, DC: **13-01-2016**
4. Trained Research Technician, Rodney Wade, BS: He has been a student research intern in lab since **19-05-2015**. Rodney has been getting trained since **19-05-2015-07-12-2015.**

o. Purchased 2 NMES units **26-10-2015**.

p. Purchased 2 FES Bikes: **24-11-2015**.

q. HRPO Approval for RICVAMC: **18-12-2015**.

r. HRPO Approval for VCU: **29-12-2015**.

s. HRPO concurrence memorandum for Bronx VA Medical Center: **29-12-2015**.

t. Working with Dr. Edward Lesnefsky, MD and Dr. Laura O'Brien, PhD to finalize the Electron Transport Chain protocol since **01-12-2015**.

u. Working with Dr. Christopher Cardozo, MD at the Bronx VA Medical Center to finalize the Western Blot protocol for protein analysis since **15-10-2015**.

v. Sub-award agreement was completed to VCU and was submitted back in **10-2015** and we are waiting for final approval.

w. The Service Agreement was submitted to the Clinical Research Unit at the VCU Medical Center: 1/20/2016.

x. Staff training for the RTI FES Bike: 2/3/2016 and 2/4/2016. The training was performed according to the protocol. Individuals who were present:
1) Ashraf Gorgey, MPT, PhD
2) Refka Khalil, DC
3) Laura O'Brien, PhD
4) Rodney Wade, BS

y. Kick-off meeting to introduce all study staff and orient them to the study operating manual (SOP):2/8/2016

z. ***First monthly*** meeting with Dr. William Carter, MD (VCU-PI) and Alison Molitor (VCU Site Research Coordinator): 2/5/2016. Meeting agenda was to discuss the process of screening, recruiting participants, and the use of the paper forms.

aa. The Service Agreement was submitted for the VCUHS Clinical Pathology Research Services (CPRS): 2/18/2016.

bb. The Service Agreement for the VCU School of Nursing (SON) laboratory was submitted: 2/22/2016.

cc. VCU IRB Amendment based on IRB request to clarify the volume of the blood used during the course of the study: 2/23/2016.

dd. VCU IRB Amendment Approval: 2/25/2016.

ee. ***Second monthly*** meeting with Dr. William Carter, MD (VCU-PI) and Alison Molitor (VCU site Research Coordinator): 4/1/2016. Meeting agenda was to discuss the progress for recruiting, screening, and enrolling participants to the study, testing process at the VCU Clinical Research unit, and to continue to have a monthly meeting on a regular basis.

ff. Laura O'Brien, PhD, a post-doctoral Research scientist, is working with Dr. Edward Lesnefsky, MD and Dr. Ashraf Gorgey, MPT, PhD to optimize the mitochondrial analysis protocol that will be used in the study.

gg. There six active participants in the study. There is one screen failure participant on 7/8/2016 and one potential participant who will be screened in 7/27/2016. The progress of each participant is listed in the table below:

Participant ID	Status	Post measurement I	Post Measurement II	Progress in the study out of 24 weeks
001-10123	Complete	Completed on 5/25/2016	Completed on 8/31/2016	Week 24
002-10187	Complete	Completed on 6/15/2016	Completed on 9/14/2016	Week 24
003-10122	Complete	Completed on 7/13/2016	Completed on 10/12/2016	Week 24
004-10006	Complete	Completed on 7/20/2016	Completed on 10/19/2016	Week 24
005-10128	Active	Completed on 8/10/2016	To be completed on 11/9/2016	Week 23
006-10142	Active	Completed on 9/28/2016	To be completed on 1/4/2017	Week 15
007-10179	Active	To be completed on 10/16/2016	To be completed on 2/15/2017	Week 9
008-Nonrandomized	Screen failed	-	-	-
009-10135	Active	To be completed 1/25/2017	To be completed 4/26/2017	Week 1 on 10/31/2016

010-10177	Active	To be completed on 2/1/2017	To be completed on 5/3/2017	Week 1 on 11/7/2016

hh. ***Third monthly*** meeting with Dr. William Carter, MD (VCU-PI) and Alison Molitor (VCU Site Research Coordinator): 5/6/2016. Meeting agenda was to discuss the process of screening and recruiting participants and enrolling participant to the study.

ii. ***Fourth monthly*** meeting with Dr. William Carter, MD (VCU-PI) and Alison Molitor (VCU site Research Coordinator): 5/27/2016. Meeting agenda was to discuss the progress for recruiting, screening, and enrolling participants to the study, the progress of the participants in the study and to continue to have a monthly meeting on a regular basis.

