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CONTRACTING ORGANIZATION: National Trauma Institute/Coalition for National Trauma Research (CNTR), San Antonio, TX

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14. ABSTRACT
The purpose of this project is to focus on three specific areas of research identified by the DoD as high priority including: better solutions for vascular injuries, improved pain management, and better approaches for airway management. Additionally, this project created the National Trauma Research Repository (NTRR) that allows for data sharing, secondary analysis and greater power to detect statistical significance. As available research funding shrinks and federal budget pressure increases, it is essential that the return from dollars invested in research be maximized by replacing the expensive and repetitive assembly and disassembly of short-lived clinical investigator networks with a stable and enduring operational infrastructure for clinical trauma research.

15. SUBJECT TERMS Vascular injury, airway management, pain management, Ketamine, National Trauma Research Repository

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1. INTRODUCTION:

Advances in trauma care in both pre-hospital and hospital settings have reduced trauma-related deaths and morbidities markedly; however, there is a substantial opportunity to further reduce deaths in the pre-hospital setting. Gaps in civilian and military pre-hospital care must be closed in order to reduce the number of potentially preventable deaths among Wounded Warriors and civilian trauma patients. The purpose of this project is to focus on three specific areas of research identified by the DoD as high priority including: better solutions for vascular injuries, improved pain management, and better approaches for airway management. These studies will extend evidenced-based pre-hospital interventions as well as populate the National Trauma Research Repository (NTRR) that will allow for data sharing, secondary analysis and greater power to detect statistical significance. As available research funding shrinks and federal budget pressure increases, it is essential that the return from dollars invested in research be maximized by replacing the expensive and repetitive assembly and disassembly of short-lived clinical investigator networks with a stable and enduring operational infrastructure for clinical trauma research.

2. KEYWORDS:

Vascular injury, airway management, pain management, Ketamine, National Trauma Research Repository, research dissemination

3. ACCOMPLISHMENTS:

Major Objectives of the Project:

Objective: To conduct research projects addressing military research gaps in airway management, pain management and vascular injury; and to develop tools to allow for the collection and dissemination of results and data from studies

Technical Objective 1: To conduct research projects addressing military research gaps in airway management, pain management and vascular injury**;** the contractor will perform Award management and compliance to include subcontracts, contract compliance, and all appropriate USAMRMC HRPO requirements.

Technical Objective 2: To develop tools to allow for the collection and dissemination of results and data from studies, including:

1) Develop a scalable repository of translational research data.
   a) Determination of common data element based on previously Coalition for National Trauma Research (CNTR) funded project and other database sources.
   b) Creation of the data dictionary
   c) Development of policies for utilization guidance which includes repository requirement documents and website development.
   d) Conduct vendor solicitation and vendor selection process based upon requirements and capabilities identified.
   e) Build a scalable repository
   f) Alpha and beta testing with previous CNTR funded studies and studies funded through this grant.

2) Provide a forum for dissemination of research outcomes to the trauma community.

Protocol 1: KETAMINE STUDY	**Timeline in Months**	**Actual completion date**	**% of completion**
Major Task 1: Prepare and adapt Research Protocol for DoD Funded Status for Study 1			
Subtask 1: Refine research protocol	1-3	06/28/2016	100%
Refine eligibility criteria, exclusion criteria, screening protocol, enrollment protocol	1-3	06/28/2016	100%
Finalize consent form and human subjects protocol	1-3	06/28/2016	100%
Coordinate IRB protocol submission	1-3	06/28/2016	100%
Submit for Military 2nd level IRB review (ORP/HRPO)	3-6	05/30/2017	100%
Submit amendments, adverse events and protocol deviations as needed	6-18	Ongoing	N/A
Milestone Achieved: Protocol for Study 1 developed	3	06/28/2016	100%
Milestone Achieved: Local IRB approval	4-5	03/20/2017	100%
Milestone Achieved: HRPO approval	8	06/21/2017	100%
Major Task 2: Data Analysis for Study 1			
Subtask 1: Monitor data collection and data quality	8-20	Closed	0%
Protocol 2: PROOVIT STUDY			
Major Task 3: Adapt PROOVIT Protocol for DoD Funded Status for Study 2			
If applicable, coordinate with sites for IRB protocol submission	1-6	01/05/2016	100%
Coordinate with sites for Military 2nd level IRB review (ORP/HRPO)	1-6	03/31/2016	100%
Submit amendments, adverse events and protocol deviations as needed	As needed	Closed	N/A
Coordinate with sites for annual IRB report for continuing review	Annual	06/28/2017	100%
Prepare and submit quarterly progress report to DoD	Qrtly	06/28/2017	100%
Milestone Achieved: Local IRB approval at all sites	3	03/29/2016	100%
Milestone Achieved: HRPO approval for all protocols	6	04/22/2016	100%
Major Task 4: Subcontract with all Study Sites for Study 2			
Verify sub-award documents: budget, budget justification, salary verification	1-3	03/22/2016	100%
Issue and execute sub-award document	1-3	04/13/2017	100%
Receive quarterly progress reports	Qtrly	03/15/2017	100%

Review quarterly progress reports	Qtrly	04/11/2017	100%
Milestone Achieved: Subawards issued for all sites	3	04/13/2017	100%
Major Task 5: Data Analysis for Study 2			
Subtask 1: Coordinate with sites and CNTR for monitoring data collection rates and data quality	4-6		100%
Perform all analyses according to specifications, share output and findings with all investigators	Ongoing		100%
Project 1: SURGICAL AIRWAY SIMULATOR			
Major Task 6: Develop High Fidelity Airway Simulator			
Execute Subaward	1	05/12/2016	100%
Develop a model base	1-4	07/01/2016	100%
Engineer hydraulic, mechanical and pneumatic systems for head movement, airway lubrication, respiration and circulation	1-4	07/01/2016	100%
Develop and integrate a programmable logic controller	1-4	07/06/2016	100%
Integrate subsystems into the infrastructure built upon the base	5-9	03/31/2017	100%
Develop a layered, high-fidelity anatomical model for face, neck and upper thorax	5-9	02/24/2017	100%
Separate the components of high-fidelity anatomical model for molding	5-9	8/31/2018	100%
Create molds of the anatomical components including bones, selected individual muscles, fascia, larynx, trachea, thyroid gland, major arteries and veins	10-12	8/31/2018	100%
Create serial iterations of the models and molds to complete engineering	10-12	8/31/2018	100%
Research materials for high anatomical and surgical fidelity laryngo-tracheal complex	10-12	08/31/2018	100%
Integrate the high-fidelity anatomical model with the base and infrastructure	13-18	8/31/2018	100%
Develop models for various anatomic wounding patterns	13-18	8/31/2018	100%
Create exchangeable sub-assemblies for reset of various wounding patterns	13-18	8/31/2018	100%
Major Task 7: Requirements Function Testing			
Confirm requirements function through volunteer use	19-24	8/31/2018	100%
Coordinate with volunteer pool to test	19-24	8/31/2018	100%

Report evaluations of volunteer testing	19-24	12/13/2018	100%
Project 2: NATIONAL TRAUMA RESEARCH REPOSITORY			
Major Task 8: Determine Data Dictionary and Vendor Requirements			
Coordinate with Steering Committee to determine Common Data Element Workgroup	1-6	03/29/2016	100%
Common Data Element Determinations	6-9	03/30/2018	100%
Develop Data Dictionary	6-9	03/30/2018	100%
Milestone Achieved: Data dictionary			
Major Task 9: Vendor solicitation and selection	1-6	08/11/2016	100%
Determine repository requirements	6-9	08/11/2016	100%
Vendor solicitation and selection process	6-9	08/11/2016	100%
Milestone Achieved: Repository requirements document	6-9	07/19/2017	100%
Milestone Achieved: Vendor Selected			
Major Task 10: Repository build and testing	9-12	06/25/2018	100%
Repository build (back and front end)	9-12	06/25/2018	100%
Alpha testing	12-15	06/25/2018	100%
Beta testing	15-18	06/25/2018	100%
Go Live	18-24	06/25/2018	100%
Milestone Achieved: Repository Live	18-24	06/25/2018	100%
Major Task 11: Website development and policy	3-9	6/25/2018	100%
Develop management policies	6-15	6/25/2018	100%
Develop website and interfaces	6-15	6/25/2018	100%
Milestone Achieved: Policies available on functional website		6/25/2018	100%
Major Task 12: Repository Hosting			
Repository hosting	37-52	3/29/2021	100%
Importing legacy studies	37-48	3/29/2021	100%
Supporting investigators with new studies	37-52	3/29/2021	100%

STUDY 1:

Protocol Title: Determining the Efficacy and Safety of Ketamine as a Battlefield Analgesic
Principal Investigator: John Fauerbach, PhD
Participating Site: Johns Hopkins University School of Medicine
HRPO Assigned A-number: A-19299.2
Abstract: Background: Early, effective pain control for acute traumatic injury is important for successful outcomes. Despite the known importance of pre-hospital pain management, few studies

have reported the use of analgesics and the type of analgesics used in combat. Ketamine has emerged recently as a potentially effective analgesic alternative to narcotics for use in combat-associated casualties. While early case reports attest to its effectiveness, these reports are anecdotal. Ketamine is the only single-agent anesthetic capable of producing a "dissociative" anesthesia, which has been useful for a variety of outpatient and inpatient surgical procedures. More than 50,000 service members have been injured in OIF, OEF, and OND and experience varying degrees of pain throughout their care. Of these injured service members, 31.8% are also diagnosed with PTSD.

Hypothesis: The addition of ketamine to narcotic analgesics will reduce significantly self-rated pain during dressing change/debridement on the Visual Analogue Scale for Pain (VAS-Pain):

Methods: Persons enrolled in the study through the informed consent process will be patients admitted to the Johns Hopkins Burn Center after sustaining burns less than 25% total burn surface area and not requiring initial endotracheal intubation. This would enable them to participate in structured interviews conducted by a psychologist assigned to the Burn Unit. These interviews would evaluate:

- The effectiveness of sub-anesthetic doses of ketamine as a sole analgesic vs. as a narcotic sparing drug for the treatment of acute post-traumatic pain
- The side effect profile of ketamine when administered in sub-anesthetic doses
- Whether the early administration of ketamine during the first three days following injury has a sustained effect on reducing the incidence or severity of Post-Traumatic Stress Disorder (PTSD)
- Whether the early administration of ketamine during the first three days following injury has a sustained effect on reducing the incidence or severity of clinical depression

Once IRB and HRPO approval is secured, patients will be randomized to a trial comparing a usual pain regimen, typically narcotics and benzodiazepines (UR-N) against a low dose ketamine regimen supplemented with usual pain medications (K+UR) on the effect of self-reported pain severity at the start of the procedure, every 5 minutes during the procedure and 5 minutes after the procedure ending, as well as the incidence and severity of PTSD and Depression at 24 hours, one week, and one month.

Military Significance: The DOD has identified capability gaps in combat casualty care. Several of the high priority gaps are well-suited for research in the civilian setting including en route care. A specific gap in these capabilities that the DoD has identified as high risk to the military and amenable to study in the civilian setting is: Ability to provide 100% acute and chronic pain management for wounded and injured soldiers, starting at the point of injury and continuing across the spectrum of care.

STUDY 2

Protocol Title: The PROspective Observational Vascular Injury Trial (PROOVIT)
Principal Investigator: Joseph DuBose, MD (Travis Air Force Base)
Lead Site: University of California at Davis
Participating Sites: Baylor College of Medicine/Ben Taub Hospital, Emory University, Loma Linda Medical Center, University of Southern California, Scripps Health, University of Maryland/R. Adams Cowley Shock Trauma, University of Tennessee – Memphis, University of Texas Health Science Center at Houston, University of Wisconsin School of Medicine and Public Health, Wright State University, East Carolina University
HRPO Assigned A-number: A-19299.1a-1m
Abstract: Background: Few if any decisions throughout the phases of vascular trauma management are guided by strong evidence. This fact is unfortunate, as many new diagnostic, therapeutic and surveillance strategies have the potential to improve morbidity and mortality

following this vexing injury pattern. The lack of evidence-based practice is even more concerning given the devastating consequences associated with mismanaged vascular trauma. To date, no studies exist that would allow the prospective aggregation of larger amounts of data pertaining to all phases of vascular trauma management.
Hypothesis: This prospective, multicenter, observational study will provide the necessary data to develop best practices and optimize the care of this unique population of patients.
Specific Aims: 1. To determine the impact of tourniquet utilization after extremity vascular injury on limb-specific complications and limb salvage; 2. To determine the optimal utilization of endovascular versus open repair modalities after vascular injury; 3. To determine the role of early anticoagulation in mitigating complications after vascular injury repair.
Study Design: This study is a prospective multi-center observational trial on the management of vascular trauma. Data and endpoints will be observational and involve no proscribed therapeutic interventions or alterations in patient care. Waiver of informed consent has been received. Institutions and providers are conducting normal diagnosis, management and surveillance procedures without interference by this study. The location and type of endovascular therapy for vascular trauma is tracked including comparison of outcomes to those following open operative repair of similar injury patterns. Finally, data elements are gathered in a wide range of age groups with vascular trauma including the challenging scenarios of pediatric and geriatric vascular injury.
Military Benefit: Hemorrhage from vascular injury, at both Non-Compressible Vascular Injury (NCVI) and Compressible Vascular Injury (CVI) sites, remains a primary cause of mortality and morbidity on modern battlefields. This study will provide linkage to crucial elements of subsequent limb salvage and long-term outcomes – data that are presently not available on any significant scale in the military realm.

PROJECT 1

Project Title: High Anatomic Fidelity Surgical Airway Training System
Principal Investigator: Robert Buckman, MD
Lead Site: Operative Experience, Inc.
HRPO Assigned A-number: Not applicable
Abstract: Background: Airway obstruction is the third most common cause of potentially-preventable combat death. Because of this, surgical management of the threatened or obstructed airway is an essential skill for special operations medics and combat surgeons. Cricothyroidostomy and tracheostomy are infrequently performed, life-saving surgical procedures required when a casualty's airway cannot be maintained by other means. Surgical airway procedures may be required at any level along the continuum of care/evacuation. Published data from recent theaters of war indicate that these emergency procedures are often performed incorrectly. Due to the limitations of existing methods of training, surgical airway management procedures are not currently taught to all combat medics. Improved, simulation-based methods of training will not only improve the training and enhance the capability of SOF medics and surgeons, but also will allow additional military healthcare providers and even combat lifesavers to be trained in this critical skill. The Defense Health Board recommended optimized airway devices and training as a research priority for the Combat Casualty Care Research Program, contributing to the identification of a Combat Casualty Care Capability Gap.
Methods: Develop a prototype surgical airway simulator that provides high anatomical and surgical fidelity and challenges trainees with increasing degrees of clinical difficulty.
This project will develop an airway simulator that is capable of accurate anatomic representation of the airway from the mouth to the lungs, simulates a variety of traumatic tissue disruption with the face and neck, bleeds realistically, and supports training in tracheostomy and cricothyroidotomy. Development includes anatomic design, engineering design, medical modeling, physical modeling, engineering and system integration.

PROJECT 2

Project Title: National Trauma Research Repository
Principal Investigator: Donald Jenkins, MD
Lead Site: The National Trauma Institute/Coalition for National Trauma Research
HRPO Assigned A-number: Not applicable

Abstract: There is a critical need for a national trauma research repository to synthesize study data for maximum use. Advances due to clinical trauma research have been accomplished largely through separate, organizationally distinct and disconnected efforts. Even when funding has derived from federal entries, individual projects have been somewhat dispersed and uncoordinated. This situation leads to research delays, duplications, inefficiencies and increased costs. To date there relatively little attention has focused on data exchange in the clinical research domain. While clinical researchers in different locations may have similar lines of investigation, the computer systems in use to store and retrieve data locally do not, and for the most part cannot, transmit, receive, combine, analyze and use shared data as information. Clinical research data are fragmented, sometimes within one facility, and can rarely be repurposed to answer additional research questions. Sharing data maximizes its value, promotes follow-up studies and minimizes duplicative data collection. Universal developments in information technology, like the creation of distributed data networks and virtual data access, provide ways to address clinical research needs that did not exist before. It is time to exploit and enhance these technologies to support clinical trauma research.

The consolidation and linkage of data sets in a shared data repository would greatly expand their use and provide a robust scientific platform; pooled data sets can create the additional statistical power necessary to improve statistical significance. This clinical research repository employing common data elements will be particularly beneficial in maximizing trauma study data because it is often difficult to obtain informed consent since the injury and the need for early interventions often coincide; the patient is often unable to give consent due to the level of consciousness; and family are often unavailable in the early stages of treatment after trauma. The ability to make aggregated research data widely available to clinical investigators is critical to reform trauma research and care because, while the practice of medicine should be evidence-based, within the field of trauma there is surprisingly little evidence to support clinical practice. The formation of a national trauma research repository will ensure maximum utilization of trauma data for translation into evidence-based practice.

The NTRR will be built as a scalable, customizable repository that is capable of receiving data feeds from other data systems through a conversion method. NTRDB will be structured such that any study can contribute any portion of its data, besides the core common data elements, and those elements remain linked to the original source as well as available for secondary analysis in concert with any other data set. The initial module will be a set of generic data elements that is as globally representative across all trauma patients as possible yet is robust enough to support a data analysis plan.

Dissemination: The goal was to comprehensively disseminate published works to the wider trauma network through a Knowledge Translation Plan thereby accelerating the adoption of research findings to improve civilian trauma and combat casualty care and outcomes

Accomplishments

TO1: To conduct research projects addressing military research gaps in airway management, pain management and vascular injury**;** the contractor will perform Award management and compliance to include subcontracts, contract compliance, and all appropriate USAMRMC HRPO requirements.

Study 1: Protocol Title: Determining the Efficacy and Safety of Ketamine as a Battlefield Analgesic

While this subject is of high interest, this study was plagued with challenges. Initially the role of the nurses on the protocol required clarification to the Institutional Review Board and ultimately a policy change addressing the procedure for sub-anesthetic, low-dose, slow infusion of ketamine for pain management was required at the facility. This process delayed the start of enrollment and contributed to the need for an extension without funding for 18 months. HRPO approval was achieved in late 2017 with a little over six months remaining in the period of performance. During a presentation by the PI to the CNTR board of directors expressed concern regarding the ability to enroll the planned number of subjects in the timeframe remaining and requested that the CNTR Science Committee chair provide close monitoring of the study. Early in 2018 a total of 3 subjects were enrolled; two were removed from the study due to high blood pressure and one withdrew due to personal reasons. The PI presented a plan of proposed changes to enhance enrollment, however, the Science Committee unanimously agreed that the study should be terminated for nonperformance.

Study 2: Protocol Title: The PROspective Observational Vascular Injury Trial (PROOVIT)
This funding source provided support for centers participating in the PROspective Observational Vascular Injury Trial (PROOVIT). As this was an existing study at the participating centers the protocol amendment (adaptation to meet DoD funding requirements) and HRPO approval was completed swiftly. A total of 1,827 subjects were enrolled, and data collection completed during the three years of support, 795 over the planned target. A table of enrollment per center is included as an appendix to this report. PROOVIT has been prolific in its publications and presentations. It remains active to this day with 4,766 patients with data from 30 centers across the nation.

Study 2: Total Participant Accrual - Cumulative

Site	Recruited	Screened	Enrolled	Completed
Baylor	132	122	119	91
East Carolina U	98	18	18	16
Emory	58	69	58	58
HSC-Tennessee	301	325	301	301
Loma Linda	443	443	192	364
Scripps	0	155	26	0
UC Davis	50	83	67	38
University of MD	0	301	247	182
USC	0	350	175	173
UT Houston	0	0	241	369
Wisconsin	64	700	30	30
Wright State	75	256	191	205
Total	**1,221**	**2,822**	**1,665**	**1,827**

Due to the large number of subjects in the PROOVIT database, Humacyte, Inc. has partnered with the PROOVIT PI and CNTR to serve as the source for Real World Data (RWD) in their study on HAV and as part of their regulatory strategy. Ongoing programs within regulatory agencies have advanced the utility of RWD for clinical development, the acceptability of RWD depends on the relevance and reliability of the data source. CNTR, through Humacyte has received Medical Technology Enterprise Consortium (MTEC) funding to support additional data collection specific to

extremity vascular injury, longitudinal outcomes, and verification of data reliability. This one-year project is expected to transition to additional funding for PROOVIT work with Humacyte.

Project 1: Project Title: High Anatomic Fidelity Surgical Airway Training System

OEI achieved the following milestones:

- Accurate representation of the airway from the mouth to the lungs. This specification required simulation of the topographical anatomy in clinically relevant areas that are directly visualized by a clinician, including the interior of the mouth and throat and certain deep structures of the face and neck that might be exposed by wounds or by surgical incisions. In addition to relevant topographical anatomy, OEI developed tissues with potential viscoelastic properties creating one of the most realistic simulator yet for surgical airway procedures.
- A head that can actively rotate side to side on a flexible neck. It is a common clinical experience that conscious or semiconscious patients with airway obstruction may make violent head movement in response to their respiratory distress and/or in response to the pain of a surgical incision in the neck. No prior surgical airway simulator has had this capability. Cadaver and anesthetized live tissue models also lack this capability. The provision of a surgical airway trainer that had active head movement was a goal of this project. It has been accomplished and is a feature of the prototype to be delivered. A flexible neck composed of a hard rubber artificial spine attached to a rotational actuator within the chest has been developed. Side-side head motion is controlled by a battery-powered remote controller. Sudden or slow, forceful head motions can be simulated.
- Surgically-relevant tissues and anatomic landmarks, including artificial analogues of the hyoid bone, thyroid and cricoid cartilages, strap muscles, cervical fascia, thyroid gland, sternocleidomastoid muscles, major blood vessels, subcutaneous tissue and skin. This specification was modified during the development of the delivered prototype. Analogues of the hyoid bone, thyroid and cricoid cartilages and cervical trachea cartilages are present in the delivered prototype. Although many models were made of the muscles of the neck, including the strap muscles and sternocleidomastoid muscles, this work proved to be largely irrelevant to the delivered model. OEI focused instead on making detailed anatomy only in the central portion of zone two of the neck, which could be reversibly sealed to contain a simulated hemorrhage and in areas of the neck of the model that are designed to simulate wounds. The critical landmark for locating the cricothyroid membrane is the sternal notch. The membrane is typically three finger breadths above this and maybe the only reliable landmark in a neck deformed by trauma. The cricoid and thyroid cartilages are palpable. The skin and subcutaneous tissue are represented in a multilayered, replaceable insert overlying the surgical airway operative area.
- Capability for simulating a variety of traumatic tissue disruptions in the face and neck. This specification has been met. The delivered prototype shows combat-relevant injuries with tissue disruption and distortion in multiple areas, including the face and tongue accompanied by hemorrhage. The upper airway of the delivered prototype is obstructed by a simulated retro-pharyngeal hematoma.
- Realistic haptic and surgical properties of the laryngeal and tracheal cartilages. OEI accomplished this difficult objective. The delivered prototype has reinforced, durable simulated cartilages that also retain some elasticity. This is an area of future research.
- Model that supports training in tracheostomy as well as cricothyroidotomy. The delivered prototype is designed principally to support training of cricothyroidotomy. Percutaneous tracheostomy can be performed on the unmodified model. OEI experienced difficulty with the use of a Seldinger technique percutaneous tracheostomy because of friction of the tip of the stylet against the silicone lining of the back of the trachea. A vertical, open

tracheostomy is a far different and more extensive operation than percutaneous tracheostomy. It requires a modified surgical section for the trachea. Although OEI made some models of this modified surgical section, including a simulated thyroid isthmus, it is not included in the deliverable prototype.

- Simulator that bleeds realistically from surgical incisions and/or from multiple patterns of traumatic tissue disruption, including direct airway wounding and cervical/fascial vascular injuries. This capability is present in the delivered prototype. OEI developed a replaceable, multilayer skin, and simultaneous tissue insert for the incision area supporting both cricothyroidotomy and tracheostomy. The potential space in this insert can be expanded with varying volumes of fluid including artificial blood. In the current prototype, multiple tubing channels provide simulated hemorrhage from pressurized reservoirs. There is currently no manifold. Potential spaces within the soft tissues of the face and neck can be percutaneously filled with blood and serve as accessory reservoirs for artificial bleeding into wounds.
- Capability of distorting or obliterating anatomic landmarks normally used to guide the creation of a surgical airway. This capability is, to a limited degree present in the delivered prototype. Although the critical landmark for locating the cricothyroid membrane is the sternal notch, as mentioned above, the two layers skin/subcutaneous insert for the surgical area can be filled sufficiently with artificial blood and other filler materials to simulate a hematoma that makes it difficult to feel the thyroid or cricoid cartilage or the cricothyroid membrane itself.
- Ability to simulate hemic drowning. The simulation of hemic drowning requires bidirectional airflow in the trachea, accompanied by major hemorrhage into the facial or cervical airway. The delivered prototype simulates airway hemorrhage but does not currently have satisfactory two-way airflow in the trachea with negative pressure ventilation. This goal has, therefore, been only partially met.
- The ability to simulate several degrees of technical difficulty required to successfully achieve a surgical airway. The specification has been partially met. Inflation of the pretracheal skin flap with blood or simulated hematoma in the delivered prototype increase the difficulty of identifying landmarks and performing cricothyroidotomy. The original intention regarding this specification contemplated the ability to deviate the trachea under the influence of space-occupying lesions such as hematomas in the lateral neck. OEI created the space-occupying lesions but was not successful in developing a trachea that had the required haptic and surgical properties and that could also be deviated under the influence of lateral pressure.
- Chest wall expansion and pulmonary analogues that expand and contract producing bidirectional airflow in the trachea with positive or negative pressure ventilation. This goal has been only partially met. The chest wall of the prototype moves to simulate active chest expansion, but the airflow within the trachea using negative pressure ventilation is poor. Positive pressure ventilation through a cricothyroidotomy or tracheostomy tube does inflate elastic long analogues which recoil to simulate exhalation.
- A design suitable for use in the field and hospital environments. The delivered prototype, constituting the upper half of a human body form is adaptable for field or hospital use. It has not been waterproofed and made durable. As it is, it could be used in a dry field environment. Point of injury training for surgical airway creation by a medic with the casualty on the ground can be simulated by placing the prototype on the floor. The electromechanical functions can be battery-powered, and all simulator functions could be controlled by a hand-held device such as a tablet or cell phone. Even in prototype form, the simulator has advantages over static task trainers, cadavers or live tissue. It can be used for training in almost any indoor environment.

- A surgical airway model capable of rapid reset with changing anatomic patterns. In the delivered prototype, the wounding patterns are fixed, although the degree of tissue swelling in various areas and the location of bleeding can be rapidly changed. The cervical skin and subcutaneous tissue insert overlying the operative area can be rapidly exchanged for reset. It is held in place with a reversible silicone adhesive was developed under the current contract. The pretracheal skin can also be repaired using silicone glue such as Sil-poxy. The cricothyroid membrane of the current prototype is also easily exchangeable. It consists of random direction fiber fabric impregnated with low durometer silicone elastomer. Like the skin flap, the cricothyroid membrane is held in place by a gel adhesive.

Technical Objective 2: To develop tools to allow for the collection and dissemination of results and data from studies.

Project 2: National Trauma Research Repository (NTRR)

The NTRR was developed by a national committee of civilian and military trauma researchers and stakeholder organizations with the functional requirements that would best serve investigators. Its purpose is to advance trauma-related research by providing the infrastructure that enables investigators to access and use clinical research data that has not previously been available. The repository makes data available for continuing use and is a cost-effective solution to the lingering challenge of funding trauma research. The NTRR allows users to enter data for active studies, upload data from data capture systems such as REDCap, peruse available data elements, study datasets, and supporting documentation from trauma research studies (e.g., protocols, consent forms, data dictionaries). It meets new data sharing requirements for researchers seeking to publish clinical trials results and supports NIH's strategic plan for data sharing. The resulting system platform is a cloud-based data repository that meets FISMA, is hosted in a secure and FedRamp compliant cloud environment, and includes multiple layers of security to include Firewall, ACNTR-Virus, Patching, Scanning, and Monitoring. It is 21 CFR Part 11 certified and meets FAIR principles.

The NTRR Steering Committee, consisting of stakeholder organizations and the DoD, provided oversight and governance of the project. Individuals were chosen because of national leadership positions, experience with database development, and/or other subject matter expertise. An Executive Committee of the larger body established four subcommittees of injury researchers and technical experts: Architecture, Regulatory/Human Subjects Protection, Data Definitions and Policies and Procedures.

National Trauma Research Repository Steering Committee

Organization Represented	Name	Home Institution
Coalition for National Trauma Research (CNTR), Clinician Scientists and Other Stakeholders	Don Jenkins, MD—Chair	Mayo Clinic
	Eileen Bulger, MD—Vice-chair	University of Washington
	Peggy Knudson, MD	UC-San Francisco
	Jerry Jurkovich, MD	Denver
	Greg Beilman, MD	University of Minnesota
	Joe DuBose, MD	Travis AFB
	Alex Valadka, MD	Virginia Commonwealth University
	Jason Sperry, MD	University of Pittsburgh
	Ellen MacKenzie, PhD	Johns Hopkins University
	Avery Nathens, MD	Sunnybrook HSC, Toronto

	Jim Ficke, MD	Johns Hopkins University
American College of Surgeons/Committee on Trauma	Ronny Stewart, MD	UTHSC—San Antonio
	Len Weireter, MD	Eastern Virginia Med. School
Department of Defense	LTC Kyle Remick, MD	CCRP, Military Deputy
	Jose Salinas, PhD	USAISR, San Antonio
	Mary Ann Spott, PhD	Dep. Dir. Joint Trauma System
	Tammy Crowder, PhD	CCCRP, Trauma Portfolio
	Frank Lebeda, PhD	MRMC, Dir. System Biology
National Institutes of Health	Matt McAuliffe, PhD	NIH, CIT, Bethesda MD

Note: Grayed background denotes members of Executive Group of the Steering Committee

NTRR Subcommittees

Architecture	Human Research Protections & Regulatory	Data Definitions	Policies & Procedures
Jose Salinas	Len Weireter	Greg Beilman	
Matt McAuliff	Peggy Knudson	Alex Valadka	Joe DuBose
Avery Nathens	Eileen Bulger	Jim Ficke	Ellen MacKenzie
Ronny Stewart	Mary Ann Spott	Jerry Jurkovich	
	Laura Brosch	Mary Ann Spott	

Note: Grayed background denotes subcommittee chair.

The subcommittees were established and charged as follow:

1. Architecture—Determine functional requirements of the physical product, reviewing how other clinical research databases are built and desired level of compatibility with related products such as the FITBIR informatics system; consider how to build the back end and front end of the database, including a plan for data quality and validation, report writing, and the user help desk.
2. Regulatory/Human Protections—Develop complete understanding of factors including protections/use of military data; established regulations in other research databases; how to meet or exceed requirements for human subject research protections; recommendations for future hosting of NTRR based on regulatory or human research protection requirements. Develop guiding policies and procedures on Data Sharing, Data Submission Requests.
3. Defining Data—Identify Common Data Elements and a well-defined data dictionary, following review of assembled elements from other trauma research databases (GLUE grant, ROC, etc.)
4. Policies & Procedures—Develop standards operating procedures and management policies for launching and maintain the NTRR.

The Architecture Subcommittee developed user requirements for NTRR which has since been transcribed into a formal Requirements Definition. CNTR/NTRR project staff identified and reviewed the top 10 programming languages for front-end and back-end (database) websites and presented this information to the Architecture subcommittee. Several existing platforms were reviewed (such as Research Electronic Data Capture (REDCap), FITBIR, and Biologic Specimen and Data Repository Information Coordinating Center (BioLINCC)). This committee also developed Use Case Scenarios for the various users of the repository. CNTR project staff developed a request for proposal (RFP) and statement of work (SOW).

Human Subject Protection/Regulatory Subcommittee drafted several policy documents based on FITBIR policies for data sharing, data contribution, data requesting, and the use of deidentified data. A Policy on Policies, which describes all regulatory references applicable to any policy, was written. The subcommittee also developed a Data Storage and Sharing Policy and a Data Access Request and Data Use Certification Policy.

The Data Definitions Subcommittee and CNTR/NTRR staff reviewed more than 30 existing research databases, registries, and repositories and over 1,000 common data elements. Trauma specific registries/repositories included in this review were the Glue Grant, FITBIR, The Prospective, Observational, Multicenter, Major Trauma Transfusion (PROMMTT) Study, The Resuscitation Outcomes Consortium (ROC), National Trauma Data Standards (NTDB), National Burn Data Standards (NBDS), and the National Emergency Medicine Information System (NEMSIS). Common data elements were ranked in order of frequency across datasets and then evaluated by the Data Definitions Subcommittee. The subcommittee recommended an initial 18 clinical CDEs and 45 study attributes or meta-study data elements. Additional clinical CDEs and unique data elements were drawn from the PROOVIT study funded by this grant.

Using the CDEs selected by the Data Definition Subcommittee, CNTR project staff have created the NTRR data dictionary with 31 standardized data attributes for each element. The dictionary uses widely accepted data definitions/parameters from existing trauma and related research registries, and data from previous and ongoing studies.

CNTR project staff continued to identify existing research and clinical repositories to review and compare and compiled a list of the top 10 programming languages for front-end and back-end (database) websites, which was presented to the NTRR Architecture subcommittee. With the committee's oversight, CNTR staff developed NTRR requirements and use cases. This work and the documents were presented to and approved by the NTRR Steering Committee on 10/28/2016. CNTR project staff developed a formal request for proposals document.

The NTRR request for proposals (RFP) was released February 1, 2017. The vendors were instructed to submit a plan with six months to construct the repository (roughly July – December 2017) followed by 12 months of hosting and technical support. The request was distributed to 3,411 recipients via Constant Contact. The announcement had 29% (989) open rate and 13% (443) click-through rate. It was posted on the National Trauma Institute website. The RFP was also submitted to the Small Business Association call for proposals website. An extensive internet search was performed to identify vendors that have done similar work. Thirteen potential vendors were identified and solicited. Interested vendors were required to submit a letter of intent by February 24, 2017. CNTR received letters of intent (7) from the following organizations: Healytics, ImageTrend, Med Star Health, National Institutes of Health Center for Information Technology (NIH CIT) with Sapient Government Services, QuesGen Systems, QuiCNTRles, and Webhead. Vendors submitted questions about the proposal to CNTR by March 1, 2017 and questions/answers document was provided by CNTR on March 9, 2017. Proposals were due March 31, 2017. Four vendors submitted proposals.

NTRR Vendor Proposals Submitted

Vendor	Development Cost	Hosting Cost	Total Cost
ImageTrend	$545,610	$88,660	$634,270
NIH CIT/Sapient	$576,064	$215,204	$791,268
QuesGen	$610,856	$524,520	$1,135,376
WebHead	$165,642	$37,706	$203,348

The NTRR Architecture Sub-committee (four reviewers) scored proposals on the strength of each vendor's technical approach/responsiveness to the RFP, relevant experience and past

performance evaluations. The aggregated scores are in the table below. Maximum possible score was 440.

NTRR Vendor Proposals Scores

Vendor	Technical Approach	Vendor Previous Experience	Total Scores*
ImageTrend	122	122	244
NIH CIT/Sapient	229	136	365
QuesGen	128	116	244
WebHead	119	76	195

NIH CIT/Sapient was the unanimous choice of the review committee. NIH CIT/Sapient proposed to customize the Biomedical Research Informatics Computation System (BRICS) to meet the functional needs of the NTRR. BRICS is a NIH-developed, disease agnostic, web-based research data repository system currently used by seven research communities including Federal Interagency Traumatic Brain Injury Research (FITBIR), Clinical Informatics for Trials and Research (CiSTAR), and the Center for Neuroscience and Regenerative Medicine (CNRM). This system already meets 80% of the NTRR requirements and can be customized to meet the remaining 20%. The proposal included maintenance and hosting on the BRICS servers, which sit in “NIH’s demilitarized zone” at the Center for Technology in Bethesda, MD. The BRICS team ensures that all software/data developed for the NTRR are in accordance with the rules of the Federal Information Security Management Act (FISMA) and all Health and Human Services information security policies.

The vendor recommendation, vendor proposal and budget were sent to the NTRR Executive Committee for review on 06/23/2017. The NTRR Executive Committee and the CNTR Steering Committee approved the selection of NIH-CIT/Sapient on 7/19/2017. In the fourth quarter of Year 2, we learned that NIH would not be able to host the NTRR. Therefore, a commercial hosting solution was researched, and Amazon Web Services was chosen.

CNTR negotiated agreements with the NIH-CIT and Sapient Governmental Service, Incorporated for repository building and hosting. The collaboration agreement between CNTR and NIH – CIT is a collaboration agreement to test, adapt and utilize NIH owned software (Biomedical Research Informatics Computing Systems (BRICS)) to create improved software that will was the foundational code for the NTRR. Under this agreement, NIH - CIT provided its BRICS source code to CNTR solely for use under this agreement. CNTR enhanced the NIH-developed BRICS capability and usability to meet the specific research objectives of CNTR. CNTR provided its contracted employee (Sapient Governmental Services, Inc.) to work on the project with the NIH-CIT investigators. The parties mutually planned the project details and determined necessary hardware and software components, configurations and technical roles of the team members from each of the parties. A mutually organized core set of system managers from CNTR, NIH-CIT and Sapient provided operational support to enable CNTR research staff to make use of the BRICS modules. The research subcontract between CNTR and Sapient Governmental Services, Inc. consisted of a 6-month period to build and test the NTRR followed by a 12-month option period to host the repository. The CNTR Executive Committee approved executing both agreements on December 15, 2017. Sapient and CNTR worked collaboratively to build the public website (10 pages) and the repository functions. In March 2018, Sapient released a demo site to CNTR staff. Work continued to configure the website and optimize functioning. The repository management policies were refined based on the website components, functions, labels, etc.

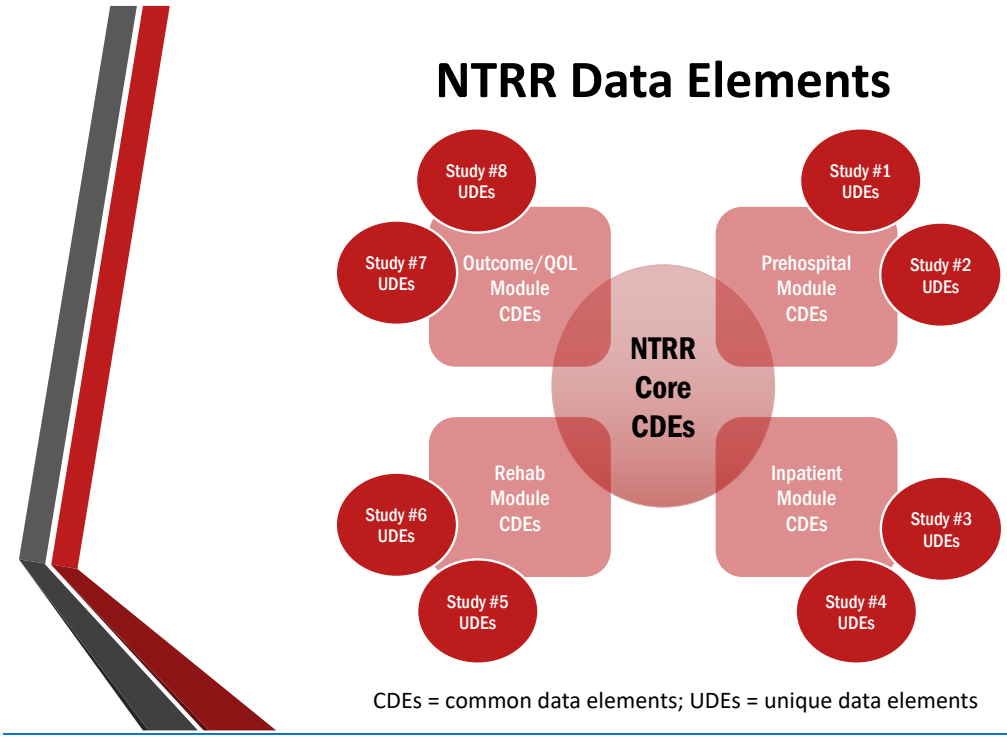
In June 2018, Sapient and CNTR conducted a two-day training on NTRR utilization for the CNTR staff. Work was completed to configure the website and optimize functioning. CNTR staff created basic common data elements and published the initial data dictionary that will be used to

populate the NTRR. CNTR staff approached several large research groups regarding contributing legacy (completed studies) data into the repository. The repository management policies and data sharing templates were finalized. The NTRR was launched on June 25, 2018 at www.ntrr-CNTR.org.

NTRR Modules include:

- ProFoRMS: manage protocols, schedule subject visits, collect data, view data and discrepancies, audit logs. Supports single or multi-site studies. Interacts with Data Dictionary
- GUID: subject specific unique identifier
- Data Dictionary: promotes data standardization approach (CDEs & UDEs). Three components – data elements, form structures, and eForms
- Data Repository: define and manage study information, contribute, upload and sore research data;
- Query and Export Data: search data elements, studies, forms, export in CSV
- Meta Study: aggregate data across multiple studies
- Account Management: manage user accounts and access
- Reports: view and download metadata associated with studies and use accounts in the system

Common data elements have been identified as core, applicable to all trauma studies across the care environment and trauma spectrum, prehospital and inpatient. While the outcome and rehabilitation data element sets are depicted below their development was beyond the scope of this funded project.



CDEs = common data elements; UDEs = unique data elements

CNTR developed repository policies and procedures to guide the data submission and

access processes. Investigators requesting data sets submit their request along with their approved study protocol for review by the Data Use Committee. Data is released to the investigator following all appropriate approvals. The public facing website allows all website visitors to brows data elements within the system. Training videos and presentations are available on the website to assist in use of the repository.

Routine system maintenance and updates were performed on the system. Legacy data are of critical importance to provide the beginning of a robust data source for secondary analysis, possibly across studies. CNTR invited all Principal Investigators of previously funded studies and major study networks such as the Resuscitation Outcomes Consortium to share their data. Several agreed and executed a Data Transfer Use Agreement (DTUA). Study data dictionaries and study materials were received. CNTR staff reviewed all the material, identified study data elements that were CDEs, built data dictionary import files for study UDEs and imported those data elements into the demo site of the NTRR. Once data elements are in the data dictionary, study forms were created using the eCRFs and Manual of Procedures to ensure collection timing and instructions were included. Following form development, each form is loaded with legacy study data for upload into the NTRR. At this point in time of this grant, funds were limited, and one part-time staff member was supported. The above process for each study takes months as these studies have 100s of data elements and sometimes thousands of subjects. A study list status is included as an attachment.

Enduring Funding: An Extension WithOut Funding (EWOF) was submitted and approved extending the period of performance to 12/29/2020. Ongoing discussions with the Combat Casualty Care Research Program regarding the possibility of enduring funding have been held over the past several years. A presentation was given by the program to the Defense Health Agency. In December 2019, Dr. Jenkins and CNTR staff met with Dr. Terry Rauch to discuss enduring funding and he was supportive. He suggested we approach the Uniformed Services University of the Health Sciences (USU) for partnership. An initial conversation between Dr. Jenkins and Dr. Elster at USU was positive. In a phone call mid-June 2020, Col Davis reported that CAPT Cohn's supervisor was briefing Dr. Rauch with updated slides. DHA had agreed to provide $1.4M in RDT&E funds as a bridge while we work on securing O&M funding. Col Laird at DHA was to be involved in this action. The bridge funds were to be added to this agreement, however, in a briefing with CDR Travis Polk, new Director of the Combat Casualty Research Program in September of 2020, he stated that the previous $1.4m in RDT&E funds were used for something else and no longer available for the NTRR. He was looking at different funding sources. While efforts have been made by CNTR staff and others over the past two years, an enduring funding solution has not been achieved. The NTRR was shutdown in February 2021. A copy of the database is secured at CNTR office and the NTRR can be brought online at any time should funding be identified.

Providing a forum for dissemination of research outcomes to the trauma community

Dissemination of trauma research was diverse and multipronged throughout the lifetime of this grant. CNTR supported the study PIs development of presentations and preparation of manuscripts and magnified those efforts through a comprehensive communications strategy. This strategy to communicate published work includes CNTR website announcements and content, blog posts, electronic communications and newsletters, white papers for external audiences, social networking, and physical distribution of reprints. CNTR communicated with the trauma stakeholder community regarding research findings via 10 communiques to 4,625 subscribers. CNTR also tweeted 75 trauma research-related messages to 641 followers. Additionally, 26 blog posts regarding trauma research advances were posted on the CNTR website (www.nationaltraumainstitute.org). The goal was to comprehensively disseminate published works to the wider trauma network through a Knowledge Translation Plan thereby accelerating the

adoption of research findings to improve civilian trauma and combat casualty care and outcomes. The outreach from the various communication techniques grew from year to year.

A more agile CNTR website (www.NatTrauma.org) was developed in July 2017 with an aim to engage more stakeholders with compelling and accessible content and raise awareness about CNTR, completed and ongoing DoD funded research and the toll of trauma in the United States. In addition, the new site provides improved insight into the diffusion of CNTR-sponsored research by linking to Altmetric scores for each resulting research publication.

Through a planned Knowledge Translation Tools page, the CNTR website serves as a portal to a full-spectrum KT pathway including access to research data, dissemination of research results, measurement of impact, synthesis of findings, and mobilization of knowledge into new guidelines and treatments. Since the launch of the new site, the number of unique visitors has held steady around 1,300 per month.

Throughout the life of this grant, CNTR attended major trauma conferences such as the American Association for the Surgery of Trauma and Eastern Association for Surgery of Trauma to raise awareness of CNTR's role in national trauma research infrastructure building and the NTRR.

Training and professional development

Nothing to report

How were the results disseminated to communities of interest?

The NTRR Communication Plan was executed to ensure that trauma researchers were aware of the repository and the research opportunities and data sharing it provides. CNTR staff exhibited the NTRR at the Eastern Association for the Surgery of Trauma annual meeting 2018-2020 and American Association for the Surgery of Trauma annual meeting 2018-2020. The article "Launch of the National Trauma Research Repository coincides with new data sharing requirements" was published in January 2019 (Price MA, et al. Trauma Surg Acute Care Open 2018. http://dx.doi.org/10.1136/tsaco-2018-000193). CNTR collaborated with the Southwest Texas Regional Advisory Council to host the first annual "National Whole Blood Summit." During the summit, a presentation title *"National Level Core Data Collection Using the National Trauma Research Repository (NTRR)"* was presented by Dr. Michelle Price and Dr. Donald Jenkins. The summit had 200 attendees. This presentation garnered interest and engaged the conference attendees including whole blood researchers in providing CNTR with a list of data elements to be considered when building whole blood CDEs into the NTRR.

Information regarding the National Trauma Research Repository was disseminated via the call for proposals, the CNTR website and other social media (see products) throughout the life of this grant. In July 2018, Dr. Jenkins and Dr. Price recorded an educational podcast for the Eastern Association for the Surgery of Trauma (posted on the EAST website). In July and August 2018, CNTR conducted an NTRR awareness campaign called "Prepare to Share" with Wolters Kluwer. This campaign encouraged researchers visiting Wolters Kluwer journal websites to contribute to or request data from the NTRR. Additionally, CNTR hosted an exhibition booth at the 2018 American Association for the Surgery of Trauma annual scientific meeting featuring the NTRR. There was a high level of interest in using the NTRR among the attendees. We distributed the NTRR information piece at the EAST Scientific Meeting in January 2019 (in addition to exhibiting the NTRR booth), and while there, arranged for three of our investigators—Eileen Bulger, Don Jenkins, and Joe DuBose—to be interviewed by the EAST Traumacast to shed a light on the activities of

CNTR and amplify our message about research partnering. The Traumacast was published the first week of March 2019 on the EAST website. The podcast was titled “Alphabet Soup! CNTR, NTRR, CNTR Oh My!” CNTR also had a strong presence at the American Association for the Surgery of Trauma Clinical Congress in Dallas in September 2019, running announcements for the National Trauma Research Repository both on the AAST website and on television screens during the meeting, and exhibiting the NTRR booth.

In May 2019, Dr. Michelle Price, and Dr. Donald Jenkins presented at the First Annual Whole Blood Summit in San Antonio, Texas. The presentation was titled “National Level Core Data Collection Using the National Trauma Research Repository (NTRR).”

The NTRR was registered as a research repository with Fairsharing, DataMed and r3data.

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

Not applicable

4. IMPACT:

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

Study 2 – PROOVIT Impact: The PROOVIT study has added knowledge to the discipline of vascular and trauma surgery in the optimal care of those with vascular injuries. The PROOVIT database currently contains over 4,000 subjects with inpatient and outpatient data fields. This database is currently being used by a commercial company, Humacyte, in their MTEC supported work as Real-World Data for current FDA conversations and in progress submissions.
Project 1 – OEI Impact: The work, findings and specific products resulting from this project resulted in major innovations and accomplishments in the field of simulator development. Lessons learned during this project will inform the development of OEI commercial products. It is too soon to judge whether the specific work, findings and products of the project will have a significant impact on the education of clinicians. However simulation-based training with more realistic and accessible simulation models, permitting more repetitions of procedures and more variation in the scenarios presented, may be expected to produce more capable practitioners with reduced requirements for live tissue and cadaver-based training.

Project 2 – NTRR Impact: The NTRR capitalized on the investment of the Department of Defense of FITBIR by leveraging that database software to create a trauma research repository. Funds provided were limited to creation and development of the database and migration of a small number of studies. All conversations with stakeholders, researchers, and potential funders have been positive with all recognizing the need for such a database and the utility of the database as created; however, its full impact is not achievable with the limited funding contained in this grant.

What was the impact on other disciplines?

Study 2 – PROOVIT: nothing to report
Project 1 – OEI: nothing to report
Project 2 – NTRR: nothing to report

What was the impact on technology transfer?

Study 2 – PROOVIT: nothing to report
Project 1 – OEI: The work funded by this grant supported continued development of high fidelity simulators at OEI.
Project 2 – NTRR: nothing to report

What was the impact on society beyond science and technology?

Study 2 – PROOVIT: nothing to report
Project 1 – OEI: nothing to report
Project 2 – NTRR: nothing to report

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

Not applicable

Actual or anticipated problems or delays and actions or plans to resolve them – nothing to report

Changes that had a significant impact on expenditures

Study 1 (Ketamine study) and Project 2 (NTRR): Study 1 was terminated for non-performance early in the period of performance. The funding originally programmed for the study was used to support the NTRR project. The NTRR database development was completed under budget with those savings being applied to support a longer timeframe for NTRR hosting.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents – nothing to report

Significant changes in use or care of human subjects – nothing to report

Significant changes in use or care of vertebrate animals – nothing to report

Significant changes in use of biohazards and/or select agents – nothing to report

PRODUCTS:

Journal publications:

1. Smith SL, Price MA, Fabian TC, Jurkovich GJ, Pruitt BA, Jr., Stewart RM, et al. The National Trauma Research Repository: Ushering in a new era of trauma research (Commentary). Shock. 2016;46(3 Suppl 1):37-41. Status: Published. Acknowledged federal support: Yes
2. Coimbra R, Kozar RA, Smith JW, Zarzaur BL, Hauser CJ, Moore FA, Bailey JA, Valadka A., Jurkovich GJ, Jenkins DH, Davis KA, Price MA, Maier RV. The Coalition for National Trauma Research supports the call for a national trauma research action plan. J Trauma Acute Care Surg. 2017 Mar;82(3):637-645. Status: Published. Acknowledged federal support: Yes
3. Loja MN, DuBose J, Sammam A, Li CS, Liu Y, Savage S, Scalea TM, Holcomb JB, Rasmussen TE, Knudson MM, AAST PROOVIT Study Group. The Mangled extremity score and amputation: Time for a revision. J Trauma Acute Care Surg. 2017 Mar;82(3):518-523. Status: Published. Acknowledged federal support: No
4. Loja MN, Galante JM, Humphries M, Savage S, Fabian T, Scalea T, Holcomb JB, Poulin N, DuBose J, Rasmussen TE; AAST PROOVIT Study Group. Systemic anticoagulation in the setting of vascular extremity trauma. Injury. 2017 Sep;48(9):1911-1916. Status: Published. Acknowledged federal support: No
5. Faulconer, E. R., et al. (2018). "Use of open and endovascular surgical techniques to manage vascular injuries in the trauma setting: A review of the American Association for the Surgery of Trauma PROspective Observational Vascular Injury Trial registry." Journal of Trauma and Acute Care Surgery 84(3): 411-417. Status: Published. Acknowledged federal support: No
6. Price et al. Launch of the National Trauma Research Repository coincides with new data sharing requirement. Trauma Surg Acute Care Open. 2018;3:e000193. doi:10.1136/tsaco-2018-000193 https://tsaco.bmj.com/content/tsaco/3/1/e000193.full.pdf Status: Published. Acknowledged federal support: Yes
7. Price MA, Bixby PJ, Phillips MJ, et al. Launch of the National Trauma Research Repository coincides with new data sharing requirements. Trauma Surgery & Acute Care Open 2018;3:e000193. doi: 10.1136/tsaco-2018-000193 Status: Published. Acknowledge federal support: Yes

Presentations -

1. Song, A., Gerold, K., McCann, U.D., Caffrey, J., Latif, A., Milner, S.M., Fauerbach, J.A. Safety and Efficacy of Ketamine as a Battlefield Analgesic for Acute Burn Pain. Poster presentation at the Asthma and Allergy Center of Johns Hopkins Bayview Medical Center in Baltimore, MD, July 27, 2016.
2. Jenkins, DH. Impact of Department of Defense Research to the National Trauma Institute. Presented at the Military Health System Research Symposium, Orlando FL, August 17, 2016.
3. *Loja MN, Wishy A, Humphries M, Savage S, Fabian T, Scalea TM, Holcomb JB, Poulin N, Galante JM, Rasmussen TE, AAST PROOVIT Study Group. Systemic anticoagulation in the setting of vascular extremity trauma. Podium Presentation, American Association for the Surgery of Trauma Annual Meeting, Maui, Hawaii, 2016.
4. *Loja MN, DuBose J, Saummann A, Li CS, Savage S, Scalea T, Holcomb JB, Rasmussen TE, Knudson MM, AAST PROOVIT Study Group. The Mangled Extremity Score and Amputation: Time for a Revision. Quickshot Podium Presentation, American Association for the Surgery of Trauma Annual Meeting, Maui, Hawaii, 2016.
5. Faulconer ER, Branco B, Loja M, Grayson K, Sampson J, Fabian T, Bee T, Holcomb JB, Brenner M, Scalea TM, Skarupa D, Inaba K, Poulin N, Rasmussen TE, DuBose JJ, AAST PROOVIT Study Group. Use of open and endovascular surgical techniques to manage vascular injuries in the trauma setting: A review of the AAST PROOVIT Registry. Podium presentation - American Association for the Surgery of Trauma Annual Meeting, Baltimore, MD, 2017.
6. Ferencz SA, DuBose JJ, Hennigan J, Nolan K, Sampson JB, Rasmussen TE, Galante JM, Bee T, Fabian TC, Menaker JA, Scalea TM, Holcomb JB, Skarupa DJ, Inaba K, Bini JK, AAST PROOVIT Study Group. Contemporary tourniquet use in extremity vascular trauma: The AAST prospective observational injury treatment (PROOVIT) registry. Quick shot presentation - American Association for the Surgery of Trauma Annual Meeting, Baltimore, MD, 2017.
7. Loja MN, DuBose JJ, Stephenson J, Kessel B, Bee T, Fabian T, Menaker J, Scalea TM, Holcomb JB, Skarupa D, Inaba K, Catalano R, Poulin N, Bini JK, Rasmussen TE, AAST PROOVIT Study Group. Pediatric vascular trauma: Current management and early outcomes. Poster presentation - American Association for the Surgery of Trauma Annual Meeting, Baltimore, MD, 2017.
8. Russo R, Galante J, DuBose JJ, Bee T, Fabian T, Holcomb JB, Brenner M, Scalea TM, Skarupa D, Inaba K, Poulin N, Turay D, Bini J. Rasmussen TE, AAST PROOVIT Study Group. Contemporary outcomes and management of blunt cerebrovascular injuries: Results from the AAST PROOVIT multicenter registry. Poster presentation - American Association for the Surgery of Trauma Annual Meeting, Baltimore, MD, 2017.
9. Research Poster presented at the Bayview Science Symposium entitled " Breaking New Ground: RCT testing the Safety, Efficacy & Opiate Sparing Effect of Ketamine Augmentation of Fentanyl for Daily Burn Wound Care Pain"
10. Research Poster presented at the Bayview Science Symposium entitled " Pain and PTSD Severity are Reciprocally Related in Burn Survivors at 6 Months Post-Discharge"
11. Training presentation to research assistants entitled "CRMS How to Enroll A Patient"

12. Jenkins, Donald H; Phillips, Monica J; Beilman, Gregory J; Bulger, Eileen M; Davis, Michael R; McAuliffe, Matthew J; Rasmussen, Todd E; Salinas, Jose; Smith, Sharon L; Spott, Mary A; Weireter, Leonard J; Price, Michelle A. Is your clinical trial ready for new data sharing requirements? Abstract Submitted to AAST Meeting, 2018. *(not accepted)*
13. Dubose JJ et al. Indications for and natural history of fasciotomy in the management of peripheral vascular injury. Abstract Submitted to EAST meeting. (not accepted)
14. Ferencz SA, DuBose JJ, et al. Contemporary tourniquet use in extremity vascular trauma: The AAST prospective observational injury treatment (PROOVIT) registry. Abstract submitted to EAST meeting. (not accepted)
15. Quintana MT, Moran, B., Scalea TM, Morrison JJ, O'Connor JV, Feliciano DV, DuBose, JJ. Urgency Categories, Same Outcome: No Difference After "Therapeutic " VS "Prophylactic" Fasciotomy. PROOVIT quickshot abstract accepted for presentation at EAST Annual Scientific Assembly. Austin, Texas, January 2019.
16. Faris K Azar, MD; Richard D Betzold, MD; Anna N Romagnoli, MD; Jeanette M Podbielski, RN; John B Holcomb, MD; Tiffany Bee, MD; Timothy Fabian, MD; David Skarupa, MD; Jonathan J Morrison, MD PhD; Deborah R Stein, MD MPH; Rosemary A Kozar, MD PhD; James V O'Connor, MD; David V Feliciano, MD; Thomas M Scalea, MD; Joseph J DuBose MD. *Submitted to AAST 2019 Meeting.* Not accepted
17. Comparison of Infrarenal and Retrohepatic Inferior Vena Cava Injuries in the Modern Era: A Review of the AAST PROOVIT Registry. *Submitted to AAST 2019 Meeting.* Not accepted
18. Ahmed F. Khouqeer, MD; Sherene Sharath, MPH, PhD; Jeanette M Podbielski, RN, CCRP; John B. Holcomb, MD; John Sharpe, MD; Tiffany Bee MD; Jonny Morrison, MD, PhD; Thomas M. Scalea, MD; David Skarupa, MD; Richard D. Catalano, MD; Jennie Kim, MD; Kenji Inaba, MD; Nathaniel Poulin, MD; Joseph Dubose, MD; Ramyar Gilani, MD. To Angio or Not To Angio: An Analysis from the AAST PROOVIT Study Group. *Submitted to AAST 2019 Meeting.* Not accepted
19. Herrold JA, Podbielski J, Holcomb J, Sharpe J, Bee T, Morrison J, Scalea T, Skaruap D, Catalano D, Kim J, Inaba K, Poulin N, Bini K, DuBose JJ. A comparison of endovascular embolization and open ligation of traumatic internal iliac artery injuries in the PROspective Observational Vascular Injury Trial (PROOVIT) registry. *Submitted to AAST 2019 Meeting.* Not accepted
20. Herrold JA, Podbielski J, Holcomb J, Sharpe J, Bee T, Morrison J, Scalea T, Skaruap D, Catalano D, Kim J, Inaba K, Poulin N, Bini K, DuBose JJ. A comparison of endovascular stenting vs open repair of traumatic iliac artery injuries in the PROspective Observational Vascular Injury Trial (PROOVIT) registry. *Submitted to AAST 2019 Meeting.*
21. Injuries to the Abdominal Aorta-Diagnosis, Management, and Outcome Data from the PROOVIT Registry. *Submitted to AAST 2019 Meeting.* Not accepted
22. Jack C. Webb, BS; Pedro G. R. Teixeira, MD; Joseph J. DuBose, MD; Carlos V. R. Brown, MD; John B. Holcomb, MD; John Sharpe, MD; Jonathan J Morrison, MD, PhD; Thomas M. Scalea, MD; David Skarupa, MD; Richard D. Catalano, MD; Jennie Kim, MD; Kenji Inaba, MD; Nathaniel Poulin, MD; John Myers, MD; John K. Bini, MD; David Feliciano, MD. Outcome Implications of Venous Management Strategy in Patients with Concomitant Arterial and Venous Femoropopliteal Injuries. *Submitted to AAST 2019 Meeting.* Not accepted

23. Christina X. Zhang MD, Jennifer M. Leonard MD PhD, Qiao Zhang MS, Joseph J. DuBose MD, Grant V. Bochicchio MD MPH, Gerald R. Fortuna, Jr, MD, Col, USAF, SFS, MC. Tranexamic Acid Administration Does Not Compromise Early Graft Patency in Trauma Patients Undergoing Arterial Repair: An Analysis of Patients from the AAST PROspective Observational Vascular Injury Treatment (PROOVIT) Registry. *Submitted to AAST 2019 Meeting.* Accepted for Poster presentation.
24. Presentation at the First Annual Whole Blood Summit in San Antonio, Texas. Price MA, Jenkins DH. National Level Core Data Collection Using the Nation Trauma Research Repository (NTRR). May 2019.
25. Christina X. Zhang MD, Jennifer M. Leonard MD PhD, Qiao Zhang MS, Joseph J. DuBose MD, Grant V. Bochicchio MD MPH, Gerald R. Fortuna, Jr, MD, Col, USAF, SFS, MC. Tranexamic Acid Administration Does Not Compromise Early Graft Patency in Trauma Patients Undergoing Arterial Repair: An Analysis of Patients from the AAST PROspective Observational Vascular Injury Treatment (PROOVIT) Registry. *Accepted for Poster presentation at AAST 2019 Meeting*.

