

AWARD NUMBER: W81XWH-15-1-0647

TITLE: Effects of Burn Injuries on Thermoregulatory and Cardiovascular Responses in Soldiers: Implications for the Standards of Medical Fitness

PRINCIPAL INVESTIGATOR: Craig G. Crandall, PhD

CONTRACTING ORGANIZATION: University of Texas Southwestern Medical Center
5323 Harry Hines Boulevard, Dallas, TX 75390

REPORT DATE: October 2020

TYPE OF REPORT: Annual Report

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

DISTRIBUTION STATEMENT: Approved for Public Release; Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. **PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.**

1. REPORT DATE (DD-MMM-YYYY) OCT-2020		2. REPORT TYPE Annual		3. DATES COVERED (From - To) 30-SEP-2019 – 29-SEP-2020	
4. TITLE AND SUBTITLE Effects of Burn Injuries on Thermoregulatory and Cardiovascular Responses in Soldiers: Implications for the Standards of Medical Fitness				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER W81XWH-15-1-0647	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Craig G. Crandall, PhD Email: CraigCrandall@TexasHealth.org				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) University of Texas Southwestern Medical Center 5323 Harry Hines Boulevard, Dallas, TX 75390				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Development Command (USAMRDC) Fort Detrick, Maryland 21702-5012				10. SPONSOR/MONITOR'S ACRONYM(S) USAMRDC	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT This project tested the hypothesis that burn survivors could exercise for 30 min without excessive elevations in core body temperature, regardless of the total body surface area (%TBSA) burned or environmental temperature. Ten subjects cycled for 60 min at 1) a moderate intensity (97±8 watts) in a thermoneutral environment (24°C, MOD_NEU), 2) a moderate intensity (100±17 watts) in a hot environment (39°C, MOD_HOT), and 3) a low intensity (65±10 watts) in a hot environment (39°C, LOW_HOT). Burn injuries were simulated by covering 0%, 20%, 40%, or 60% of the individual's %TBSA with an absorbent material that prevented sweat evaporation. Changes in gastrointestinal temperature (ΔT_{core}) were analyzed at 15-min increments throughout exercise. For the MOD_NEU trial, there were no differences in ΔT_{core} between the %TBSA coverage bouts at any time point during exercise. For the MOD_HOT trial, there were no differences in ΔT_{core} at 15 and 30 min of exercise regardless of the %TBSA coverage, while ΔT_{core} was appreciably elevated ($P < 0.05$) at 45 and 60 min of exercise for 20%+ TBSA bouts. For the MILD_HOT trial, there were no differences in ΔT_{core} at any time point between %TBSA bouts, with the sole exception of 60% simulated burn having a slightly greater ΔT_{core} ($0.3 \pm 0.34^\circ\text{C}$; $P < 0.05$) at 60 min of exercise relative to the 0% TBSA bout. These data indicate that individuals with up to 60% of their TBSA burned could exercise at a moderate intensity for 30 min, even in hot environmental conditions, without excessive elevations in body core temperature. Thus, burn survivors can benefit from exercise, without the risk of excessive hyperthermia, for up to 30 min in the heat or at least 60 min in an air-conditioned space.					
15. SUBJECT TERMS Army's Standards of Medical Fitness; burn injury; thermoregulation; sweating; heat dissipation; environmental temperature; body surface area burned; donor site					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT UU	18. NUMBER OF PAGES 15	19a. NAME OF RESPONSIBLE PERSON USAMRDC
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U			19b. TELEPHONE NUMBER (include area code)

Table of Contents

1. INTRODUCTION.....	4
2. KEYWORDS	4
3. ACCOMPLISHMENTS.....	4
What were the major goals of the project? (Goals to be accomplished and status.)	4
What was accomplished under these goals? (Detailed progress and results.).....	4
What opportunities for training and professional development has the project provided?	8
How were the results disseminated to communities of interest?.....	8
Plans for the next reporting period to accomplish the goals.....	8
4. IMPACT.....	8
What was the impact on the development of the principal discipline(s) of the project?.....	8
What was the impact on other disciplines?.....	8
What was the impact on technology transfer?.....	8
What was the impact on society beyond science and technology?	9
5. CHANGES/PROBLEMS.....	9
Changes in approach and reasons for change	9
Actual or anticipated problems or delays and actions or plans to resolve them.....	9
Changes that had a significant impact on expenditures.....	9
Significant changes in use or care of human subjects	9
Significant changes in use or care of vertebrate animals.....	11
Significant changes in use of biohazards and/or select agents	11
6. PRODUCTS.....	11
Website(s) or other Internet site(s)	12
Technologies or techniques	12
Inventions, patent applications, and/or licenses	12
Other Products	12
7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS.....	13
What individuals have worked on the project?.....	13
Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?	14
What other organizations were involved as partners?	14
8. SPECIAL REPORTING REQUIREMENTS	14
9. APPENDICES.....	14