jj. ***Fifth monthly*** meeting with Dr. William Carter, MD (VCU-PI) and Alison Molitor (VCU site Research Coordinator): 7/1/2016. Meeting agenda was to discuss the progress for recruiting, screening, and enrolling participants to the study, the progress of the participants in the study and to continue to have a monthly meeting on a regular basis.

kk. ***Sixth monthly*** meeting with Dr. William Carter, MD (VCU-PI) and Alison Molitor (VCU site Research Coordinator): 9/30/2016. Meeting agenda was to discuss the progress for recruiting, screening, and enrolling participants to the study, the progress of the participants in the study and to continue to have a monthly meeting on a regular basis.

ll. RICVAMC site submitted the continuing review for the Human Research Protection Office (HRPO) on Wednesday 9/28/2016.

mm. VCU-site submitted the continuing review for the Human Research Protection Office (HRPO) on Thursday 10/13/2016.

nn. The Human Research Protection Office (HRPO) continuing review approval for both the RICVAMC and VCU sites has been received on Tuesday 10/18/2016.

Recruitment

oo. Testing at the RICVAMC site and admission at the VCU Clinical Research unit of the fourth participant in the study: 4/20/2016 to 4/21/2016

pp. Testing at the RICVAMC site and admission at the VCU Clinical Research unit of the

Scheduled the fifth participant enrolled in the study: 5/11/2016-5/12/2016).

qq. First participant completed the first 12 weeks of the study: 5/23/2016

rr. Post Measurement I testing for the first participant at the RICVAMC site and admission at the VCU Clinical Research unit: 5/25/2016 to 5/26/2016

ss. Second participant completed the first 12 weeks of the study: 6/10/2016

tt. Post Measurement I testing for the second participant at the RICVAMC site and admission at the VCU Clinical Research unit: 6/15/2016 to 6/16/2016

uu. Testing at the RICVAMC site and admission at the VCU Clinical Research unit of the sixth participant in the study: 7/13/2016 to 7/14/2016.

vv. Out of our target recruitment, we have successfully recruited nine participants: four had completed the study, four of them are currently active at different stages of the study and one of the participants has been a screen failure due to failure to respond to the electrical stimulation.

What opportunities for training and professional development has the project provided?

Nothing to Report.

How were the results disseminated to communities of interest?

Nothing to Report.

What do you plan to do during the next reporting period to accomplish the goals?

Future plans: Recruit 8 subjects by March 2017, continue training the enrolled participants according the protocol and to meet our target for the second year to have 16 participants enrolled in the study.

6. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

Our preliminary data suggests that 12 weeks of Neuromuscular Electrical Stimulation (NMES)-induced resistance training or passive movement prior to 12 weeks of Functional Electrical Stimulation (FES)-induced cycling improves metabolic profile and increases thigh muscle size. Furthermore, RT+FES prevented the increase in leg fat mass experienced by the PM (Passive Movement) + FES group. This suggests that RT (Resistance Training) +FES may be used to decrease the detrimental decline in metabolic and body composition profiles after SCI. Furthermore, an increase in metabolic profile with this exercise intervention may prevent the development of type II diabetes, cardiovascular disease, and insulin resistance after SCI.

What was the impact on other disciplines?

Nothing to Report.

What was the impact on technology transfer?

Nothing to Report

What was the impact on society beyond science and technology?

The findings from the current study are likely to impact the rehabilitation community and provide evidence based findings to the significance of restoring lean mass following SCI.

CHANGES/PROBLEMS:

Changes in approach and reasons for change: Nothing to Report

Actual or anticipated problems or delays and actions or plans to resolve them: Nothing to Report

Changes that had a significant impact on expenditures: Nothing to Report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents: Nothing to Report

Significant changes in use or care of human subjects: Nothing to Report

Significant changes in use or care of vertebrate animals: Not applicable

Significant changes in use of biohazards and/or select agents: Not applicable

7. **PRODUCTS:**

Publications, conference papers, and presentations.

Nothing to report

Journal publications.

Nothing to report

Books or other non-periodical, one-time publications.

Nothing to report

Other publications, conference papers, and presentations.

