



TASK ORDER NUMBER: W81XWH-15-9-0001

MTEC RESEARCH PROJECT NUMBER: MTEC-17-08-Multi-Topic-0340

EGS NUMBER: MT17008.034

TITLE: MTEC-17-08-MT-0340; The Effects of Complete and Partial Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) with Pharmacologic Treatment in Swine Models of Hemorrhagic Shock, Traumatic Brain Injury, and Complex Vascular Injuries.

PRINCIPAL INVESTIGATOR: Hasan B Alam, MD, Research Project Lead

PERFORMING ORGANIZATION: Regents of the University of Michigan
3003 S State Street
Ann Arbor, MI 48105
Phone Number: 734-936-5823

CONTRACTING ORGANIZATION: Medical Technology Enterprise Consortium (MTEC)

REPORT DATE: 10/25/2020

TYPE OF REPORT: Annual Report

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

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188



Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.					
1. REPORT DATE 10/21/20		2. REPORT TYPE Annual		3. DATES COVERED 09/25/19-10/25/20	
4. TITLE AND SUBTITLE MTEC-17-08-MT-0340; The Effects of Complete and Partial Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) with Pharmacologic Treatment in Swine Models of Hemorrhagic Shock, Traumatic Brain Injury, and Complex Vascular				5a. CONTRACT NUMBER W81XWH-15-9-0001	
				5b. GRANT NUMBER N/A	
				5c. PROGRAM ELEMENT NUMBER (Can be blank if don't know)	
6. AUTHOR(S); Hasan B Alam, MD; Rachel Russo, MD; Yongqing Li, MD, PhD; Michael Kemp, MD; Glenn Wakem, MD E-Mail:hasan.alam@nw.org				5d. PROJECT NUMBER MT17008.034	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER N/A	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) AND ADDRESS(ES) Regents of the University of Michigan, 3003 S state Street, Ann Arbor MI 48109				8. PERFORMING ORGANIZATION REPORT NUMBER 4 2019-511 -001 [REDACTED]	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Development Command Fort Detrick, Maryland 21702-5012				10. SPONSOR/MONITOR'S ACRONYM(S)	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S) N/A	
12. DISTRIBUTION / AVAILABILITY STATEMENT Distribution Unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT The goal of this project is to provide practical solutions for the control of non-compressible torso hemorrhage. We plan to achieve this objective by combining two innovative strategies to make REBOA more practical for the military and austere use, and by testing these approaches in clinically realistic large animal models. Specific Aim 1: Determine the effects of c-and pREBOA, with and without VPA, on brain lesion size and edema, spinal cord injury, damage to organs distal to the aortic occlusion (e.g. kidney, liver, bowel, muscles), and global ischemia-reperfusion injury in swine models of combined controlled hemorrhagic shock (HS) and severe traumatic brain injury (TBI). Specific Aim 2: Study the consequences of c- and pREBOA, with and without VPA treatment, on hemorrhage control, long-term survival, neurological outcomes, and multiple organ injury, in swine models of combined uncontrolled HS and TBI. Specific Aim 3: Elucidate the underlying physiological and cellular mechanisms that are altered					
15. SUBJECT TERMS					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			19b. TELEPHONE NUMBER (include area code)
Unclassified	Unclassified	Unclassified	Unclassified		

TABLE OF CONTENTS

Annual Technical Report

1. Project Status	
a. Accomplishments.....	5
b. Reportable Outcomes	6
c. Progress Detail	7
2. Future Plans	14
3. Problems / Issues	14
a. Current Problems / Issues	
b. Anticipated Problems / Issues	
4. Financial Health	14
5. Personnel Effort	14
6. Protocol and Activity Status.....	15
a. Human Use Regulatory Protocols	
b. Use of Human Cadavers for RDT&E, Education or Training	
c. Animal Use Regulatory Protocols	

Annual Business Report

1. Current Staff	17
2. Current Expenditures	17
3. Status of Milestones	18
4. Deviation from Project Plan	19

Annual Technical Status Report for

MTEC-17-08-MT-0340; The Effects of Complete and Partial Resuscitative
Endovascular Balloon Occlusion of the Aorta (REBOA) with Pharmacologic Treatment in Swine
Models of Hemorrhagic Shock, Traumatic Brain Injury, and Complex Vascular Injuries.
MT17008.034

Reporting Period: Effective Date – 7/26/2019-10/25/2020

University of Michigan (Awardee)
Hasan B Alam, MD, Research Project Lead
Co-Investigators Rachel Russo, MD; Yongqing Li, MD, PhD
Hasan B Alam, MD Research Project Technical POC

Regents of the University of Michigan
3003 S State Street
Ann Arbor, MI 48105
Phone Number: 734-936-5823
Email address: alamh@umich.edu and zoev@umich.edu