Podcasts -

1. Donald Jenkins & Michelle A Price. The National Trauma Research Repository #105. Eastern Association for the Surgery of Trauma – Traumacast. Continuing education podcast posted 7/17/2018 https://www.east.org/education/online/traumacasts/detail/1163/the-national-trauma-research-repository
2. Eastern Association for the Surgery of Trauma (EAST) Podcast titled Alphabet Soup! CNTR, NTRR, CNTR Oh My!. March 2019. https://www.east.org/education/online/traumacasts/detail/1183/alphabet-soup-CNTR-ntrr-cntr-oh-my

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

CNTR website www.NatTrauma.org,
NTRR website, currently defunct https://ntrr-CNTR.org

- **Technologies or techniques**

During the course of this contract, OEI developed an anatomically-accurate, multiple-tissue, physical model of the head, face, neck, airway and upper chest. The simulator delivered by OEI under this contract is unique in several respects: 1) The face and neck skin, airway structures and sub-surface soft tissues have visual and tactile properties unprecedented in prior airway simulators, 2) Capability has been developed to incorporate viscoelastic tissues within the face, neck and airway of the simulator, 3) Combat-relevant patterns of airway distortion and obstruction have been simulated, 4) The head and neck of the simulator can be actively rotated by remote control, 5) Simulated chest expansion occurs with negative or positive pressure ventilation, 6), Bleeding channels in the tissues allow the simulation of soft tissue hemorrhage in the face and neck, 7) A replaceable, multilayer skin/subcutaneous tissue insert incorporating a potential space can simulate a hematoma in the anterior neck, that obscures some of the landmarks for surgical airway, 8) The multi-laminar skin/subcutaneous insert is attached to the pre-tracheal area using a unique adhesive, 9) The simulator is adaptable to support cricothyroidotomy or tracheostomy, 10) The simulator is modular and adaptable for incorporation a full body manikin. As indicated by the above list, most but not all of our proposed specifications have been met in the prototype simulator that we are delivering under this contract.

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

Project 2 – OIE Airway Simulator: We filed a provisional US patent, #62/522, 479, in June, 2017, covering the apparatus and methods for incorporating viscoelastic tissues into medical training simulators. A follow-up non-provisional patent was subsequently filed. We have not received a patent office action on the non-provisional patent as of this date. The intellectual property for which we have filed a claim did not arise out of this research project. The patent application was filed during the term of this contract, but the technical invention predated its application to this project.

- **Other Products**

1. Human Subjects Policies/procedures from NTRR
2. NTRR Requirements Document
3. NTRR Use Case Document
4. Knowledge Translation Plan
5. Clinical report forms, staff training and other materials for the ketamine study
6. New CNTR website www.NatTrauma.org, social media materials, communications
7. High Anatomic Fidelity Surgical Airway Training. Conducted at University of Texas Health - San Antonio, January 2019.
8. NTRR Study List Status
9. NTRR 6-panel display
10. NTRR CDE Sheet
11. Postcard-Data Sharing

6. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

Name	Project Role	Nearest person month worked	Contribution to the project
Donald Jenkins	Principal Investigator	.60	Oversight of entire project
Amy Flores	Controller	7.65 Years 2-5	Subaward financial and contract management, tracking grant expenditures
Elisia Stevens	Executive Assistant	1.8 Year 3	Coordinating Steering Committee meetings, drafting minutes, planning face to face steering committee meetings.
Ana Guerrero	Executive Assistant	6.4 Years 1-5	Coordinating Steering Committee meetings, drafting minutes, planning face to face steering committee meetings.
Monica Phillips	Research Operations Director	17.2 Years 1-6	Assist in data element review. Attends all committee meetings
Pam Bixby	Communications	10.3 Years 1-5	Responsible for the communication and dissemination tasks of the projects.
Sharon Smith	Project Administrator	15.84 Years 1-5	Managing Steering Committee meetings, agenda, process. Establishment of working groups.
Michelle Price	Co-Investigator/ Program Manager	23.94 Years 1-6	Conducting research on existing registries, platforms, and common data elements. Coordinating subcommittee work and meetings. Communicating with stakeholders and potential collaborators at DoD, NIH, academic trauma centers and trauma professional organizations.
Roy Estrada	Project Manager	2.46 Year 1	Coordinated initial committee meetings and drafted charters.
Edward Shipper	Research Fellow	1.7 Year 5	Responsible for study data element creation.
Lizette Villarreal	Program Manager	4.57 Years 3-5	Responsible for regulatory oversight and coordination of regulatory reviews and reporting for the research subawards.

Other Collaborating Organizations

Organization	Location	Contribution to Project
Baylor College of Medicine/Ben Taub General Hospital	1504 Taub Loop, Houston, TX 77030	PROOVIT Clinical Site (PI: Dr. Ramyar Gilani)
Emory University	201 Dowman Drive, Atlanta, GA 30322	PROOVIT Clinical Site (PI: Dr. Ravi Rajani)
Loma Linda Medical Center	11234 Anderson Street, Loma Linda, CA 92354	PROOVIT Clinical Site (PI: Dr. Richard Catalano)
University of Southern California	1983 Marengo Street, Los Angeles, CA 90033	PROOVIT Clinical Site (PI: Dr. Kenji Inaba)
Scripps Health	4077 Fifth Avenue, San Diego, CA 92103	PROOVIT Clinical Site (PI: Dr. Michael Sise)
University of California, Davis	2315 Stockton Boulevard, Sacramento, CA 95817	PROOVIT Clinical Site (PI: Dr. Joseph Galante)
University of Maryland/R. Adams Cowley Shock Trauma	22 S. Greene Street, Baltimore, MD 21201	PROOVIT Clinical Site (PI: Dr. Thomas Scalea)
University of Tennessee – Memphis	920 Court Street, Memphis, TN 38163	PROOVIT Clinical Site (PI: Dr. Timothy Fabian)
University of Texas Health Science Center at Houston	6410 Fannin Street, Houston, TX 77030	PROOVIT Clinical Site (PI: Dr. Laura Moore)
University of Wisconsin School of Medicine and Public Health	750 Highland Avenue, Madison, WI 53276	PROOVIT Clinical Site (PI: Dr. Suresh Agarwal)
Wright State University	1 Wyoming Street, Dayton, OH 45409	PROOVIT Clinical Site (PI: Dr. John Bini)
University of Texas Health Science Center at San Antonio	7703 Floyd Curl Drive, San Antonio, TX 79230	PROOVIT Statistical Analysis (PI: Dr. Joel Michalek)
Johns Hopkins University	600 North Wolfe Street, Blalock 1415, Baltimore, MD 21287	Ketamine Clinical Site (PI: Dr. John Fauerbach)
Operative Experience, Inc.	500 Principio Parkway West, Suite 300, North East, MD 21901	Airway Management Simulator Development (PI: Dr. Robert Buckman)

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

Nothing to report. This is a final report.

What other organizations were involved as partners? Nothing to report

7. SPECIAL REPORTING REQUIREMENTS

A QUAD chart is included in the appendices.

8. APPENDICES:

1) Quad Chart
2) Safety and Efficacy of Ketamine as a Battlefield Analgesic for Acute Burn Pain. Poster presentation
3) High Fidelity Simulator for Training Airway Management of Combat-Relevant Wounds of the Face and Neck
4) Smith SL, Price MA, Fabian TC, Jurkovich GJ, Pruitt BA, Jr., Stewart RM, et al. The National Trauma Research Repository: Ushering in a new era of trauma research (Commentary). Shock. 2016;46(3 Suppl 1):37-41.
5) Impact of Department of Defense Funded Research at the National Trauma Institute
6) National Trauma Institute's Knowledge Translation Plan: Moving Knowledge into Action
7) Coimbra R, Kozar RA, Smith JW, Zarzaur BL, Hauser CJ, Moore FA, Bailey JA, Valadka A., Jurkovich GJ, Jenkins DH, Davis KA, Price MA, Maier RV. The Coalition for National Trauma Research supports the call for a national trauma research action plan. J Trauma Acute Care Surg. 2017 Mar;82(3):637-645.
8) Song, A., Gerold, K., McCann, U.D., Caffrey, J., Latif, A., Milner, S.M., Fauerbach, J.A. Safety and Efficacy of Ketamine as a Battlefield Analgesic for Acute Burn Pain. Poster presentation at the Asthma and Allergy Center of Johns Hopkins Bayview Medical Center in Baltimore, MD, July 27, 2016.
9) Loja MN, DuBose J, Sammam A, Li CS, Liu Y, Savage S, Scalea TM, Holcomb JB, Rasmussen TE, Knudson MM, AAST PROOVIT Study Group. The Mangled extremity score and amputation: Time for a revision. J Trauma Acute Care Surg. 2017 Mar;82(3):518-523.
10) Loja MN, Galante JM, Humphries M, Savage S, Fabian T, Scalea T, Holcomb JB, Poulin N, DuBose J, Rasmussen TE; AAST PROOVIT Study Group. Systemic anticoagulation in the setting of vascular extremity trauma. Injury. 2017 Sep;48(9):1911-1916.
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12) Ferencz SA, DuBose JJ, Hennigan J, Nolan K, Sampson JB, Rasmussen TE, Galante JM, Bee T, Fabian TC, Menaker JA, Scalea TM, Holcomb JB, Skarupa DJ, Inaba K, Bini JK, AAST PROOVIT Study Group. Contemporary tourniquet use in extremity vascular trauma: The AAST prospective observational injury treatment (PROOVIT) registry. Quick shot presentation - American Association for the Surgery of Trauma Annual Meeting, Baltimore, MD, 2017.
13) Loja MN, DuBose JJ, Stephenson J, Kessel B, Bee T, Fabian T, Menaker J, Scalea TM, Holcomb JB, Skarupa D, Inaba K, Catalano R, Poulin N, Bini JK, Rasmussen TE, AAST PROOVIT Study Group. Pediatric vascular trauma: Current management and early outcomes. Poster presentation - American Association for the Surgery of Trauma Annual Meeting, Baltimore, MD, 2017.
14) Russo R, Galante J, DuBose JJ, Bee T, Fabian T, Holcomb JB, Brenner M, Scalea TM, Skarupa D, Inaba K, Poulin N, Turay D, Bini J. Rasmussen TE, AAST PROOVIT Study Group.

Contemporary outcomes and management of blunt cerebrovascular injuries: Results from the AAST PROOVIT multicenter registry. Poster presentation - American Association for the Surgery of Trauma Annual Meeting, Baltimore, MD, 2017.

15) Research Poster presented at the Bayview Science Symposium entitled " Breaking New Ground: RCT testing the Safety, Efficacy & Opiate Sparing Effect of Ketamine Augmentation of Fentanyl for Daily Burn Wound Care Pain"
16) Research Poster presented at the Bayview Science Symposium entitled " Pain and PTSD Severity are Reciprocally Related in Burn Survivors at 6 Months Post-Discharge"
17) Training presentation to research assistants entitled "CRMS How to Enroll A Patient"
18) Faulconer, E. R., et al. (2018). "Use of open and endovascular surgical techniques to manage vascular injuries in the trauma setting: A review of the American Association for the Surgery of Trauma PROspective Observational Vascular Injury Trial registry." Journal of Trauma and Acute Care Surgery 84(3): 411-417.
19) Jenkins, Donald H; Phillips, Monica J; Beilman, Gregory J; Bulger, Eileen M; Davis, Michael R; McAuliffe, Matthew J; Rasmussen, Todd E; Salinas, Jose; Smith, Sharon L; Spott, Mary A; Weireter, Leonard J; Price, Michelle A. Is your clinical trial ready for new data sharing requirements? Abstract Submitted to AAST Meeting, 2018. (not accepted)
20) Dubose JJ et al. Indications for and natural history of fasciotomy in the management of peripheral vascular injury. Abstract Submitted to EAST meeting.
21) Ferencz SA, DuBose JJ, et al. Contemporary tourniquet use in extremity vascular trauma: The AAST prospective observational injury treatment (PROOVIT) registry. Abstract submitted to EAST meeting.
22) Price et al. Launch of the National Trauma Research Repository coincides with new data sharing requirement. Trauma Surg Acute Care Open. 2018;3:e000193. doi:10.1136/tsaco-2018-000193 https://tsaco.bmj.com/content/tsaco/3/1/e000193.full.pdf.
23) Donald Jenkins & Michelle A Price. The National Trauma Research Repository #105. Eastern Association for the Surgery of Trauma – Traumacast. Continuing education podcast posted 7/17/2018
24) Price MA, Bixby PJ, Phillips MJ, et al. Launch of the National Trauma Research Repository coincides with new data sharing requirements. Trauma Surgery & Acute Care Open 2018;3:e000193. doi: 10.1136/tsaco-2018-00019
25) High Anatomic Fidelity Surgical Airway Training. Conducted at University of Texas Health - San Antonio, January 2019.
26) Herrold JA, Podbielski J, Holcomb J, Sharpe J, Bee T, Morrison J, Scalea T, Skaruap D, Catalano D, Kim J, Inaba K, Poulin N, Bini K, DuBose JJ. A comparison of endovascular embolization and open ligation of traumatic internal iliac artery injuries in the PROspective Observational Vascular Injury Trial (PROOVIT) registry. Submitted to AAST 2019 Meeting.
27) Injuries to the Abdominal Aorta-Diagnosis, Management, and Outcome Data from the PROOVIT Registry. Submitted to AAST 2019 Meeting.
28) Jack C. Webb, BS; Pedro G. R. Teixeira, MD; Joseph J. DuBose, MD; Carlos V. R. Brown, MD; John B. Holcomb, MD; John Sharpe, MD; Jonathan J Morrison, MD, PhD; Thomas M. Scalea, MD; David Skarupa, MD; Richard D. Catalano, MD; Jennie Kim, MD; Kenji Inaba, MD; Nathaniel Poulin, MD; John Myers, MD; John K. Bini, MD; David Feliciano, MD. Outcome Implications of Venous Management Strategy in Patients with Concomitant Arterial and Venous Femoropopliteal Injuries. Submitted to AAST 2019 Meeting.
29) Ahmed F. Khouqeer, MD; Sherene Sharath, MPH, PhD; Jeanette M Podbielski, RN, CCRP; John B. Holcomb, MD; John Sharpe, MD; Tiffany Bee MD; Jonny Morrison, MD, PhD; Thomas M. Scalea, MD; David Skarupa, MD; Richard D. Catalano, MD; Jennie Kim, MD; Kenji Inaba, MD; Nathaniel Poulin, MD; Joseph Dubose, MD; Ramyar Gilani, MD. To Angio or Not To Angio: An Analysis from the AAST PROOVIT Study Group. Submitted to AAST 2019 Meeting.
30) Presentation at the First Annual Whole Blood Summit in San Antonio, Texas. Price MA, Jenkins

DH. National Level Core Data Collection Using the Nation Trauma Research Repository (NTRR). May 2019.
31) Christina X. Zhang MD, Jennifer M. Leonard MD PhD, Qiao Zhang MS, Joseph J. DuBose MD, Grant V. Bochicchio MD MPH, Gerald R. Fortuna, Jr, MD, Col, USAF, SFS, MC. Tranexamic Acid Administration Does Not Compromise Early Graft Patency in Trauma Patients Undergoing Arterial Repair: An Analysis of Patients from the AAST PROspective Observational Vascular Injury Treatment (PROOVIT) Registry. Accepted for Poster presentation at AAST 2019 Meeting.
32) Quintana MT, Moran, B., Scalea TM, Morrison JJ, O'Connor JV, Feliciano DV, DuBose, JJ. Urgency Categories, Same Outcome: No Difference After "Therapeutic " VS "Prophylactic" Fasciotomy. PROOVIT quickshot abstract accepted for presentation at EAST Annual Scientific Assembly. Austin, Texas, January 2019.
33) NTRR 6-panel display
34) NTRR CDE Sheet
35) Postcard-Data Sharing
36) NTRR Legacy Study Table

A National Coordinating Center for Trauma Research

PI: Donald Jenkins, MD **Org:** National Trauma Institute

Study/Product Aim(s)

Hypothesis: The civilian trauma research community can be used as a surrogate for military combat casualty care research, maximizing the return from dollars invested by replacing the expensive and repetitive assembly and disassembly of short-lived clinical investigator networks with a stable and enduring operational infrastructure for clinical trauma research.

- Technical Objective 1: To manage specific research projects addressing military research gaps in airway management, pain management and vascular injury.
- Project 1: Determining the Efficacy and Safety of Ketamine as a Battlefield Analgesic;
- Project 2: High Anatomic Fidelity Surgical Airway Training system;
- Project 3: The PROspective Observational Vascular Injury Trial (PROOVIT);
- Technical Objective 2: Develop tools to allow for the collection and dissemination of results and data from studies.

NTRR Launched in June 2018 at www.nti-ntrr.org

Timeline and Cost (direct + indirect)

Activities	FY16	FY17	FY18	FY 19	FY20
Ketamine Study					
Airway Simulator Development					
PROOVIT					
NTRR Development					
Total Budget ($M)	$1.1M	$1.2M	$1.2M	$1.1M	

Goals and Milestones

CY16 Goal –
☑ HRPO approval for studies; Subcontracting complete; Studies commence
☑Common Data Elements and NTRDB functional requirements

CY17 Goals
☑Airway simulator developed
☑ NTRR developer solicited and chosen

CY 18 Goals
☑Ketamine study concludes
☑PROOVIT study concludes

CY19 & CY20 Goals
☑ NTRR development continues

Comments/Challenges/Issues/Concerns: No enduring funding for NTRR.

Budget: $4,642,861 Actual: $4,642,861

Rene Smith, MSN, RN rene.k.smith.civ@mail.mil

Safety and Efficacy of Ketamine as a Battlefield Analgesic for Acute Burn Pain

Alex Song, Kevin Gerold, Una D. McCann, Julie Caffrey, Asad Latif, Stephen M. Milner, James A. Fauerbach

[1] Departments of Plastic and Reconstructive Surgery, Anesthesia and Critical Care Medicine, Psychiatry and Behavioral Science, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Introduction

- The acutely painful, twice-daily wound care necessitates finding effective analgesic medication regimens with fewer side effects than morphine
- Morphine analgesic is the usual care (UC-O) of burn patients
- UC-O requires repeated dosages which can lead to opiate induced hyperalgesia and morphine tolerance
- Ketamine is an analgesic that blocks nociceptive signals to the brain via a pathway that differs from opiate analgesics and thus may have opiate sparing effects
- Ketamine may also reduce symptoms of PTSD and depression

Background

- Wound care occurs 1-2 times per day
- Repeated wound care may cause increased sensitivity of nociceptive receptors and risk for developing chronic pain
- Few studies have been conducted testing the efficacy of ketamine augmentation of opiates for acute burn wound care or ketamine's hypothesized opiate sparing effect

Objectives

The study is conducted to address the following objectives:

Primary

- Whether ketamine augmentation to usual opiate care (K+O) reduces burn pain during wound care
- Whether ketamine is associated with opiate sparing effect during wound care

Secondary

- Whether the prevalence and severity of Acute Stress Disorder (ASD),PTSD, and depression are reduced by the K+O condition to UC-O
- Whether symptoms of pain-related anxiety and pain-related catastrophizing are reduced by the K+O condition compared to UC-O
- How the K+O condition can improve sleep quality and effect duration
- How emotion regulation and trauma resilience can moderate pain-related anxiety and catastrophizing

Study Design

- Double-blind, parallel-group, randomized controlled trial
- Sample is drawn from population of consecutive admissions to Johns Hopkins Burn Center
  - 300 Screened, 150 enrolled
- Groups are stratified based on Total Body Surface Area (TBSA)
  - 60% of sample will be small burns (≥2% and ≤ 20% TBSA)
  - 40% of the sample will be "moderate" burns (>20% and ≤40% TBSA)

Participant Inclusion Criteria:

- Acute burn injury with TBSA ≥2% & ≤40%.
- Adults 18-65 years of age admitted to the JHBC with acute burns
- Estimated length of stay ≥7 days
- Pain in Emergency Room during initial wound evaluation (NAS ≥6)

Participant Exclusion Criteria:

- Requiring endotracheal intubation and sedation
- Diminished Level of Consciousness / Cognitive Function (MMSE ≤20)
- Diminished Capacity – Incapable of providing informed consent
- PMH: Insensate (e.g., SCI)
- Safety: Contra-indication (e.g., potential drug interactions, medical comorbidities)

Materials and Methods

The following will be measured (see Figure 2 for measures and timing):

Comparing effectiveness of K+O to UC-O in reducing severity of acute pain

- *Self-reported pain* using a Numerical Analog Scale (NAS) – measurement is standardized by applying pressure at wound, proximal and distal regions, before, during and after wound care
- *Sympathetic arousal* using the Itamar Watch-PAT 200
- *Time to maximal pain relief* – time taken to achieve lowest pain rating on NAS from the time that each wound care procedure begins
- *Recollection of pain* using NAS
- *Satisfaction with wound care* using a visual analog scale

Opiate sparing effect

- Frequency of requests for additional analgesic medications

Post-treatment effect

- During a follow-up assessment, 1 month after the study protocol:
  - *ASD/PTSD* using the Diagnostic and Statistical Manual of Mental Disorders IV – Text Revision (DSM IV-TR)
  - *Depression* using the Beck Depression Inventory (BDI-II)
  - *Sleep and sympathetic reactivity* using the Itamar Watch-PAT 200
  - *Trauma Resilience* using the Trauma Resilience Scale
  - *Optimism* using the Life Orientation Test
  - *Emotion Regulation* using the Emotion Regulation Scale State

Study Diagram and Participant Flow

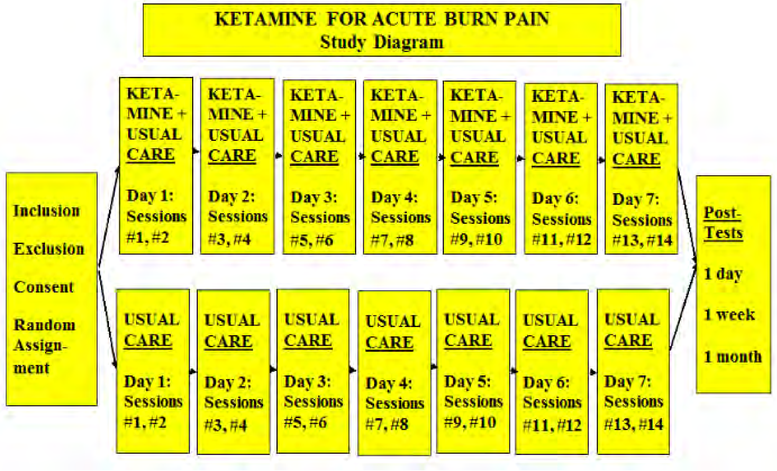


Figure 1

- 1.25 months
- 1 day pretest baseline
- 7 days of twice daily interventions
- Follow-up at 1 day, 1 week and 1 month after the 7th day (14th session)

Assessment: Measures and Timing

Ketamine For Acute Burn Pain: Assessment Diagram

PRIOR TO RANDOM-IZATION: (Examples)	BASELINE: PREBURN MONTH (Retrospective)	Days: 1 – 7 Sessions #1 - #14:	Days: 3, 5, 7 Sessions: #6, #10, #14 Additional measures as follows:	POST-TESTS After final procedure:
Inclusion TBSA: ≥2% & ≤40% **Exclusion** Pain <6/10 in ER **Stratification** TBSA: ≥2%-≤20% >20%-≤40%.	**Month Before Burn** (Retrospective) Pain – Average NAS Type, Location Pain Medications Pain Anxiety Symptom Scale (PASS) Pain Coping Questionnaire. Pain Catastrophizing PTSD (SCL-C) Depression (BDI-II) Behavior Inhibition / Behavior Activation Scales (BIS/BAS) Post-Trauma Resilience Scale (PTRS) Emotion Regulation Scale (ERS)	**Before Session (~1 hour)** Burn Pain NAS Every 10 minutes during procedure at: Wound Proximal to wound Distal to wound Pain Medications Acute Stress Disorder Depression **During Session** Burn Pain: NAS every 10 minutes during procedure: - Locations as above Additional Analgesic Medications **After Session** Burn Pain: NAS 1 hour & 6 hours Pain Management Satisfaction	**Prior to Session** Pain Anxiety (PASS) Pain Coping Pain Catastrophizing All other pre-session measures as shown in prior box for Sessions 1-14. **During Session** All intra-session measures as shown in prior box for Sessions 1-14 **After Session** All post-session measures as shown in prior box for Sessions 1-14.	**Day 1** Burn Pain (Mean 24-hr NAS) at Locations: Wound Proximal to wound Distal to wound Pain Medications Pain Management Satisfaction **Week 1:** All Day 1 post-test follow-up measures as above. **1 Month:** All Day 1 & 6 post-test follow-up measures, plus: PTSD (SCL-C) Depression (BDI-II) Resilience (PTRS) Emotion Regulation (ERS)

Figure 2

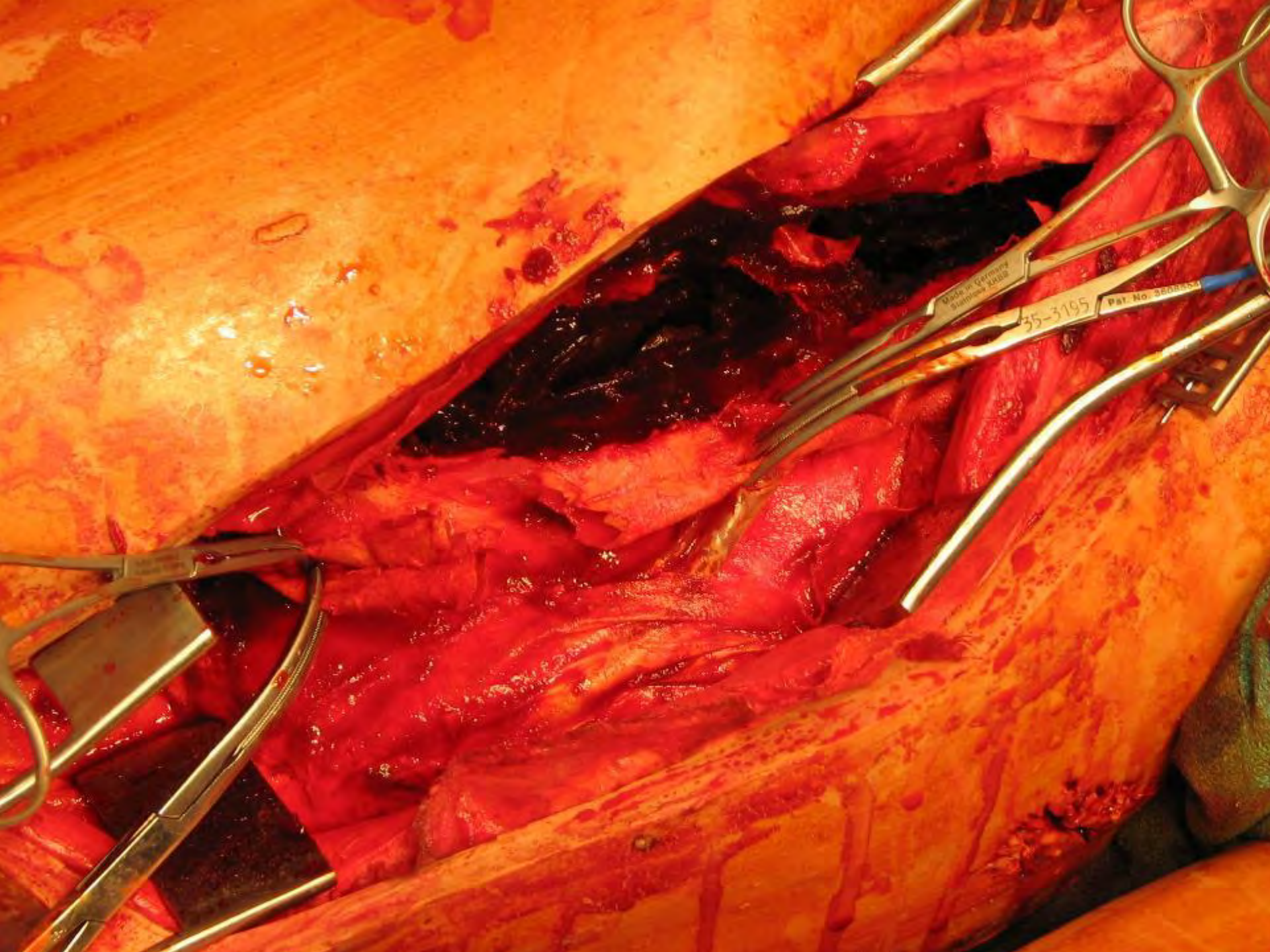
High fidelity simulator for training airway management of combat-relevant wounds of the face and neck

Train medics and surgeons

:

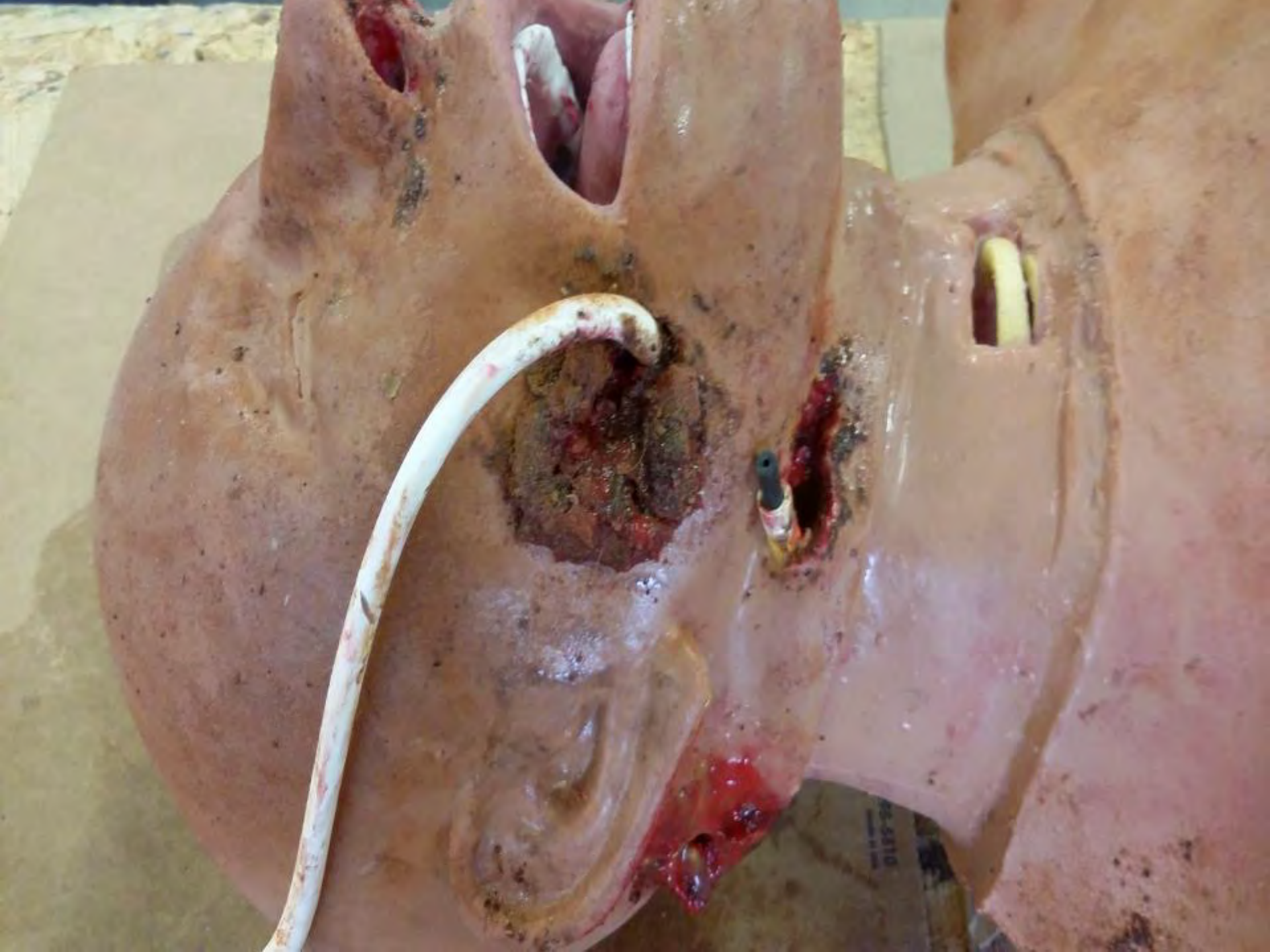
Biofidelic Emulation™ vs Simulation

electromechanical mechanisms within realistic surgical anatomy and tissues


35-3195

We are engineering electromechanical and hydraulic systems
to fit within a unique, high anatomical fidelity construct of the head, face, neck and upper chest.

Anatomic and tissue modelling



SHOCK, Vol. 46, Supplement 1, pp. 37–41, 2016

THE NATIONAL TRAUMA RESEARCH REPOSITORY: USHERING IN A NEW ERA OF TRAUMA RESEARCH (COMMENTARY)

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ABSTRACT—Despite being the leading cause of death in the United States for individuals 46 years and younger and the primary cause of death among military service members, trauma care research has been underfunded for the last 50 years. Sustained federal funding for a coordinated national trauma clinical research program is required to advance the science of caring for the injured. The Department of Defense is committed to funding studies with military relevance; therefore, it cannot fund pediatric or geriatric trauma clinical trials. Currently, trauma clinical trials are often performed within a single site or a small group of trauma hospitals, and research data are not available for secondary analysis or sharing across studies. Data-sharing platforms encourage transfer of research data and knowledge between civilian and military researchers, reduce redundancy, and maximize limited research funding. In collaboration with the Department of Defense, trauma researchers formed the Coalition for National Trauma Research (CNTR) in 2014 to advance trauma research in a coordinated effort. CNTR's member organizations are the American Association for the Surgery of Trauma (AAST), the American College of Surgeons Committee on Trauma (ACS COT), the Eastern Association for the Surgery of Trauma (EAST), the Western Trauma Association (WTA), and the National Trauma Institute (NTI). CNTR advocates for sustained federal funding for a multidisciplinary national trauma research program to be conducted through a large clinical trials network and a national trauma research repository. The initial advocacy and research activities underway to accomplish these goals are presented.

KEYWORDS—Advocacy, clinical trials network, data-sharing, injury, research funding, trauma

Trauma is the leading cause of death among individuals 46 years and younger, and the single largest cause for years of life lost in the United States (1). In a review of mortality data from 2000 to 2010, Rhee et al. (1) found a 22.8% increase in trauma deaths in contrast with a decrease in deaths from cancer and heart disease. In the United States, 199,756 persons suffered fatal injury in 2014 and 30,888,063 were treated in emergency departments for non-fatal injuries in 2013 (2). Medical treatment and work loss costs for civilian fatal and non-fatal injuries in the United States totaled more than $586 billion in 2010 (2). In Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), Operation New Dawn (OND), Operation Inherent Resolve (OIR), and Operation Freedom's Sentinel (OFS), there have been 52,407 injured U.S. military and Department of Defense (DoD) civilians and 6,881 deaths from trauma (3). These statistics point to the dramatic burden of injuries on the health of this country in both civilian and military sectors.

It continues to surprise many that trauma, as a disease category, receives so little research funding support from the Federal government. This problem has been reviewed and restated many times over the last 50 years, and 2016 marks the 50-year anniversary of the publication that first cited the problem: ''Research in trauma has suffered from the lack of recognition of trauma as a major public health problem. The most significant obstacle at present [to trauma research efforts] is the lack of long-term funding. Unpredictability of financial support hinders recruitment of competent scientists and technicians, retention of key personnel, and procurement of necessary equipment'' (4). While this may be the first significant national publication about the lack of trauma research funding, the Institute of Medicine Committee on Injury Prevention and Control stated in 1999 that ''the nation's current investment in injury research is not commensurate with the magnitude of the problem'' and that ''without a national commitment, the field of injury science will stagnate and the unnecessary toll of injury will persist'' (5). In a 2015 report, the Agency for Healthcare Research and Quality stated that the highest condition-related expenditure total among adults ages 18 to 64, and third highest for all ages, was for treatment of trauma-related disorders (6). Without dedicated research funding, this major healthcare problem continues to worsen.

Support for sustained, long-term investment is limited, and there is diminished funding from both public and private sponsors at a time when scientific opportunity has never been greater (7). National Institutes of Health (NIH) funding of clinical trauma research is disproportionate to the burden of the disease, and by that metric, ranks last among 27 disease categories (8). In comparison with the HIV/AIDS NIH funding that exceeds the economic burden of that disease by 17%, NIH funding of injury research is 12% less than the economic burden of injuries (8).

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One way of addressing these challenges lies in sharing clinical research data, as ''an opportunity to expand the investment of the clinical trial beyond its original goals at minimal costs'' (9). As the trauma research community seeks ways to extend available funds, the creation of a national repository for trauma clinical research data that makes data available for enduring use is a potentially viable and cost-effective solution. While it would not result in any additional funding, it would effectively allow for much more data analysis and knowledge translation, which can result in improved patient care.

Single-instance use of research data and the inability to access the research data of others following study closure and publication limit the effectiveness of available trauma research funding. Advances due to clinical trauma research have been accomplished largely through separate, organizationally distinct, and disconnected efforts. Individual large and successfully accomplished projects have been usually dispersed and uncoordinated by their very design and funding. This situation leads to research delays, duplications, inefficiencies, and increased costs—all part of a knowledge translation process that averages an excruciating 17 years (10).

While clinical researchers in different locations may have similar lines of investigation, the computer systems in use to store and retrieve data locally ''do not, and for the most part cannot, transmit, receive, combine, analyze and use shared data as information'' (8). In fact, it is built into the research design and data privacy tenets, directed by an Institutional Review Board, that this type of sharing cannot occur in these types of studies and research databases. Clinical research data are fragmented, sometimes within one facility, and can rarely be repurposed to answer additional research questions. Sharing data maximizes the value, promotes secondary analyses, and minimizes duplicative data collection (8, 9). Universal developments in information technology, like the creation of distributed data networks and virtual data access, provide ways to address clinical research needs that did not exist before (9). It is time to exploit and enhance these technologies to support clinical trauma research, speed up knowledge translation, and enhance the development of evidence-based trauma care practices.

BENEFITS OF CLINICAL DATA-SHARING

The Institute of Medicine reports that ''a cultural change has occurred in which the conversation around data sharing has moved from whether it should happen to how it can be carried out'' (11). Data-sharing platforms or repositories already exist for the Federal Interagency Trauma Brain Injury Research (FITBIR), the National Database for Autism Research (NDAR), the National Heart, Lung and Blood Institute (NHLBI), the Alzheimer's Disease Neuroimaging Initiative (ADNI), and other disease areas. FITBIR was developed as a joint DoD-NIH effort to share data across the entire traumatic brain injury (TBI) research field and to facilitate collaboration between laboratories, as well as interconnectivity with other information platforms. Advantages of data-sharing are numerous:

- Data-sharing reinforces open scientific inquiry and encourages diversity of analysis and opinion; enables exploration of novel topics not envisioned by the initial investigators; and facilitates the education and engagement of new researchers.
- Data-sharing avoids duplication of multiple, separate databases and results in conservation of research funds, ultimately leading to availability of funds for other studies and more investigators.
- Transfer of research and knowledge between military and civilian researchers and care providers is supported and increased in a concrete and measurable way. Research gaps are more easily identified and addressed.
- Many trauma studies require use of an expensive and lengthy process to obtain Exception from Informed Consent (i.e., community consent in place of individual consent for inclusion in a research project). This is necessary because victims of traumatic injury are frequently unconscious or otherwise unable to provide consent. Further, consent from a legally authorized representative usually can only be obtained later in the care trajectory, and life-saving intervention is necessary before the trauma victim is even identified. The ability to use data resulting from these studies may aid in the reduced need for unnecessary repetition of this process, effectively stretching limited trauma research funding.

NATIONAL TRAUMA INSTITUTE (NTI)

The National Trauma Institute (NTI), a non-profit organization chartered in 2006, has as its central purpose to advocate for trauma research funding. The members of NTI's Board of Directors are from across the United States; represent trauma and acute care surgery, emergency medicine (American College of Emergency Physicians (ACEP)), burns (American Burn Association (ABA)), neurosurgery (American Association of Neurological Surgeons (AANS)), orthopaedic surgery (Orthopaedic Trauma Association (OTA)); and include non-voting representatives from Army, Navy and Air Force medical departments. NTI has generated and/or managed nearly $55 million in trauma research funds (almost all of it in federal funds) over the past 10 years. NTI's purpose is to raise funds for trauma research, yet uniquely it does no research itself; instead, it directs those funds to the trauma clinical investigator community. Since 2008, NTI has received federal contracts to fund studies of more than 60 investigators at institutions in 35 cities and 22 states. In total, these studies have generated 16 publications (12–27), two manuscripts under review, and 23 presentations at national, regional, state, or local trauma meetings, adding substantially to the knowledge in injury care science.

In 2012, NTI leadership met with personnel within the DoD, including the Medical Research and Materiel Command (MRMC) and the Combat Casualty Care Research Program. A discussion of the challenges to adequately fund trauma research included the issue of how to make extended use of the data that result from available funding. The DoD had already funded the creation of the FITBIR platform and asked if the same could be done for the broader trauma research community. Once established, all federal trauma funding solicitations will include the requirement that funded investigators

must contribute data from studies funded by the DoD to the repository. This would create a new standard for federally-funded trauma research. Conceptually, this is precisely how the DoD Trauma Registry was developed. While not a primarily research-oriented data registry, research by ''outsiders'' can and has been carried out using the data collected for other purposes.

Following this meeting, NTI considered the concept fully. Leaders were well aware of the difficulties and risks of, first, accepting the highly technical and demanding challenge, and second, achieving success and utilization by the national trauma research community. After examination, NTI determined that a national trauma clinical research repository could be achieved if developed carefully and with the leadership and involvement of key trauma organizations and professionals and began advocating for the funding of this project within the DoD budget. In 2013, NTI developed a white paper and delivered a request for $5 million to United States House and Senate offices during the annual congressional appropriations process. The request stated that, if approved, the funds should be added to the DoD's Research, Development, Testing and Evaluation (RDT&E) program. Because of the impact on injured Americans as well as on U.S. service members wounded in combat, Congress did provide $5 million in the FY2014 Defense Health Program Research and Development budget to establish the National Trauma Research Repository (NTRR) for the purposes outlined above. Following the proposal submission and peer-review process within the DoD, NTI was the selected contractor for the NTRR.

Data stored in a fully developed and robust NTRR will cover the entire patient care trajectory: from injury prevention, to point of injury, en route care, hospital care, and finally rehabilitation/outcomes. This will be the central repository for the clinical data resulting from both military and civilian federally funded trauma research and will be a free, web-based application with a user-friendly interface for trauma researchers to contribute and access data.

CHALLENGES TO SUCCESS

Sharing data is a complex task. Beyond the challenge of encouraging full participation from investigators, including those funded by federal, state or private means, there are other challenges that include understanding the interests and privacy of study participants who volunteered their data as well as the interests of study investigators. Study investigators invest significant personal energies into the design, conduct, and analysis of studies, and tend to guard research data to retain ownership and property rights, avoid competition, reduce duplication, protect confidentiality and privacy, or avoid misuse by unqualified persons (28). Policies and procedures to protect patient and investigator rights while making data available to secondary researchers require specific and meticulous formulation (29). These are significant challenges that could undermine NTRR's success and must be addressed by project planners. Much of the work necessary to avoid these pitfalls has been accomplished or is underway, most recently by FITBIR and NADR.

PLANS FOR NTRR

The initial step was to establish a Steering Committee that includes members of stakeholder organizations and the DoD, among others, who will provide oversight and governance of the project. Individuals were chosen because of national leadership positions, experience with database development, and/or other subject matter expertise. An Executive Committee of the larger body established four subcommittees of injury researchers and technical experts: Architecture, Regulatory/Human Subjects Protection, Data Definitions and Policies and Procedures. The Architecture Subcommittee will determine functional requirements of the physical product, review structures of clinical research repositories, determine the desired level of compatibility with other repositories, application requirements including data quality and validation, report writing, and user support. The Regulatory/Human Protection Subcommittee will develop policies on human subjects protections and make recommendations for hosting of NTRR. The Data Definitions subcommittee will identify Common Data Elements to be included following review of assembled elements from trauma research repositories and other widely used common data elements. The Policies and Procedures subcommittee will develop standards, policies, and procedures such as data sharing, data submission requests, data access requests, and standard operating procedures. These subcommittees began their work in Spring 2016.

COALITION FOR NATIONAL TRAUMA RESEARCH

In 2014, the American Association for the Surgery of Trauma (AAST) and NTI began discussing the need for a unified, stronger voice to advocate for further funding of trauma research. This discussion, initially held at the headquarters of the American College of Surgeons Committee on Trauma (ACS COT), escalated rapidly, and several months later the Coalition for National Trauma Research (CNTR) was formed to include not only AAST and NTI, but also the ACS COT, the Eastern Association for the Surgery of Trauma (EAST), and the Western Trauma Association (WTA) (30).

CNTR's membership and the participation of members of national trauma organizations is a critical success factor in the NTRR. The CNTR Steering Committee includes representatives from each organization within CNTR and the DoD, and is focused not only on the development of NTRR, but also the development of a unified national trauma research agenda that establishes priorities and eliminates redundancies, a robust trauma research infrastructure that includes a Trauma Clinical Trials Network, and consistent and significant federal funding for research that increases the understanding of injury and informs clinical practice. In 2015, CNTR held its first Trauma Research Advocacy Day in Washington, DC, when 40 trauma surgeons traveled from across the United States to visit with key congressional contacts. This resulted in the addition of $10 million to the FY 2016 DoD budget, specifically to supplement DoD's efforts for the establishment of a National Trauma Clinical Trials Network. CNTR returned to Washington, DC in 2016 to request further funding to supplement DoD efforts in

support of the research network, again with a similar number of trauma surgeons so that its message reached the greatest number of key House and Senate members.

A collaborative approach, utilizing the experience and expertise of study investigators, is the most productive method of data-sharing to ensure reliability and quality of the manuscripts produced. CNTR is leveraging the expertise within ACS COT, DoD, data coordinating centers and research leaders from recent trauma multi-institutional randomized clinical trials such as the Glue Grant, ROC, and METRC. Even with the inherent challenges of developing a data-sharing platform, the generation, dissemination, and sharing of research data are key ingredients in contributing to scientific progress and the public good (29). The NTRR is an important piece of CNTR's knowledge translation plan, which encompasses robust dissemination of research outcomes via traditional and emerging channels, powerful new measurement tools that follow and gauge qualitative as well as quantitative uptake of information across sectors and platforms, and finally, review and synthesis that enable translation of knowledge into evidence-based practices. As planning and implementation steps continue, CNTR is committed to the rigorous and transparent development of NTRR in a way that involves the leaders and representatives of the national trauma research community.

CONCLUSION

Three components of a national approach to advance trauma care through research are a national research agenda, a trauma clinical trials network, and a research data repository. Clearly, these components require sustained funding at the federal level. Annual congressional special interest funds are short-term solutions to the problem, do not address the scope and impact comprehensively, and are meant to address or initiate one or two key and urgently needed capabilities for DoD/civilian sectors. Military-relevant trauma research has no safety net. It is a well-known phenomenon that as combat operations winds down after a conflict, combat casualty care research funding declines drastically (31). Civilian trauma care research needs cannot be met over the long term, as DoD priorities fluctuate over time. Additionally, research focused on several key patient populations and some injury treatments would likely never by funded by the DoD, e.g., research for the care of injured pediatric and geriatric populations.

A National Trauma Research Action Plan (NTRAP) supported by both Congress and the White House is essential to a mid-term strategy. This could be modeled in part after the National Research Action Plan (NRAP), which was issued as an Executive Order in 2013 to address improving access to mental health services for veterans, service members, and military families (32). NTRAP would require no appropriation and may be a plank for a future administration's platform for national healthcare.

The longer term solution for the country in this topic area is an enduring asset provided through a National Institute of Trauma supporting a National Clinical Trauma Research Program. This solution requires widespread public support and a congressional act that would insure that planned, programmed, and coordinated research occurs and the problem of trauma injury in America is finally addressed. In the meantime, NTI and CNTR will develop a robust NTRR and technology-driven knowledge translation plan to meet the current needs of trauma research community to leverage and make the most of the limited research funding available today.

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Impact of Department of Defense Funded Research at the

NATIONAL TRAUMA INSTITUTE

Funding Research ■ Changing Practice ■ Creating Awareness

Disclosure

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Management of Blunt Abdominal Trauma and Splenic Injury

- First casualty Masirah Island Oman 30 Sep 2001
- ATV crash, unknown TOI, LOC, handlebar sign to LUQ abdomen
- iStat Hgb 12 and stable, no peritonitis
- FAST trace fluid in the pelvis
- Serial observation (12 ground transport, no CT scanner, no fluoro, no REBOA, warm fresh whole blood on the hoof)
- 3 day hospital LOS, serial outpatient f/u, stayed in deployed environment

Splenic Injury Prospective Outcomes Trial: An American Association for the Surgery of Trauma Multi-Institutional Study

- Principal Investigator: Ben Zarzaur, MD, MPH at University of Tennessee Health Science Center
- First multi-institutional, long-term prospective study of patients with blunt splenic injury
- Funded by the DoD through the National Trauma Institute for $299,422 (NTI-NCH-10-020 & W81XW-11-1-0841)
- Results presented as AAST Plenary Paper in 2014 and published in the J of Trauma Acute Care Surgery in 2015 (Vol 79;3, 335-342)

Impact on the management of blunt splenic injury

- After the first 24 hour of nonoperative management, risk of splenectomy is rare:
  - 3.1% during inpatient phase of care
  - 0.27% during 180 days after discharge
- The benefits of splenic preservation techniques (angiography and embolization) are unclear. This study highlighted the need for further large scale multicenter trials that randomize to either management with angiography and embolization or nonoperative management.

National Trauma Institute Mission

- To generate funds for clinical trauma research
- To discover new funding opportunities
- To advocate for trauma research across federal entities as well as other agencies
- To distribute those funds to clinical investigators, but to do no research ourselves

National Trauma Institute Origins

- 2003: Began as local organization of 3 Level 1 Trauma Centers (TRISAT); based within University of Texas Health Science Center at San Antonio
- Product of both civilian and military trauma centers
- 2003-2006: Worked within UTHSCSA to achieve earmarks/federal appropriations
  - $4.2M total awarded for local trauma research/education & training; recruitment of first civilian burn center director at BAMC, funding salary for 5 years
- 2006: Reorganized as national non-profit entity
  - New Mission: to address lack of federal trauma research funding
  - New Leadership: National Board of Directors

NTI Board of Directors includes members of…

- American Association for the Surgery of Trauma
- Eastern Association for the Surgery of Trauma
- Western Trauma Association
- Shock Society
- American College of Emergency Physicians
- Orthopedic Trauma Association
- American Association of Neurological Surgeons
- US Army Institute of Surgical Research
- US Navy
- US Army
- US Air Force

NTI Research Priorities

- Hemorrhage
  - Non-compressible (truncal/torso)
  - Blood Products
  - Resuscitation
  - Shock and bleeding
  - Coagulopathy
  - Systemic and local hemostatic therapy
- Airway and Ventilation
- Infection
  - Eliminating hospital acquired infections in the ICU
  - Antibiotic utilization
- Disaster Preparedness
  - Mass casualty
  - Transportation of the critically ill
- Burn
  - New skin
  - Off the shelf skin
- Technology development

NTI Trauma Studies Funding Rounds

FIRST

- Issued first Request for Proposals (RFP) October 1, 2009 with $1.4M available funds
- 85 pre-proposals
- 15 full proposals reviewed on February 5, 2010
- 7 selected for funding March, 2010

SECOND

- Issued second RFP June 10, 2010 with $2.46M available funds
- 92 pre-proposals
- 21 full proposals reviewed on August 30, 2010
- 9 selected for funding January, 2011

NTI Funded Studies

16 Lead Sites

43 Participating Sites

NTI Research in 35 cities in 22 states

Funded Awards

PI Name	Institution	Study	$ Awarded	Participating Sites
Martin Croce	UTenn HSC	Multicenter Prospective Evaluation of the Ventilator Bundle in Injured Patients	$225,000	5
Joel Baseman	UTHSC - San Antonio	*Mycoplasma Pneumoniae* in the ICU	$190,000	5
Fred Pieracci	U Co. Denver	A Multicenter, Randomized, Double-blind Comparison of Intravenous Iron Supplementation to Placebo for the Anemia of Traumatic Critical Illness	$188,541	3
Shahid Shafi	Baylor Hosp, Dallas	Comparative Effectiveness of Clinical Care Processes in Resuscitation and Management of Moderate to Severe Traumatic Injuries	$225,000	3
Jason Sperry	U. Pittsburgh	Characterization of the Effects of the Early Sex-Hormone Environment Following Injury	$225,000	Single Center
Mitchell Cohen	UC-SF	Timing and Mechanism of Traumatic Coagulopathy	$225,000	2
Carrie Sims	U. Penn.	Vasopressin Supplementation during the Resuscitation of Hemorrhagic Shock	$125,000	Single Center
Ben Zarzaur	AAST/PI: UTenn HSC	Splenic Injury Prospective Outcomes Trial	$299,422	11

Funded Awards (continued)

PI Name	Institution	Study	$ Awarded	Participating Sites
Jay J Doucet	UC San Diego	Detection and Management of Non-Compressible Hemorrhage by Vena Cava Ultrasonography	$230,000	3
Jean-Francois Pittet	U AL Birmingham	Effect of Antioxidant Vitamins on Coagulopathy and Nosocomial Pneumonia after Severe Trauma	$300,000	Single Center
Mark Cipolle	Christiana HCS, DE	The Safety and Efficacy of Platelet Transfusion in Patients Receiving Antiplatelet Therapy that Sustain Intracranial Hemorrhage	$130,500	Single Center
Henry Cryer	UCLA	Transfusion of Stored Fresh Whole Blood in a Civilian Trauma Center: A Prospective Evaluation of Feasibility and Outcomes	$200,000	Single Center
Suresh Agarwal	Boston Med Center	Acute Lung Injury Ventilation Evaluation (ALIVE) Trial	$295,172	5
Robert Maxwell	UTenn HSC, Chattanooga	Methicillin-Resistant Staphylococcus aureus in a Trauma Population: Does Decolonization Prevent Infection?	$180,000	1
Martin A Schreiber	Oregon Health & Science University	Thrombelastography (TEG®) based dosing of enoxaparin for thromboprophylaxis: a prospective randomized trial	$675,761	3
Lena M. Napolitano	U Mich Health System, Ann Arbor	Hepcidin and Anemia in Trauma	$154,109	Single Center

Initial Scientific Contributions

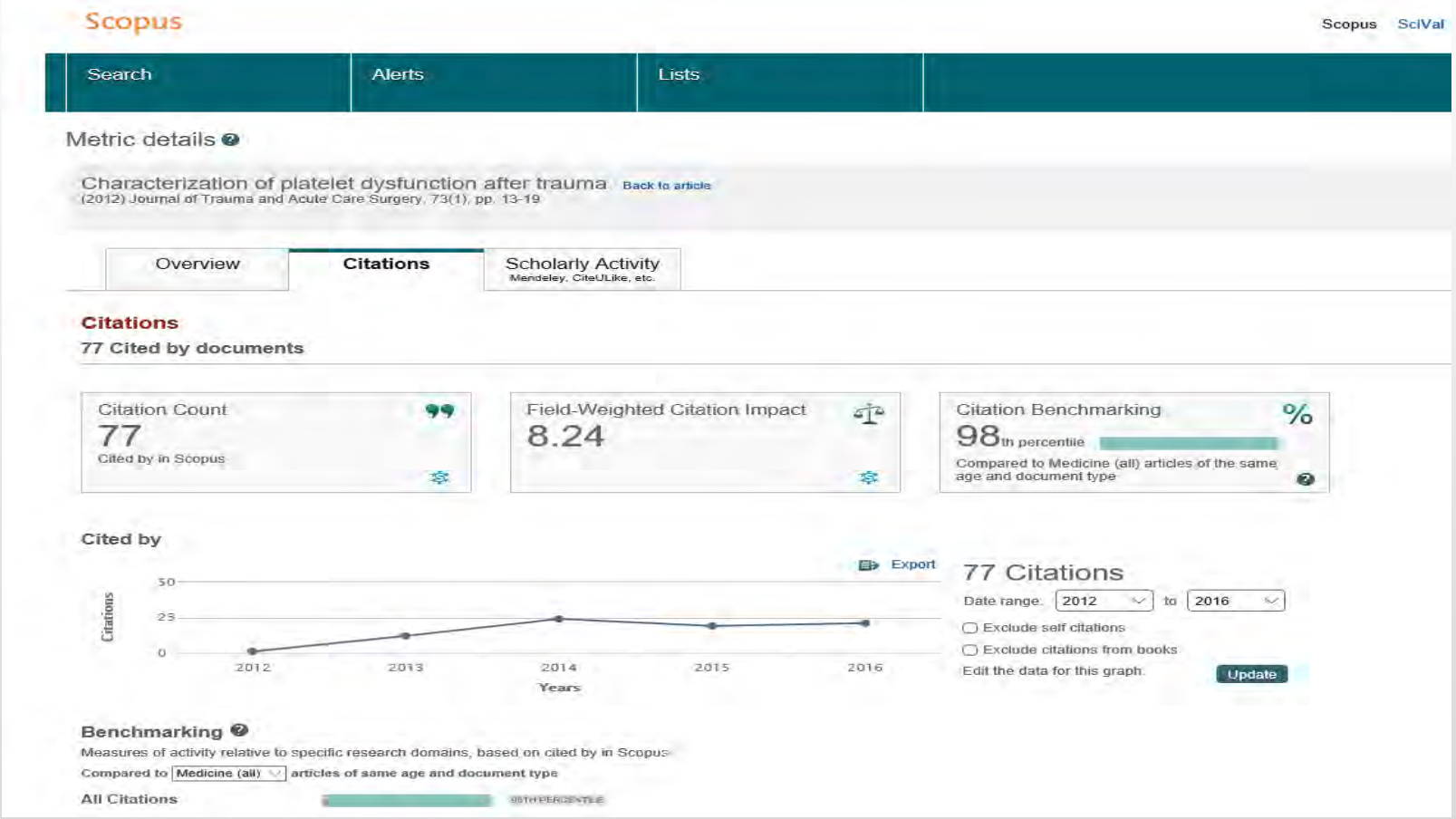
- Sixteen peer-reviewed publications
- Two publications in press
- One manuscript submitted/under review
- Sixteen national, 2 regional and 6 local presentations
- Ten of the 13 completed studies have published or submitted a manuscript (76%)
- Two PIs received additional funding through NTI applications to the Joint Warfighter Medical Research Program ($500K each)
- Twelve PIs trained junior researchers, fellows, residents or students on their study

Timing and Mechanism of Traumatic Coagulopathy

- Principal Investigator: Mitchell Cohen, MD, at University of California San Francisco
- Funded by the DoD through the National Trauma Institute for $224,950 (W81XWH-10-1-0924 & NTI-TRA-09-034)
- Prospective, multi-institutional observational study to characterize coagulation parameters in the severely injured, to use systems biology to identify the central mediators involved in coagulopathic phenotypes and to develop a predictive model to support diagnosis and treatment

Timing and Mechanism of Traumatic Coagulopathy (PI: Mitchell J. Cohen, MD)

The most cited publication from this study is the 2013 *JOT* manuscript *Characterization of platelet dysfunction after trauma*. It has been cited 77 times.



