Science & Technology Efforts & Programs

PREVENTION, MITIGATION, AND TREATMENT OF BLAST INJURIES

FY15 REPORT TO THE EXECUTIVE AGENT

DoD Blast Injury Research Program Coordinating Office ■ US Army Medical Research & Materiel Command

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FOREWORD FROM THE DIRECTOR

Sean Johnson, a First Lieutenant (1LT) in the 101st Airborne Division, was on foot patrol in Afghanistan when a roadside bomb exploded nearby and sent him hurtling in the air. He suffered wounds to his right arm and leg, but his body armor and helmet protected him from penetrating shrapnel and ball bearings. Staff Sergeant (SSG) Joseph Mata, a member of the same division, was inside a mine resistant ambush protected (MRAP) vehicle when it hit an improvised explosive device (IED) and flew nearly 15 feet. Both Service Members were wearing personal protective equipment (PPE) developed by the United States (US) Army's Program Executive Office (PEO) Soldier. In addition to developing body armor, helmets, uniforms, and small arms for Service Members, PEO Soldier analyzes damaged equipment for the Joint Trauma Analysis and Prevention of Injury in Combat (JTAPIC) Program. After the Service Members returned from tour, PEO Soldier, in an official ceremony at Fort Benning, presented 1LT Johnson with his side armor plate and SSG Mata with his helmet to recognize both their service and components of the protection system that saved their lives.[1]

The development of life-saving PPE and other protection systems, including vehicular, begin with collaborative medical and nonmedical research on traumatic events and their injurious consequences. The collective efforts of multidisciplinary researchers in the Department of Defense (DoD) Blast Injury Research Program combine knowledge of blast events, mechanism of injury, and product performance to develop new strategies that protect the Service Member in training and in the field, whether mounted or on foot. Notable advances in treatment and rehabilitation are saving lives, reducing injury, and speeding the recovery and reintegration of Service Members into their military roles and civilian lives. The DoD Blast Injury Research Program and the Program Coordinating Office (PCO) play a critical role in supporting the Service Member by facilitating collaboration across the research, development, test and evaluation (RDT&E) communities; disseminating blast injury research information; identifying blast injury knowledge gaps; and shaping medical research programs to fill identified gaps.

This annual report to the Executive Agent (EA) describes the DoD Blast Injury Research Program's Fiscal Year 2015 (FY15) efforts to address the entire spectrum of blast injuries. It highlights significant accomplishments, explores the remaining challenges, and suggests action for advancing the state of the science. By disseminating information on the DoD Blast Injury Research Program to researchers, policymakers, military leaders, and the general public, we hope to demonstrate the power of collaboration and the breadth of partnerships within the diverse blast injury research community. We also want to build confidence in the DoD's commitment to preventing, mitigating, and treating the full range of blast injuries, including the long-term consequences on quality of life and return to duty.

I am pleased to present this report to the EA on behalf of the vast network of dedicated professionals who are the foundation of this program.

Michael J. Leggieri, Jr.
Director, DoD Blast Injury Research Program Coordinating Office

ACKNOWLEDGMENTS

The Blast Injury Research Program Coordinating Office is enormously grateful to the many individuals and organizations across the Department of Defense (DoD) who contributed to this report and the work it summarizes. Particular recognition goes out to the collaborative science and technology efforts that are leading the way toward improved strategies for the prevention, mitigation, and treatment of blast injuries. The dedication of the scientists, clinicians, engineers, and operators who support DoD blast injury research represent a commitment to the health and well-being of Service Members and their Families. In addition, we would like to thank the reviewers for their valuable insights and feedback.

Photo credits, top to bottom: US Navy; Devin Pisner/US Navy; Lieutenant Colonel Robert Couse-Baker/US Air Force.

EXECUTIVE SUMMARY

Enemy use of explosive devices is on the rise, resulting in a high number of casualties with blast injuries. While technological advancements are improving survivability from blast events, Service Members are surviving attacks with lasting blast injuries ranging from hearing loss to amputation to traumatic brain injury (TBI). Even relatively mild symptoms of blast injuries (e.g., tinnitus, dizziness, disorientation) can have major effects on operational readiness and quality of life. To address these effects, the US DoD is investing significant resources into medical and nonmedical research on the prevention, mitigation, and treatment of blast injuries.