Submitted: <10/25/2020>

1. Project Status

a. Accomplishments

1. Wrote and revised protocol. Obtained IACUC and ACRUO approval.
 - a. First draft of protocol submitted for veterinary review 15-MAY-2019
 - b. Revised in response to IACUC questions 31-MAY-2019
 - c. Revised in response to IACUC questions 24- JUN-2019
 - d. Revised in response to IACUC questions 18-JUL-2019
 - e. Revised in response to IACUC questions 5-AUG-2019
 - f. Revised in response to IACUC questions 22-AUG-2019
 - g. Obtained IACUC approval 9-SEP-2019
 - h. Submitted to ACRUO 10-SEP-2019
 - i. Revised in response to ACRUO questions 03-JAN-2020
 - j. Revised in response to ACRUO 07-JAN-2020
 - k. Obtained ACRUO approval 27-JAN-2020
 - l. Milestone 1 completed.
 - m. Submitted approvals to MTEC.
 - n. Received first allocation for funds
2. Began model development experiments
 - a. Equipment ordered. Delivered. Personnel training updated.
 - b. Animals ordered. Delivered. Acclimated. 27-JAN – 6-FEB-2020
 - c. Completed in-service with Transonic Engineer, Cole McLarty
 - d. Completed in-service with Prytime Engineer, Curtis Franklin. 5-FEB-2020
 - e. Model development experiments
 - i. 6-FEB-2020
 - ii. 12-FEB-2020
 - iii. 25-FEB-2020
 - iv. 03-MAR-2020 – determined need for fluoroscopy to troubleshoot pREBOA-PRO
 - v. Obtained access to fluoroscopy. Additional training. Arranged for Prytime Engineer, Curtis Franklin to be on site.
 - vi. Lab shut down for COVID-19. Obtained special permission to complete planned experiment.
 - vii. 20-MAR-2020 – Learned new insights about the pREBOA-PRO, novel device
 - viii. Experiments on hold through JUL-2020 due to COVID-19 restrictions
 - ix. Applied for and received approval to perform complex procedures during COVID-19 restrictions – July-2020
 - x. Short-term survival model with 40% hemorrhage developed and tested in July 2020/August 2020: model compared complete occlusion with standard ER-REBOA catheter versus partial occlusion (without provider titration) using novel catheter pREBOA-PRO (see below)
3. Completed data analysis on previously performed animal model development experiments
 - a. Last analyzed pre-COVID data 07-APR-2020
 - b. Presented pre-COVID data at lab meeting 10-APR-2020
4. Fine-tuned the Standard Operating Procedures for future model development experiments to be carried out at Northwestern
 - a. Last modified 21-JUN-2020
5. Established the preliminary plan for relocating the lab, including starting initial recruitment of personnel, inventory of equipment with moving plan, and submission of the animal protocols for this experiment to the IACUC at Northwestern
 - a. 15-JUN-2020
6. Published manuscript describing the performance characteristics of the pREBOA-PRO catheter as observed during the model development experiments completed thus far
 - a. Russo RM, Franklin CJ, Davidson AJ, et al. A new, pressure-regulated balloon catheter

for partial resuscitative endovascular balloon occlusion of the aorta (REBOA) [published online ahead of print, 2020 Apr 27]. *J Trauma Acute Care Surg.* 2020;10.1097/TA.0000000000002770. doi:10.1097/TA.0000000000002770

- b. Submitted for publication 10-APR-2020
 - c. Accepted for publication 13-APR-2020
 - d. Published online ahead of print 27-APR-2020
 - e. Proofs revised for print 19-MAY-2020
 - f. Published in hard copy AUG-2020
7. Accepted for presentation at 2020 Military Health System Research Symposium, initially planned for August in Florida, that has since been cancelled due to COVID-19 with no plan to reschedule or replace with a virtual conference
 - a. Submitted for presentation 04-APR-2020
 - b. Accepted for presentation 03-JUN-2020
 8. Published abstract relating to the design and the performance of the pREBOA-PRO catheter as observed during the model development experiments completed thus far
 - a. Russo RM, Franklin CJ, Davidson AJ, et al. Technical Innovation in Partial Aortic Occlusion: A Brief Review of the pREBOA-PRO. [Abstract, published online ahead of print, 2020 July 8]. 2020 Military Health System Research Symposium. [conference cancelled for COVID]. Available at <https://mhsrs.amedd.army.mil/>. Accessed on July 16, 2020.
 - b. Submitted 03-JUN-2020
 - c. Accepted for publication 13-JUN-2020
 - d. Published online 8-JUL-2020
 9. Established the MTEC add-on project proposal to investigate the use of our Super-Continuum Infrared Spectroscopy of Cytochrome-C-Oxidase (SCISCO) system [patent pending] to detect and monitor brain injury
 - a. Submitted 22-APR-2020
 - b. Approved 01-MAY-2020
 10. Obtained approval for add-on proposal from U of M
 - a. Executed 9/18/2020
 11. Modified the statement of work and milestones to include the addition of the new add-on Project.
 - a. Revised 22-JUN-2020
 12. Analyzed short-term model data assessing resuscitation requirements and end levels of organ injury biomarkers
 - a. Last analyzed 22-SEP-2020
 - b. Demonstrated improvement in resuscitation requirements and lower end levels of organ injury biomarkers in partial occlusion cohort.
 13. Drafted manuscript entitled: "A Novel Partial Resuscitative Endovascular Balloon Aortic Occlusion (pREBOA) Device That Requires Minimal Provider Titration"
 - a. Submitted OCT-2020 to *Journal of Trauma and Acute Care Surgery*
 - b. Highlights the minimal return of distal femoral arterial wave form as the target for partial occlusion
 - c. Highlights the ability to achieve partial occlusion without need for significant provider titration
 - d. Emphasizes the improvement in resuscitation requirements and end levels of organ injury biomarkers in the partial occlusion (pREBOA-PRO) cohort

b. Reportable Outcomes

1. Russo RM, Franklin CJ, Davidson AJ, et al. A new, pressure-regulated balloon catheter for partial resuscitative endovascular balloon occlusion of the aorta (REBOA) [published online ahead of print, 2020 Apr 27]. *J Trauma Acute Care Surg.* 2020;10.1097/TA.0000000000002770. doi:10.1097/TA.0000000000002770
2. Russo RM, Franklin CJ, Davidson AJ, et al. Technical Innovation in Partial Aortic Occlusion: A

Brief Review of the pREBOA-PRO. [Abstract, published online ahead of print, 2020 July 8]. 2020 Military Health System Research Symposium. [conference cancelled for COVID]. Available at <https://mhrs.amedd.army.mil/>. Accessed on July 16, 2020. Accepted for presentation at 2020 Military Health System Research Symposium, initially planned for August in Florida, that has since been cancelled with no plan to reschedule or replace with a virtual conference.

c. Progress Detail

Overview

The first quarter of this project was dedicated to perfecting the study design and obtaining protocol approval. During this time, we leveraged the expertise of our team, our industry partner, and our university resources to prepare for our experiments. Our in-service with Cole McLarty from Transonic assisted our team with understanding aortic and carotid flow measurement in translational swine models. Many existing studies of partial REBOA techniques use blood flow measurements to guide balloon inflation/deflation and to define end points for partial REBOA. The major criticism of this approach is that flow measurements are not available in clinical practice. New end points to define partial REBOA must be defined using clinically available measurements. Our in-service with Curtis Franklin included a table-top demonstration and in-vivo application of the catheter with an introduction to its features and functionality. With Curtis's help we have been able to show our method of performing pREBOA with the pREBOA-PRO device can bridge this gap. We have been able to use clinically available measurements to define partial REBOA end-points that correlate with flow measurements that confer survival benefits in animal models.