1. INTRODUCTION

The U.S. Army's Standards of Medical Fitness pertaining to a prior burn injury is based upon the findings of only three studies, from a total of 9 subjects with burns of >40% body surface area (BSA; N=4, 3, and 2), and report contradictory findings. Equally low number of subjects were assessed in individuals with <40% BSA burned in those studies. Notably, we know nothing about the interactive effects of differing workload requirements (e.g., metabolic heat generation associated with military service) and the environmental conditions soldiers often operate in on the safety and well-being of a soldier with a prior burn injury. Further, we know nothing about the effects of differing body sizes, location of burn injury, and/or how a soldier's uniform/body armor may affect thermoregulatory and cardiovascular responses during military operations of a soldier with a burn injury. Clearly, there is insufficient information to make conclusions regarding the potential detrimental effects of a prior burn injury at the level necessary to include such recommendations in the Standards of Medical Fitness. The proposed work will provide clear and scientifically supported guidelines that will culminate in recommendations for a revision of the US Army's Standards of Medical Fitness for burn injuries to more accurately predict the consequences of the injury on the safety and wellbeing of the burned soldier. This information will also have direct impact on the accession/retention of the burned soldier, potentially allowing highly trained, but burned, soldiers to remain in service and thereby realizing cost savings to the Army that would otherwise be spent on training replacements. Finally, the obtained information will benefit the civilian burn community, and those who treat such individuals, through specific recommendations that are dictated in part by the activity level and/or environmental conditions such individuals participate in, with a goal of mitigating the risk of heat-related injuries in this population.

2. KEYWORDS

Army's Standards of Medical Fitness; burn injury; soldier; thermoregulation; sweating; heat dissipation; exercise; metabolic heat generation; environmental climate; temperature; humidity; body surface area burned; donor site; fitness.

3. ACCOMPLISHMENTS

What were the major goals of the project? (Goals to be accomplished and status.)

Specific Aim 1: Identify whether the fraction of unburned skin is an accurate predictor of impaired heat dissipation (months 1-24)

- STATUS: In progress

Specific Aim 2: Determine the extent to which a burn injury is detrimental for an individual's ability to thermoregulate is dependent upon ambient temperature and exercise intensity (months 1-48)

- STATUS: In progress

Specific Aim 3: Evaluate the influence of burn location on thermoregulatory responses (months 32-54)

- STATUS: Completed Y4Q1

Specific Aim 4: Identify whether the donor site contributes to impaired thermoregulatory responses in burned subjects (months 1-54)

- STATUS: COMPLETED Y3Q3

Specific Aim 5: Predicting the thermoregulatory safe zone for individuals with burn injuries (months 54-60)

- STATUS: In progress

What was accomplished under these goals? (Detailed progress and results.)

Specific Aim 1: Identify whether the fraction of unburned skin is an accurate predictor of impaired heat dissipation (months 1-24)

1a: Work was completed and reported in the annual technical report year 2 and will be presented again in full in the final technical report.

1b: Data collection for this protocol is ongoing. This protocol compares thermoregulatory responses to exercise in hyperthermic conditions between groups of burn survivors with similar burn injuries (% body surface area) but with disparate overall body surface areas. Three burn survivors were scheduled to complete these trials by March 2020, however those trials were put on hold due to COVID-19. We are hopeful that travel restrictions will shortly be lifted such that these individuals can travel to Dallas and complete these trials.

Specific Aim 2: Determine the extent to which a burn injury is detrimental for an individual's ability to thermoregulate is dependent upon ambient temperature and exercise intensity (months 1-48)

2a: Work was completed and reported in the annual technical report year 3 and will be presented again in full in the final technical report.

2b:

Abstract Title: Interaction of Exercise Intensity and Simulated Burn Injury Size on Thermoregulation

The US Department of Defense's Medical Standards for Appointment, Enlistment, Or Induction into the Military Services exclude personnel with burn injuries covering 18% or more of their body surface area (BSA). However, this requirement does not consider the metabolic heat loads associated with physical activities of different intensities that may influence a burn survivor's ability to perform his/her duties. Purpose: To test the hypothesis that the elevation in internal body temperature during exercise in a hot environment is influenced by the combination of exercise intensity and BSA burned. Methods: Ten healthy participants (8 males, 2 females; 32±9 y; 75.3±11.7 kg) completed eight exercise trials on a cycle ergometer, each with different combinations of metabolic heat productions (Low: 4 W/kg, Moderate: 6 W/kg) and simulated BSA burn, in a hot environmental chamber (39.9±0.3°C, 20.1±1.5% RH). Burns were simulated by covering 0%, 20%, 40%, or 60% of participants' BSA with a highly absorbent, vapor-impermeable material. Gastrointestinal temperature (TGI) was recorded, with the primary analysis being the increase in TGI after 60 minutes of exercise. Results: We identified an interaction effect for the increase in TGI ($p < 0.01$), suggesting TGI was influenced by both intensity and simulated burn BSA. Regardless of the percentage BSA burn simulated, the increase in TGI was similar across low-intensity trials ($0.70 \pm 0.26^\circ\text{C}$, $p > 0.11$ for all). However, during moderate-intensity exercise, the increase in TGI was greater for the 60% ($1.78 \pm 0.38^\circ\text{C}$; $p < 0.01$) and 40% BSA coverage trials ($1.33 \pm 0.44^\circ\text{C}$; $p = 0.04$), relative to 0% ($0.82 \pm 0.36^\circ\text{C}$). There were no differences in TGI responses between 0% and 20% trials. Conclusion: These data suggest that exercise intensity influences the relationship between burn injury size and thermoregulatory responses in a hot environment.

