AWARD NUMBER: W81XWH-20-2-0032

TITLE: Plasma Resuscitation Without Lung Injury (PROpOLIs)

PRINCIPAL INVESTIGATOR: Leopoldo Cancio, MD

CONTRACTING ORGANIZATION: Coalition for National Trauma Research, San Antonio, TX

REPORT DATE: October 2023

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

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5b. GRANT NUMBER
W81XWH-20-2-0032

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

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8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Development Command
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12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release, Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT
This study evaluates the administration of plasma for resuscitation after burn injury and its effect on 24 hour and total resuscitation volumes and resuscitation related morbidities at five Burn Centers across the US. Institutional Review Board and HRPO approval for protocol and several centers has been achieved. Logistics to support the study are in place.

15. SUBJECT TERMS
Resuscitation, burn, injury, blood

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
					USAMRDC
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**	Unclassified	32	**19b. TELEPHONE NUMBER** *(include area code)*
Unclassified	Unclassified	Unclassified			

Standard Form 298 (Rev. 8-98)
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TABLE OF CONTENTS

1. **INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

This study evaluates the administration of pathogen reduced plasma for resuscitation after burn injury and its effect on 24 and total resuscitation volumes and resuscitation related morbidities at five Burn Centers across the US. Its aims include (1) To determine whether administration of plasma during burn resuscitation results in decreased total resuscitation volumes compared to standard-of-care crystalloid-based resuscitation. (2) To determine whether plasma administration during burn resuscitation reduces ARDS. (3) To determine the effect of plasma administration on inflammation and the endotheliopathy of burns. Ninety-four subjects will be enrolled.

2. **KEYWORDS:**

Resuscitation, burn, injury, blood, plasma

3. **ACCOMPLISHMENTS:**

Throughout this year site initiation training was provided to participating sites ending with all sites open to enrollment. This coordination included blood bank training and coordination with plasma providers in each state to supply the plasma product.

A Defense Health Agency (DHA) Data Sharing Agreement Application (DSAA) was submitted and the Data Sharing Agreement approved 3/30/2023. The DSA was renewed 9/29/2023 and expires on 9/29/2024.

An initial Data and Safety Monitoring Board (DSMB) meeting was held in January 2023.

An Extension WithOut Funding (EWOF) was submitted and approved extending the period of performance to 9/29/2024. An amendment to extend the period of performance has been issued to all subawardees.

Dr. Cancio presented study progress at an In Progress Review in July 2023. A subsequent meeting with CAPT Polk, Combat Casualty Care Research Program was held in August 2023 to further discuss the study. The challenges to enrollment across all sites were discussed and potential options moving forward to include possibly changing the study design to achieve a no greater than minimal risk assessment as both the standard of care and intervention are approved by the FDA. Dr. Cancio is to send a White Paper outlining potential solutions to CAPT Polk.

PROPOLIS	Timeline (months)	Description of effort expended in this report period	Status
Major Task 1: Adapt PROPOLIS protocol for DoD Funded Status			
Coordinate with Sites for IRB agreement to use WIRB	1-3	Continuing review submitted and approved by WCG_IRB	100%

