U.S. Army Institute of Surgical Research (USAISR)

“For Combat Wounded”

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Director of Research, USAISR
30 March 2017
Disclaimer

• The opinions or assertions presented here are those of the author and do not represent those of the US Army or the Department of Defense.

• Conflicts of Interest: None
Purpose

• Overview of the US Army Institute of Surgical Research
  – Mission
  – History
  – Capabilities
  – Areas of Research
  – Points of Contact
Mission and Vision

**Mission**
Optimize Combat Casualty Care

**Vision**
The World’s Premier Research Organization for Combat Wounded

- **Research** – Conduct a comprehensive and sustainable research and development program to deliver knowledge and material solutions to optimize survival and functional recovery in combat casualties and civilian patients with trauma and burns, while also providing expert analysis and input to shape future requirements and directions in combat casualty care.

- **Burn Center** - Serves as the sole facility caring for combat burn casualties, beneficiaries and civilian emergencies within the Department of Defense. The Burn Center provides interdisciplinary care by a team of approximately 300 medical professionals providing cutting edge surgical services and promoting optimal recovery, restoration of function, and community reintegration of our burn survivors.
A Long History of Research - Clinical Collaboration

Established as Surgical Research Unit at Halloran General Hospital, Staten Island, New York 1943 – 1947 (Staff 12)

- Move to Brooke Army Medical Center – 1947

-Renamed US Army Institute of Surgical Research - 1970

Army Burn Unit
Brooke General Hospital
1949 - 1996

U.S. Army Institute of Surgical Research at Brooke Army Medical Center
1996 to Present (Staff >700)

Evolving Mission
- Antibiotics in Wound Care (1943)
- Innovative Surgical Techniques & Develop (1947)
- Thermal Injury (1949)
- Full Spectrum Combat Casualty Care (1996)
USAISR Personnel and Facilities

### USAISR Total Personnel (as of FEB17)

<table>
<thead>
<tr>
<th>Military</th>
<th>Civilians</th>
<th>IPAs</th>
<th>Contractor</th>
<th>TOTAL</th>
</tr>
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<tbody>
<tr>
<td>193</td>
<td>239</td>
<td>1</td>
<td>419</td>
<td>852</td>
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### Number of Research Personnel (as of 28MAR17)

<table>
<thead>
<tr>
<th>Military</th>
<th>Civilians</th>
<th>IPAs</th>
<th>Post Docs</th>
<th>Contractors</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>92</td>
<td>68</td>
<td>1</td>
<td>42</td>
<td>162</td>
<td>366 (43%*)</td>
</tr>
</tbody>
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* percent of 28 FEB 2017 totals

**Animal Research Facilities:** 53,170 sf; large and small animal experimental surgery, imaging, ICU, housing (Bldg 3611 (BHT1) 31,037sf; Bldg 3610 (BHT2) 22,033sf)

**Laboratory Facilities:** 53,179 sf; shared with NAMRU-SA, USAF (Bldg 3611 (BHT1) 17,371 sf; Bldg 3610 (BHT2) 35,808 sf)

**Location:** Joint Base San Antonio - Fort Sam Houston, San Antonio, TX, on the San Antonio Military Medical Center (SAMMC) Campus, in the Battlefield Health and Trauma Research Center (BHT) and the 4th Floor Consolidated Tower in SAMMC (Burn Center)
MISSION
The United States Army Institute of Surgical Research Burn Center serves as the sole facility caring for combat burn casualties, beneficiaries and civilian emergencies within the Department of Defense. The Burn Center provides interdisciplinary care by a team of approximately 300 medical professionals providing cutting edge surgical services and promoting optimal recovery, restoration of function, and community reintegration of our burn survivors.

Only DoD Burn Center

Since 2003
>1200 Military Burn Casualties
>3800 Civilian Burn Patients
>1000 Transported by Burn Flight Team World-wide

![Graph showing the number of patients treated each fiscal year from FY 2003 to FY 2016. The graph includes two categories: ACUTE and READM. The number of patients treated each year is indicated by bars. The highest number of patients treated in FY 2016 is 181, and the lowest is 3 for FY 2003. The graph shows a steady increase in patient numbers over the years.]
CORE RESEARCH FACILITIES AND CAPABILITIES
Research Support Division

- **Laboratory Support:**
  - clinical chemistry, hematology, coagulation, blood gas and microbiological services

- **Animal Husbandry**
  - Animal feeding, care, facilities, environmental enrichment

