AWARD NUMBER: W81XWH-17-2-0069

TITLE: "Electroceutical Dressing Against Traumatic and Burn Wound Biofilm Infection"

PRINCIPAL INVESTIGATOR: Rodney Chan, MD

CONTRACTING ORGANIZATION: The Metis Foundation
San Antonio, Texas 78205

REPORT DATE: October2019

TYPE OF REPORT: Annual

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**
Oct 2019	Annual	**September 30, 2018 – September 29, 2019**

4. TITLE AND SUBTITLE
"Electroceutical Dressing Against Traumatic and Burn Wound Biofilm Infection"

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-17-2-0069

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
The Metis Foundation
300 Convent Street, Suite 1330
San Antonio, Texas 78205-1357

8. PERFORMING ORGANIZATION REPORT NUMBER

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

U.S. Army Medical Research and Materiel Command
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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

During the reporting period, tasks completed include obtaining the proper agreements required to conduct the study. The study protocol and regulatory documents were prepared and submitted to both the IRB and HRPO for approval. Approval was obtained for both levels of review. Post approval the collaborating study site was transferred from Ohio State University to Indiana University. An amendment to the grant and IRB protocol have been completed. HRPO approval for the site change is currently pending.

15. SUBJECT TERMS
Biofilm, biofilm mitigation, biofilm infection, wireless electroceutical dressing, wound infections, wound healing, skin repair.

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			USAMRMC
Unclassified	Unclassified	Unclassified	Unclassified	13	**19b. TELEPHONE NUMBER** *(include area code)*

TABLE OF CONTENTS

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

The purpose of this Prospective, randomized, placebo-controlled clinical trial is to test the efficacy of the wireless electroceutical dressing (WED) in preventing as well as treating wound infection and its effect on wound healing. Addressing the W81XWH-17-DMRDP-MID-CSA topic area on therapeutics with a particular focus on evaluation of a FDA approved device for optimum preventive or directive therapies for combat-related or trauma-induced wound infections.

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

Electroceutical dressing, biofilm prevention, infection treatment, wound, wound healing.

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer 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.

Specific Aim 1 and 2: Obtain all necessary IRB approvals to conduct the proposed clinical trial
Status: Local IRB approval obtained; HRPO approval pending

Major Task 1: Prepare regulatory documents and study protocol for proposed study
Status: Completed

Subtask 1: Coordinate with Sites for cooperative research and development agreements (CRADA) submission
Status: Completed

Subtask 2: Coordinate with Sites for material transfer agreements
Status: Completed

Subtask 3: Coordinate with Sites for nondisclosure agreements (NDAs)
Status: Completed

Subtask 4: Submit study protocol (including: eligibility, screening protocol, consent forms etc.)
Status: Completed, January 25, 2018

Subtask 5: Military 2nd level IRB review (HRPO)

Status: Completed

Milestones Achieved: Local IRB/REB approval at USAISR
Status: Completed

Major Task 2: Patient screening and enrollment, surgery, imaging and sample collection
Status: In progress. Enrollment began Y2Q3

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 and 2: Obtain all necessary IRB approvals to conduct the proposed clinical trial

Major Task 1: Prepare regulatory documents and study protocol for proposed study (Part 1 and Part 2)

We have achieved the milestones in year 1 for this major task by obtaining both local IRB and HRPO approval. In year 2, we have received approval for continuation.

Major Task 2: Patient screening and enrollment, surgery, imaging and sample collection

The task is currently in progress.

Major Task 3: Data analysis

Data analysis has not yet been started.

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.

In order to accomplish the goals of this project, subject enrollment will continue and be completed. The results of the data collected from the subject enrollments will be analyzed for dissemination through conference presentation and manuscript publication.

4. **IMPACT:** Describe 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 Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer 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.

This project has experienced issues with

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.

Delays in enrollment completion has been a problem encountered during this reporting period. An amendment was sent to and approved on 10 May 2019 by the IRB to change the inclusion criteria. During this period a total of 1213 patients were screened in total; post amendment approval we had some success in screening 770 patients in which eight enrollments were completed. Currently, the pace enrollment is still slower than we anticipated in our timeline. Further analysis of the screening gave us insight on how to capture more study candidates to meet our enrollment goal. An amendment was submitted to the IRB (approval pending) on 23 September 2019 with additional changes to increase our potential subject population.

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

The human subjects' research protocol was amended twice with approvals, one amendment is pending approval. Changes include the following for each amendment.

Amendment 1- Change of research site from Ohio State University to Indiana. Addition of research staff.