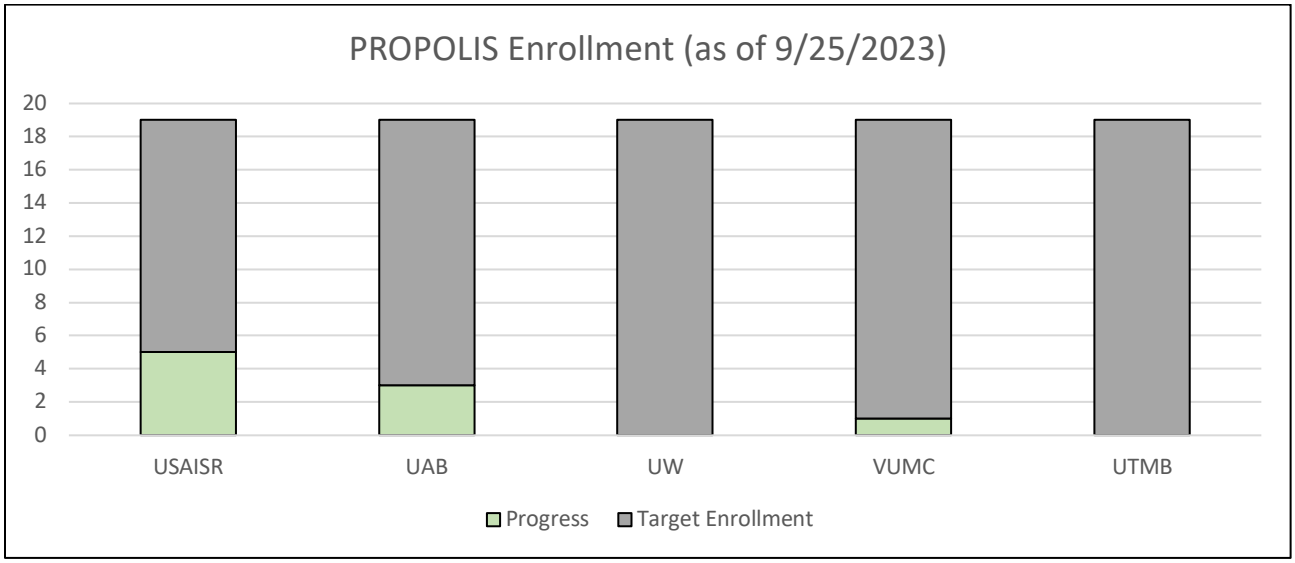
Coordinate with Sites for Military 2nd level IRB review (ORP/HRPO)	1	Continuing review submitted and approved by HRPO.	100%
Submit amendments, adverse events and protocol deviations as needed	As needed		ongoing
Submit annual WIRB report for continuing review	Annually	Submitted in 1/2023. Continuing review approved.	annually
Prepare and submit quarterly progress report to DoD	Quarterly	Quarterly reports were submitted for quarter 1, 2, and 3.	ongoing
Milestone Achieved: Central IRB approval at all sites	3		100%
Milestone Achieved: HRPO approval	6		100%
Major Task 2: Subcontract with all Study Sites			
Verify subaward documents: budget, budget justification, salary verification	1-3	Subaward documents have been reviewed for all site subawards.	100%
Issue and execute subaward documents	3	All subawards are fully executed.	100%
Submit quarterly progress reports	Quarterly	The monthly teleconference is currently serving as the quarterly report from sites.	ongoing
Review quarterly progress reports	Quarterly	Sites progress in submitting to WCG-IRB, HRPO, etc is monitored monthly.	ongoing
Milestone Achieved: Subawards issued for all sites	3		100%
Major Task 3: Patient Enrollment			
Educate and train research staff on study protocol and data collection procedures	1-6	• Monthly meetings are held via teleconference. A study webpage on the CNTR webpage has been created and has all study related resource documents and trainingshttps://www.nattrauma.org/research/research-policies-templates-guidelines/propolis-project-page/ To see the PROPOLIS Staff pages of the website – the password is PROPOLIS1. • Site initiation presentation created, and meetings were held with UAB, VUMC, and UTMB.	ongoing
Identify patients for study inclusion and collect initial data	1-6	All sites open to enrollment	Ongoing
Validate data collected quarterly	1-6	DCC works directly with sites for data validation.	Ongoing
Follow-up data collection	1-6		Ongoing
Coordinate with Sites & CNTR for monitoring data collection rates and data quality	1-16		Ongoing
Milestone Achieved: Completion	24		

of study; 94 patients enrolled			
Major Task 4: Data Analysis and Knowledge Translation			
Perform all analyses according to specifications, share findings with all investigators	24-29	Have not started.	
Comprehensive analysis of enrolled patients with intended publication	30-33	Have not started	
Dissemination of results, MHSRS, journal publications, electronic/print broadcasts through NTI	34	Have not started	
Milestone Achieved: Complete National Trauma Research Action Plan incorporating *findings from Aims 1-4*	36	Have not started	
Milestone Achieved: Identify optimal metrics to assess long term functional outcomes (Aim 2)	36	Have not started	
Milestone Achieved: Develop the NTRAP investigator toolkit	36	Have not started	

Enrollment:

Target Enrollment (per quarter)	**Q1**	**Q2**	**Q3**	**Q4**	**Q1**	**Q2**	**Q3**	**Q4**	**Q1**	**Q2**	**Q3**	**Q4**	
All Sites	-	-	12	12	12	12	12	12	12	10	-	-	**94**
Target Enrollment (cumulative)	**-**	**-**	**12**	**24**	**36**	**48**	**60**	**72**	**84**	**94**	**94**	**94**	**94**
Target and Actual enrollment by site													
UW			0	0	0	0	0	0	1	0	0	0	
USAISR			0	0	0	0	0	0	0	4	1	0	
UAB			0	0	0	0	0	0	0	0	3	0	
UTSW			0	0	0	0	0	0	0	0	n/a		
UTMB			0	0	0	0	0	0	0	0	0	0	
VUMC			0	0	0	0	0	0	0	0	0	1	
Actual Enrollment (cumulative)			0	0	0	0	0	0	0	4	8	9	

Site Enrollment Progress:



What opportunities for training and professional development has the project provided?

Nothing to report

How were the results disseminated to communities of interest?

Nothing to report

What do you plan to do during the next reporting period to accomplish the goals?

1. Continue enrollment at all sites except UW.
2. Submit White Paper outline possible next steps to CCCRP.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

Nothing to report.

What was the impact on other disciplines?

Nothing to report.

What was the impact on technology transfer?

Nothing to report.

What was the impact on society beyond science and technology?

Nothing to report.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

Nothing to report.