DoD Directive (DoDD) 6025.21E (5 July 2006) formalized the DoD's blast injury research efforts. This directive established the DoD Blast Injury Research Program and assigned EA responsibilities to the Secretary of the Army (SECARMY). EA responsibilities include recommending DoD blast injury prevention and treatment standards, ensuring DoD-sponsored blast injury research programs address the Services' needs, and sharing blast injury research information among medical and nonmedical communities.

Following a series of delegations, the Commander, US Army Medical Command (MEDCOM) assumed EA authority for the DoD Blast Injury Research Program and established the PCO at the US Army Medical Research and Materiel Command (USAMRMC) to assist in fulfilling EA responsibilities and functions. The PCO coordinates the DoD's blast injury research on behalf of the EA to ensure that critical knowledge gaps are filled, to avoid costly and unnecessary duplication of effort, and to accelerate the fielding of prevention and treatment strategies through collaboration and information sharing. This report highlights the PCO's FY15 activities that support the congressional intent for a coordinated DoD blast injury research program. Over the past year, the PCO continued to chair the North Atlantic Treaty Organization (NATO) Human Factors and Medicine (HFM) Research Task Group (RTG) on "Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods, and Standards" (HFM-234); direct the Military Health System (MHS) Blast Injury Prevention Standards Recommendation (BIPSR) Process; sponsor the fourth annual International State-of-the-Science (SoS) Meeting on the Biomedical Basis for mild TBI (mTBI) Environmental Sensor Threshold Values; and plan the fifth International SoS Meeting on the question, "Does Repeated Blast-Related Trauma Contribute to the Development of Chronic Traumatic Encephalopathy (CTE)?"

In accordance with DoDD 6025.21E, the PCO fosters international collaboration to support the prevention, mitigation, and treatment of blast injuries. The PCO Director chairs the NATO HFM-234 (RTG), which includes 17 members representing nine NATO nations. Its objective is to develop tools that will guide current and future blast injury research efforts in support of the Service Member. The task group initiated a comprehensive dictionary of blast injury research terms to facilitate communication and collaboration across research and operational communities, as well as guidance documents for conducting blast injury epidemiological studies, reproducing relevant blast exposure conditions in the laboratory, and using animal models in blast injury research. These guidance documents will promote standardized study and data collection methodologies, facilitate cross-study comparisons, and advance the state of the science. In FY15, the HFM-234 (RTG) completed a final draft of its first product: guidelines for conducting epidemiological studies of blast injury. Plans are underway to publish this document as an official NATO report for international dissemination. The dictionary, guidelines for reproducing blast exposures in the laboratory, and guidelines for using animal models in blast injury research will be completed by the end of the HFM-234 (RTG)'s term in FY16.

Photo credit (opposite page): US Army Sergeant Harley Jelis/New York National Guard

The EA is responsible for recommending blast injury prevention standards to the Assistant Secretary of Defense for Health Affairs (ASD(HA)) who approves them as DoD standards. To support this key EA responsibility, the PCO developed the BIPSR Process—the DoD's first unbiased, stakeholder-driven critical assessment methodology for recommending biomedically valid blast injury prevention standards. These standards support weapon system health hazard assessments, combat platform occupant survivability assessments, and protection system development and performance testing. In FY15, the BIPSR Process for the lower extremity blast injury type was completed; progress was also made in analyzing standards for preventing blast-related spine and back injuries and upper extremity injuries. The PCO also introduced a new, streamlined BIPSR Process in a web-based collaboration environment that will significantly reduce the time required to review standards for all injury types. The new process, known as iBIPSR, is currently being used to evaluate standards for preventing auditory injuries.

