# 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 #:** FDG20170021A **DATE:** 24 Jan 19

**PROTOCOL TITLE** Development for a Swine (*Sus scrofa*) model of Controlled Hemorrhage and Lung Contusion.

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

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

**INITIAL APPROVAL DATE:** 20 Jul 17 **LAST TRIENNIAL REVISION DATE:** 19 Jul 18

**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* | 58 | 0 | 36 |
| | | | |
| | | | |

**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 ( ) _X__ 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 | 2 Oct 17 | Biosample collected/methods |
| 2 | 16 Nov 17 | Personnel |
| 3 | 15 Feb 18 | Procedural |
| 4 | 19 Jun 18 | Personnel |

**6. FUNDING STATUS:** Funding allocated: $114,135.00 Funds remaining: $

**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.

None

**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?

None

**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?

None

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

We found that REBOA did not cause progression of pulmonary contusions. We had hypothesized that REVOA would make the pulmonary contusions worse and that EVAC would mitigate this progression of injury. Because we did not see a worsening of the pulmonary contusion, we did not test the EVAC arm of the study.

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

Two abstracts have been written and submitted for presentation. A publication is currently being drafted with plans for submission to Journal of Trauma and Acute Care Surgery in March of 2019. The abstracts are attached at the end of this report.

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

The objectives were met. We have demonstrated that REBOA does not worsen the size of pulmonary contusions. We have also found that in animals with a pulmonary contusion, the proximal blood pressure during the period of occlusion is attenuated when compared to animals without pulmonary contusions.

**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.)

**Abstract #1:**

**Title:** Use of Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) in a Swine Model of Hemorrhagic Shock and Chest Trauma

**Introduction:** REBOA limits hemorrhage and augments blood pressure (BP) in trauma patients with non-compressible torso hemorrhage. Thoracic injury is considered an absolute contraindication to REBOA theoretically due to the increase in proximal BP, but data is limited. We examined the effects of chest trauma on REBOA response in a swine model of hemorrhagic shock.
**Methods:** Twelve anesthetized swine were randomized to blunt chest trauma with a captive bolt device or no trauma. All animals then underwent controlled hemorrhage followed by 60 minutes of Zone 1 REBOA, resuscitation with shed blood, and critical care until euthanasia at six hours. Physiologic parameters were continuously monitored. Blood samples and computed tomography images were obtained at intervals.
**Results:** There were no baseline differences between groups. Animals with chest trauma had lower mean arterial pressures (105.7±1.4 mmHg vs. 121.9±1.3 mmHg, P<0.001) and heart rates (154±2 vs. 166±2, P<0.001) during REBOA. Both groups had similar declines in their PaO2:FiO2 ratios after REBOA (-131±31 vs -126±31, P=0.91). Troponin levels rose significantly over time but did not differ between groups. There was no change in the size (402±107 mL vs 356±119 mL, P=0.78) or density (-406±52 Hounsfield Units (HU) vs -299±72 HU, P=0.26) of the pulmonary contusions in chest trauma pigs during the experiment.
**Conclusions:** Proximal BP augmentation during REBOA is diminished following chest trauma. Catheter manufacturer instructions recommend monitoring balloon inflation by monitoring for an increase in BP, which may not be as large in patients with chest trauma. Pulmonary contusions did not get larger or denser following aortic occlusion.

**Abstract #2:**

**Title:** Monitoring Pulmonary Contusion During Prolonged Field Care: A Pilot Study Comparing Ultrasound to Computed Tomography for Serial Imaging of Lung Contusion in a Porcine Trauma Model

**Background:** Pulmonary contusion, caused by either blunt or penetrating traumatic mechanisms, is a challenging clinical problem. The gold standard for diagnosis is computed tomography (CT); patients are then typically followed with serial chest imaging to monitor the progression of the contusion. However, these technologies may not be available in austere conditions under a delayed evacuation scenario. Portable ultrasound (US) technology is ideal for serial imaging in resource limited environments. US has not been sufficiently studied for imaging pulmonary contusions. This pilot study compares serial US to CT for imaging pulmonary contusions in a porcine trauma model.
Methods: Five anesthetized swine were instrumented and underwent controlled hemorrhage of 25% blood volume. A standardized right sided lung contusion was created with the use of a captive bolt gun fired five times directly on the chest wall. Animals were mechanically ventilated with a positive end expiratory pressure of 8 cm of water and a fraction of inspired oxygen of 0.4. Animals were resuscitated according to a prespecified protocol using shed blood followed by isotonic crystalloids and norepinephrine to maintain their mean arterial pressure between 65 and 75 mmHg. Physiologic parameters were monitored continuously. CT and US imaging was obtained before injury and 120, 240, and 360 minutes after injury. US images were acquired by two different operators at each time point using a standardized protocol. Each operator scored the degree of lung injury by recording the number of B-lines in each quadrant of the right thorax. Continuous variables were compared using Student's t-test and bivariate correlation was calculated with Pearson's r. Statistical significance was defined as $p < 0.05$.
**Results:** On CT imaging prior to injury, the mean right lung volume was 1373±261 mL and the mean right lung radiodensity was -675±27 Hounsfield units (HFU). The mean size of the contusion 120 minutes after injury was 16.7±12.4%. The mean radiodensity of the contusion at 120 minutes was -315±81 HFU. The mean ratio of arterial oxygen partial pressure to fraction of inspired oxygen was significantly lower at 120 minutes after injury compared to baseline (564±24 vs 422±114 mmHg, p=0.03). At 120 minutes after injury, the US scores for lung injury were well correlated with the size of the pulmonary contusion as a percentage of the right lung volume on CT (Pearson's r=0.69, r-squared=0.48, p = 0.03). There was no significant correlation between US scores and size of the contusion on CT imaging at the two later time points. The interclass

correlation coefficient (ICC) between ultrasound operators was 0.10 at baseline, 0.77 at 120 minutes, 0.35 at 240 minutes, and 0.81 at 360 minutes.

**Conclusions:** This porcine trauma model produced a substantial pulmonary contusion on CT imaging with a significant decrease in lung function. US performed moderately well early after injury to detect pulmonary contusion severity, but was not effective at the later time points. The variable ICCs at different time points reflects the operator-dependent nature of US imaging, suggesting that standardization and training are required before US can be an effective method for diagnosing pulmonary contusions. Despite these limitations, this pilot study demonstrates that ultrasound may be a useful technology for the diagnosis of pulmonary contusion in austere condition and further research is warranted.

**(PI / TC Signature)**

**2/4/19**

**(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:**

**Methods:**

**Results:**

**Conclusion:**

**Grant Number:**_____

**From:**_____

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