

**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 #:** FDG20170029A

**DATE:** 6 June 2018

**PROTOCOL TITLE:** The Effect of Prolonged Hypothermia on Extremity Ischemia in a Porcine Model (*Sus scrofa*) of Hemorrhage.

**PRINCIPAL INVESTIGATOR (PI) / TRAINING COORDINATOR (TC):** Capt Harris Kashtan

**DEPARTMENT:** SGSE

**PHONE #:** 916-397-1188

**INITIAL APPROVAL DATE:** 17 August 2017

**LAST TRIENNIAL REVISION DATE:** N/A

**FUNDING SOURCE:** SG

**1. RECORD OF ANIMAL USAGE:**

<b>Animal Species:</b>	<b>Total # Approved</b>	<b># Used this FY</b>	<b>Total # Used to Date</b>
<i>Sus scrofa</i>	16	7	7

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

- |  |   |  |
|--|---|--|
| <input type="checkbox"/> Training: Live Animal                     | <input type="checkbox"/> Medical Readiness  | <input type="checkbox"/> Prolonged Restraint       |
| <input type="checkbox"/> Training: non-Live Animal                 | <input type="checkbox"/> Health Promotion   | <input type="checkbox"/> Multiple Survival Surgery |
| <input type="checkbox"/> Research: Survival (chronic)              | <input type="checkbox"/> Prevention         | <input type="checkbox"/> Behavioral Study          |
| <input checked="" type="checkbox"/> Research: non-Survival (acute) | <input type="checkbox"/> Utilization Mgt.   | <input type="checkbox"/> Adjuvant Use              |
| <input type="checkbox"/> Other (            )                      | <input type="checkbox"/> Other (Treatment ) | <input type="checkbox"/> Biohazard                 |

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

**4. PROTOCOL STATUS:**

**\*Request Protocol Closure:**

- Inactive, protocol never initiated
- Inactive, protocol initiated but has not/will not be completed
- 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**

<b>Amendment Number</b>	<b>Date of Approval</b>	<b>Summary of the Change</b>
None		

6. **FUNDING STATUS:** Funding allocated: \$32,865.00 Funds remaining: \$ 5,000.00

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)

None

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

None

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.

After completion of the first portion of the experiment, we determined that the benefit from hypothermia decreased significantly with time. As such, we did not feel that it would be beneficial to proceed with the survival portion of the experiment.

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).

This protocol was presented at the UC Davis 2018 Research Symposium and has been selected for presentation at the 2018 MHSRS in August. Upon completion of the manuscript, it will also be submitted to a journal, although which is TBD at this time.

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

The protocol objectives were met in the sense that we determined that the benefits we saw at 4 hours of hypothermia did not seem to continue for 8 hours of ischemic time. This information is beneficial to our war fighters in that it tells us that we should start external cooling once a tourniquet is applied but should seek definitive care as soon as possible, preferably before 8 hours has elapsed.

**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.)

Introduction: Tourniquet use in the military has drastically improved survival from vascular injury, however, prolonged limb ischemia can result in permanent limb disability. We hypothesized that external cooling could decrease the severity of ischemia-reperfusion injury to pelvic limbs exposed to prolonged ischemia.

Materials and Methods: Following controlled hemorrhage, we induced extremity ischemia in 6 pigs with a zone 3 resuscitative endovascular balloon occlusion of the aorta (REBOA). The animals were then randomized to either control or external cooling using ice packs and cooling blankets for 8 hours, followed by a critical care period of 3 hours. Ischemic injury was then quantified with serum creatinine kinase activity, serum myoglobin concentrations, serum lactate dehydrogenase, peroneus tertius compartment pressures, and muscle and nerve biopsies.

Results: While lab markers of muscle breakdown tended to be lower in those animals receiving external cooling, these differences were not statistically significant. There were also no significant differences in hemodynamic data, muscle compartment pressure data, or urine output data.

Conclusion: While we saw trends toward less ischemic injury in those animals receiving external cooling, ultimately our study did not show a statistical difference between our two test groups. Previous studies from our group showed a large benefit from external cooling during 4 hours of extremity ischemia, however, it does not appear that such benefit maintained with prolonged cooling.

  
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HARRIS KASHTAN, Capt, USAF, MC

7/14/18  
\_\_\_\_\_  
(Date)

**Attachments:**

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

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

**Objectives:**

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**Methods:**

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While we saw trends toward less ischemic injury in those animals receiving external cooling, ultimately our study did not show a statistical difference between our two test groups. Previous studies from our group showed a large benefit from external cooling during 4 hours of extremity ischemia, however, it does not appear that such benefit is maintained with prolonged cooling.

**Grant Number:** \_\_\_\_\_

**From:** SG5M \_\_\_\_\_

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