The Science of Conducting Trauma Research

- National Trauma Institute Research Group, Price MA, Beilman GJ, Fabian TC, Hoyt DB, Jurkovich GJ, Knudson MM, MacKenzie EJ, Marshall VS, Overton KE, Peitzman AB, Phillips MJ, Pruitt BA, Jr., Smith SL, Stewart RM, Jenkins DH. The National Trauma Institute: Lessons learned in the funding and conduct of sixteen trauma research studies. J Trauma Acute Care Surg. 2016 (epub ahead).
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National Trauma Research Repository

- A robust, well-utilized and scalable repository for data resulting from current and future clinical trauma research
- All federally funded clinical trauma investigators will be eligible to contribute their data.
- Coordination between agencies and civilian academic and professional trauma organizations will further utilization, cooperation and collaboration.

10 Years of Advocating for Trauma Research

- Works with Congressional offices to seek sponsors and supporters to augment the Defense Health Agency budget for trauma research
- NTI works with principle investigators (PIs) and institutions to obtain funding through a competitive proposal process
- NTI has generated and/or managed $55M in trauma research funding since 2003

Coalition for National Trauma Research (CNTR)

- In 2014, CNTR formed to advocate for adequate, sustained federal funding for trauma clinical research studies and infrastructure
- CNTR successfully advocated for additional $10M in DoD budget for FY2016 for a clinical trauma research network
- Advocating for additional $10M in the DoD budget for FY2017 (supported by 15 senators and 69 representatives from a total of 25 states or 10% of both houses)
- Received notification of first DoD award to CNTR for *Multi-institutional Multidisciplinary Injury Mortality Investigation in the Civilian Pre-Hospital Environment (MIMIC*) to investigate potentially preventable deaths in the prehospital setting with 6 statewide medical examiner offices, the National Association of Medical Examiners and Johns Hopkins Bloomberg School of Public Health

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NTI Knowledge Translation Plan→Moving Knowledge into Action

Knowledge translation: "Ensuring that stakeholders are aware of and use research evidence to inform their health and healthcare decision-making."

The private and public sectors together spend billions of dollars each year on biomedical, clinical and health services research; healthcare student and professional training; patient safety; and risk management. Despite this investment, healthcare systems still sometimes fail to deliver effective (or the most effective) treatments, services and drugs to all who need them, and health professionals may fail to provide the optimal level of care, as evidenced in studies. One of the most consistent findings from clinical and health services research is the failure to translate research into practice and policy. Evidence-practice gaps result in poorer health outcomes that can affect quality of life and productivity.

NTI's Knowledge Translation Plan transcends the traditional publication, presentation and—often years in process—public dissemination of data and results following scientific inquiry. This plan is in accordance with OSTP's 2013 policy memorandum calling for increased access to the results of federally funded scientific research. But because access is necessary but not sufficient to ensure knowledge translation (Ellen et al. cited in Grimshaw, 2012), NTI implements a robust, multi-media effort for access, dissemination, measurement, synthesis and translation that will result in new evidence-based practices that impact public health in a meaningful way. It seeks to be an effective learning system, as defined in the NASEM June 2017 report, one that supports "broad, rapid, meaningful change in practice."

The primary goals of this plan are to improve information flow to the trauma research community and enhance follow-on research; affect agency and government funding, policies and services; and enhance clinical practices. All goals are intended to affect the long-term intention, which is improved health outcomes for the traumatically injured, and enhanced public health overall.

A secondary goal is to identify translational research lags that can and should be decreased in order to shorten the time required for scientific inquiry to translate to new practices and improved outcomes. Knowledge translation barriers that contribute to lags include sheer volume, access, and lack of critical appraisal and research literacy skills. Further systemic barriers include financial and structural disincentives, peer group and professional issues, and difficulties working between and across professional health disciplines (Grimshaw, et al. Implementation Science 2012, 7:50, p. 6). NTI's Knowledge Translation Plan aims to overcome these barriers.

ACCESS

Access to research data will be achieved through research data and publication submissions to:

- Open source research libraries like ResearchGate
- Research data clearinghouses such as clinicaltrials.gov
- The National Trauma Research Repository (NTRR) and the National Trauma Data Base (NTDB)
- FITBIR and other topic-specific repositories, as appropriate

- Defense Technical Information Center (DTIC: www.dtic.mil). Because the Department of Defense provides much of the funding awarded to NTI research projects, NTI will interface with DTIC and, where appropriate, require researchers to submit their peer-reviewed, refereed manuscripts in final form to this repository in order to increase access. DTIC shares technical information related to funded studies with all DoD and affiliated industry and academic groups, provides collaboration tools, and performs research analyses. The DTIC's 12-month embargo ensures that manuscripts are published in scholarly journals before being made public. This powerful repository helps users monitor federally-funded research, identify research gaps, and forecast investment opportunities.
- Once a study is completed, its data will be uploaded into the National Trauma Research Repository (NTRR), now under construction. The NTRR will facilitate the sharing of information and yield long-term collective value. Aside from increased access to study data for researchers, a robust NTRR will result in increased visibility of research priorities and investment opportunities, avoidance of redundant research, and cost savings. It also meets the OSTP's guidance to increase public access to research results funded by the federal government.

DISSEMINATION

First, NTI expects that funded researchers will publish and present their findings in traditional high-impact venues including peer-reviewed journals and scientific conferences and other assemblies. New open-access journals such as *Trauma Surgery and Acute Care Open* and other publishing platforms like F1000Research provide high quality and speedier opportunities to disseminate research results, and NTI encourages funded researchers to publish in these forums as well.

In addition, primary investigators are encouraged to engage in less formal dissemination such as during grand rounds, lectures, department meetings and board presentations.

Following publication in peer-reviewed journals, primary investigators will submit a Publication Report form, which, in turn, signals NTI to activate its Dissemination Checklist. The checklist includes collaboration with the PI's institution on media, provision of a research summary to relevant medical organizations, announcements via NTI's contact list, posts to social media, and more.

NTI will disseminate research results in the popular, science, and health media using one or more technology-enabled platforms such as PRNewswire, AAAS EurekAlert!, and Meltwater. Individual dissemination efforts will encompass social media output on platforms such as Twitter and Facebook, with NTI connecting to all research funding recipients and amplifying their related posts. NTI is building a following among members of the trauma community, and will continue to add both depth and breadth within the follower base.

In order to provide the full range of functionality required of a research institution, NTI will construct a new state-of-the-art website. The NationalTraumaInstitution.org site will provide access and dissemination functionality, enabled by a flexible and searchable content management system to post and archive publications as they become available. The site's blog will be a forum for expert commentary on the archived work. In addition, the NationalTraumaInstitution.org website will host and moderate a robust community of interest surrounding trauma-related research, with multiple forums dedicated to the streams of research being explored. The website will also provide detailed information about the Trauma Clinical Trials Network to be tapped for the multi-institutional studies involved in the funded research, and about the participating clinical centers in any given study.

As new dissemination technologies and means of interaction and engagement emerge, NTI will grow to encompass them within its knowledge translation plan.

Already, NTI has a proven track record of dissemination—with 76% of NTI-funded studies resulting in one or more peer-reviewed publication(s) or manuscripts under review within two years. On average, only 29% of completed clinical trials have published within two years of study completion. (Chen R, Desai NR, Ross JS, Zhang W, Chau KH, Wayda B, Murugiah K, Lu, DY, Mittal A, Krumholz HM. Publication and reporting of clinical trials results: cross sectional analysis across academic medical centers. *BMJ*. 2016;352:i637).

MEASUREMENT

NTI expects its funded research to have a reach beyond the scholarly ecosystem, which means it must look beyond the Impact Factor (IF) and measure more than academic citations. IF has been the leading indicator of research impact since the 1950s. IF is a way to demonstrate research quality and impact, drawing on the data in the Web of Science (a subscription-based scientific citation indexing service used to calculate IF). In today's digital environment, however, IF has its limitations because it has become impossible, using this system of bibliometrics alone, to see the full picture of an article's impact. Alternate impact indicators are the Immediacy Index, calculating how soon after publication an article is cited, and the Cited Half-Life, which shows how often an article is referenced after being published, and there are others. None of them, however, accounts for alternative research outputs—they all rely on traditional scientific publication and conference presentation output.

Thus, NTI will combine traditional measures of scholarly impact with alternative metrics, as well as a variety of public relations measures such as PESO (paid, earned, shared, owned), to understand and quantify how research is being used in public policy and how scholars, practitioners and health agencies are viewing, saving, sharing and discussing research online. NTI will follow and analyze non-citation based, article-level indicators of impact—gathered from mentions of research in nontraditional online outlets. Such metrics will track research dissemination beyond academia; show attention, reception and response to a published work prior to its being cited; and apply to non-traditional research outputs like community forums, data-sets, and blog posts.

Every publication resulting from a NTI-funded study will be tagged with electronic retrieval information (i.e., Digital Object Identifier) to enable such enhanced tracking and analysis of reach and impact. NTI may need to become a member of a DOI Registration Agency such as DataCite or CrossRef if typical publishers of trauma-related research are not assigning DOIs.

SYNTHESIS, SUMMARY & TRANSLATION

Individual studies rarely provide sufficient evidence to support practice or policy changes—and in fact, can often be misleading. One of the most consistent findings from clinical and health services research is the failure to translate research into practice and policy. Research translation is complex and iterative: replication and evidence synthesis is needed before translation can occur (Grimshaw, 2012). NTI will facilitate this process with the development of a National Trauma Research Repository (NTRR), now under construction.

The NTRR will be the central repository for the clinical data resulting from both military and civilian federally funded trauma research and will be a free, web-based application with a user-friendly interface for trauma researchers to contribute and access data. The data-sharing enabled by the NTRR will reinforce open scientific inquiry, encourage diversity of analysis and opinion, more quickly bring to light research gaps, enable exploration of novel topics not envisioned by the initial investigators, and facilitate the education and engagement of new researchers. The NTRR will also facilitate knowledge translation between military and civilian researchers and care providers.

NTI will formally interface with the Eastern Association for the Surgery of Trauma (EAST) GRADES system for establishing Clinical Practice Guidelines and with American Association for the Surgery of Trauma (AAST) presentation and educational avenues such as webinars and scientific assemblies. It is through these established and respected channels that evidence-based practices emerge and become adopted within centers of care.

NTI will work with existing entities that undertake to review and synthesize research for the purpose of knowledge translation, including AHRQ Evidence-Based Practice Centers (EPCs - http://www.ahrq.gov/research/findings/evidence-based-reports/centers/index.html). NTI can nominate trauma treatment as a topic for analysis (AHRQ encourages topic nominations, weighting burden of disease and cost as important criteria. A quick search on "trauma" brought up just a handful of EPC reports, most on traumatic brain injury or injury related to violence, which indicates the agency has not already established trauma as a subject area for research synthesis, even though it is the third most costly medical condition, at $671 billion a year in health care costs and lost productivity, responsible for nearly 200,000 lives every year.) AHRQ has established EPCs at Brown University, the Mayo Clinic, Johns Hopkins, Oregon Health & Science University, Vanderbilt, and other hospital systems where NTI already has strong trauma center connections. Alternatively, or in addition, NTI may pursue establishment as an AHRQ EPC in order to be directly involved in the production of evidence reports related specifically to trauma-related care. Such reports are used for informing quality measures, educational materials and tools, clinical practice guidelines and research agendas.

Cochrane is another research synthesizer—an independent, global network of researchers, professionals, and care-givers—that seeks to improve health through informed, high-quality, relevant and up-to-date synthesized research evidence (http://www.cochrane.org/). Cochrane supports more than 50 review groups—including an anesthesia, critical and emergency care group (HQ in Denmark: http://ace.cochrane.org/) and an injuries group (HQ in London: http://injuries.cochrane.org/). NTI will pursue a partnership with Cochrane to insure that the knowledge translation process runs its full course.

ACCELERATING THE ADOPTION OF EVIDENCE-BASED PRACTICES

Morris et al. (J R Soc Med 2011:104:510-520) examined the literature related to the supposed 17-year gap in the conversion of basic science to patient benefit, determining that due to vast variations in what is measured, it's difficult to calculate an average. The conclusion is that research translation is complex and iterative, the type of research will affect the lag time to patient benefit, and a certain amount of lag is necessary and desired. The crucial questions to answer relate to identifying the specific contributions to lag (grant award process, ethical approvals process, publication and replication process, guideline preparation, and so forth) and which are beneficial or necessary and which unnecessary. Pinpointing the unnecessary gaps, and working to relieve those lags in the translation process will be a secondary goal of NTI's knowledge translation plan.

The National Trauma Institute has already undertaken an examination of gaps experienced by researchers it has funded, finding lags inherent in the regulatory approval process at one or more institutional levels, including IRB approval, DoD HRPO approval, the waiver of informed consent process, FDA approval, issues relating to multi-site and subcontracting. NTI will replicate this work with awarded studies in order to identify additional hurdles and tighten lags.

NTI's Knowledge Translation Plan identifies the key audiences to whom research knowledge will be transferred (researchers, policymakers and federal agencies, funders, practitioners/hospitals), how it will be transferred, the ways in which transference will be measured, and the practices and outcomes that are impacted (see attached spreadsheet).

The Coalition for National Trauma Research supports the call for a national trauma research action plan

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Several forums have been convened in the last two decades regarding civilian research priorities in trauma, including but not limited to National Institutes of Health (NIH) roundtables, Centers for Disease Control meetings, and others.[1–3] In 2015, the NIH and American College of Surgeons (ACS) convened a group of 60 leading researchers and clinicians to develop a national surgical disparities research agenda.[4] Most recently, the National Academies of Sciences, Engineering and Medicine (NASEM) released a report calling for a national, integrated, military-civilian plan to achieve zero preventable deaths after injury.[5] This aim (zero preventable deaths) is similar to other national goals to spur progress in treatment research for challenging health conditions such as infectious disease (i.e., "the countdown to the cure" for HIV) and cancer (i.e., the "moonshot" to end cancer).[6,7] Among the recommendations in that report was the formation of a National Trauma Research Action Plan requiring a resourced, coordinated, joint approach to trauma care research.[5] With the emergence of new scientific and clinical paradigms, the need for an updated research agenda is evident. As new knowledge is incorporated into clinical practice and new challenges in clinical care are identified in both civilian and military environments, research remains the driving force behind advances in the care of injured patients. Overlapping priorities among the military casualty care and civilian trauma care communities mandate the formulation of a new combined research agenda.

The current ongoing military conflicts in Iraq and Afghanistan and the global war on terror have brought to light the need for strong collaboration between civilian and military sectors in clinical care, training, education, and particularly in research. The NASEM report examined how the US military's use of focused empiricism to reduce morbidity and mortality after injury might have implications for improving care in civilian settings.[8] Research manpower and capacity are clearly abundant in the civilian sector, and the US Department of Defense (DoD) is of utmost importance in research funding and priorities (Fig. 1). Currently, DoD funding represents more than 80% of the United States federal government's annual investment in trauma care research.[8]

In 2014, the American Association for the Surgery of Trauma (AAST) and National Trauma Institute (NTI) began discussing the need for a unified, stronger voice to advocate for additional trauma research funding, as well as a mechanism to conduct large multi-institutional clinical trials. This discussion, initially held at the headquarters of the ACS, escalated rapidly. Several months later, the Coalition for National Trauma Research (CNTR) was formed to include not only the AAST and NTI, but also the ACS Committee on Trauma, Eastern Association for Surgery of Trauma (EAST), and Western Trauma Association (WTA).[10] CNTR is focused on developing a centralized national trauma research agenda that establishes priorities and eliminates redundancies in both civilian and military injury treatment, building a robust trauma research infrastructure that includes a Trauma Clinical Trials Network, and securing consistent and significant federal funding for research that increases the understanding of injury and informs clinical practice.[11,12]

CNTR's Executive Committee established three working committees: the Clinical Trials Network Committee (CTN), the National Trauma Research Repository Committee, and the Research Agenda (RA) Committee. The CTN Committee is charged with developing a national clinical trials network, comprising trauma research centers of various sizes and capabilities, using a fair and publicly available process with representative geographic distribution. This committee collaborates and coordinates activities with the AAST Multi-Institutional Trials Committee as well as the CNTR RA Committee. The National Trauma

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1. Unit-based prehospital trauma registries
2. Food and Drug Administration (FDA)-approved freeze-dried blood products (such as plasma and platelets)
3. Clinicopathological review of every U.S. Combat fatality, including preventable death analyses from combat units
4. Development and testing of non-compressible torso and junctional hemorrhage control devices
5. Optimized airway devices and training
6. Optimized fluid resuscitation for casualties with TBI and shock
7. Training and evaluation methods for Traumatic Combat Casualty Care (TCCC) skills
8. Impact of TCCC interventions in preventing Post Traumatic Stress Disorder (PTSD) and TBI, including the role of analgesia in preventing PTSD
9. Combat casualty care monitoring devices
10. Impact of Tactical Evacuation (TACEVAC) provider level and skill sets on survival

Figure 1. Defense Health Board research, development, training, and evaluation high priorities.[9]

Research Repository Committee is charged with establishing a multidisciplinary steering committee that will guide the planning, development, and implementation of an electronic database that combines civilian trauma registries, such as the National Trauma Data Bank of the ACS, and—as permissible—military trauma data repositories to create the "big data" necessary to define and explore critical issues. Additionally, the trauma research repository is envisioned to contain the data elements of all studies funded and implemented through CNTR activities. The RA Committee is charged with developing a national trauma research agenda that reflects scientific questions and research gaps, both civilian and military, based on a review of relevant and recent work groups or publications by other trauma organizations or entities. The committee's charge also includes prioritizing the agenda so that resources will be directed toward the questions needing answers first, and clinical trials related to these questions will evolve over the next five to 10 years.

METHODS

The CNTR RA Committee is comprised of 10 expert scientist-practitioners in the care of injured patients. AAST, WTA, EAST, and NTI each nominated surgeons and/or injury researchers to serve on the committee (Table 1). A member of the CNTR Executive committee served as an ex officio member of the committee. Using conference call technology, the RA Committee met three times during January and February 2015. Each member was asked to review DoD documents and literature provided,[1,2,9,13] and to list research topics/priorities and gaps in three domains: clinical, translational, and mechanistic trauma research. A modified Delphi process was used for the collection of research priorities.[1] Topics were compiled after three rounds of analysis and comments by the committee members. There was a high level of concurrence among committee members in identifying the research topics and gaps (80%). The committee members determined that the "Clinical" and "Translational" domains should be combined, and hence, the final product is organized into two domains, clinical/translational and mechanistic. The lists were reviewed by the RA Committee members and approved for discussion with the CNTR Executive Committee.

In addition to a list of priorities, the RA Committee was asked to provide a condensed prioritized document, which would be aligned with the gap analysis already performed by the DoD for military casualty care research. The priority areas are, therefore, those that are intended to be relevant for both the civilian and military sectors. Specifically, the RA Committee was asked to provide three major focus areas with described goals and specific projects suggested. The final work condensed the lists of research topics. The research priorities were presented to the CNTR leadership. The Executive Committee of CNTR reviewed the RA Committee's work and considered it a comprehensive template to guide future funding and research programs.

RESULTS

There are three major focus areas in which there is considerable overlap between military casualty care research and civilian trauma care research needs. These are acute resuscitation topics, central nervous system trauma, and transfer to definitive care (Table 2). Under the clinical/translational domain, the research priorities focus on three areas. The first large area focuses globally on resuscitation, including optimal timing for and type of resuscitation fluids, endpoints for resuscitation, methods of hemorrhage control, and the identification and management

TABLE 1. CNTR Research Agenda Committee

Member	Representation/Affiliation
Raul Coimbra, MD (Chair)	AAST
Ronald V. Maier, MD (Co-Chair)	AAST
Alex Valadka, MD	AAST
Jason W. Smith, MD, PhD	EAST
Ben L. Zarzaur, MD	EAST
Jeff A. Bailey, MD	NTI
Frederick A. Moore, MD	NTI
Carl J. Hauser, MD	WTA
Rosemary A. Kozar, MD, PhD	WTA
Gregory J. Jurkovich, MD	CNTR Executive Committee—Ex officio member

of coagulopathies and their contribution to posttraumatic thromboembolic disorders. Sequelae of massive resuscitation, including the development of multisystem organ dysfunction and wound healing dyscrasias, were included in this topic area. The second large area under the clinical/translational domain is specific patient populations, with a focus on patients with central nervous system injury. Optimal management strategies in these two disparate populations and outcomes are included. The final large category under the clinical/translational domain focuses on the prehospital environment and the development of trauma systems of care. Specific to this area is the development of registries to facilitate data capture. Details of the clinical/translational domain are illustrated in Figure 2.

The second major domain for trauma research priorities is mechanistic. Topics for study in this domain include mechanisms of immune modulation, the impact of genomics on the response to trauma and outcome trajectories, and the identification of novel targets for therapy (Fig. 3). Although mechanistic research is not the focus of CNTR, it is important for the advancement of trauma research as a whole.

DISCUSSION

In examining the multitude of priorities and needs for trauma research, the RA Committee was particularly interested in examining scientific questions that would address both civilian and military trauma surgeon needs. To that end, the three major topics (Table 2) of acute resuscitation, central nervous system injury, and the interface between field (prehospital) care and definitive (hospital) care rose to the top.

In the area of acute resuscitation, it was determined that focused research efforts yielding the greatest benefit to injured patients (and soldiers) would be clinical trials on novel fluid resuscitation strategies that could potentially minimize ischemia and reperfusion injury, and prevent or treat the development of coagulopathy. It was theorized that a combination of new or developing pharmacologic agents, blood substitutes, or more durable forms of blood and plasma storage (lyophilized or dried formulations) could address these needs. It was determined that prospective, randomized trials comparing different treatment strategies including, but not limited to, forms of inflow occlusion (resuscitative endovascular balloon occlusion of the aorta), aortic cross-clamping, direct hemorrhage control and novel packing agents, etc., in severe traumatic shock are also needed to refine the indications and results of each method. Studies are also needed to determine the safety, efficacy, and effectiveness of modulators of inflammation and coagulation, specifically blood component therapy, procoagulation complexes, fibrinogen, and other procoagulant agents. This would include the specific role of modulators on perception and treatment of pain. Additionally, the effect of resuscitation strategies on the development of heterotopic ossification and functional limb outcomes should be prioritized.

Central nervous system injury, a second major area of interest that crosses multiple disciplines, encompasses both direct impact and blast injury. The committee selected three specific goals of research: better methods of diagnosing and characterizing brain injury; better methods of preventing brain injury and its sequelae, and better methods of predicting outcome of brain injuries to provide the resources needed for recovery. Multimodal imaging and biomarkers can be used for diagnosis, follow-up, and determination of outcomes following TBI. Multiwell plates to measure biomarkers known to be related to TBI-could be used to create a risk index to predict intracranial hemorrhage in mild to moderate injury patients, and to predict progression of injury in moderate to severely injured patients. The correlation of clinical data, biomarkers, and imaging could lead to the development of more timely and specific treatment strategies. In addition, the biomarker levels could be used to improve selectivity of patients who require cerebral computed tomography following mild to moderate injury to reduce overall radiation exposure and to improve prediction/detection of progression of brain injury, as well as identification of patients who require earlier or more frequent re-imaging or surgical intervention. TBI studies should have long-term follow-up to estimate and measure quality of life; to validate CDE, Patient Reported Outcomes Measurement Information System (PROMIS), Quality of Life in Neurological Disorders, and NIH Toolbox initiatives; and to utilize neurocognitive testing. This would include impact on recovery from concomitant extremity injury, especially when blast is the mechanism.

The third overlapping area of civilian and military trauma care is the interface between field care and hospital care. This area includes the most time-sensitive injuries, and the research agenda suggests that focus areas that might lead to improved outcomes by the most rapid interventions include physiologic derangements, improved communication strategies and tools between these areas of care, and finally, novel management strategies for the prehospital/field arena. The study of the interface between the prehospital system and the definitive care

TABLE 2. Overlapping Trauma Research Priorities in Military and Civilian Settings

Major Areas	Goals	Specific Projects
Acute resuscitation	Hemorrhage control and resuscitation	Novel fluids, components or transfusion, modulation of coagulation, and inflammation
Central nervous system injury	Diagnosis, brain protection, outcomes	Multimodal imaging, biomarkers of injury, prevention/limitation of secondary brain injury, outcome predictions by multimodal monitoring, maxillofacial trauma related to TBI
Scene to definitive care interface	Improve physiology, communication, and management interface	Advanced monitoring, automated decision support technology, wireless data and image transmission, interface hospital-based physicians with prehospital nonphysicians, prehospital hemorrhage control strategies

Clinical/Translational

RESUSCITATION

- Optimal resuscitation strategies
- Shock resuscitation
  - Fluids
    - Freeze-dried plasma
    - Blood products
      - Whole blood
      - 1:1:1 component therapy
      - 1:1 component therapy
      - Plasma alone
      - Cold-stored platelets
  - Genomics/Proteomics – defining trends in inflammatory response to blunt trauma and identifying possible biomarkers to guide resuscitation and predict outcome trajectories
  - Novel adjuncts to resuscitation: Modulation of coagulation/inflammation
    - Drugs
    - Fibrinogen
  - End points
    - Cardiovascular Reserve Monitor-Driven Resuscitation from Hemorrhagic Shock
    - Tissue oxygenation monitoring
    - Use of transesophageal echocardiography and/or transthoracic ultrasonography in optimizing shock resuscitation
    - Develop novel technology to assist clinicians in shock resuscitation (computer software guided resuscitation, new technologies to monitor patients, etc.)
  - Attenuation of metabolic demand and extension of viability (suspended animation)
  - Extremity injury management effects of resuscitation, including the development of heterotopic ossification

HEMORRHAGE CONTROL

- Novel means of hemorrhage control
- Endovascular hemorrhage control
- Development of innovative technologies to be used in pre-hospital management of hemorrhaging patient
- REBOA- identify optimal patients, device, technique +/- imaging
- Prospective trial on the utilization of REBOA in trauma patients with hemorrhagic shock. Comparison of REBOA to resuscitative thoracotomy.
- Determine effect of REBOA on mortality, identify ideal time and patient population to utilize REBOA.
- Determine institutional characteristics hospital type, trauma level, location of resuscitation bay, presence/absence of in house trauma attending, vascular attending, interventional radiology attending, hybrid operating room, etc. for evaluation of extremity salvage and functional outcome in those with extremity injury.

COAGULATION/COAGULOPATHY

- Development of strategies to utilize thromboelastography (TEG) to control traumatic coagulopathy
- Effect of new class of anticoagulants (e.g., rivaroxaban) on bleeding risk in elderly
- Acute coagulopathy of trauma
  - Identification
  - Prevention
  - Correction
    - Procoagulant concentrates
    - Tranexamic Acid (TXA)
- The role of TEG in the management of coagulopathy after trauma, focused on the impact of patient co-morbidities and medication use.
- Optimal platelet storage and preservation

Figure 2. Clinical/translational trauma research priorities.

- Understanding the interplay between coagulation and inflammation after trauma
- Approaches to correct acute coagulopathy during massive transfusion.

BIOMARKERS/GENETIC PROFILING/POCT/RISK MODELING

1. Biomarkers to predict:
   - Injury severity
   - Injury severity response – time
   - Shock and shock response
   - Inflammation following severe injury and shock
   - TBI (GFA, NSE, S100 and ceruloplasmin)
   - Polytrauma
   - Early biomarkers of severe injury (predict transfusion, need for surgery)
   - Early biomarker of increased venous thromboembolism (VTE) risk
   - Early biomarker of increased heterotopic ossification risk
   - Early biomarker of increased pain and long term pain syndromes

2. Therapeutic targets
   - Human specific genes or gene pathways
   - Signaling

3. Development of applications for risk prediction
   - Creation of an application that incorporates complex risk models including Trauma and Injury Severity Score (TRISS), Revised Injury Severity Classification (RISC/RISCII) as well as injury specific risk adjustors (like out unplanned intubation risk calculator) that can be used to rapidly predict risk at time of patient admission. +/- incorporation of technology into an electronic medical record (EMR). May include continuous updates with information that is gathered over time such as Acute Physiology and Chronic Health Evaluation (APACHE), Sequential Organ Failure Assessment (SOFA) etc., that can be used to give a daily "overall risk" for mortality like a "5th" vital sign that will be displayed to physicians whenever vital signs are checked and may prompt an upgrade or downgrade in level of care based on risk. This may also be used to predict functional extremity outcome and development of pain syndromes.

VENOUS THROMBOEMBOLISM (VTE)/DEEP VEIN THROMBOSIS (DVT)

- Optimal strategy for VTE prophylaxis (dosing interval, algorithm, dose adjustments)
- Oral anti-Xa inhibitor for inpatient VTE prophylaxis
- Duration of VTE prophylaxis post-discharge
- Long term morbidity for patients with VTE after trauma
- DVT Prophylaxis
  - Continuation and duration of Lovenox after discharge, and the immobility factor?
  - Prolonged VTE prophylaxis after spine injury: quadrapalegic vs paraplegic?
  - When is it safe to start prophylaxis after spine surgery?
- Trial to determine the safety and efficacy of early pharmacologic VTE prophylaxis in trauma patients with spinal fractures with and without spinal cord injury. Variables of interest include type of fracture, patient demographics, surgical intervention. Outcomes include bleeding, progression of neurological injury, need for surgery, epidural hematoma, VTE, mortality.

TRAUMATIC BRAIN INJURY (TBI)

- Optimal resuscitation strategies after TBI
- Intracranial pressure (ICP) monitors and outcome
- Interstitial oxygenation monitoring and optimization
- Hypernatremia in TBI: bolus vs. infusion, dose, sodium target, and duration
- Comparative efficacy of reversal strategies for patients on anticoagulants and anti-platelet agents. Examine effects, if any, of prothrombin complex concentrate (PCC), plasma, platelet transfusion, desmopressin (DDAVP), dialysis, or other reversal agents on progression of brain injury, need for surgical intervention in TBI, mortality, complications, and neurological outcome.
- Impact of New Technologies and Assays:
  - TEG
  - Thrombogram
  - "Plavix" assay

Figure 2. Continued

facility is important to allow for the development of better care at the scene and during transport in civilian as well as in military austere settings.

In most urban systems, transport time is short, and there is very little time for interpretation of data prior to implementing life-saving interventions. In the battlefield, this time from injury

ORGAN FAILURE/SEPSIS/Multiple Organ Failure (MOF)/Intensive Care Unit (ICU) Care

- Organ insufficiency and failure
  - Risk stratification and early identification
  - Organ replacement therapy
    - Cardiopulmonary
    - Hepatic
    - Renal based on AKIN classification
    - Pulmonary – extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS)
- Modern classification and assessment of post traumatic sepsis and MOF
- Impact of nutrition and mobility on outcomes after ICU admission
- ECLS after trauma
- Study feasibility of developing regional centers of excellence in resource intense therapies – i.e., – ECMO / ECLS
- Computer based algorithm to detect risk of clinical deterioration/transfer to ICU for patients on floor/Intensive Medicine Unit (IMU)
- The timing of an optimal method of tracheostomy: examining the possible benefits of early tracheostomy in specific patient populations and outcomes relative to the technique used.
- Sedation and analgesia regimen to limit delirium after traumatic and septic shock
- Closed loop clinical decision support to provide basic ICU care (e.g. ICP management, ventilator management, resuscitation)
- Early exercise and physical therapy in the ICU
- Optimize perioperative care to limit acute kidney injury
- Optimal antibiotics in treating nosocomial infections
- Strategies to limit nosocomial infections
- Polymerase chain reaction (PCR) based early detection of bacterial pneumonia
- Effect of prolonged shock on organ injury and recovery
- Effect of aortic occlusion on organ injury and MOF
- Effect of aortic occlusion on functional extremity salvage

ELDERLY

- Long term outcomes after trauma in the elderly – functional recovery and mortality
- Quality improvement for geriatric trauma
- Elderly TBI - Effectiveness of pathways and bundles
  - Cohort elderly patients in a unit
  - Establishing sleep/wake immediately
    - Dim the lights at 9pm on at 7am
    - Soothing music
  - Swallow evaluation and timing
  - The role of early enteral tube feeding in patients with altered levels of consciousness in the prevention of aspiration
  - Mobility
- Elderly rib fractures
  - Mobility
  - Respiratory therapy
  - Pain control algorithm
- Performance improvement and outcomes assessment of the geriatric trauma patient, with a focus on the identification of appropriate metrics
- Ethical decision making in Elderly trauma patients

TRAUMA SYSTEM/TRAUMA CENTERS/REGISTRIES

- Development of formula/paradigm for optimal placement of trauma centers (Can we develop an echelon system within the US?)
- Study feasibility of developing surgical strike teams for rapid deployment to rural hospitals or disaster areas for management of (multiple?) bleeding patients
- Develop technology to automate population of registries with data
- EHR and Registry Interaction
  - Data acquisition
    - Epidemiology
    - Mechanism

Figure 2. Continued

        - Physiology
        - Injury Severity
        - Biomarkers
        - Interventions
        - Co-morbidity
        - Morbidity
        - Autopsy
        - Pre-hospital data management
            - Registries
            - Automated data collection
            - Remote virtual management augmentation
    - Analytics
        - Performance metrics and outcomes
        - Risk identification and adjusted benchmarks
    - Enhanced interoperability and data sharing

- Preventable causes of mortality
- Evaluation of impact of hybrid OR's. Outcomes of interest mortality/morbidity following orthopedic injuries, vascular injuries, time to definitive control of hemorrhage, need for repeat surgical/interventional procedures, transfusion requirements, cost/charges. Variables to study, presence/absence of hybrid OR, location of hybrid OR, service primarily involved (vascular, IR, trauma surgery), teaching facility, trauma level, hospital size, trauma volume, percent penetrating injuries.

PREHOSPITAL

- Novel pre-hospital diagnostics and therapeutics
- Optimal use of blood products in the pre-hospital setting
- Optimal use of military CCCT techniques in the civilian pre-hospital environment (Tourniquets, Combat Gauze, Celox, etc.)
- Pre-hospital (pre-surgical) hemorrhage control
    - Truncal (thoracic, abdominal, pelvic)
    - Junctional
    - Extremity (including analysis of salvage and function)
- Advanced pre-hospital resuscitation during prolonged transportation times
- Video streaming to trauma centers from pre-hospital (scene and ambulance)
- Real time data streaming of physiologic data from pre-hospital to trauma centers
- Pre-injury environment/transportation and relationship to post-injury recovery and outcome following major trauma

WOUND HEALING AND PAIN CONTROL

- Novel methods of optimizing wound healing, especially in craniomaxillofacial injury as well as prevention of heterotopic ossification in extremity injury
    - New Drugs
    - Gene Therapy
    - Others
- Novel use of current pain agents, continuous versus bolus and utilization of novel pain control agents to optimize recovery and long term functional outcomes

Figure 2. Continued

to definitive care may be longer, as it would be in many rural or austere environments. The development and testing of miniaturized biomonitoring systems that allow advanced assessment and interpretation of the physiologic response to injury, linked to automated decision support systems that inform medics about interventions needed in a timely fashion, may improve prehospital trauma care. These data points, as well as real-time video streaming at the scene and during transport, could be transmitted wirelessly to definitive care facilities (trauma centers, forward surgical hospitals) for resource mobilization and team preparation. Studies could be designed to measure the impact of data and image transmission from the prehospital to the hospital setting in terms of resource utilization, timing of interventions (e.g., intubation, chest tube placement, diagnostic peritoneal aspiration, etc.), improved resuscitation (e.g., early use of blood or novel agents), and cost. Ultimately, the data transmitted from the prehospital phase of care should be incorporated into trauma registries.

In selected groups of bleeding patients, the development and application in the prehospital phase of novel techniques and/or drugs to achieve bleeding control should be performed. Studies on the effectiveness of prehospital administration of blood, blood components, and procoagulant factors should be performed. Techniques (devices or substances) used to temporarily control junctional or cavitary hemorrhage should be tested. Time to definitive care and monitoring of physiologic

- Mechanisms contributing to age-related outcomes after trauma
- Genomics of trauma to predict outcomes
- Mechanisms of coagulopathy of trauma and TBI
- Identify novel methods/compounds for restoring hemostasis following hemorrhagic shock induced coagulopathy
- Influence of microbiota of outcomes after trauma
- Mechanism of immune suppression/alteration following severe TBI
- Molecules as therapeutic targets after hemorrhage
- Identify alternative resuscitation strategies/methods for correcting shock and its underlying physiologic derangements.
- Acute Coagulopathy of Trauma (ACOT)
- Ischemia reperfusion identification and prevention/treatment
- Attenuation of metabolic demand and extension of viability (suspended animation)
- Biomarkers and genetic profiling
    - Injury Severity
    - Injury severity response – time
    - Shock
    - TBI
    - Polytrauma including extremity salvage and function
- Therapeutic targets
    - Human specific genes
    - Signaling
- Improved animal models of injury (polytrauma models, humanized mice)
- Human specific genes
- Mechanism of trauma induced coagulopathy
- Gut and lung microbiome (effect on SIRS, effect on nosocomial infection)
- Exosomes as mediator of SIRS
- Regenerate or reverse extremity dysfunction with stem cell therapy
- Extend survival and limit organ failure after hypotensive resuscitation
- Regenerate or reverse TBI and SCI with stem cell therapy
- Optimal fluid resuscitation for shock resuscitation
- Regenerate or reverse craniomaxillofacial injury with stem cell therapy
- Early genomic and proteomics responses to trauma and septic shock
- Tracking and treatment of late inflammation and immunosuppression after trauma and septic shock
- Mechanisms of diminished resistance to infection after injury
- Mechanisms of the perpetuation of inflammation (and thus organ failure) after injury
- Non-antibiotic means of diminishing infection and the emergence of resistant organisms.

Figure 3. Mechanistic trauma research priorities.

response to resuscitation may impact type and degree of options for extremity injury reconstruction and will be subject to thorough investigation, especially in the multiple injuries patient.

In conclusion, research in the areas of acute resuscitation, central nervous system injury, and the interface between field (pre-hospital) care and definitive (hospital) care addresses gaps in knowledge that impact the care of both civilian and military critically injured patients. The DoD's Combat Casualty Care Research Program and the military's learning health system have already resulted in knowledge or materiel solutions in these areas.[8] Successful execution of the research agenda proposed herein would go a long way to address the NASEM report goal of achieving zero preventable deaths after injury.[5] CNTR views the NASEM report to be in complete alignment with its mission and will continue to advocate for the development of a National Trauma Research Action Plan.[14]

AUTHORSHIP

R.C., R.V.M., G.J.J., and M.A.P. conducted the literature search. R.C., R.V.M., A.V., J.W.S., B.L.Z., J.A.B., F.A.M., C.J.H., R.A.K., G.J.J. served on the CNTR Research Agenda Committee. R.C., R.V.M., and G.J.J. conducted data analysis. R.C., R.V.M., G.J.J., D.H.J., K.A.D., and M.A.P. wrote the article. R.C., R.A.K., A.V., J.A.B., G.J.J., D.H.J., K.A.D., M.A.P., R.V.M. assisted with critical revisions.

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The authors declare no conflicts of interest.

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Safety and Efficacy of Ketamine for Acute Burn Pain in Austere Conditions

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JOHNS HOPKINS BURN CENTER

Participating Sites

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- Department of Plastic & Reconstructive Surgery
- Department of Anesthesia & Critical Care Medicine
- Department of Psychiatry & Behavioral Sciences
- Department of Neuroscience

Johns Hopkins Institute For Clinical and Translational Research

Johns Hopkins Bayview Medical Center

- Johns Hopkins Burn Center
- Nursing
- Research Pharmacy

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Background/Scientific Rationale

The Problem: Acute Burn Pain Management in Austere Conditions

Standard of Care for Acute Burn Wounds

- Wound Care Sessions: Twice daily for adults with acute intermediate and/or deep partial thickness burns.
- Pain During Each Sessions: Severe pain during dressing removal, debridement, wound cleansing, re-application of topical ointment, and dressing replacement. Especially during the first week.
- Standard Pain Management: intravenous opiate medications (i.e., fentanyl).

Military & Civilian:

- Urgent need: for a well-controlled and rigorously designed study with sufficient power to test definitively the hypothesis that fentanyl when augmented with low-dose, slow-infusion ketamine provides superior analgesia in the acute burn setting.
- Findings from acute burn centers are likely to generalize to a number of austere trauma settings, including injuries sustained in a battlefield setting.

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Background/Scientific Rationale

Opiates as Mainstay for Acute Burn Pain Management

Opioid Treatments:

- Opiate Side Effects:
  - Diminished cognitive & physical function
  - Suppression: Respiratory, Cardiac & Digestion/Excretion
- Comorbidities & Outcomes
  - Impaired cognitive and physical function on core military tasks
  - Downward Spiral: Tolerance-Dependence-Addiction
  - Under-treated Acute Pain-Central Sensitization-Chronic Pain
  - Chronic Pain associated with higher rates of Opiate Dependence, PTSD, Depression

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Background/Scientific Rationale:
Ketamine Augmentation of Opiate Medications for Acute Burn Pain Management

Ketamine: Opioid Augmentation, Sub-anesthetic, low-dose, slow infusion

- Ketamine Side Effects:
  - **Diminished response time** but not precision on key military tasks
  - **Dissociation, confusion** – less severe, less frequent, briefer duration with low-dose, slow infusion
- **Comorbidities & Outcomes:** Abuse potential, Possible neurotoxicity (high doses, administered quickly via IV, in chronic abusers)

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Low Dose Ketamine for Analgesia in Acute Pain

The evidence base is solid and expanding for the safety and efficacy of ketamine either alone or as adjuvant analgesia in:

Emergency Department

- Multiple systematic reviews/meta-analyses
- Safe, Effective, across diverse severe pain populations

Pre-hospital Transport

- Multiple publications, consistent pain reduction findings
- *Safe, Effective, in transport, EMTs*

Ketamine Analgesia: Mechanism & Relation to Opioid Effect

NMDA Receptor function – Potentiates painful stimuli (hyperalgesia, central sensitization);

KETAMINE – NMDA Receptor Antagonist with “slow off rate”

Also, in combination with Opiates:

- Augments opioid mu-receptor function by potentiating “downstream” opioid-induced phosphorylation and thus requiring lower opioid doses for equal phosphorylation.
- Delays opioid receptor desensitization, improves resensitization, thus prolonging opiate effect

Ketamine for Mood Disorder and Posttraumatic Stress Disorder

The evidence base is also solid and expanding for the safety and efficacy of ketamine for PTSD and Major Depressive Disorder:

Ketamine: Low dose, slow infusion - Rapid relief for 1-2 weeks

Chronic PTSD:

- Accruing military & civilian samples, diverse trauma

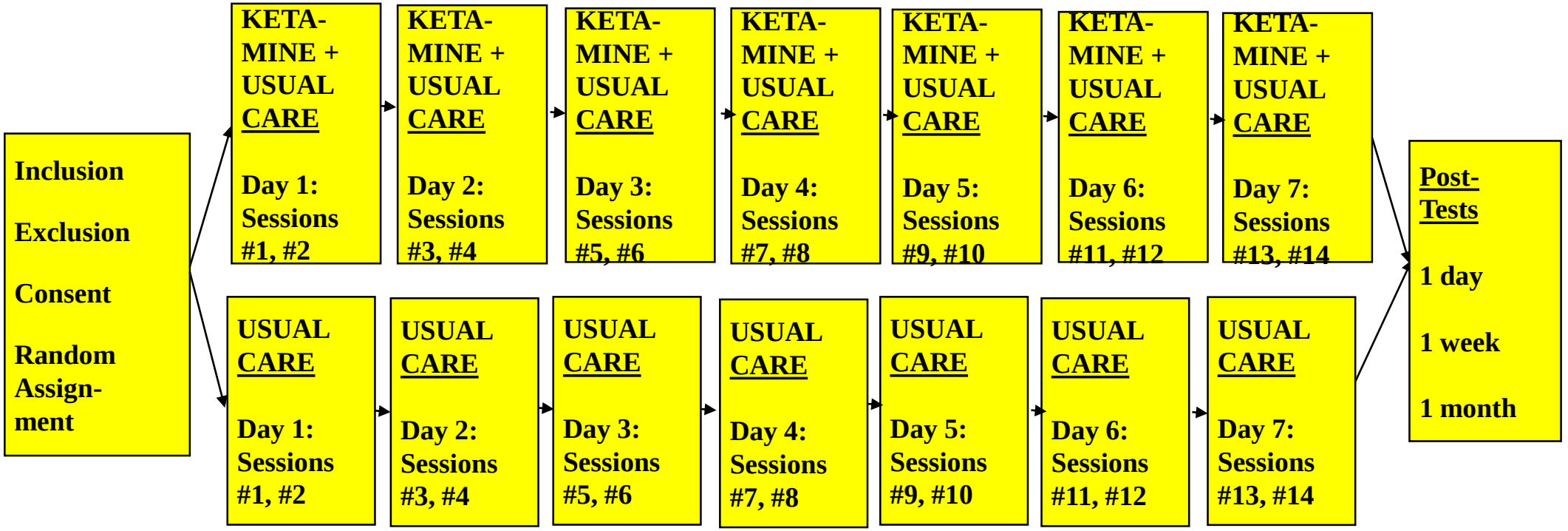
Treatment Resistant MDD:

- Years of failed drug trials

Suicidal Ideation / Imminent Risk of Suicide

- Possible Treatment Component: Cognitive Impairment

KETAMINE FOR ACUTE BURN PAIN
Study Design & Flow Diagram



DESIGN: This is a randomized, controlled, parallel group trial, utilizing repeated treatments, Triple-blinding

Study Hypotheses/Aims

Specific Aim #1: To test the safety and effectiveness of ketamine augmentation to usual care relative to Usual Care alone in reducing the severity of acute nociceptive pain during burn wound care.

a. *Mean Pain; *mean Pain Unpleasantness
b. *Time to Maximal Pain Relief
c. *Recall Effect on Pain
d. *Sympathetic Arousal (HR, HRV, BP, RR)
e. *Satisfaction with Pain Management
f. Central Sensitization: Secondary Hyperalgesia; Allodynia.

*Average of 14 sessions, and, Trajectory across sessions 1-14 and follow-up.

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Study Hypotheses/Aims

Specific Aim #2: To determine whether adjunctive ketamine is associated with opiate sparing.

Opiate Sparing Effect: Significant mean group difference across treatment arms in the request for supplemental analgesic medications.

Prior Findings: Ketamine in one study were reported to be equally effective as opiates but much more rapid in achieving maximum pain relief in burn wound care

Measure: Requests for Additional Analgesic Medications (i.e., RAAMs) for acute nociceptive pain during each wound care sessions (7 Days, 14 Sessions).

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Study Hypotheses/Aims

There are Two Secondary Outcomes:
Rates and symptom severity of:
1) Posttraumatic Stress Disorder (i.e., ASD and PTSD), and
2) Major Depressive Disorder (MDD):

Prior Findings:
Pain and PTSD are highly correlated, and, are reciprocally related over time (Mutual Maintenance Theory).

Ketamine drastically reduces chronic PTSD and chronic Treatment Resistant Depression for up to 2 weeks.

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Study Hypotheses/Aims

There are 12 mediators of outcome:

RISK FACTORS

Preburn:

- Pain History
- Drug/Alcohol History
- Psychiatric History
- Trauma History

Sympathetic Arousal

Pain-related Anxiety

Pain Catastrophizing

PROTECTIVE FACTORS

Sleep (quality, duration)

Emotion Regulation

Pain Coping

Optimism

Trauma Resilience

Benefit Finding

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Study Sample & Methods

SAMPLE: 94-104 acute adult burn patients hospitalized in the Johns Hopkins Bayview Medical Center's Johns Hopkins Burn Center (Burn Intensive Care Unit) who have sustained burns ≥2% and ≤40% total body surface area (TBSA ≥2% & ≤40%).

ASSIGNMENT: Subjects will be randomly assigned to either a fentanyl ("usual care") + saline (UC) condition, or to fentanyl (usual care) plus ketamine (K + UC) condition.

STUDY DRUG ARM: Subjects in the K + UC condition will receive low-dose, slow-infusion ketamine (see information below on medications, dosing, timing etc.).

USUAL CARE ARM: Subjects in the UC condition will receive fentanyl plus normal saline instead of fentanyl plus ketamine.

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KETAMINE STUDY ARM (Fentanyl PLUS Ketamine)

i. Ketamine Loading Dose (Study Drug, slow infusion) = 0.3 mg/kg

Initiated 10-minutes prior to wound care and infused over 3 minutes.

THEN, …

ii. Fentanyl Loading Dose = 1 mcg / kg

This is given to participants in both Group 1 and Group 2 starting at <1 minute before wound care is initiated.

THEN, …

iii. Ketamine (Study Drug, Infusion): 2.5 mcg/kg/min

Initiated immediately following the Loading Dose and continued for the duration of the session.

USUAL CARE STUDY ARM (Fentanyl PLUS Saline)

i. Saline Loading Dose (Placebo, slow infusion) = An identical volume of saline as that in 0.3 mg/kg of ketamine.

Initiated 10-minutes prior to wound care and infused over 3 minutes.

THEN, …

ii. Fentanyl Loading Dose (Usual Care, Injection) = 1 mcg / kg

This is given to participants in both Group 1 and Group 2 starting at <1 minute before wound care is initiated.

THEN, …

iii. Saline (Placebo, Infusion): 2.5 mcg/kg/min

An identical volume of saline as that in 2.5 mcg/mg/min of ketamine.

Initiated immediately following the Loading Dose and continued for the duration of the session.

*PRN: Provided to participants when additional pain relief is requested.

- PRN Fentanyl (injection) :

  PRN = 1 mcg / kg based on Pain NAS score >3.

- Criteria for providing PRN fentanyl are based on customary nursing practices, including a self-reported NAS pain >3/10 but also involves nursing judgment, observation of patients, vitals, etc.

- ***Request*** not Delivery: Request for Additional Analgesic Medication (RAAM), and, Reported Present Pain Intensity >3/10.

KETAMINE FOR ACUTE BURN PAIN
Assessment Diagram

PRE-RANDOM-IZATION:

Inclusion
TBSA: ≥2% & ≤40%

Exclusion
Pain: 1st NAS in ER AND BICU <6/10; Insensate, Lacks Capacity; Intubated; LOS<~4 days

Allocation Strategy:
Group Allocation, in random blocks of 2, 4, 6

BASELINE: PREBURN MO

Pain – (Month)
Average, Type, Location
Pain Medications
Brief Pain Inventory (BPI)
Pain Anxiety (PASS)
Pain Coping Q.
Catastrophizing Q
Med Side Effects (SEM-O.K.™)

PTSD Hx (LETE)
Depression (BDI-II)
Suicide Risk Scale

Post-Trauma Resilience Scale
Emotion Regulation Scale

SF-12
DSM V Adult Psycho-pathology Screen (lifetime, 12 months)

Days: 1 – 7 Sessions #1 - #14

Pre—Session (~1-hr)
Burn Pain: Mean pain since last Session
Pre-procedure:
Wound
Proximal to wound
Distal to wound
- **Pain Medications**

Sleep-Pain Diary

Intra-Session
Burn Pain: Mean pain every 10 minutes during session:
- **Mean pain since last NAS**
- **Locations (above)**

Additional Pain Meds

Post-Session
Burn Pain Recall:
NAS @ 1 hr (AM, PM)
NAS @ 6 hrs (AM only)
- **Mean Dsg Change**

Pain & Unpleasantness
Pain Mgmt Satisfaction

Days: 3, 5, 7: Sessions: #6, #10, #14 .

Pre—Session
Pain Anxiety (PASS)
Pain Coping
Pain Catastrophizing
PTSD (Davidson Trauma Scale)
Depression (BDI-II)
**All other pre-session measures as shown in prior box for Sessions 1-14.

Intra-Session
*All intra-session measures as shown in prior box for Sessions 1-14.

***Post-Session**
*All post-session measures as shown in prior box for Sessions 1-14.

POST-TESTS

1 Day
Burn Pain (Mean 24-hr NAS) at Locations:
Wound
Proximal to wound
Distal to wound
Pain Medications
Pain Management Satisfaction
PTSD (Davidson Trauma Scale)
Depression (BDI-II)
Benefit Finding (BF)
Emotion Regulation Scale (ERS)

1 Week:
*All post-session measures as shown above for 24-hour follow-up.

1 Month:
*All post-session measures as shown for 1- & 7-Day follow-ups.
Burn Specific Health Scale (BSHS),
SF-12

Ketamine RCT: Staff, Coverage

Wound Care & Outcome Coverage

- Enrollment Rate:
  - 12 Participants/Month, 3 Participants/week
- Staff Coverage:
  - SESSIONS: 14 Total Shifts/week, 4 hours/Shift, 3 Part/shift
  - OUTCOME: 3 follow-ups/Participant (1 Day, 1 week, 1 month)

Shift (AM/PM)	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
AM (9a-1p)	Rayyan	Emily	Amanda	Emily	Amberly	Emily	Rayyan
PM (9p-1a)	Shanna	Rayyan	Emily	Shanna	Emily	Amberly	Amberly

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Ketamine Sample: Target & Actual

Target Accrual Rate:

- 100 Participants in 8 Months (Nov ‘17–June ‘18)
- 12 Participants/Month, 3 Participants/week

Actual Eligible Admission Rate (5-year mean):

- 350 annual mean admission rate
- Adjusted for 8 months: 233 admits, 30/month (7/week)
- 2-4 eligible/week, 3 enrolled/week = 96 total

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Challenges/Lessons Learned

- DoD Grants:
  - Steep Learning Curve
    - Several Stages of Approval
    - Ambiguous Expectations, Time Frames & Funding Release
- Funding Release
  - Prolonged Delay “Post-Award“
    - Study Staff – could not be hired
    - Faculty Time – protected time not available
- Hospital Policy Changes
  - Ketamine – Clinical Application vs IRB-Approved
- Team Turnover:
  - JHBC Director Retired
  - Nurse Manager: 1 Resigned, 1 Interim Manager, 1 New Manager
  - Nursing Turnover (new training required)

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NEW KNOWLEDGE FROM TRIAL / DESIGN

Dose Response to Ketamine:

- Does impact improve with repeated sessions?
- This has vast implications for combat casualties in austere conditions with delayed evacuation, as well as for their ongoing analgesia once they have been moved to a field hospital.

Dual Target Variables:

- Pain and PTSD have never been targeted by ketamine in the same trial, using repeated treatments, in humans, and only a few times in preclinical studies.

Ketamine as Prevention:

- Treating acute pain to prevent central sensitization and chronic pain - Likely to have implications for opiate dependence and disability.
- Reducing symptoms of acute stress disorder and depression to prevent syndromal PTSD and depression

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Related Research Presentations/Publications

Posters

Annual JHU Undergraduate Competition: DREAM

- Ketamine for Acute Burn Pain

Annual Post Doctoral Research Pot Pouri; NIDA & the JHU Behavioral Biology Research Unit

- Ketamine for Acute Burn Pain, Opiate Sparing, Acute Stress Symptoms

Paper Presentations

American Burn Association – Spring, 2018

1. Pain and PTSD: A Test of the Mutual Maintenance Model
2. Acute Pain: Does PTSD Mediate Transition to Chronic Pain?
3. Acute PTSD: Does Pain Mediate Transition to Chronic PTSD?

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IRB Approved: Change in Research (09/28/2017)
Remaining Steps:

- ICU RNs, Fellows, PA providers
  - Training in specifics of the study (Yvette Wilson, Emily Werthman)
  - IRB – Change in Research: Study Staff, (Fauerbach)
- HRPO Review
- Drug Order Set Build –
  - Takes ~1-week after IRB approval. Tad Edwards
- Screen, Recruit, Enroll, …

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Future Directions

1. Multicenter RCT Replication and Extension: Refine methods, procedures, measures from knowledge gained here. Focus Aims & Hypotheses on direct relevance to military & civilian contexts of most austere conditions.

2. Next-Generation War Plans: Prolonged time lapse before extrication – repeated, effective wound care, acute pain and distress management.

3. Deployment-Ready Ketamine Delivery Device: low dose, slow-infusion ketamine in austere conditions, multiple sessions and days, tamper proof, lightweight

4. Zero Preventable Deaths and Disability: Integrate acute pain and psychological distress management with the DOD's initiative.

5. Cornerstone for the Military-Civilian Program: integrate acute care into prevention of chronic disability in the cross-fertilization and continuous training of military and civilian.

NATIONAL TRAUMA INSTITUTE

The mangled extremity score and amputation: Time for a revision

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BACKGROUND: The Mangled Extremity Severity Score (MESS) was developed 25 years ago in an attempt to use the extent of skeletal and soft tissue injury, limb ischemia, shock, and age to predict the need for amputation after extremity injury. Subsequently, there have been mixed reviews as to the use of this score. We hypothesized that the MESS, when applied to a data set collected prospectively in modern times, would not correlate with the need for amputation.

METHODS: We applied the MESS to patient data collected in the American Association for the Surgery of Trauma PROspective Vascular Injury Treatment registry. This registry contains prospectively collected demographic, diagnostic, treatment, and outcome data.

RESULTS: Between 2013 and 2015, 230 patients with lower extremity arterial injuries were entered into the PROspective Vascular Injury Treatment registry. Most were male with a mean age of 34 years (range, 4–92 years) and a blunt mechanism of injury at a rate of 47.4%. A MESS of 8 or greater was associated with a longer stay in the hospital (median, 22.5 (15, 29) vs 12 (6, 21); $p = 0.006$) and intensive care unit (median, 6 (2, 13) vs 3 (1, 6); $p = 0.03$). Of the patients' limbs, 81.3% were ultimately salvaged (median MESS, 4 (3, 5)), and 18.7% required primary or secondary amputation (median MESS, 6 (4, 8); $p < 0.001$). However, after controlling for confounding variables including mechanism of injury, degree of arterial injury, injury severity score, arterial location, and concomitant injuries, the MESS between salvaged and amputated limbs was no longer significantly different. Importantly, a MESS of 8 predicted in-hospital amputation in only 43.2% of patients.

CONCLUSION: Therapeutic advances in the treatment of vascular, orthopedic, neurologic, and soft tissue injuries have reduced the diagnostic accuracy of the MESS in predicting the need for amputation. There remains a significant need to examine additional predictors of amputation following severe extremity injury. (*J Trauma Acute Care Surg.* 2017;82: 518–523. Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.)

LEVEL OF EVIDENCE: Prospective, prognostic study, level III.

KEY WORDS: Mangled; trauma; vascular; extremity; amputation.

The decision on whether to proceed with amputation or reconstruction of a mangled extremity is perhaps one of the most difficult for civilian trauma surgeons, as these types of injuries are seen relatively infrequently. Factors considered in the decision-making process include patient's age, physiologic condition at presentation, associated injuries, soft tissue factors, and the potential for salvaging a useful limb.[1] The Mangled Extremity Severity Score (MESS) was developed 25 years ago at Harborview Medical Center in Seattle by Johansen et al.[2] in an attempt to create a tool that accurately predicted the need for amputation. The MESS takes into consideration the degree of skeletal and soft tissue injury, limb ischemia, the presence of shock, patient's age, and ischemia time. It has been widely used since its inception despite continued questions over its prognostic accuracy. The use of this scoring system, or any other such scoring system, is further questioned given the major advances that have been made in the management of severely mangled extremities, including increased use of tourniquets in both civilian and military settings, numerous new hemostatic agents, advanced tissue transfer techniques, and novel vascular interventions.

