AWARD NUMBER: W81XWH-17-1-0513

TITLE: Pulsed Electromagnetic Field Therapy for Accelerating Peripheral Nerve Regeneration and Preserving Neuromuscular Junctions

PRINCIPAL INVESTIGATOR: Thomas L. Smith, PhD

CONTRACTING ORGANIZATION: Wake Forest University Health Sciences
Winston Salem,NC 27157

REPORT DATE: September 2018

TYPE OF REPORT: Annual Report

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
September 2018	Annual Report	15 Aug 2017-14 Aug 2018

4. TITLE AND SUBTITLE

Pulsed Electromagnetic Field Therapy for Accelerating Peripheral Nerve Regeneration and Preserving Neuromuscular Junctions

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-17-1-0513

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Thomas L. Smith, PhD

E-Mail: tsmith@wakehealth.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Wake Forest University Health Sciences
Medical Center Boulevard
Winston-Salem, NC 27157

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Major accomplishments include receipt of IACUC and ACURO approvals for all animal protocols, receipt and installation of a PEMF cage system providing commercially available PEMF waveforms, and initiation of experiments in Specific Aims 1 and 2. The PEMF cage system is installed in a dedicated room in the Wake Forest vivarium. Caging does not interfere with the PEMF waveform.

Eight rats were placed on study to address Specific Aims 1 and 2. Initial gait analysis was performed, the sciatic nerve was transected and repaired, and the animals received PEMF treatment for four months. Animals will have functional testing utilizing EMG and muscle force generation the first week in November 2018.

A second cohort of 8 rats will be trained and initiated on the project the week of November 12, 2018. A second PEMF system constructed by the Wake Forest Center for Nanotechnology and Molecular Materials will be installed in the dedicated vivarium room in November 2018 and will permit simultaneous running of sham-PEMF exposure rats.

Initiation of Specific Aim 3 (ability of PEMF to sustain neuromuscular junctions) – Animals on study December 2018

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			19b. TELEPHONE NUMBER *(include area code)*
Unclassified	Unclassified	Unclassified	Unclassified		USAMRMC

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

TABLE OF CONTENTS

1. **INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

Peripheral nerve injuries often accompany blast and shrapnel wounds. Repair of peripheral nerves requires a relatively long period of recovery. Pulsed electromagnetic field (PEMF) exposure offers an FDA approved intervention that has the potential to accelerate nerve recovery. The proposed studies will study PEMF treatments in rats with transected and repaired sciatic nerves. The rate and degree of functional motor recovery will be assessed in animals with and without treatment. In addition, the ability of PEMF to maintain neuromuscular junction integrity and function following denervation will be studied.

2. **KEYWORDS:** *Provide a brief list of keywords (limit to 20 words).*

Nerve injury, pulsed electromagnetic fields, motor nerve function, neuromuscular junctions, sciatic nerve, gait.

3. **ACCOMPLISHMENTS:** *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.*

What were the major goals of the project?
List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

Major goals:

Specific Aim 1- In-vivo effects of Pulsed Electromagnetic Fields (PEMF) on peripheral nerve axonal regrowth will be examined in rats subjected to sciatic nerve injury and repair.

- Major Task 1: Obtain regulatory approval for animal studies
  - Milestone Achieved November 8, 2017
- Major Task 2: Construct apparatus to deliver PEMF to test subjects –
  - Milestone achieved November 20, 2018. Second apparatus constructed by Wake Forest Center for Nanotechnology June 2018.
- Major Task 3: Perform surgeries on animals and enroll in PEMF protocol. – First cohort of 8 rats initiated in protocol on May 14, 2018

Specific Aim 2 - Assess functional outcomes of PEMF exposure on peripheral nerve injury/repair

- Major Task 4: Perform gait analysis on animals in Specific Aim 1. – First cohort of 8 rats initiated on May 1, 2018. These animals came off PEMF exposure on September 14, 2019. Data are being analyzed.

Specific Aim 3 – Determine whether PENF exposure has the ability to sustain neuromuscular junction morphology following denervation of muscle.

- Major task 1: subject subjects to PEMF following denervation of muscle. – To be initiated in December 2018

What was accomplished under these goals?
For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

Specific Aim 1- In-vivo effects of Pulsed Electromagnetic Fields (PEMF) on peripheral nerve will be regrowth will be examined in rats subjected to sciatic nerve injury and repair.