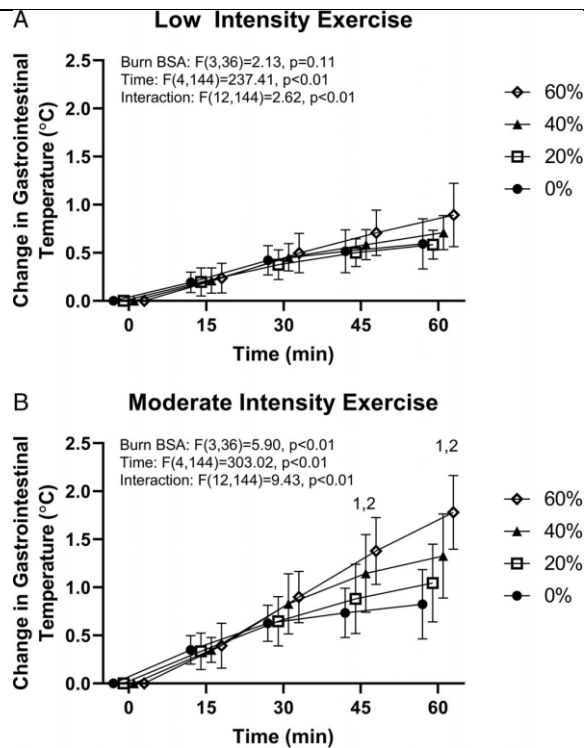


FIGURE 1 —Change in T_{GI} during 60min of exercise at low (A, $\sim 4 \text{ W}\cdot\text{kg}^{-1}$) and moderate (B, $\sim 6 \text{ W}\cdot\text{kg}^{-1}$) exercise intensity with 0%, 20%, 40%, and 60% simulated BSA burn. 140% simulated burn different from 0% at the indicated time points within exercise intensity ($P < 0.05$). 260% simulated burn different from 0% at the indicated time points within exercise intensity ($P < 0.01$). For the moderate-intensity trial, one 40% and three 60% simulated burn values for the 60-min time point are end of exercise values due to these participants ending exercise prematurely For the moderate-intensity trial, at 30 min, the 60% simulated burn trial approached significance ($P = 0.0508$) relative to the 0% trial.

Key Findings or Accomplishments:

- **These data suggest that individuals with up to 60% body surface area burned can perform mild exercise in the heat for up to 60 minutes with no greater impairment in temperature regulation than non-burned individuals. With moderate intensity exercise, individuals with 40% body surface area burned or greater may experience greater body temperature than individuals without burns and with 20% body surface area burned.**

Aim 2c: Work was completed and reported in the annual technical report year 4 and will be presented again in full in the final technical report.

Aim 2d: Data collection for this protocol is ongoing. This protocol compares thermoregulatory responses to exercise in hyperthermic conditions between groups of burn survivors with burn injuries spanning 20%, 40%, or 60% of total body surface area. Three burn survivors were scheduled to complete these trials by March 2020 to complete data collection, however those trials were put on hold due to COVID-19. We are hopeful that travel restrictions will shortly be lifted such that these individuals can travel to Dallas and complete these trials.

Specific Aim 3: Evaluate the influence of burn location on thermoregulatory responses (months 32-54)

3a: Work was completed and reported in the annual technical report year 4 and will be presented again in full in the final technical report.