In 2013, the AAST Multicenter Trials Committee initiated a prospective registry designed to collect data specific to vascular injuries. The PROspective Observational Vascular Injury Treatment (PROOVIT) registry includes extensive treatment and outcome data from multiple major trauma centers with the aim of informing practice and protocols to improve outcomes.[3] The purpose of our study was to use the PROOVIT database to re-evaluate the MESS on data collected prospectively in modern times. The hypothesis was that MESS would be predictive of the need for amputation.

METHODS

Patient data were collected from the AAST Multicenter PROspective Observational Vascular Injury Treatment (PROOVIT) registry. The details describing this large database have been previously described. In brief, it is a prospectively collected

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TABLE 1. Mangled Extremity Severity Score (MESS) Components Prospectively Collected in the PROOVIT Registry

A. Skeletal/Soft tissue injury
1. Low energy (stab wound, simple fracture, low-energy gunshot wound)
2. Medium energy (open or multiple fractures, dislocation)
3. High energy (high-speed motor vehicle collision or rifle gunshot wound)
4. Very high energy (above plus gross contamination)
B. Limb ischemia*
1. Pulse reduced or absent but perfusion normal
2. Pulseless; paresthesia, diminished capillary refill
3. Cool, paralyzed, insensate, numb
C. Shock
0. Systolic blood pressure always > 90 mm Hg
1. Systolic blood pressure transiently < 90 mm Hg
2. Systolic blood pressure persistently < 90 mm Hg
D. Age (years)
0. <30
1. 30–50
2. >50

*Score doubled for ischemia time > 6 hours.

database of injuries to named arterial and venous structures from 14 Level I trauma centers across the country.[3] The database includes patients' demographics, mechanism of injury, concomitant injuries, and intraoperative and postoperative variables for patients entered during the index hospital stay only. The database is actively accruing data from follow-up clinic visits and readmissions, and these data were not included in this study.

Lower extremity named arterial injuries were identified between February 2013 and August 2015. Each component of the MESS was obtained prospectively during data collection using the scoring system shown in Table 1. The MESS was calculated for each patient by adding the numerical scores of the skeletal/soft tissue injury, limb ischemia, shock, and age scores. If there were greater than 6 hours of ischemia time, the ischemia score was doubled. There were 57 patients in which one component of the MESS (skeletal/soft tissue injury, shock, or ischemia) was missing. The missing data were found to be missing at random with $p = 0.59$ compared to the nonmissing variable of age. The missing data were then treated using multiple imputation with 20 imputations. There was no difference in the correlation of MESS or its components before or after use of multiple imputation, suggesting that the bias imposed by the missing data is minimal. The percentage increase in standard error due to the missing values was 6.9% for MESS, 0.03% for shock, 0.02% for skeletal score, and 0.6% for ischemia score.

A MESS of 8 was chosen based on a prior study from the original creators of the scoring system, who suggested in their 2016 publication that a threshold of 8 was more appropriate in a modern setting.[4] A receiver operating characteristic (ROC) analysis was performed, which demonstrated that a MESS of 5 was a better balance of sensitivity and specificity than a MESS of 8. The ROC curves can be found in Figure 1.

Statistical analysis was performed using SAS version 9.4 (SAS Institute Inc, Cary, NC, USA). Univariable logistic regression was used to look at the correlation of the MESS, as well as each MESS component, with the risk of amputation. Odds ratios comparing amputation versus limb salvage were generated. Age, sex, injury mechanism (blunt, penetrating, or mixed blunt and penetrating), injury type (transection, flow-limiting lesion, occlusion, pseudoaneurysm, or other), arterial injury location (femoral, popliteal, below-popliteal arteries, or multilevel injury), use of shunting, prehospital tourniquet use, fasciotomy performed at any time during the admission, injury severity score (ISS), and concomitant vein, nerve, or orthopedic injury were assessed for confounding. Of note, the database did not distinguish the severity of vein, nerve, or orthopedic injury; it reports a binary value of injured or not injured. Independent predictors of amputation were identified by univariable logistic regression. Significant variables ($p \leq 0.1$) were injury mechanism, the presence of a transection, arterial injury location, ISS, concomitant nerve, or orthopedic injury. A multivariable logistic regression with these confounders was performed of the MESS, and separately of the MESS components, with the binary outcome of amputation compared to limb salvage. These were performed separately due to the confounding nature of including both MESS and its components in the same model. The area under the receiver operating characteristic (AUROC) curve for the logistic regression model including MESS was 0.86 [95% confidence interval [CI], 0.79–0.93]. The Hosmer-Lemeshow goodness-of-fit test had a $p = 0.93$. The AUROC for the model, which included the components age score, skeletal score, ischemia score, and shock score was 0.88 [95% CI, 0.82–0.94], and the

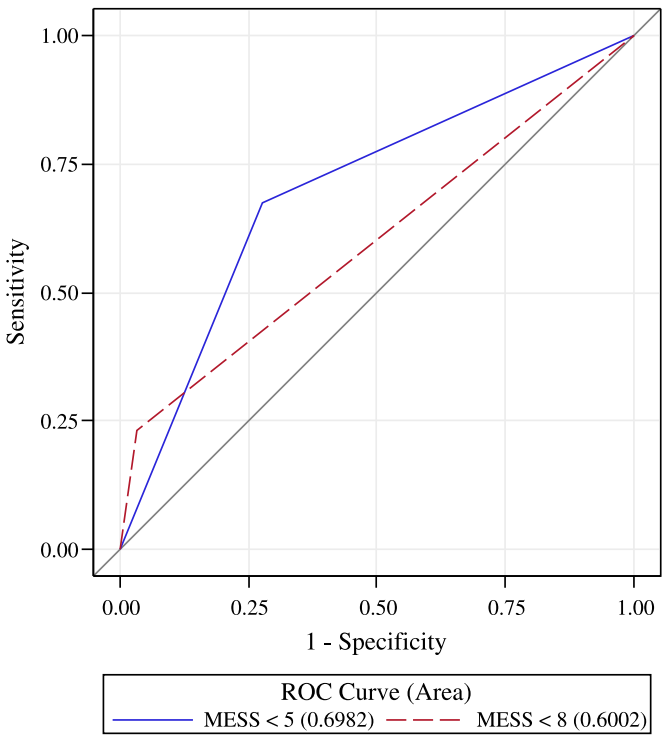

Figure 1. Receiver operator characteristic (ROC) curve for a MESS cutoff of 5 versus 8. A MESS cutoff of 5 was found to have the best balance of sensitivity and specificity, however, only was predictive of MESS in 20.2% of patients. A MESS of 8 was predictive of amputation in 43.2% of patients.

Hosmer-Lemeshow was nonsignificant with $p = 0.29$. The probability of amputation was modeled using univariable logistic regression to predict amputations with a MESS cutoff of 5 and 8. Finally, demographics of patients with the MESS cutoff of 8 were compared using Wilcoxon rank-sum test and Fisher exact test. A $p < 0.05$ was considered statistically significant.

RESULTS

Between February 2013 and August 2015, 230 patients with lower extremity arterial injuries were entered into the PROOVIT registry. The cohort consisted predominantly of men (87.8%) with an average age of 34 ± 15.3 years (range, 4–92 years). The mechanism of injury was reported as blunt in 109 patients (47.4%), penetrating in 114 patients (49.6%), and mixed blunt and penetrating in the remainder (Table 2). Isolated femoral injuries were found in 102 patients (44.3%) and isolated popliteal injuries in 60 patients (26.1%). Sixty-three injuries to arteries distal to the popliteal artery were identified (27.4%), and five injuries were to both the above- and below-knee arterial beds. The injury to the artery was most often a transection, present in 45.7% of patients. There were 50 concomitant venous injuries (21.7%). Ninety-four percent of these venous injuries were repaired at the time of initial operation and the remainder ligated. There were 94 concomitant orthopedic injuries (40.9%) and 33 nerve injuries (14.4%).

Twenty-two patients had a prehospital tourniquet applied (9.6%). Ninety-four (40.9%) fasciotomies were performed during the index hospitalization, including 40 prophylactic fasciotomies at the initial procedure, 48 therapeutic fasciotomies at the initial procedure, and 5 delayed fasciotomies (one was not categorized). A temporary shunt was used for damage control in 17 patients (7.4%).

We modeled the probability of amputations based on MESS and determined that MESS greater than or equal to 8 was predictive of in-hospital amputation in only 43.2% of patients. Receiver operating characteristic analysis (Fig. 1) showed the best balance of sensitivity and specificity was a MESS of 5 (AUROC, 0.70 [95% CI, 0.62–0.77]) compared to a MESS of 8 (AUROC, 0.60 [95% CI, 0.54–0.67]; $p = 0.02$). However, a MESS of 5 was only predictive of amputation in 20.2% of cases. Based on prior studies and this increase in ability to predict amputation, a MESS of 8 was chosen for further analysis. Sixteen patients had a MESS of greater than or equal to 8 (7.0%). The median MESS was 4 (25th percentile (Q1), 3; 75th percentile (Q3), 6). The median skeletal injury component score was 2 (1, 3), the median ischemia score was 2 (1, 2), the median shock score was 0 (0, 1), and the median age score was 1 (0, 1). Patients with a MESS of 8 or greater were on average older (48.3 years old vs 32.8, $p < 0.0003$), and were more likely to have sustained a blunt injury (81.3% vs 44.9%, $p = 0.004$). Patients with a MESS of 8 or greater had a higher median ISS (21 vs 10.5, $p = 0.0003$), although they had no difference in mean abbreviated injury score of the extremity, admission systolic blood pressure, or GCS (Table 2). There were more concomitant nerve (68.8% vs 10.3%, $p < 0.001$) and orthopedic injuries (68.8% vs 38.8%, $p = 0.02$) when MESS was greater than or equal to 8. There was no difference in concomitant venous injuries between the groups (Table 2).

Primary or secondary amputations were performed in 43 patients (18.7%, median MESS, 6 (4, 8)), including 21 primary amputations performed for damage control (9.1%). Limbs were ultimately salvaged in 187 patients (81.3%; median MESS, 4 (3, 5); $p < 0.001$; Table 3). There were 12 deaths (5.2%) in the total cohort.

Univariable logistic regression was performed, looking at age, sex, injury mechanism, injury type, arterial injury location, use of shunting, prehospital tourniquet use, fasciotomy performed at any time during the admission, ISS, and concomitant vein, nerve, or orthopedic injury for confounding. Blunt injuries were associated with amputation with an odds ratio of 6.4 [95% CI, 2.7–15.1] compared to penetrating injuries ($p < 0.0001$). Transection was associated with amputation with an odds ratio of 2.4 [95% CI, 1.2–4.7] ($p = 0.014$). Popliteal arterial injuries were associated with a 6.8-fold higher risk of amputation than femoral arterial injuries [95% CI, 2.7–17.3] ($p < 0.001$). Injury severity score

TABLE 2. Comparison of Demographics Between Patients with Mangled Extremity Severity Score (MESS) < 8 and MESS ≥ 8

		MESS Score		
	All	MESS < 8	MESS ≥ 8	
Variable	(n = 230)	(n = 214)	(n = 16)	p
Age, mean ± SD	34 ± 15.3	32.8 ± 14.7	48.3 ± 15.6	0.0003
Male, n (%)	202 (87.8)	187 (87.4)	15 (93.8)	0.4
Injury mechanism				0.004
Blunt, n (%)	109 (47.4)	96 (44.9)	13 (81.3)	
Penetrating, n (%)	114 (49.6)	112 (52.3)	2 (12.5)	
Mixed blunt and penetrating, n (%)	7 (3.0)	6 (2.8)	1 (6.3)	
Injured artery:				0.7
Femoral, n (%)	102 (44.3)	97 (45.3)	5 (31.3)	
Popliteal, n (%)	60 (26.1)	55 (25.7)	5 (31.3)	
Distal to popliteal artery, n (%)	63 (27.4)	57 (26.6)	6 (37.5)	
Multiple levels, n (%)	5 (2.2)	5 (2.3)	0 (0)	
Transection, n (%)	105 (45.7)	93 (43.5)	12 (75)	0.01
Flow-limiting defect, n (%)	44 (19.1)	42 (19.6)	2 (12.5)	0.4
Occlusion, n (%)	38 (16.5)	36 (16.8)	2 (12.5)	0.5
Pseudoaneurysm, n (%)	9 (3.9)	9 (4.2)	0 (0)	0.5
Other injury type, n (%)	41 (17.8)	40 (18.7)	1 (6.3)	0.2
Median ISS (Q1, Q3)	11 (9, 19)	10.5 (9, 18)	21 (17, 26)	0.0003
Median AIS-extremity (Q1, Q3)	3 (3, 4)	3 (3, 4)	3 (3, 4)	0.1
Mean admission SBP ± SD	120.9 ± 30.0	121.4 ± 29.9	115.9 ± 31.7	0.5
Median GCS (Q1, Q3)	15 (14, 15)	15 (15, 15)	15 (14, 15)	0.7
Concomitant venous injury, n (%)	50 (21.7)	46 (21.5)	4 (25)	0.5
Vein repaired, n (%)	47/50 (94.0)	43/46 (93.4)	4/4 (100%)	0.4
Concomitant nerve injury, n (%)	33 (14.4)	22 (10.3)	11 (68.8)	<0.001
Concomitant orthopedic injury, n (%)	94 (40.9)	83 (38.8)	11 (68.8)	0.02
Prehospital tourniquet, n (%)	22 (9.6)	20 (9.4)	2 (12.5)	0.5
Temporary shunt used, n (%)	17 (7.4)	17 (7.9)	0 (0)	0.3
Fasciotomy, n (%)	94 (40.9)	89 (41.6)	5 (31.3)	0.3

Q1, lower quantile (25th percentile).
Q3, upper quantile (75th percentile).
AIS, abbreviated injury score; GCS, Glasgow coma score; SBP, systolic blood pressure.

TABLE 3. Mangled Extremity Severity Score (MESS) Elements Compared Between Patients Who Underwent Amputations and Those Who Did Not; Before and After Adjustment for Significant Confounders of Injury Mechanism, Arterial Transection, Arterial Injury Location, ISS, and Concomitant Nerve and Orthopedic Injuries

MESS Elements	Amputations Median (Q1, Q3) (n = 43)	Limb Salvage Median (Q1, Q3) (n = 187)	*p* Value Unadjusted	*p* Value Adjusted
Skeletal/Soft tissue score	3 (2, 3)	1 (1, 3)	<0.001	0.50
Limb ischemia	2 (1, 3)	1 (1, 2)	<0.001	0.79
Shock	0 (0, 1)	0 (0, 1)	0.21	0.20
Age score	1 (0, 1)	1 (0, 1)	0.22	0.22
Total MESS	6 (4, 8)	4 (3, 5)	<0.001	0.18

Q1, lower quantile (25th percentile).
Q3, upper quantile (75th percentile).

was only weakly associated with amputation with an odds ratio of 1.02 [95% CI, 1.00–1.05] ($p = 0.08$). Concomitant nerve and orthopedic injuries were associated with amputation with an odds ratio of 11.6 [95% CI, 5.1–26.5] and 6.8 [95% CI, 3.2–14.7], respectively ($p < 0.0001$ for each). Age, sex, use of shunting, prehospital tourniquet use, fasciotomy performed at any time during the admission, and concomitant vein injury were not significantly associated with amputation and were not included in the final model. After controlling for confounding factors, the overall MESS and its components were no longer different between salvaged and amputated limbs (Table 3). After adjustment, concomitant nerve injury was the only factor that remained an independent predictor of amputation (odds ratio, 6.9 [95% CI, 2.3–21.2]; $p = 0.001$).

A MESS of 8 or greater was associated with a longer stay in the hospital (median, 22.5 (15, 29) vs 12 (6, 21); $p = 0.006$) and intensive care unit (6 (2, 13) vs 3 (1, 6), $p = 0.03$). There was a higher percentage of both primary traumatic amputations performed for damage control (50.0% vs 6.1%, $p < 0.001$) and overall amputations (62.5% vs 15.4%, $p < 0.001$) in the group of patients with a MESS of 8 or greater. There was no statistically significant difference in the number of re-interventions or in death between the groups (Table 4).

DISCUSSION

The original MESS was developed in 1990 by a retrospective review of 25 consecutive patients with lower extremity injuries.[2] The same authors subsequently applied the scoring system to a group of 26 comparable patients studied prospectively. In the original study, the MESS for salvaged limbs ranged from 3 to 6, whereas the MESS for the amputated limbs ranged from 7 to 12. These authors concluded that in their hands, a MESS of 7 or greater predicted amputation with 100% accuracy. Subsequent authors were unable to obtain this degree of accuracy and developed alternative scoring systems. These systems include the Limb Salvage Index; the Predictive Salvage Index; the Nerve Injury, Ischemia, Soft-tissue Injury, Skeletal Injury, Shock and Age of Patient Score (NISSA); and the Hannover Fracture Scale.[1] Each contains various elements of patients' characteristics at presentation (e.g., age, presence of shock), structural injury (e.g., concomitant bone, muscle, skin, nerve, vascular, injury, degree of contamination), and treatment factors (e.g., warm ischemia time, time to treatment).[5–8] These five scoring systems were prospectively evaluated in 2001 by Bosse et al.[9] as part of the Lower Extremity Assessment Project (LEAP) study group. A total of 556 high-energy injuries were evaluated including ischemic limbs, type III-A, III-B, and III-C tibial fractures, severe distal tibial fractures (open pilon fractures or type III-B ankle fractures), hindfoot fractures, and isolated soft tissue injuries of the lower extremities. This extensive analysis could not validate the clinical use of any of these scoring systems. The scores did have high specificity in predicting limb-salvage potential but had a low sensitivity in predicting the need for amputation. A subsequent study by the LEAP group showed that none of these scoring systems were predictive of functional recovery in patients who underwent successful limb reconstruction.[10]

Recent re-evaluations of the MESS have continued to question its validity. Menakuru et al.[11] found that of 148 patients, a MESS greater than 7 had a sensitivity of only 44% and a specificity of 70% in predicting amputation. Recent systematic reviews further confirm the unreliability of the MESS. Fodor et al.[12] concluded that MESS correctly identified the need for amputation in only 25% of cases, whereas Schiro et al.[13] found the range of reported accuracy of a MESS greater than 7 to be anywhere between zero percent and 93.4% in the literature. The MESS has also been evaluated in combat-related injuries. Sheean et al.[14] reported on 155 patients treated for type III open tibia fractures in US military service personnel, involving primarily blast injuries. One hundred ten had successful limb salvage, and 45 underwent primary amputation. The mean MESS values for amputees was 5.8 and for those that were salvaged was 5.3 ($p = 0.057$). The sensitivity and specificity of a MESS of 7 or greater in predicting the need for amputation in the combat setting were 35% and 87.8%, respectively (positive predictive value of 50%). These military surgeons concluded that the MESS was not useful in battlefield-related injuries. Additional studies on

TABLE 4. Comparison of Outcomes Between Patients with MESS < 8 and MESS ≥ 8

	All (n = 230)	MESS < 8 (n = 214)	MESS ≥ 8 (n = 16)	*p*
Total units packed red blood cells, median (Q1, Q3)	3 (0, 8)	3 (0, 8)	8 (2.5, 10)	0.07
Hospital length of stay, median (Q1, Q3)	12 (6, 22)	12 (6, 21)	22.5 (15, 29)	0.006
Days in Intensive Care Unit, median (Q1, Q3)	3 (1, 6)	3 (1, 6)	6 (2, 13)	0.03
Reintervention required, n (%)	35 (15.2)	32 (15)	3 (18.8)	0.5
Damage control primary traumatic amputation, n (%)	21 (9.1)	13 (6.1)	8 (50)	<0.001
All amputations, n (%)	43 (18.7)	33 (15.4)	10 (62.5)	<0.001
Death, n (%)	12 (5.2)	10 (4.7)	2 (12.5)	0.2

Q1, lower quantile (25th percentile).
Q3, upper quantile (75th percentile).

battlefield-related extremity vascular injuries did find that those with preserved limbs but high MESS scores (≥7) had higher levels of dysfunction as rated with the Short Musculoskeletal Function Assessment tool.[15]

In another contemporary analysis of the mangled lower extremity, de Mestral et al.[16] retrospectively examined a cohort of patients entered into the National Trauma Databank between 2007 and 2009. A total of 1354 patients were identified, with a 21% amputation rate. These authors found that the presence of a severe head injury, shock in the emergency department, and a high-energy mechanism of injury were associated with early amputation. Unfortunately, the National Trauma Databank does not contain sufficient data to accurately calculate the MESS score, which is why the PROOVIT database project is so important. A recent study from Austria looked at early failed attempts at salvage in open lower limb fractures demonstrating that in addition to MESS, other important predictors of secondary amputations included complex fractures, severe soft tissue damage, and the need for fasciotomy.[17] In 60% of these patients, failed limb salvage resulted from infectious complications and 40% from a failed vascular reconstruction.

In 2015, Aarabi et al. from Seattle presented their data on the use of MESS 25 years after its creation. In their series of 48 patients with mangled extremities complicated by acute arterial insufficiency, 81% were salvaged (MESS mean of 4.8) and 19% required amputation (MESS mean of 9.1).[4] In their series, the 77% of those who went on to secondary amputation had a popliteal artery injury. These authors also reported that MESS independently predicted the cost and length of hospitalization; on average, for every 1-point increase in MESS, the hospital cost increased by almost $6000.

Our study found blunt injuries, vessel transection, popliteal injuries, and concomitant nerve and orthopedic injuries were associated with the need for amputation, and were more predictive than an isolated MESS score. Although patients who underwent limb salvage had a lower MESS score on average, this was not significant after adjustment for confounders. Mangled Extremity Severity Score was a very poor predictor of amputation in this cohort, predicting only 43.2% of amputations.

This analysis includes 10 patients who died without receiving an amputation. The PROOVIT database does not distinguish if the limb was viable when the patient died, but these are included in the limb salvage category, representing a potential confounding variable. Mangled limbs without arterial injuries are not included in the PROOVIT database. In addition, although these data were prospectively obtained, incomplete or inaccurate data entry is an inherent flaw across all database studies. In this study, patients with missing MESS components were included as missing, meaning that some patients could have a falsely low total MESS. This was evaluated by correcting the missing values using multiple imputation, and no difference was found in the analysis. The increase in standard error was minimal for the missing component analysis and 6.9% for overall MESS. The missing data were also found to be missing at random compared to nonmissing variables; and thus, we conclude that although bias may be present, it is minimal for this study. Furthermore, this study reflects modern practice only among major Level I academic institutions across the country. Practice patterns of the larger enrolling centers may have dictated some of the trends observed.

While our data are robust, prospectively collected, and this series is relatively large, we do acknowledge that future investigations will need to examine the long-term outcomes of the patients with salvaged limbs. Late amputations (performed after the first hospitalization) may be required for limb dysfunction, persistent infections/open wounds, or in patients with chronic pain, as these problems can contribute to significant physical, psychological, financial, and social distress for these patients.[18] As the LEAP study group has demonstrated, in selected patients, the long-term quality of life may be the same in those with amputations and successful prosthetics, as it is in patients with limb salvage.[19]

Prehospital use of a tourniquet, damage control, balanced resuscitation, use of vascular shunts to reduce ischemia time, early fasciotomy, aggressive wound care, microsurgical abilities, and advanced tissue coverage techniques have all contributed to our increased ability to care for patients with mangled extremities. At this juncture, we advocate for the use of a team approach to decision making regarding limb salvage rather than the use of a score. Experienced surgeons from vascular, trauma, orthopedic, and plastic surgical disciplines evaluating the patient at the bedside and the patient's limb collaboratively ultimately contributes to the best outcome for the patient and for the extremity. Additionally, continued re-evaluation in the hospital and after discharge with long-term functional outcome data is needed to inform practice decisions and to assure the best quality of life for individual patients with limb-threatening mangled extremities.

AAST PROOVIT STUDY GROUP

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M.N.L., A.S., J.D., M.M.K. contributed to study design, literature search, data analysis, data interpretation, manuscript writing, and critical revision of the manuscript. C.-S.L., Y.L., contributed to study design, data analysis, and critical revision of the manuscript. S.S., T.S., J.B.H., T.E.R. contributed to study design, data collection, data interpretation, and critical revision of the manuscript. AAST PROOVIT Study Group contributed to data collection and critical revision of the manuscript.

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DISCLOSURE

The authors declare no conflicts of interest.

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Systemic anticoagulation in the setting of vascular extremity trauma

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ABSTRACT

Introduction: There is conflicting data regarding if patients with vascular extremity trauma who undergo surgical treatment need to be systematically anticoagulated. We hypothesized that intraoperative systemic anticoagulation (ISA) decreased the risk of repair thrombosis or limb amputation after traumatic vascular injury of the extremities.

Methods: We analyzed a composite risk of repair thrombosis and/or limb amputation (RTLA) between patients who did and did not undergo ISA during arterial injury repair. Patient data was collected in the American Association for the Surgery of Trauma PROspective Vascular Injury Treatment (PROOVIT) registry. This registry contains demographic, diagnostic, treatment, and outcome data.

Results: Between February 2013 and August 2015, 193 patients with upper or lower extremity arterial injuries who underwent open operative repair were entered into the PROOVIT registry. The majority were male (87%) with a mean age of 32.6 years (range 4–91) and 74% injured by penetrating mechanism. 63% of the injuries were described as arterial transection and 37% had concomitant venous injury. 62% of patients underwent ISA. RTLA occurred in 22 patients (11%) overall, with no significant difference in these outcomes between patients who received ISA and those that did not (10% vs. 14%, $p = 0.6$). There was, however, significantly higher total blood product use noted among patients treated with ISA versus those that did not receive ISA (median 3 units vs. 1 unit, $p = 0.002$). Patients treated with ISA also stayed longer in the ICU (median 3 days vs. 1 day, $p = 0.001$) and hospital (median 9.5 days vs. 6 days, $p = 0.01$).

Discussion: In this multicenter prospective cohort, intraoperative systemic anticoagulation was not associated with a difference in rate of repair thrombosis or limb loss; but was associated with an increase in blood product requirements and prolonged hospital stay. Our data suggest there is no significant difference in outcome to support use of ISA for repair of traumatic arterial injuries.

Background

Routine intraoperative systemic anticoagulation (ISA) is a mainstay of therapy in elective arterial reconstruction and treatment of acute limb ischemia [1]. In the setting of trauma, surgeons have been reluctant or unable to systemically anticoagulate patients when performing arterial repair due to concern for potential local and systemic bleeding [2]. It is unclear if the improved patency seen with elective vascular repair can be generalized to traumatic arterial repair, particularly in patients

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with acute traumatic coagulopathy or resuscitation-associated coagulopathy. There is limited and conflicting retrospective data in the literature correlating improved patency or limb salvage with use of ISA during traumatic arterial injury repair [3–9]. Retrospective reviews of patients who received ISA during lower extremity arterial injury repair report a limb salvage rate of 85–91% [2,5,7,8]. Other reviews, however, report lower limb salvage rates of 83–84% with similar injuries, despite routinely not giving ISA [4,10]. Comparative studies have shown no statistically significant difference in outcome between patients who are given ISA and those who are not [6,7]. Proponents, however, argue that the risks of ISA are minimal, and may decrease the risk of distal in situ thrombus or microvascular thrombosis [5,9]. We hypothesized that intraoperative systemic anticoagulation (ISA) decreased the risk of repair thrombosis or limb amputation (RTLA) after traumatic vascular injury of the extremities.

Methods

Patient data was collected from the American Association for the Surgery of Trauma (AAST) Multicenter PROspective Observational Vascular Injury Treatment (PROOVIT) registry. The details of this registry have been previously described [11]. This is a prospectively-collected database of injuries to named arterial and venous structures from fourteen Level I trauma centers across the United States. The database includes demographic, diagnostic, treatment, and outcome data for the index hospital stay. The registry is accruing data from clinic and readmission follow up.

Patients with upper or lower extremity arterial injuries who underwent open arterial revascularization between February 2013 and August 2015 were identified. Patients treated with arterial ligation, primary traumatic amputation, endovascular repair or embolization were excluded. Arterial injuries to the upper extremity utilized for analysis included individual injuries to the brachial or distal forearm arteries. The rare combined brachial and radial artery injuries were categorized as brachial artery injuries. Arterial injuries to the lower extremity included individual injuries to the femoral, popliteal or distal to the popliteal artery. Method of repair included autologous conduit, synthetic interposition or bypass graft and primary repair. Patients treated with vein interposition or bypass, vein patch or autologous artery as a conduit were included in the autologous category. ISA was defined as systemic anticoagulation with unfractionated heparin (UFH) utilized during the initial operation or vascular repair. Intraoperative regional anticoagulation was not included in this study. The total mangled extremity severity score (MESS) was calculated

Table 1
Demographics of included patients, analyzed by intraoperative anticoagulation status.

		Intraoperative Systemic Anticoagulation		
Factor	All	Received	Not Received	p-value
Mean age (SD)	32.6 (15.3)	32.2 (15.1)	33.4 (15.7)	0.6*
Male, n (%)	167/193 (87)	109/119 (92)	58/74 (78)	0.02†
Injury mechanism				0.5†
Blunt, n (%)	47/193 (24)	32/119 (27)	15/74 (20)	
Penetrating, n (%)	142/193 (74)	85/119 (71)	57/74 (77)	
Mixed blunt and penetrating, n (%)	4/193 (2)	2/119 (2)	2/74 (3)	
Specific mechanism				0.5†
Gunshot, n (%)	80/193 (42)	53/119 (45)	27/74 (37)	
Stabbing, n (%)	29/193 (15)	16/119 (13)	13/74 (18)	
Motor Vehicle Collision, n (%)	25/193 (13)	17/119 (14)	8/74 (11)	
Other, n (%)	59/193 (31)	33/119 (28)	26/74 (35)	
Injury description				0.5†
Flow limiting defect, n (%)	33/193 (17)	22/119 (19)	11/74 (15)	
Occlusion, n (%)	24/193 (12)	18/119 (15)	6/74 (8)	
Pseudoaneurysm, n (%)	6/193 (3)	3/119 (3)	3/74 (4)	
Transection, n (%)	121/193 (63)	71/119 (60)	50/74 (68)	
Other injury type, n (%)	9/193 (5)	5/119 (4)	4/74 (5)	
Median ISS (Q1, Q3)	9 (9, 16)	10 (9, 16)	9 (5, 16)	0.1§
Mean admission SBP (SD)	120.9 (28.5)	120.5 (29.8)	121.6 (26.6)	0.8*
Median GCS (Q1, Q3)	15 (15, 15)	15 (15, 15)	15 (15, 15)	0.7§
Median AIS-extremity (Q1, Q3)	3 (3, 3)	3 (3, 3)	3 (2, 3)	0.06§
Median MESS (Q1, Q3)	4 (3, 6)	4 (3, 6)	4 (3, 5)	0.08§
Median Skeletal/Soft tissue Score (Q1, Q3)	1 (1, 2)	1 (1, 2)	1 (1, 1)	0.1§
Median Limb Ischemia Score (Q1, Q3)	1 (1, 2)	2 (1, 2)	1 (1, 1)	<0.001§
Median Shock Score (Q1, Q3)	0 (0, 1)	0 (0, 1)	0 (0, 1)	0.9§
Median Age Score (Q1, Q3)	0 (0, 1)	0 (0, 1)	1 (0, 1)	0.3§
Concomitant vein injury, n (%)	71/193 (37)	44/119 (37)	27/74 (37)	0.9†
Vein repaired, n (%)	63/71 (89)	40/44 (91)	23/27 (85)	0.7†
Concomitant nerve injury, n (%)	63/193 (33)	31/119 (26)	32/74 (43)	0.02‡
Concomitant orthopedic injury, n (%)	66/193 (34)	43/119 (36)	23/74 (31)	0.6†

ISS = Injury severity score.
AIS = Abbreviated injury score.
SBP = Systolic blood pressure.
GCS = Glasgow coma score.
MESS = Mangled extremity severity score.
SD = standard deviation.
Q1 = Lower quantile (25th percentile).
Q3 = Upper quantile (75th percentile).
* Two-tailed *t*-test.
† Pearson's Chi-square.
‡ Chi-square with Yates' continuity correction.
§ Wilcoxon Rank-Sum.

as originally described by Johansen et al., from the prospectively obtained components described in Appendix B in the Supplementary material [12].

The primary endpoint was a composite risk of RTLA during the index admission, between patients who did and did not undergo ISA during arterial injury repair. Secondary endpoints included need for reintervention after initial operation for any reason, total units of packed red blood cells (PRBC) required in the first 24 h, length of intensive care unit (ICU) stay and length of total hospital stay.

Statistical analysis was performed using Stata Version 14.1 (StataCorp, College Station, TX, USA). Differences in demographics for patients who received ISA and were compared using the Wilcoxon rank-sum test for ordinal variables and two-sample *t*-test for continuous variables. The Fisher's exact test was used for 2×2 contingency tables with 20 or less patients in any category. P-values are reported as double the 1-sided exact probability. Pearson's chi-squared test with Yates' correction for continuity was used for 2×2 contingency tables when there were between 21 and 40 patients in a given category. Pearson's chi-squared test was used for all larger contingency tables. A p-value < 0.05 was considered statistically significant.

Results

Between February 2013 and August 2015, 193 patients with upper or lower extremity arterial injuries who underwent open arterial repair were entered into the PROOVIT registry from 14 Level-1 trauma centers. The 14 centers contributed between 1 and 52 patients each (mean 13.8, median 4), with five centers being the largest contributors with over 25 patients each. ISA was given to 119 patients in total (62%). The patients were predominantly male, with a mean age of 32.6 years (range 4–91, Table 1). Men were more likely to receive ISA than women (92% ISA were male vs. 78% without ISA were male, p = 0.02). Most injuries were penetrating in nature (74%), and were most often caused by gunshot wounds (42%). The injury identified was most often a transection (63%). There were no differences in ISS, admission systolic blood pressure, or Glasgow coma score (GCS) between patients who received ISA and those who did not. There was a trend towards higher AIS-extremity in patients who received ISA compared to those who did not, but it did not reach statistical significance (median of 3 (25th percentile (Q1) – 75th percentile (Q3) 3–3) vs. 3 (Q1–Q3 2–3), p = 0.06). MESS did not differ between patients who received ISA than those who did not (median of 4 (Q1–Q3 3–6) vs. 4 (Q1–Q3 3–5), p = 0.08). When each component was analyzed individually, however, patients who received ISA had a higher limb ischemia score compared to those who did not (median of 2 (Q1–Q3 1–2) vs. 1 (Q1–Q3 1-1), $p < 0.001$).

In total, there were 71 concomitant venous injuries (37%), of which 63 were repaired (89%). The remaining 8 injured veins were ligated. Sixty-three patients had concomitant nerve injuries (33%), and 66 patients had associated orthopedic injury (34%). There were no significant differences in concomitant venous or orthopedic injuries between patients who received ISA and those who did not. Patients with concomitant nerve injuries were less likely to receive ISA (26% with ISA vs. 43% without, p = 0.02).

Forty-three patients had a pre-hospital tourniquet placed (22%). Most patients had an ischemia time (from time of injury to time of definitive repair) between 3 and 6 h (54%, Table 2). Damage-control temporary shunt placement was used in 9 patients (5%), 8 of whom received ISA. Arterial repair with autologous conduit was performed in 103 patients (53%), including 100 vein interposition or bypass grafts, 2 vein patches and one autologous artery used as conduit. The artery was repaired primarily in 81 patients (42%), and with synthetic graft in 8 patients (4%). Patients who underwent a repair with any autologous conduit were more likely to receive ISA than not (62% vs. 39%, p = 0.001). Twenty-eight patients (15%) required a revision of the arterial repair during the initial operation (Table 2). There was no difference in administration of ISA in patients who required immediate revision (17% with ISA vs 11% without, p = 0.3). Extremity fasciotomies were performed in 78 patients, including 13 involving the upper extremity. Patients who underwent fasciotomy at any time during the initial hospitalization were more likely to have received ISA than not (48% vs. 28%, p = 0.01). Patients who had an operative time of greater than 6 h were more likely to receive ISA than not (10% vs. 5%, p = 0.04).

There were 96 and 97 injuries to the upper and lower extremity, respectively. There were no combined upper and lower extremity injuries, and no combined above- and below-knee arterial injuries. There were two combined brachial and radial injuries. ISA was given for popliteal arterial injuries in 84% (26/31) of cases, in 67% (39/58) of femoral and in only 38% (3/8) of below-popliteal injuries

Table 2
Management of injuries, analyzed by intraoperative anticoagulation status.

Factor	All	Intraoperative Systemic Anticoagulation		p-value
		Received	Not Received	
Pre-hospital Tourniquet, n (%)	43/193 (22)	24/119 (20)	19/74 (26)	0.4‖
Time from Injury to Repair				0.4†
Less than 3 h, n (%)	41/193 (21)	23/119 (19)	18/74 (24)	
3–6 h, n (%)	104/193 (54)	71/119 (60)	33/74 (45)	
Greater than 6 h, n (%)	33/193 (17)	20/119 (17)	13/74 (18)	
Temporary shunt utilized, n (%)	9/193 (5)	8/119 (7)	1/74 (1)	0.2‖
Repair Method				0.001†
Autologous repair, n (%)	103/193 (53)	74/119 (62)	29/74 (39)	
Primary repair, n (%)	81/193 (42)	38/119 (32)	43/74 (58)	
Synthetic graft utilization, n (%)	8/193 (4)	7/119 (6)	1/74 (1)	
Immediate revision required intraoperatively, n (%)	28/193 (15)	20/119 (17)	8/74 (11)	0.3‖
Fasciotomy, n (%)	78/193 (40)	57/119 (48)	21/74 (28)	0.01‡
Intraoperative time				0.04†
Less than 3 h, n (%)	78/193 (40)	42/119 (35)	36/74 (49)	
3–6 h, n (%)	84/193 (44)	60/119 (50)	24/74 (32)	
Greater than 6 h, n (%)	16/193 (8)	12/119 (10)	4/74 (5)	

† Pearson's Chi-square.
‡ Chi-square with Yates' continuity correction.
‖ 1-tailed Fisher's exact test, doubled.

Table 3
Analysis of intraoperative anticoagulation status and outcome, by artery injured.

			Amputations		RTLA	
Artery Injured	Total Injuries	ISA Received	ISA Received	ISA Not Received	ISA Received	ISA Not Received
Brachial artery, n (%)	47/193 (24)	32/47 (68)	0/32 (0)	0/15 (0)	3/32 (9)	2/15 (13)
Forearm arteries, n (%)	49/193 (25)	19/49 (39)	1/19 (5)	0/30 (0)	1/19 (5)	1/30 (3)
Femoral artery, n (%)	58/193 (30)	39/58 (67)	2/39 (5)	2/19 (11)	4/39 (10)	3/19 (16)
Popliteal artery, n (%)	31/193 (16)	26/31 (84)	4/26 (15)	1/5 (20)	4/26 (15)	3/5 (60)
Distal to popliteal, n (%)	8/193 (4)	3/8 (38)	0/3 (0)	1/5 (20)	0/3 (0)	1/5 (20)

RTLA = Repair thrombosis and/or amputation.
ISA = intraoperative systemic anticoagulation.

($p < 0.001$, Table 3). The total limb salvage rate was 94% (182/193). Popliteal artery injuries had the lowest rate of limb salvage (84%, 26/31). Lower extremity amputations were more frequent than upper extremity amputations (10% of lower extremity injuries (10/97) vs. 1.0% of upper (1/96), $p = 0.005$). Rates of amputation and RTLA by artery injured and ISA status can be found in Table 3. Results were not analyzed for statistical significance given small numbers per group.

RTLA occurred in 22 patients (11%), including 11 amputations and 13 instances of graft thrombosis (Table 4). There was no significant difference in RTLA between patients who received ISA and those that did not (12/119 (10%) vs. 10/74 (14%), $p = 0.6$).

There was significantly higher total blood product use among patients treated with ISA versus those that did not receive ISA (median 3 units (Q1–Q3 0–8)) vs. 1 unit (Q1–Q3 0–4, $p = 0.002$). There was a longer length of ICU (median 3 days (Q1–Q3 1–6) vs. 1 day (Q1–Q3 0–3), $p = 0.001$) and hospital length of stay (median 9.5 days (Q1–Q3 4–18.5) vs. 6 days (Q1–Q3 2–13), $p = 0.01$) in patients treated with ISA compared to those who were not. Nineteen patients required return to the operating room for reintervention during the index hospitalization (10%), including the 13 with repair thrombosis, one with hematoma, three with flow-limiting stenosis, one with a pseduoaneurysm and one with an infection. There was no difference in need for reintervention between patients who underwent ISA and those who did not (9/119 (8%) vs. 10/74 (14%), $p = 0.2$). There were no deaths or hemorrhagic strokes in the total cohort.

Discussion

Anticoagulation has been investigated as a modifiable risk factor to improve outcomes for patients with extremity arterial injuries. Early use of anticoagulation has been argued to minimize distal and small vessel thrombosis and therefore improve outflow patency [5,9]. Despite the dogma for using anticoagulation in vascular repair, in patients undergoing repair of traumatic vascular injuries there is minimal and conflicting data in the literature correlating the use of ISA with improved outcomes. Routine anticoagulation in the absence of contraindications has been recommended by multiple groups [5,8,9,13], but has been found to have no difference by other groups [4,6,7,10]. Wagner et al. found a significantly lower amputation rate when ISA was used, in a review of 99 traumatic popliteal artery injuries (8% vs. 31%, $p < 0.01$) [8]. They did not, however, account for other confounding patient characteristics like degree of limb ischemia at presentation. Daugherty et al. compared patients with popliteal injuries who received ISA over two sequential five-year periods. Between 1967–1972, 13 patients received ISA with a limb salvage rate of 46%; in contrast to 7 patients who did not receive ISA and had a limb salvage rate of 43%. Between 1972–1977, 11 patients received ISA and the total limb salvage improved to 91% [5]. They also report using improved operative techniques including extra-anatomic bypass in the latter time period, which could account for the difference in outcome. Melton et al. looked at 102 patients with popliteal artery injuries, 79% of whom were given ISA with or without thrombolysis [7]. While there was a trend towards improved limb salvage in patients treated with anticoagulation and/or thrombolysis compared to no treatment ($p = 0.05$), there was no significant difference in limb salvage in subgroup of 46 patients who were given ISA alone ($p = 0.19$) [7]. Humphries et al. performed a modern retrospective review of 123 patients with extremity injuries, in which 56% of patients received ISA [6]. They found no difference in RTLA with use of ISA (OR 0.74, $p = 0.6$) [6]. Similarly, we found no significant association between ISA and amputation and/or repair thrombosis.

Table 4
Outcomes after repair, analyzed by intraoperative anticoagulation status.

		Intraoperative systemic anticoagulation		
Outcome	Total	Received	Not received	p-value
Median total units PRBC (Q1, Q3)	2 (0, 6)	3 (0, 8)	1 (0, 4)	0.002[§]
Median days of ICU stay (Q1, Q3)	2 (0, 5)	3 (1, 6)	1 (0, 3)	0.001[§]
Median days of total hospital stay (Q1, Q3)	8 (3, 17)	9.5 (4, 18.5)	6 (2, 13)	0.01[§]
Re-intervention required after repair, n (%)	19/193 (10)	9/119 (8)	10/74 (14)	0.2[‖]
Composite endpoint RTLA, n (%)	22/193 (11)	12/119 (10)	10/74 (14)	0.6[‖]
Amputation, n (%)	11/193 (6)	7/119 (6)	4/74 (5)	1.0[‖]
Thrombosis, n (%)	13/193 (7)	6/119 (5)	7/74 (10)	0.4[‖]

RTLA = Repair thrombosis and/or amputation.
PRBC = Packed red blood cells.
ICU = intensive care unit.
Q1 = Lower quantile (25th percentile).
Q3 = Upper quantile (75th percentile).
[§] Wilcoxon Rank-Sum.
[‖] 1-tailed Fisher's exact test, doubled.

The limb salvage rate observed in this study is consistent with modern studies [9], with 94% limb salvage. Popliteal artery injuries continue to have the poorest limb salvage rates. There is no appreciable improvement in the overall limb salvage rate of popliteal arteries since the 1980s; 84% in this modern study compared to historically reported rates of 83–100% [3–5,7,8,13] despite improvements in hospital and pre-hospital care.

The biggest limitation of any database is the detailed information that are not collected. Specifically, data regarding other adjuvant anticoagulation strategies including use of local heparinized-containing irrigation intraoperatively, transexemic acid, dextran, anticoagulation or antiplatelet agents given postoperatively, use of thrombectomy catheters, and details regarding specific ISA dose, pre- or post-administration activated clotting time levels were not collected in the PROOVIT database. These factors could be significant cofounding variables and warrant further investigation.

One main reason anticoagulation is withheld during arterial repair for a trauma patient is the concern for bleeding complications due to concomitant injuries. Anticoagulation given to patients with traumatic arterial injuries without absolute contraindications has been reported to have no increase in the rate of bleeding complications [5,6,9,10,14]. Wagner et al. found no hemorrhagic complications in the 71 patients given intraoperative systemic anticoagulation [8]. Humphries et al. found that use of ISA did not significantly change intraoperative blood loss (637 mL vs 926 mL, $p = 0.23$) or overall bleeding complications (42% vs 45%, $p = 0.95$) [6]. Golob et al. found a total complication (major and minor) rate of 21% in 114 patients given anticoagulation after traumatic injury [15]. Our study found significantly higher total PRBC use in patients receiving ISA, as well as longer hospital and ICU stays despite similar ISS, MESS and GCS between the groups. However, the outcomes of thrombosis, amputation, stroke or death were unchanged between the groups. The PROOVIT database does not currently include data regarding specific bleeding complications or strict contraindications for anticoagulation (i.e. intracavitary hemorrhage, need for multiple operations), and therefore these potential confounders will be missed.

Though prospectively obtained, this database reflects modern practice only among major Level I academic institutions across the country. Practice patterns of the 5 centers with higher enrollment may dictate some of the trends observed. The database did not collect information on the level of training or specialty of the operating surgeon. This study focused on open arterial repairs, as there were only two identified endovascular repairs undertaken for extremity arterial trauma recorded in the PROOVIT database for this time period. Use and outcomes of endovascular techniques for extremity trauma is being actively explored [16,17], but outcomes associated with these technologies will require additional investigation as experience matures. This preliminary report focuses on in-hospital outcomes following traumatic arterial injury repair, and does not include delayed amputations that may be required long term for limb dysfunction, delayed repair thrombosis or infection. A power calculation determined that to detect a 3% difference in rate of amputation, 1496 total patients should be analyzed. A more robust data set with information on outcomes will be obtained as the PROOVIT database continues to mature.

In this study, anticoagulation given during an operation was not associated with improved graft patency or limb salvage. Furthermore, ISA use was associated with prolonged hospital stay and increased blood product use. Our data suggest that for traumatic arterial injuries, there is no significant difference in outcome to support use of ISA. Further investigation regarding the risks of ISA for traumatic vascular injuries is needed.

Authorship

This work represents the original efforts of the investigators. All listed authors contributed to study design, data collection, data interpretation, and manuscript development.

Disclosure

The authors declare no conflicts of interest.

Acknowledgements

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Appendix A.

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Appendix B. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.injury.2017.03.020.

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USE OF OPEN AND ENDOVASCULAR SURGICAL TECHNIQUES TO MANAGE VASCULAR INJURIES IN THE TRAUMA SETTING: A REVIEW OF THE AAST PROOVIT REGISTRY

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Invited Discussant: [discussant]

Introduction: Vascular trauma data have been submitted to the American Association for the Surgery of Trauma PROspective Observational Vascular Injury Trial (PROOVIT) database since 2013 from multiple level I and II trauma centers throughout the United States. To date over 2,500 records have been submitted. We present preliminary data from the registry to describe the current use of endovascular surgery in vascular trauma.

Methods: We reviewed registry data from March 2013 to December 2016 with permission from the PROOVIT review panel. All patients who had an injury to a named artery, excepting forearm and lower leg, were included. Arteries were grouped into anatomical regions (neck, thoracic outlet, thorax, upper limb, major abdominal, abdominal branches and lower limb) and regions (compressible and non-compressible) for analysis. This review was limited to patients with non-compressible transection, partial transection, or flow limiting defect injuries. In addition to descriptive statistics, we developed multivariate linear models to assess the relationships between study variables.

Results: 1143 patients from 22 institutions had 1 or more arterial injuries in the regions defined. Median age was 32 years (interquartile range [IQR] 23-48) and 76% were male. Mechanisms of injury were 49% blunt, 41% penetrating, and 1.8% of mixed aetiology. Gunshot wounds accounted for 73% of all penetrating injuries. Endovascular techniques were used least often in limb trauma (upper limb 3% (n=7/203), lower limb 5% (n=18/381)) and most commonly in patients with blunt injuries to more than one region (50%, n=116/231). Penetrating wounds to any region were preferentially treated with open surgery (74%, n=341/459) with endovascular and combined approaches only accounting for 34 cases (7%). The most common indication for endovascular treatment was blunt non-compressible truncal injuries (NCTI). Patients with transection, partial transection or flow limiting NCTI treated with endovascular surgery had higher overall injury burden as reflected by injury severity scores and longer associated hospital stays, but required less packed red blood cells (PRC), and had lower in hospital mortality than those treated with open surgery on univariate analysis. On multivariate analysis of this NCTI group, low hemoglobin and abdominal injury were independent predictors of mortality, and amongst survivors, type of injury, hemoglobin, lactate, and vasopressor use were predictors of PRC use in the first 24 hours.

Conclusion: Our review of the PROOVIT registry demonstrates that both endovascular and open surgery is being performed for vascular injuries in all regions of the body. These findings support the use of endovascular treatment of vascular injuries in the severely injured, but additional investigation is needed to define indications and optimal utilization of endovascular technologies in the setting of vascular trauma.

CONTEMPORARY TOURNIQUET USE IN EXTREMITY VASCULAR TRAUMA: THE AAST PROSPECTIVE OBSERVATIONAL VASCULAR INJURY TREATMENT (PROOVIT) REGISTRY

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and the *AAST PROOVIT Study Group*

Introduction: Correct tourniquet application can be a lifesaving technique prior to definitive surgical treatment of extremity vascular trauma. After World War II, tourniquet use had fallen out of favor due to potential complications such as nerve damage and limb loss. Current guidelines recommend tourniquet use to control hemorrhage from penetrating lower extremity trauma. There are many reports of successful tourniquet use in military conflicts; however, only a few small studies have evaluated their use in the civilian trauma population. We aimed to describe the contemporary use of tourniquets in the management of civilian extremity vascular trauma and evaluate the associated outcomes.

Methods: We reviewed data from the multicenter AAST Prospective Observational Vascular Injury Treatment (PROOVIT) registry from Feb 2013 to Dec 2016. This data included key elements of vascular trauma presentation, diagnosis, management and outcomes. Data was compared with student t-tests and propensity score matching using R software. Controls were matched using the covariates Injury Severity Score, Abbreviated Injury Score of the extremity, initial systolic blood pressure, initial Glasgow Coma Scale score, initial lactate level, and age. Patients with multiple arterial injuries were excluded from analysis.

Results: A total of 623 patients with extremity arterial injuries from 14 centers were included for analysis. Pre-hospital tourniquets were placed in 17.5% of patients with extremity arterial injury. The overall number of amputations following any arterial extremity injury was low with or without the placement of a tourniquet, and not statistically different when compared to propensity matched controls (tourniquet 0.04 vs control 0.10; p=0.12). There was no statistical difference between the in-hospital mortality rates when tourniquets were used (tourniquet 0.08 vs control 0.04; p=0.18). In patients with brachial artery injuries the use of tourniquets was associated with a reduced average hospital length of stay (11.3 days vs 17.0 days; p=0.23) and average ICU length of stay (3.5 days vs 7.0 days; p=0.04). When compared to controls, tourniquet use did not significantly affect 24-hour packed red blood cell (pRBC) transfusion requirement (tourniquet 7.98 vs control 7.12; p=0.35), need for post-operative therapeutic anticoagulation (tourniquet 0.65 vs control 0.68; p=0.36), or the rate of infection in the affected limb (tourniquet 0.01 vs control 0.02; p=0.45).

Conclusion: The PROOVIT registry shows that in contemporary civilian practice, tourniquets are used for extremity arterial injury in just 17.5% of cases, a rate much lower than previously reported for both civilian and military settings. Tourniquet use was not associated with an increased rate of amputation, in-hospital mortality, 24-hour pRBC transfusion, or subsequent infection in the affected limb when compared to matched controls. There was a statistically significant shorter ICU length of stay in patients who had tourniquets placed for brachial artery injuries. There was also a trend toward shorter overall hospital length of stay by over 5 days in

this group as well, which while not statistically significant, may have important clinical implications.

Poster # 97

PEDIATRIC VASCULAR TRAUMA: CURRENT MANAGEMENT AND EARLY OUTCOMES

Melissa N. Loja MD, MAS, Joseph Dubose* MD, Jacob Stephenson* MD, Boris Kessel* MD, Tiffany Bee* MD, Timothy Fabian* MD, Jay Menaker* MD, Thomas Scalea* MD, John B. Holcomb* MD, David Skarupa* MD, Kenji Inaba* MD, Richard Catalano MD, Nathaniel Poulin* MD, John K. Bini* MD, Todd E. Rasmussen* MD, University of California, Davis

Introduction: The hospital course and early outcome of vascular injuries in the pediatric population is not well known due to a paucity of literature, and infrequent occurrence. We sought to describe pediatric vascular injuries including hospital treatment strategies and discharge outcomes using a multicenter, prospectively collected database.

Methods: We included patients 16 years or younger from patient data collected from the American Association for the Surgery of Trauma PROspective Vascular Injury Treatment (PROOVIT) registry. This registry contains demographic, diagnostic, treatment, and in-hospital outcome data for patients with vascular injuries.

Results: Between February 2013 and December 2016, 2,673 patients were enrolled into the PROOVIT registry. 83 of these patients were aged 16 years or younger (3% incidence). The majority were male (80%) with a mean age of 13.5 years (range 3-19). 60% (50/84) were injured by penetrating mechanism including 25 gunshot wounds and 7 stabbings. 36% were injured by a blunt mechanism. Hard signs of vascular injury were present in 41 patients. 61% (51/83) of patients were taken to the operating room immediately. CT scans were performed for diagnosis in 24% (20/83) of patients, most frequently for lower extremity injuries (7/20). The median ISS was 10 (25th percentile 5 – 75th percentile 18). 72% (60/83) of the injuries were to an extremity, 11% to the neck (9/83), and 17% to the abdomen or chest (14/83). Of the extremity injuries, 20% patients (12/60) had a pre-hospital tourniquet placed. 65% of extremity injuries were treated with open repair (39/60). Neck trauma was most commonly treated with observation in 5/9 patients. Abdomen or chest trauma was treated most frequently with open operations (6/14), followed by endovascular intervention (4/14). Overall mortality was 6.4% (5/83).

Conclusions: Pediatric vascular injuries are most frequently penetrating injuries to the extremities, commonly treated with open interventions. The use of endovascular techniques is rare for vascular trauma in this population. Mortality from vascular injuries in the modern era is rare.

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CONTEMPORARY OUTCOMES AND MANAGEMENT OF BLUNT CERBROVASCULAR INJURIES: RESULTS FROM THE AAST PROOVIT MULTICENTER REGISTRY

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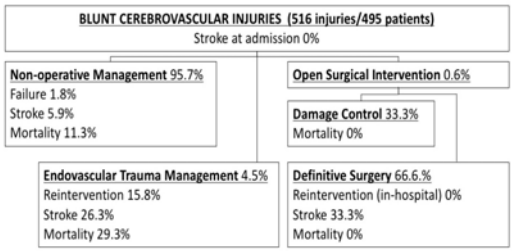
Invited Discussant: [discussant]

Introduction: In 2010 the Eastern Association for the Surgery of Trauma (EAST) published guidelines for the treatment of blunt cerebrovascular injuries. Analysis of prospectively collected data following the implementation of these guidelines can help inform future practices.

Methods: The American Association for the Surgery of Trauma PROspective Vascular Injury Treatment (PROOVIT) registry was used to collect demographic, diagnostic, treatment, and outcome data on cerebrovascular injuries.



Results: A total of 516 blunt cerebrovascular artery injuries (bCVIs) in 495 patients from 19 centers (18 ACS Level I and 1 ACS Level II) have been captured since February 2013. Most injuries occurred in males (63.4%, 327/516) with a median age of 38.0 years (IQR 28) and a documented Injury Severity Score greater than 15 in 63.2% (326/516), primarily from motor vehicle collision (67.2%, 347/516). Injuries to the common carotid (4.3%, 22/516), internal carotid (45.5%, 235/516), and vertebral (50.2%, 259/516) arteries were identified, with multiple injuries identified in 21 patients (4.2%). bCVI severity was distributed as follows: Grade I and II (intimal tear or flow limiting defects): 34.9%, III (pseudoaneurysm): 12.1%, IV and V (occlusion or transection): 24.1%. Treatment was as follows: Grades I and II: non-operative management (NOM) 96.9%, endovascular trauma management (EVTM) 2.5%, open surgical intervention (OSI) 0.3%; Grade III: NOM 96.0%, EVTM 4.0%, OSI 0%; Grade IV and V: NOM 92.8%, EVTM 5.6%, OSI 1.6%. Anti-thrombotic agents were used in 57.2% of injuries, (NOM 58.1%, EVTM 77.8%, OSI 0%; p=0.49). Failure of NOM occurred in 1.8% of injuries. EVTM required re-intervention in 15.8% with none requiring open revision. In-hospital re-intervention was not required after OSI in any patient. Stroke after initiation of management occurred in 6.8% of bCVIs (NOM 5.9%, EVTM 26.3%, OSI 33.3%; p <0.001). Overall hospital mortality was 12.3% (NOM 11.3%, EVTM 29.3%, OSI 0%; p=0.11). Follow-up is available for 80 injuries (15.5%) for a median of 2.0 months (IQR 2.0 mo). During the available follow up period, out of hospital stroke rate was 0% and reintervention was necessary for only 1 injury (0.2%) after open repair due to flow-limiting stenosis.

Conclusions: Initial data suggests that management of bCVI largely follows the EAST guidelines. However, NOM predominated even in higher grade injuries. The number of bCVIs requiring intervention was small, but data suggests OSI and EVTM may be associated with a higher rate of stroke than NOM.

Breaking New Ground: RCT testing the Safety, Efficacy & Opiate Sparing Effect of Ketamine Augmentation of Fentanyl for Daily Burn Wound Care Pain

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Introduction

Severe burns are intensely painful and increase risk of chronic pain, PTSD, and major depression (1). Wound care requires painful twice-daily wound care to prevent infection and promote healing. Repeated aversive stimulation of peripheral nociceptors may develop central sensitization and chronic pain (2). Notably, shared symptoms of chronic pain and PTSD are reciprocally related (3). Further, PTSD increases sensitivity to acute pain (4), central sensitization (5) and increased rates of chronic pain (6). Chronic pain, in turn, exacerbates PTSD severity (1). Opiates are ubiquitous in managing burn wound care pain, yet, opiates alone are insufficient (7) as they do not block all μ opioid receptors - thus tolerance and secondary hyperalgesia increase (2). Hyperactivity of the N-methyl-D-aspartate receptor (NMDAR) is the underlying mechanism of sensitization to noxious stimuli and opioid non-responsiveness (8). Ketamine is a selective, non-competitive NMDAR-blocker which enhances opioid efficacy by enhancing μ-opioid receptor-mediated signaling (ERK1/2 signaling) thus reducing desensitization and increasing resensitization and preventing opioid-induced hyperalgesia (9). Low-dose, slow infusion Ketamine has been shown safe and effective for acute burn (10) and chronic pain (11). Ketamine has also been shown to relieve treatment-resistant chronic depression (12), and chronic PTSD perhaps by increasing supply of brain derived neurotropic factor (BDNF) protein (13)

Aims, Design, Treatment Arms

Specific Aims: To evaluate the safety and efficacy of Ketamine in reducing wound care pain, and to evaluate the opiate sparing effects. Secondary aims include investigating the effect on diagnoses and symptom trajectory of depression, PTSD and sleep disturbance.