(1) Over the last three months, we have presented three symposiums accepted in two national meetings:

a. Two symposiums will be presented at the American Congress of Rehabilitation Medicine in Chicago: 11/2016

i. Training Outcomes of Functional Electrical Stimulation, Testosterone and Exoskeleton in Persons with Spinal Cord Injury

Chair: Ashraf S. Gorgey (ACRM 2016)
Presenters: Ashraf S. Gorgey, Therese Johnston, Gail Forrest

ii. Cellular Adaptations in Response to Different Training Paradigms after Spinal Cord Injury

Chair: Ashraf S. Gorgey (ACRM 2016)
Presenters: Ashraf S. Gorgey, Ceren Yarar-Fisher, Kevin McCully

b. One Symposium was presented at the ISCOS Meeting in Vienna, Austria: 09/2016

i. Different Application Forms of Electrical Stimulation in Persons with SCI, Presenters: Vanesa Bochkezanian and Ashraf S. Gorgey

c. We have three abstracts accepted for presentation in the ISCOS meeting

(2) Peer-reviewed Scientific Journals - We had 3 papers accepted for publication since the last report.

1. **Gorgey AS,** Timmons MK, Dolbow DR, Bengel J, Fugate-LausKC Michener LA, Gater DR. Electrical stimulation and blood flow restriction increase wrist extensor cross-sectional 137 area and flow meditated dilatation following spinal cord injury. Eur J Appl Physiol. 138 116(6):1231-44 (2016).
2. Moore P, **Gorgey AS**, Wade R, Khalil R, Khan R, Adler R. Neuromuscular Electrical Stimulation and Testosterone did not

Influence Heterotopic Ossification Size after Spinal Cord Injury. World Journal of Clinical Cases. Accepted

3. O'Brien LC, **Gorgey AS**. Skeletal muscle mitochondrial health and spinal cord injury. World J Orthop 2016; 7(10): 628-637 Available from: URL: http://www.wjgnet.com/2218-5836/full/v7/i10/628.htm
4. Dolbow DR, **Gorgey AS**, Khalil R, Gater DR. Effects of a Fifty-Six Month Electrical Stimulation Cycling Program after Tetraplegia: Case Report. J Spinal Cord Med. Accepted.

5. **Gorgey AS,** Graham ZA, Bauman WA, Cardozo C, Gater DR. Abundance in proteins expressed after functional electrical stimulation cycling or arm cycling ergometry training in persons with chronic spinal cord injury. J Spinal Cord Med. 2016 Oct 13:1-10.

6. **Gorgey AS**, Ghatas MP. Novel Rehabilitation Paradigm for Restoration of Hand Functions after Tetraplegia. Commentary letter on "Restoring cortical control of functional movement in a human 33 with quadriplegia. Journal of Neural Regen Res. 2016 Jul;11(7):1058-9.

7. Wade R, **Gorgey AS**. Skeletal muscle conditioning may be an effective rehabilitation intervention preceding functional electrical stimulation cycling. Neural Regen Res. 2016 Aug;11(8):1232-3

We have currently three papers currently under peer review in different journals.

1. **Gorgey AS,** Moore P, Wade R, Gill R, Lavis T, Adler R. Intramedullary Femoral Fixation may attenuate Testosterone Action on Muscle Size in a Person with Complete SCI. Submitted to European J PMR

2. Beal C**, Gorgey AS**, Moore P, Wong N, Adler R, Gater DR. Higher dietary intake of Vitamin D influences cholesterol and insulin sensitivity independent of body composition in Men with Chronic Spinal Cord Injury. To be submitted to Journal of Spinal Cord Medicine.

3. O'Brien LC, Wade RC, Segal L, Chen Q, Savas J, Lesnefsky EJ, **Gorgey AS**. Mitochondrial mass and activity as a function of body composition in individuals with spinal cord injury. Under review at Journal of Applied Physiology.

Website(s) or other Internet site(s)

Nothing to report

Technologies or techniques

Nothing to report

Inventions, patent applications, and/or licenses

Nothing to report

Other Products

Nothing to report

8. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	Ashraf Gorgey, MPT, PhD
Project Role:	Principal Investigator
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	12
Contribution to Project:	Ashraf Gorgey, MPT, PhD monitors all aspects of recruitment, data collection as well as supervising individuals with SCI during exercise. He coordinates grant-related activities and financial oversight for the CDMRP award. He manages pre and post award activities related to the grant, and carry out budget expenditures, fulfill staffing and space requirements and ensures deadlines are met for any required administrative reporting. He monitors all expenses associated with grant budget, verify that expenses are appropriate based on the approved budget for the grant, monitor payments owed to Virginia Commonwealth