Actual or anticipated problems or delays and actions or plans to resolve them

Participating Sites:

a. UAB – The initial delay due to lack of blood bank staffing was resolved through additional resources provided at UAB Department of Surgery expense. The Burn Navigator implementation process took longer than anticipated due to UAB IT issues/processes and staff wanting a single sign on (SSO). All have been resolved. The Site Initiation presentation was held in February of 2023. Training across all staff and disciplines has been conducted. Site is actively screening. However, there UAB is working through timing the standard of care blood specimens draw time to closely align with the research blood specimen timeline. This issue is requiring IT support and staff education and has been resolved.

b. VUMC –VUMC enrollment was delayed this year due to a broken Blood Bank refrigerator that took several weeks for parts and repair. VUMC was able to actively screen and enroll as of the middle of August 2023.

c. UTSW –The site PI attempted to resolve the delay related to blood bank processes to account for plasma product in blood bank software and blood bank staffing. However after multiple meetings the staffing in the blood bank at Parkland remains a challenge. The blood bank leadership doesn't anticipate being able to participate until 2024. Dr. Cancio and the site PI met and determined the best course of action was to close the site. ***The site has been removed from the study and the subward has been terminated.***

d. UW – This site was the first to initiation screening (October of 2022). However their eligible to enrolled percentage remained at 0%. Dr. Cancio and Dr. Stewart met and while UW has attempted to enroll, their Burn Center receives many patients from far away therefore outside the 8 hour enrollment window. It was agreed to have the site pause enrollment as of August 1, 2023.

Enrollment:

Due to the low enrollment and challenges across site Dr. Cancio reviewed all the screening data and determined the main reason why eligible patients have missed enrollment is the time it takes to identify, contact, and consent the patient's Legally Authorized Representative (LAR). Consent of the LAR is required because critical injury and intensive care (e.g., intubation, narcotics administration) interfere with the patient's own ability to provide consent. Meanwhile, the study requires that infusion of plasma begin by the 8th postburn hour (within 8 hours of burn, not of admission). Many burn patients are received by the burn center hours postburn, decreasing the available time window in which to obtain consent. To help address this challenge, we are using smart-phone enabled electronic consent (e-consent). However, our screening data indicate that we are still missing too many eligible enrollees. Our screening log as of 3 June 2023 shows that the median time from burn injury to screening (for patients who were screened within the 8-hour window) was 4.0 hours. This indicates that timely screening is possible. However, the leading cause for missed enrollments of otherwise eligible patients is non-availability of the LAR in a timely fashion. To date, up to 50% more patients could have been enrolled if the LAR had been available. All sites are exhausting all avenues to contact LARs however enrollment remains a challenge. This issue was discussed at the IPR in July 2023 and the follow on meeting with CCCRP in August 2023. As stated above, Dr. Cancio to submit a White Paper to CAPT Polk outlining possible solutions including study redesign.

Changes that had a significant impact on expenditures

None

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

None

Significant changes in use or care of vertebrate animals

Not applicable.

Significant changes in use of biohazards and/or select agents

Not applicable.

6. PRODUCTS:

- **Publications, conference papers, and presentations**

Journal publications.

Nothing to report

Books or other non-periodical, one-time publications.

Nothing to report.

Other publications, conference papers and presentations.

Nothing to report

- **Website(s) or other Internet site(s)**

Nothing to report.

- **Technologies or techniques**

Nothing to report

- **Inventions, patent applications, and/or licenses**

Nothing to report.

- **Other Products**

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name	Project Role	Nearest person month worked	% Effort	Contribution to the project
Leopoldo Cancio	Principal Investigator	1.2	10%	Oversight and leads all aspects of the study.
Monica Phillips	Project Manager	2.4	20%	Performing administrative support for the study. Schedules and supports monthly meetings. Works with all sites regarding human subjects protection, site initiation, education and training, and data collection.
Joel Baker	Research Coordinator	1.0	12%	Research Coordinator at ISR to support this study at the ISR. Mr. Baker left employment as of 7/31/2023.

Shannon Gutierrez	Research Coordinator	.92	23%	Ms. Gutierrez replaced Mr. Baker starting in July 2023. She will perform duties of the Research Coordinator at USAISR.
Pam Bixby	Communications	1.2	10%	Responsible for maintaining and updating study webpage and other communications.
Ana Guerrero	Administrative	0.6	5%	Receives subaward invoices, verifies, and processes for approval. Meeting support.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Dr. Cancio:
Additional closed studies: Ex vivo Heparin-Free ECLS.
Current studies added:

a. Title: Development and validation of innate immunome-targeted therapy to create a pro-survival and organ-protective phenotype after hemorrhage at the point of injury
b. Title: Commercialization and Clinical Assessment of Large Surface Area Burn Treatment for Prolonged Field Care and Long-Term Care

Pending studies include:

a. Title: Use of Low-Flow Extracorporeal Life Support in Burned Patients as Ultra-Lung Protective Method

What other organizations were involved as partners?

Organization	Location	Contribution to Project
Institute of Surgical Research and US Army Burn Center	3698 Chambers Pass, JBSA Fort Sam Houston, TX 78234-6315	Dr. Leopoldo Cancio (Study PI)
University of Washington	325 9th Ave, Seattle, WA 981014-2420	Dr. Barclay Stewart (Site PI)
University of Washington	325 9th Ave, Seattle, WA 981014-2420	Dr. Dagmar Amtmann (DCC PI)
University of Alabama, Birmingham	1720 2nd Avenue South, Birmingham, AL 35294.0111	Dr. Jan Jensen (Site PI)
Vanderbilt University	3319 West End Avenue, STE	Dr. Robel Beyene (Site PI)

Medical Center	970, Nashville, TN 37203-6856	
University of Texas Medical Branch	815 Market Street, Galveston, TX 77550-2725	Dr. Steven Wolf (Site PI)
University of Texas Southwestern	5323 Harry Hines Blvd E6.202, Dallas, TX 75390	Dr. Samuel Mandel (Site PI)
University of Maryland	800 West Baltimore Street, Baltimore, MD 21201-1100	Dr. Rosemary Kozar (Site PI)
Cerus Corporation	1220 Concord Avenue, Concord, CA 94520	Dr. Larry Corash, Consultant

8. SPECIAL REPORTING REQUIREMENTS

QUAD CHARTS:
A QUAD chart is included as an appendix.