Trial Design: Double-blind, parallel-group, randomized, controlled trial with repeated-exposure analogous to contexts with repeated exposure to severe pain (e.g., combat wounds). All participants will receive standard clinical care for acute burn injury. Both groups will receive the assigned study drug during twice-daily wound care for the 7-day study period (up to 14 sessions).

Treatment Arms: Augmentation Arm (ketamine plus Fentanyl) and Usual Care Arm (placebo plus Fentanyl). The Augmentation Arm will receive low dose, slow-infusion ketamine (0.3 mg/kg loading dose and 2.5 mcg/kg/min infusion during wound care) in addition to fentanyl (1 mcg/kg loading dose and 1mcg/kg PRN during wound care). The Usual Care Arm will receive a saline-placebo infusion (identical volume to ketamine loading dose and ketamine infusion) in addition to fentanyl (as above).

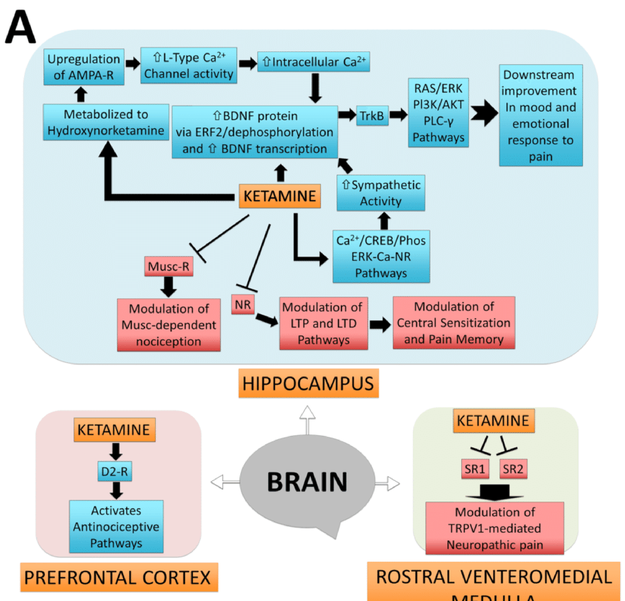
Inclusion

- **TBSA** ≥2% and ≤40% admitted to JHBMC
- **Age** ≥ 18 years and ≤ 70 years

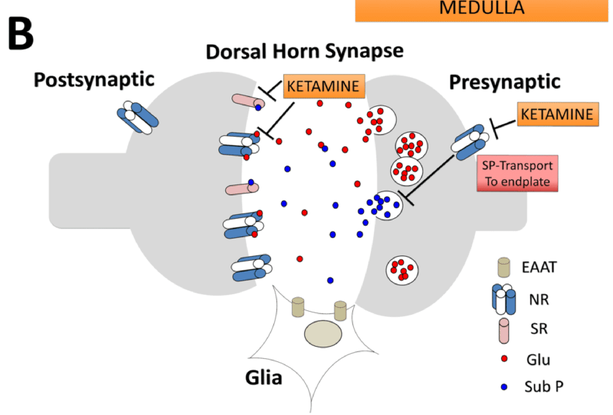
Exclusion

- **Pain** <5/10 in ER
- Insensate
- Lacks Capacity
- Intubated
- LOS <3 days

A. Ketamine's Central Mechanisms of Action on Mood (blue) and Pain (pink)



B. Ketamine's Mechanisms of Action at Dorsal Horn Synapses



Methods

Validated measures are given at 3 stages:

1. Baseline Measures (pre-injury moderators and event-related data): demographic information, injury descriptors, previous exposure to traumatic events (Life Events Checklist), and general health information prior to burn injury (SF-12 Health Survey).

2. Wound Care Measures (before, during, after each session): Pain, pain unpleasantness, and satisfaction with pain relief (numeric analogue scales), and positive and negative affect are collected from patients every 10 minutes during daily wound care sessions for the 7-day study protocol. Opiate sparing is assessed via total opiate equivalent dosages of analgesic (e.g., PRN fentanyl) and other medications administered during wound care.

3. Follow-Up Measures (1-day, 1-week, 1-month after last study session): pruritus, medication usage, pain recall, pain relief satisfaction, health and function (Burn-Specific Health Scale-Brief, SF-12 Health Survey),and appearance satisfaction (Satisfaction With Appearance Scale).

Conclusions

Ketamine has recently emerged as a potentially effective analgesic alternative to narcotics for use in combat associated casualties. Further, it has shown promise in managing PTSD and chronic pain in independent studies and thus may be the key to simultaneously addressing both conditions, especially since the two are intricately connected and concurrently fuel each other through the mutual maintenance model (e.g. the shared symptoms of one increase that of the other and vice versa). Thus, the study will evaluate the safety and opiate-sparing effects of standard of care opiate (fentanyl) augmented with low-dose, slowly infused ketamine for the treatment of pain, hyperalgesia, and allodynia during acute burn wound care. In addition, it will be observed if study-drug participants have reduced symptoms of acute stress disorder, posttraumatic stress disorder, major depressive disorder and sleep disturbance during the study and for up to one-month follow-up.

References & Acknowledgements

References and Measures available upon request.

External Funding: The contents of this poster were developed under a grant from the National Trauma Institute (NTI) and the Department of Defense (DOD). The opinions and assertions contained in this poster are the private ones of the authors and are not to be construed as official or reflecting the views of NTI, DOD, the Federal Government, or the Uniformed Services University of the Health Sciences.

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Johns Hopkins Bayview Medical Center, Office of the Vice Dean for Research
Johns Hopkins University, Office of the Provost

Pain and PTSD Severity are Reciprocally Related in Burn Survivors at 6 Months Post-Discharge

A. Gehrke, MS, E. Presseller, L. Quiroga, MD, J. Caffrey, DO, J.A. Fauerbach, PhD

Johns Hopkins Burn Center, Psychiatry & Behavioral Sciences, Plastics & Reconstructive Surgery, Johns Hopkins University School of Medicine, Baltimore, MD, USA; Uniformed Services University of the Health Sciences, Bethesda, MD.

Introduction

Burn pain starts with injury and continues with daily wound care. The present study investigated the relationship of acute pain and chronic posttraumatic stress disorder (PTSD) to chronic pain in burn survivors. Chronic, moderate-severe graft site pain is reported by 28% of burn survivors at 6 weeks and 21% at 6 months[2] and PTSD is reported by 2-40% of burn survivors 3-6 months post-burn.[3] Veterans with PTSD had greater pain severity and disability.[4] Predictors of chronic pain[5] and PTSD[6] are known in burns and other populations,[7] yet theory-driven knowledge of their reciprocity remains limited.[8] The Mutual Maintenance Model posits that pain and PTSD symptoms are reciprocally exacerbating and reinforcing.[1]

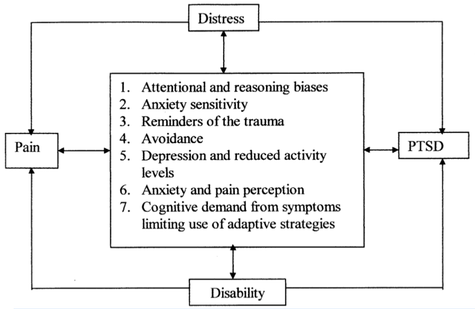


Figure 1. Chronic Pain and Posttraumatic Stress Disorder: mutual maintenance[1]

Objectives

- To investigate the specific relationship between chronic pain at 6 months and PTSD symptoms at 6 months post-discharge in burn injury survivors
- To assess the applicability of the Mutual Maintenance Model to the relationship between burn pain and burn-related PTSD.

Materials and Methods

Burn Model System data (1994 to 2014) were analyzed. The predictor variables were acute pain at discharge (Acute Pain-DC: Short Form-McGill Pain Questionnaire, SF-MPQ), and PTSD at 6 months (PTSD-6, Davidson Trauma Scale). The outcome of interest was chronic pain at 6 months post-discharge (Chronic Pain-6, SF-MPQ). Linear regression examined the association of Acute Pain-DC and Chronic PTSD-6 and their interactions (i.e., Acute Pain-DC X PTSD-6) with Chronic Pain-6. Post-hoc multivariate linear models also regressed Acute Pain-DC and PTSD-6 on the Chronic Pain-6 subscales, Affective Pain and Sensory Pain.

Note. References for measures available upon request.

Results

Sample characteristics (N= 166 with complete data) include: Caucasian (70%), male (69%), mean age 42 years (SD = 15). Injury severity descriptors include: mean TBSA burned 14.65% (SD = 15.6), and length of stay 21.5 days (SD = 23.4). The overall regression models for Chronic Pain-6, Chronic Pain-6 (Affective), and Chronic Pain-6 (Sensory) were significant ($R^2 = 0.45, 0.42, 0.42$, $p = 0.001, 0.001, <0.001$ respectively). See Figure 2 for detailed results.

Outcome	Predictor	*B*	SE *B*	B	*T*	*p*
Chronic Pain-6	Chronic Pain-DC	0.14	0.10	0.13	1.42	.159
	PTSD-6	0.09	0.04	0.29	2.36	.019
	Chronic Pain-DC X PTSD-6	0.00	0.00	0.31	1.92	.057
	Constant	1.74	1.45		1.20	.232
Chronic Pain-6 (Sensory)	Chronic Pain-DC (Sensory)	0.14	0.10	0.13	1.40	.164
	PTSD-6	0.04	0.03	0.18	1.24	.216
	Chronic Pain-DC (Sensory) X PTSD-6	0.01	0.00	0.40	2.30	.023
	Constant	1.80	1.21		1.49	.138
Chronic Pain-6 (Affective)	Chronic Pain-DC (Affective)	0.06	0.08	0.07	0.71	.476
	PTSD-6	0.04	0.01	0.48	5.28	.000
	Chronic Pain-DC (Affective) X PTSD-6	0.00	0.00	0.16	1.31	.193
	Constant	0.09	0.28		0.32	.752

Figure 2. Results

Note. DC = At discharge, 6 = 6 months post-discharge, Chronic Pain = Short Form McGill Pain Questionnaire; PTSD = Davidson Trauma Scale

Conclusion

As hypothesized, the Mutual Maintenance Model was supported. Accounting for the influence of acute pain, chronic PTSD at 6 months post-discharge was significantly associated with chronic pain at 6 months post-discharge. Results also indicate that the interaction of acute sensory pain at discharge and chronic PTSD at 6 months post-discharge was significantly related to chronic sensory pain 6 months post-discharge. As such, efforts to prevent or treat chronic pain and PTSD in acute care and rehabilitation will likely reduce their chronicity. See Figures 3 and 4 for potential interventions and their mechanisms.

External Funding: The contents of this poster were developed under a grant from the National Institute on Disability, Independent Living, and Rehabilitation Research (NIDILRR grant number 90DP0035). NIDILRR is a Center within the Administration for Community Living (ACL), Department of Health and Human Services (HHS). The opinions and assertions contained in this poster are the private ones of the authors and are not to be construed as official or reflecting the views of NIDILRR, ACL, HHS, the Federal Government, the Department of Defense, or the Uniformed Services University of the Health Sciences.

Acknowledgements:

National Trauma Institute

Department of Defense

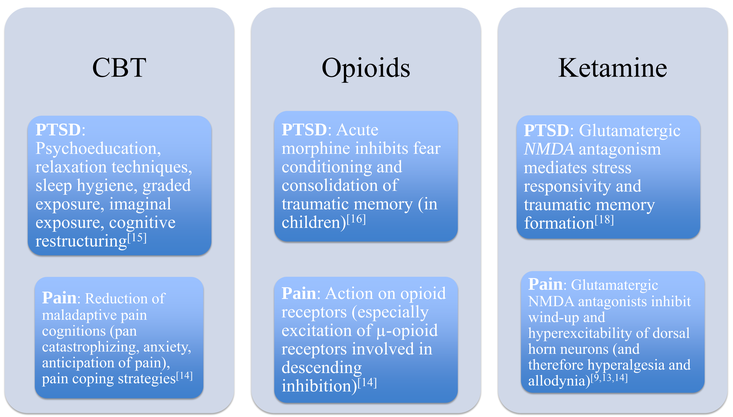
National Institute on Disability and Independent Living Rehabilitation and Research

Johns Hopkins Bayview Medical Center, Office of the Vice Dean for Research

Figure 3. Potential treatment interventions

	Burn Survivors	General Population
Chronic Pain	• Acute non-opioid analgesics (including NMDA antagonists)[9] • Centrally-acting pharmacological agents (antidepressants, anticonvulsants, NMDA antagonists)[10] • Surgical intervention[11] • Fat grafting[12]	• Pharmacotherapies (ketamine, lidocaine, acetaminophen, opioids, SSRIs, SNRIs)[13,14] • Cognitive Behavioral Therapy[14]
PTSD	• CBT with modules addressing consequences of physical injury[15] • Acute morphine (in children)[16]	• Cognitive Therapy • Exposure Therapy • EMDR[17] • Pharmacotherapies (SSRIs, risperidone, topiramate, venlafaxine, ketamine)[17,18]

Figure 4. Potential mechanisms of treatments effective for both pain and PTSD



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3) Check Eligibility
4) Enroll

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CRMS-63686 Evaluating the Safety, Efficacy and Opiate Sparing Effects of Ketamine in a Setting Analogous to Austere Battlefield Conditions

CRMS Status: Active
IRB Number: IRB00089761
Department/Division: Psychiatry - Behavioral Medicine
PI: Fauerbach, James
Lead Study Coordinator:
Lead Research Nurse:

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Protocol Number
CRMS-63686

CRMS Number
CRMS-63686

NCT Category
Treatment

NCT Code
03305055

Short Title
Evaluating the Safety, Efficacy and Opiate Sparing Effects of Ketamine in a Setting Analogous to Aus

Epic Research: Active Flag and Study Team Notification of Inpatient Admission
Display Research Active Flag, Notify Team of Admission

Approved

CRMS Status
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PI
Fauerbach, James

PI's Site
Bayview Med Cntr

PI's Primary Affiliation
Psychiatry & Behavioral Sciences

PI's Primary Department
Psychiatry - Behavioral Medicine

Johns Hopkins Authored?
Yes

Is this a Clinical Trial?
Yes

IRB Number
IRB00089761

Phase
Phase IV

IRB
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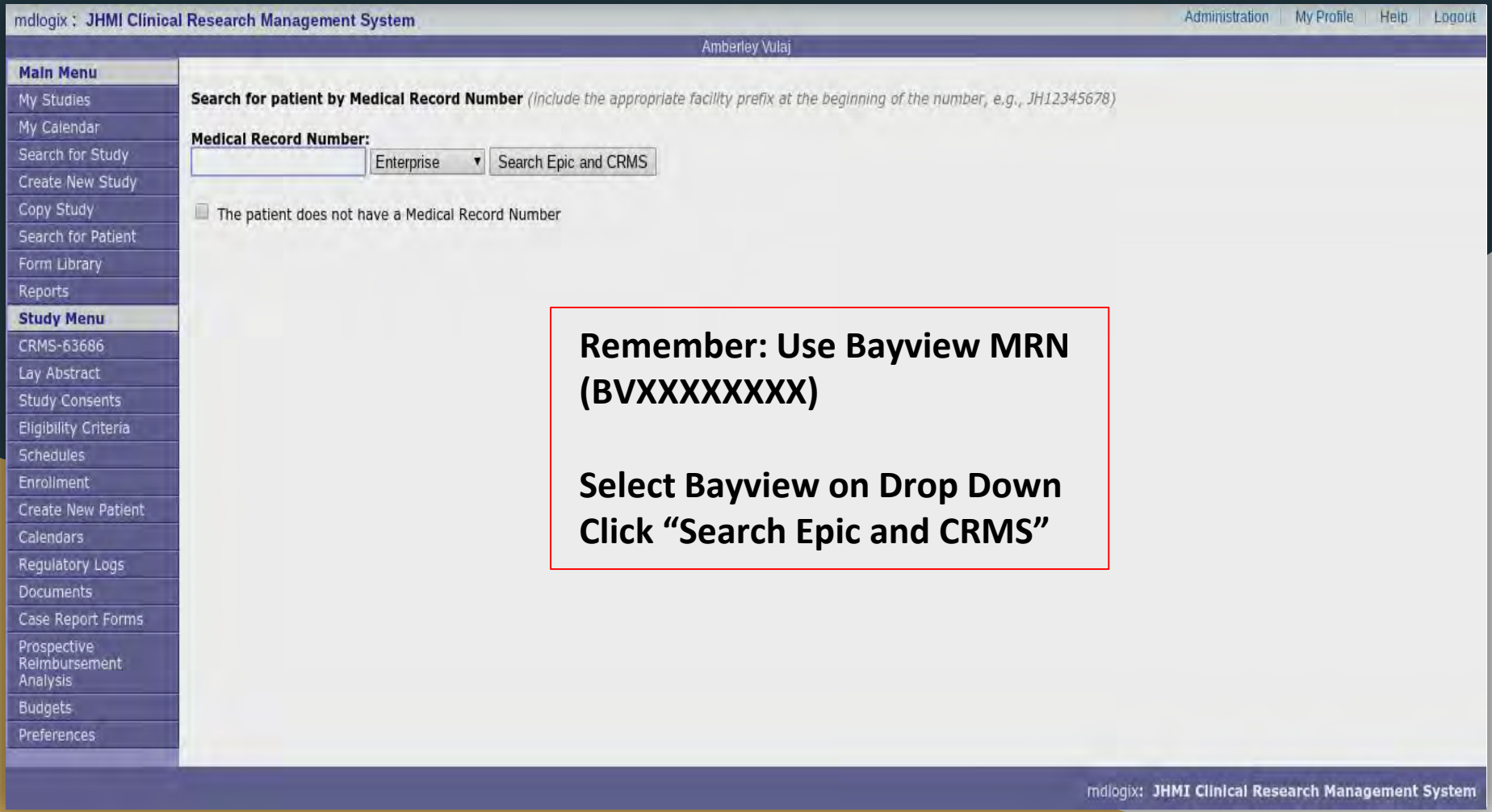
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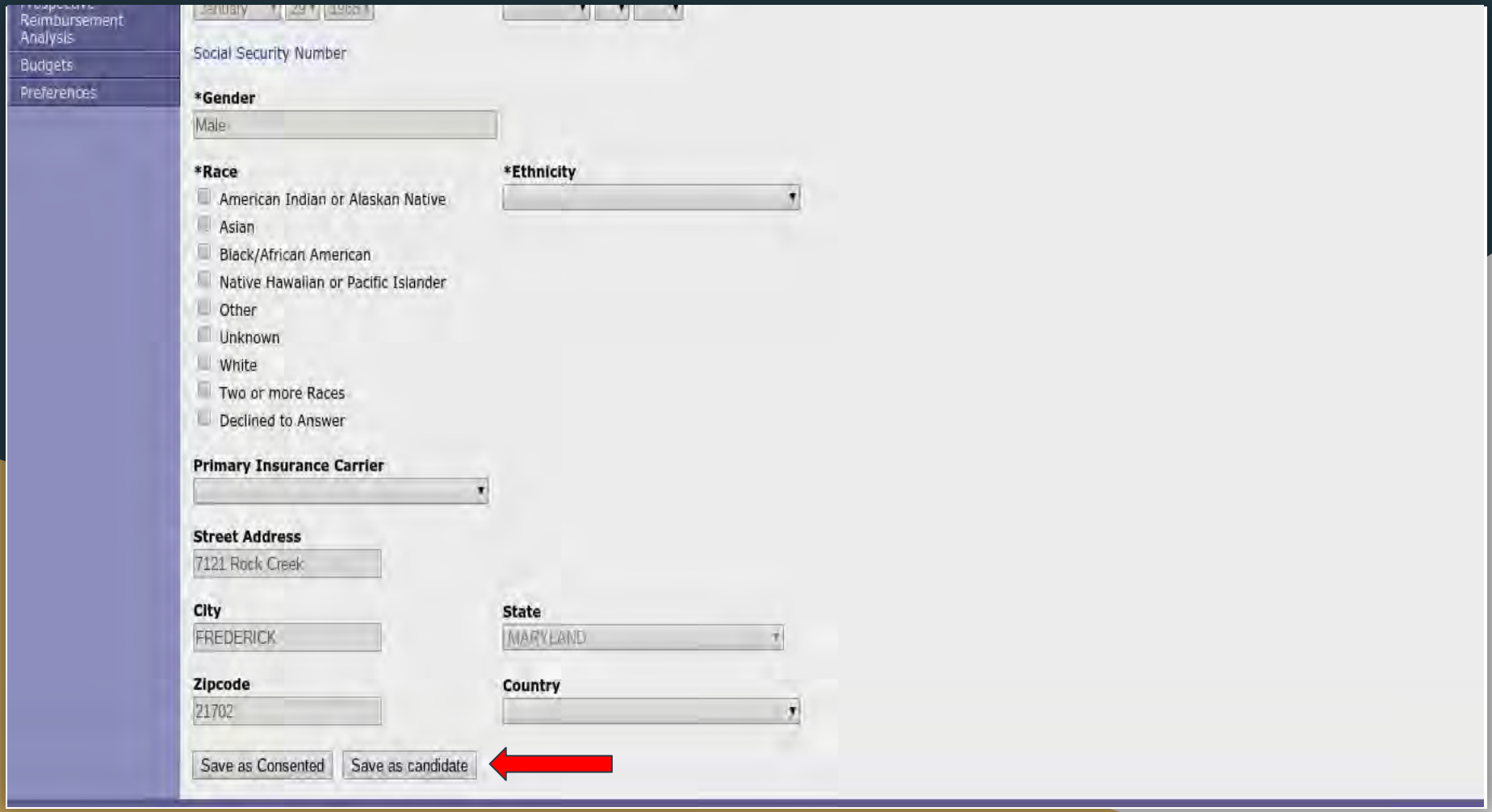
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Needham, Cara

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JHH - JH26823506
Bayview - BV02087391
Howard County - HC01138109

Social Security Number
Date of Birth 06/08/1987
Date of Death
Gender Female
Race White
Ethnicity Non-Hispanic

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New Consent

Site:
Bayview Med Cntr

***Consent:**
RCT Ketamine Augmentation vs. Usual Care for Acute Pain During Burn Wound Care(Main)-11/28/2017

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***Date consented**

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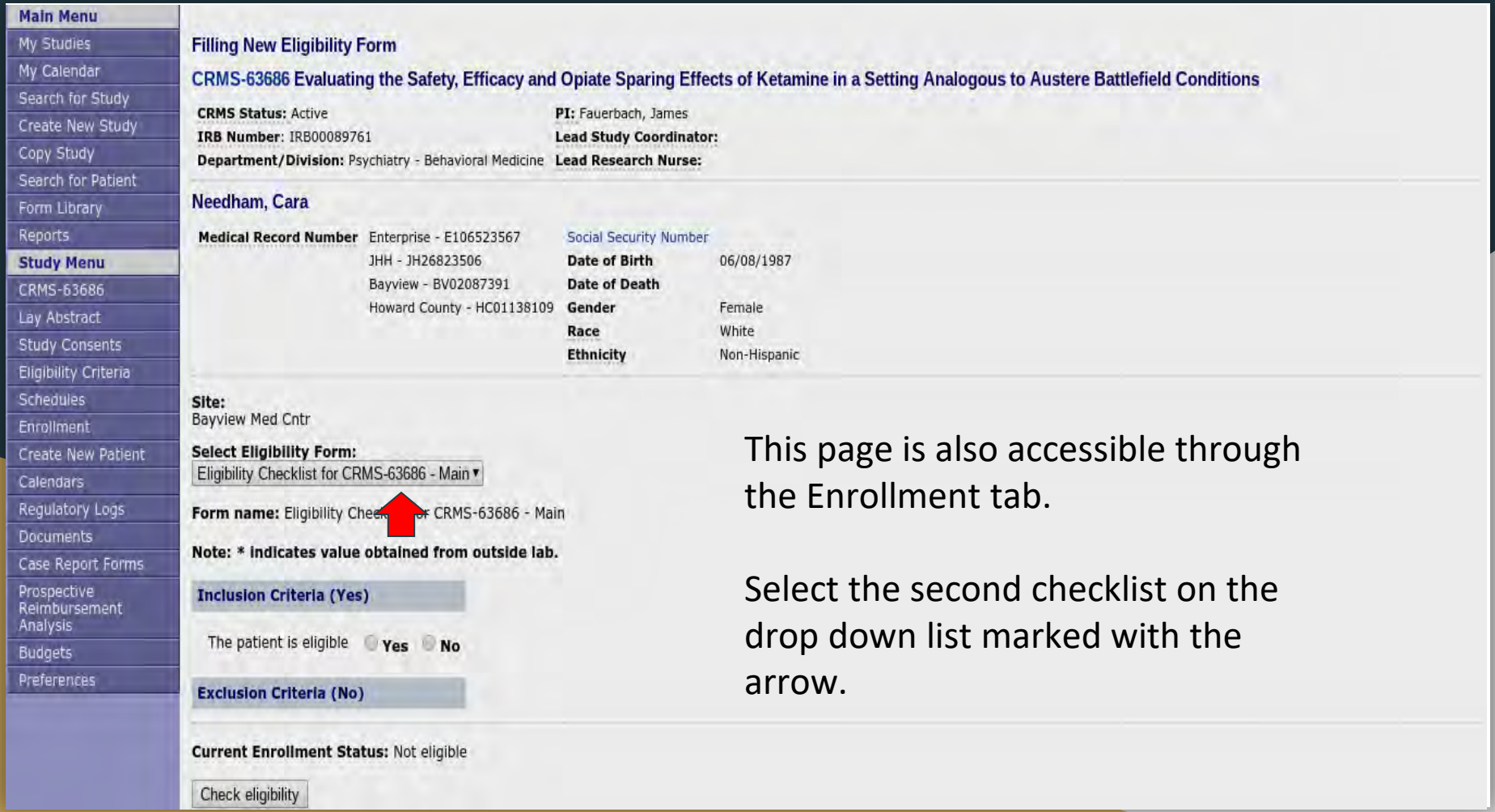

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Inclusion Criteria (Yes)

Does the patient have an acute burn injury with TBSA greater than 2% and less than 40%?	Yes No
Is the patient older than 18 and younger than 70 years of age?	Yes No
Is the estimated length of stay on the day of admission for this patient greater than around 5 days?	Yes No
Did the patient report a pain rated NAS of at least 5 in the Emergency Room during initial wound evaluation/debridement or on admission to the BICU while undergoing debridement?	Yes No

Exclusion Criteria (No)

Does the patient require endotracheal intubation or sedation?	Yes No
Does the patient show a Diminished Level of Consciousness/Cognitive Function (MMSE less than or equal to 20)?	Yes No
Does the patient show a Diminished Capacity (incapable of providing informed consent)? If so, please explain.	Yes No
Is there a concern for the patient's safety due to contra-indication? (e.g., potential drug interactions, medical comorbidities)	Yes No

Is the estimated length of stay on the day of admission for this patient greater than around 5 days? Yes No

Did the patient report a pain rated NAS of at least 5 in the Emergency Room during initial wound evaluation/debridement or on admission to the BICU while undergoing debridement? Yes No

Exclusion Criteria (No)

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Is there a concern for the patient's safety due to contra-indication? (e.g., potential drug interactions, medical comorbidities) Yes No

Is the patient insensate to pain in the burn wound location? (e.g., SCI; peripheral neuropathy) Yes No

Current Enrollment Status: Not eligible

Check eligibility

Save Close without saving changes

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Is the estimated length of stay on the day of admission for this patient greater than around 5 days?	○ Yes ◉ No
Did the patient report a pain rated NAS of at least 5 in the Emergency Room during initial wound evaluation/debridement or on admission to the BICU while undergoing debridement?	○ Yes ◉ No
Exclusion Criteria (No)	
Does the patient require endotracheal intubation or sedation?	◉ Yes ○ No
Does the patient show a Diminished Level of Consciousness/Cognitive Function (MMSE less than or equal to 20)?	◉ Yes ○ No
Does the patient show a Diminished Capacity (incapable of providing informed consent)? If so, please explain.	◉ Yes ○ No
Is there a concern for the patient's safety due to contra-indication? (e.g., potential drug interactions, medical comorbidities)	◉ Yes ○ No
Is the patient insensate to pain in the burn wound location? (e.g., SCI; peripheral neuropathy)	◉ Yes ○ No

Needham, Cara is Not eligible for study CRMS-63686

Current Enrollment Status: Not eligible [Check eligibility]

[View PDF] [Start new checklist] [Save] [Close without saving changes]

***Eligibility Checked By:** Bayview Med Cntr [Vulaj, Amberley] [Mark as Eligible] [Mark as NOT eligible] [Override]

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Enroll the following patient(s): *(0 of 100 patients enrolled)*

Name	Enrollment Status	Subject number	Date on Study	Message
Needham, Cara	Not eligible	*		must be "Eligible" to enroll

*Patients must have a subject number to enroll

Enroll Cancel

Use of open and endovascular surgical techniques to manage vascular injuries in the trauma setting: A review of the American Association for the Surgery of Trauma PROspective Observational Vascular Injury Trial registry

Edwin R. Faulconer, MBBS, Bernardino C. Branco, MD, Melissa N. Loja, MD, Kevin Grayson, PhD, James Sampson, MD, Timothy C. Fabian, MD, John B. Holcomb, MD, Thomas Scalea, MD, David Skarupa, MD, Kenji Inaba, MD, Nathaniel Poulin, MD, Todd E. Rasmussen, MD, *and* **Joseph J. Dubose, MD***, Fairfield, California*

BACKGROUND: Vascular trauma data have been submitted to the American Association for the Surgery of Trauma PROspective Observational Vascular Injury Trial (PROOVIT) database since 2013. We present data to describe current use of endovascular surgery in vascular trauma.

METHODS: Registry data from March 2013 to December 2016 were reviewed. All trauma patients who had an injury to a named artery, except the forearm and lower leg, were included. Arteries were grouped into anatomic regions and by compressible and noncompressible region for analysis. This review focused on patients with noncompressible transection, partial transection, or flow-limiting defect injuries. Bivariate and multivariate analyses were used to assess the relationships between study variables.

RESULTS: One thousand one hundred forty-three patients from 22 institutions were included. Median age was 32 years (interquartile range, 23–48) and 76% (n = 871) were male. Mechanisms of injury were 49% (n = 561) blunt, 41% (n = 464) penetrating, and 1.8% (n = 21) of mixed aetiology. Gunshot wounds accounted for 73% (n = 341) of all penetrating injuries. Endovascular techniques were used least often in limb trauma and most commonly in patients with blunt injuries to more than one region. Penetrating wounds to any region were preferentially treated with open surgery (74%, n = 341/459). The most common indication for endovascular treatment was blunt noncompressible torso injuries. These patients had higher Injury Severity Scores and longer associated hospital stays, but required less packed red blood cells, and had lower in hospital mortality than those treated with open surgery. On multivariate analysis, admission low hemoglobin concentration and abdominal injury were independent predictors of mortality.

CONCLUSION: Our review of PROOVIT registry data demonstrates a high utilization of endovascular therapy among severely injured blunt trauma patients primarily with noncompressible torso hemorrhage. This is associated with a decreased need for blood transfusion and improved survival despite longer length of stay. (*J Trauma Acute Care Surg.* 2018;84: 411–417. Copyright © 2017 Wolters Kluwer Health, Inc. All rights reserved.)

LEVEL OF EVIDENCE: Therapeutic/care management, level III.

KEY WORDS: Vascular trauma; noncompressible torso hemorrhage; endovascular trauma management.

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With the advancement of endovascular techniques and technology, the traditional methods of open vascular exposure and vessel repair or bypass are no longer the only option available when faced with a case of vascular trauma.[1] Increased availability of hybrid operating rooms and advancements in industry technology, such as refinements in wires, catheters, and stents, has enhanced management options for those with a vascular injury.[2,3] Examples of current endovascular use in trauma include angioembolization of pelvic injuries in hemodynamically unstable pelvic injuries, stent use in blunt aortic injury and emerging techniques, such as aortic balloon occlusion as part of resuscitation.[4–6] Despite these advances, hemorrhage remains the second highest cause of death in trauma, and noncompressible torso hemorrhage (NCTH) accounts for the highest number of preventable deaths in this group.[7–9] Endovascular techniques for hemorrhage control with subsequent definitive open or endovascular management are gaining popularity for vascular injuries in noncompressible regions due to the minimally invasive nature of the technology.[10,11] Based on observational data, in certain blunt

injury patterns, such as pelvic arterial trauma associated with a fracture and thoracic aortic injuries, endovascular intervention is becoming the primary treatment modality.[5,12,13] For other noncompressible vascular injuries, endovascular management is not yet as mainstream. Temporary proximal balloon occlusion for hemorrhage control is one technique that is evolving in trauma centers and the prehospital setting as an alternative to open resuscitative thoracotomy.[14–16] By using this minimally invasive technique for proximal control, it may be possible to rapidly control vascular injuries, reestablish a proximal perfusion pressure, and extend life for further assessment, open surgical repair, or a definitive endovascular solution.

The PROspective Observational Vascular Injury (PROOVIT) registry was established in 2013 by the American Association for the Surgery of Trauma to collect data specific to vascular trauma and the management of these injuries. To date, over 2,500 different injuries are included in the database. The aim of this study was to report the incidence of arterial injuries in the registry to date and to analyse injuries in noncompressible regions of the body to assess mortality and hospital resource use associated with open surgical and endovascular management strategies.

METHODS

Enrolled trauma centers submit data directly to the PROOVIT Study through the online data collection portal developed by the American Association for the Surgery of Trauma. Ethical approval for participation in the study and for data submission was received by each center before joining the study through local institutional review boards. Approval for this review of the data was granted by the PROOVIT Study review panel. Following approval, anonymized records for admissions between March 1, 2013, and December 31, 2016, were studied.

Patients who sustained an arterial injury were identified and included in the study. We excluded injuries distal to the knee and elbow. Data extracted included age, gender, mechanism of injury, vessel injury location and grade, admission details, management details, hospital resource utilization, and mortality. Figure 1 summarizes the methodology in the form of a flow chart.

Arteries were first grouped into the anatomic regions of neck, thoracic outlet, thorax, upper limb, major abdominal, abdominal branches, and lower limb for descriptive purposes. Arteries in the major abdominal group included abdominal aorta, and common and external iliac. The abdominal branch arteries included all other named arteries in the abdomen and pelvis. Descriptive analyses of demographics, injury patterns, and presenting features were performed for all regions. Anatomic regions were further grouped into whether they were compressible or noncompressible zones and management strategies were compared in these two groups. For detailed analysis of the noncompressible group by treatment option, patients managed nonoperatively and those with injuries defined as pseudoaneurysms or occlusions were excluded from the cohort. Pseudoaneurysms were overwhelmingly managed with endovascular techniques, and it was felt that these were likely to be stable injuries. Occlusive injuries,

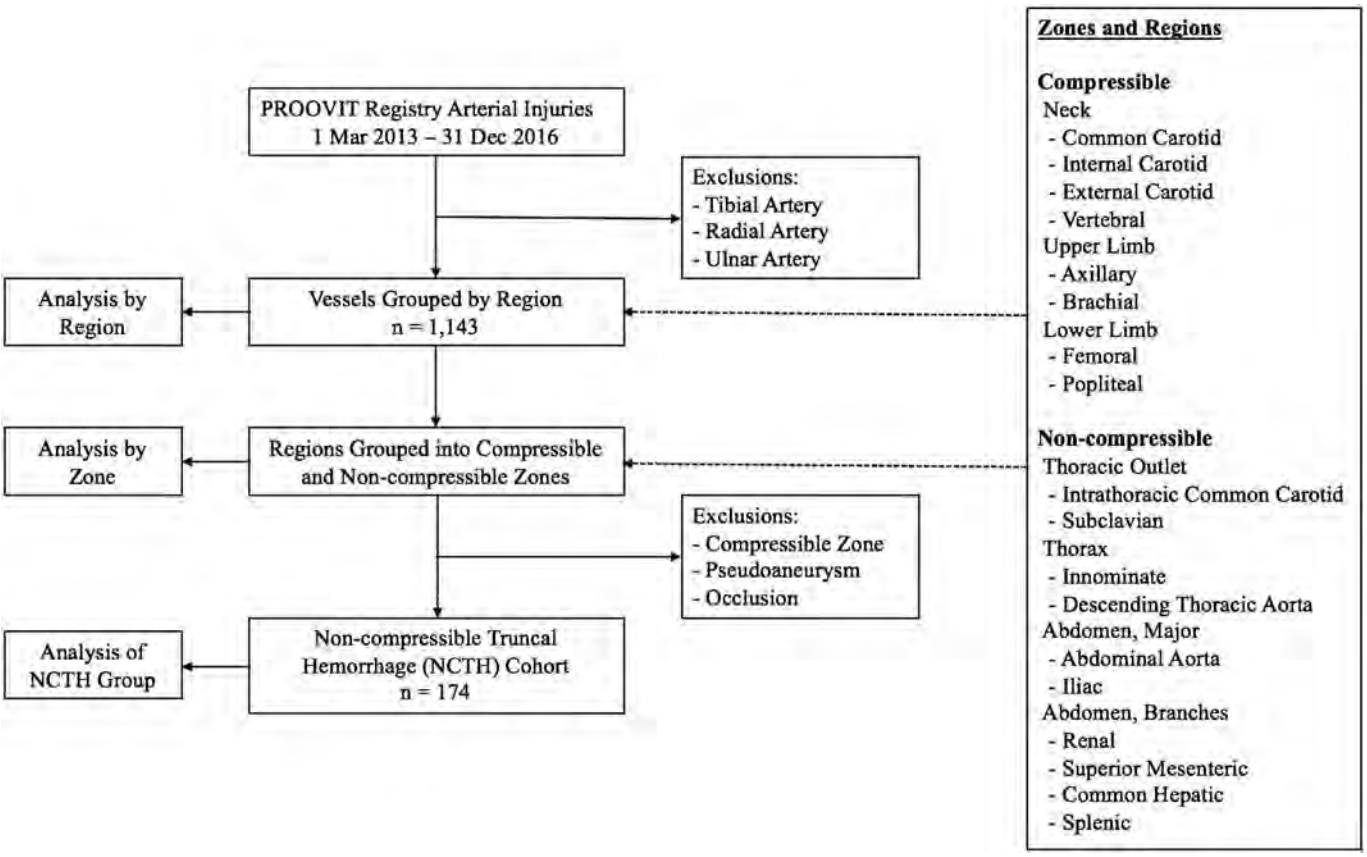

Figure 1. Schematic of study showing inclusions and exclusions for different stages of analysis.

by definition, are not bleeding. This left surgically managed injuries defined as "transection" and "partial transections or flow-altering injury" within noncompressible regions of the body to form the NCTH intervention group for analysis of outcomes by operative strategy. Where both open and endovascular approaches were reported, because of the heterogeneous nature of this small group and the fact that they had undergone definitive open repairs with simultaneous temporary or definitive endovascular procedures, they were considered as having undergone open surgery for purposes of comparison. Primary outcomes were hospital resource use and mortality.

Data were collected using a standard spreadsheet program (Excel for Mac v15.30, Microsoft Corporation, Redmond, WA) and statistical analysis was performed using a statistical software package (Stata for Mac v14.2, Stata Corp, Bryan, TX). Categorical data are reported as frequencies and percentages and compared using chi-square statistics. Continuous variables are reported as medians with interquartile ranges (IQR) and comparisons performed with Student's *t* tests. If data points were missing, they were excluded from that calculation and the denominator reduced. To identify independent predictors for hospital resource use and mortality, variables that on bivariate analysis were significant at *P* less than 0.2 were entered in a forward stepwise logistic regression model. Statistical significance was considered to be *P* less than 0.05 in all cases.

RESULTS

Between March 1, 2013, when the registry opened, and December 31, 2016, 1,143 trauma patients with one or more arterial injuries fitting the study inclusion criteria were submitted by 22 different Level I institutions (median, 31.5; IQR, 11.5–76.75 per institution). Most patients were young adults (median 32, IQR 23–48) males (76%, n = 871) with few comorbidities (Table 1). Nearly half of the injuries were listed as blunt (49.1%, n = 561) with penetrating wounds accounting for 40.5% (n = 464) of cases. A mixed blunt and penetrating injury was described in 1.8% (n = 21) and injury pattern was not specified in the remaining 8.4% (n = 97) of cases. Motor vehicle collisions were responsible for 61.3% (n = 344) of blunt injuries. Gunshots were the most common cause of penetrating injuries (73.5%, n = 341). Within the whole cohort of arterial injuries, transection (36.8%, n = 421) and partial transection or flow limiting defect (24.8%, n = 283) were more commonly described than occlusion (10.1%, n = 115).

When named arteries were grouped by anatomic region (Table 2 and Fig. 2), lower-limb arteries (33.3%, n = 381) accounted for the largest group of single region injuries and a combination of thoracic outlet and thorax arteries (18.1%, n = 207) accounted for the largest number of multi-region injuries. The Injury Severity Score (ISS) was highest in patients with vascular injuries to the thorax and documented hard signs of injury (active hemorrhage, developing hematoma, or distal ischemia) were more commonly seen in extremity trauma than torso injuries. When considering a single region injury pattern only, upper limb had the lowest median ISS value of 10, and thorax had the highest median value of 24 in this cohort.

Table 3 describes the management strategies used for arterial injuries to compressible and noncompressible regions by injury mechanism. Of the 456 injuries to noncompressible regions, blunt injuries accounted for 78.1% (n = 356) of the cases and open surgery or combined open and endovascular surgery was performed in only 13.8% (n = 33) of cases. In contrast to the blunt injuries, 68.0% (n = 68) of the penetrating noncompressible vascular injury patients underwent open or combined open and endovascular surgery.

TABLE 1. Epidemiology of PROOVIT Patients With Arterial Injury Entered March 2013 to December 2016 (n = 1,143) (Excludes Forearm, Hand, Lower Leg, and Foot Arteries)

Demographics	
Male, n (%)	871 (76%)
Age, median (q1, q3)	32 (23, 48)
Premorbid comorbidities and medications	
Chronic kidney disease, n (%)	15 (1.3%)
Insulin-dependent diabetes mellitus, n (%)	49 (4.3%)
Anticoagulation therapy, n (%)	25 (2.2%)
Antiplatelet therapy, n (%)	39 (3.4%)
Injury type	
Blunt, n (%)	561 (49.1%)
Penetrating, n (%)	464 (40.5%)
Mixed, n (%)	21 (1.8%)
Not specified	97 (8.4%)
Most common mechanism of injury by type	
Blunt, motor vehicle collision, n (% of blunt)	344 (61.3%)
Blunt, pedestrian versus automobile, n (% of blunt)	77 (13.7%)
Penetrating, gunshot, n (% of penetrating)	341 (73.5%)
Penetrating, stabbing, n (% of penetrating)	70 (15.0%)
Mixed, motor vehicle collision, n (% of mixed)	10 (47.6%)
Arterial injury pattern	
Transection, n (%)	421 (36.8%)
Occlusion, n (%)	115 (10.1%)
Partial transection or flow limiting defect, n (%)	283 (24.8%)
Pseudoaneurysm, n (%)	135 (11.8%)

TABLE 2. Presentation Details for Anatomic Regions Injured (n = 1,143)

Region	n	ISS, med (q1, q3)	Hard Signs of Arterial Injury, n (% of Region)	Soft Signs of Arterial Injury, n (% of Region)
Single region				
Neck	52	21 (13.75, 29)	52 (100%)	28 (53.8%)
Thoracic outlet	44	20 (13, 32.75)	14 (31.8%)	17 (38.6%)
Upper limb	203	10 (6, 16)	108 (53.2%)	130 (64.0%)
Thorax	4	26 (17.5, 42)	0	1
Abdomen, major	148	22 (17, 34)	42 (28.4%)	55 (37.2%)
Abdomen, branches	80	25 (17, 38)	24 (30.0%)	24 (30.0%)
Lower limb	381	11.5 (9, 19.75)	179 (47.0%)	253 (66.4%)
Multiregion				
Thorax and thoracic outlet	207	32 (22, 41)	25 (12.1%)	34 (16.4)
Other multiregion	24	—	—	—

Major abdominal arteries include abdominal aorta, and common and external iliac. The abdominal branch arteries include all other named arteries in the abdomen and pelvis.

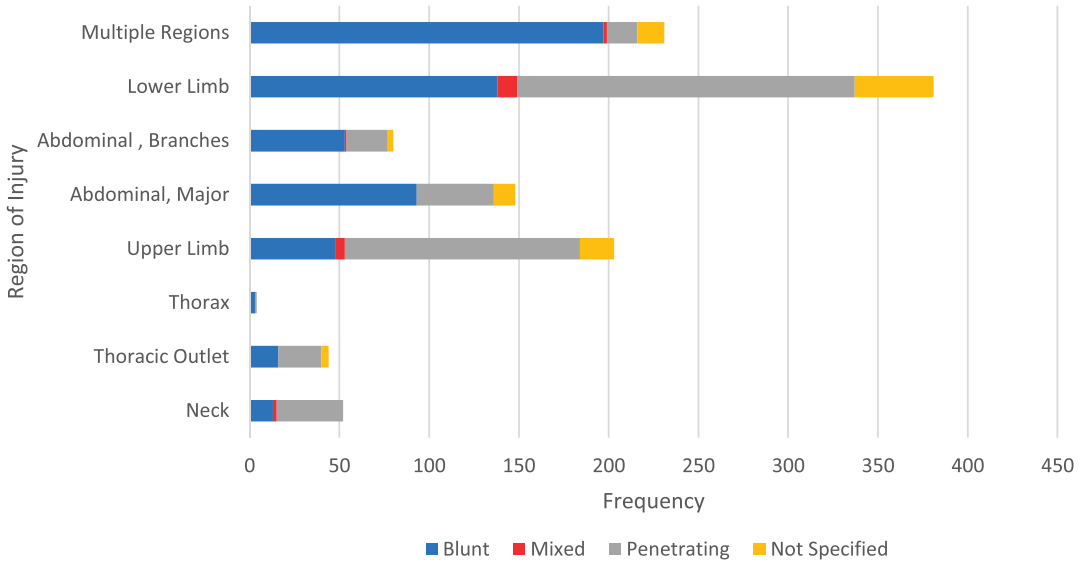

Figure 2. Mechanism of injury distribution by region of injury.

After exclusion of occlusive and pseudoaneurysm injuries and those not managed surgically from the noncompressible cohort, 174 patients made up the NCTH group who underwent surgical management. This group contained 138 males (78.1%) and 36 females with a median age of 36 (IQR, 24.25–54 years). Blunt mechanism of injury was more common than penetrating (109 vs. 65). Ninety-six injuries were to the abdomen/pelvis, 76 to the thoracic outlet or thorax and thoracic outlet and two patients had injuries to all three of these regions. Table 4 details the differences between those patients managed with open compared to endovascular surgery. The endovascular group had a significantly higher ISS on presentation (29 [21, 38] vs. 21 [16, 34]; $P = 0.020$), longer stays on intensive care unit (ICU) (7 [3, 18] vs. 3 [0, 13], $P = 0.009$) and in hospital (17 [7, 32] vs. 9 [2, 24]; $P = 0.003$) but required less packed red cell units (2 [0, 8] vs. 10 [4,24]; $P < 0.005$) than the open surgery group. Mortality rates were significantly lower in the endovascular group (10.8% vs. 39.5%, $P < 0.005$).

Multivariate Analysis

Multivariate regression analysis of mortality, packed red blood cell (PRBC) use in survivors, and hospital length of stay was performed using independent variables of PRBC use, hospital length of stay, treatment strategy, type of injury, admission lactate, hemoglobin (Hb), systolic blood pressure, use of vasopressors in first 24 hours, and NCTH subregion (abdomen vs. thorax/thoracic outlet).

Only Hb and PRBC use were independent predictors of mortality. When analyzing PRBC use as a dependent variable in survivors, admission lactate, penetrating injury, and the use of vasopressors in the first 24 hours were independently predictive. Hospital length of stay predictors in survivors included abdominal injuries and the use of vasopressors in the first 24 hours. In all three of these models, R^2 or pseudo-R^2 values were between 0.3 and 0.4.

TABLE 3. Management Strategies for Compressible and Noncompressible Regions by Injury Mechanism, n = 1,014

Description (n)	Conservative	Open Surgery	Endovascular Surgery	Combined Open and Endovascular
Compressible				
Blunt (199)	53 (26.6%)	130 (65.3%)	12 (6.0%)	4 (2.0%)
Penetrating (359)	69 (19.2%)	276 (76.9%)	5 (1.4%)	9 (2.5%)
Noncompressible				
Blunt (356)	164 (46.1%)	33 (9.3%)	143 (40.2%)	16 (4.5%)
Penetrating (100)	15 (15.0%)	65 (65.0%)	17 (17.0%)	3 (3.0%)

DISCUSSION

Our review of arterial injuries from the PROOVIT registry, focusing on NCTH patterns, shows evidence of use of both

TABLE 4. Resource Utilization and Outcomes for Transection and Partial Transection Injuries in Noncompressible Regions by Management Strategy (n = 174)

Noncompressible Transection, Partial Transection or Flow-Limiting Defect	Open Surgery	Endovascular Surgery	*P*
n	77	97	
Age, median (q1, q3)	31 (23, 48)	40 (25, 55)	0.032*
ISS, median (q1, q3)	21 (16, 34)	29 (21, 38)	0.020*
Admission systolic BP, median (q1, q3)	88 (73, 126)	116 (95, 137)	<0.005*
Admission Hb, median (q1, q3)	11.5 (10, 13)	12 (11, 14)	<0.005*
Admission pH, median (q1, q3)	7.16 (6.97, 7.28)	7.25 (7.19, 7.32)	<0.005*
Admission lactate, median (q1, q3)	6.65 (3.18, 11.6)	3.8 (2.3, 4.9)	<0.005*
Ventilator days, median (q1, q3)	2 (0.5, 5.5)	4 (0, 14)	0.280
ICU days, median (q1, q3)	3 (0, 13)	7 (3, 18)	0.009*
PRBC units in first 24 h, median (q1, q3)	10 (4, 24)	2 (0.8)	<0.005*
Hospital LOS, median (q1, q3)	9 (2, 24)	17 (7, 32)	<0.005*
In hospital mortality, n (% of group)	30/76 (39.5%)	10/93 (10.8%)	<0.005*

*denotes significance of <0.005.

open and endovascular surgical techniques to manage vascular injuries throughout the body. Vascular injuries across the spectrums of mechanism of injury, severity, type, and location are being managed with both techniques. Despite this, penetrating injuries are more commonly being managed with open surgery. These data show an increasing tendency to manage blunt NCTH injuries by endovascular means. In these cases, despite longer length of stay, transfusion requirements, and mortality rates were lower compared with the patients managed with open surgery. The ICU and hospital stays were longer likely due to the higher number of survivors in a group with a higher ISS value on admission. However, despite the obvious statistical difference in PRBC requirements and mortality when comparing the endovascular and open surgery NCTH groups, type of surgery was not an independent predictor of mortality, PRBC use, or hospital length of stay on multivariate regression analysis. This may indicate that there is more to the pattern of injury or presentation that is not available for comparison in the registry, and the low R^2 values seen on multivariate analysis support this assumption that a large proportion of the model is unaccounted for by the current variables. In Chang et al.'s[1] recent retrospective multicenter review of NCTH across four Level I trauma centers, a similar pattern was described in their data. They theorized that the endovascularly managed patients may be more stable and not actively exsanguinating, whereas those managed by open techniques were more urgent. In our data set, the subgroup of NCTH treated with open surgery had worse baseline vital signs than the endovascular group. This would suggest that the endovascular group were more stable, and therefore, the clinicians may have had more time to investigate and plan surgery rather than be forced into an immediate operation.

In this review, Level I trauma centers provided the majority of the data. The PROOVIT registry records location of procedure but not specialty or grade of the treating physician. There has been an increase in the rate of use of endovascular techniques to approach vascular trauma as seen in other reviews, and our data support these findings. There are many factors which influence the choice of surgical approach including patient factors, urgency of the procedure, facilities, available staff, and institutional protocols. It is not possible to tell from the data in the PROOVIT registry which factors are influencing the trauma team's decision making in each individual case.

The definitions and management strategies of NCTH were reviewed by Morrison and Rasmussen in 2012 and this review recently updated.[11,17] In their definition of NCTH injuries need to be from one of four anatomic categories (thoracic cavity, solid organ, named axial torso vessel or pelvic fracture with ring disruption) and include the presence of hemorrhagic shock or the need for immediate surgery to control bleeding. The results from our subset of 174 arterial injuries in noncompressible zones satisfy this NCTH criterion as only surgically managed patients were included. It might, however, be more accurate to describe our cohort as being arterial NCTH rather than the broader NCTH definition offered by Morrison and Rasmussen.

We sought to assess differences in outcomes of mortality and hospital resource use when adapting endovascular or open surgical strategies in arterial NCTH. A previous review of the PROOVIT registry presented the first year of data but numbers were too small to analyze different regions and treatments in detail.[18] This review has shown a significant difference in the NCTH outcomes between the two treatments but fails to prove that treatment is the sole reason for these differences. Branco et al.[19] published the largest US review of registry data on arterial injury outcomes for endovascular therapy to date using data from the National Trauma Data Bank (NTDB) between 2002 and 2010. They showed an increase in the use of endovascular techniques in blunt and penetrating causes over the nine years of the study and compared outcomes by matching the open and endovascular cohort groups. Although they conclude that endovascular is associated with lower mortality rates, this conclusion relates to the whole study and is not specific to noncompressible regions. Because the NTDB does not offer details on vessel injury descriptions such as occlusion, transection, and pseudoaneurysm, it is likely that their cohort is a mixture of these different injury patterns and therefore different from our cohort where occlusion and pseudoaneuryms have been excluded.

Two recent studies analyzing specific noncompressible vascular injuries include Branco and colleagues dual-center study on axillosubclavian injuries between 2002 and 2010 and Lauerman and colleagues[10,20] review of iliac injuries in the NTDB between 2002 and 2006. In the axillosubclavian study, the authors showed a trend of lower ventilator, ICU and hospital stays in matched endovascularly managed patients but not statistical significance. In the iliac NTDB review, both venous and arterial injuries were included, and the authors showed a higher rate of endovascular therapy use compared with open surgery in blunt patients with associated pelvic fractures. They did not attempt to compare mortality or resource use by treatment. It is difficult to compare our results and outcomes with either of these studies. Surgical practice continues to change over time, and our data are from a more recent period. This study also has different definitions for inclusion, and we have not attempted to match the different treatment groups.

This review has focussed on the type of surgery performed. While the PROOVT registry does account for damage control techniques, it does not address whether these techniques are open or endovascular in type. resuscitative endovascular balloon occlusion of the aorta is an endovascular technique gaining favour in trauma centers instead of open resuscitative thoracotomy in certain instances.[4] A separate registry monitoring its use in the US reported 1 year results showing no survival benefit between the two techniques.[21] It is not possible to tell in our review whether resuscitative endovascular balloon occlusion of the aorta was used in either the hybrid or endovascular groups. We have focused on the overall technique used to manage the injury.

As with any registry data, there are limitations to the accuracy of the data as a representation of practice on a wider scale. This review includes data on vascular injuries from 22 trauma centers across the United States, which represent a small percentage of the number of institutions who submit data to the NTDB. The PROOVIT institutions are categorized by level and by volume but the exact number of admissions for the period studied are not recorded, so the incidence of these injuries cannot be calculated. In this review, we did not address time delays to surgery, duration of procedure or whether the patient had a planned period of nonoperative observation before surgery. In the combined group, it is difficult to establish if patients had initial damage control using one technique, and then definitive management using another or whether the hybrid approach

was planned from the outset. Admission independent variables are the first recorded results in hospital. These data show significant differences between the admission vital signs of the NCTH groups undergoing different surgical approaches. By excluding missing data points in the analysis, it is possible that we have produced some bias in this analysis but it was felt that this was the appropriate way of presenting the data given its nature as a descriptive study of registry data. The PROOVIT registry does not account for prehospital vital signs, resuscitation efforts before presenting to the emergency department, or delays between injury and assessment which may greatly affect outcomes in vascular trauma and may influence the outcomes of this study if known. Despite these limitations, our results show an interesting pattern of lower mortality and transfusion amounts but longer hospital and ICU stay between patients with blunt NCTH vascular injuries managed with endovascular or open surgery.

CONCLUSION

Our review of the PROOVIT registry demonstrates utilization of endovascular therapy among severely injured blunt trauma patients primarily with noncompressible torso hemorrhage. In that population, endovascular therapy was associated with low requirements for blood transfusion and high survival rates but longer hospital length of stay than surviving patients treated with open surgery. Additional investigation is needed to define indications and optimal utilization of endovascular technologies in the setting of vascular trauma.

AUTHORSHIP

E.R.F., J.J.D., and B.C.B. were responsible for initial planning and data acquisition. E.R.F., M.N.L., and K.G. analyzed the data and performed the statistics. E. R. F. drafted the article. M.N.L., K.G., B.C.B., J.S., T.B.F., T.C.H., T.S., D.S., K.I., T.E.R., N.P., and J.J.D. provided advice and critical editing of the article. E. R. F. takes responsibility for the content of the article.

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DISCLOSURE

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DISCUSSION

Dr. J. David Richardson (Louisville, Kentucky): In the mid-1990s the AAST constituted the Multi-Institutional Trials Committee and I was actually privileged to be the chair of that group initially and for several years.

In 1997, exactly 20 years ago, the first paper from that group was published after presentation at this meeting on what was then the current management of blunt aortic rupture.

It's interesting, these things, even though there may not be trials, per se, that paper actually changed practice management a great deal by showing that the clamp-and-sew technique was inferior, really, to bypass in the treatment of blunt aortic rupture.

Now the original plan for the Committee was that we would do actual trials but logistics, review board issues, ethical concerns really make that unworkable.

Instead, that original paper outlined the current state of treatment with a huge data base of contemporaneously treated patients and in that spirit the PROOVIT trial, I think, now does the same thing.

Any time you can get treatment over a period of just three or four years on over 1,100 patients with vascular injuries, that makes it, in my view, a very valuable paper, regardless of any limitations it might have.

In the interest of time I'll ask only two questions.

The authors state the most common indication for endovascular treatment was – quote – blunt, non-compressible torso injuries, but didn't provide much granularity in that in terms of what type of vessels were treated and exactly how that treatment went.

I think your paper would be greatly enhanced by perhaps adding a table on that, to wit, how many if any of these endovascular treatments were embolizations of pelvic fractures, for example. You didn't mention that. I'm not sure if those were even included.

It's important to know that detail to distinguish between a technique in use for 40 years versus the more novel applications of stents or embolizations of non-pelvic vessels.

Then now many were endographs, if any – I would presume some were – for blunt aortic injuries? It all would be useful to know. And, again, I think actually adding a table to your manuscript would be very helpful.

My second question is perhaps a more philosophical one. You are probably unable to answer it. But do you have data or at least some general sense of who is doing the treatment, particularly on these penetrating extremity injuries? Are these done by vascular surgeons or acute care trauma surgeons?

One of the promises of acute care surgery was that surgeons would manage a broad spectrum of injuries, including vascular problems; but in my view of the landscape that is not often true or often not true, although in many places it is. So do you have data or opinions on my observations?

Regardless, I think this is an excellent paper and I certainly commend it to everyone for their review.

Dr. Edwin R. Faulconer (Davis, California): Dr. Richardson, thank you very much for your kind words and your comments.

The question about granularity on the non-compressible hemorrhage group and what is being managed within this data set. The pelvic embolizations, as was presented by the last presenter, tend to fall outside of this registry because the registry does not go down into very small, unnamed pelvic vessels. Very significant pelvic injuries might be in the data set but the majority of the pelvic fractures with angioembolization probably aren't making it into this registry. The blunt aortic injuries, however, are.

In the endovascular group of 97 patients that we presented, within the non-compressible trauma group 54 percent of these are thoracic injuries rather than abdominal or pelvic injures. And of these thoracic injuries all but one are blunt.

This is in contrast to the open surgical patients. They're more abdominal; they're more penetrating; and they're actually only got a 25 percent rate of thoracic injury. They are different groups. We accept that. And that's why we're not trying to say that one technique is better. It is clear in the multivariate analysis that the techniques don't make a significant difference as don't show up as independent variables in this data set.

I think with more numbers we could do that comparison much better but with the numbers we've got at the moment we kept the statistical analysis to non-compressible trauma.