	University based on the grant sub-award budget.
Funding Support:	None
Name:	Refka Khalil, DC
Project Role:	RICVAMC Research Coordinator
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	12
Contribution to Project:	Refka Khalil, DC prepares regulatory submissions, recruits subjects, reviews subject for eligibility, obtains informed consent, reviews medical records, evaluate subject's condition at study visits, performs study procedures, and maintains regulatory and subjects documents.
Funding Support:	None
Name:	Laura O'Brien, PhD
Project Role:	Research Scientist
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	10
Contribution to Project:	Laura O'Brien, PhD performs study procedures, data collection, data analysis, and working to optimize the mitochondrial analysis protocol for the study.
Funding Support:	None

Name:	Rodney Wade, BS
Project Role:	Research Technician
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	10
Contribution to Project:	Rodney Wade, BS performs study procedures, data
Funding Support:	None
Name:	Alison Molitor
Project Role:	VCU Research Coordinator
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	10
Contribution to Project:	Alison Molitor prepares regulatory submissions, recruits subjects, reviews subject for eligibility, obtains informed consent, reviews medical records, evaluate subject's condition at study visits, performs study procedures, and maintains regulatory and subjects documents.
Funding Support:	None

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to Report

What other organizations were involved as partners?

1. **Organization Name:** Virginia Commonwealth University

   Location of Organization: Richmond, VA, USA

   Partner's contribution to the project: **Facilities and Collaboration**

2. **Organization Name:** James J. Peters Bronx VA Medical Center

   Location of Organization: Bronx, New York USA

   Partner's contribution to the project: **Collaboration**

2) **SPECIAL REPORTING REQUIREMENTS**

a. **COLLABORATIVE AWARDS:** Nothing to report

b. **QUAD CHARTS:**

Skeletal Muscle Hypertrophy and Cardio-Metabolic Benefits after Spinal Cord Injury

SCI140119.CDMRP W91ZSQ
W81XWH-15-1-0671

PI: Ashraf Gorgey, MPT, PhD Org: McGuire Research Institute, Inc Award Amount: $1,908,055.00

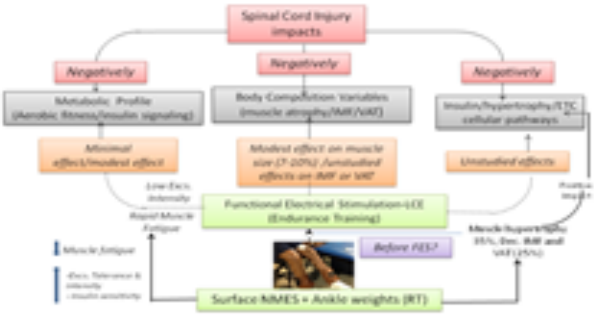
Study/Product Aim(s)

* *Aim #1:* To determine the impact of 12+12 weeks of NMES+FES-LEC on oxygen uptake, insulin sensitivity and glucose uptake in adults with SCI compared to control + FES-LEC.
* *Aim #2:* To determine the impact of 12+12 weeks of NMES+FES-LEC on skeletal muscle size, infiltration of intramuscular fat, visceral adiposity as well as fatigue resistance compared to control+ FES-LEC.
* *Aim #3 (translational exploratory aim):* To determine the impact of 12+12 weeks of NMES+FES-LEC on determinants of energy metabolism, protein molecules involved in insulin signaling, muscle hypertrophy and oxygen uptake and electron transport chain proteins compared to control + FES-LEC only.

Approach

Forty eight participants will be randomly assigned into neuromuscular electrical stimulation+ functional electrical stimulation (NMES+FES) or control (passive movement) + FES groups (PM+FES) for 24 weeks .

Rationale of the Study



Timeline and Cost

Activities CY	16	17	18	19
Adapt Research Protocol for RICVAMC, VCU, JJ VAMC)	X			
Coordinate Study Research Staff and Purchase Equipment	X			
Participant Recruitment, Therapy, Participant Evaluation	Ongoing			
Data management, data analysis and final report				
Estimated Budget ($K)	$193,191	$199,939	$199,990	$199,739

Updated: 10/25/2016

Goals/Milestones (Example)

CY11 Goal – System demonstration
☑ Functionality tests of integrated firmware and software
CY12 Goals – System validation
☐Investigate earplug designs based on collected features
☐Complete formal attenuation and comfort trials of earplugs
CY13 Goal – Production readiness
☐ Validate design architecture for digital ear canal volumetric shape capture and data workflow
CY14 Goal – Navy suitability testing
☐ Field test on aircraft carrier flightdeck

Comments/Challenges/Issues/Concerns

- If timelines change, comment here.
- If off by more than one quarter in spending, comment here.

Budget Expenditure to Date
Projected Expenditure:
Actual Expenditure:

3) **APPENDICES:** Nothing to Report