9. APPENDICES:

a. Quad Chart
b. IPR Presentation
c. Support Document – Dr. Cancio

Plasma Resuscitation WithOut Lung Injury (PROpOLIs)

DM090167
W81XWH2020032

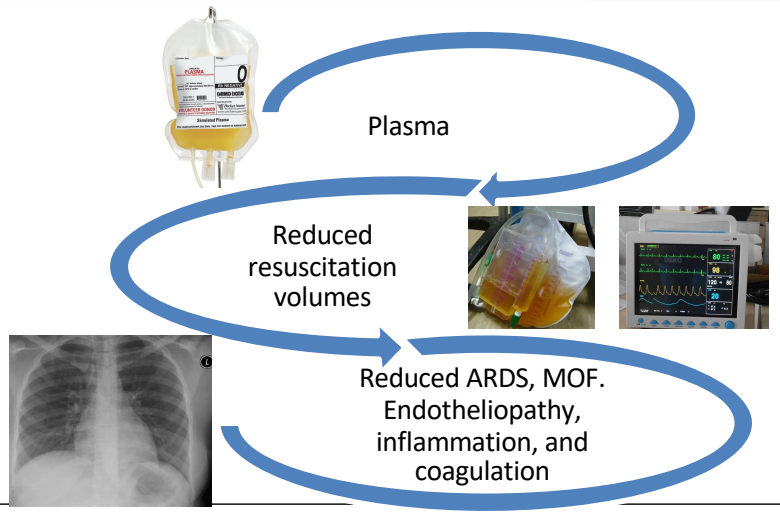
PI: Dr. Leopoldo Cancio **Org: Coalition for National Trauma Research (CNTR)** **Award Amount: 2,485,163**

Study/Product Aim(s)

- To determine whether administration of Pathogen-Reduced Plasma during burn resuscitation results in decreased total resuscitation volumes compared to standard-of-care crystalloid-based resuscitation
- To determine whether Pathogen-Reduced Plasma administration during burn resuscitation reduces ARDS
- To determine the effect of Pathogen-Reduced Plasma administration on the endotheliopathy, and inflammation of burns.

Approach

This is an open-label, phase IV, multicenter, randomized controlled prospective clinical trial in patients with burns. The study model is parallel (between-patient). The intervention to be tested is Pathogen-Reduced Plasma for burn shock resuscitation vs. standard-of-care resuscitation.



Accomplishment:. UTMB IRB approved. Eight subjects enrolled.

Timeline and Cost

Activities CY	21	22	23
Adapt Protocol			
Issue Subawards			
Patient Enrollment			
Data Analysis and Dissemination			
Estimated Budget ($K)	**$769**	**$874**	**$841**

Updated: June 30,2023

Goals/Milestones

CY21 Goal – Adapt Protocol
x IRB approval at all sites
☐ HRPO approval
CY21 Goals – Subcontracts
☒ Subawards issued for all sites
CY21 and CY 22 Goal – Patient Enrollment
☐ Subject enrollment goal of 94
CY23 Goal – Data Analysis and Dissemination
☐ Analyze Data
☐ Disseminate findings

Comments/Challenges/Issues/Concerns

- Various delays related to blood bank processes/staffing, burn navigator implementation

Budget Expenditure to Date

Projected Expenditure: $2,485,163
Actual Expenditure: $1,222,292

PROPOLIS:

Plasma Resuscitation without Lung Injury

(W81XWH2020032)

PI: L. Cancio MD

PI Organization: US Army Institute of Surgical Research

Date: 18 July 2023

Project Information

- Principal Investigator: *Leopoldo C. Cancio*
- PI's Organization: *US Army Institute of Surgical Research*
- DoD Award Number: *W81XWH2020032*
- Key Sub-Awards:
  - *Participating burn centers: Univ. of Alabama at Birmingham; Vanderbilt; Univ. of Texas Southwestern (Dallas); US Army Institute of Surgical Research; Univ. of Washington; UT Medical Branch (Galveston).*
  - *Data Coordinating Center: Univ. of Washington.*
  - *Lab: Univ. of Maryland.*
- Period of Performance: *30 SEP 2020 – 29 SEP 2023*
- Total Funding / Project Cost / Budget:
- Additional Key Partners / Institutes: *Coalition for National Trauma Research, San Antonio, TX (CNTR)*
- Grant / Contract Officer Representative: *Christie Vu*
- Grant / Contract Specialist / Science Officer: *Jonathan Monti*
- Funding Mechanism Type: *Cooperative Agreement*
- Solicitation / Award Mechanism Title / Number: *DMRDP (Multi-Domain Lifesaving Trauma Innovations (MuLTI) Award, W81XWH-19-S-CCC1)*
- Related government funding: *n.a.*