3b:

Abstract Title: Burn Injury Does Not Exacerbate Heat Strain during Exercise while Wearing Body Armor

Introduction: Although evaporative heat loss capacity is reduced in burn-injured individuals with extensive skin grafts, the thermoregulatory strain due to a prior burn injury during exercise-heat stress may be negligible if the burn is located underneath protective clothing with low vapor permeability. Purpose: To test the hypothesis that heat strain during exercise in a hot-dry environment while wearing protective clothing would be similar with and without a simulated torso burn injury. Methods: Ten healthy individuals (8M/2F) underwent three trials wearing: Uniform (combat uniform, tactical vest, and replica torso armor plates), Uniform with a 20% total body surface area (TBSA) simulated torso burn (Uniform + Burn), or shorts (and sports bra) only (Control). Exercise consisted of treadmill walking (5.3 km·h⁻¹; 3.7 ± 0.9% grade) for 60 min at a target heat production of 6.0 W·kg⁻¹ in 40.0 ± 0.1°C; 20.0 ± 0.6% relative humidity conditions. Measurements included rectal temperature, heart rate, rating of perceived exertion, and thermal sensation. Results: No differences in rectal temperature ($P \geq 0.85$), heart rate ($P \geq 0.99$), thermal sensation ($P \geq 0.73$), or rating of perceived exertion ($P \geq 0.13$) occurred between Uniform + Burn and Uniform trials. In the Control trial, however, core temperature, heart rate, thermal sensation, and rating of perceived exertion were lower compared to the Uniform and Uniform + Burn trials ($P \leq 0.04$ for all). Conclusion: A 20% TBSA simulated torso burn injury does not further exacerbate heat strain when wearing a combat uniform. These findings suggest that the physiological strain associated with torso burn injuries is not different from non-injured individuals when wearing protective clothing during an acute exercise-heat stress.

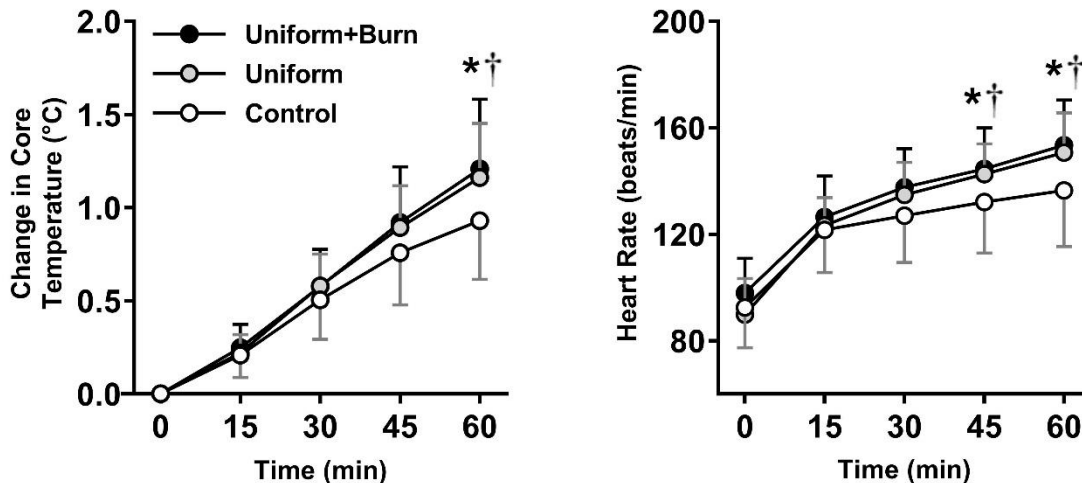


Figure 2: The change in core temperature (left) and heart rate responses (right) throughout exercise at 40°C and 20% RH while wearing military protective clothing (Uniform), military protective clothing with a simulated burn injury (Uniform + Burn), or shorts and shoes only (Control). * difference between Control and Uniform + Burn ($P < 0.05$). † difference between Control and Uniform ($P < 0.05$). Values are mean ± SD for 10 participants.

Key Findings or Accomplishments:

- **These data suggest the deleterious effects of a torso burn injury appear to be negated by the wearing of body armor.**

Specific Aim 4: Identify whether the donor site contributes to impaired thermoregulatory responses in burned subjects (months 1-54)

Work was completed and reported in the annual technical report year 4 and will be presented again in full in the final technical report.

Specific Aim 5: Predicting the thermoregulatory safe zone for individuals with burn injuries (months 54-60)

This work is pending the completion of Aim 2d and 1b. Preliminary analyses on simulated burn data indicate that metabolic heat production (exercise intensity), extent of body surface area burned, body mass, air temperature and age significantly account for variability in body temperature responses.

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

Though the project was not intended to provide training or professional development opportunities, training has nonetheless taken place as a result of the performed work. Specifically, Joseph Watso, Ph.D. and Luke Belval, Ph.D. have been provided training through this project. As a result of this project, each of these individuals received training in the following areas: IRB approvals, subject recruitment (both uninjured and burned subjects), data collection and management, data analysis and reporting, and presentation of the data. Regarding the last point, data from these studies have been presented by trainees at weekly “Works in Progress” meetings and at the American College of Sports Medicine annual meeting.

How were the results disseminated to communities of interest?

The obtained data have been presented at the following local, national, and international meetings in verbal or poster formats: internal “Works in Progress”, the Military Health System Research Symposium, the American Burn Association meeting and the American College of Sports Medicine annual meeting. The manuscripts for Aims 1a, 2a and 3b were published and the manuscript for Aim 2b was accepted for publication in *Medicine and Science in Sports and Exercise*.

