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AWARD NUMBER: W81XWH-14-2-0161

TITLE: Improving Diagnosis of Sepsis After Burn Injury Using a Portable Sepsis Alert System

PRINCIPAL INVESTIGATOR: Ravi S. Radhakrishnan, MD, MBA, FACS, FAAP

RECIPIENT: The University of Texas Medical Branch at Galveston
Galveston, TX 77555

REPORT DATE: October 2015

TYPE OF REPORT: Annual

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

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	**2. REPORT TYPE**	**3. DATES COVERED**
October 2015	Annual	30 Sep 2014 - 29 Sep 2015

4. TITLE AND SUBTITLE

Improving Diagnosis of Sepsis After Burn Injury Using a Portable Sepsis Alert System

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-14-2-0161

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Ravi S. Radhakrishnan, MD, MBA, FACS, FAAP
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The University of Texas Medical Branch at Galveston
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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
The University of Texas Medical Branch at Galveston
301 University Boulevard
Galveston, TX 77555-5302

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

Background: Sepsis is the leading cause of death after significant burn injury. Severely burned patients (TBSA >20%) have sepsis rates < 40%. Early initiation of antibiotics within 1 hour of recognition of sepsis is the only factor associated with better survival. Diagnosis of sepsis after burn injury is not amenable to standard sepsis criteria. To address this problem, the American Burn Association developed specific criteria to prompt sepsis workup. Despite these guidelines, these findings can be subtle leading to delays in recognition of sepsis. **Hypothesis:** Best practice guidelines using 'new vital signs' of heart rate variability, regional tissue oxygenation, and noninvasive cardiac output can diagnose burn sepsis earlier, reducing morbidity and mortality. **Rationale:** Heart Rate Variability (HRV), regional Tissue Oxygenation, and non-invasive Cardiac Output (CO), have shown promise in detecting sepsis in other patient populations. These modalities have not been evaluated for sepsis detection after burn injury. **Specific Aims/Study Design:** 1. Prospectively collect traditional and 'new vital signs' and compare the diagnostic accuracy, time to diagnosis, and prediction of outcome. 2. Develop a best practice guideline for the early diagnosis and treatment of sepsis in the burn patient, integrating current and new vital signs, and incorporating these into a bedside decision-support tool. 3. Design and conduct a prospective, multicenter, randomized study to test the efficacy of the newly developed bedside tool in detecting sepsis. **Relevance:** The use of 'new vital signs' will provide an improved assessment of burn sepsis, enabling earlier detection of sepsis. The results of the study may change the standard of burn care if it is found that 'new non-invasive vital signs' can detect sepsis earlier, leading to earlier initiation of antibiotics and improved morbidity and mortality.

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**			USAMRMC
Unclassified	Unclassified	Unclassified	Unclassified	19	**19b. TELEPHONE NUMBER** *(include area code)*

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.

Despite multiple advances in critical care and resuscitation, sepsis is the leading cause of death in patients who sustain a significant burn injury. Our over-arching hypothesis is that best practice guideline using 'new vital signs' of heart rate variability, regional tissue oxygenation, and noninvasive cardiac output can be used to diagnose sepsis earlier, reducing morbidity and mortality after burn injury.

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

Burn injury, sepsis, mortality, heart rate variability, regional tissue oxygenation, noninvasive cardiac output

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 and objectives 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.

Task 1. Test the efficacy of "new noninvasive vital signs" of HRV, regional tissue oxygenation, and noninvasive cardiac output in detecting sepsis after burn injury. Proposed Timeline: Months 0-18. Patients to be enrolled: 20. Patients enrolled to date: 3. Adjusted completion date: Month 20.
Task 2. Identify and use best conventional and "new" vital signs for early detection of burn sepsis to create a best practice guideline for identification of burn sepsis. Proposed Timeline: Months 6-18. Adjusted completion date: Month 22.
Task 3. Create decision support tool using best practice guidelines. Proposed Timeline: Months 12-24. Adjusted completion date: Month 24.
Task 4. Validate the efficacy of the bedside decision support tool to detect burn sepsis using multicenter, prospective study, bedside laptops, and patient sensors. Proposed Timeline: Months 24-48.

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.

