60th Medical Group (AMC), Travis AFB, CA

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)

FINAL REPORT SUMMARY

(Please type all information. Use additional pages if necessary.)

PROTOCOL #: FDG20170030A **DATE:** 15 April 2019

PROTOCOL TITLE: Developing Novel Methods to Predict Fluid Responsiveness in a Porcine (*Sus scrofa*) Model of Shock.

PRINCIPAL INVESTIGATOR (PI) / TRAINING COORDINATOR (TC): Dr. Austin Johnson

DEPARTMENT: SGSE **PHONE #:** 608-712-7152

INITIAL APPROVAL DATE: 21 Nov 17 **LAST TRIENNIAL REVISION DATE:**

FUNDING SOURCE: Air Force Surgeon General's Office.

1. RECORD OF ANIMAL USAGE:

Animal Species:	Total # Approved	# Used this FY	Total # Used to Date
Sus scrofa	12	11	11

2. PROTOCOL TYPE / CHARACTERISTICS: (Check all applicable terms in **EACH** column)

___ Training: Live Animal ___ Medical Readiness ___ Prolonged Restraint

___ Training: non-Live Animal ___ Health Promotion ___ Multiple Survival Surgery

___ Research: Survival (chronic) ___ Prevention ___ Behavioral Study

_x__ Research: non-Survival (acute) ___ Utilization Mgt. ___ Adjuvant Use

___ Other ( ) ___ Other (Treatment) ___ Biohazard

3. PROTOCOL PAIN CATEGORY (USDA): (Check applicable) ___ C _x__ D ___ E

4. PROTOCOL STATUS:

***Request Protocol Closure:**

___ Inactive, protocol never initiated

___ Inactive, protocol initiated but has not/will not be completed

__X_ Completed, all approved procedures/animal uses have been completed

5. Previous Amendments:

List all amendments made to the protocol. **IF none occurred, state NONE. Do not use N/A.**

For the Entire Study Chronologically

Amendment Number	Date of Approval	Summary of the Change
1	11 July 18	Personnel
2	7 Aug 18	Procedure

6. FUNDING STATUS: Funding allocated: $30,030 Funds remaining: $ 0.00

7. PROTOCOL PERSONNEL CHANGES:

Have there been any personnel/staffing changes (PI/CI/AI/TC/Instructor) since the last IACUC approval of protocol, or annual review? ___ Yes __X_ No

If yes, complete the following sections (Additions/Deletions). For additions, indicate whether or not the IACUC has approved this addition.

ADDITIONS: (Include Name, Protocol function - PI/CI/AI/TC/Instructor, IACUC approval - Yes/No)

NAME	PROTOCOL FUNCTION	IACUC APPROVAL

DELETIONS: (Include Name, Protocol function - PI/CI/AI/TC/Instructor, Effective date of deletion)

NAME	PROTOCOL FUNCTION	DATE OF DELETION

8. PROBLEMS / ADVERSE EVENTS: Identify any problems or adverse events that have affected study progress. Itemize adverse events that have led to unanticipated animal illness, distress, injury, or death; and indicate whether or not these events were reported to the IACUC.

The first experimental animals were enrolled as expected. We found that determining fluid responsive solely by cardiac output is difficult in this model as cardiac output continues to increase throughout the experiment, primarily because the pigs were able to have very high heart rates that increased throughout the experiment. Therefore, fluid responsiveness by traditional definitions were difficult to model. A stroke volume definition will be needed for all algorithm development.

9. REDUCTION, REFINEMENT, OR REPLACEMENT OF ANIMAL USE:

REPLACEMENT (ALTERNATIVES): Since the last IACUC approval, have alternatives to animal use become available that could be substituted in this protocol without adversely affecting study or training objectives?

No.

REFINEMENT: Since the last IACUC approval, have any study refinements been implemented to reduce the degree of pain or distress experienced by study animals, or have animals of lower phylogenetic status or sentience been identified as potential study/training models in this protocol?