Your second question I can't answer, as you suggested. I can tell you where in the Hospital these operations are being done: whether they are being done in a hybrid suite or whether they are being done in an interventional radiology suite, but I can't tell you who is doing them. I can't tell you whether it's a resident or a fellow or an attending and what their subspecialty or training is. And that may be something that can be brought in in the future or in trials or prospective studies.

IS YOUR CLINICAL TRIAL READY FOR NEW DATA SHARING REQUIREMENTS?

Jenkins, Donald H; Phillips, Monica J; Beilman, Gregory J; Bulger, Eileen M; Davis, Michael R; McAuliffe, Matthew J; Rasmussen, Todd E; Salinas, Jose; Smith, Sharon L; Spott, Mary A; Weireter, Leonard J; Price, Michelle A.

Introduction: Increasing data sharing and avoiding duplication of studies have been ongoing challenges in medical research. In order to address these issues and create a standard for data sharing among medical researchers, the International Committee of Medical Journal Editors (ICJME) will start requiring the use of data sharing plans as part of a clinical trial manuscript submission beginning in July 2018. ICJME journal members include *The Journal of the American Medical Association* and *The New England Journal of Medicine,* and many medical journals follow its recommendations (e.g., requiring trial registration at clinicaltrials.gov). To address this new requirement, the Department of Defense (DoD) funded the development of the new National Trauma Research Repository (NTRR).

Methods: The NTRR is designed to be a central, cloud-based repository for the clinical data resulting from both military funded and civilian research efforts. Access to the system is through web-based applications developed jointly with the National Institutes of Health – Center for Information Technology. Repository data will cover the entire patient care trajectory: from injury prevention, point of injury, en route care, hospital care, rehabilitation and long-term outcomes. The system allows researchers to share original data sets and request shared data sets for secondary analyses. The NTRR uses common data elements (CDEs) to improve data quality and opportunities for comparison and combination of data from multiple studies. To identify the initial CDEs, a review of data elements from more than 20 large trauma study data dictionaries (including PROOVIT, PROMMT, ROC and METRC) and the NIH Common Data Element Resource Portal was conducted.

Results: Over 500 data elements from 20 trauma-related research data dictionaries were reviewed to identify the most frequently used CDEs in trauma research. The most frequently used CDEs were organized into the following data storage modules: Core and study metadata (submitted by all studies), Prehospital, Inpatient, Rehabilitation, and Outcomes/Quality of Life. Studies contributing data to the NTRR are categorized to the appropriate phase of care module. Importantly, NTRR's data structure allows researchers to add unique data elements (UDEs) to the NTRR data dictionary for their study and use by other researchers. This will further promote data harmonization across trauma studies.

Conclusion: The NTRR was developed to facilitate data sharing in order to optimize the use of clinical trauma research data and collaboration across the trauma research community. The NTRR data dictionary contains the most frequently used CDEs among trauma research studies organized into phase of care modules. The NTRR will provide trauma researchers with a unique and novel tool to conduct exploratory analyses of shared data sets, to create and implement a data sharing plan, to adopt CDEs for study data dictionaries, and to meet new medical journal data sharing requirements.

Abstract Submitted for 2019 EAST Meeting

Introduction: Fasciotomy remains an important adjunct in the management of peripheral vascular injuries, yet the indications for and natural history of this intervention are not well elucidated.

Methods: The AAST PROOVIT registry was utilized to identify patients undergoing four compartment fasciotomy of the leg after femoropopliteal arterial injuries. Outcomes following fasciotomy for both therapeutic and prophylactic indications were compared, including whether primary skin closure or split-thickness skin grafting (STSG) was performed.

Results: From 2013 to 2018, 530 patients with femoropopliteal artery injuries were identified, of whom 272 (51.5%) underwent surgical management. Fasciotomy was performed at the initial operation in 55.5% (151/272) of patients, with 92.1% (139/151 surviving to discharge; of interest, delayed fasciotomy was performed at reoperation in only 5.8% (7/121) patients in this group. Among survivors, fasciotomies were classified as "therapeutic" in 58.3% (81/139) and "prophylactic" in 41.7% (58/139). There were no significant differences between these two groups, including amputation rate (14.8% vs. 8.6%, $p = 0.272$) and the rate of primary skin closure (54.0% vs. 53.4%, $p = 0.919$) of the fasciotomy site. Comparison of rates of primary skin closure versus STSG coverage revealed only that skin closure was more likely among patients who were more severely injured (ISS 16.0 vs. 10.0, $p = 0.039$; Extremity AIS 3.3 vs. 2.8, $p = 0.007$). Primary skin closure was achieved at a median of 5.0 days vs. 11.0 days for STSG ($p = 0.001$)

Conclusion: Over 55% of patients undergoing repair of a femoral or popliteal artery injury have a fasciotomy of the leg performed at the same operation, and delayed fasciotomies are very uncommon in the modern era. A "therapeutic" indication for fasciotomy continues to be more common than "prophylactic", while outcomes are identical in both groups.

Submitted to EAST 2019

Title: Contemporary Tourniquet Use in Extremity Vascular Trauma: The AAST PROspective Observational Vascular Injury Treatment (PROOVIT) Registry

Background: Correct tourniquet application can be a lifesaving intervention prior to definitive surgical treatment of extremity vascular trauma. Only a few small studies have evaluated tourniquet use in civilian trauma. We aimed to describe the contemporary use of tourniquets in the management of civilian extremity vascular trauma and evaluate the associated outcomes.
Methods: Data was analyzed from the multicenter AAST PROOVIT registry (Feb 2013-Dec 2016) using student t-tests and propensity-score matching using R-software. Controls were matched using Injury Severity Score(ISS), Abbreviated Injury Score of the extremity(AIS extremity), initial systolic blood pressure(SBP), initial Glasgow Coma Scale(GCS) score, lactate level, and age. Patients with multiple arterial injuries were excluded.
Results: 623 patients were included for analysis. Pre-hospital tourniquets were placed in 14.9% of patients with extremity arterial injury. The amputation rate following any extremity arterial injury, with or without placement of a tourniquet, was not statistically different when compared to propensity-matched controls (tourniquet 0.04 vs none 0.10;p=0.12). There was no statistical difference between in-hospital mortality with tourniquet placement (tourniquet 0.08 vs control 0.04;p=0.18). Tourniquet use did not significantly affect 24-hour packed red blood cell (pRBC) transfusion requirement (tourniquet 7.98 vs none 7.12;p=0.35), need for post-operative therapeutic anticoagulation (tourniquet 0.65 vs none 0.68;p=0.36), or the rate of infection in the affected limb (tourniquet 0.01 vs none 0.02;p=0.45).
Conclusion: The PROOVIT registry shows that in contemporary civilian practice, tourniquets are used for extremity arterial injury in just 14.9% of cases, much lower than previously reported. Tourniquet use was not associated with an increased rate of amputation, in-hospital mortality, 24-hour pRBC transfusion, or subsequent infection in the affected limb. As the national rollout of the Stop the Bleeding campaign gains momentum, we should continue to advocate for pre-hospital tourniquets, as the life-saving benefit does not appear to be offset by increased morbidity or mortality.

Level of Evidence: Level III, Prospective cohort study, prognostic
Keywords: vascular injury, tourniquet, exsanguination, trauma, amputation

Trauma Surgery & Acute Care Open

Launch of the National Trauma Research Repository coincides with new data sharing requirements

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NTRR IS LAUNCHING

Previous analyses of research data have shown that many trauma studies cannot be replicated or validated due to a variety of factors, including lack of access to study data, lack of access to protocol information, and inability to replicate procedures used in the study. New data sharing rules for federally funded studies have been put in place to address factors associated with this issue.

To address these new data sharing requirements, beginning this month, investigators conducting research on trauma and critical care will be able to maximize the utility of the data they produce with the launch of the National Trauma Research Repository (NTRR). The system was developed as a resource to support new and emerging data sharing needs within the trauma research community and is envisioned to be a key piece of the national trauma research infrastructure. It is funded by the Department of Defense (DoD) and developed by the National Trauma Institute (NTI) to promote collaboration, accelerate research, and advance knowledge on the treatment of trauma. When it becomes fully functional, the NTRR will be a comprehensive repository offering thousands of data points from hundreds of studies, enabling investigators to query across studies for their own research objectives.

The NTRR was developed by trauma researchers for trauma researchers. A national committee was convened of civilian and military trauma researchers and stakeholder organizations to define the functional requirements of the repository that would best serve investigators.[1] The NTRR allows users to peruse available data elements, study data sets, and supporting documentation (eg, protocols, consent forms, data dictionaries). Investigators contributing data to the NTRR can upload completed data sets and supporting documents at the completion of a study or as the study is being conducted. All studies will submit core data elements and study metadata (information about the study). Use of common data elements (CDEs) is encouraged to improve data harmonization and opportunities for comparison and combination of data from multiple studies. The system also allows researchers to use unique data elements, or UDEs, if a CDE for that variable is not available. When the data set is complete and validated, it will receive a digital object identifier (DOI) to allow contributing researchers to be acknowledged in publications resulting from secondary analyses.

The NTRR is organized in four modules representing the entire patient care trajectory: prehospital care, inpatient care, rehabilitation, and long-term outcomes/quality of life issues. Access to the system is through a web-based interface developed by the National Institutes of Health (NIH) – Center for Information Technology and enhanced by the NTI. Hosted in a secure Amazon Web Services cloud environment, the repository conforms to standards set forth in the Federal Information Security Management Act, which provides a standardized approach for assessing, monitoring, securing, and authorizing cloud computing products. Specific security controls in place for the NTRR include firewalls, application monitoring software and integrated cloud tools for operating system scanning, SSL (Secure Sockets Layer), antivirus and password encryption technology, and security audits and inspections.

Uploading trauma research data into the NTRR will fulfill both funder and publisher obligations to share and help to create a rich resource to support trauma investigations over time. Although it will take years to build out the repository and for it to be used at full capacity, the NTRR holds great promise for the responsible stewardship of data, respecting the contributions of study participants, the efforts of trialists, and the sources of public funding whose ultimate goal is to improve patient outcomes and minimize death and disability.

NTRR ENTERS AN EMERGING DATA SHARING LANDSCAPE

Over the past 15 years, the concept of data sharing has grown from a few disease-specific efforts such as traumatic brain injury and Parkinson's disease to almost universal expectations by research funding entities and journal editors. Those requiring various degrees of sharing include academic journal publishers and a wide variety of funding agencies, from government entities like the DoD and the NIH to private philanthropies like the Bill & Melinda Gates Foundation and Wellcome Trust, to corporate entities like Medtronic and GlaxoSmithKline.[2 3]

Perhaps the earliest funder to recognize the benefits of data sharing, the NIH initially published its Statement on Sharing Research Data in 2003.

Declaring that "data sharing is essential for expedited translation of research results into knowledge, products, and procedures to improve human health," the NIH requires applicants seeking $500 000 or more in grant funding to include a plan for data sharing in their proposals.[4] Likewise, since 2011, the National Science Foundation (NSF) has required funding proposals to include a data management plan describing how they will conform to the NSF policy on the dissemination and sharing of research results.[5] Such plans are expected to address the types of data and other materials to be produced during the study, the data and metadata standards to be used, policies for access and sharing, policies for reuse, and plans for archiving and preserving access to data and other research products.

In 2013, the White House Office of Science and Technology Policy (OSTP) asserted that federal agencies will work to develop policies to make the results of federally funded research freely available to the public and for requiring researchers to better account for and manage the digital data resulting from federally funded research.[6] After OSTP's mandate, the DoD issued its guidance in 2015, with a "Plan to Establish Public Access to the Results of Federally Funded Research." The plan provides a framework for increasing public access to both scholarly publications and the scientific data that underlie them—for the research and programs funded in part or wholly by the DoD. "Having DoD components work together within this proposed framework will yield synergies and innovations no single component can achieve alone," explained its authors (p2).[7] According to the plan, those submitting research proposals must include a data management plan that largely follows what is required by the NSF, and must upload research outputs—including peer-reviewed scholarly publications and data sets—to an online repository maintained by the Defense Technical Information Center.[7]

In 2014, *The Public Library of Science* (*PLOS*) was one of the first publishers to make data sharing a requirement for those investigators whose articles are accepted for publication in its journals.[8 9] *British Medical Journals*, *Springer Nature*, and many other publishers now have data policies requiring or recommending data statements and data sharing.[8 10] In 2017, the International Committee of Medical Journal Editors (ICMJE) revised its *Uniform Requirements for Manuscripts* (renamed *Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals*) to include a mandate that the results of clinical trials must contain a data sharing statement beginning in July 2018, and that clinical trials that begin enrolling participants on or after 1 January 2019 must include a data sharing plan in the trials' registration (table 1).[11–13] The ICMJE—a small working group of general medical editors including the *British Medical Journals*, *Journal of the American Medical Association*, *New England Journal of Medicine*, *PLOS Medicine*, and the *US National Library of Medicine*—has a great deal of clout. Most medical journal editors follow the ICMJE's recommendations. Trauma clinical trials researchers will recall that the ICMJE's recommendation requiring trial registration (eg, www.clinicaltrials.gov) was quickly adopted by nearly all medical journals. An informal survey of editors of the journals in which trauma investigators often publish revealed that they are aware of ICMJE's mandate and are developing their own data sharing policies.

Therefore, researchers who have had little incentive to share data now find that there is no choice but to do so, as more members of the research community recognize that data resulting from publicly funded clinical trials are a public good, to be made openly available with as few restrictions as possible.[14] The NTRR is the mechanism that trauma researchers can now use to meet such funder and publisher requirements.

Table 1 Examples of data sharing statements that fulfill the ICMJE requirements

	Example 1	Example 2	Example 3	Example 4
Will individual participant data be available (including data dictionaries)?	Yes.	Yes.	Yes.	No.
What data in particular will be shared?	All of the individual participant data collected during the trial, after deidentification.	Individual participant data that underlie the results reported in this article after deidentification (text, tables, figures, and appendices).	Individual participant data that underlie the results reported in this article after deidentification (text, tables, figures, and appendices).	Not available.
What other documents will be available?	Study protocol, statistical analysis plan, informed consent form, clinical study report, analytic code.	Study protocol, statistical analysis plan, analytic code.	Study protocol.	Not available.
When will data be available (start and end dates)?	Immediately after publication—no end date.	Beginning 3 months and ending 5 years after article publication.	Beginning 9 months and ending 36 months after article publication.	Not applicable.
With whom will the data be shared?	Anyone who wishes to access the data.	Researchers who provide a methodologically sound proposal.	Investigators whose proposed use of the data has been approved by an independent review committee (learned intermediary) identified for this purpose.	Not applicable.
What types of analyses are authorized to be conducted?	Any purpose.	To achieve aims in the approved proposal.	For individual participant data meta-analysis.	Not applicable.
By what mechanism will data be made available?	Data are available indefinitely at (include link).	Proposals should be directed to xxx@yyy. To gain access, data requesters will need to sign a data access agreement. Data are available for 5 years at (include link).	Proposals may be submitted up to 36 months after article publication. After 36 months the data will be available in our university's data warehouse but without investigator support other than deposited metadata. Information regarding submitting proposals and accessing data is at (include link).	

ICMJE, International Committee of Medical Journal Editors.
[a]Reprinted with permission from the Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals at http://www.icmje.org/icmje-recommendations.pdf.[13]

DATA SHARING BRINGS BOTH BENEFITS AND CHALLENGES

The purpose of data sharing is to make research data available for reuse, validation, meta-analysis, and replication.[15] The purported benefits of data sharing include replication of previous findings, comparisons with independent data sets, testing of additional hypotheses, teaching, and improving patient safety.[16] Evidence has shown that data sharing practices may also help correct for publication bias (the publication or non-publication of research findings depending on the nature and direction of the results) and outcome reporting bias (the selective reporting of some outcomes but not others).[17] Individual researchers benefit from data sharing via increased visibility, improved output connections, and reduced inefficiencies. The research community benefits from advances in reproducibility, improved long-term data archiving, and a reduction in unnecessary studies. Society benefits from data sharing by increased innovation, easier access to research, and scientifically informed policy making.[18] Of course, the ultimate goal of responsible sharing of clinical trial data is to increase scientific knowledge that leads to better therapies for patients.[19]

As with any new paradigm, difficulties and weaknesses become apparent in the first attempts to meet new expectations and goals—the higher the expectations, the greater the likelihood there will be challenges in meeting them. The challenges associated with data sharing are real. Researchers are concerned about the barriers to data sharing, even as the benefits are well documented and requirements for doing so come due.[8] Still at issue are the resources required to prepare data for sharing, the potential for other users to misinterpret data, and the possibility that the original researchers—the ones who did all the work to design and conduct the trials—may not be able to publish as many articles using the data as they might otherwise have.[14] In a recent survey of more than 7700 researchers, *Springer Nature* reported that among the medical sciences researchers surveyed (2683 respondents), 39% shared data neither through supplements nor repositories.[8] These respondents identified the following barriers to data sharing:

- "Unsure about copyright and licensing" (44%).
- "Organizing data in a presentable and useful way" (40%).
- "Not knowing what repository to use" (37%).
- "Lack of time to deposit data" (25%).
- "Costs of data sharing" (21%).[8]

Risks, burdens, and challenges also include protecting the privacy of trial subjects, safeguarding intellectual property and proprietary information, checking invalid secondary analyses that could harm public health, providing enough time for researchers to analyze their own data and receive recognition before sharing, and addressing the costs.[19]

The NTRR is working to overcome such challenges and will continue to refine its policies and processes as new issues arise. To address the concern researchers may have that their ability to produce publications will be compromised, the NTRR holds to a 1 year embargo from the time of the first study publication before making data available for sharing. Further, the NTRR will limit access to data by requiring researcher credentials and institutional endorsement. Requesting investigators will be required to have institutional review board approval for their planned secondary analyses. They will be encouraged to collaborate with the contributing investigator and required to cite the original data source (via DOI). Shared data will either be deidentified or be limited data sets with appropriate institutional data use agreements. With these safeguards in place, the NTRR administrators expect to minimize the potential for misinterpreting or misusing the data.

IT'S YOUR NATIONAL TRAUMA RESEARCH REPOSITORY: HELP TO BUILD THIS RESOURCE AND IMPROVE PATIENT OUTCOMES

Data sharing platforms encourage transfer of research data and knowledge between civilian and military researchers, reduce redundancy, and maximize limited research funding.[1] Optimizing the research life cycle now involves responsible data stewardship, as opposed to ownership. The old paradigm—in which individual investigators maintain indefinite ownership of the data resulting from their publicly funded work—results in now unacceptable research waste, including hidden data and irreproducible findings.[20] Single-instance use of research data and the inability to access data resulting from studies limit the impact of trauma research funding. Especially in fields such as trauma, where research funding has never been free-flowing and in the past decade has become even more difficult to come by, it is imperative to make every research dollar count. As the trauma research community seeks to maximize available research funds, the NTRR makes data available for enduring use and will effectively allow for more data analysis and knowledge translation, which can result in improved patient care.

Still in its infancy, the NTRR needs trauma investigators' participation to realize the vision of advancing the field of trauma research to achieve improved outcomes for injured patients. Become a data steward and help build YOUR National Trauma Research Repository. You can find additional information and detailed implementation guidance on the NTRR website (www.ntrr-nti.org).

Contributors MAP and PJB conducted the literature search and contributed to the planning, writing, and critical revision of the article. All authors contributed to the writing and critical revision of the article.

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Competing interests None declared.

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The National Trauma Research Repository - #105

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07/17/2018

Drs. Don Jenkins and Michelle Price from the National Trauma Institute introduce the National Trauma Research Repository (NTRR) an exciting new undertaking that aims to combine data from previous and future trauma research sources, such as PROPPR, PROMMTT, the Glue Grant, DOD, etc. They also discuss how researchers can access these data and contribute their own data to the ever-growing repository. Got a project idea for a large national database? **Check out NTRR** to see if this could work for you.

Disclaimer Statement:
The National Trauma Research Repository is sponsored by the Department of the Army, Prime award #W81XWH-15.2.0089. The U.S. Army Medical Research Acquisition Activity, 820 Chandler Street, Fort Detrick MD21702-5014 is the awarding and administering acquisition office. The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the view of the Department of the Army or the Department of Defense.

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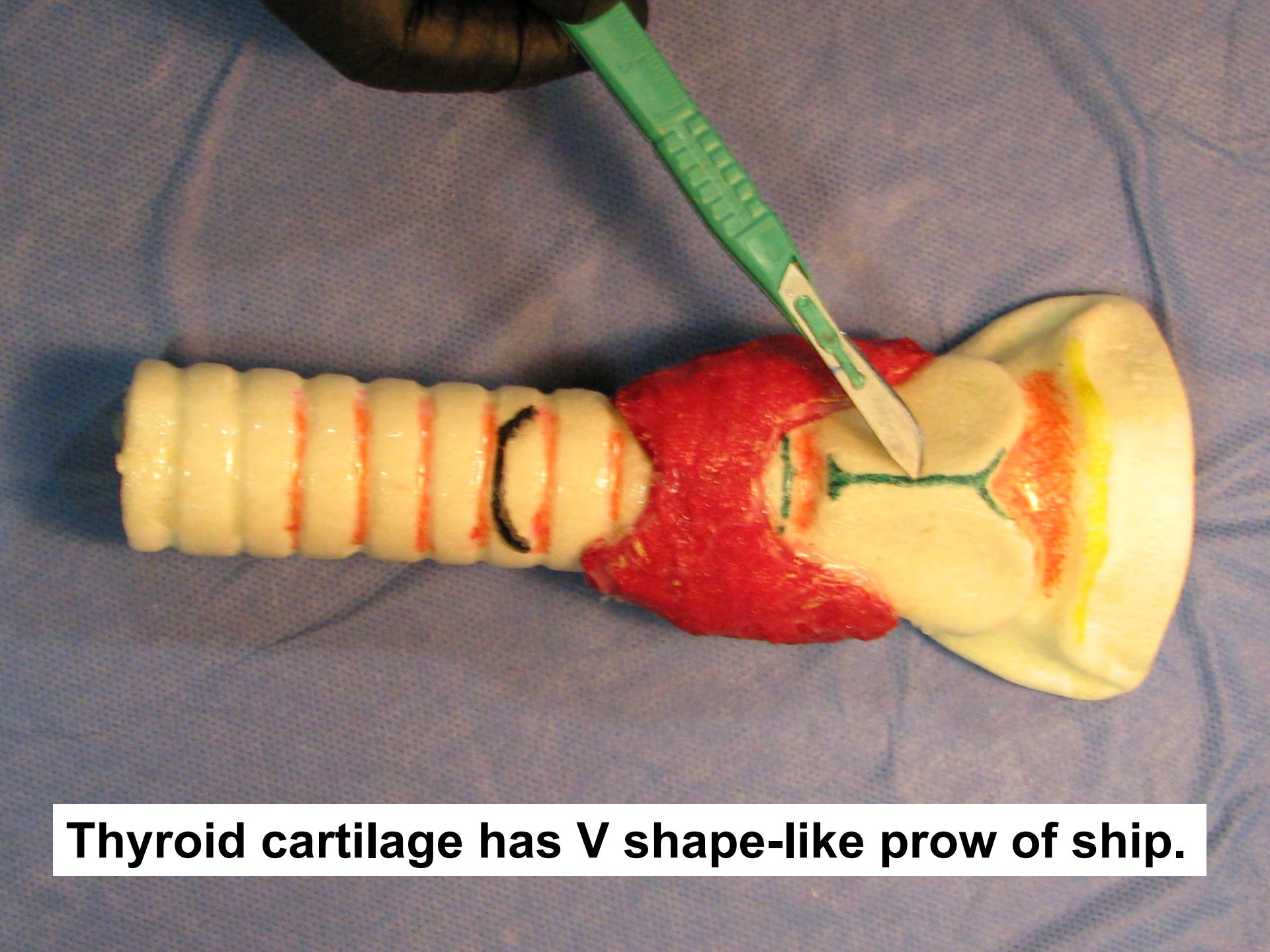
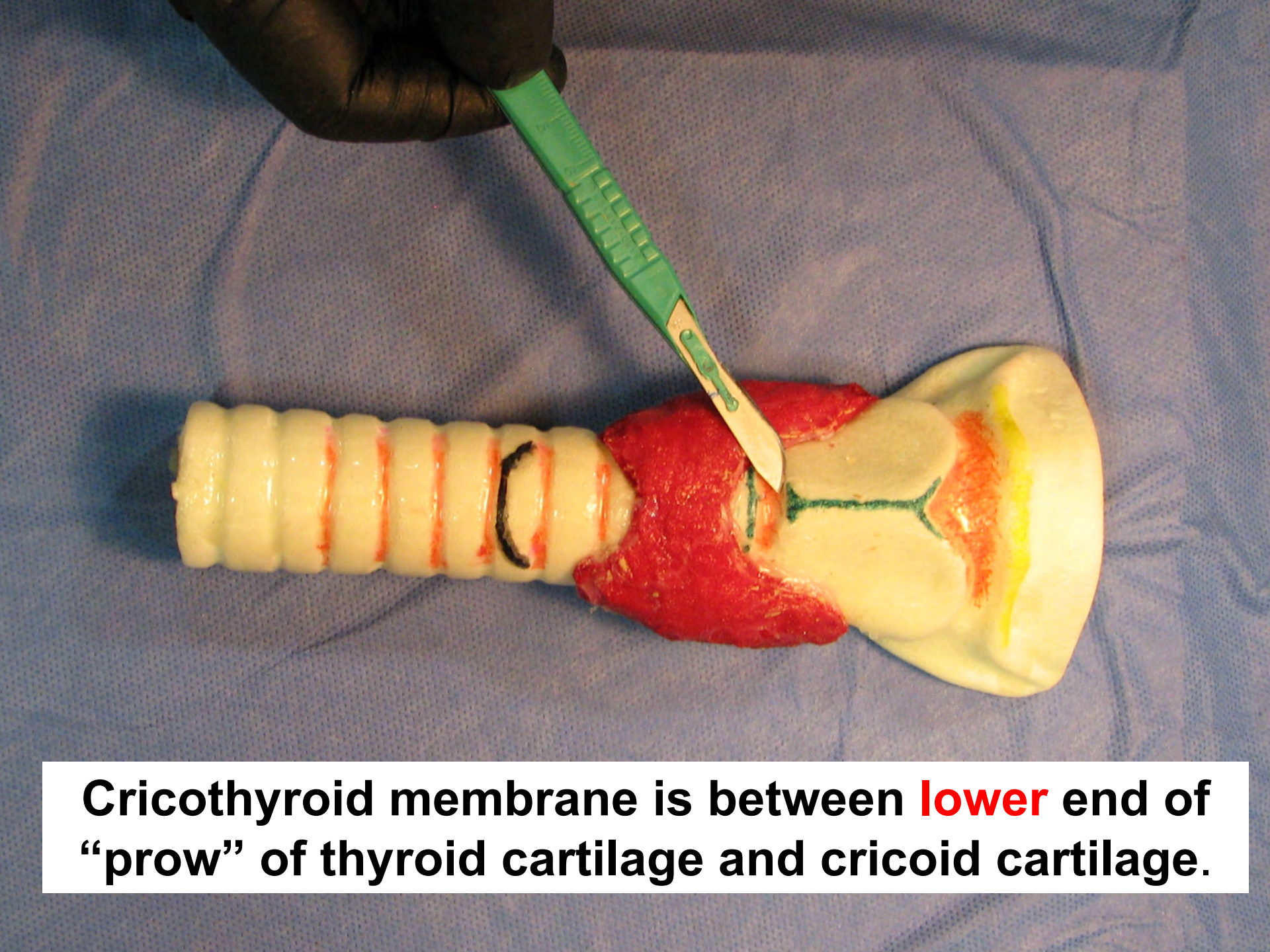
Cricothyroidotomy

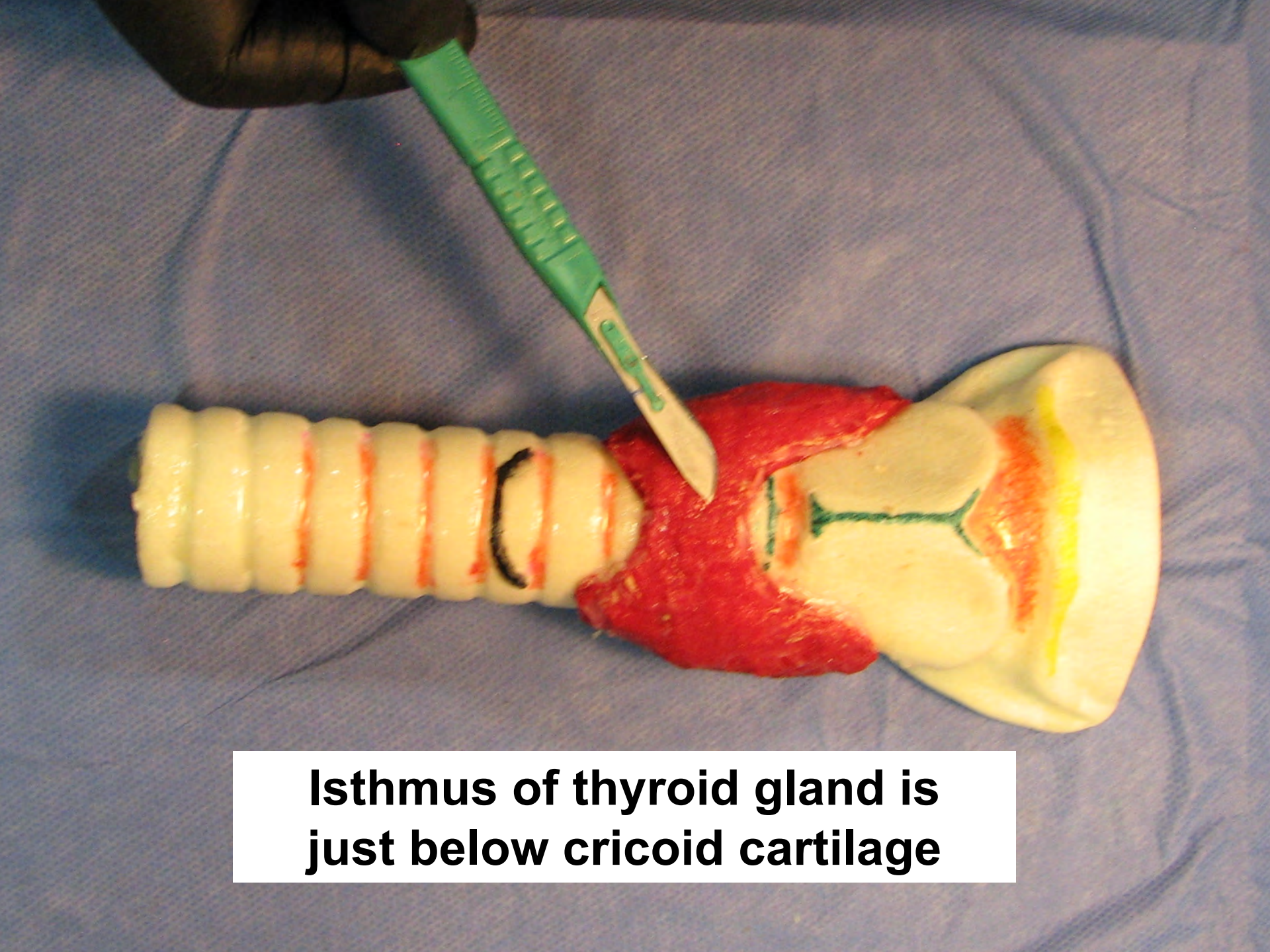
Surgical Anatomy

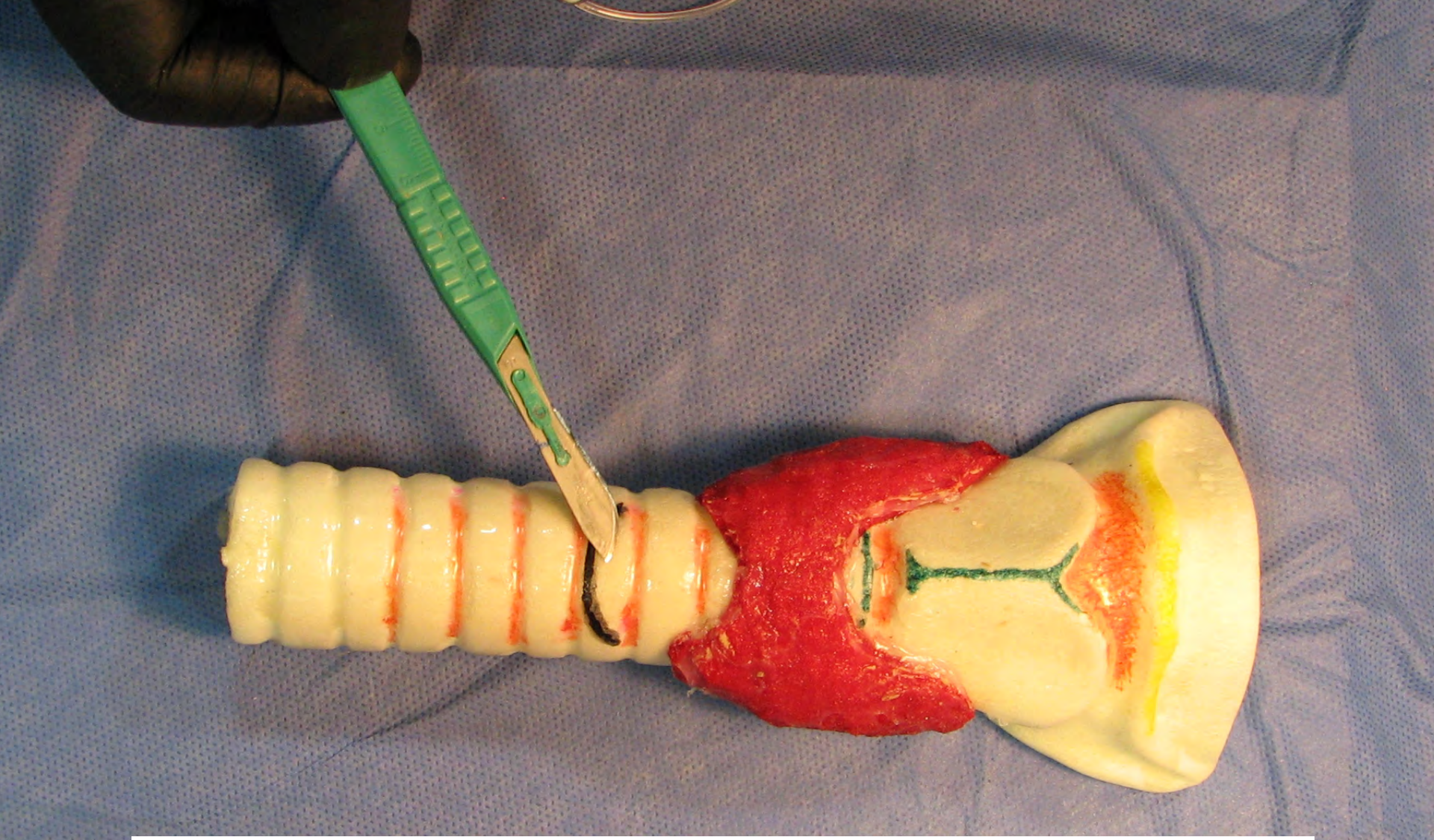


Thyroid cartilage has V shape-like prow of ship.

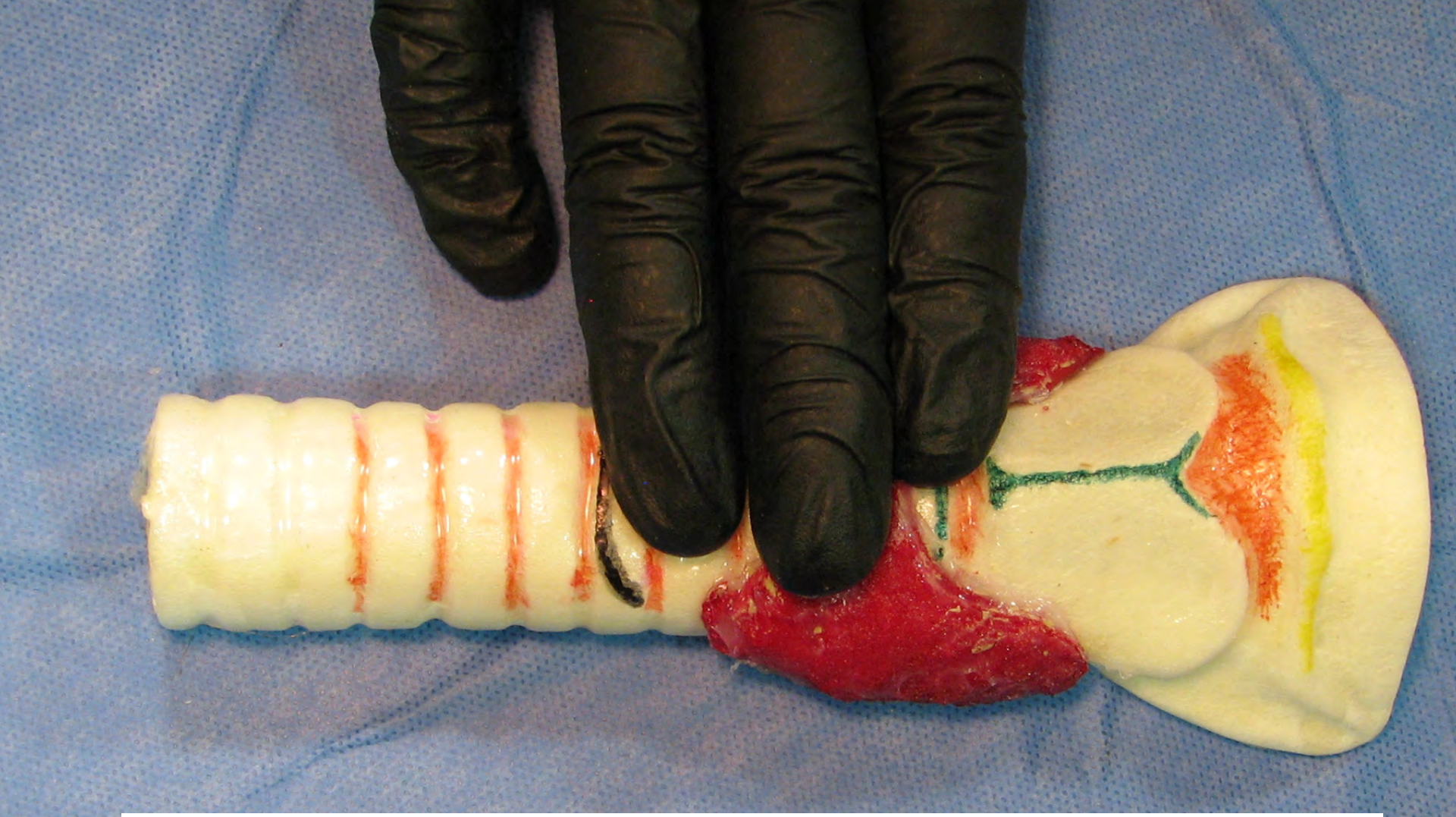


Cricothyroid membrane is between lower end of "prow" of thyroid cartilage and cricoid cartilage.


Isthmus of thyroid gland is
just below cricoid cartilage



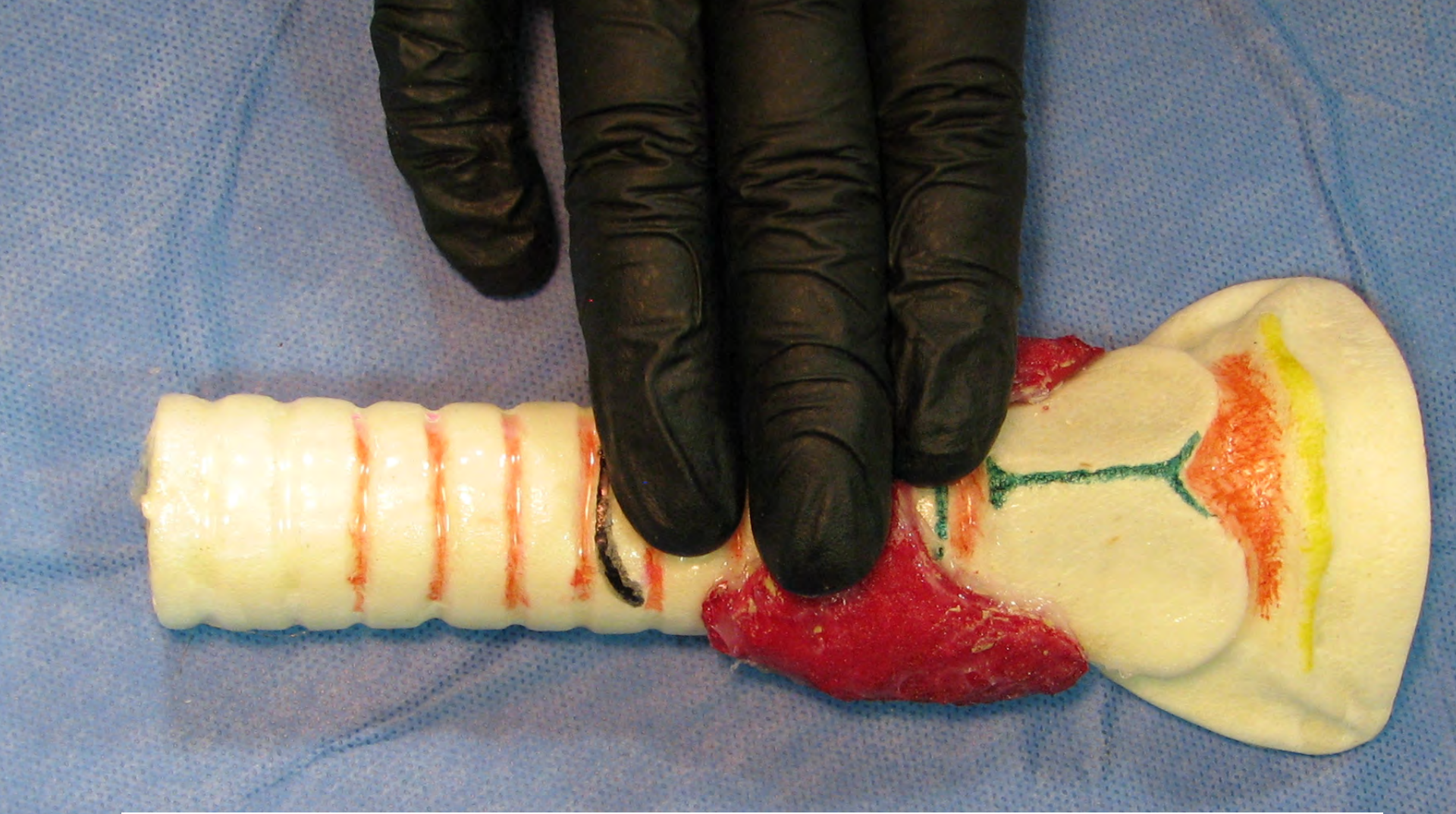
Black line indicates level of sternal notch where trachea passes behind sternum



Cricothyroid membrane is about 3 fingers above sternal notch in adult male.

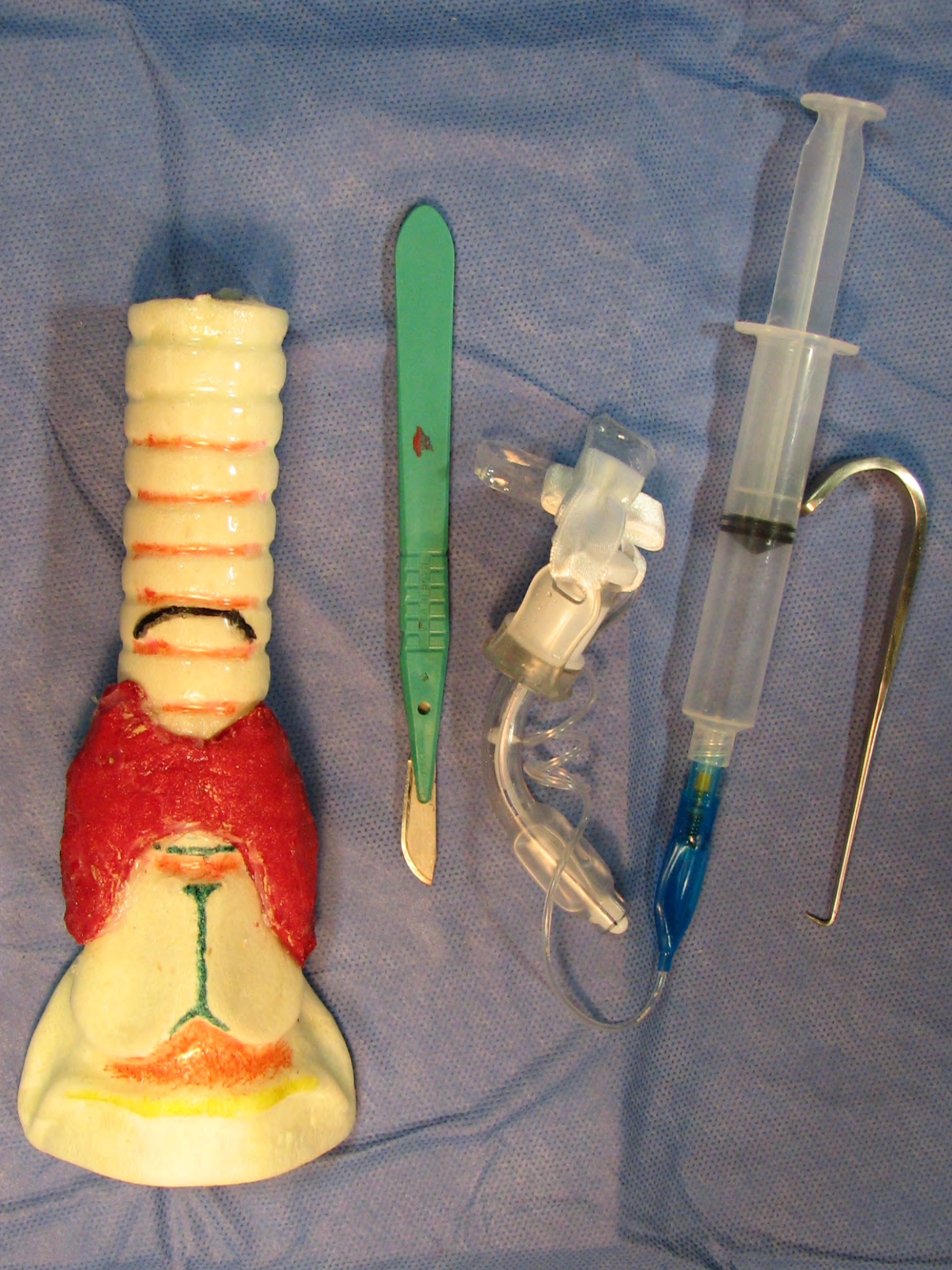
Sternal notch

Most important landmark to locate level of cricothyroid membrane



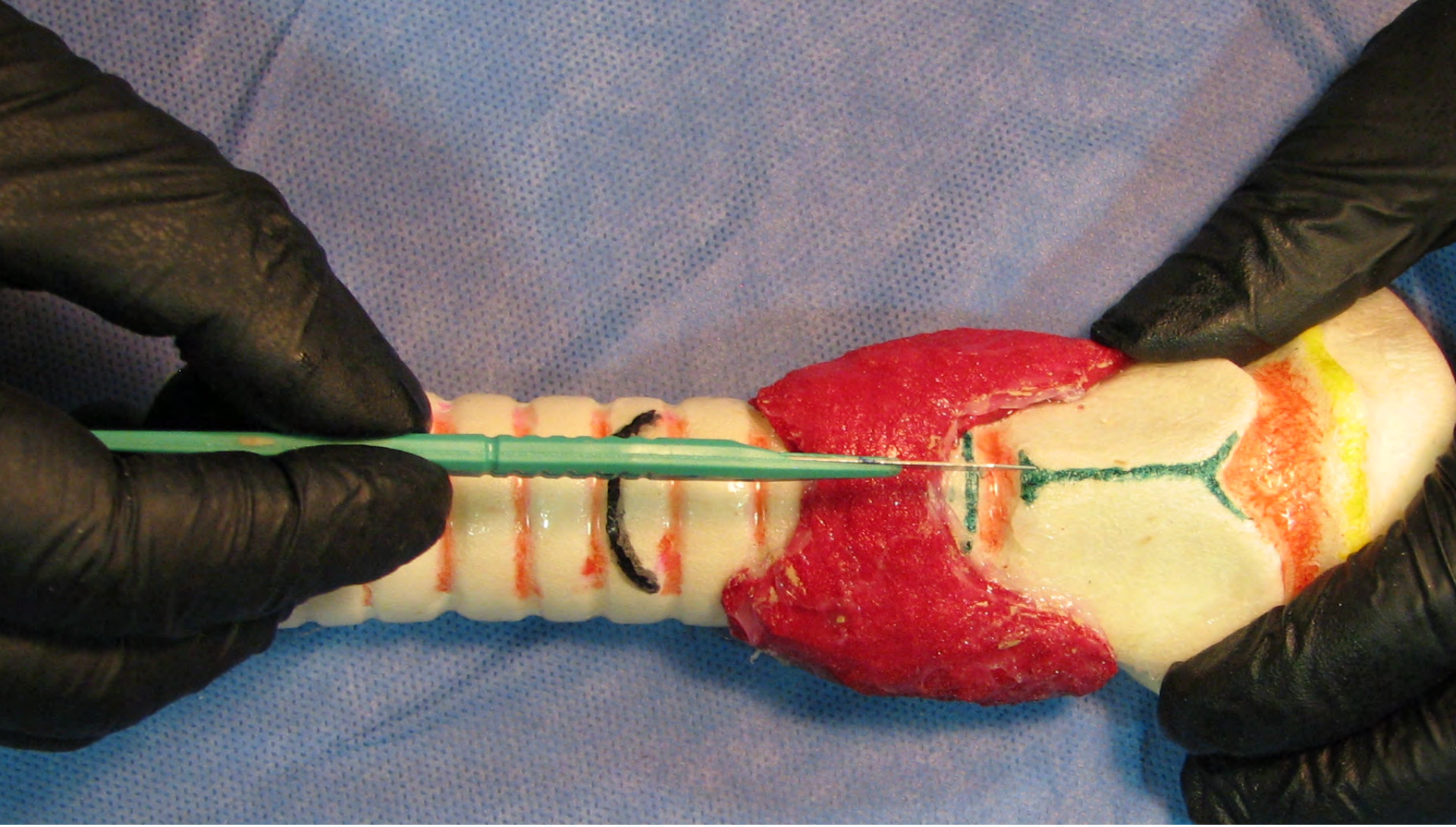
REMEMBER:Cricothyroid membrane is about 3 fingers above sternal notch in adult male.

CRIC Procedure

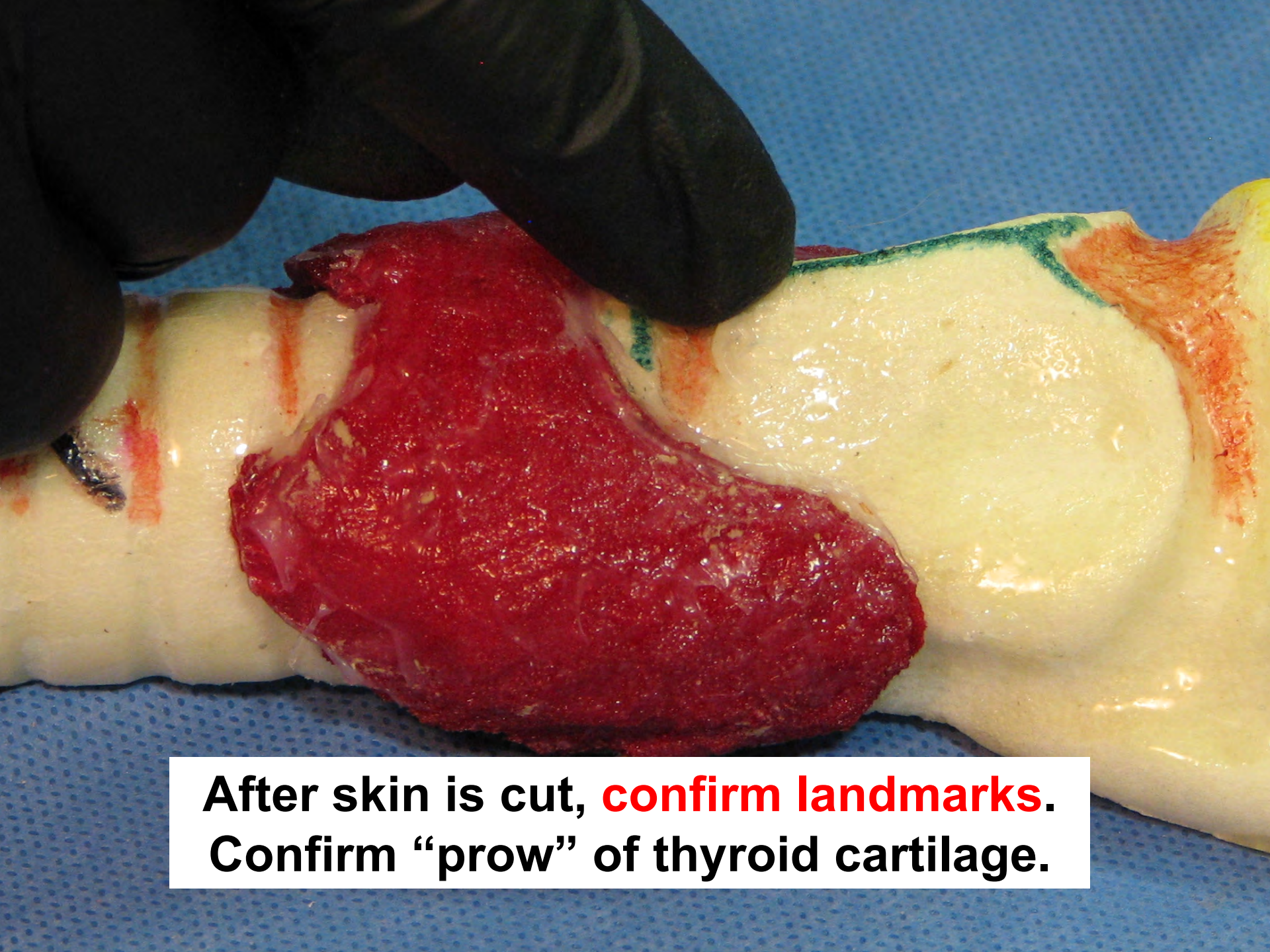


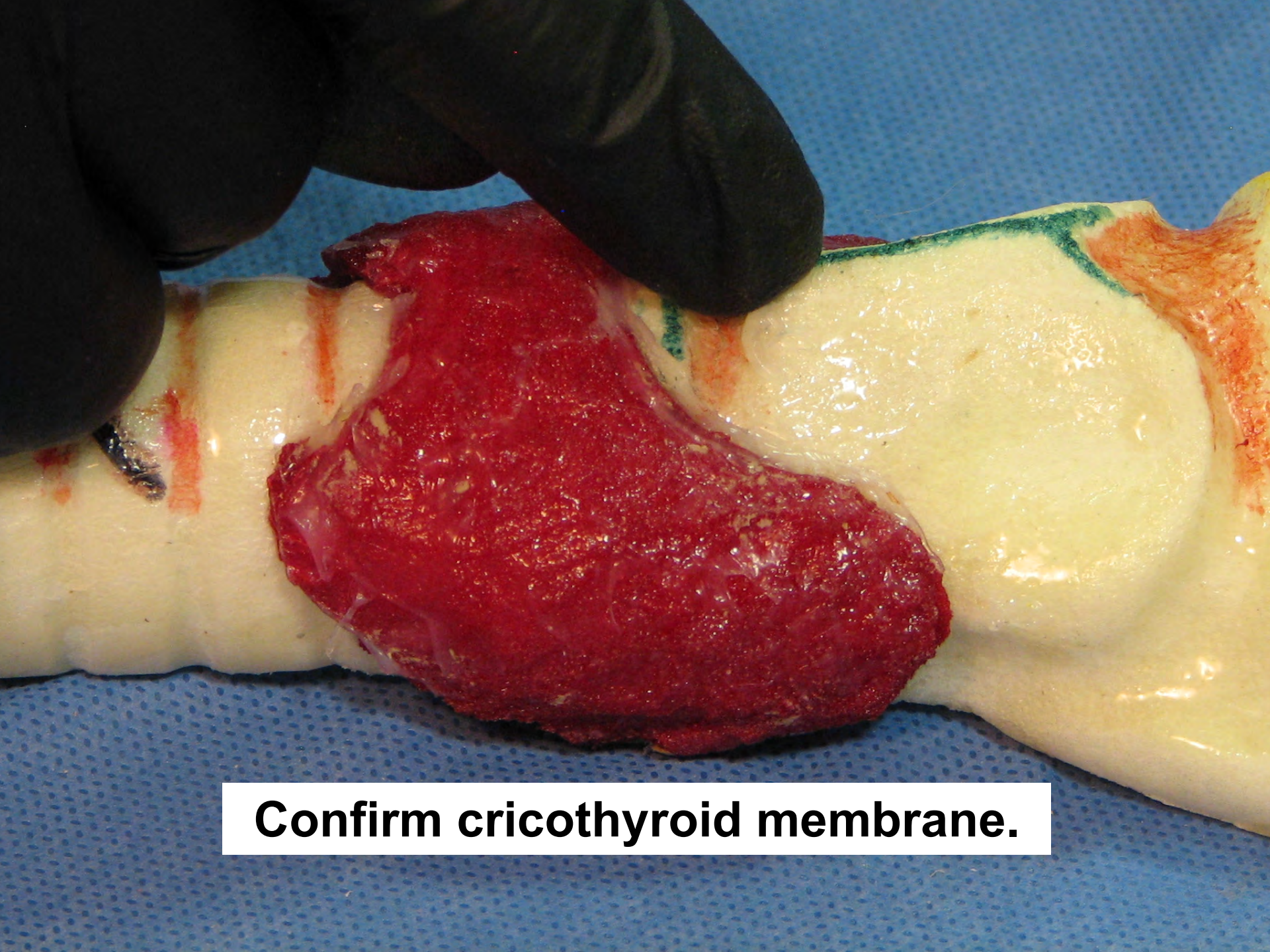
Step 1

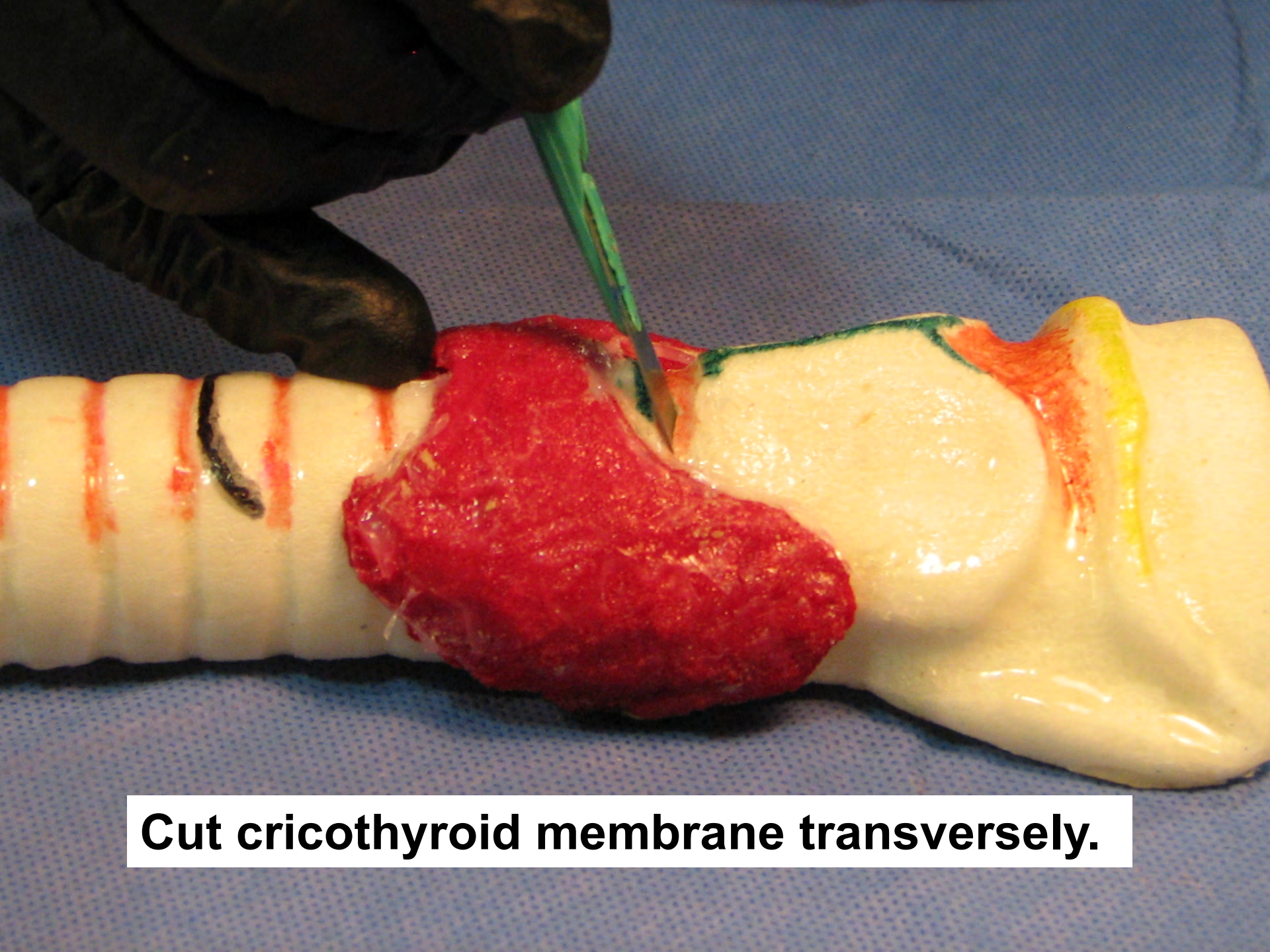
Find sternal notch



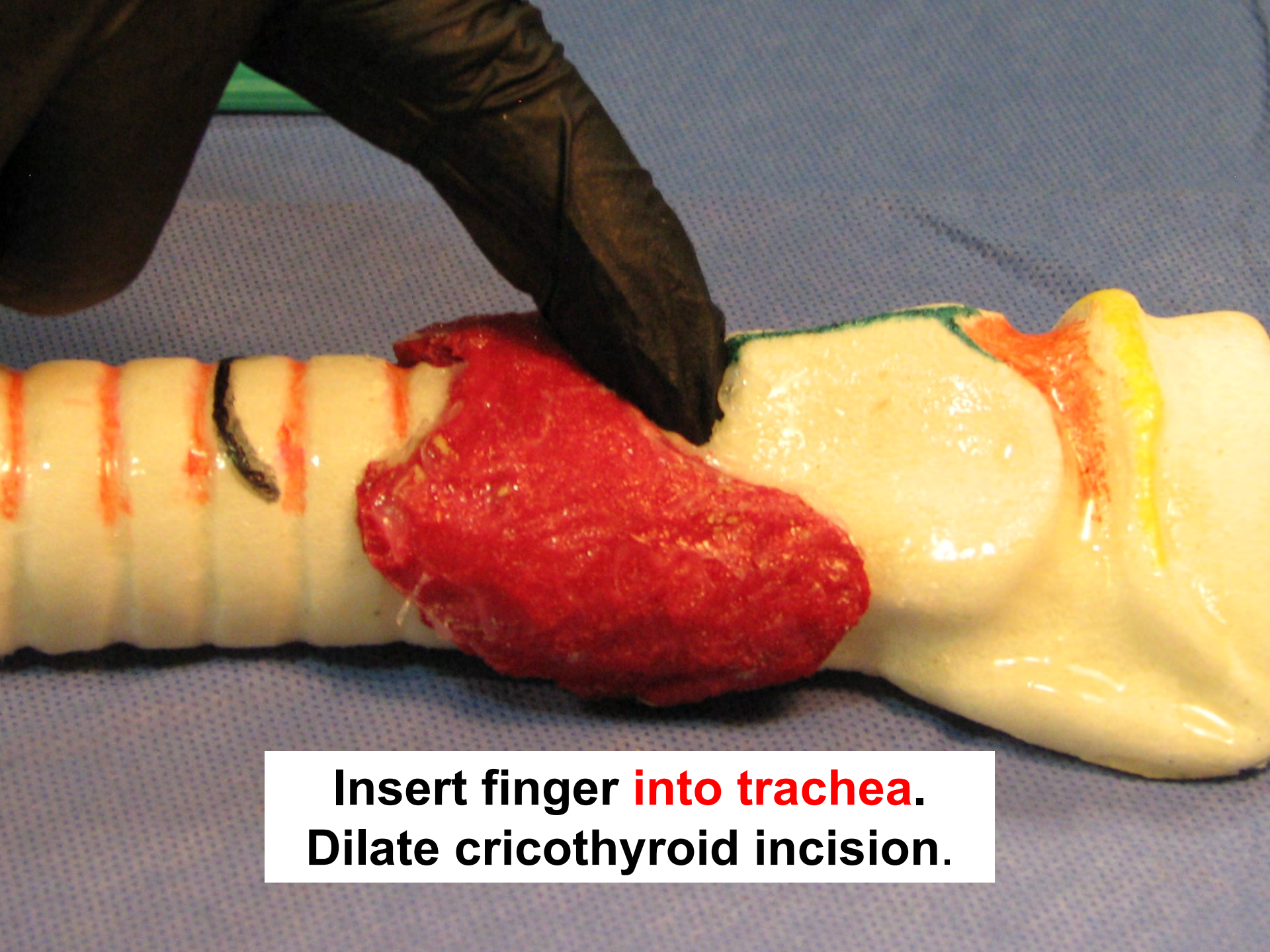
Make 3 cm vertical incision through skin.
Start 3 finger breadths above sternal notch.