The second quarter of this project focused on model development. We solidified the degree of hemorrhage we plan to use, the instrumentation, anesthetic management, and approach to partial REBOA. We made appropriate changes in the protocol and had the amendments approved. We fine-tuned the use of the pREBOA-PRO catheter to establish partial REBOA in our swine and settled on a degree of occlusion for future experiments. Much of the second quarter was dedicated to understanding the functionality of the pREBOA-PRO during and after hemorrhage. Prior to our work, the pREBOA-PRO had only been tested in ex-vivo flow chambers and in euvoletic swine. Many factors influence aortic flow, particularly during hemorrhagic shock. Understanding this complex relationship in pre-clinical models will be key to guiding the use of the pREBOA-PRO in clinical practice.

During the third quarter the lab was shut down due to COVID-19. No experiments could be performed and all effort was required to be remote. As such the quarter was devoted to analysis of model development data to facilitate the completion of the model development milestone as soon as animal experiments are allowed again.

Furthermore, we applied for additional funding and laid the groundwork for the add-on project that will allow the development of a new Super-Continuum Infrared Spectroscopy of Cytochrome-C-Oxidase (SISCCO) prototype to be developed remotely within the restrictions imposed by COVID-19. This novel laser-based device is designed to non-invasively detect changes in tissue oxygenation and energy production. We believe these measurements will aid in the diagnosis and monitoring of brain injury and hemorrhagic shock. We updated the statement of work and the milestones to reflect this new addition.

In the fourth quarter we worked diligently to be able to open the lab. We established a health and safety plan that was approved by our laboratory safety committee and public health advisors. We obtained approval to open and were able to resume model development. We then selected the duration of occlusion we will use to study. The aim of this proposal is to extend the survivable duration of aortic occlusion. Current clinical practice guidelines recommend complete aortic occlusion (REBOA) be limited to 15 minutes. The average pre-hospital transport time in military environments is 90 minutes but may be longer. We will aim to extend the survivable duration of aortic occlusion beyond 2 hours using a combination of partial REBOA achieved with the pREBOA-PRO catheter to reduce ischemia and valproic acid to enhance cellular ischemia tolerance. Thus far, we have been able to achieve survival following 2 hours of aortic occlusion with our partial REBOA technique.

We were further able to compare the ischemic impact of 2 hours of partial REBOA performed with the pREBOA-PRO to 2 hours of complete occlusion achieved with the standard ER-REBOA. Thus far we demonstrated that partial REBOA achieved in this way provided equivalent blood pressure support with less ischemic burden than complete REBOA. We were additionally able to achieve a steady degree of partial REBOA with stable hemodynamics throughout the occlusion period without the need to manipulate the balloon during treatment.

Results summary

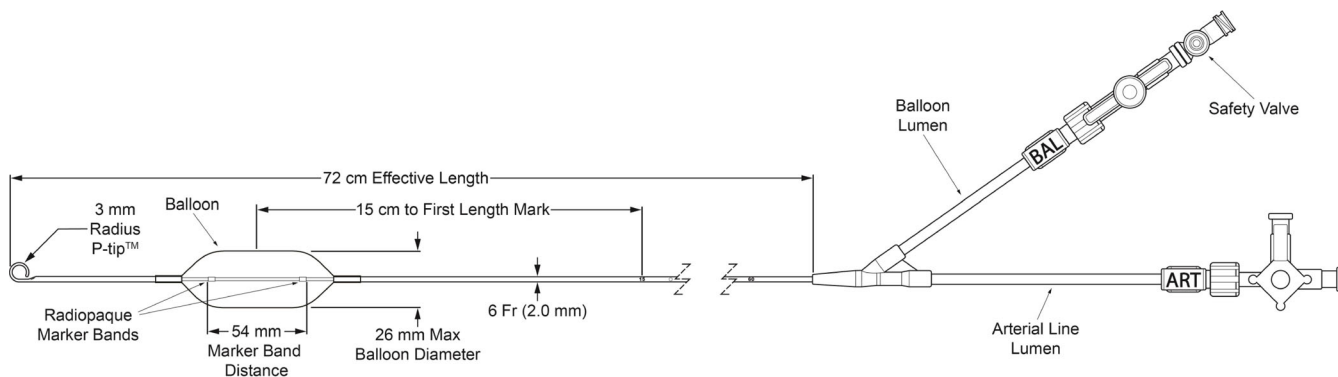
Model development – we investigated the performance characteristics of the pREBOA-PRO catheter to determine the most suitable degree of occlusion to standardize the degree of “partial REBOA” across future animal experiments. We found a reproducible metric with results depicted in the figure below.

We compared 2 hours of partial REBOA to 2 hours of complete REBOA and demonstrated that

- 1) pREBOA achieved the same proximal (upstream from the balloon) blood pressure improvement as cREBOA
- 2) pREBOA resulted in less distal ischemia than cREBOA and
- 3) pREBOA resulted in lower resuscitation requirements

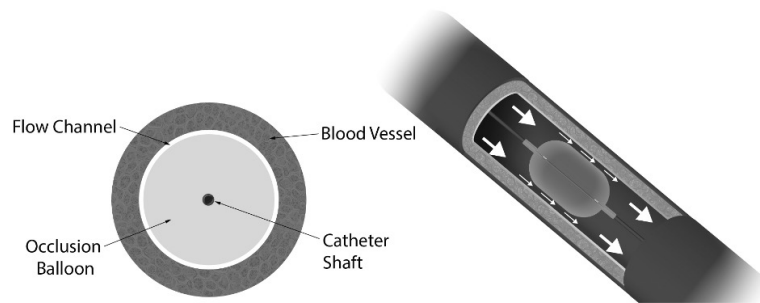
We also demonstrated the feasibility of achieving partial REBOA with a novel catheter using return of distal waveform as the end-point. This study marks the first pre-clinical study to evaluate the efficacy of this common clinical end-point (used in Japan and in the field by US special forces teams). We also demonstrated that, for the first time, pREBOA could be sustained for 2 hours without manipulating the balloon at all. The fact that animals in the pREBOA group had decreasing lactate following reperfusion while the cREBOA animals had persistently high lactate (at levels that have previously been above the threshold for survivability based on longer-term survival models in this same hemorrhage model), indicates that high-grade pREBOA carried out in this way may provide a longer period of safe occlusion than is currently achieved with other techniques. Future studies in longer-term survival models will be needed to evaluate this endpoint. These findings have been submitted for peer-reviewed publication to the Journal of Trauma and Acute Care Surgery.