- **Veterinary Medical and Surgical Support**
  - Anesthetic preparations, monitoring and recovery for animal protocols, and assist with procedures as needed

- **Anatomic Pathology:**
  - assists with protocol development, provides necropsy and animal disposal, histology, molecular pathology (IHC, and extraction of RNA, DNA, and protein from FFPE tissues), and histopathological analysis reports
Vivarium

- 53,170 sq ft
- Large Animal Capacity
  - Over 100
- Small Animal capacity
  - Over 1500
- 8 operating rooms
- CT, mCT, Radiograph, SEM, confocal microscope, In vivo Imaging System
- Large Animal ICU (24/7)
- Biosafety Level 2
- AAALAC Accredited
Selected Additional Capabilities

• Animal models in trauma (established and new)
• >50,000 sq ft laboratory space
• Flow cytometry
• Analytical chemistry
• Intra-vital microscopy
• Coagulation biochemistry
• Platelet function
• Assay and method development
• Cell culture
• Research Blood Bank
• BHT Center for Human Integrative Physiology - Lower body negative pressure for simulation of hemorrhagic shock to study cardiovascular responses in normal human volunteers
• Syndaver and other artificial systems for testing for device evaluation and development
• Statistics
Clinical Trials

• Dedicated team of clinical research personnel to enable and facilitate clinical studies – prospective and retrospective, single and multi-center

• Extensive experience in clinical studies in burn patients

• Studies in trauma, orthopedic, and other patient populations also possible through partnering with BAMC

• Rare capability bringing together basic scientists and clinical researchers to form cutting edge, multidisciplinary teams

• Establishing GMP/GLP

POC: LTC Kevin Akers, MD – kevin.s.akers.mil@mail.mil
RESEARCH PROGRAMS
USAISR Research Programs Span The Continuum of Care

Emerging Challenge: Prolonged Field Care
- Iraq & Afghanistan casualties to forward surgical team (FST) in ~60 min
- Future conflicts may require stabilization for up to 72 h before FST

How can we stabilize patients and move advanced capabilities forward toward the point of injury?
• Damage Control Resuscitation
• Coagulation and Blood
• Extremity Trauma and Regenerative Medicine
• Multi-Organ Support Technology (MOST)
• Comprehensive Intensive Care Research
• Tactical Combat Casualty Care
• Combat Trauma and Burn Research
• Systems of Care for Complex Patients
• Medical Countermeasures for Ocular Trauma
• Dental and Maxillofacial Trauma
Research Task Areas (Therapeutic Areas)

• Damage Control Resuscitation (Dr. Michael Dubick)
  – Develop methods and products to stop bleeding, replace lost blood volume, and mitigate the pathophysiologic consequences of severe bleeding

• Coagulation and Blood (LTC(P) Andre Cap)
  – Improve the safety, efficacy, and logistical supportability of blood products, identify mechanisms of coagulation dysfunction in trauma, diagnostics and therapeutics to restore normal function

• Extremity Trauma and Regenerative Medicine (Dr. Josh Wenke)
  – Focused on infection control and healing in extremity trauma; Reconstruction/regeneration of volumetric and segmental defects of muscle and bone; and rehabilitation following extremity trauma.
Research Task Areas (Therapeutic Areas)

- Multi-Organ Support Technology (Dr. Lee Cancio)
  - Comprehensive research and development to develop and optimize methods to minimize damage and sustain vital organ function following severe trauma in a setting of delayed definitive care

- Comprehensive Intensive Care Research (Dr. Jose Salinas)
  - Computer engineering solutions for automation and decision support in the care of severely injured casualties

- Tactical Combat Casualty Care (Dr. Kathy Ryan)
  - Integrative and translational research focused on patient care under the unique set of tactical, environmental, and patient factors associated with the pre-ROC 2 environment, including ground and air transport.
• Combat Trauma and Burn Injury Research (Dr. Robert Christy)
  – Improve burn wound stabilization, repair, healing, scar minimization, and functional recovery. Also includes study of the molecular mechanisms and improved treatments for battlefield pain control

• Systems of Care for Complex Patients (COL Elizabeth Mann-Salinas)
  – Develop, refine, and sustain teams, processes, and systems to optimize casualty care across vast geographical distances and 10 or more patient hand-offs among teams from the point of injury to definitive care
• Medical Countermeasures for Ocular Trauma (COL Jeffery Cleland)
  – Procedures and products to repair and restore the eye and vision following severe injury. Will expand to include auditory trauma and regeneration in next 2 years.