No

REDUCTION: Since the last IACUC approval, have any methods been identified to reduce the number of live animals used in this protocol?

No..

10. PUBLICATIONS / PRESENTATIONS: (List any scientific publications and/or presentations that have resulted from this protocol. Include pending/scheduled publications or presentations).

None to date.

11. PROTOCOL OBJECTIVES: (Were the protocol objectives met, and how will the outcome or training benefit the DoD/USAF?)

The objectives to date have been met. Data analysis and algorithm generation continues on the data research side. These algorithms will be used in new automated critical care platforms that are under development at the CIF.

12. PROTOCOL OUTCOME SUMMARY: (Please provide, in "ABSTRACT" format, a summary of the protocol objectives, materials and methods, results - include tables/figures, and conclusions/applications.)

Objectives: The use of intravenous fluids to improve blood pressure for patients in shock is difficult. Only 50% of patients will respond to fluids with an increase in blood pressure. The objective of this study was to develop a dataset of different states of fluid responsiveness that can be used for new algorithms to identify patients who are fluid responsive.

Materials and Methods: Eleven Yorkshire-cross swine were subjected to a shock state. Five animals underwent a hemorrhage followed by 45 minutes of aortic occlusion to create an ischemia-reperfusion shock state. Six animals underwent a continuous infusion of pseudomonas to create a bacteremia shock state. Once hypotension was achieved, animals underwent stepwise boluses with IV fluids until they were no longer fluid responsive. Physiologic and ventilation waveforms were collected continuously. ABGs were collected every 30 minutes.

Results: Animals in the ischemia-reperfusion arm remained fluid responsive for the entirety of the experiment with continuous increases in blood pressure with each full 500 mL bolus of fluid. This group of animals were found to have severe bowel edema. Animals in the pseudomonas arm continued to have increases in blood pressure throughout the study which decreased with increasing total fluid administered. On pressure-volume loop analysis, cardiac output increased throughout the study but stroke volume only increased during the first 60-90 minutes of fluid administration before leveling off. Increases in cardiac output after this period were predominantly due to increases in heart rate. Fluid responsive algorithm generation is ongoing based off stroke volume changes instead of cardiac output or blood pressure changes.

Conclusions: Ischemia-reperfusion models using REBOA remain fluid responsive. Sepsis-bacteremia models must use stroke volume as an indicator of fluid responsiveness and not blood pressure or cardiac output.

4/14/19

(PI / TC Signature) **(Date)**

Attachments:
Attachment 1: Defense Technical Information Center (DTIC) Abstract Submission **(Mandatory)**

Attachment 1

Defense Technical Information Center (DTIC) Abstract Submission

This abstract requires a brief (no more than 200 words) factual summary of the most significant information in the following format: Objectives, Methods, Results, and Conclusion.

Objectives: The use of intravenous fluids to improve blood pressure for patients in shock is difficult. The objective of this study was to develop a dataset of different states of fluid responsiveness that can be used for new algorithms to identify patients who are fluid responsive.

Methods: Eleven Yorkshire-cross swine were subjected to a shock state. Five animals underwent an ischemia-reperfusion injury and six animals underwent a bacteremia model. Animals then underwent stepwise boluses with IV fluids until they were no longer fluid responsive.

Results: Animals in the ischemia-reperfusion arm remained fluid responsive for the entirety of the experiment. Animals in the bactermia arm continued to have increases in blood pressure and cardiac output throughout the study. Stroke volume only increased during the first 60-90 minutes of fluid administration. Increases in cardiac output after this period were predominantly due to increases in heart rate. Fluid responsive algorithm generation is ongoing based off stroke volume changes instead of cardiac output or blood pressure changes.

Conclusion: Ischemia-reperfusion models using REBOA remain fluid responsive. Sepsis-bacteremia models must use stroke volume as an indicator of fluid responsiveness and not blood pressure or cardiac output.

Grant Number:_____
From:_____
****If you utilized an external grant, please provide Grant # and where the grant came from. Thank you.**