Scientific Overview

- Overview / Background / Purpose:
  - ***Burn shock*** *occurs during the 1st 24-48 hrs postburn, in burns > 20% of the total body surface area (TBSA).*
  - *It features* ***hypovolemia*** *caused by loss of plasma from the intravascular to the interstitial spaces.*
  - *Since the 1960s, resuscitation has centered on large volumes of i.v. crystalloid solution (lactated Ringer's, LR). This causes* ***edema*** *(lung, wounds, extremities, etc.).*
  - *Colloids like albumin or plasma may decrease the volume required.*
  - ***Plasma*** *may also protect the endothelial glycocalyx, reversing burn shock.*

- Main methodology(ies) to accomplish the research: *Multicenter, randomized, open-label, controlled clinical trial.*

- Expected Outcomes: *Since medics will carry lyophilized plasma soon, we'll learn how best to use plasma for burn shock resuscitation.*

Scientific Overview (Continued)

- Hypothesis(es) / Research Question
  - *Administration of plasma for resuscitation after burn injury will 1) reduce 24-hour and 48-hour resuscitation volumes and 2) reduce the incidence of acute respiratory distress syndrome, multi-organ failure and other resuscitation-related morbidities.*

- Specific Aims / Objectives
  - *To determine whether administration of Pathogen-Reduced Plasma during burn resuscitation results in decreased total resuscitation volumes compared to standard-of-care crystalloid-based resuscitation.*
  - *To determine whether Pathogen-Reduced Plasma administration during burn resuscitation reduces ARDS.*
  - *To determine the effect of Pathogen-Reduced Plasma administration on the endotheliopathy and inflammation of burns.*

Research Methodologies

- Methodologies used for the research process:
- *This is a randomized controlled clinical trial*
- *Inclusion (partial list): burn size >20% TBSA, age 18-65 years*
- *Patients must be enrolled within 8 hours of burn*
- *Arms:*
  - *Experimental arm: pathogen-reduced plasma at 1 ml*kg*TBSA for 24 hrs*
  - *Control arm: LR at 1 ml*kg*TBSA for 24 hrs*
  - *Both arms: LR at 10 ml*TBSA/hr, titrate with Burn Navigator decision support*
- *Primary outcome: volume of fluid received during the 1st 24 hours postburn*

- Lessons learned from any design/methods challenge or failure, as applicable:
  primary challenge relates to getting LAR consent within 8 hrs of injury (see below)

- Describe validation methods, especially in model base work: *n.a.*

LR, lactated Ringer's solution
TBSA, total body surface area, %

Results to Date

- Provide Status of Aims/Objectives/Tasks completed or in progress to date, and their Significance: *Currently 3 centers open to enrollment with 10 subjects enrolled.*

- IRB/ORP/HRPO/ACURO approval update, as applicable (see back-up slides): *IRB approval at 5/6 sites; HRPO approval at 4/6*

- Description of completed proofs of concept, prototypes, and/or demonstrations: *n.a.*

- Rationale for deviations or alteration from original SOW or hypotheses: *n.a.*

- Any challenges, risks anticipated, and or risks realized (Issues), as well as mitigation strategies employed, and status of issue(s) resolution: *next slide*

Challenges

- *UAB: blood bank staffing; Burn Navigator IT issues/processes. Issues resolved; site is actively screening.*
- *VUMC: requested 6 mo. delay pending burn center verification; need new blood bank refrigerator; anticipate repair completion in two weeks.*
- *UTSW: blood bank staffing; not able to participate until 2024. The site has been removed from the study and the subward has been terminated.*
- *USAISR: blood bank had concerns re ABO compatibility; issue has been resolved; actively enrolling.*
- *Overall: non-availability of blue top tubes for blood samples during COVID (resolved); delay in availability of pathogen-reduced plasma*
- *Due to these delays an extension without funding will be necessary, will be submitted at the appropriate time.*
- *Enrolling and consenting within 8 hours of injury is a challenge in these patients. All sites are actively employing strategies to enroll on off hours and draw the biospecimens. All eligible patients that are unable to be enrolled are discussed at the monthly meeting with the most common reason "unable to approach in time".*

UAB, Univ. of Alabama at Birmingham; VUMC, Vanderbilt;
UTSW, Univ. of Texas Southwestern (Dallas); USAISR, US Army Institute of Surgical Research

Deliverables

Deliverable Type	Description of Product Delivered	Data Rights	Delivery Schedule
Knowledge Product	JTS Clinical Practice Guideline	n.a.	Upon completion of the study.
Data	Data from the study will be available for further analysis.	To be determined.	Upon completion of the study.

Transition Strategies

- Discuss transition strategies for the deliverables of the funded research project.
  - *The transition partner for this project is the Joint Trauma System (JTS).*
  - *The PI and team are closely linked to the JTS.*
  - *The PI is the DoD subject matter expert on burns and contributes to the JTS Burn Clinical Practice Guidelines.*

- List any intellectual property or proprietary information needed…:
  - *N.A.*

JOINT TRAUMA SYSTEM CLINICAL PRACTICE GUIDELINE (JTS CPG)

Burn Wound Management in Prolonged Field Care (CPG ID: 57)

This Role 1 prolonged field care (PFC) guideline is intended to be used after Tactical Combat Casualty Care (TCCC) Guidelines, when evacuation to higher level of care is not immediately possible.

