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 #: FDG20170028A **DATE:** 2 April 2019

PROTOCOL TITLE: Limited Survival Pilot Study to Evaluate Endovascular Perfusion Augmentation for Critical Care (EPACC) after Endovascular Intervention in a Porcine Model (*Sus scrofa*) of Resuscitation following Long Bone Fracture and Hemorrhagic Shock.

PRINCIPAL INVESTIGATOR (PI) / TRAINING COORDINATOR (TC): Capt Carl Beyer

DEPARTMENT: SGSE **PHONE #:** 941-223-8572

INITIAL APPROVAL DATE: 21 Aug 17 **LAST TRIENNIAL REVISION DATE:** 16 Aug 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	18	12	16

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
_X_ Research: Survival (chronic)	___ Prevention	___ Behavioral Study
___ 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	16 Nov 17	Personnel
2	16 May 18	Procedural/Anesthetic/Analgesic/Antibiotic/Study Agent
3	11 Jul 18	Personnel
4	20 Sep 18	Animal Use

6. **FUNDING STATUS:** Funding allocated: $ 55,000 Funds remaining: $ 0

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?

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?

The last two animals were not required to achieve the goals of this protocol.

10. **PUBLICATIONS / PRESENTATIONS:** Poster Presentation at MHSRS 2018: 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. See attached abstract.

11. **PROTOCOL OBJECTIVES:** The protocol objectives were met. This pilot study demonstrated that 24-hour survival after endovascular intervention is feasible in a swine model of hemorrhagic shock. This knowledge will benefit the USAF as researchers continue to optimize this life-saving technology and study it over longer, more clinically relevant time periods. Furthermore, this pilot study suggests that continued endovascular perfusion augmentation during critical care (EPACC) following hemorrhage control may not be helpful and other technologies should be pursued for use during critical care following hemorrhage control. Last, additional data collected during model development allowed a pilot study evaluating ultrasound for the diagnosis of pulmonary contusion.

12. PROTOCOL OUTCOME SUMMARY:

Objectives: The objective of this pilot study was to develop a 24-hour survival model following the use of aortic occlusive technology in a swine model of hemorrhagic shock. Furthermore, the study compared the consequences of using endovascular perfusion augmentation versus standard critical care in this model.

Methods: Anesthetized swine underwent pulmonary contusion, lower extremity fractures, and 30% hemorrhage. Animals were randomized to receive either: no intervention, endovascular perfusion augmentation, or standard critical care after 90 minutes of full or partial aortic occlusion. Animals were survived for 24 hours.

Results: All animals in the control group (n=3) and partial aortic occlusion group (n=3) survived for the full 24 hours. No animals survived 24 hours after complete aortic occlusion (n=3), with a mean survival time of 6 hours. The use of automated endovascular perfusion augmentation in this model required massive fluid boluses of over 20 liters in a 12-hour period and led to elevated lactate concentrations (3.59 mmol/L) compared to animals without endovascular perfusion augmentation (2.89 mmol/L).

Conclusion: This pilot study demonstrated that 24-hour survival after partial aortic occlusion is feasible in a swine model of hemorrhagic shock. Automated endovascular perfusion augmentation led to massive fluid resuscitation and did not improve outcomes.

(PI / TC Signature)

6 May 2019

(Date)

Attachments:
Attachment 1: Defense Technical Information Center (DTIC) Abstract Submission
Attachment 2: MHSRS 2018 Abstract Accepted for Poster Presentation

Attachment 1
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Grant Number: No grant number.

Attachment 2
MHSRS 2018 Abstract Accepted for Poster Presentation

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

Authors: Carl Beyer, MD, Guillaume Hoareau, DVM PhD, Eduard Poltavskiy, PhDc, Lauren Walker, Ian Stewart, MD, Michael Johnson, MD

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.