- Major Task 1: Obtain regulatory approval for animal studies
  - Milestone Achieved November 8, 2017
- Major Task 2: Construct apparatus to deliver PEMF to test subjects –
  - Milestone achieved November 20, 2018. Second apparatus constructed by Wake Forest Center for Nanotechnology June 2018.
- Major Task 3: Perform surgeries on animals and enroll in PEMF protocol. – First cohort of 8 rats initiated in protocol on May 14, 2018
  - These aseptic surgeries consist of transecting the sciatic nerve followed by immediate primary repair. Rats then are pair housed within the PEMF exposure cages and are subjected to specific PEMF waveforms for 6 hours per day, five days per week.

Specific Aim 2 - Assess functional outcomes of PEMF exposure on peripheral nerve injury/repair

- Major Task 4: Perform gait analysis on animals in Specific Aim 1. – First cohort of 8 rats initiated on May 1, 2018. These animals came off 4 months of PEMF exposure on September 14, 2019. Data are being analyzed.
  - Gait analysis was performed prior to nerve injury/repair using a digiGait system for gait analysis. Rats were subsequently studied at 2, 3, and 4 months post-injury.

Specific Aim 3 – Determine whether PEMF exposure has the ability to sustain neuromuscular junction morphology following denervation of muscle.

- Major task 1: subject rats to PEMF following denervation of muscle. – To be initiated in December 2018

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

Nothing to report

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Nothing to report

What do you plan to do during the next reporting period to accomplish the goals?
If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

Specific Aims 1 and 2 – Continue to enroll rats on PEMF exposure protocols. The longest exposure periods of 4 months will be initiated first on the remaining 12 rats for this cohort and the shorter exposure periods will be initiated. This sequence will allow us to complete the studies in a timely fashion. Specific Aim 3 – These studies to examine the potential for PEMF to maintain neuromuscular rjunction integrity will be initiated in the 2nd quarter of year two.

4. **IMPACT:** D*escribe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:*

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Nothing to report

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to report

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to report

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to report

5. CHANGES/PROBLEMS: *The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:*

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

No major changes in approach were experienced. A minor change was made to utilize a solenoid-typed PEMF coil rather than a Helmholz-type coil. This change was made upon the recommendation of Orthofix, a major supplier of medical instrumentation for PEMF therapy. By utilizing a solenoid coil around the animal's home cage, a more consistent PEMF field was obtained, insuring uniform exposure of the animal to the correct waveform intensity, regardless of where they are located within their cage.

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

Nothing to report

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

Not applicable

Significant changes in use or care of vertebrate animals

Nothing to report

Significant changes in use of biohazards and/or select agents

Nothing to report

6. **PRODUCTS:** *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."*

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report

Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report

Other publications, conference papers and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Nothing to report

- **Website(s) or other Internet site(s)**

List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Not applicable

- **Technologies or techniques**

Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

Nothing to report

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to report

- **Other Products**
  Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:
  - *data or databases;*
  - *physical collections;*
  - *audio or video products;*
  - *software;*
  - *models;*
  - *educational aids or curricula;*
  - *instruments or equipment;*
  - *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
  - *clinical interventions;*
  - *new business creation; and*
  - *other.*

Nothing to report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?
Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change".

Name: Thomas L. Smith, PhD
Project Role: Principal Investigator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1.2 calendar months
Contribution to Project: Dr. Smith developed the animal model for use in this application and completed all animal surgeries. He has worked closely with his team to review, analyze, and interpret experimental results.
Funding Support: W81XWH-17-1-0513

Name: Zhongyu Li, MD, PhD
Project Role: Co-Investigator

Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 0.24 calendar months
Contribution to Project: Dr. Li's role for this project has been to provide expertise as needed with respect to experimental design, nerve injury and repair surgeries, and data interpretation.
Funding Support: W81XWH-17-1-0513

Name: Xue (Amy) Ma, MD, PhD
Project Role: Co-Investigator
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 6 calendar months
Contribution to Project: Dr. Ma's role for this project has been to assist Dr. Smith in nerve injury and repair as well as functional testing at specific time points. She also is the primary person responsible for histologic preparation of the tissues being studied.
Funding Support: W81XWH-17-1-0513

Name: Eileen Elsner
Project Role: Laboratory Technician
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 6 calendar months
Contribution to Project: Ms. Elsner has assisted Dr. Smith in acquisition of animals and general animal husbandry. She has prepared the surgical suites and ensured appropriate supplies have been available for animal surgeries. She has also monitored the animals during daily PEMF exposure.
Funding Support: W81XWH-17-1-0513