Design characteristics of the pREBOA-PRO:

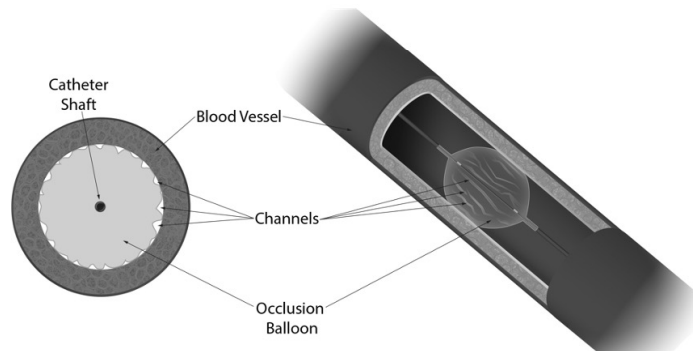


The pREBOA-PRO™ catheter. The 7F compatible pREBOA-PRO™ is built on the same chassis as its predicate, the ER-REBOA™. The combination of the atraumatic P-tip™, integrated superelastic nitinol tube and external aortic zone marks on the catheter shaft aid the ability to place the device when imaging is not available. The semi-compliant balloon containing flow channels is capable of full and controlled partial occlusion in vessels up to 26mm. A safety valve set to release at < 0.5 ATM prevents over-inflation of the balloon. The “ART” lumen can be used to monitor pressure proximal to the balloon or to insert a guidewire (up to 0.025”).

ER-REBOA (standard balloon for complete occlusion)

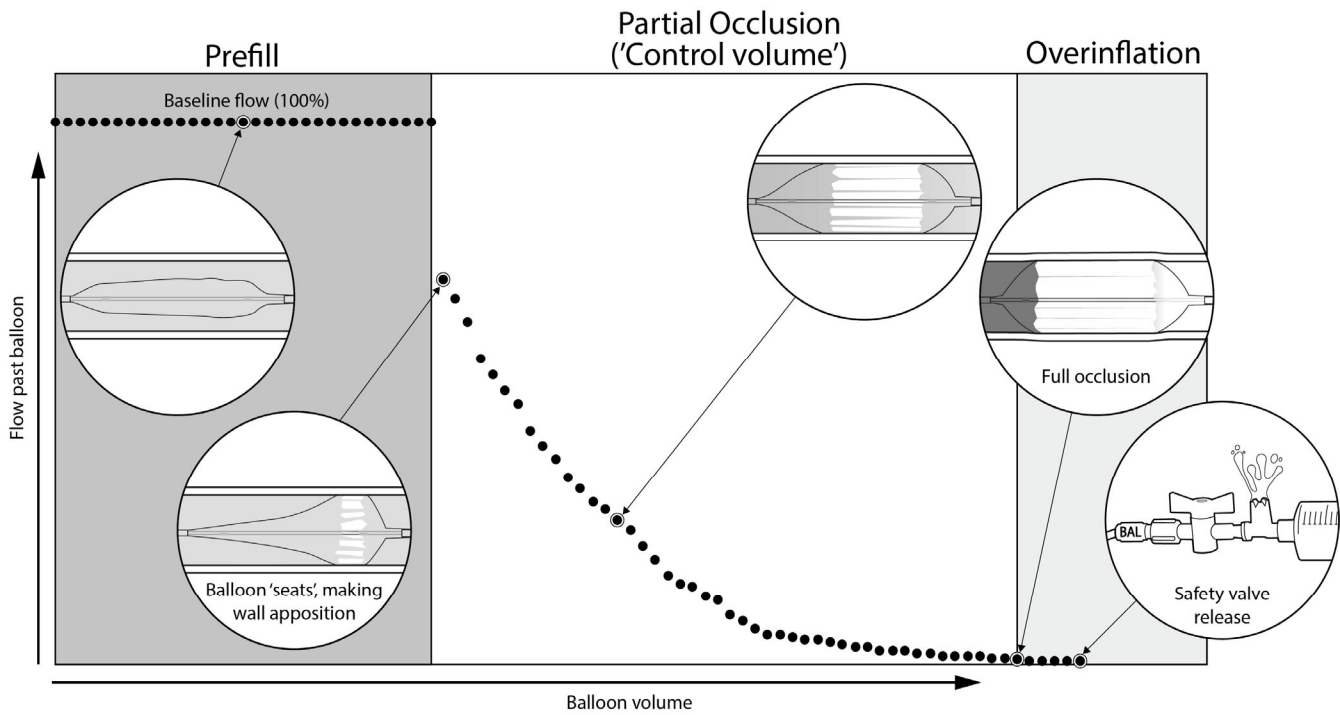


pREBOA-PRO (novel balloon for partial occlusion)