1. Post-doctoral Fellow (Min Zhu) hired. He has developed and tested the data collection system. Data now able to stream directly from bedside to secure servers in PI lab for analysis. Testing complete on system and ready to accept patient data. Nonin and Cardiotronic devices tested with Phillips bedside monitor. Current data collection system integrates and timestamps all data from various sources to allow accurate analysis.
2. IRB and HRPO approval obtained.
3. New Phillips data acquisition boards installed in every bedspace in burn unit. Will allow for data capture of multiple patients at lower cost than previously outlined.
4. Obtained device and sensors from Nonin. Obtained additional sensors from Cardiotronic.
5. RAID Server to store patient data with appropriate backup to prevent data loss has been ordered.
6. Workstation to analyze data obtained. Preliminary data analysis is being performed on data collected.
7. Since completion of Y1Q3, we have begun enrolling patients. We have identified 4 patients who meet eligibility requirements for the study. We have enrolled and collected data on 3 of these patients (15% of proposed number) At this rate, we expect to complete enrollment of patients for prelim portion of the study by month 28. Our initial proposed timeframe for this goal was month 18. Our initial delays in capturing patient data were related to creating a more cost-effective and efficient data collection system than initially proposed. This will allow us to collect data on more patients simultaneously than initially proposed. .

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.

Continue to enroll eligible patients from the Blocker Burn Unit. We will continue to analyze the data obtained to create and modify our predictive algorithm for sepsis as more data becomes available.

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.

In the initial grant proposal, we proposed the usage of a PowerLab device to obtain data from the patient bedside monitor. While this methodology is possible, we found a more cost effective means to obtain data. We worked with the Philips monitor support staff to obtain cards to install in each monitor to allow digital export of data from the patient monitor. This has allowed us to save money while obtain data from multiple patients at once. While the means of collecting this data has changed marginally, the overall scope of the project remains the same.

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.

As outlined above, we have attempted to obtain a more cost effective method to obtaining patient data. In identifying this alternative and installing it, our project was delayed by approximately 9 months. With this increased capability to enroll patients, we feel that we will likely be able to enroll more patients in a shorter time and lessen the delay. We have applied for an extension for year one funding as well.

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.

We were able to identify a more cost effective methodology to obtain patient data from the Philips monitor. This will allow us to shift the savings to obtain more patient sensors to enroll more patients.

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

None

Significant changes in use or care of vertebrate animals.

Not applicable.

Significant changes in use of biohazards and/or select agents

Not applicable.

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.

Nothing to report.

- **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: Ravi Radhakrishnan
Project Role: PI
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1
Contribution to Project: Dr. Radhakrishnan has obtained IRB/HRPO approval. Working with Min Zhu, he has created and tested the data acquisition system. Finally, he has identified and obtained more cost effective methods to obtain patient data from monitors. Have also assisted in enrolling patients in the study.

Name: Min Zhu
Project Role: Postdoctoral Fellow
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 7
Contribution to Project: Dr. Zhu has completed work on integration and collection of data signals from varied monitors. He has developed and tested his system to capture raw data efficiently from the bedside monitors, which is now ready to acquire data from patients. The database and storage infrastructure to allow for storage and analysis of the data once collected has been created and resides on our current computers. He is currently working with our collected data to begin decision support algorithm development.

Name: Omar Nunez-Lopez
Project Role: Research Associate/Fellow
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1
Contribution to Project: Dr. Nunez-Lopez has worked on patient enrollment, ensuring that data is collected appropriately from patients, assisting bedside nursing with adherence to data collection protocols, and ensuring that sensors are in proper position for data collection.

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.

See attached updated Other Support for Drs. Radhakrishnan and Kramer (Attachment 1).

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.*

Nothing to report.

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.

Attachment 2: Quad Chart

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.

ATTACHMENT 1

CHANGES IN ACTIVE SUPPORT

Radhakrishnan, Ravi S

Total Active EffortPct: 7%

W81XWH-14-2-0161 (PI: Radhakrishnan, Ravi S) 09/30/14-09/29/18 5%
Dept of Defense $145,167
"Improving Diagnosis of Sepsis After Burn Injury Using a Portable Sepsis Alert System"

Goal: To provide an improved assessment of burn sepsis, enabling earlier detection of sepsis leading to earlier initiation of antibiotics and improved morbidity and mortality.