• Dental and Maxillofacial Trauma (Dr. Kai Leung)
  – Develop knowledge and materiel solutions to stabilize patients and improve healing, function, and aesthetic outcomes after severe combat-related cranio-maxillofacial injury
Mission Conduct medical, craniofacial, and biomedical research, which focuses on ways to enhance the health, safety, performance and operational readiness of Navy and Marine Corps personnel and addresses their emergent medical and oral/facial problems in routine and combat operations.

Combat Casualty Care & Operational Medicine Directorate
Research that focuses on developing novel treatment methodologies and testing of medical devices and agents that save the lives of warfighters and extends survival one golden hour at a time.

Craniofacial Health & Restorative Medicine Directorate
Integrated research focused on innovative solutions to address craniofacial injuries, dental needs, and related environmental stewardship.

State of the Art Laboratory Facilities, including a 45,000 square foot animal facility with NHP capability

Contact: Chief Science Director: Dr. Sylvain Cardin (sylvain.cardin.civ@mail.mil)
**Mission**
Provide comprehensive, far forward research in order to enhance patient stabilization, preparation for movement, staging, and in-flight/in-transit care.
End state: focused translational research that will advance knowledge for treatment of injury and disease

**Mission Objectives**
- **Improve care** during evacuation and transport of casualties
- **Study capability gaps** to solve scientific en route care needs
- Collaborate through **joint research**
- Perform **translational** outcomes based research
- Develop **evidence based care** and clinical practice guidelines

**Infrastructure**
Director (Emergency Medicine Physician)
Senior scientist (PhD, RN)
Program manager
Research nurse coordinators
Statistical and regulatory compliance support

**Location**
U.S. Army Institute of Surgical Research/ USAF 59th MDW/ST
Joint Battlefield Health and Trauma Research Institute
U.S. Army Institute of Surgical Research

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**Areas of Current Research**

**Pre-Hospital Care**
- Pre-Hospital Life Saving Interventions in a Combat Setting

**MEDEVAC**
- TACEVAC – to enable development of CPGs
- Provider type (influence on procedures and outcomes)
- Transport time and outcomes in specific patient population types

**Critical Care Air Transport (OIF/OEF to CONUS)**
- Documentation and transfer of information
- Evaluation of safe blood hemoglobin levels for CCATT transport
- Blood transfusion requirements for burn and inhalation injuries
- Analgesic use (opioid, ketamine, epidural) via CCATT
- Ventilation methods via CCATT
- Non-trauma critically ill patients transported via CCATT

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**Future Research**
- En route Care Outcomes: Evidence based care for TCCET/MERT/CCATT/TACEVAC/MEDEVAC
- Hospital Based Clinical Trials: Resuscitation, ultrasound, analgesics
- Preclinical Studies: Pre-hospital resuscitation; serum marker for hemorrhagic shock
- Devices: Monitoring, documentation, decision support

**Collaboration**
- **Joint Collaboration – DoD and Civilian**
  - USAISR Burn Center and Pain Task Area
  - USAISR Critical Care Monitoring Task Area
  - USAISR Tactical Combat Casualty Care Task Area
  - Navy Medical Research Unit (NAMRU)
  - JTS - Department of Defense Trauma Registry (DoDTR)
  - USAF CCATT Pilot Unit
  - Air Force Special Operations Command (AFSOC)
  - University of Cincinnati, UNC-Chapel Hill
  - SAMMC Department of Emergency Medicine, Toxicology
  - Southwest Texas Regional Advisory Council (STRAC)

**Resident/Fellow Research Mentoring**
- SAUSHEC - emergency medicine medical and surgery
- Fellows in pulmonary, surgery, pre-hospital care
- United Kingdom research fellow
- Mentoring staff physicians, academic faculty
Major Partnerships/Collaborations

230 Active Cooperative Research and Development Agreements (CRADA), Material Transfer Agreements (MTA), and Educational Partnership Agreements (EPA)

- Multiple-collaborator teams
- Industry
- Academia
- Government
- International
Partnering and Collaboration are Essential to Consistently Deliver Advanced Products to the Battlefield
Comments and Questions
• Damage Control Resuscitation
• Coagulation and Blood
• Extremity Trauma and Regenerative Medicine
• Multi-Organ Support Technology (MOST)
• Comprehensive Intensive Care Research
• Tactical Combat Casualty Care
• Combat Trauma and Burn Research
• Systems of Care for Complex Patients
• Medical Countermeasures for Ocular Trauma
• Dental and Maxillofacial Trauma
Damage Control Resuscitation