Plans for the next reporting period to accomplish the goals

The primary focus for the next reporting period is to complete data collection for the remaining subjects in Aims 1b and 2d. We need 3 remaining participants to complete these Aims and these individuals have been identified, however, we are unable to test them due to COVID-19 travel restrictions and precautions. We also will work on Aim 5, which will analyze and synthesize the data from our participants to inform guidelines and parameters for the Army to utilize to determine limits for soldiers with burns.

4. IMPACT

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

Impact statements from the work completed during the prior reporting period:

Data from 2B suggest that the Army’s Standard of Medical Fitness cutoff of $\geq 40\%$ BSA burned is overly cautious for soldiers who are expected to perform mild intensity work in the heat, while this BSA cutoff is appropriate for soldiers who are expected to perform moderate intensity work in the same climate.

Data from Aim 3B suggest to the military that a burn on the chest is not detrimental for body temperature regulation when the individual is wearing body armor.

What was the impact on other disciplines?

The obtained data will be of interest to the civilian burn rehabilitation community. Exercise is critical for appropriate rehabilitation. That said, burned individuals are often hesitant to perform aerobic exercise training for fear that they may experience a heat-related injury. The information presented herein will be very beneficial to the rehabilitation community by instructing them that burn survivors can perform exercise without an additional risk of hyperthermia if the exercise is moderate in intensity and the individuals is exercising in an air conditioned area. Moreover, even in settings of elevated environmental temperatures, if the work intensity is mild, individuals with severe burn injuries can exercise without a risk of excessive hyperthermia.

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

IMPORTANT REMINDER – Award recipient organization is required to obtain prior written approval from the awarding agency Contracting/Grants Officer whenever there are significant changes in the project or its direction such as significant change in scope or the Statement of Work (e.g. removal, change, or addition of aims/tasks or animal model change), change in PI or key personnel, reduction of 25% FTE, or significant change in budget.

Changes in approach and reasons for change

Nothing to report.

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

Due to COVID-19 data collection is currently delayed for the remaining burn survivors in Aim 1 and Aim 2. We are currently awaiting the removal of travel bans for previously identified participants. We have remained in communication with the participants and plan to have them complete their testing and the remaining analyses when these travel restrictions are removed.

Changes that had a significant impact on expenditures

Nothing to report.

Significant changes in use or care of human subjects

TOTAL PROTOCOL(S): 4

PROTOCOL (1 of 4 total):
 IRB Protocol Number:
 HRPO Protocol Number: A-18991.1
 Protocol PI: Craig G. Crandall, PhD
 Protocol Site: University of Texas Southwestern Medical Center
 Protocol Title: Effects of Burn Injuries on Thermoregulatory and Cardiovascular Responses in Soldiers: Implications for the Standards of Medical Fitness - Aim 1
 Target approved for clinical significance: 85 subjects
IRB INITIAL APPROVAL DATE: 12/14/2015
HRPO INITIAL APPROVAL DATE: 12/24/2015
CONTINUING REVIEW APPROVAL DATES:
 - 07/07/2016 HRPO
 - 06/01/2017 HRPO
 - 08/10/2018 HRPO
 - 12/13/2019 HRPO

AMENDMENTS:
 - Amendment 1, HRPO approved 06/01/2017, to add one study visit for non-burned subjects and remove the requirement to have a pregnancy test performed within the first 10 days of the menstrual cycle for women of child bearing age; also previously enrolled subjects who return to complete the added visit will be re-consented

ADVERSE EVENTS OR UNANTICIPATED PROBLEMS:
 - None

ENROLLMENT STATUS:
 - Number of subjects recruited/original planned target: 66/85
 - Number of subjects screened/original planned target: 66/85
 - Number of patients enrolled/original planned target: 44/85
 - Number of patients completed/original planned target: 44/85

PROTOCOL (2 of 4 total):

IRB Protocol Number:

HRPO Protocol Number: A-18991.2

Protocol PI: Craig G. Crandall, PhD

Protocol Site: University of Texas Southwestern Medical Center

Protocol Title: Effects of Burn Injuries on Thermoregulatory and Cardiovascular Responses in Soldiers: Implications for the Standards of Medical Fitness - Aim 2

Target approved for clinical significance: 85 subjects

IRB INITIAL APPROVAL DATE: 12/14/2015

HRPO INITIAL APPROVAL DATE: 12/24/2015

CONTINUING REVIEW APPROVAL DATES:

- 07/06/2016 HRPO
- 06/09/2017 HRPO
- 08/10/2018 HRPO
- 12/13/2019 HRPO

AMENDMENTS:

- Amendment 1, HRPO approved 07/06/2016, to add a cohort of burn subjects to the protocol, thereby increasing enrollment to 85 subjects (from 35 subjects) plus other minor changes
- Amendment 1, HRPO approved 06/09/2017, to add Parkland as a recruiting site