Contributors

Leopoldo C. Cancio, MD
Doug Powell, MD
Britton Adams, NREMT-P, ATP
Kenneth Bull, MD
Alexander Keller, MD
Jennifer Gurney, MD
Jeremy Pamplin, MD
Stacy Shackelford, MD
Sean Keenan, MD

Publication Date 13 Jan 2017

JOINT TRAUMA SYSTEM CLINICAL PRACTICE GUIDELINE (CPG)

Burn Care (CPG ID: 12)

Addresses burn injury assessment, resuscitation, wound care, and specific scenarios including chemical and electrical injuries. Reviews considerations for the definitive care of local national patients, including pediatric patients, who are unable to be evacuated from theater.

Contributors

MAJ Ian R Driscoll, MC, USA
COL Elizabeth A Mann-Salinas, AN, USA
CPT Nathan L Boyer, MC, USA
LTC Jeremy C Pamplin, MC, USA
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MAJ Julie A Rizzo, MC, USA
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COL (Ret) Evan M Renz, MC, USA
CAPT Zsolt T Stockinger, MC, USN
COL Jennifer Gurney, MC, USA

First Publication Date: Jul 2007 | Publication Date: 11 May 2016 | Supersedes CPG dated 13 Nov 2013

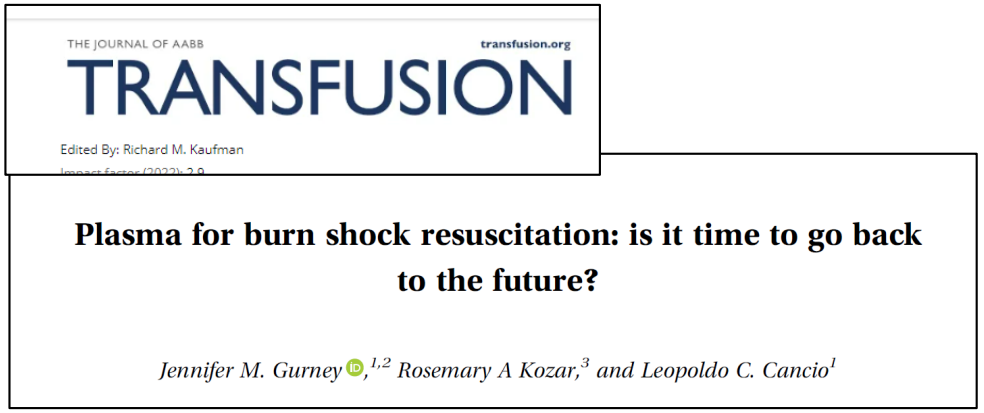
Anticipated Impact
as an Outcome of Research

- Based upon work to date, discuss anticipated significant impacts of completion of this project:
  - Military medicine: *We will learn whether plasma should be used on the battlefield for burn shock resuscitation. Since plasma will become available, this is a critical question.*
  - Civilian medicine: *Results broadly applicable to burn care in the US/worldwide.*
  - Technology commercialization*: n.a.*
  - Commercial industry partners: *This study uses pathogen-reduced plasma, which is produced by a propriety process (Cerus Corp.). But it does not directly assess that particular process in comparison with other methods of plasma preparation.*
  - Academic arena: *This work examines the effect of resuscitation strategy on the endothelial glycocalyx, with broad relevance to other shock states such as hemorrhage, sepsis, cardiac arrest, others.*
  - Possible impacts outside of medicine: *n.a.*

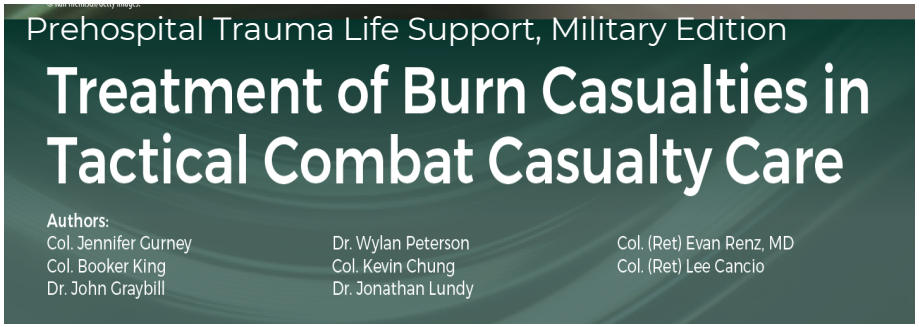
- What are the "next steps" and/or further research needed?
  - *In view of slow accrual, we will apply for a no-cost extension; we recently submitted a pre-proposal to Joint Warfighter Medical Research Program to support more sites and an Exception From Informed Consent application to the FDA.*
  - *In the future, if lyophilized plasma becomes available in the civilian market, a future evaluation of that product(s) for burn resuscitation should be considered.*