• Accomplishments
  – Extremity and Junctional Tourniquets
  – 2nd and 3rd Generation Hemostatic Dressings and devices

• Focus Areas - Reduce KIA/DOW
  – Hemostatic Resuscitation – Restore volume, provide clotting factors and oxygen carrying capacity, avoid coagulopathy
  – Avoid giving blood products to those who do not need them
  – Prevent hypothermia
  – Improve immune dysfunction and tissue stabilization
  – Prolonged Field Care

POC: Dr. Michael Dubick – michael.a.dubick.civ@mail.mil
Coagulation and Blood Research Program

• Accomplishments
  – Supported SOCOM Expanded Access IND for French Freeze-Dried Plasma
  – Clinical practice guidelines for the use of tranexamic acid, whole blood, and coagulation diagnostics (ROTEM)
  – Army Science and Technology Objective: Improved Platelets Storage – Liquid Stored Platelets with 14d shelf-life (vs. 5d)
  – Lead for DoD clinical trial on Zika detection at 21 US DoD Blood Centers

• Focus Areas
  – Understanding basic mechanisms of trauma-induced coagulopathy
  – Developing improved platelet storage systems
  – Developing blood product pathogen reduction technologies
  – Mesenchymal Stem Cells
  – Prolonged Field Care

POC: LTC Andre Cap – andrew.p.cap.mil@mail.mil
Accomplishments

- Defining injury patterns and resulting outcomes
- Debrided skin as a source for stem cells

Focus Areas

- Segmental defects (bone and muscle)
- Volumetric Muscle Loss
- Wound contamination and infection
- Autologous stem cells for muscle/skin/bone defects
- Major Extremity Trauma Research Consortium (>20 civ and 4 military centers; Dr. Wenke programmatic lead)
  - Bone Defect Reconstruction and Fracture Healing
  - Prevention and Treatment of Acute and Chronic Infections
  - Diagnosis and Treatment of Compartment Syndrome
  - Outcomes of Limb Salvage and Amputation
  - Post Acute Care and Rehabilitation Outcomes
  - Wound Care and Closure

• Prolonged Field Care

POC: Dr. Josh Wenke – joseph.c.wenke.civ@mail.mil
Multi-Organ Support Technology (MOST)

Accomplishments

• Animal models of smoke, burn, blunt injury, hemorrhagic shock in large and small animal ICU (72 hours)

Focus Areas

• Stem cells and their products
  – MSC mitigate lung failure in ARDS after inhalation injury
  – Working to isolate beneficial component and eliminate prothrombotic character (conditioned media, etc.)

• Extracorporeal Life Support for forward care
  – Exploring low-flow CO2 removal versus full (larger ECLS)
  – Heparin-free ECLS (new coatings and catheters)

• Resuscitative Endovasc Balloon Occlusion of Aorta (REBOA)
  – Development of “partial” REBOA to enable controlled perfusion distal to balloon (for more prolonged use)
  – Define physiology of REBOA resuscitation under various conditions

• Prolonged Field Care

POC: Dr. Lee Cancio – leopoldo.c.cancio.civ@mail.mil
Comprehensive Intensive Care Research
Decision Support for Acute Burn Fluid Resuscitation (Mobile & Clinical)

Accomplishments

• Burn Resuscitation Decision Support System-Clinical (BRDSS-C) – FDA cleared device; calculates fluid resuscitation volume based on patient status as decision support in burn resuscitation
• BRDSS-Mobile - FDA cleared device for deployed setting

Focus Areas

• R&D to develop novel health information technologies to enhance clinical decision making
• Intelligent Focused Assessment with Sonography for Trauma (iFAST)
  • Exclusive license signed and finalized
• Closed Loop Burn Resuscitation: BRDSS-A
  • Working with FDA on design

POC: Dr. Jose Salinas, PhD  jose.salinas4.civ@mail.mil or LTC (Ret) Seriomelvin maria.l.seriomelvin.civ@mail.mil
Accomplishments

• Developed and integrated the CRI machine-learning algorithm (based on waveform feature extraction) into field-ready medical monitor with accurate (>95%) prediction of hemodynamic decompensation (class III shock).
• Developed Intrathoracic Pressure Regulation Therapy for improving central circulation in shock

Focus Areas

– R&D to deliver diagnostic and procedural solutions which support the spectrum of TCCC
– Evidence to support the TCCC doctrine
– Physiological monitoring in the prehospital setting
– Pre-hospital pain management
– Airway and ventilatory support
– Prevention of acute kidney injury (new start FY18)

POC: Kathy L. Ryan, PhD: kathy.l.ryan.civ@mail.mil
**Combat Trauma and Burn Injury Research**

- **Integrated Approach:** Burn injury is complex and requires inter-disciplinary collaboration between basic science, translational and clinical researchers – pain management in wound care is integrally related to both treatment and outcome.