Name: Daniel Lara, MD
Project Role: Postdoctoral Fellow
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 2 calendar months
Contribution to Project: Assist with decellularization/oxidation of rat sciatic nerves f
Funding Support: Wake Forest University Health Sciences, General Surgery training grant

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Thomas L. Smith, PhD
PREVIOUS PROJECTS
Title: Degenerative Disc Regeneration with the Use of Amniotic Tissue: Pilot Study
Time Commitment: 0.48 calendar months (4%)
Role: Principal Investigator
Supporting Agency: NuTech Medical, Inc.
Update: Project ended 1/1/2018

Title: Treatment of Spinal Cord Injury Using Keratin Biomaterials
Time Commitment: 1.2 calendar (10%)
Role: Principal Investigator
Supporting Agency: Errett Fisher Foundation
Update: Project ended 12/31/2017

Title: Exercise Countermeasures for Knee and Hip Joint Degradation during Spaceflight.
Time Commitment: 0.74 calendar months (7%)
Role: Co-Investigator (PI: Willey)
Supporting Agency: NASA NNX15AB506
Update: Dr. Smith's effort on this project ended 6/30/18

Title: Capped F10 for Next Generation Fluoropyrimidine Therapy of Colon Cancer.
Time Commitment: 0.12 calendar months (1%)
Role: Co-Investigator (PI: Gmeiner)
Supporting Agency: NC BioTechnology Center
Update: Project ended 7/31/2017

NEW PROJECTS
Title: Treatment of Spinal Cord Injury Using Keratin Biomaterials
Time Commitment: 1.2 calendar (10%)
Role: Principal Investigator
Supporting Agency: Errett Fisher Foundation
Program Official: Carmen Caruth
E-mail: carmenc@cityofws.org
Period of Performance: 1/1/14-12/31/2018 NCE
Level of funding: $107,533 annually
Project Goals: The goals of this project are to confirm that keratin treatment can produce the M2 macrophage type in human primary cells, determine the best route of administration of the keratin in a rat SCI model, and show that keratin treatment can have a beneficial effect in the most clinically relevant SCI injury model, crush injury.

Title: Recruitment of Endogeneous Neural Stem/Progenitor Cells for the Treatment of Spinal Cord Injury
Time Commitment: 0.36 calendar months (3%)
Role: Principal Investigator
Supporting Agency: Errett Fisher Foundation
Program Official: Carmen Caruth
E-mail: carmenc@cityofws.org
Period of Performance: 7/1/17-6/30/2019
Level of Funding: $190,000
Project Goals: This research aims to understand and overcome barriers associated with the recruitment of endogenous NSPCs and to harness their regenerative potential through examining cellular health and activities such as autophagy and pyroptosis. Additionally, this project tests the potential of two neuroprotective treatments to synergistically reduce neuroinflammation while supporting NSPC survival for the treatment of SCI.

Title: Evaluating the use of sub-atmospheric pressure to promote bone healing.
Time Commitment: 0.60 calendar months (5%)
Role: Principal Investigator
Supporting Agency: Wake Forest University Health Sciences, Department of Plastic Surgery
Program Official: Stan Gordon, Department Administrator
E-mail: sgordon@wakehealth.edu
Period of Performance: 7/1/17-7/31/2019
Level of Funding: $35,536
Project Goals: The objective of this study is to apply sub-atmospheric pressure to facilitate bone healing as well as improve the integration of bone graft using a rat model.

Zhongyu Li, MD, PhD
No changes in active support

Xue (Amy) Ma, MD, PhD
Title: Exercise Countermeasures for Knee and Hip Joint Degradation during Spaceflight.
Time Commitment: 3 calendar months (25%)
Role: Postdoctoral Fellow (PI: Willey)
Supporting Agency: NASA NNX15AB506
Update: Dr. Ma's effort on this project ended 6/30/2017

Title: Acceleration of regeneration of large-gap peripheral nerve injuries using acellular nerve allografts plus amniotic fluid derived stem cells (AFS).
Time Commitment: 7.2 calendar months (60%)
Role: Postdoctoral Fellow
Update: Dr. Ma's effort changed to a Collaborator on 9/1/2016

Title: Acceleration of Schwann Cells with Co-Culturing Amniotic Membrane and Amniotic Fluid Stem Cells
Time Commitment: 1.44 calendar months (12%)
Role: Principal Investigator
Supporting Agency: NuTech Medical, Inc.
Update: Dr. Ma's effort changed to a Collaborator on 8/31/2017

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were

involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

Organizational name: Orthofix
Location of Organization: 345 Plano Parkway
Lewisville, TX 75056
Partner's contribution: Orthofix, a major supplier of PEMF equipment in the medical device industry, graciously loaned Wake Forest School of Medicine a complete, functional cage system for delivering the PEMF waveform approved in our grant. This system utilizes solenoid coils for generation of the PEMF signal. This system compliments but does not replace the PEMF system constructed by the Wake Forest Center for Nanotechnology and Molecular Materials.