ADVERSE EVENTS OR UNANTICIPATED PROBLEMS:

- None

ENROLLMENT STATUS:

- Number of subjects recruited/original planned target: 75/85
- Number of subjects screened/original planned target: 75/85
- Number of patients enrolled/original planned target: 67/85
- Number of patients completed/original planned target: 60/85

PROTOCOL (3 of 4 total):

IRB Protocol Number:

HRPO Protocol Number: A-18991.3

Protocol PI: Craig G. Crandall, PhD

Protocol Site: University of Texas Southwestern Medical Center

Protocol Title: Effects of Burn Injuries on Thermoregulatory and Cardiovascular Responses in Soldiers: Implications for the Standards of Medical Fitness - Aim 3

Target approved for clinical significance: 40 subjects

IRB INITIAL APPROVAL DATE: 08/06/2018

HRPO INITIAL APPROVAL DATE: 10/03/2018

CONTINUING REVIEW APPROVAL DATES:

- 12/13/2019 HRPO

AMENDMENTS:

- None

ADVERSE EVENTS OR UNANTICIPATED PROBLEMS:

- None

ENROLLMENT STATUS:

- Number of subjects recruited/original planned target: 22/20
- Number of subjects screened/original planned target: 22/20
- Number of patients enrolled/original planned target: 22/20
- Number of patients completed/original planned target: 20/20

PROTOCOL (4 of 4 total):

IRB Protocol Number:

HRPO Protocol Number: A-18991.4

Protocol PI: Craig G. Crandall, PhD

Protocol Site: University of Texas Southwestern Medical Center

Protocol Title: Effects of Burn Injuries on Thermoregulatory and Cardiovascular Responses in Soldiers: Implications for the Standards of Medical Fitness - Aim 4

Target approved for clinical significance: 30 subjects

IRB INITIAL APPROVAL DATE: 12/21/2015

HRPO INITIAL APPROVAL DATE: 12/24/2015

CONTINUING REVIEW APPROVAL DATES:

- 08/26/2016 HRPO
- 08/21/2017 HRPO
- 08/26/2018 HRPO
- 08/20/2019 HRPO closure memo issued

AMENDMENTS:

- Amendment 1, IRB approved 08/24/2016, minor changes for personnel change
- Amendment 2, IRB approved 09/28/2017, minor changes for enrollment increase from 18 subjects to 30 subjects

ADVERSE EVENTS OR UNANTICIPATED PROBLEMS:

- None

ENROLLMENT STATUS:

- Number of subjects recruited/original planned target: 21/30
- Number of subjects screened/original planned target: 21/30
- Number of patients enrolled/original planned target: 21/30
- Number of patients completed/original planned target: 20/30

Significant changes in use or care of vertebrate animals

No animal use research is involved.

Significant changes in use of biohazards and/or select agents

No biohazard or select agent research is involved.

6. PRODUCTS

Journal publications

1. Cramer, M.N., G. Morales, M. Huang, K. Kouda, P.Y.S. Poh, C.G. Crandall. Exercise Core Temperature Response with a Simulated Burn Injury: Effect of Body Size. *Med Sci Sports Exerc* 2020 Mar; 52(3): 705-711. doi: 10.1249/MSS.0000000000002160.
 - a. Original Manuscript
 - b. Published
 - c. Aim 1a
 - d. DoD Funding Acknowledged
2. Cramer, M.N., G. Morales, M. Huang, K. Kouda, P.Y.S. Poh, C.G. Crandall Exercise Thermoregulation with a Simulated Burn Injury: Impact of Air Temperature. *Med Sci Sports Exerc.* 2020 Mar; 52(3): 712-719. doi: 10.1249/MSS.0000000000002184
 - a. Original Manuscript
 - b. Published
 - c. Aim 2a
 - d. DoD Funding Acknowledged
3. Fischer M, Cramer MN, Huang M, Belval LN, Watso JC, Cimino FA, Crandall CG. Burn Injury does Not Exacerbate Heat Strain during Exercise while Wearing body Armor. *Med Sci Sports Exerc* Oct 2020; 52(10): 2235-2241. doi: 10.1249/MSS.0000000000002375
 - a. Original Manuscript
 - b. Published
 - c. Aim 3b
 - d. DoD Funding Acknowledged
4. Belval LN, Cramer MN, Morales G, Huang M, Cimino FA, Watso JC. Interaction of Exercise Intensity and Simulated Burn Injury size on Thermoregulation. *Med Sci Sports Exerc (in press)*.
 - a. Original Manuscript

- b. In Press
- c. Aim 2b
- d. DoD Funding Acknowledged

Books or other non-periodical, one-time publications

Nothing to Report.