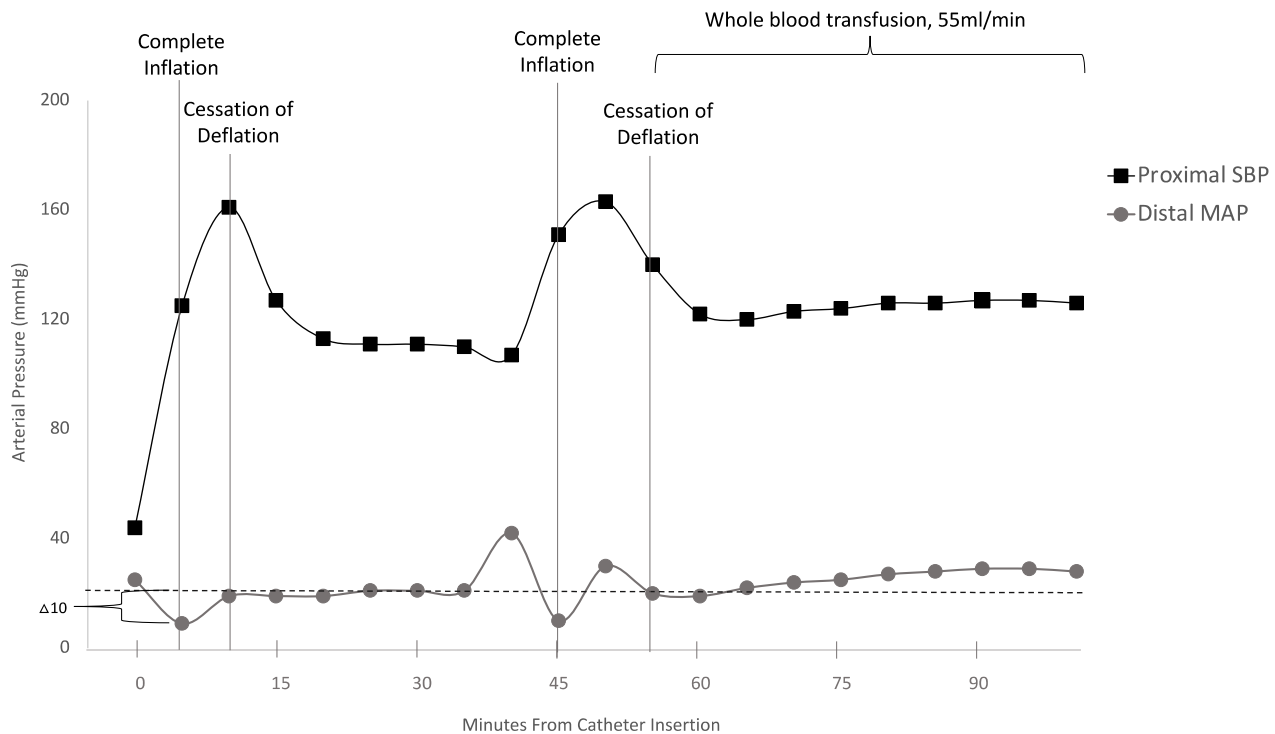


During Inflation/Deflation

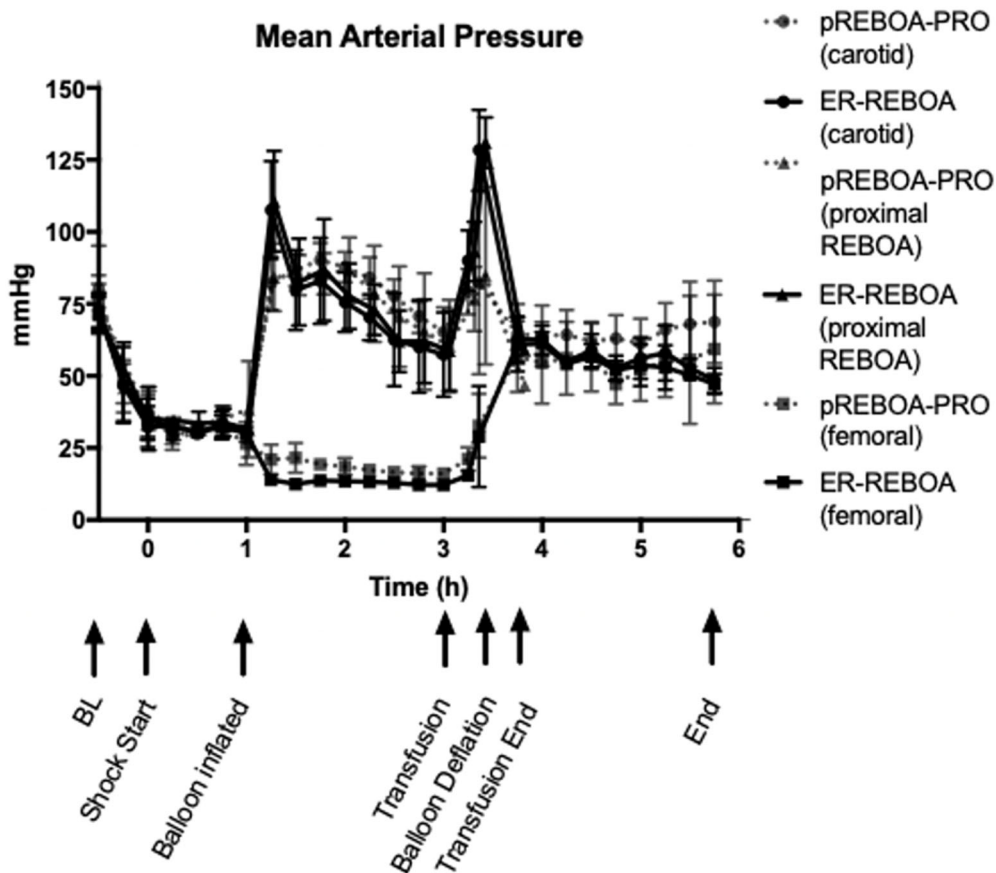
Images of the ER-REBOA and pREBOA-PRO devices. The ER-REBOA, created for complete occlusion, is inflated in a symmetrical fashion such that there should be simultaneous apposition of the balloon to the wall of the aorta at all points. Due to the semi-compliant nature of the balloon, the pREBOA-PRO which was created for partial occlusion creates ridges, or channels, at the periphery during inflation/deflation. Blood may flow through these channels when the pREBOA-PRO is not fully inflated. If the pREBOA-PRO is insufflated sufficiently, it is capable of creating a complete occlusion.



The pREBOA-PRO utilizes a semi-compliant balloon with flow channels. During inflation, the balloon achieves wall apposition with flow channels present in the balloon material, which permits a limited amount of flow to pass by the balloon until full occlusion is reached. Balloon inflation or deflation progresses in stages as the balloon changes shape with changes in volume. The stages of balloon inflation with pREBOA-PRO are 1) Prefill, during which volume added to the balloon has minimal impact on flow. The expanded balloon does yet contact the wall of the aorta; 2) Partial occlusion, in which the balloon is in contact with the wall of the aorta and distal flow is permitted through open flow channels of varying size. The volume of fluid in the balloon during the period of pREBOA is termed “control volume” as it is during this period that changes in balloon volume “control” the degree of distal flow. 3) Full occlusion, in which no distal flow is permitted but intra-balloon pressure has not yet started to rise; and 4) Over-inflation, in which additional balloon volume causes intra-balloon pressure to increase. Safety valve release occurs when the intra-balloon pressure reaches 0.5ATM.