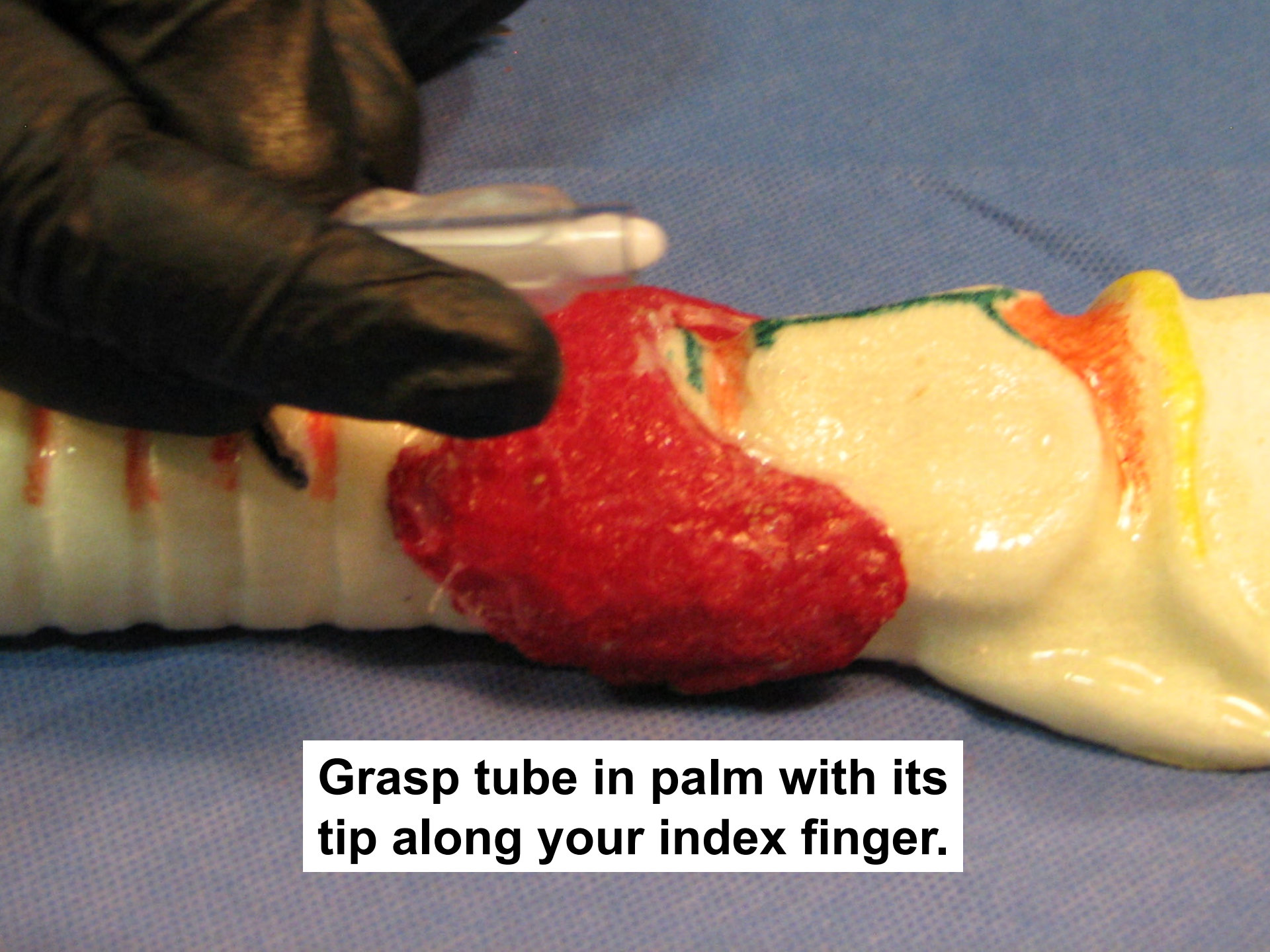

After skin is cut, confirm landmarks.
Confirm “prow” of thyroid cartilage.

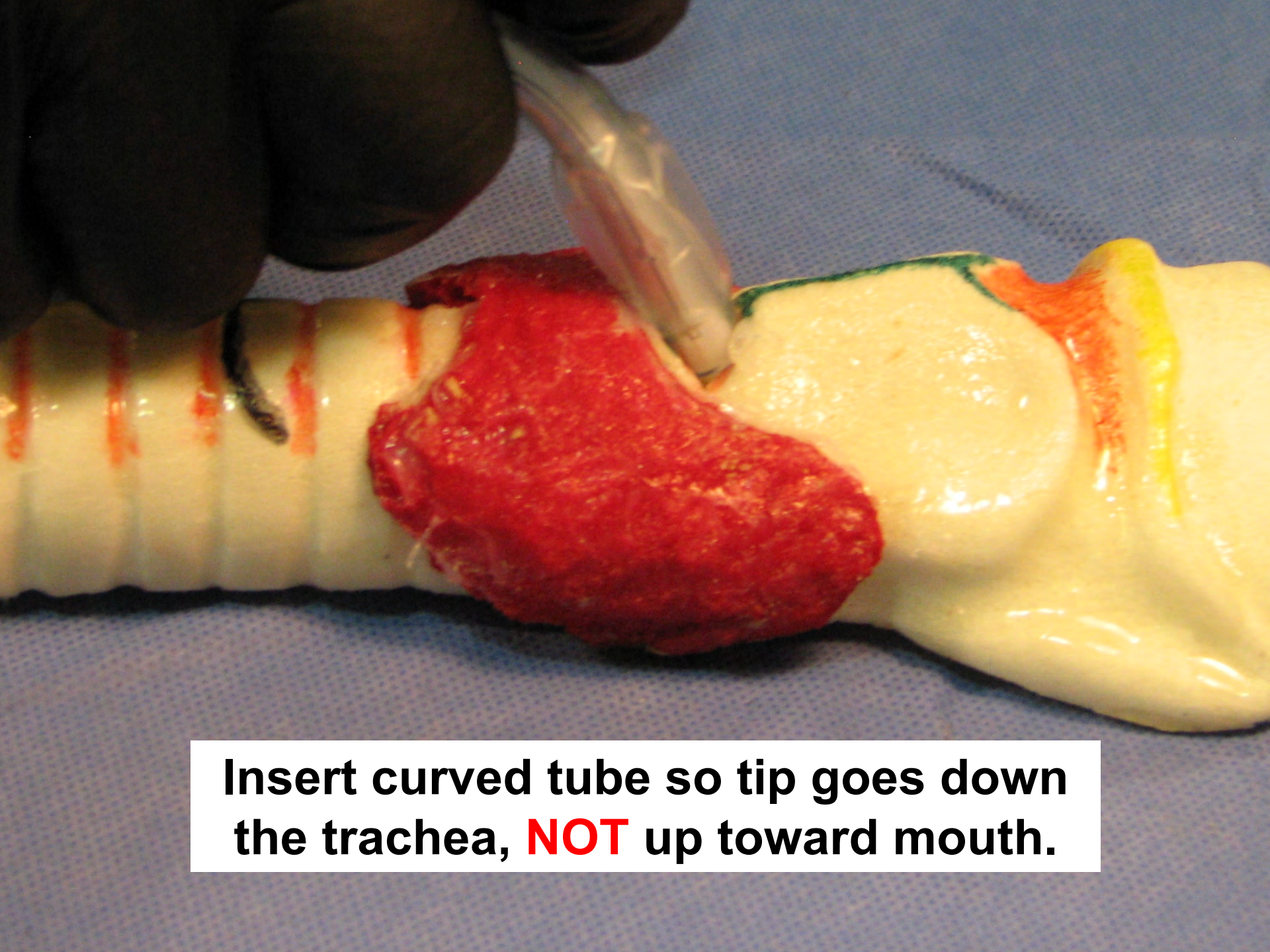

Confirm cricothyroid membrane.



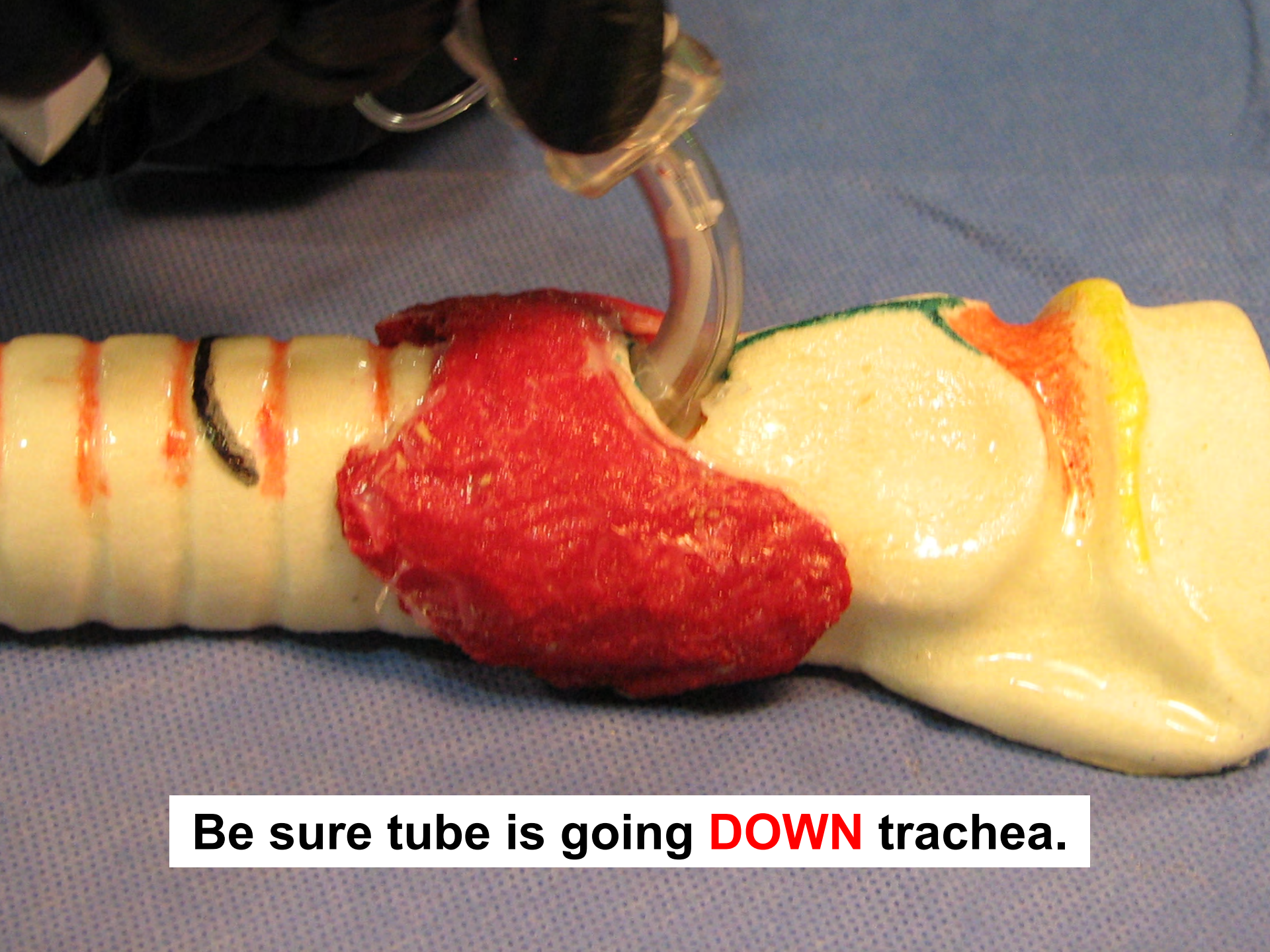
Cut cricothyroid membrane transversely.


Insert finger into trachea.
Dilate cricothyroid incision.


Grasp tube in palm with its
tip along your index finger.

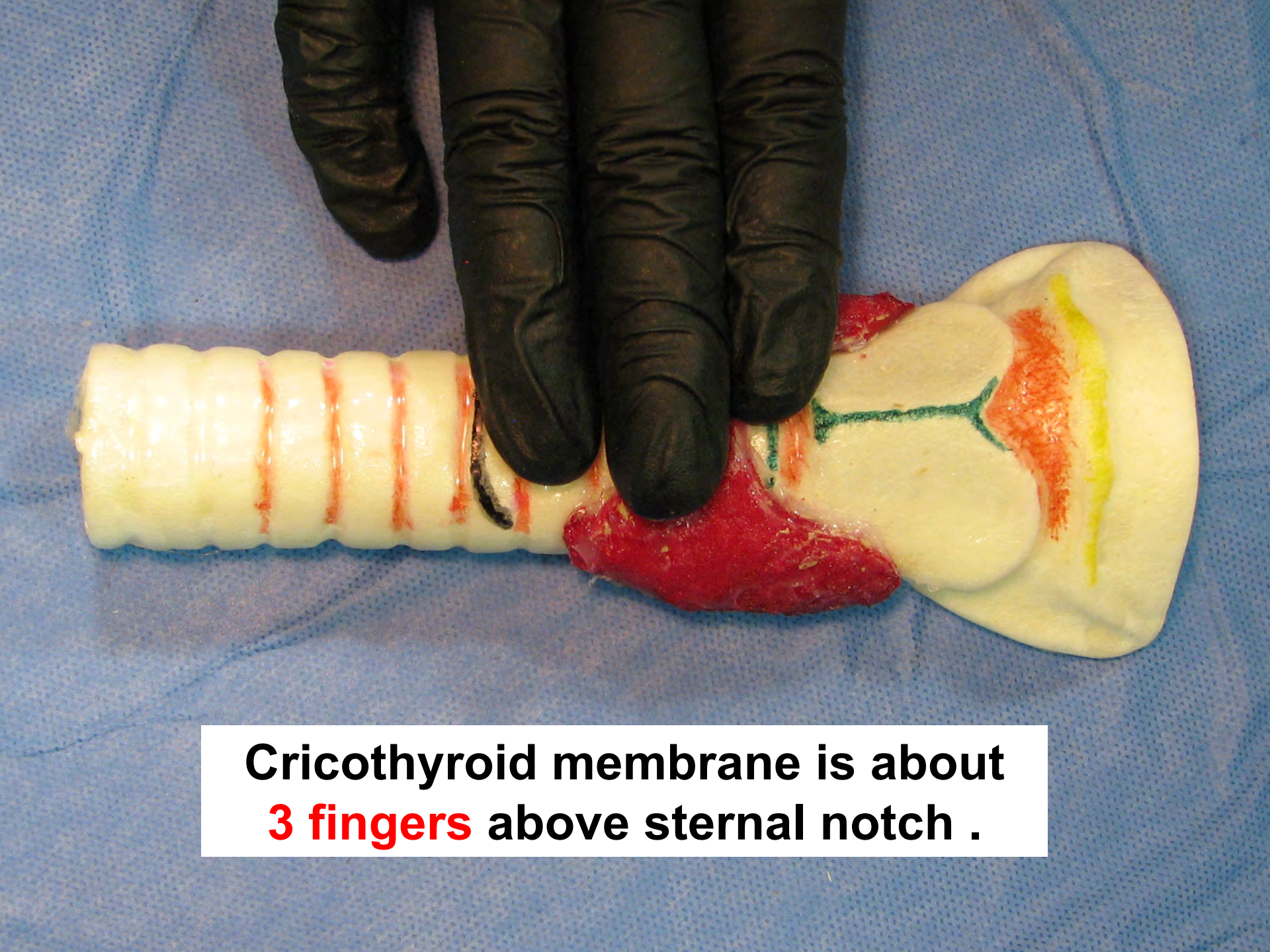


Insert curved tube so tip goes down the trachea, NOT up toward mouth.

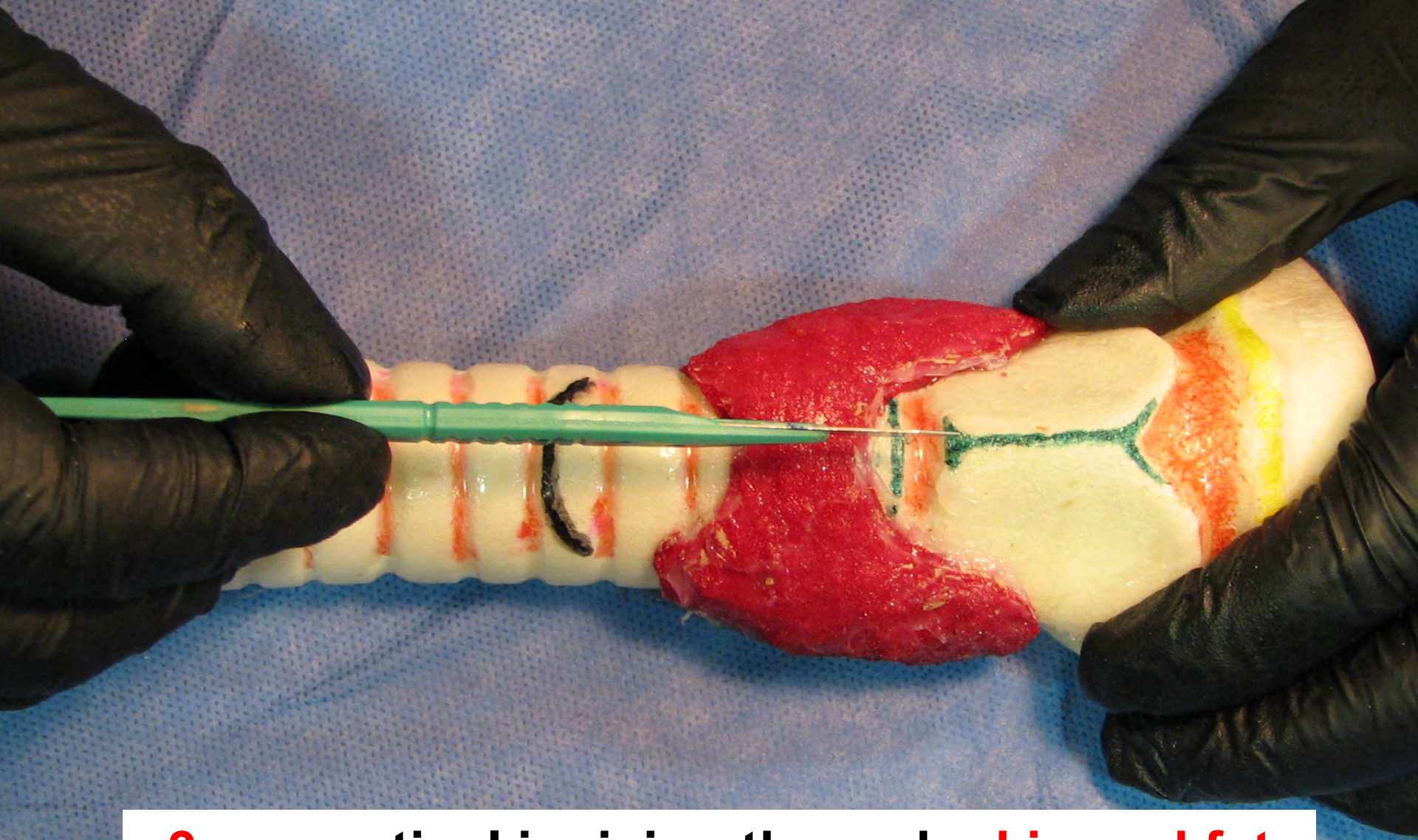

Be sure tube is going DOWN trachea.


CASUALTY: Obstructed airway

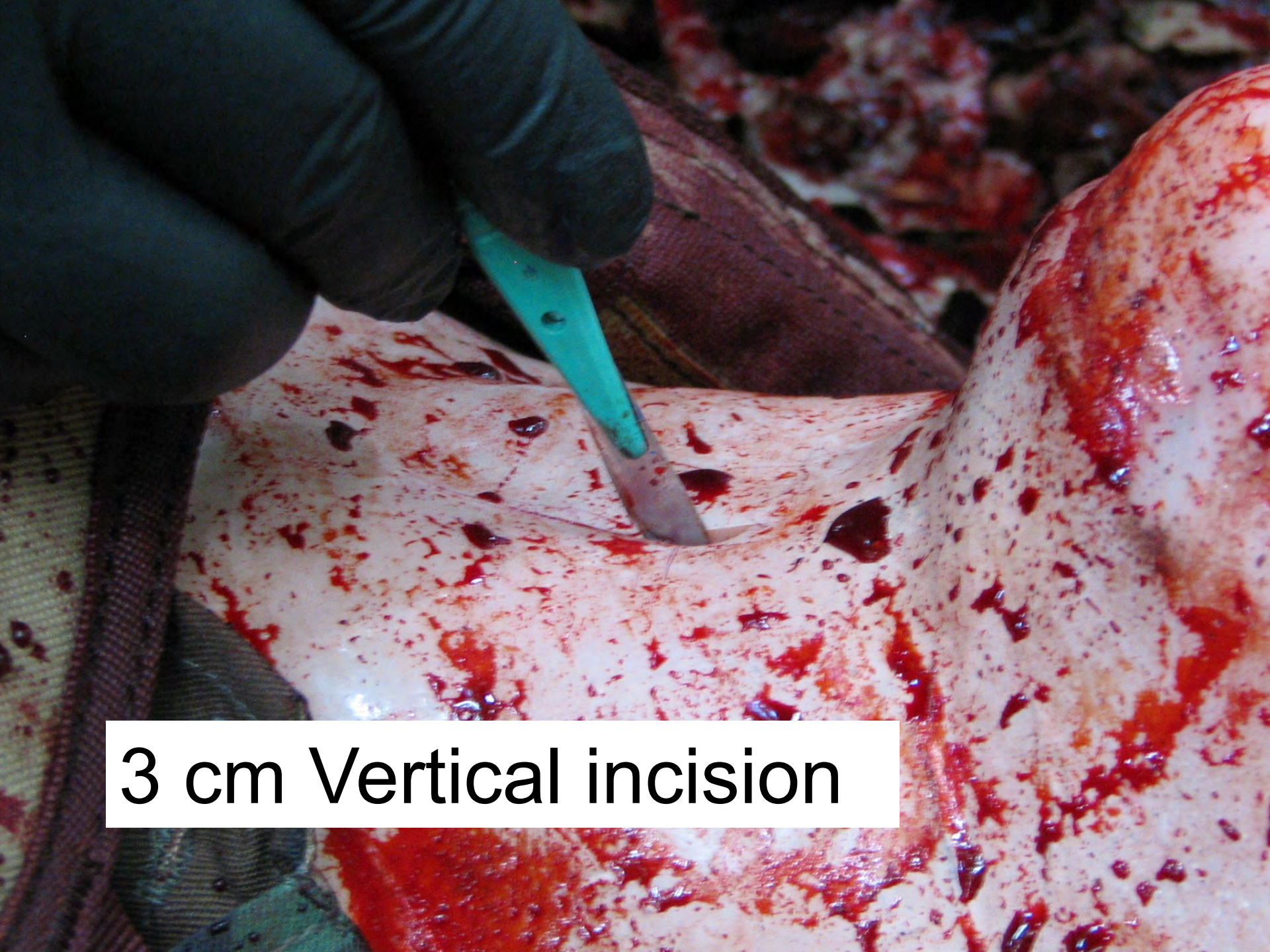

FIND STERNAL NOTCH



Cricothyroid membrane is about
3 fingers above sternal notch .

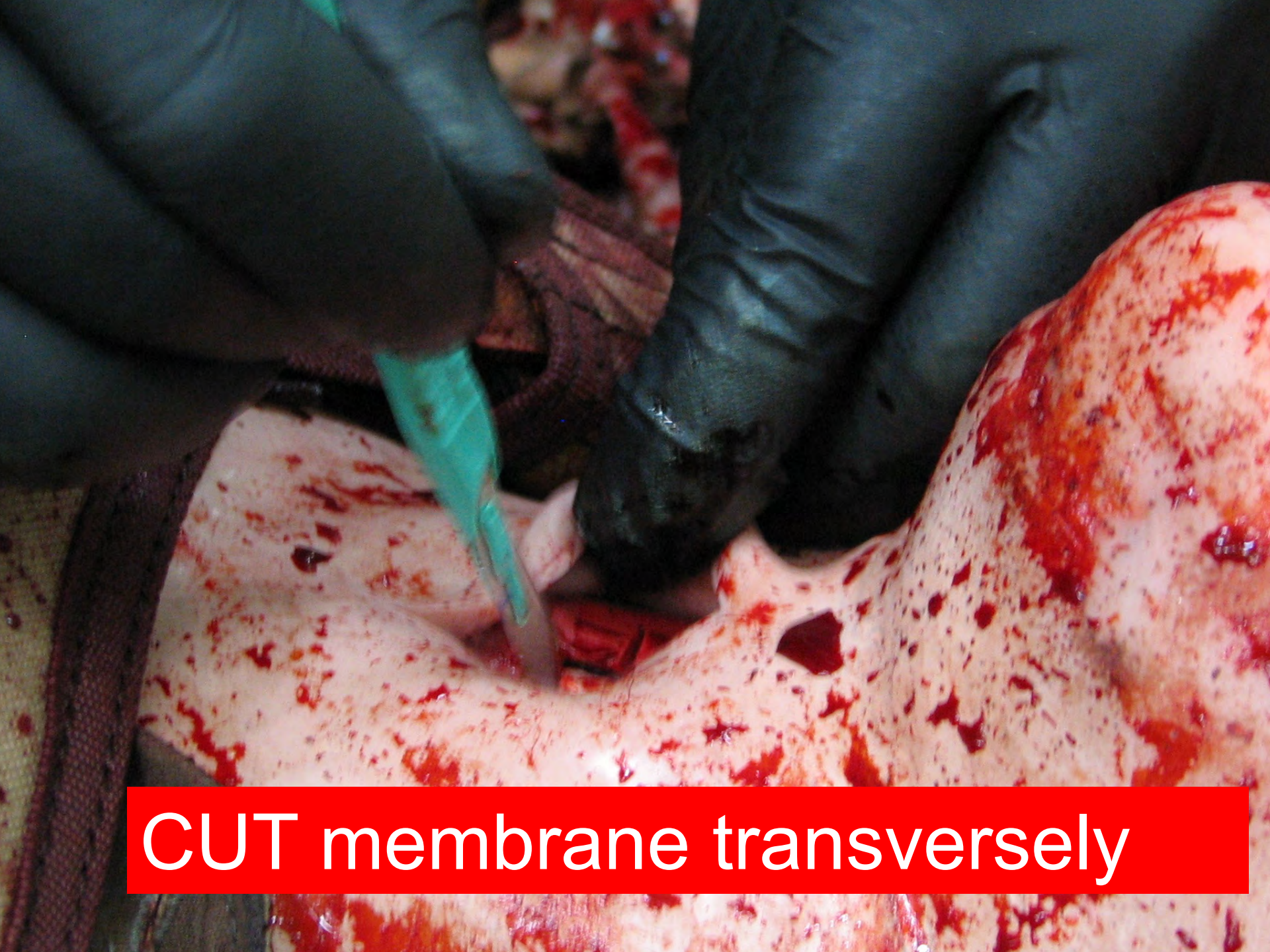


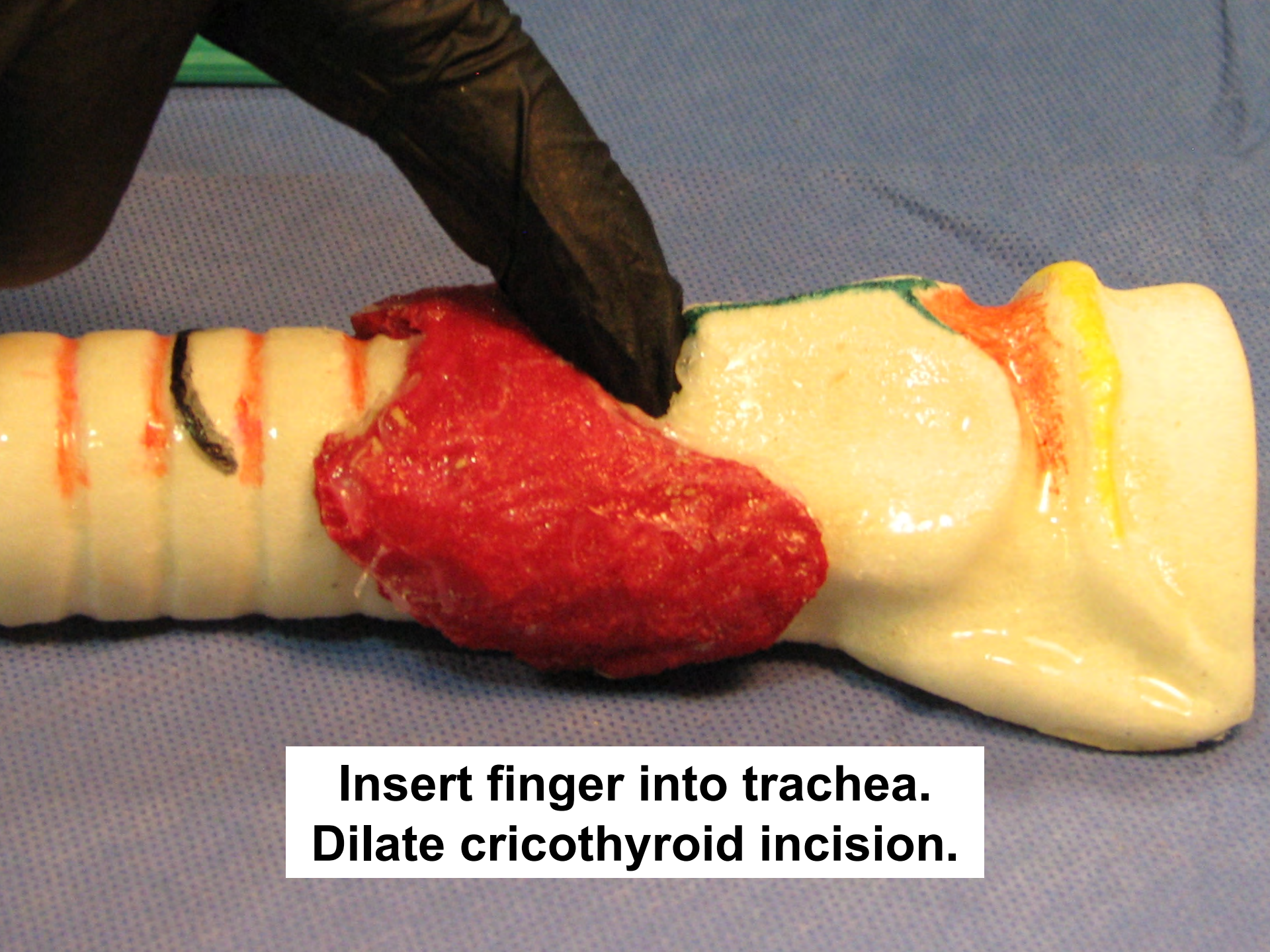
3 cm vertical incision through skin and fat
3 fingers above sternal notch.

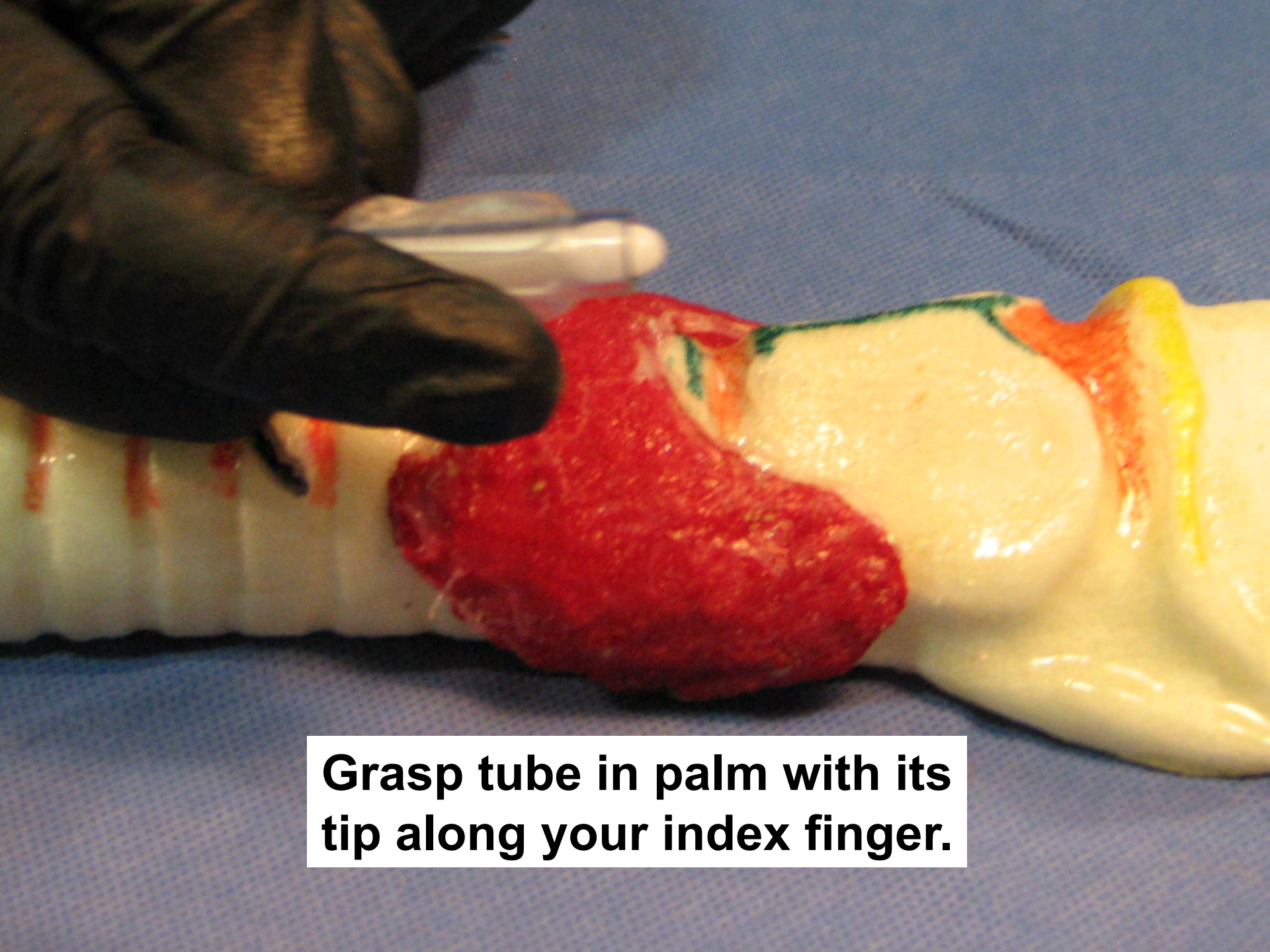

3 cm Vertical incision

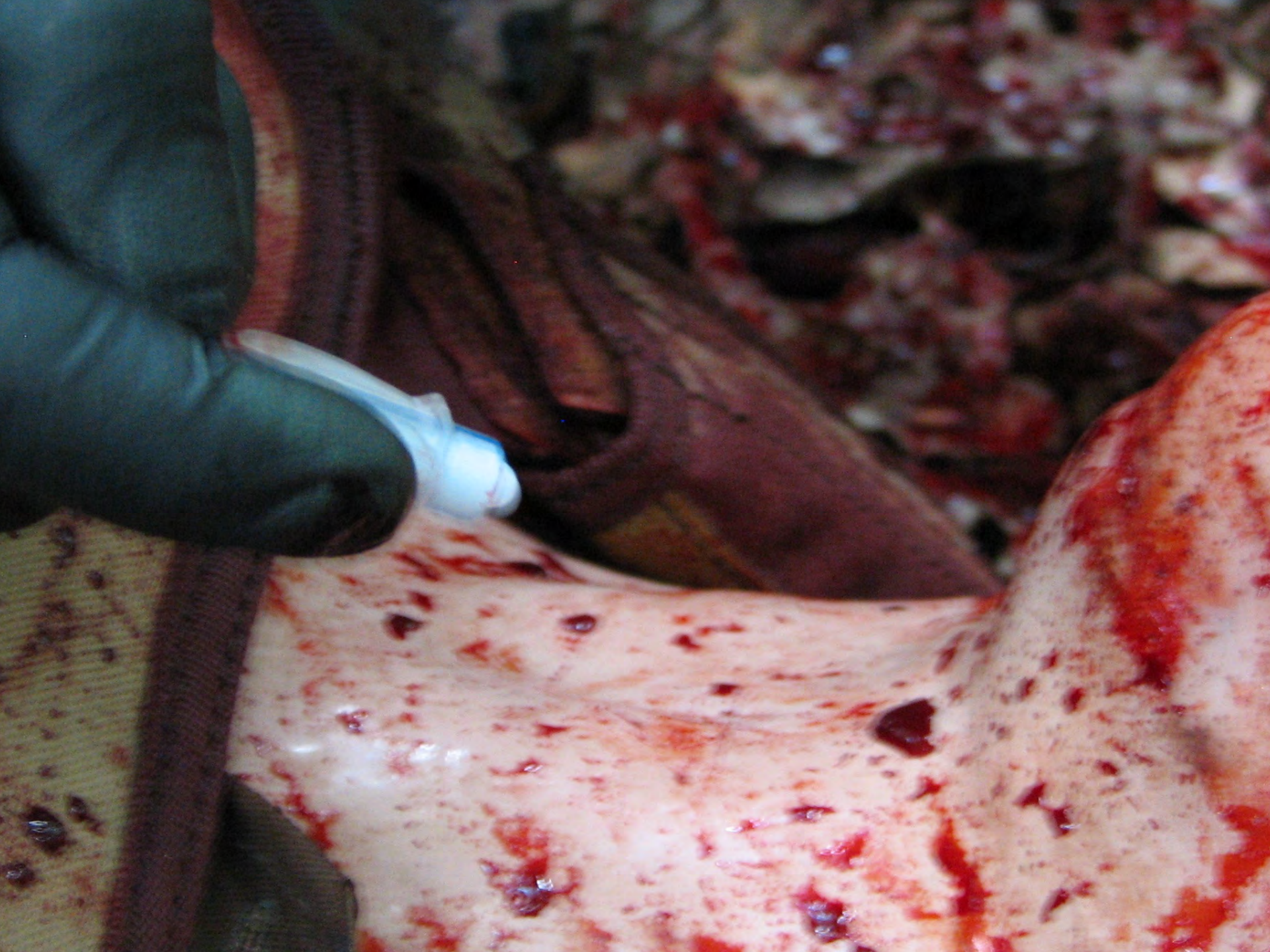

After skin is cut, confirm landmarks.

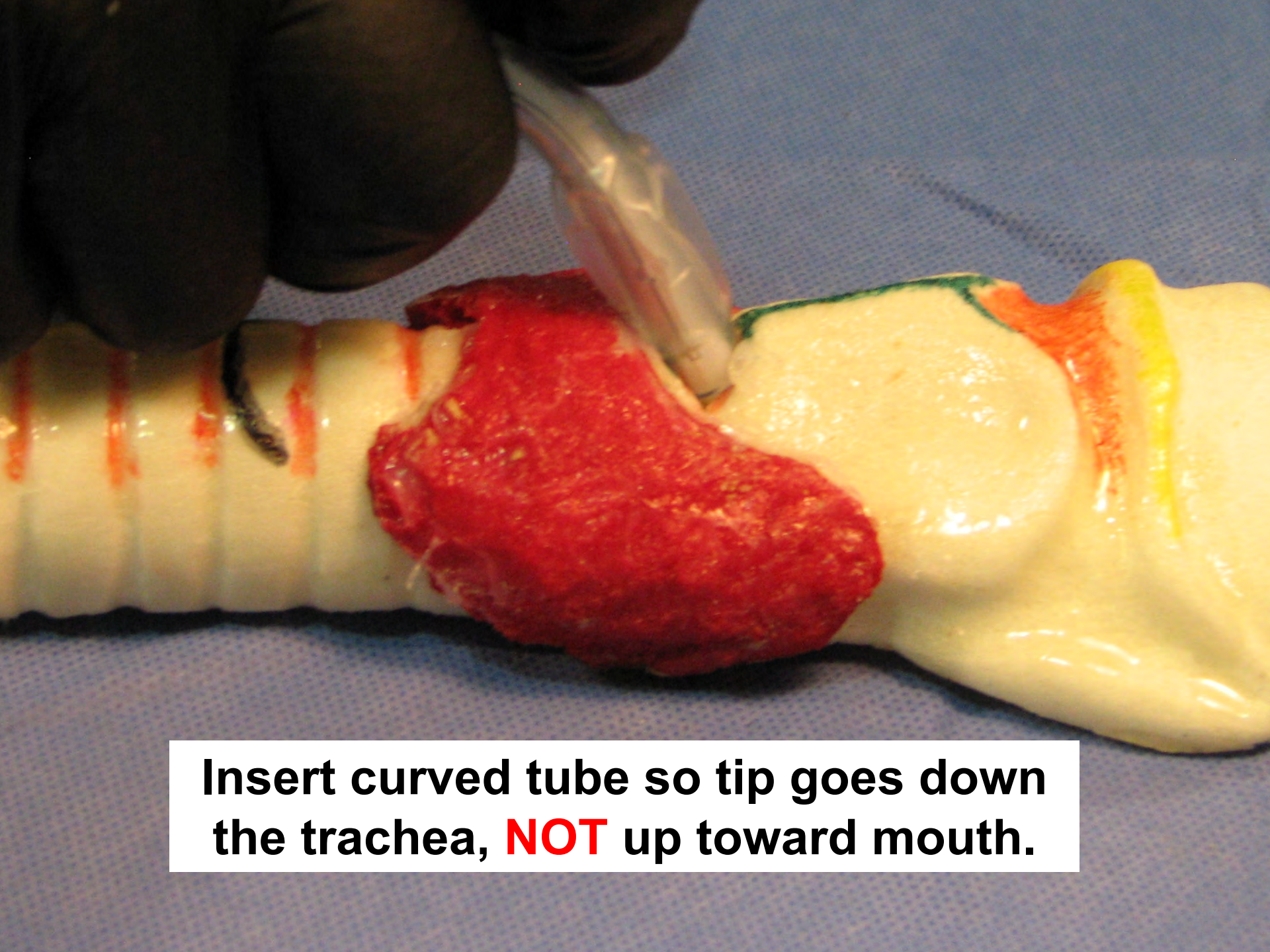

Confirm landmarks

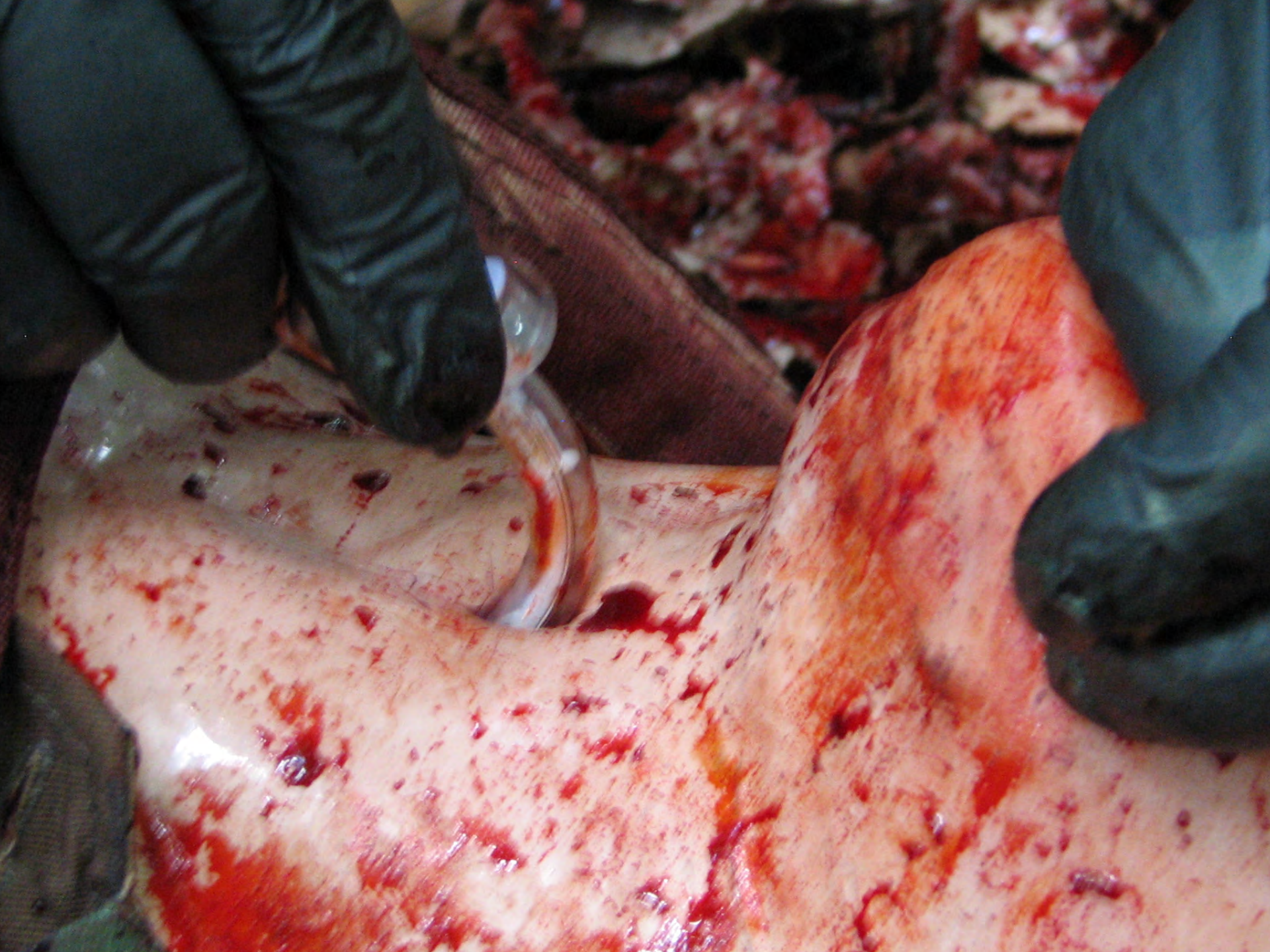

CUT membrane transversely

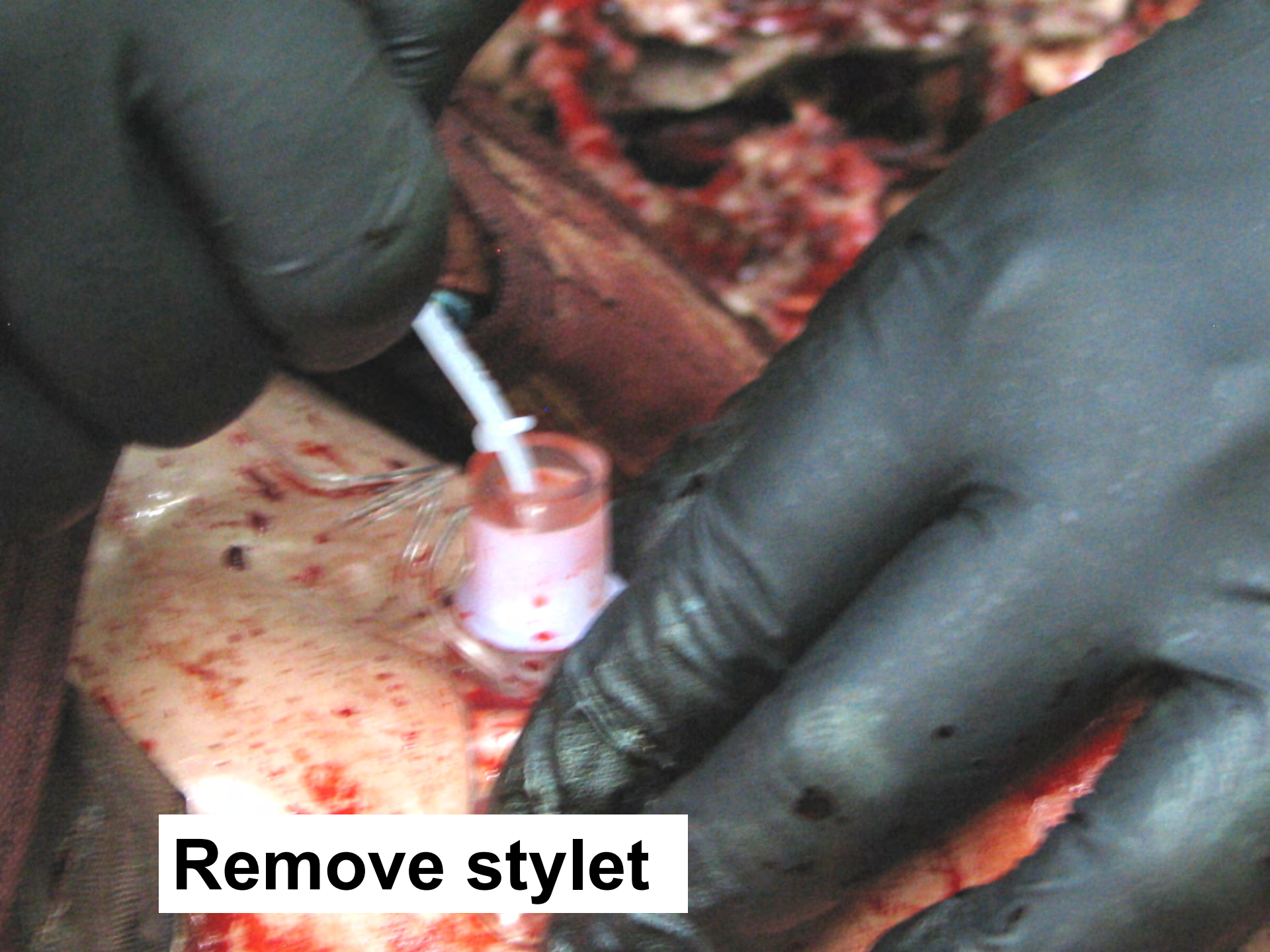

Insert finger into trachea.
Dilate cricothyroid incision.

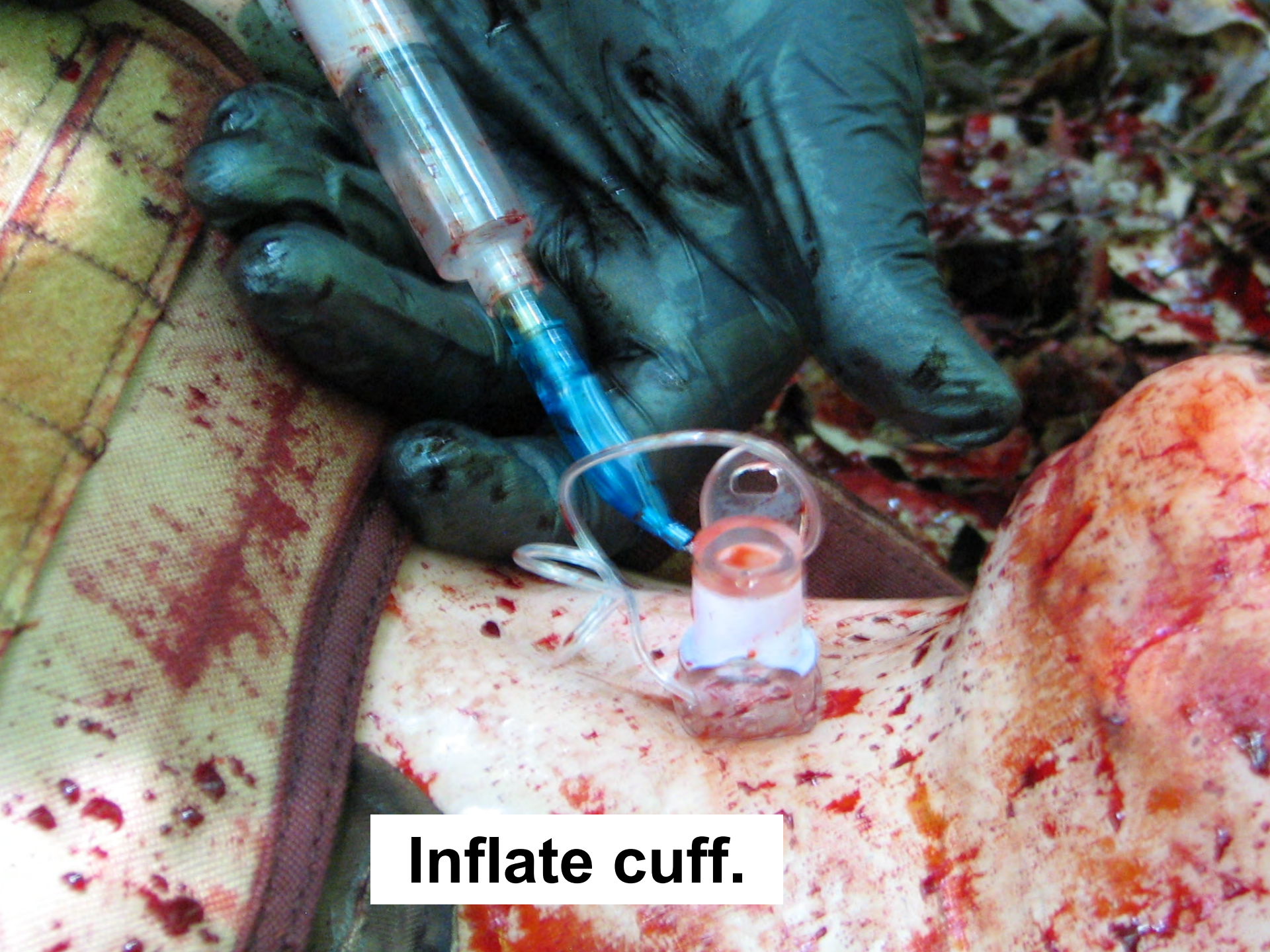

Grasp tube in palm with its tip along your index finger.