Amendment 2- Revision of inclusion criteria, addition of Silhouette Star assessment tool, change of location of site performing colony forming unit analysis, and update to the study timeline.

Amendment 3- Revision of research staff

Amendment 4- Clarification of patient population, revision to inclusion criteria to allow for the use of legally authorized representative for consenting, change of biopsy (day 4) as optional, addition of subject compensation, and revision of treatment area size definition.

Significant changes in use or care of vertebrate animals.

N/A

Significant changes in use of biohazards and/or select agents

N/A

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).*

None

  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).*

None

  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.*

None

- **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.

None

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be 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. State whether an application is provisional or non-provisional and indicate the application number. 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;*
  - *biospecimen 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."

Example:

Name: *Mary Smith*
Project Role: *Graduate Student*
Researcher Identifier (e.g. ORCID ID): *1234567*
Nearest person month worked: *5*

Contribution to Project: *Ms. Smith has performed work in the area of combined error-control and constrained coding.*
Funding Support: *The Ford Foundation (Complete only if the funding support is provided from other than this award).*

Name: Victoria Hatem
Project Role: Research Coordinator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *12*
Contribution to Project: *Ms. Hatem has performed work in the area of protocol design, regulatory preparation, IRB submission, IRB communications, HRPO submission, and protocol execution.*

Name: Rodney Chan
Project Role: Principal Investigator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *12*
Contribution to Project: *Dr. Chan has performed work in the area of protocol design and study oversight.*

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.

Nothing to report.

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.*

Indiana University has provided support in processing and analysis of the punch biopsy samples. Histology, Colony Forming Unit counts and scanning Electron Microscopy are included in this support.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating 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.

Title: Electroceutical Dressing Against Traumatic and Burn Wound Biofilm Infection

Log No. DM170113

Contract #: W81XWH-17-2-0069

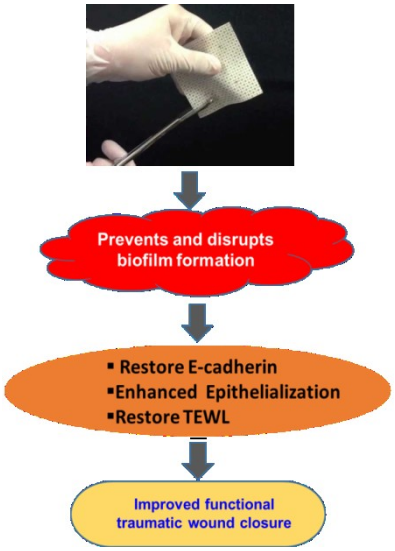
PI: Dr. Rodney Chan, MD **Org:** Metis Foundation **Award Amount:** $2.2 M

Aim: To evaluate Procellera® , a novel FDA 510(k) cleared antimicrobial wound dressing in a prospective, randomized, controlled clinical study on biofilm burden in patients with either traumatic or burn wounds.

Hypothesis: Low electric field created by a moisture-activated elemental silver and zinc WED will reduce microbial load, enhance wound healing and restore skin barrier function of infected wounds.

Focus Area: Therapeutics

Approach: The current application is based on our observation that low magnitude electric field is effective in both preventing as well as dismantling bacterial biofilm and improving wound closure. We will investigate bacterial burden, wound healing and re-epithelialization at the wound site using established clinical and laboratory based methods.



Key features of treatment:

- Low Electric field (~1V) and microcurrent technology
- Kills and prevents bacterial growth
- Accelerates wound closure and improves barrier function.
- No heat/pain
- No adverse effects documented No
- power supply or battery needed
- Can be self applied
- Conforms to wound size and shape
- Long shelf life and storage at room temperature
- Non-invasive
- Reduces cost of follow-up care

Biofilm infection negatively impacts host wound healing. This proposal will study the efficacy of an FDA cleared device, suitable for field use, as a preventative barrier to infection while supporting wound closure.

Timeline and Costs

Activities	CY 17	CY 18	CY19
Approvals + Initiation of study			
Enrollment of subjects			
Data analysis and study closeout			
Estimated Budget ($K)	$1,091,912	$1,093,398	

Goals/Milestones (2 year period)

CY18 Milestones–

- ❑ Local IRB approved May 09, 2018
- ❑ 2nd level HRPO Approval

CY19 Goals –

- ❑ Enrollment of subjects
- ❑ Data analysis
- ❑ Study closeout

Budget Expenditure to Date (September 30, 2017 – October 29, 2019)

Projected Expenditure Years 01-02: $2,185,310.00

Actual Expenditure: $747,616.67