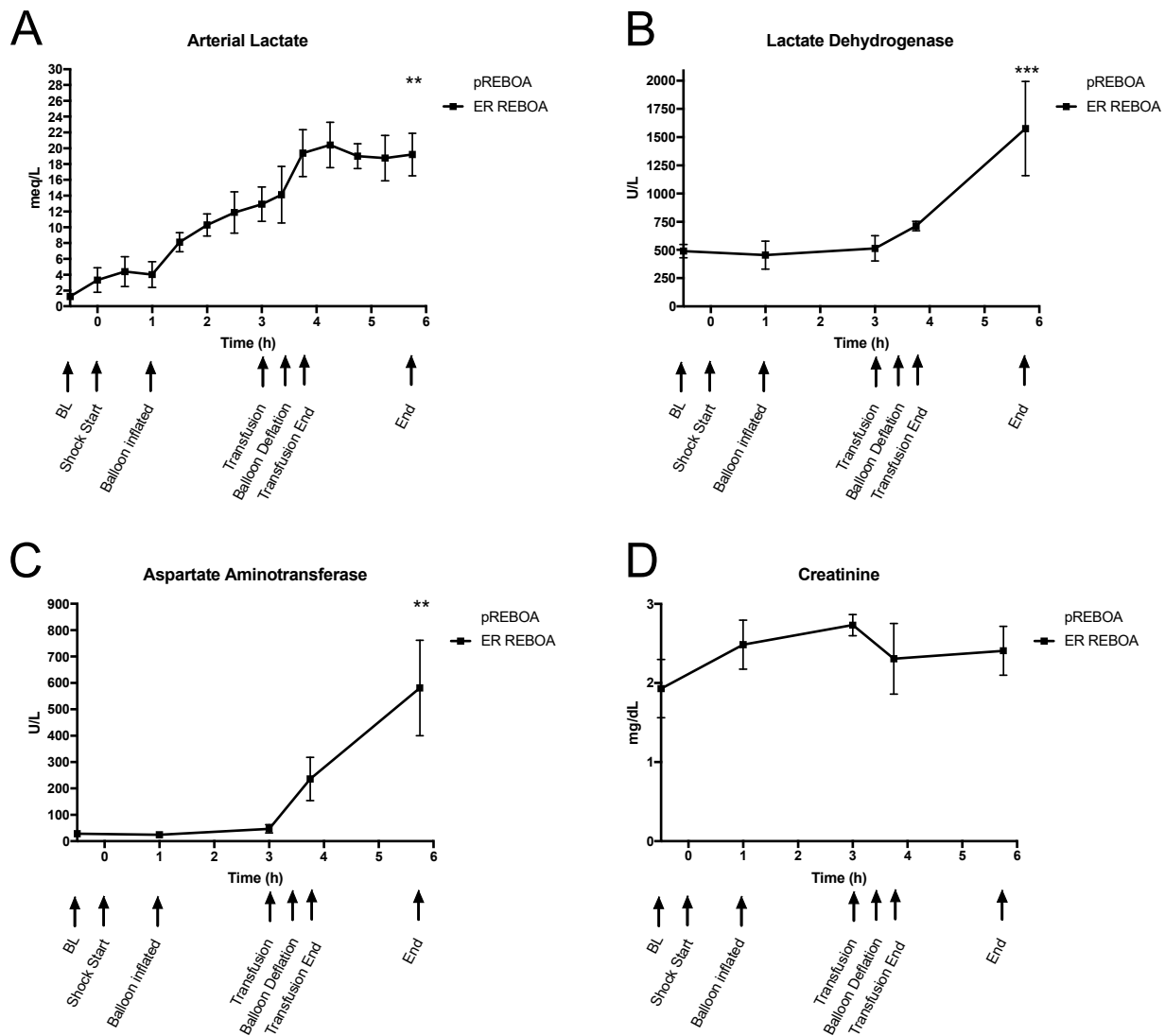


Initial observations assessing the hemodynamic stability of targeting a distal MAP (d-MAP) goal on two consecutive cycles of inflation/deflation following an hour of un-resuscitated stage 4 hemorrhagic shock in a swine. In each cycle the pREBOA-PRO was completely inflated until activation of the pressure-release valve. Volume was removed until d-MAP increased by 10mmHg. No further changes were made in balloon volume after cessation of deflation. In each cycle, proximal systolic blood pressure (p-SBP) continued to rise after occlusion, even as volume was removed from the balloon. While d-MAP stabilized immediately, p-SBP stabilized 10 minutes following cessation of balloon deflation. During whole blood transfusion blood pressure increased steadily without any adjustment to balloon volume.

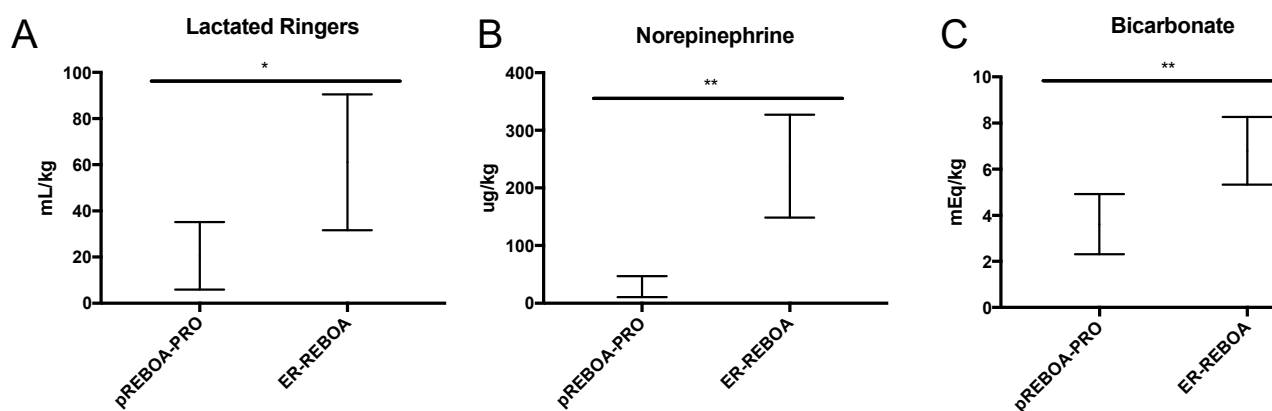


Comparison of Mean Arterial Pressures throughout hemorrhage, shock, balloon occlusion, deflation, and resuscitation.