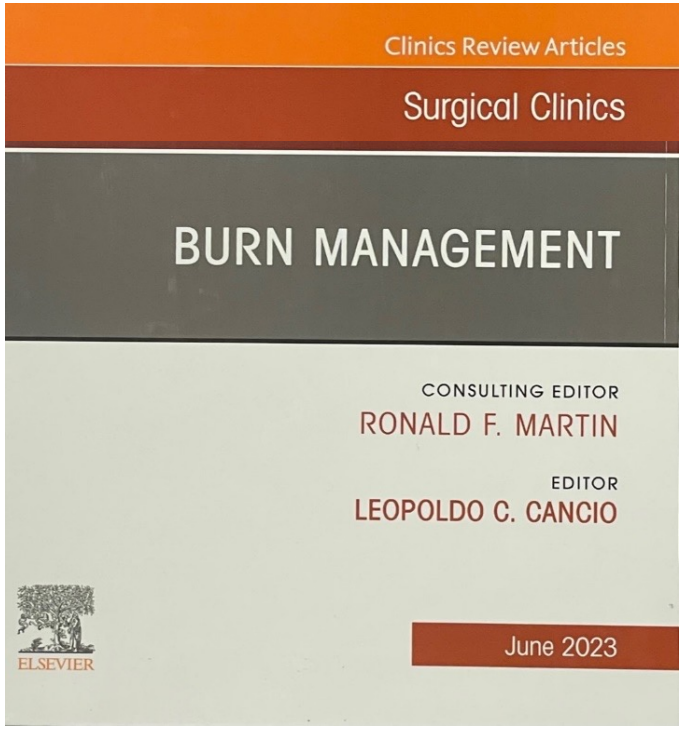
Publications

- List / Describe all Publications and/or Presentations…:
  - *Study concept/design presented at Surgical Biology Club III (conjunction with American College of Surgeons)*
  - *See images*



- List / Describe intended future Publications / Presentations:
  - *Work likely to be presented at the American Burn Association*





Conclusions

- PI comments regarding overall progress:
  - *Successes:*
  - *The study is one of the first multicenter RCTs of burn-shock resuscitation ever conducted.*
  - *A operational consortium of 6 burn centers in 3 states, a Data and Safety Monitoring Board (DSMB), and a Data Coordinating Center (University of Washington) has been built with the support of the Coalition for National Trauma Research.*
  - *Burn resuscitation practice is being protocolized in this study using Burn Navigator decision support software, which was developed at the USAISR for use on the battlefield.*
  - *Effective use of electronic consent using the DCC server has been implemented and has been shown to be invaluable in obtaining LAR consent*
  - *The study has identified and documented problems with early LAR consent, which will be used to support an application to the FDA for exception from informed consent if additional funding is obtained from Joint Warfighter.*

- For researchers near the beginning of the project, summarize: *n.a.*

BACK-UP SLIDES

***Note*: Please complete the Back-Up slides, though they will NOT be briefed as part of your presentation.**
They can be used to answer questions and/or clarify discussion points presented on template slides.

Intellectual Property / Government Rights

- Provide any inventions and intellectual property rights derived as a direct result of this funding. Include items (but not limited to)
  - Patents / licensures: *none*
  - Copyrights: *none*
  - Trademarks: *none*
  - Licensures: *none*
- Describe any data (technical data and/or software and prototypes) that will be available to the government (CDRLs)
- Additionally, identify Government rights to the data and intellectual property
  - Licenses: *none*
  - Products: *none*
  - Software: *none*
  - Materiel Solutions: *none*
  - SBIR data rights: *none*

Include any/all deliverable information that will (or is expected to) have associated rights to make it for government use only, or that is proprietary. Two (2) slides maximum

SUPPORT
Cancio, Leopoldo C.

CURRENT

Title: Anti-Complement Therapy to Improve Mortality and Morbidity for Traumatic Hemorrhage during Prolonged Field Care and Prolonged Damage Control Resuscitation
Principal Investigator: Yansong Li (The Geneva Foundation/UTHSCSA)
Time Commitment: 5%
Supporting agency: USAMRAA/BAA
Period of Performance: 2019-24
Funding:
Goal: determine the effectiveness of the anti-ComC therapy aimed to reduce morbidity and mortality after trauma and hemorrhage during PFC and PDCR.
Role: Associate investigator

Title: Development and Validation of a Novel Immunotherapy for Traumatic Hemorrhage
Principal Investigator: Yansong Li, MD (The Geneva Foundation/UTHSCSA)
Time Commitment: 5%
Supporting agency: CDMRP/PRMRP-TTDA
Period of Performance: 2020-5
Funding:
Goal: test whether early administration of Coversin and/or CX-01 will ameliorate inflammation, mitigate, MOF, reduce resuscitation fluid requirement, and increase survival chances through modulating inflammation dysregulation, improving metabolism, and reducing ETP after TH during PFC.
Role: Associate investigator

Title: Multicenter Implementation Trial of Targeted Normoxia Strategy to Define Oxygen Requirements for Combat Casualty Care**:** An Approach to Reduce Warfighter Morbidity, Deployed Logistical Burden of Oxygen, and Readiness Costs
Principal Investigator: Adit Ginde, MD (University of Colorado-Denver)
Time Commitment: 2%
Supporting Agency: Medical Technology Enterprise Consortium (MTEC-19-08-MuLTI)
Period of Performance: 2019-2024
Funding:
Goal: Determine the feasibility, safety, and effectiveness of the targeted normoxia approach to conserve oxygen and improve clinical outcomes in major burn patients.
Role: Site principal investigator