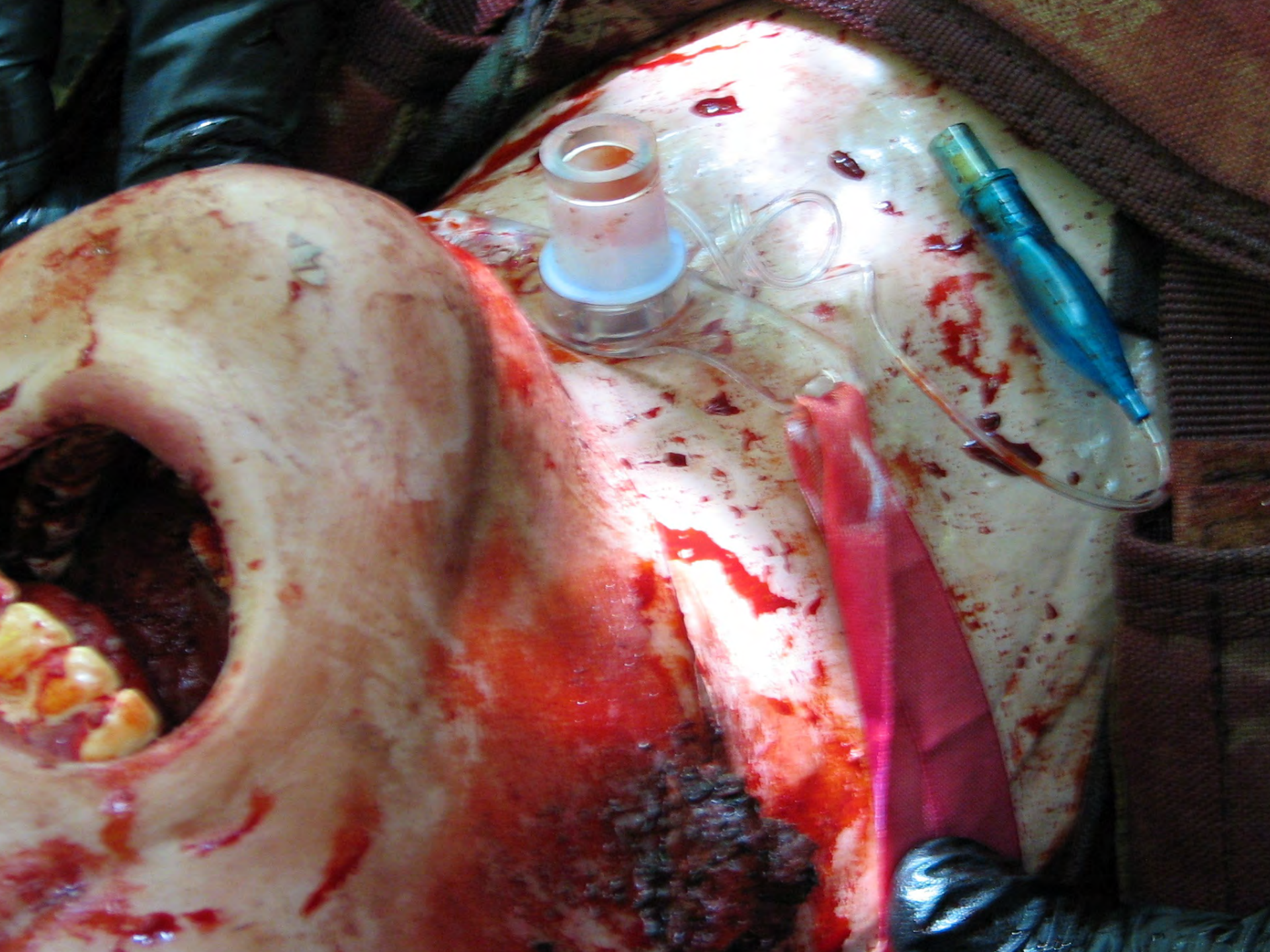



Insert curved tube so tip goes down the trachea, NOT up toward mouth.




Remove stylet


Inflate cuff.



Title: A comparison of endovascular embolization and open ligation of traumatic internal iliac artery injuries in the PROspective Observational Vascular Injury Trial (PROOVIT) registry.

Authors: Herrold JA, Podbielski J, Holcomb J, Sharpe J, Bee T, Morrison J, Scalea T, Skaruap D, Catalano D, Kim J, Inaba K, Poulin N, Bini K, DuBose JJ,

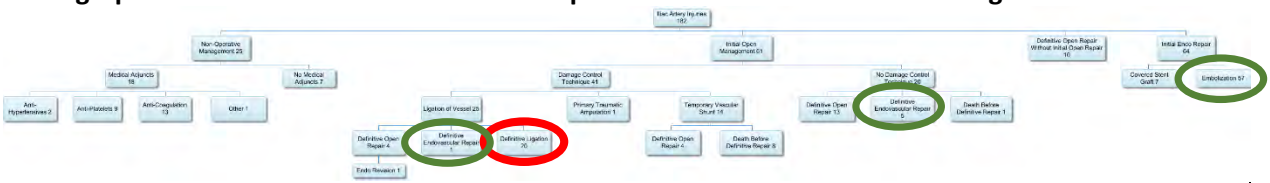
Background: Iliac artery injuries account for up to 6.5% of reported vascular injuries, and isolated injuries carry a mortality of 19.3%, while combined arterial and venous injuries carry a mortality of 48.7%. Endovascular embolization (EE) is an increasingly common and minimally invasive alternative to open ligation (OL) for internal iliac injuries. The purpose of this study is to compare demographics and outcomes of EE and OL.

Methods: A retrospective cohort study was performed using PROOVIT registry data from February 2013 to December of 2018. Cohorts were created to compare patients who sustained internal iliac artery injuries who were treated with endovascular embolization to those who were treated with open ligation of the injured vessel. Demographic, clinical, and outcome data were compared using chi-squared tests for proportions and two-sample t-tests for means. The primary outcome was in-hospital mortality and secondary outcomes were lengths of stay, ventilator days, and blood product usage.

Results: 182 patients with injuries to the common, internal, or external iliac arteries were identified from the registry. 65 patients underwent endovascular embolization (EE) of the internal iliac artery, and 20 patients underwent definitive open ligation (OL). These two groups comprised the two cohorts of the study. In comparing the EE and OL cohorts, there was a statistically significant difference in mean age (50.3 vs 33.3 year, $p = 0.0046$), percentage of penetrating injury (10.8% vs 60%, $p < 0.0001$), mean systolic blood pressure on admission (120.1 vs 81.3 mmHg, $p = 0.0010$), mean GCS on admission (10.6 vs 7.2, $p = 0.0103$), mean head AIS (1.7 vs 0.3, $p < 0.0001$), mean abdomen AIS (2.7 vs 3.6, $p = 0.0015$), and presence of hard signs of vascular injury (35.9% vs 65.0%, $p = 0.0219$). However, there was no statistically significant difference in overall mean ISS (26.9 vs 27.3, $p = 0.9145$). Compared to patients who underwent OL, patients who underwent EE had significantly lower in-hospital mortality (21.9% vs 57.9%, $p = 0.0027$), more ventilator days (8.1 vs 2.9 days, $p = 0.0031$), more ICU days (12.1 vs 3.4, $p = 0.0163$), and more total hospital days (24.5 vs 10.9, $p = 0.0306$). On average, patients who underwent EE required fewer total units of PRBC in the first 24 hours (9.3 vs 16.5, $p = 0.0105$), and fewer units of PRBC & platelets during procedures (5 vs 11.2, $p = 0.0168$ and 1.2 vs 3.3, $p – 0.0168$). One EE patient required reintervention for repair-related complications, and no OL patients required reintervention, but this was not statistically significant ($p = 0.5768$). Neither cohort sustained thrombosis, flow-limiting stenosis, or pseudoaneurysm of the repair, nor infections requiring reintervention, or amputation related to the repair.

Conclusions: In our review of the PROOVIT registry examining management of internal iliac injuries, more patients undergoing OL presented with hypotension and penetrating mechanisms likely to require emergent open intervention. When comparing management approaches overall, however, EE was associated with improved in-hospital mortality, reduced blood product utilization, and no difference in procedure-related complications, despite longer hospital and ICU lengths of stay. These findings suggest that EE may have a beneficial role in hemorrhage control among amenable patients with these injuries, although additional study is required on this topic.

Demographic and Clinical Data of Patient Groups for Embolization vs Definitive Ligation



	Endo Repair (N = 65)	Open Repair (N = 20)	P-Value
Age	50.3 ± 24.8	33.3 ± 14.1	0.0046
Male	63.1 (41)	80.0 (16)	0.1591
Penetrating	10.8 (7)	60.0 (12)	<0.0001
SBP on Admission	120.1 ± 37.8	81.3 ± 56.9	0.0010
GCS on Admission	10.6 ± 5.1	7.2 ± 4.9	0.0103
ISS	26.9 ± 13.2	27.3 ± 15.7	0.9145
Head AIS	1.7 ± 1.8	0.3 ± 0.75	<0.0001
Chest AIS	1.9 ± 1.3	1.6 ± 1.8	0.3955
Abdomen AIS	2.7 ± 1.1	3.6 ± 0.9	0.0015
Extremity AIS	2.8 ± 1.2	2.3 ± 1.4	0.2225
Hard Signs of Vascular Injury Present	35.9 (23)	65.0 (13)	0.0219
Soft Signs of Vascular Injury Present	68.8 (44)	50 (10)	0.1266

Continuous variables are presented as mean ± standard deviation. Categorical variables are presented as % (No.).

Outcomes of Patient Groups for Endovascular Embolization vs Definitive Ligation

	Endo Repair (N = 65)	Open Repair (N = 20)	P-Value
In-Hospital Mortality	21.9 (14)	57.9 (11)	0.0027
Ventilator Days	8.1 ± 10.6	2.9 ± 4.4	0.0031
ICU Days	12.1 ± 14.4	3.4 ± 8.2	0.0163
Hospital Days	24.5 ± 25.3	10.9 ± 16.0	0.0306
Total Units of PRBC in First 24 hours	9.3 ± 9.4	16.5 ± 13.9	0.0105
Total Crystalloid Used During Procedures (L)	1.3 ± 1.5 (46/65)	1.8 ± 1.6 (15/20)	0.2237
Total Colloid Used During Procedures (mL)	210.2 ± 646.9 (44/65)	352.1 ± 494.3 (12/20)	0.4845
Total Units PRBC Used During Procedures	5.0 ± 8.6 (55/65)	11.2 ± 8.6 (19/20)	0.0085
Total Units Plasma Used During Procedures	4.1 ± 7.4 (56/65)	9.0 ± 7.5 (18/20)	0.0174
Total Units Platelets Used During Procedures	1.2 ± 2.8 (54/65)	3.3 ± 4.4 (18/20)	0.0168
Total Units Cryoprecipitate Used During Procedures	0.9 ± 4.5 (49/65)	2.1 ± 3.7 (16/20)	0.3515
Need for re-operation/intervention during initial hospitalization	1.5 (1)	0 (0)	0.5768
Thrombosis of repair	0	0	N/A
Flow limiting stenosis of repair	0	0	N/A
Pseudoaneurysm of repair	0	0	N/A
Infection resulting in need to re-operate	0	0	N/A
Amputation in treated limb	0	0	N/A

Continuous variables are presented as mean ± standard deviation. Categorical variables are presented as % (No.).

INJURIES TO THE ABDOMINAL AORTA – DIAGNOSIS, MANAGEMENT, AND OUTCOME: DATA FROM THE PROOVIT REGISTRY

Introduction: Traumatic injuries to the abdominal aorta (AAI) are rare and entail significant risk of morbidity and mortality.

Methods: Data on AAI was collected from the AAST PROspective Observational Vascular Injury Treatment (PROOVIT) registry

Results: Of 3,598 cases in the registry, 73 (0.02%) cases involved injury to the abdominal aorta. The injury was blunt in 48 cases (65.8%) and penetrating in 19 cases (26%). Motor vehicle accident was the most common mechanism of injury – 38 cases (65.8%).

Diagnosis was made by contrast enhanced computed tomography (CTA) in 34 (46.6%) cases, by operative exploration in 21 (28.8%) cases, and by conventional angiography in 2 cases (2.7%). The injury to the abdominal aorta was transection in 12 cases (16.4%), partial transection or flow-limiting defect in 34 cases (46.6%), and pseudoaneurysm in 8 cases (11%). Initial operative management was performed in 22 cases (30.1%). Damage control techniques were used in 9 of those cases. The most common method was primary repair, used in 11 cases, synthetic graft interposition or bypass was used in 4 cases, autologous vein interposition or bypass in 1 case, and other types of vascular repair in 2 cases. There were 10 cases of endovascular repair of the abdominal aortic injury (13.7%).

10 patients in the cohort died (13.7%). When comparing survivors with mortalities, the following factors were of statistical significance: AIS abdomen (3.3 vs 4.75, p=0.003), GCS (12.7 vs 5.8, p=0.000), hemoglobin (12.91 vs 10.57, p=0.018), hemorrhage as a hard sign of injury (12% vs 50%, 0.005). Diagnosis in operative exploration was associated with mortality (26% vs 70%, p=0.012), whereas diagnosis on CTA was associated with survival (62% vs 20%, p=0.033). The association of mortality with type of injury and mode of treatment were not of statistical significance.

Conclusions: AAI is a rare injury, and injury patterns, diagnosis and management remains highly variable.

OUTCOME IMPLICATIONS OF VENOUS MANAGEMENT STRATEGY IN PATIENTS WITH CONCOMITANT ARTERIAL AND VENOUS FEMOROPOPLITEAL INJURIES

Jack C. Webb, BS; Pedro G. R. Teixeira, MD; Joseph J. DuBose, MD; Carlos V. R. Brown, MD; John B. Holcomb, MD; John Sharpe, MD; Jonathan J Morrison, MD, PhD; Thomas M. Scalea, MD; David Skarupa, MD; Richard D. Catalano, MD; Jennie Kim, MD; Kenji Inaba, MD; Nathaniel Poulin, MD; John Myers, MD; John K. Bini, MD; David Feliciano, MD

INTRODUCTION: Optimal management for associated venous injuries encountered during repair of arterial femoropopliteal injuries is controversial and it remains unclear whether potentially complex venous reconstructions are warranted. The aim of this study was to evaluate how the management of associated venous injuries impacted the outcome of patients with femoropopliteal arterial injuries using a multicenter prospective registry.

METHODS: All patients with combined arterial and venous femoropopliteal injuries in the prospective registry (2013-2018) were identified and those with documentation of management of the venous injury were included in the study. Patient demographics, presenting physiology, injury severity scores, fluids and blood products utilization, use of systemic anticoagulation and antiplatelet therapy were abstracted. The population was stratified by venous management stragegy (Vein Ligation [VL] versus Vein Repair [VR]), and compared with univariate analysis. The primary outcome was failure of the arterial repair. Secondary outcomes included amputation, need for reintervention, need for fasciotomy, and definitive fasciotomy closure.

Variables	Repair (n=22)	Ligation (n=18)	*p-value*
Age	32.6±13.0	29.6±13.5	0.72
Male sex	81.8%	100%	0.14
Penetrating	72.7%	83.3%	0.47
SBP <90 mmHg	13.6%	16.7%	1.00
GCS ≤8	9.1%	5.6%	1.00
ISS ≥16,	50.0%	55.6%	0.73
Head AIS ≥4	0%	0%	1.00
Chest AIS≥4	4.5%	0%	1.00
Abdomen AIS≥4	4.5%	0%	1.00
Extremity AIS≥4	40.9%	50.0%	0.56
Hemoglobin	11.5±2.0	11.8±2.0	0.65
pH <7.2	18.2%	22.2%	1.00
Lactate >4	59.1%	55.6%	0.82
INR >1.5	13.6%	11.1%	1.00
Total PRBC in 24hr	6.9±9.0	6.9±6.7	0.91
Massive Transfusion	31.8%	27.8%	0.78
Time to operation			
< 1 hour	4.5%	11.1%	0.07
1-3 hours	36.4%	33.3%	
3-6 hours	50.0%	44.4	
>6 hours	9.1%	11.1%	
Operation lenght			
1-3 hours	27.3%	22.2%	0.91
3-6 hours	50.0%	61.1%	
>6 hours	22.7%	16.7%	
Perioperative fluids			
Crystalloids, L	3.31±2.36	3.04±2.68	0.73
PRBC, units	6.1±9.4	4.6±4.7	0.54
FFP, units	3.1±7.2	2.1±3.1	0.57
Platelets, units	0.7±1.5	0.4±0.9	0.47
Intra-op anticoagulation	81.8%	83.3%	1.00
Post-op anticoagulation	81.8%	66.7%	0.30
Post-op antiplatelet	45.5%	50.0%	0.77
Post-op anti-thrombotic	90.9%	72.2%	0.21

RESULTS: Over 6 years, 40 patients with combined arterial and venous femoropopliteal injuries and documented venous injury management strategy were admitted to participating 22 trauma centers. The associated venous injury was treated with ligation in 18 (45%) and repair in 22 (55%) patients. Patients in both groups were not significantly different (Table). Patient undergoing VR had higher arterial repair failure rates (18.2% vs 5.6%), need for reintervention (22.7% vs 11.1%) and amputation (18.2% vs 5.6%), but none of these differences were statistically significant. VL patients were more likely to undergo a prophylactic fasciotomy (55.6% vs. 18.2%, OR[95% CI]: 5.62[1.34-23.44], p=0.01), however significantly more patients in the VR group required a therapeutic fasciotomy, with the resulting total fasciotomy rates being comparable in both groups (88.9% vs 77.3%, OR[95% CI]: 2.35[0.39-13.90], p=0.42. Fasciotomy closure was achieved 75.0% in the VL group compared to 64.7% in the VR group (p=0.70).

CONCLUSION:
In the small subset of patients from the PROOVIT registry with doucmented combined femoropopliteal arterial and venous injury, venous repair offered no outcome benefit compared to venous ligation. Patients undergoing venous ligation received more prophylactic fasciotomies, but the overall need for fasciotomy was not different due to more therapeutic fasciotomies being performed in the patients with a vein repair.

TO ANGIO OR NOT TO ANGIO: AN ANALYSIS FROM THE AAST PROOVIT STUDY GROUP.

Ahmed F. Khouqeer, MD; Sherene Sharath, MPH, PhD; Jeanette M Podbielski, RN, CCRP; John B. Holcomb, MD; John Sharpe, MD; Tiffany Bee MD; Jonny Morrison, MD, PhD; Thomas M. Scalea, MD; David Skarupa, MD; Richard D. Catalano, MD; Jennie Kim, MD; Kenji Inaba, MD; Nathaniel Poulin, MD; Joseph Dubose, MD; Ramyar Gilani, MD

Introduction

The use of a completion angiogram post-traumatic extremity arterial open repair remains an area of debate. Guidelines, however, recommend routine completion angiograms with a paucity of supporting data. We hypothesize that completion angiography is not necessarily associated with improved procedural outcomes and therefore not obligatory.

Methods

Using data from the American Association for the Surgery of Trauma PROspective Vascular Injury Treatment (PROOVIT) registry, we included open repairs of peripheral arterial injuries (axillary, brachial, radial, ulnar, common/superficial/deep femoral, popliteal, anterior tibial, posterior tibial, peroneal arteries). Ligated injuries and immediate amputations were excluded. We divided the cohort into two groups, Completion Angiogram (CA) and No-Completion Angiogram (NCA). The outcomes of interest were: immediate revisions, reoperations, and amputations. Arterial injuries were modeled with multiple factors that could affect the repair and its outcome. Multivariable logistic and linear regressions were used to assess the influence of demographics, diagnostic factors, and pre, intra, and postoperative factors on the use of CA.

Results

Between February 2013 and January 2018, data on 397 patients with 429 peripheral vascular injuries were available. CA was utilized in 92 injuries (21.5%). A greater proportion of CA injuries required immediate revision (22.8% vs 7.4% NCA group, $p< 0.001$). However, there was no difference between groups in need for reoperation (CA 15.2% VS NCA 11.3%, $p=0.30$) or amputation (9.0% CA vs 4.0% NCA, $p=0.06$). Among the repairs without immediate revision, there was also no difference in reoperation (CA 4.2% VS NCA 7.7%, $p=0.30$), or amputation (5.6% CA vs 3.5% NCA, $p=0.40$). The adjusted odds of reoperation increased with immediate revision (OR= 11.79, 95% CI (5.53, 25.1), $p< 0.001$) among the entire cohort. Even when stratified by CA use, reoperation odds were still higher after immediate revision despite CA(OR= 5.6, 95% CI (0.98, 31.5), $p\leq0.05$). Furthermore, more amputations were observed in injuries with reoperation compared to those without reoperation (21.6% vs 2.7%, $p<0.001$). The CA group had a higher Injury Severity Score mean (ISS) (CA=15.3 [SD=11.4] vs NCA=11.7[SD=7.7], $p<0.001$) as well as a higher Abbreviated Injury Scale mean (AIS) (CA=3.2 [SD=0.84] vs NCA=2.7[SD=0.89], $p<0.001$). There was no difference between the two groups in the Mangled Extremity Severity Score (MESS) mean (CA=5 [SD=1.6] vs NCA=6 [SD=1.9], $p=0.6$). Brachial and ulnar artery injuries received fewer CA (CA 16% vs NCA 26.7%, $p= 0.04$; CA 1% vs NCA 14%, $p<0.001$), respectively, while femoral arteries received more CA (CA 42.4% vs NCA 18.9%, $p<0.001$). CA was more likely to be utilized if a vascular shunt was used (OR= 2.1, 95% CI [0.12, 0.38], $p< 0.001$), and if systemic anticoagulation was administered (OR= 4.8, 95% CI [2.44, 9.48], $p< 0.001$). The presence of palpable pulses was associated with lower odds in utilization of CA (OR= 0.22, 95% CI [0.12, 0.38], $p< 0.001$).

Conclusion

Utilization of CA occurred in approximately 20% of injuries. When CA was used, there was an increase in the performance of revisions. However, CA with revision was indeed associated with higher rates of reoperation suggesting the influence of factors that cannot be ascertained by CA. Contrarily, repair not requiring revision is equivalent whether CA is performed or not. Performance of high quality repair at initial operation with close clinical monitoring is the bedrock of peripheral vascular trauma with CA playing a much more selective role than mandated by guidelines.

National Level Core Data Collection Using the National Trauma Research Repository

Donald Jenkins, MD
Michelle Price, PhD

National Whole Blood Summit

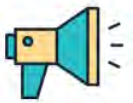
May 22, 2019

Disclosure

- The U.S. Army Medical Research Acquisition Activity, 820 Chandler Street, Fort Detrick MD 21702-5014 is the awarding and administering acquisition office.
- This work was supported by the Office of the Assistant Secretary of Defense for Health Affairs, through the Defense Medical Research and Development Program under Award No. W81XWH-15-2-0089. Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the Department of Defense.
- Principal Investigator: Donald Jenkins
- Project Title: “A National Coordinating Center for Trauma Research”
- Contractor: National Trauma Institute

NATIONAL TRAUMA INSTITUTE

NTI's mission is to reduce trauma death & disability by:



- Increasing research funding for trauma, a major public health and security challenge

- Coordinating clinical studies and research infrastructure to improve trauma survivor outcomes

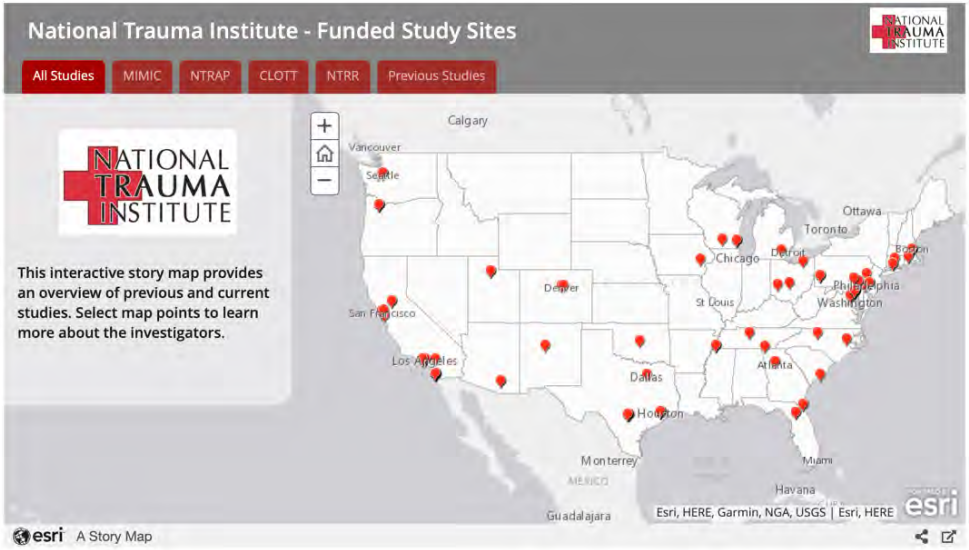
- Translating trauma research discoveries to advance medical care quickly and save lives

https://www.nattrauma.org

Coordinating Clinical Studies and Research Infrastructure

With an agenda focused solely on advancing the field of traumatic injury care, NTI has secured and managed funding for:

- 22 studies
- 35 cities
- 25 states
- 70 + investigators
- 52 + institutions
- > $90M in funding



https://www.NatTrauma.org/research/

Sharing Clinical Trial Data (Institute of Medicine, 2015)

Recommendation 1: Stakeholders in clinical trials should foster a culture in which data sharing is the expected norm, and should commit to responsible strategies aimed at maximizing the benefits, minimizing the risks, and overcoming the challenges of sharing clinical trial data for all parties.

https://www.nap.edu/catalog/18998/sharing-clinical-trial-data-maximizing-benefits-minimizing-risk

Research Repository Benefits

- Allows for secondary analysis of completed datasets at little cost, optimizing financial and human resources
- Enable meta-analysis of multiple datasets using common data elements
- Reinforces the use of harmonized data elements that improves the ability to combine data from multiple studies
- Enables replication of findings through re-analysis of pooled data files
- Promotes the publication of new clinical research findings with effective use of existing data
- Reinforces the principles of open scientific discovery
- Supports *FAIR Guiding Principles* to make data Findable, Accessible, Interoperable and Reusable (Wilkinson et al., 2016)

Benefits of Data Harmonization with CDEs

- Enable meta-analysis of multiple study datasets that use standardized common data elements (CDEs)
- Increases potential interoperability between clinical research data and patient care data
- Facilitates the development of data dictionaries and clinical report forms for at study outset (CDE attributes are predetermined)
- Supports *FAIR Guiding Principles* to make data Findable, Accessible, Interoperable and Reusable (Wilkinson et al., 2016)

NTRR History

- NTRR initiated in 2012 meeting between DoD representatives and NTI, when they said they want a repository, eventually to require federally funded researchers to share their data
- Needed because scarcity of funds and expense of research means research data needs to be useful for other studies etc.
- 2013 NTI advocated for Congressional funding, various supporting US Representatives, resulted in funds that included $3.2M for initial development of NTRR in 2014
- 2016 NASEM report included recommendation to ensure sharing of common data

International Committee of Medical Journal Editors
New Requirements for Clinical Trials Data Sharing

- As of July 1, 2018 clinical trials must include data sharing plans at the time of manuscript submission
- As of January 1, 2019 firm data sharing arrangement required for publication submission
- Trauma journal editors are aware, still working on their responses and policies

EDITORIAL

Data Sharing Statements for Clinical Trials
A Requirement of the International Committee of Medical Journal Editors

Darren B. Taichman, MD, PhD; Peush Sahni, MB, BS, MS, PhD; Anja Pinborg, MD; Larry Peiperl, MD; Christine Laine, MD, MPH; Astrid James, MB, BS; Sung-Tae Hong, MD, PhD; Abraham Haileamlak, MD; Laragh Gollogly, MD, MPH; Fiona Godlee, FRCP; Frank A. Frizelle, MB, ChB, FRACS; Fernando Florenzano, MD; Jeffrey M. Drazen, MD; Howard Bauchner, MD; Christopher Baethge, MD; Joyce Backus, MSLS

The International Committee of Medical Journal Editors (ICMJE) believes there is an ethical obligation to responsibly share data generated by interventional clinical trials because trial partici-

nisms are not in place to mandate universal data sharing at this time. Although many issues must be addressed for data sharing to become the norm, we remain committed to this goal.

JAMA, 2017. **317**(24): p. 2491-2492.

NTRR Aims

- Hypothesis: the civilian trauma research community can be used as a surrogate for military combat casual care, maximize the return from dollars invested by replacing the expensive and repetitive assembly and disassembly of short-lived clinical investigator networks with an enduring infrastructure for clinical trauma research.
- Requires development of tools to allow for collection and dissemination of results and data from studies
- Specific aims:
  - To design and implement the trauma clinical research repository
  - To identify common data elements (CDEs) from currently funded studies, both NTI and others
  - To review and evaluate existing trauma data sources to ensure inclusion and to encourage future use by researchers

NTRR Steering Committee

Organization Represented	Name	Home Institution
Coalition for National Trauma Research (CNTR), Physicians and Other Stakeholders	Don Jenkins, MD—Chair *	UTHSCSA
	Eileen Bulger, MD—Vice-chair*	University of Washington
	Peggy Knudson, MD	UC-San Francisco
	Jerry Jurkovich, MD	UCSD
	Greg Beilman, MD	University of Minnesota
	Joe DuBose, MD	Travis AFB
	Alex Valadka, MD	Virginia Commonwealth University
	Jason Sperry, MD	University of Pittsburgh
	Ellen MacKenzie, PhD	Johns Hopkins University
	Avery Nathens, MD	Sunnybrook HSC, Toronto
	Jim Ficke, MD	Johns Hopkins University
American College of Surgeons/Committee on Trauma	Ronny Stewart, MD	UTHSC—San Antonio
	Len Weireter, MD	Eastern Virginia Med. School
Department of Defense	LTC Kyle Remick, MD*	CCRP, Military Deputy
	Jose Salinas, PhD*	USAISR, San Antonio
	Mary Ann Spott, PhD	Dep. Dir. Joint Trauma System
	Frank Lebeda, PhD*	MRMC, Dir. System Biology
National Institutes of Health	Matt McAuliffe, PhD	NIH, CIT, Bethesda MD

NTRR Subcommittees

Repository Architecture	Human Research Protections & Regulatory	Data Structure & Definitions	Management Policies & Procedures
Jose Salinas	Len Weireter	Greg Beilman	
Matt McAuliff	Peggy Knudson	Alex Valadka	Joe DuBose
Avery Nathens	Eileen Bulger	Jim Ficke	Ellen MacKenzie
Ronny Stewart	Mary Ann Spott	Jerry Jurkovich	
	Laura Brosch	Mary Ann Spott	

Planning and Implementation

- Formed oversight committees in Fall 2015
- Issued RFP for development of NTRR, resulted in contract with Sapient Governmental Inc.
- Coordinated with DoD Trauma Registry, NTDB, TQIP
- Launched NTRR in June 2018
- Importing legacy data from ROC Hypertonic Saline study; PROHS, PROPPR, and completed NTI studies
- Will also include NTRAP, CLOTT and MIMIC data as those studies are completed by PIs and NTI
- Other studies have included NTRR in proposal budgets for their data sharing plans
- Identifying CDEs across the continuum of care and clinical research

www.NTRR-NTI.org

GIVE A LITTLE, GET A LOT

Give a little: Data

Get a lot of: Access, Visibility, Analysis, Impact, Collaborators, Expediency, Evidence, Results

The NTRR thrives as a research resource when investigators contribute data from trauma clinical research trials.

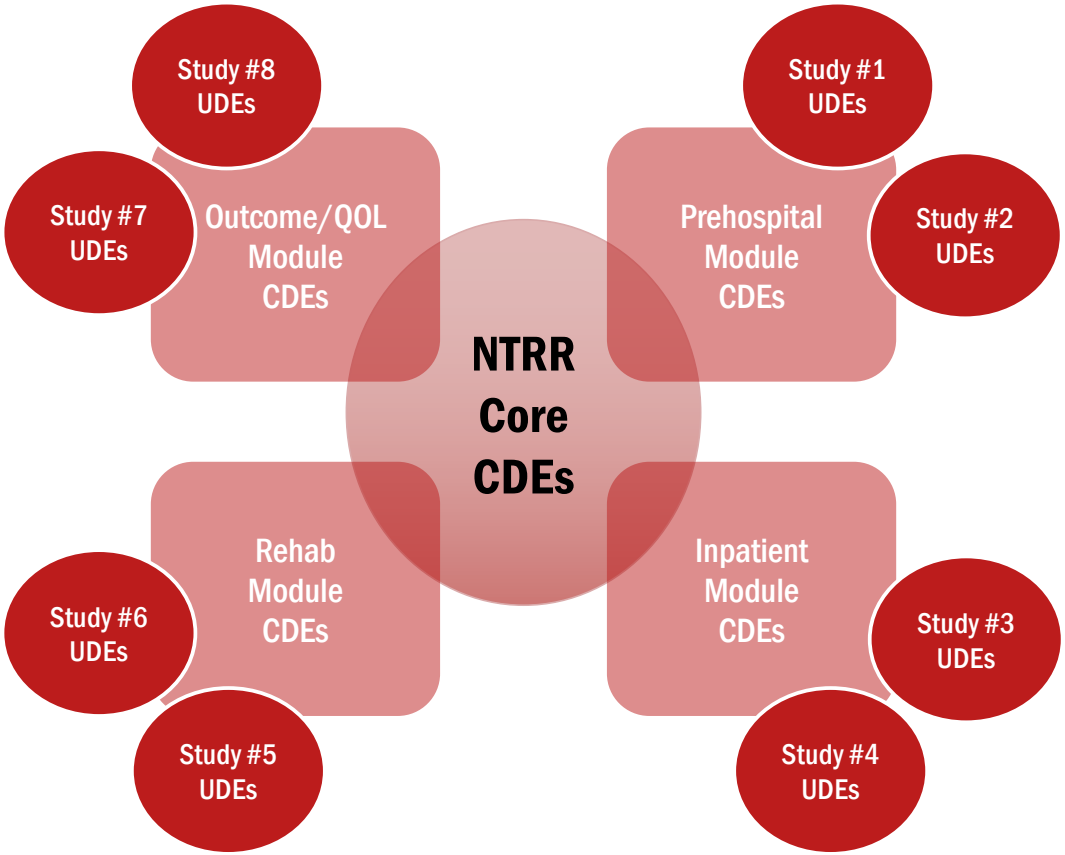
The NTRR is a key piece of the national research infrastructure supporting the trauma research environment. Developed by the National Trauma Institute in partnership with the National Institutes of Health Center for Information Technology, Sapient Governmental Services and the Coalition for National Trauma Research, the NTRR will be a vast repository offering thousands of data points from hundreds of studies, which investigators can query for their own research.

With the NTRR, trauma researchers now have access to a unique and novel tool to conduct exploratory analyses of shared data sets, to create and implement a data sharing plan, to adopt common data elements (CDEs) for study data dictionaries, and to meet new medical journal data sharing requirements.

Research repositories provide a multitude of benefits, and the NTRR will

- Facilitate the publication of new research using existing data, expanding the return on investments made in clinical trials
- Enable replication of findings
- Minimize the need to recruit patients for research studies, as secondary analyses may answer more research questions than originally asked
- Minimize delays, duplications, inefficiencies and costs related to conducting disparate and uncoordinated research
- Speed knowledge translation, enhance the development of evidence-based trauma care practices

NTRR Data Modules and Elements



Study Metadata CDEs & Documents

CDEs = common data elements; UDEs = unique data elements

Data Element	NTRR Core	Prehospital Core	Inpatient Core	Prehospital Study #1	MIMIC
Date of Birth	x	x	x	x	
Person Sex	x	x	x	x	
Ethnicity	x	x	x	x	
Race	x	x	x	x	
Mechanism of Injury	x	x	x	x	
Injury Date/Time	x	x	x	x	
Comorbid conditions	x	x	x	x	
Abbreviated Injury Score, PreDot	x	x	x	x	
Abbreviated Injury Score, Severity	x	x	x	x	
Injury Severity Score	x	x	x	x	
ED Heart Rate First, Last, Lowest with d/t		x	x		
ED Respiratory Rate First, Last, Lowest with d/t		x	x		
ED Systolic Blood Pressue First, Last, Lowest with d/t		x	x		
ED Diastolic Blood Pressure First, Last, Lowest with d/t		x	x		
ED GCS Total, individual components, and qualifiers		x	x		
ED Arrive Date/Time		x	x		
ED Discharge Date/Time		x	x		
ED Discharge Disposition Location		x	x		
Complications		x	x		
PH Heart Rate First, Last, Lowest with d/t		x		x	
PH Respiratory Rate First, Last, Lowest with d/t		x		x	
PH Systolic Blood Pressure First, Last, Lowest with d/t		x		x	
PH Diastolic Blood Pressure First, Last, Lowest with d/t		x		x	
Prehospital pRBC given (units)		x			
Prehospital whole blood given (units)		x			
PH Interventions		x		x	
Hospital Admit d/t			x		
Hospital Discharge date			x		
Hospital Discharge Disposition			x		
Hospital Procedures			x		
Intent of Injury				x	
Place of Injury				x	
Weather Conditions				x	
Work-related				x	
Mass Casualty Incident				x	

Research Data Repository vs. NTDS Data

	MIMIC	
Data Element	Research Data	NTDS Data
Date of Birth		x
Sex		x
Race		x
Mechanism of Injury		x
Height		x
Weight		x
Location of Injury	x	
Intent of Injury	x	
Place of Injury	x	
Weather Conditions	x	
Event witnessed	x	
PROOVIT – More than 100 study elements with approximately 13 elements available in a trauma registry		
MIMIC -- More than 100 study elements with approximately 0 elements available in a trauma registry, as the population is prehospital deaths.		
SPOT Trial – More than 100 study elements with approximately 20 elements available in a trauma registry		

Study Metadata

- Imports study registration and results data from www.clinicaltrials.gov
- Study protocol, data dictionary, clinical report forms, policies and procedures
- Information about the principal investigator, team, sites, funding
- Links to publications of the study findings
- A Digital Object Identifier (DOI) and formal dataset citation (to ensure that the contributing investigators are correctly cited for generating the original data)

Security on the NTRR Site

- The NTRR platform is hosted in a secure Amazon Web Services (AWS) cloud environment conforming to standards set forth in the Federal Information Security Management Act (FISMA) providing a standardized approach for assessing, monitoring, securing and authorizing cloud computing products.
- Specific security controls in place for NTRR include:
  - Firewalls
  - Application monitoring software and integrated cloud tools for operating system scanning
  - SSL (Secure Sockets Layer), Data, Anti-Virus and Password encryption technology
  - Security audits and inspections

Accessing the NTRR

- **No Account Necessary** for public pages describing submitted data, the data dictionary, how to guides, policies and procedures or requesting data
- **Data Submission Accounts** are for researchers and their teams submitting data for sharing
- Account requests will be reviewed and approved by the NTRR Data Access Committee

How do I see data elements in the system?

- Ntrr-nti.org
- Data dictionary
  - View data elements and their attributes
  - View data forms (collections of data elements)
- An account is not necessary

NTRR: National Trauma Research Repository

HOME ABOUT CONTACT DATA NEWS GET STARTED LOGIN

DATA DICTIONARY

Data Elements | Form Structure | Helpful Documents

PUBLISHED DATA ELEMENTS

The library below contains all published and approved common and unique data elements from NTRR's data dictionary.

Search Locations ▾ [ ] Whole Word or Phrase

Narrow your search

Status
- [x] Awaiting Publication
- [x] Published

Modified Date

Element Type
- [ ] Unique Data Element
- [ ] Common Data Element

Disease (?)
- [ ] Trauma

more

Population
- [x] Adult

Show 25 entries RESET ALL DOWNLOAD ALL 22 RESULTS

Title	Variable Name	Type	Modified Date	Status
Abbreviated injury scale (AIS) - Body region	AISBodyRegion	CDE	2018-06-29	Published
Abbreviated injury scale (AIS) - Dictionary version type	AISDictionaryVersionTyp	CDE	2018-06-29	Published
Abbreviated injury scale (AIS) - injury clinical description text	AISInjuryDesriptionTxt	CDE	2018-06-29	Published
Abbreviated injury scale (AIS) - Injury severity score	AISInjurySeverityScore	CDE	2018-06-29	Published
Abbreviated Injury Score (AIS) - Predot	AISPreDot	CDE	2018-06-29	Published
Age in years	AgeYears	CDE	2018-06-29	Published
Comorbidities	Comorbidity	CDE	2018-06-29	Published
Comorbidity Other	ComorbidityOTH	CDE	2018-06-29	Published

NTRR National Trauma Research Repository

Common Data Element: Abbreviated injury scale (AIS) - Body region

Listed below are the details for the data element.

- General Details

Version: 1.0

Element Type: Common Data Element

Title: Abbreviated injury scale (AIS) - Body region

Variable Name: AISBodyRegion

Short Description: The six body regions assessed with the 6 point intermediate ordinal severuly scale

Definition: The six body regions assessed with the 6 point intermediate ordinal severuly scale

Notes:

Creation Date: 2018-06-21

Historical Notes:

References:

- Basic Attributes

Data Type: Alphanumeric

Input Restrictions: Single Pre-Defined Value Selected

Pre-Defined Values:

Search:

PERMISSIBLE VALUE	DESCRIPTION	OUTPUT CODE

NTRR Data Submission Process

1. Submit a Data Submission Account form/receive an account
2. Create a study in the data repository & designate who will have access to the study (for data entry, data access, etc.)
3. Compare your data to the data elements in the NTRR data dictionary
4. Contact NTRR to create unique data elements for your study
5. De-identify the data set
6. Upload data set to the NTRR
   - Use ProFORMS for live data capture
   - Upload a CSV file from Excel or REDCap

NTRR data validation tool will validate the data prior to uploading them

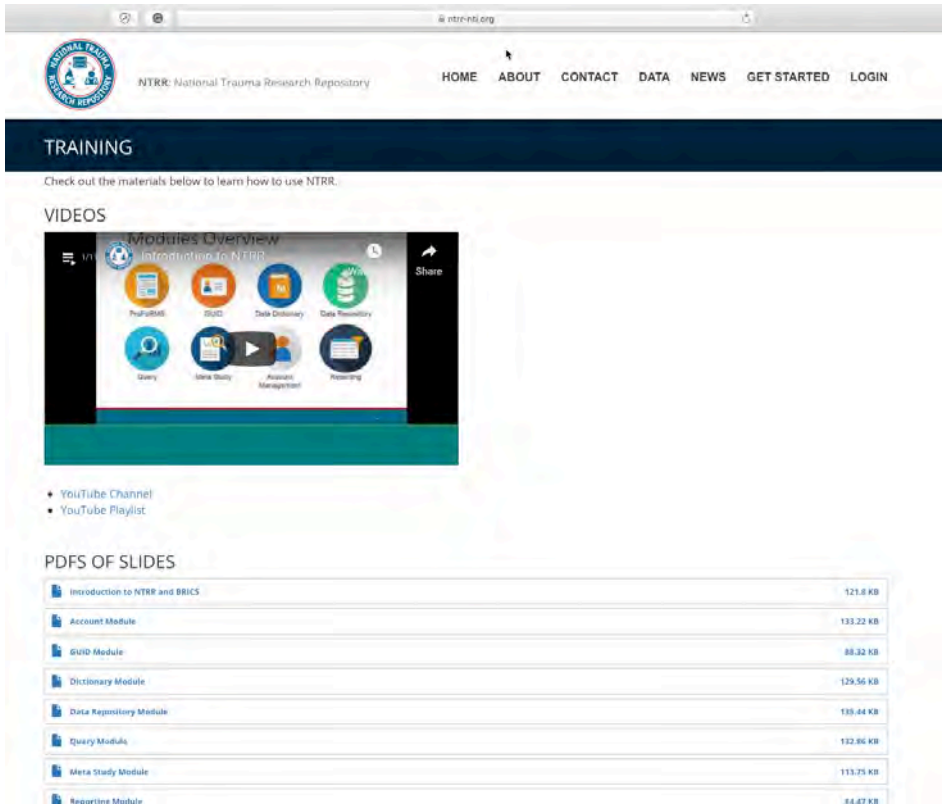
NTRR Data Access Process

1. View details of studies that have been or will be submitted
   - Study abstract, aims
   - Data forms/elements
   - Publications
   - Summary data
2. Use the query tool to filter the data based on research question(s) of interest
3. Submit a data request for the data (reviewed by the NTRR Data Access Committee)
   - Describe the intended use/research questions
   - Submit institutional review board approval and investigator's CV
   - Sign data use agreement with reporting requirement

[NTRR Staff will curate the requested dataset and securely send it to the requestor.]

NTRR User Training

- YouTube Channel video
- PDF Slides
- Quick Start Guide



NTRR Rollout & Promotion

- Distribute marketing materials (logo, URL, postcards, messages, trade booth)
- Publish data sharing commentaries in trauma journals
- Exhibit at relevant conferences and assemblies (EAST, MHSRS, ACS, AAST)
- Register NTRR with international data repository sites
- Contact major studies to request data (ROC, PROMPT, PROPPR, others?)
- Podcasts for AAST and EAST
- Constant contact (+3000) announcement when data become available

NTRR Publications & Presentations

- Smith SL, Price MA, Fabian TC, Jurkovich GJ, Pruitt BA, Jr., Stewart RM, et al. The National Trauma Research Repository: Ushering in a New Era of Trauma Research (Commentary). Shock. 2016;46(3 Suppl 1):37-41.
- Jenkins, DH. Impact of Department of Defense Research to the National Trauma Institute. Presented at the Military Health System Research Symposium, Orlando FL, August 17, 2016.
- Price et al. Launch of the National Trauma Research Repository coincides with new data sharing requirement. Trauma Surg Acute Care Open. 2018;3:e000193. doi:10.1136/tsaco-2018-000193
- Recorded EAST Traumacast: The National Trauma Research Repository - #105 https://www.east.org/education/online/traumacasts/detail/1163/the-national-trauma-research-repository
- Recorded EAST Traumacast: Alphabet Soup! NTI, NTRR, CNTR Oh My! #116 https://www.east.org/education/online/traumacasts/detail/1183/alphabet-soup-nti-ntrr-cntr-oh-my

Populating the NTRR

PROMMTT

PRospective, Observational, Multi-center Major Trauma Transfusion Study

PROPPR

Pragmatic, Randomized Optimal Platelet and Plasma Ratios

CLOTT

MIMIC

[NTI LEGACY STUDIES]

…OTHERS?

ROC

Potential Whole Blood CDEs

- Preservative used
- Age of blood
- Leukoreduction
- Irradiation
- Platelets
- Low titer limit
- Donors
- Recipient (male, female, adult, children)
- Recipient blood type
- Hemolysis markers
- Outcomes
- Clinical endpoints
- # of units given first 24 hours
- # units given total stay

Discussion
&
Questions

Abstract Submitted for 2019 EAST Meeting

Introduction: Fasciotomy remains an important adjunct in the management of peripheral vascular injuries, yet the indications for and natural history of this intervention are not well elucidated.

Methods: The AAST PROOVIT registry was utilized to identify patients undergoing four compartment fasciotomy of the leg after femoropopliteal arterial injuries. Outcomes following fasciotomy for both therapeutic and prophylactic indications were compared, including whether primary skin closure or split-thickness skin grafting (STSG) was performed.

Results: From 2013 to 2018, 530 patients with femoropopliteal artery injuries were identified, of whom 272 (51.5%) underwent surgical management. Fasciotomy was performed at the initial operation in 55.5% (151/272) of patients, with 92.1% (139/151 surviving to discharge; of interest, delayed fasciotomy was performed at reoperation in only 5.8% (7/121) patients in this group. Among survivors, fasciotomies were classified as "therapeutic" in 58.3% (81/139) and "prophylactic" in 41.7% (58/139). There were no significant differences between these two groups, including amputation rate (14.8% vs. 8.6%, $p = 0.272$) and the rate of primary skin closure (54.0% vs. 53.4%, $p = 0.919$) of the fasciotomy site. Comparison of rates of primary skin closure versus STSG coverage revealed only that skin closure was more likely among patients who were more severely injured (ISS 16.0 vs. 10.0, $p = 0.039$; Extremity AIS 3.3 vs. 2.8, $p = 0.007$). Primary skin closure was achieved at a median of 5.0 days vs. 11.0 days for STSG ($p = 0.001$)

Conclusion: Over 55% of patients undergoing repair of a femoral or popliteal artery injury have a fasciotomy of the leg performed at the same operation, and delayed fasciotomies are very uncommon in the modern era. A "therapeutic" indication for fasciotomy continues to be more common than "prophylactic", while outcomes are identical in both groups.

Tranexamic Acid Administration Does Not Compromise Early Graft Patency in Trauma Patients Undergoing Arterial Repair: An Analysis of Patients from the AAST PROspective Observational Vascular Injury Treatment (PROOVIT) Registry

Christina X. Zhang MD, Jennifer M. Leonard MD PhD, Qiao Zhang MS, Joseph J. DuBose MD, Grant V. Bochicchio MD MPH, Gerald R. Fortuna, Jr, MD, Col, USAF, SFS, MC

Introduction:

Since 2010, there has been increased use of tranexamic acid (TXA) to reduce mortality in trauma patients with major bleeding. Previous studies with perioperative transfusions of TXA in coronary artery bypass grafts have shown no reduction in graft patency or increased thrombotic complications. However there have not been any studies investigating TXA and the rate of thrombosis in trauma patients undergoing vascular repairs. Our study investigated the relationship between TXA and in-hospital graft patency for trauma patients with vascular injuries undergoing arterial repairs.

Methods:

We analyzed a subset of patients from the PROOVIT registry who underwent open or endovascular definitive arterial repair using a graft or stent. Patients who received TXA were compared to those who did not. The primary outcome of the study was in-hospital graft patency. Graft occlusion was defined by the need for repeat operations or interventions due to either thrombosis or stenosis of initial arterial repair. Data were analyzed using students t-test and $\chi 2$ test.

Results:

There were 898 cases of arterial injuries identified over 755 patients (4.6% cervical injuries, 30.4% torso injuries, 27.5% upper extremity injuries, and 37.5% lower extremity injuries). There were 100 cases in the TXA group, and 798 cases in the non-TXA group. There was no significant difference in the rate of graft thrombosis/stenosis between the TXA and non-TXA groups (10% vs 7%, $p=0.26$). TXA administration was also not associated with an increased rate of distal ischemia (stroke, bowel ischemia, or extremity amputation) (10% vs 8.5%, $p=0.62$). In the TXA group, graft occlusions most commonly occurred after repairs of brachial or femoral artery injuries. In the non-TXA group, graft occlusions most frequently occurred after popliteal artery repair. Arterial graft occlusion was only significantly associated with the need for immediate perioperative revision during the initial surgery (42% vs. 7%, $p<0.0001$) and was unrelated to the use of TXA.

Conclusion:

The administration of TXA did not compromise early graft patency in trauma patients undergoing arterial repairs. Although this study does not take into consideration time and dose of TXA in these high risk patients, clinicians should be comfortable administering TXA to trauma patients with arterial injuries without concern for increased risk of graft occlusion. Future research should factor in the time and dose of TXA in this high risk population.

Abstract Submitted for 2019 EAST Meeting

Introduction: Fasciotomy remains an important adjunct in the management of peripheral vascular injuries, yet the indications for and natural history of this intervention are not well elucidated.

Methods: The AAST PROOVIT registry was utilized to identify patients undergoing four compartment fasciotomy of the leg after femoropopliteal arterial injuries. Outcomes following fasciotomy for both therapeutic and prophylactic indications were compared, including whether primary skin closure or split-thickness skin grafting (STSG) was performed.

Results: From 2013 to 2018, 530 patients with femoropopliteal artery injuries were identified, of whom 272 (51.5%) underwent surgical management. Fasciotomy was performed at the initial operation in 55.5% (151/272) of patients, with 92.1% (139/151 surviving to discharge; of interest, delayed fasciotomy was performed at reoperation in only 5.8% (7/121) patients in this group. Among survivors, fasciotomies were classified as "therapeutic" in 58.3% (81/139) and "prophylactic" in 41.7% (58/139). There were no significant differences between these two groups, including amputation rate (14.8% vs. 8.6%, $p = 0.272$) and the rate of primary skin closure (54.0% vs. 53.4%, $p = 0.919$) of the fasciotomy site. Comparison of rates of primary skin closure versus STSG coverage revealed only that skin closure was more likely among patients who were more severely injured (ISS 16.0 vs. 10.0, $p = 0.039$; Extremity AIS 3.3 vs. 2.8, $p = 0.007$). Primary skin closure was achieved at a median of 5.0 days vs. 11.0 days for STSG ($p = 0.001$)

Conclusion: Over 55% of patients undergoing repair of a femoral or popliteal artery injury have a fasciotomy of the leg performed at the same operation, and delayed fasciotomies are very uncommon in the modern era. A "therapeutic" indication for fasciotomy continues to be more common than "prophylactic", while outcomes are identical in both groups.

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DATA SHARING ELEVATES YOUR RESEARCH

The National Trauma Research Repository (NTRR) is a Department of Defense-funded, cloud-based data repository for clinical trauma research data.

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DATA SUBMISSION PROCESS

- Execute a Data Transfer and Use Agreement with the National Trauma Institute.
- Certify data as de-identified or as a limited data set.
- Certify that an appropriate IRB has considered the risks and that the data have been de-identified in accordance with federal regulations.
- Upload your data -- it is typically embargoed for one year following your first publication.

Contact Help@NTRR-NTI.org to begin the data sharing process.

COMMON DATA ELEMENTS

Common Data Elements (CDEs) are those data collected for every subject of every trauma study, an intentionally small set. The NTRR will also upload Unique Data Elements (UDEs), specific to a given study or number of studies. To date, the NTRR includes the following CDEs:

CORE DATA SET

- Person Sex
- Ethnicity USA Category
- Race USA Category
- Comorbidities
- Injury date/time
- ICD version and external cause codes
- Injury Severity Score
- Abbreviated Injury Scale version, body region, severity score, clinical description and PreDot

PREHOSPITAL DATA SET

- Vital Signs - Heart Rate, Respiratory Rate, Systolic Blood Pressure, and Diastolic Blood Pressure - first, last, highest, lowest with date/time
- Glasgow Coma Score with date/time
- Unit counts of blood products transfused in the prehospital setting, including packed red blood cells, fresh frozen plasma, freeze dried plasma, and whole blood

INPATIENT DATA SET

- Vital Signs in the Emergency Department - Heart Rate, Resipiratory Rate, Systolic Blood Pressure, and Diastolic Blood Pressure - first, last, highest, lowest with date/time
- Glasgow Coma Score with date/time
- Unit counts of blood products transfused in the Emergency Department, including packed red blood cells, fresh frozen plasma, freeze dried plasma, whole blood, platelets, cryoprecipitate
- Emergency Department admission and discharge date/time
- Emergency Department discharge location - list from NTDS
- Weight/Height
- Hospital admission and discharge date/time
- Hospital discharge disposition - list from NTDS
- Complications

DATA SHARING ELEVATES YOUR RESEARCH

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The National Trauma Research Repository (NTRR) supports data sharing among trauma investigators, enabling them to share their study data, collaborate on secondary analyses, and combine and analyze data across studies.

Most federal funding sources- including the NIH, DoD and NSF-require data sharing for funded research.

Most major medical journals now require researchers reporting results of clinical trials to submit data sharing plans.

NATIONAL TRAUMA RESEARCH REPOSITORY

In 2018, the National Trauma Institute (NTI) and Sapient Government Services (the developer of the NIH's Federal Interagency Traumatic Brain Injury Research Informatics System, or FITBIR) created the National Trauma Research Repository. The NTRR is a centralized, cloud-based data repository and discovery portal. For more information, contact Help@NTRR-NTI.org.

BENEFITS & GUARANTEES

- The NTRR facilitates new research using existing data, expanding the return on investments made in clinical trials.
- Investigators receive scholarly credit for sharing their data through linkage to the original study's Digital Object Identifier (DOI) and the creation of a unique DOI for the data set.
- Data uploaded to the NTRR are typically embargoed for use by others for at least a year.
- Investigators requesting data must meet access criteria and fulfill acknowledgement requirements (original investigator/study) when publishing studies using the data.

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NATIONAL TRAUMA INSTITUTE

Study	PI	Lead Institution	Funding Source	Contract Number	Enrolled subjects	Estimated # data elements	Agreed to submit Data	DTUA Executed	Data Dictionary Received	Data elements created	Data Elements Imported	Data Received	Data Imported
Pragmatic, Randomized Optimal Platelet and Plasma Ratios (PROPPR)	Charles Wade	UT Houston	NHLBI; DoD; Defense Research and Development Canada	U01HL077863; CRR-120612	680	484	x	x	x	x	x	x	In progress
Prospective Observational Multicenter Major Trauma Transfusion (PROMMTT)	Hossein Rahbar.	UT Houston	DoD/NIH through CTSA for DCC infrastructure	W81XWH-08-C-0712/UL1 RR024148	1245	400							
Multicenter Observational Prehospital Resuscitation on Helicopter Study (PROHS	Charles Wade	UT Houston	NIH/DoD	U01HL077863; CRR-120612	1058	298	x	x	x	in progress		x	
Prehospital Air Medical Plasma (PAMPer)	Jason Sperry		DoD	W81XWH-12-2-0023	501		x						
Resuscitation Outcomes Consortium (ROC) Hypertonic Saline Trial Shock Study (HS) and Traumatic Brain Injury Study (TBI)		ROC	Multi	NIH 5U01HL077863-05	2226	865	x		x	in progress			
Fit-to-Fly" Biomarkers after Severe Traumatic Brain Injury with or without Additional Severe Trauma ("Multitrauma")	Deborah Stein		Multi		84	90	x	x	n/a	x	x	x	x
Thromboelastography (TEG®) based dosing of enoxaparin for thromboprophylaxis: a prospective randomized trial	Martin Schreiber	OHSU	DoD	W81XWH-11-10841	96		x						
Transfusion using Stored Fresh Whole Blood	Henry Cryer	UCLA	DoD	W81XWH-11-10841	66		x		x				

Vasopressin Supplementation during the Resuscitation of Hemorrhagic Shock	Carrie Sims	University Pennsylvania	DoD	W81XWH-10-1-0924	25								
Timing and Mechanism of Traumatic Coagulopathy	Mitch Cohen	UCSF	DoD	W81XWH-10-1-0924	317								
Multicenter Prospective Evaluation of the Ventilator Bundle in Injured Patients	Martin Croce	UT Memphis	DoD	W81XWH-08-1-0758	630		x	x					
Detection and Management of Non-Compressible Hemorrhage by Vena Cava Ultrasonography	Jay Doucet	UCSD	DoD	W81XWH-11-10841	59		x						
Methicillin-Resistant Staphylococcus aureus in a Trauma Population: Does Decolonization Prevent Infection?	Robert Maxwell	UT Chattanooga	DoD	W81XWH-11-10841	56		x						
Transfusion of Stored Fresh Whole Blood in a Civilian Trauma Center: A Prospective Evaluation of Feasibility and Outcomes	Mark Cipolle	Christiana	DoD	W81XWH-11-10841									
Hepcidin and Anemia in Trauma	Lena Napolitano	U Michigan	DoD	W81XWH-11-10841	98								
Characterization of the effects of the early sex-hormone environment following injury.	Jason Sperry	UPMC	DoD	W81XWH-10-1-0924	293		x						
Splenic Injury Prospective Outcomes Trial	Ben Zarzaur	UT Memphis	DoD	W81XWH-11-10841	383		x		x				
A Multicenter, Randomized, Double-blind Comparison of Intravenous Iron Supplementation to both Enteral Iron Supplementation and Placebo for the Anemia of Traumatic Critical Illness	Fred Pierraci	Denver	DoD	W81XWH-08-1-0758	150		x						

Multiinstituional Multidisciplinary Injury Mortality Investigation in the Civilian Prehospital Environment (MIMIC) - data available 2021	Brian Eastridge	NTI	DoD	W81XWH-170200010	3000		x						
The Pathogenisis of Post Traumatic Pulmonary Embolism: A Prospective Multicenter Investigation by the CLOTT study group (CLOTT) - data available 2021	Peggy Knudson	UCSF	DoD	W81XWH-17-2-0673	9400		x						
Prospective ObservationalVascular Injury Treatment (PROOVIT) Registry	Joe DuBose		DoD	W81XWH-15-2-0089	6773								
Management of Non-compressible Hemorrhage using Vena Cava Ultrasound	Jay Doucet	UCSD	DoD	W81XWH-15-1-0079	102		x						
Transfusion using Stored Fresh Whole Blood	Henry Cryer	UCLA	DoD	W81XWH-15-2-0039	60		x						
National Trauma Research Action Plan	Eileen Bulger	NTI	DoD	W81XWH18C0179			x					Anticipate available 2021	
Hemorrhage Control for Major Traumatic Vascular Injuries Phase II	Laura Moore	UT Houston	DoD	W81XWH-14-1-0112			x	x					
Microbiome study	Susannah Nicholson	UTHSCSA					x						
Safety/Efficacy of Platelet Transfusion in patients receiving antiplatelet therapy that sustains intracranial hemorrhage	Mark Cipolle	Christiana	DoD	W81XWH-11-10841									
27					27,302	427.4	20	5	6		1		1