Partial REBOA achieved with the pREBOA-PRO provides equivalent proximal blood pressure support compared to complete occlusion achieved with the ER REBOA while allowing significantly more distal perfusion throughout the treatment period. Data are presented as group mean \pm standard error. MAP – mean arterial pressure; bpm – beats per minute; BL – baseline; pREBOA-PRO – partial REBOA; ER-REBOA – complete REBOA.



Laboratory markers of organ injury. Laboratories including (A) arterial lactate, (B) lactate dehydrogenase, (C) aspartate aminotransferase, and (D) creatinine are presented as group means \pm standard error. Statistical significance of $p < 0.01$ or $p < 0.001$ are designated as ** or *** respectively. Statistically lower levels of end lactate, lactate dehydrogenase, and aspartate aminotransferase were demonstrated in pREBOA animals. BL – baseline; pREBOA-PRO – partial occlusion; ER-REBOA – complete occlusion.



Resuscitation requirements following balloon deflation. Presented variables include (A) volume of lactated ringers required to maintain CVP of 6mmHg, (B) norepinephrine dosing to maintain goal MAP of 55-60mmHg, (C) and bicarbonate dosing to temporize pH<7.2. Data are presented as group means \pm standard error. Statistical significance of $p<0.05$ or $p<0.01$ are designated as * or ** respectively. pREBOA-PRO – partial REBOA; ER-REBOA – complete REBOA.

2. Future Plans

Over the next year, our group intends to evaluate longer survival models beyond that currently tested with the novel catheter pREBOA-PRO. We also intend to assess how the addition of valproic acid dosing alters the tolerated duration of REBOA aortic occlusion, anticipating that we will be able to extend the tolerated duration.

3. Problems / Issues

SOW was updated for the transfer and covid 19 delays when we modified for MOD 1 addendum.

a. Current Problems / Issues

Waiting on transfer to Northwestern University to finalize and Protocol approval through Northwestern and ACURO.

b. Anticipated Problems / Issues

None

4. Financial Health

We have utilized all funds from our first milestone payment and have exceeded those funds by \$7700. With the project transferring to Northwestern and our next milestone payment will be issued to that institution we will need to work together so these funds are recovered for University of Michigan out of the next milestone payment.

5. Personnel Effort

Personnel for the first year of the project.

Personnel	Role	Percent Effort
Hasan B. Alam	Project Leader	20% Until 8/31/20
Rachel Russo	Co-Investigator/Team Leader	50% Until 7/31/20
Jonathan Eliason	Co-Investigator	5% Until 7/31/20
Yongqing Li	Co-Investigator	25% Until 8/31/20
Baoling Liu	Research Specialist	30% Until 8/31/20

Kiril Chtraklin	Research Specialist	33.3% Until 8/31/20
Maggie McLaughlin	Research Associate	50% until July 6, 2020
Zoe Vanella	Project Manager	30% Until 8/31/20

6. Protocol and Activity Status

- a. **Human Use Regulatory Protocols:** None
- b. **Use of Human Cadavers for RDT&E, Education or Training:** Not Applicable
- c. **Animal Use Regulatory Protocols:**

Protocol [ACURO Assigned Number]: PRO00009167

Title: "MTEC-17-08 Multi-Topic-0340: The Effects of Complete and Partial Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) with Pharmacologic Treatment in Swine Models of Hemorrhagic Shock, Traumatic Brain Injury, and Complex Vascular Injuries"

Target required for statistical significance:

Target approved for statistical significance:

Submitted to and Approved by: IACUC and ACURO

Hasan Alam General Surgery

2920B TC

Ann Arbor 48109-5331

Dear Dr. Alam:

The Institutional Animal Care & Use Committee (IACUC) has reviewed the animal use application referenced below. The proposed animal use procedures are in compliance with University guidelines, State and Federal regulations and the standards of the "Guide for the Care and Use of Laboratory Animals. This project has been approved. There may be additional issues that need to be addressed prior to initiation of the associated research. It is your responsibility, as Principal Investigator, to secure all the necessary requirements and recommendations and notify funding agencies of changes made to the study. Committee approval must be obtained prior to making changes from what is originally stated in the protocol. An amendment must be approved prior to the implementation of the change.

Contact the ACU

Office for further information.

The United States Department of Agriculture (USDA), Department of Defense (DOD), and University policy require an annual administrative review of any animal use protocols funded by the DOD or approved to use USDA-covered species. Your continued animal use approval is contingent upon the completion of this online form. Additionally, your renewal application must be submitted, reviewed and approved in a timely manner prior to the expiration date of the current protocol. You will receive notification prior to the deadlines for both the annual review and protocol expiration.

The University's Animal Welfare Assurance Number on file with the NIH Office of Laboratory Animal Welfare (OLAW) is A3114-01, and most recent date of accreditation by the Association for the Assessment and Accreditation of Laboratory Animal Care International (AAALAC, Intl.) is November 22, 2017. If you receive news media inquiries concerning any aspect of animal use or care in this project, please contact James Erickson, News and Information Services, (734) 647-1842. If you have a security concern regarding the animals or animal facilities, or if you need emergency veterinary medical care, contact Joseph Piersante, Chief Operations Officer, at (734) 763-3434. UMPD will contact the appropriate veterinarian.