Aims: 1) Prospectively collect traditional and 'new vital signs' and compare the diagnostic accuracy, time to diagnosis, and prediction of outcome; 2). Develop a best practice guideline for the early diagnosis and treatment of sepsis in the burn patient, integrating current and new vital signs, and incorporating these into a bedside decision-support tool; 3) Design and conduct a prospective, multicenter, randomized study to test the efficacy of the newly developed bedside tool in detecting sepsis.

Role: Principal Investigator
Contact: Thomas Winter, 301-619-2665, thomas.s.winter2.civ@mail.mil
Overlap:

******New award effective 1/15/2015******
1 R01 GM112936-01 (PI: Finnerty, Celeste) 01/15/15-12/31/19 1%
National Institutes of Health $259,620
"Effects of Chronic Catecholamine Exposure on Post-burn Scarring"

Goal: Understanding the mechanisms underlying aberrant wound healing and scarring, and their reversal by propranolol, will lay the foundation to develop additional anti-scarring therapies for the severely burned.

Aims: Aim 1. Determine the effects of chronic catecholamine exposure and β-blockade on wound healing and hypertrophic scars. Aim 2. Quantitate the effects of β-blockade on scar composition. Aim 3. Determine the effects of β-blockade on β-AR expression, activity, and binding partners of dermal fibroblasts.

Role: Co-Investigator
Contact: Tseng, Hung H., 301-496-0810, tsengh@mail.nih.gov
Overlap: None

******New award effective 3/1/2015******
5R01NS077963-03 (PI: Radhakrishnan, Ravi S) 03/01/15-02/29/16 1%
UT Health Science Center at Houston $61,978
"Subaward: Phase 2 Pediatric Autologous Bone Marrow Mononuclear Cells for Severe Traumatic Brain Injury"

Goal: To determine the effect of intravenous infusion of autologous BMMNC on brain structure and neurcognitive/functional outcomes after severe TBI in children.

Aims: 1. Determine the effect of autologous BMMNC on CNS white matter (WM), Gray matter (GM) structural preservation. 2. Determine if autologous BMMNC infusion preserves structural integrity of GM and WM regions of interest and improves functional and neurocognitive deficits in children after TBI

Role: Principal Investigator
Contact: Karen S. Niemeier, UT Houston Sponsored Projects Administration, 713-500-3999
Overlap: None

ACTIVE OTHER SUPPORT AS OF 10/28/2015

KRAMER, George C., PhD

ACTIVE **Total Active EffortPct: 50%**

N0001412C0556 (Kramer) 08/27/12-12/27/15 33%
Office of Naval Research $1,317,532
"Decision Support and Closed Loop Drug Delivery for Trauma Care"
Major Goal(s): Our goal was to deliver a clinical solution to fluid resuscitation for combat casualties in the absence of advanced caregivers.
Role: Principal Investigator
Sponsor Contact: Office of Naval Research, 875 N Randolph St, Arlington, VA 22217; (703) 696-5031
Overlap: None

W81XWH1210598 (Kinsky) 09/30/12-09/29/16 10%
US Army Medical Research Acquisition Activity $304,783
"Smart Oxygen Monitors to Diagnose and Treat Cardioplumonary injuries"
Major Goal(s): The proposed project integrates non- invasive, commercial off the shelf (COTS) products with autonomous systems. Specifically, oxygenation data, which is continuously streamed and displayed in real-time, will be used to construct patient status and treatment algorithms. Our project goal is to implement novel recognition decision support systems with early warning alarms and display and/or initiate recommended therapies. These smart- oxygenation- systems (SOS) will identify oxygenation deficits in pulmonary function or circulation.
Role: Co-investigator
Sponsor Contact: US Army Medical Research Acquisition Activity, 820 Chandler Street, Fort Detrick, Maryland 21702
Overlap: None

3350 (Kramer) 08/27/14-08/26/16 1%
Potrero Medical Inc. $0
"Evaluation of a Novel Electronic Urine Output Monitor (eUOM)"
Major Goal(s): 1) By comparing a standard-of-care (Bard® Medical's CritiCore® System) electronic urine output monitor (eUOM) and standard urinary drainage tube to the Accuryn eUOM and Anti-Airlock Drainage Tube, we gain knowledge regarding the quality of standard of care UO data.
Role: Principal Investigator
Sponsor Contact: Potrero Medical Inc., 101 Mississippi Street, San Francisco, CA 94107
Overlap: None

