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

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)

FINAL REPORT SUMMARY

PROTOCOL #: FDG20180031A **DATE:** 09/09/2019

PROTOCOL TITLE: Comparison of intermittent and partial resuscitative endovascular balloon occlusion of the aorta (REBOA) in a porcine (*Sus scrofa*) model of non-compressible torso hemorrhage.

PRINCIPAL INVESTIGATOR (PI) / TRAINING COORDINATOR (TC): Guillaume L Hoareau

DEPARTMENT: CIF **PHONE #:** (215) 275-0395

INITIAL APPROVAL DATE: 20 Sep 2018 **LAST TRIENNIAL REVISION DATE:** Not Applicable

FUNDING SOURCE: AF Surgeon General's Office

1. RECORD OF ANIMAL USAGE:

Animal Species:	Total # Approved	# Used this FY	Total # Used to Date
Sus scrofa	17	17	17

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	9 Jul 19	Personnel

6. FUNDING STATUS: Funding allocated: $ 39,890.00 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? _x__ Yes ___ 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
Lindsay Bach	AI	Yes
Timothy Guenther	AI	Yes

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

NAME	PROTOCOL FUNCTION	DATE OF DELETION
Connor Caples	AI	16 Aug 19
Marguerite Spruce	AI	16 Aug 19
Kaeli Yamashiro	AI	16 Aug 19

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.

Four animals had to be excluded from the study due to the REBOA balloon bursting during use. Lot numbers for these were collected and forwarded to the manufacturer, Prytime Medical, Inc.

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?

None

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

Submitted to the Journal of Trauma and Acute Care Surgery.

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

Objectives were met despite have to exclude four animals due to device failure. We established that compared to intermittent REBOA, partial REBOA reduced the time spent at full occlusion and the number of precipitous drops in proximal MAP while delivering more distal aortic flow but not increasing total blood loss in this highly lethal injury model.

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: Partial resuscitative endovascular balloon occlusion of the aorta (pREBOA) and intermittent-REBOA (iREBOA) are techniques to extend the therapeutic duration of REBOA by balloon titration for distal flow or cyclical balloon inflation/deflation to allow transient distal flow, respectively. We hypothesized that manually-titrated pREBOA would reduce blood losses and ischemic burden when compared to iREBOA.

Material and methods: Following 20% blood volume controlled hemorrhage, 10 anesthetized pigs underwent uncontrolled hemorrhage from the right iliac artery and vein. Once in hemorrhagic shock, animals underwent 15 minutes of complete Zone 1 REBOA followed by 75 minutes of either pREBOA or iREBOA (N=5/group). After 90 minutes, definitive hemorrhage control was obtained, animals were resuscitated with the remaining collected blood, and then received 2 hours of critical care.

Results: There were no differences in mortality. Animals randomized to iREBOA spent a larger portion of the time at full occlusion when compared to pREBOA (74.0±5.5% versus 30.0±20.0%, respectively; p<0.01). While the average blood pressure during the intervention period was equivalent between groups, this was offset by large fluctuations in blood pressure and significantly more rescue occlusions for hypotension with iREBOA. Despite lower maximum aortic flow rates, the pREBOA group tolerated a greater total amount of distal aortic flow during the intervention period (median [IQR]; 20.9 [20.1-23.0]L vs 9.8 6.8-10.3]L; p=0.03) with equivalent abdominal blood losses. Final plasma lactate and creatinine concentrations were equivalent, although iREBOA animals had increased duodenal edema on histology.

Conclusions: Compared to iREBOA, pREBOA reduced the time spent at full occlusion and the number of precipitous drops in proximal MAP while delivering more distal aortic flow but not increasing total blood loss in this highly lethal injury model. Neither technique demonstrated a survival benefit. Further refinement of these techniques is necessary before clinical guidelines are issued.

10/10/2019

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

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

Attachment 1

Defense Technical Information Center (DTIC) Abstract Submission

Objectives: Partial resuscitative endovascular balloon occlusion of the aorta (pREBOA) and intermittent-REBOA (iREBOA) extend the duration of REBOA. We hypothesized that pREBOA would reduce blood losses and ischemic burden when compared to iREBOA.

Methods: Ten anesthetized pigs underwent controlled and uncontrolled hemorrhage. Animals then underwent 15 minutes of complete Zone 1 REBOA followed by 75 minutes of pREBOA or iREBOA. After 90 minutes, definitive hemorrhage control was obtained, animals were resuscitated with shed blood, and received 2 hours of critical care.

Results: There were no differences in mortality. iREBOA animals spent longer at full occlusion (74.0±5.5% versus 30.0±20.0%, respectively). While the average blood pressure during the intervention period was equivalent between groups, this was offset by large fluctuations in blood pressure and significantly more rescue occlusions for hypotension with iREBOA. Despite lower maximum aortic flow rates, the pREBOA group tolerated a greater total amount of distal aortic flow during the intervention period with equivalent abdominal blood losses. Final plasma lactate and creatinine concentrations were equivalent, although iREBOA animals had increased duodenal edema on histology.

Conclusions: pREBOA reduced the time spent at full occlusion and precipitous drops in MAP while delivering more distal aortic flow but not increasing total blood loss.

Grant Number:_____

From:_____

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