Sincerely,

Dr. Daniel Myers, D.V.M., MPH Professor of Surgery
Chairperson, Institutional Animal Care and Use Committee

STATUS: Approved

IACUC approved 09/09/2019

ACURO Approved 01/09/2020

Annual Business Status Report for

MTEC-17-08-MT-0340; The Effects of Complete and Partial Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) with Pharmacologic Treatment in Swine Models of Hemorrhagic Shock, Traumatic Brain Injury, and Complex Vascular Injuries.
MT17008.034

Reporting Period: Effective Date – 9/25/2019-10/25/2020

University of Michigan (Awardee)
Hasan B Alam, MD, Research Project Lead
Co-Investigators Rachel Russo, MD; Yongqing Li, MD, PhD
Hasan B Alam, MD Research Project Technical POC

Regents of the University of Michigan
3003 S State Street
Ann Arbor, MI 48105
Phone Number: 734-936-5823
Email address: alamh@umich.edu and zoev@umich.edu

Submitted: <10/25/2020>

1. CURRENT STAFF

<i>Personnel</i>	<i>% of Effort on project</i>
Project Leader	20%
Co-Investigator/Team Leader	50%
Co-Investigator	5%
Co-Investigator	25%
Research Specialist	30%
Research Specialist	33.3%
Research Associate	50%
Project Manager	30%

2. CURRENT EXPENDITURES

A. Fixed Priced Contracts:

MTEC Milestone Number	Milestone Description	Due Date	Government Funds
MTEC Milestone Number	Milestone Description	Due Date	Government Funds
1	Obtain IACUC and ACURO Approvals	10/15/2019 Completed 01/09/2020	\$269,367
2		2/15/20	\$1.00
	Total Expenditures		\$269,367

B. In Kind Contributions:

2) In-Kind: Prytime Medical Device Inc. In-Kind Contribution

Prytime Medical Device Inc. In-Kind Contribution

Funding Source (Cash)	This Period	Cumulative to Date
Cash	\$0.00	\$0.00
Labor Dollars	\$268.21	\$4,855.53
Indirect Labor Rates (Overhead/Fringe Benefits)	\$26.82	\$4,426.83
Travel	\$0.00	\$1,703.63
General & Administrative Services	\$0.00	\$0.00
Equipment (New)	\$0.00	\$0.00
Material	\$8,395.20	\$33,835.20
Other Direct Costs	\$0.00	\$0.00
Other *	\$0.00	\$0.00
Sub-Total	\$8,690.23	\$44,821.19

Funding Source (In-Kind)	This Period	Cumulative to Date
Use of Existing Equipment (Estimated fair market value)	\$0.00	\$0.00
Use of Existing Software (Estimated fair market value)	\$0.00	\$0.00
Intellectual Property (Estimated fair market Value)	\$0.00	\$0.00
Space (Land or buildings)	\$0.00	\$0.00
Sub-Total	\$8,690.23	\$44,821.19
Cost Share Total	\$8,690.23	\$44,821.19

3. STATUS OF MILESTONES All project milestones from the Milestone Payment Schedule, in the project award, should be accounted for below.

MTEC Milestone Number	Milestone Description	Due Date	% Completed this Reporting Period	Cumulative % Complete
1	Obtain IACUC and ACURO Approvals	10/15/2019	100%	100%
Sub task 1.1	Deliverable for task 1: Submit IACUC approval to funding agency			
2	Quarterly Report Y1Q1	10/25/2019	-Prj Not started No report	----
3	Quarterly Report Y1Q1	1/25/2020	100%	100%
	March - July COVID-19 Pandemic Shutdown all Large Animal Experiments			
4	Quarterly Report Y1Q2	4/25/2020	100%	100%
5	Quarterly Report Y1Q3	7/25/2020	100%	100%
	8/31/20 Alam Lab Moves to Northwestern University		completed	completed
6	Task 2 and 2.1: Islam Team - Improve and optimize SCISCCO breadboard design Blueprint for design and operating parameters	9/30/20(3 months after funded)	40%	40%
7	Annual Report Y1	10/25/2020	100%	100%
8	Task 3 and 3.1Islam Team - Build SCISCCO prototype that can be transported to remote labs. Tested performance metric for SCISCCO prototype	12/31/2020 (6 months after funded)	Not Started	Not Started
9	Quarterly Report Y2Q1	1/25/2021	Not Started	Not Started
10	Task 4 Complete model Optimization Experiments	3/15/2021	60%	60%
	Sub task 4.1Complete Animal Experiment			
	Sub task 4.2 Deliverable for task 4, Analysis Report of Experimental Data		Not Started	Not Started
11	Quarterly Report Y2Q2	4/25/2021	Not Started	Not Started
12	Sub task 3.2Islam Team - Deliver SCISCCO Operation with software and algorithms for display of relevant information for user:	4/30/2021	Not Started	Not Started

13	Quarterly Report Y2Q3	7/25/2021	Not Started	Not Started
14	Task 5: Complete 50% Experiment 1	9/15/2021	Not Started	Not Started
	Subtask 5.1 Complete 50% Animal Experiment		Not Started	Not Started
	Subtask 5.2 Deliverable for task 5: Analysis Report of Experimental Data		Not Started	Not Started
15	Annual Report Y2	10/25/21	Not Started	Not Started
16	Task 6: Complete remaining 50% Experiment 1	1/15/2022	Not Started	Not Started
	Subtask 6.1 Complete remaining 50% Animal Experiment		Not Started	Not Started
	Subtask 6.2 Deliverable for task 6: Analysis Report of Experimental Data		Not Started	Not Started
17	Quarterly Report Y3Q1	1/25/2022	Not Started	Not Started
18	Quarterly Report Y3Q2	4/25/2022	Not Started	Not Started
19	Task 7: 50% Experiment 2	6/15/2022	Not Started	Not Started
	Sub task 7.1 Complete 50% Experiment 2		Not Started	Not Started
	Sub task 7.2 Deliverable for task 7: Analysis Report of Experimental Data		Not Started	Not Started
20	Quarterly Report Y3Q3	7/25/2022	Not Started	Not Started
21	Task 8: Complete remaining 50%	9/30/2022	Not Started	Not Started
	Sub task 8.1 Complete Experiment 2		Not Started	Not Started
	Sub task 8.2 Deliverable for task 4: Analysis Report of Experimental Data		Not Started	Not Started
22	Task 9 Final Analysis of all Physiological Data	10/25/2022	Not Started	Not Started
23	Task 10 Publish findings in Peer Reviewed Journal	10/25/2022	Not Started	Not Started
24	Final Report	10/25/2022	Not Started	Not Started

4. DEVIATION FROM PROJECT PLAN

Covid 19 Pandemic shut down all operations and we were under a "Stay Home, Stay Safe" order from our Governor. University of Michigan restarted research, clinical, administrative activities through June 2020. We were allowed to restart large animal experiments in July. We submitted a revised SOW with add-on project and the transition of the lab to Northwestern University which was approved.