- Collaboration : Jane Jacob, PhD, Vice President for Research and Clinical Affairs
  - Erik Waldorf, PhD, Principal Scientist and Research Manager
    - Dr. Waldorf oversaw the transportation and installation of the Orthofix PEMF system

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: *For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to* ***https://ers.amedd.army.mil*** *for each unique award.*

QUAD CHARTS: *If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.*

9. APPENDICES:

Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

“Pulsed electromagnetic field therapy for accelerating peripheral nerve regeneration and preserving neuromuscular junctions.”

ERMS/Log Number – OR160258

Award Number Here – W81XWH-17-0513

PI: Thomas L. Smith, PhD **Org:** Wake Forest University Health Sciences **Award Amount: $616,937**

Study/Product Aim(s)

Specific Aim 1 (SA1): *In –vivo* effects of PEMF on peripheral nerve axonal regrowth will be examined in rats subjected to sciatic nerve injury and repair. Sham-PEMF exposure will serve as a control group.

Specific Aim 2 (SA2): Functional outcomes of muscle force generation and gait analysis of SA 1 rats will be studied longitudinally.

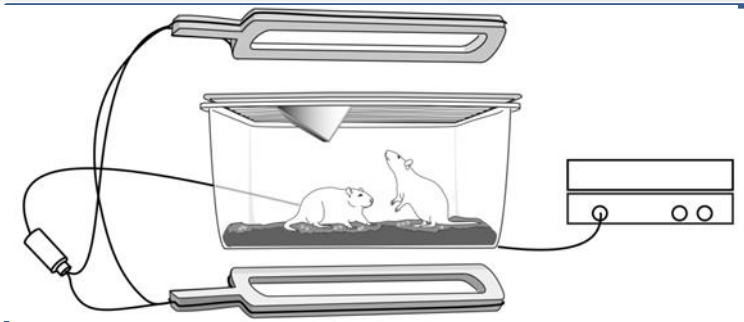
Specific Aim 3 (SA3): Ability of PEMF to maintain neuromuscular junction integrity after denervation will be studied in cohorts separate from Aims 1&2

Approach

SA1 - A Lewis rat model of sciatic nerve injury and repair will be studied . Cohorts with PEMF treatment will be compared to cohorts with Sham-PEMF treatment. Histologic outcomes will be gathered.

SA2 - Motor function (muscle force and gait) in animals from Aim 1 will be studied

SA3 – Post-synaptic NMJ preservation will be studied with PEMF or Sham-PEMF treatments following permanent denervation



Rats with sciatic nerve injury will be treated with an FDA-approved PEMF waveform. Controls will receive Sham-PEMF. Functional and histologic outcomes will be compared between the treatment groups. A different set of rats will be chronically denervated and treated as above to preserve the post-synaptic motor end plates for reinnervation.

Accomplishments: - All animal approvals (IACUC and ACURO) have been obtained.
- PEMF coil apparatus has been installed in vivarium, tested, and verified.
- Initial cohort of rats place on 4 month exposure study, results under analysis

Timeline and Cost

Activities CY	17	18	19	
Aim 1: In-vivo PEMF histology effects				
Aim 2: in-vivo PEMF function & gait				
Aim 3: In-Vivo NMJ PEMF effects				
Estimated Budget ($K)	**$55.9**	**$97.7**	**$000**	

Updated: July 31, 2018

Goals/Milestones (Example)

CY17 Goals –
- construction of PEMF apparatus - accomplished
- Receive IACUC & ACURO approval for studies - accomplished
- SA 1 & 2 in-vivo studies initiated

CY18 Goals –
- Conclude SA 1&2 Studies
  - publish results from SA 1&2
- Initiate SA 3 studies

CY 19 Goals –
- Complete SA 3 studies
  - publish results from SA 3 studies

Comments/Challenges/Issues/Concerns

Budget Expenditure to Date

Projected Expenditure: $223,637

Actual Expenditure: $153,595