Other publications, conference papers, and presentations

1. Belval LN, Cramer MN, Huang M, Morales G, Cimino FA, Watso JC, Crandall CG. Interaction Between Exercise Intensity and Burn Size Affects Body Temperature During Exercise in the Heat. 2020 ACSM Annual Meeting (Cancelled due to COVID-19). *Medicine & Science in Sports & Exercise*. 52(7S): 534, June 2020.
 - a. Invited Talk
 - b. Presented
 - c. Directly related to Aim 2b
 - d. DoD Funding Acknowledged
2. Cimino FA, Cramer MN, Morales G, Huang M, Belval LN, Watso JC, Crandall CG. The Effect of Burn Location on Internal Body Temperature Responses During Exercise in The Heat. 2020 ACSM Annual Meeting (Cancelled due to COVID-19). *Medicine & Science in Sports & Exercise*. 52(7S): 534, June 2020.
 - a. Invited Talk
 - b. Presented
 - c. Directly related to Aim 3a
 - d. DoD Funding Acknowledged
3. Fischer M, Cramer MN, Huang M, Belval LN, Watso JC, Cimino FA, Secher NH, Crandall CG. A Torso Burn Injury Does Not Exacerbate Thermoregulatory Strain During Exercise-Heat Stress While Wearing A Military Combat Uniform. Experimental Biology 2020 (Cancelled due to COVID-19). *FASEB J*, 34(S1).
 - a. Posted
 - b. Presented
 - c. Directly related to Aim 3b
 - d. DoD Funding Acknowledged
4. Crandall CG, Cramer MN, Huang M, Morales G, Belval LN, Watso JC, Fischer M. Burn Survivors Can Exercise for 30 Min, Even in the Heat, Without a Risk of Excessive Hyperthermia. American Burn Association 52nd Annual Meeting. *Journal of Burn Care & Research*. 41(S1): S48-S49, March 2020.
 - a. Invited Talk
 - b. Presented
 - c. Related to Aim 2
 - d. DoD Funding Acknowledged

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: Craig Crandall, PhD
Project Role: PI
Researcher Identifier: <https://orcid.org/0000-0001-7792-9713>
Nearest person month worked: 4
Contribution to Project: Dr. Crandall has worked extensively with the lab team while planning and implementing data collection and analysis.
Funding Support: Dr. Crandall receives extramural funding from the Department of Defense and the NIH.

Name: Benjamin Levine MD
Project Role: Collaborator
Researcher Identifier: <https://orcid.org/0000-0001-9064-7251>
Nearest person month worked: 1
Contribution to Project: Dr. Levine provides medical oversight to this project, as well as assists in the interpretation of the findings.
Funding Support: Dr. Levine receives funding through the NIH, NASA, and from clinical revenue

Name: Karen Kowalske, MD
Project Role: Collaborator
Researcher Identifier: <https://orcid.org/0000-0003-2729-3328>
Nearest person month worked: 1
Contribution to Project: Dr. Kowalske assists with subject recruitment and the interpretation of the findings.
Funding Support: Dr. Kowalske receives funding from the Burn Model Systems grant and from clinical revenue.

Name: Naomi Kennedy RN, BSN
Project Role: Research Nurse
Researcher Identifier: N/A
Nearest person month worked: 1
Contribution to Project: Naomi has assisted with subject screening and consenting, data collection, and subject safety.
Funding Support: Ms. Kennedy receives extramural funding support from grants to Dr. Crandall from the Department of Defense and the NIH.

Name: Luke Belval, Ph.D.
Project Role: Postdoctoral Fellow
Researcher Identifier: <https://orcid.org/0000-0003-0929-8061>
Nearest person month worked: 4
Contribution to Project: Dr. Belval has taken over the primary responsibilities of this project follow the departure of Dr. Matthew Cramer who to a Research Scientist position within the Canadian government. Dr. Belval assists with all aspects of the study, from recruitment through data analysis. This contribution has been quite extensive as each subject requires multiple visits to the laboratory to accomplish the stated aims.
Funding Support: Dr. Belval receives extramural funding support from the Department of Defense and the NIH.

Name: Joseph Watso, Ph.D.
Project Role: Postdoctoral Fellow
Researcher Identifier: <https://orcid.org/0000-0001-7840-0643>
Nearest person month worked: 1
Contribution to Project: Dr. Watso assists with data collection.

Funding Support:	Dr. Watso receives extramural funding support from the Department of Defense.
Name:	Frank Cimino, M.S.
Project Role:	Research Associate
Researcher Identifier:	N/A
Nearest person month worked:	3
Contribution to Project:	Mr. Cimino assists with subject recruitment, scheduling, and assisted with data collection and reduction.
Funding Support:	Mr. Cimino receives extramural funding support from grant to Dr. Crandall from the Department of Defense and the NIH.
Name:	Ileana Hill, RN, BSN
Project Role:	Research Nurse
Researcher Identifier:	N/A
Nearest person month worked:	3
Contribution to Project:	Ileana has assisted with subject screening and consenting, data collection, and subject safety.
Funding Support:	Ms. Hill receives extramural funding support from grants to Dr. Crandall from the Department of Defense and the NIH.