- **Focus Areas – Burn Injury and Pain**
  - Detecting and preventing infection and sepsis
  - Modulating the systemic inflammatory response
  - Skin regeneration
  - Scar modification to prevent contractures and improve cosmesis
  - Screen and evaluate of novel therapeutics in animal models of human pain conditions
  - Testing of novel interventions, devices, and treatment regimens for the management of pain
  - Evaluation of the effects of treatments for pain on long-term outcomes
  - Investigation of the molecular mechanisms underlying the effects of pain and the response to analgesics and anesthetics on pain, pathophysiology, and comorbidities

POC: Robert J. Christy, PhD: robert.j.christy12.civ@mail.mil
Goal: Define best combat casualty care practice through research on practice variability and patient outcomes in all military roles of care

- **Focus Areas - Readiness**
  - Defining optimal skill set for deploying professional medical personnel
  - Development of automated guidelines for delivery of combat casualty care
  - Cooperative Communication Systems – improving team communication to improve patient safety
  - Comparison of live tissue vs. high fidelity simulation for extracorporeal life support training
  - Evidence-based preceptorship program for clinical and operational competency
Medical Countermeasures for Ocular Trauma

- **Mission:** Advance procedures, methods and modeling that protect, repair and restore the eye and vision from injuries sustained by our Warfighters

- **Focus Areas – Stabilize, Treat, Repair Eye Trauma**
  - Amniotic Membrane to Treat Corneal Wounds
  - Development of an In Vitro Model of Proliferative Vitreoretinopathy (PVR)
  - Nanotechnology-Based Approach for Treating Corneal Endothelial Damage
  - Blast Effects on the Eye, Vision, and Pain/Inflammation
  - Ocular Wound Chamber as a Novel Instrument to Protect and Treat Eyes of Burn Patients
  - Engineering therapeutics to treat corneal chemical burns
  - Optic nerve regeneration
  - Incorporating auditory trauma in near future

POC: COL Jeffrey Cleland – jeffrey.m.cleland4.mil@mail.mil
Recent Accomplishments:

- Established a quantitative rabbit ear biofilm-impaired wound model to test the effects of anti-inflammatory agents and pro-resolving mediators on wound healing and scar formation
- Built an *in vitro* and *in vivo* platform for high-throughput testing of more effective anti-biofilm therapeutics
- Developed a clinically relevant small animal mandible model
- Established a porcine, full-thickness burn model

Current Focus Areas: Dental and Maxillofacial

- Dental
  - Development of Novel Molecules for Plaque Control-Antiplaque chewing gum
- Mitigation of Biofilm
  - Biofilm-Impaired Wound Healing
  - Formulation of anti-biofilm agents
  - Genomic responses of *Pseudomonas* in wounds
- Regenerative Medicine
  - Craniomaxillofacial (CMF) Bones
  - CMF Soft Tissues
- Mitigation of Face Scars/Burns
  - Face Restoration Project
  - Wound bed modulation

POC: Dr. Kai Leung – kai.p.leung.civ@mail.mil
USAISR Deliverables

Major Innovations Delivered to Field
2004 – Hemcon Dressing
2005 – Combat Tourniquet
2007 – Damage Control Resuscitation
2008 – Combat Gauze Dressing
2009 – Burn Resuscitation Decision Support

- Hemostasis Innovations
- Fluid warmers to prevent hypothermia
- Hypothermia prevention kit
- Intraosseus Infusion Systems
- Resuscitation Innovations – Damage Control
  - Hemostatic (balanced) resuscitation
  - Freeze dried plasma (FDP)
- Antibiotics by medics
- Burn resuscitation guidelines
- Needle thoracentesis
- Ultrasound to diagnose pneumothorax
- Individual/vehicle First Aid kit
- Extracorporeal organ support
  - Renal replacement therapy
  - Lung support
- Impedance threshold device for cardiac arrest and hypovolemia
- Device for early detection of shock (CRI)
- Battlefield burn prevention
End