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 #: FDG20170017A **DATE:** 1 March 2018

PROTOCOL TITLE: Development and Validation of a Simplified Renal Replacement Therapy Suitable for Prolonged Field Care in a Porcine (*Sus scrofa*) Model of Acute Kidney Injury.

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

DEPARTMENT: SGSE **PHONE #:** 215-275-0395

INITIAL APPROVAL DATE: 23 March 2017 **LAST TRIENNIAL REVISION DATE:** N/A

FUNDING SOURCE: SG

1. RECORD OF ANIMAL USAGE:

Animal Species:	Total # Approved	# Used this FY	Total # Used to Date
Sus scrofa	23	7	12

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	18 May 17	Personnel
2	16 Nov 17	Personnel

6. FUNDING STATUS: Funding allocated: $104,108.00 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
Mrs. Lauren Walker	AI	Yes
Maj Robert Faulconer	AI	Yes

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

NAME	PROTOCOL FUNCTION	DATE OF DELETION
Maj Robert Faulconer	AI	16 November 2017

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.

There was no adverse event with this protocol, which was executed in compliance with the IACUC.

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).

Validation of an improvised field expedient method for renal replacement therapy in a porcine AKI model. Military Health System Research Symposium 2018, FL.

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

The objectives were met. The results will be used to advocate for increased availability of forward renal

replacement therapy capacity.

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/Background:

Acute kidney injury (AKI) is a serious complication in combat casualties and renal replacement therapy (RRT) is vital for those with severe AKI. Access to RRT for US military combat casualties in war theaters is currently limited and those platforms can easily be overwhelmed. We propose to validate a simple RRT system compatible with prolonged field care (PFC) and austere environments in a porcine (Sus scrofa) model of AKI. We hypothesized that our improvised RRT (IRRT) system would require similar volumes of custom-made dialysate to achieve comparable creatinine and electrolytes concentrations and similar resuscitation requirements, when compared to conventional RRT (CRRT).

Materials and methods:

Twelve swine were anesthetized and instrumented. A 20cm Niagara® temporary dialysis catheter (Bard Access Systems, Salt Lake City, UT) was introduced into the right external jugular vein. Bilateral nephrectomies were performed. Animals were given intravenous heparin and underwent Zone 3 balloon occlusion of the aortic for 2 hours. Animals were randomized to either CRRT (NxStage System One®, NxStage Medical, Lawrence, MA) or IRRT. In the IRRT group, the arterial line of the dialysis catheter was connected to a Belmont® rapid infuser (Belmont Instrument Corporation, Billerica, MA) which was then connected to a Gambro® dialysis cartridge (Baxter International, Deerfield, IL), and subsequently to the venous line of the dialysis catheter. The ultrafiltrate was collected from the dialysis cartridge into a urometer and quantified. Replacement fluid solutions were custom-made with FDA-approved electrolytes stock solutions and infused in the system pre-pump. In the CRRT group, commercially available replacement fluids were used. At the end of the 2-hour occlusion period, the aortic balloon was deflated and animal received 4 hours of RRT. Animals were treated with isotonic crystalloids boluses and norepinephrine to maintain their mean arterial pressure between 65 and 75 mmHg.

Results:

While serum creatinine concentration was significantly higher than baseline from T120 until the end of the experiment, there was no difference in serum creatinine between groups (p=0.84). Similarly, there was no difference in serum calcium, magnesium, or phosphorus between groups (p=0.1, 0.68, and 0.14, respectively). While there was a difference between groups in serum potassium concentration over time (p=0.02), significance was lost in pairwise comparison at specific time points. There was no difference in serum potassium concentration at the end of the experiment [Median (IQR) - CRRT 5.25 (4.96-5.41) mmol/L; IRRT 6.0 (5.79-6,12) mmol/L, p=0.11]. There was no difference in dialysate [96.4 (94.3-97.8) mL/kg] and [98.9 (95.0-100.0) mL/kg (p=0.42)] or ultrafiltrate [96.5 (94.1-99.0) mL/kg] and [96.0 (92.4-98.7) mL/kg (p=0.75)] volumes between the CRRT and IRRT groups, respectively. There was no difference in sodium (p=0.17), chloride (p=0.14), calcium (0.08), magnesium (p=0.27), bicarbonate (p=0.27), or dextrose (p=0.31) between the commercially available and the custom-made replacement fluid. There was no difference in serum lactate (p=0.29) between groups. While serum lactate was significantly increased over time (p=0.0001), there was no difference in isotonic crystalloids (p=1), or norepinephrine (p=0.81) required for resuscitation between groups.

Conclusion:

We established that the IRRT system achieved similar electrolyte concentrations as CRRT with equivalent volumes of dialysate. Electrolytes concentration in the custom-made replacement fluids were comparable to the commercially available product. Additionally, resuscitation requirements and end-points were similar between the two groups. The IRRT system may prove helpful for the treatment of severe AKI in PFC or austere environments.

Guillaume Hoareau

Signature numérique de Guillaume Hoareau
Date : 2018.03.15 14:02:40 -07'00'

3/15/18

Guillaume L. Hoareau, DVM, PhD **(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:

To validate a RRT system compatible with prolonged field care (PFC). We hypothesized that our improvised RRT (IRRT) system would have similar performance to conventional RRT (CRRT).

Methods:

Twelve swine were anesthetized. A dialysis catheter was introduced. Bilateral nephrectomies were performed. The aorta was occluded in Zone 3 for 2 hours. Animals were randomized to CRRT or IRRT. In the IRRT group, the arterial line of the dialysis catheter was connected to a Belmont® rapid infuser which was then connected to a Gambro® dialysis cartridge, and subsequently to the venous line of the dialysis catheter. Replacement fluids were made with stock solutions. At the end of the 2-hour occlusion, animals received 4 hours of RRT. Animals were treated with isotonic crystalloids and norepinephrine to maintain their mean arterial pressure.

Results:

There was no difference in serum creatinine, electrolytes, dialysate or ultrafiltrate volumes between the groups. There was no difference between the commercial and the custom-made replacement fluids. There was no difference in serum lactate, isotonic crystalloids, or norepinephrine required for resuscitation.

Conclusion:

The IRRT system achieved similar performance as the CRRT. The IRRT system may prove helpful for the treatment of severe AKI in PFC.