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. Crandall has received two grants funded by the NIH, one addressing cooling strategies for burn survivors and the cardiovascular responses of the elderly to heat stress. These grants do not impact the support for the present project.

What other organizations were involved as partners?

Nothing to Report.

8. SPECIAL REPORTING REQUIREMENTS

QUAD CHART

Convert this report to a PDF file and append updated quarterly Quad Chart in PDF as an appendix.

9. APPENDICES

Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

Nothing to report.

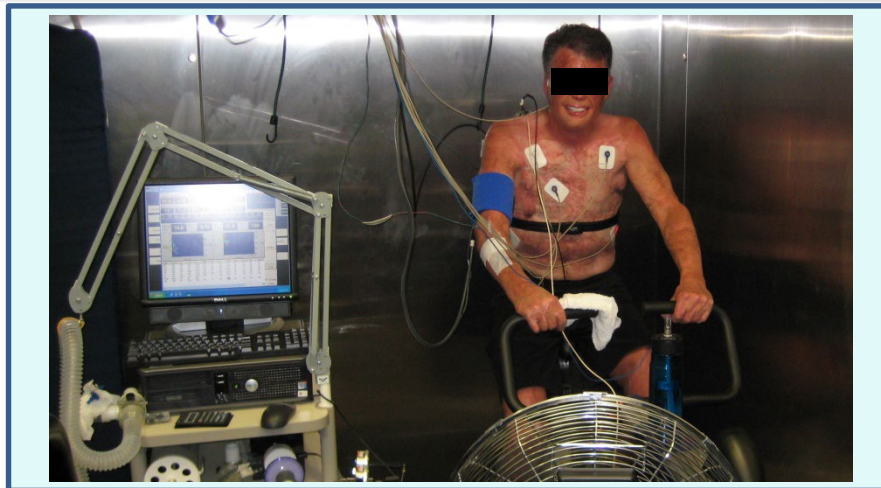


Study/Product Aim(s)

- Aim 1: Absolute body surface area (BSA) available for heat dissipation (i.e., uninjured skin) more accurately predicts thermoregulatory and cardiovascular consequences during a thermal stress relative to the current standard of using %BSA burned.
- Aim 2: The extent to which a burn injury is detrimental to an individual is dependent on the ambient temperature at a given exercise intensity and the exercise intensity within a given environment.
- Aim 3: Does the location of the burn injury influence thermoregulatory responses?
- Aim 4: Does the donor site contribute to compromised thermoregulatory responses in burned individuals.
- Aim 5: Identification of an upper limit for which a soldier with a prior burn injury could be expected to maintain a safe core body temperature across differing metabolic demands and environmental conditions.

Approach

The above questions will be addressed primarily by measuring thermoregulatory responses (e.g., core and skin temperatures) during exercise in neutral and hyperthermic environments at various workloads (e.g. rate of metabolic heat generation) in individuals with simulated burn injuries and in actual burn patients.



Accomplishment: We are very close to completing Aim 2B (only 1 subject needed and she has completed 5 of the 9 visits). We completed Aims 2C, 3A, and 3B.

Timeline and Cost

Activities	CY	16	17	18	19	20
Aim 1: Body surface area		[Green bar spanning 2016-2020]				
Aim 2: Effect of workload and climate		[Green bar spanning 2017-2020]				
Aim 3: Burn location					[Green bar spanning 2019-2020]	
Aim 4: Donor site		[Green bar spanning 2016-2019]				
Aim 5: Compilation						[Green bar in 2020]
Estimated Budget (\$K)		\$431	\$375	\$395	\$399	\$419

Goals/Milestones

CY16 Goal – Obtain IRB and HRPO approvals. Initiate data collection for Aim 1A.

CY17 Goals – Complete Aims 1A and initiate Aims 2.

CY18 Goal – Continue data collection for Aims 1B, all Aim 2s, and Aim 4.

CY19 Goal – Complete data collection for Aim 2 and initiate data collection for Aim 3.

CY20 Goal – Complete data collection for Aims 1B, 3, and 4. Complete the synthesis of the obtained data and provide guidelines regarding burn injury size/location, environmental condition, and workload by which a burned soldier could safely perform his/her duties.

Comments/Challenges/Issues/Concerns

- Like most laboratories throughout the United States, COVID-19 has shut down our laboratory, we are only just able to resume data collection. However, travel restrictions for out of town subjects remains prohibited. During the prior 7+ month we have focused data analysis, manuscript writing, and Aim 5.

Budget Expenditure to Date

Projected Expenditure: \$2,017,168

Actual Expenditure: \$1,734,703