HHSF223201450003 A (Kramer) 09/15/14-09/14/17 1.5%
Food and Drug Administration $72,551
"Collection of Physiological Data Prior to Shock"
Major Goal(s): This project is to provide physiological data, using a large animal model of hemodynamic shock.
Role: Principal Investigator
Sponsor Contact: U.S. Food and Drug Administration, 10903 New Hampshire Avenue, Silver Spring, MD 20993
Overlap: None

HHSF223201450003A (Kramer) 09/15/14-09/14/17 1.5%
Food and Drug Administration $50,518
"Collection of Physiological Data Prior to Shock"
Major Goal(s): This project is to provide physiological data, using a large animal model of hemodynamic shock.
Role: Principal Investigator
Sponsor Contact: U.S. Food and Drug Administration, 10903 New Hampshire Avenue, Silver Spring, MD 20993
Overlap: None

W81XWH1420161 (Radhakrishan) 09/30/14-09/29/18 3%
Dept of Defense $145,167
"Improving Diagnosis of Sepsis after Burn Injury Using a Portable Sepsis Alert System"
Major Goal(s): To determine best practice guideline using ‘new vital signs’ of heart rate variability, regional tissue oxygenation, and noninvasive cardiac output can be used to diagnose sepsis earlier, reducing morbidity and mortality after burn injury.
Role: Co-investigator
Overlap: None

Improving Diagnosis of Sepsis after Burn Injury Using a Portable Sepsis Alert System

Log Number: 13214029
Award Number: W81XWH-14-2-0161

PI: Ravi S. Radhakrishnan **Org:** University of Texas Medical Branch **Award Amount:** $1,247,316

Study/Product Aim(s)

Task 1. Test the efficacy of "new noninvasive vital signs" of HRV, regional tissue oxygenation, and noninvasive cardiac output in detecting sepsis after burn injury. Timeline: Months 0-26.
Task 2. Identify and use best conventional and "new" vital signs for early detection of burn sepsis to create a best practice guideline for identification of burn sepsis. Timeline: Months 6-26.
Task 3. Create decision support tool using best practice guidelines. Timeline: Months 12-26.
Task 4. Validate the efficacy of the bedside decision support tool to detect burn sepsis using multicenter, prospective study, bedside laptops, and patient sensors. Timeline: Months 24-48.

Approach

3 patients enrolled. Continue patient enrollment with goal of completing initial patient cohort enrollment in next 10-12 months. Begin work on multi-variable predictive index for sepsis.

	SDRR (ms)	pNN50 (%	SD1/SD2	CSI	CVI	VLF Powe	LF Power	HF Power
Nonseptic	75.1	8.98	0.62	1.90	4.60	1,699	4,538	5,730
Septic	32.8	0.7	0.7	1.5	4.1	432.2	902.9	699.6
P Value	0.0022	0.0039	0.0117	0.0130	0.0348	0.0231	0.0187	0.0224

	HR	SV	CO	ICON	SpO2	MAP
Nonseptic	158.02	1.23	0.19	110.33	95.07	54.78
Septic	167.87	1.17	0.19	77.08	93.06	44.02
P Value	0.11	0.42	0.50	0.01	0.08	0.07

Comparison of Advanced Cardiovascular Indices in Septic and Non-Septic Extremely Low Birthweight (<1000g) Neonates. These data are the result of analysis similar to that proposed in this grant obtained from septic neonates. Similar analysis is being done on available historic data sets from our center to identify predictive indices in burn sepsis.

Activities FY	15	16	17	18
Collect Preliminary Data and Create Multivariable Algorithm				
Create Multivariable algorithm and portable decision support tool				
Conduct Prospective Multicenter Study				
Estimated Budget ($K)	$307K	$267K	$395K	$332K

Goals/Milestones

FY15 Goal –
☑Complete IRB approval
☑Obtain HRPO approval
☑Obtain Monitors, Data analysis computers
☑Begin Patient Enrollment

FY16 Goals
☐Complete Initial Patient Enrollment
☐Develop Multivariable Algorithm
☐Create Portable Decision Support Tool

Comments/Challenges/Issues/Concerns
- Current Expenditures behind projected figures. Proper data collection system created and necessary data analysis tools ordered. Patient enrollment and data collection to continue.

Budget Expenditure to Date
Projected Expenditure: $271,682
Actual Expenditure: $129,034

Updated: October 23, 2015.