Title: PROPOLIS (Plasma Resuscitation WithOut Lung Injury)
Principal Investigator: Leopoldo C. Cancio
Time Commitment: 10%
Supporting Agency: Defense Medical Research and Development Program (DMRDP), Joint Program Committee-6 (JPC-6)/CCCRP Multi-Domain Lifesaving Trauma Innovations (MuLTI) Award, W81XWH-19-S-CCC1.
Period of Performance: 2019-2023
Funding:
Goal: Randomized controlled multicenter clinical trial of plasma (Pathogen-Reduced Plasma) vs. crystalloid solution for burn shock resuscitation.
Role: Principal investigator

Title: STAT – Standard Therapy plus Active Therapy to Improve Mobility, Long-term Activity and Quality of Life for Severely Burn Injured Patients after Skin Graft Surgery
Principal Investigator: Soman Sen, MD (University of California, Davis)
Time Commitment: n.a.
Supporting Agency: Military Burn Research Program
Period of Performance: FY 2019-23
Funding:
Goal: In burn patients, compare a standardized approach to rehabilitation (STAT protocol, which emphasizes four active components--mobility, strengthening, cardiovascular fitness and functional training), to standard of care
Role: Site principal investigator

Title: VItamin C in Thermal injuRY: The VICToRY Trial. A Phase III Multi-Center Randomized Trial
Principal Investigator: Darren Heyland (Queen's University, Kingston, ON)
Time Commitment: 5%
Supporting Agency: Military Burn Research Program (W81XWH-21-MBRP-CTRA)
Period of Performance: 2022-6
Funding:
Goal: Multicenter randomized controlled trial of high-dose vitamin C in burn patients
Role: Site principal investigator

Title: Compensatory Reserve Measurement (CRM) during Burn Shock Management
Principal Investigator: Garrett Britton (USAISR)
Time Commitment: 2.5%
Supporting Agency: Military Burn Research Program (W81XWH-21-MBRP-CTRA)
Period of Performance: 2022-5
Funding:
Goal: Single-site evaluation of the CRM in patients presenting in burn shock and undergoing resuscitation
Role: Associate investigator

Title: Restoring Immune Function to Critically Ill Burn Patients
Principal Investigator: Isaiah Turnbull (Washington University at St. Louis)
Time Commitment: 5%
Supporting Agency: Military Burn Research Program (W81XWH-21-MBRP-CTRA)
Period of Performance: 2022-6
Funding:
Goal: Determine the ability of clinically available immune adjuvants to restore ex-vivo immune function to immunosuppressed burn sepsis patients
Role: Site principal investigator

Title: Development and validation of innate immunome-targeted therapy to create a pro-survival and organ-protective phenotype after hemorrhage at the point of injury
Principal Investigator: Yansong Li, MD (The Geneva Foundation/UTHSCSA)
Time Commitment: 5%
Supporting agency: CDMRP/PRMRP-TTDA
Period of Performance: 2023-7
Funding
Goal: determine the effectiveness of early IM administration of a therapeutic regimen of nomacopan + PMX205, or CX-01+ ethyl pyruvate aimed to attenuate morbidity and mortality after TH at the POI during PFC.
Role: Associate investigator

Title: Burns for Prehospital Providers Program (BPPP).
Principal Investigator: Jeffrey Carter, MD (Louisiana State University)
Time Commitment: 5%.
Supporting Agency: MTEC-22-01-BurnTraining, W81XWH-15-9-0001.
Period of Performance: TBD.
Funding: TBD.
Goal: Develop a curriculum and simulators to teach personnel how to take care of burns in an austere environment.
Role: Site principal investigator

PENDING

None; no proposals under review

PREVIOUS (LAST 5 YEARS)

Title: Evaluation of C1 inhibitor and C5 monoclonal antibody in pre- and early hospital animal models of trauma and hemorrhage
Principal Investigator: Leopoldo C. Cancio, MD
Time Commitment: 5%
Supporting agency: USAMRAA/BAA
Period of Performance: 2016-9
Funding:
Goal: develop and validate C1 inhibitor and C5 monoclonal antibody for prehospital and hospital treatment of trauma and hemorrhage.
Role: Principal investigator

Title: Comparative evaluation of bone-marrow-derived and adipose-derived stem cells in swine model of prolonged field care
Principal Investigator: Ben Antebi, PhD (USAISR)
Supporting Agency: CCCRP
Period of Performance: FY 17-19
Funding:
Role: Associate investigator

Title: Preclinical Production and Characterization of Extracellular Vesicles Derived from Mesenchymal Stem Cells
Principal Investigator: Arezoo Mohammadipoor, PhD (USAISR)
Time Commitment: 5%
Supporting Agency: CCCRP
Period of Performance: FY 2018-2020
Funding:
Goal: Produce, characterize, and evaluate extracellular vesicles derived from mesenchymal stem cells for use following combat injury.
Role: Associate investigator

Title: Ex vivo Heparin-Free ECLS
Principal Investigator: Andriy I. Batchinsky, MD (USAISR and University of the Incarnate Word)
Time Commitment: 5%
Supporting Agency: CCCRP
Period of Performance: FY 2020-2022
Funding:

Goal: Develop and evaluate novel antithrombogenic coatings for extracorporeal devices which obviate the need for systemic anticoagulation.
Role: Associate investigator

OVERLAP
None