The larger blast injury research community looks to the EA to identify blast injury knowledge gaps and to facilitate collaboration among the world's blast injury research experts. These two roles help shape medical research programs that can in turn fill the gaps and meet the needs of the Services. To support these EA responsibilities, the PCO established the International SoS Meeting Series to address specific blast injury issues important to the DoD. These annual working meetings convene research experts and stakeholders to determine what is known about specific blast injury issues and to identify gaps requiring additional medical research. In FY15, the PCO executed the fourth International SoS Meeting on the Biomedical Basis for mTBI Environmental Sensor Threshold Values. The PCO also planned the fifth International SoS Meeting on the question, "Does Repeated Blast-Related Trauma Contribute to the Development of CTE?" Meeting materials are posted to the PCO website (https://blastinjuryresearch.amedd.army.mil).

This report devotes two chapters to highlighting the programs and efforts of two critical organizations in the field of blast injury research, development, and clinical care: the Extremity Trauma and Amputation Center of Excellence (EACE) and the Vision Center of Excellence (VCE). To advance research and clinical practice for extremity trauma occurring at the DoD and US Department of Veterans Affairs (VA), the EACE serves as a hub for vetting new ideas, synchronizing competing interests, eliminating research redundancies, and standardizing evidence-based practice and clinical recommendations. VCE addresses injuries and disorders of the visual system by facilitating the identification of research capabilities within and between the DoD and VA, leveraging information management systems, promoting collaboration, identifying evidence-based best practices, and supporting the continuous transfer of scientific and medical knowledge.

The research accomplishments, initiatives, and activities highlighted in this FY15 annual report reflect the extent of collaboration within the blast injury research community. This report details 140 accomplishments that extend the knowledge base for blast injury research and establish new tools and strategies for preventing, mitigating, and treating blast injuries. These accomplishments were sourced from 31 DoD organizations and partners representing the RDT&E communities as well as the operational and clinical care communities. For example, the US Army Hyperbaric Oxygen Therapy (HBO2) Clinical Trial focused on treatment development using HBO2 for chronic post-concussion syndrome (PCS) after mTBI in active duty Service Members.

The results of the phase II pilot study of hyperbaric oxygen for persistent post-concussive symptoms (HOPPS) showed that HBO2 oxygen provided no differential benefit relative to room air breathing in terms of short-term relief (six weeks post-treatment) for PCS after mTBI. Long term follow-up (LTFU) of participants from this and other studies showed no consistent trends to support the hypothesis that chamber exposure with 1.5 atmospheres absolute (ATA) HBO2 was associated with long-term improvement in PCS. In another example, investigators at the Walter Reed Army Institute of Research (WRAIR) are using an animal model to understand the effect of blast exposure on tau phosphorylation; their work has demonstrated a decrease in the activity and expression of tissue non-specific alkaline phosphatase (TNAP) following blast exposure and an associated increase in the phosphorylation of tau, which reveals the potential role of TNAP in the development of tauopathy after blast exposure. A US Air Force (USAF)-sponsored animal model study found that six hours of hypobaria worsened the histologic and neurologic markers of injury in rats with mild or moderate TBI. Administration of an anti-inflammatory drug improved the behavioral and histologic effects. The US Army Research Laboratory (ARL) has successfully designed and developed a manikin with an advanced pelvis component that will be used to test the effectiveness of protective undergarments and overgarments during an underfoot blast. As a last example, researchers at the Naval Health Research Center (NHRC) and Naval Medical Center San Diego (NMCSD) reviewed electronic medical records for Service Members who sustained combat-related amputations and found that 28 percent of patients had deep vein thrombosis (DVT) and/or pulmonary embolism diagnoses, with risk factors that include an increase in the number of ventilator days, units of blood transfused, and units of fresh frozen plasma transfused.

Photo credit: Specialist Derek Niccolson/US Army

Prophylactic medication significantly decreased the likelihood of DVT and pulmonary embolism, supporting the use of prophylactics and post-injury surveillance. These and other accomplishments submitted to the PCO for inclusion in this report represent a significant body of work in the field and should inspire confidence among Service Members, their Families, and the general public—major advances are helping to protect each Service Member from potential blast injuries and support those injured throughout their treatment and recovery.

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CHAPTER 1:

INTRODUCTION

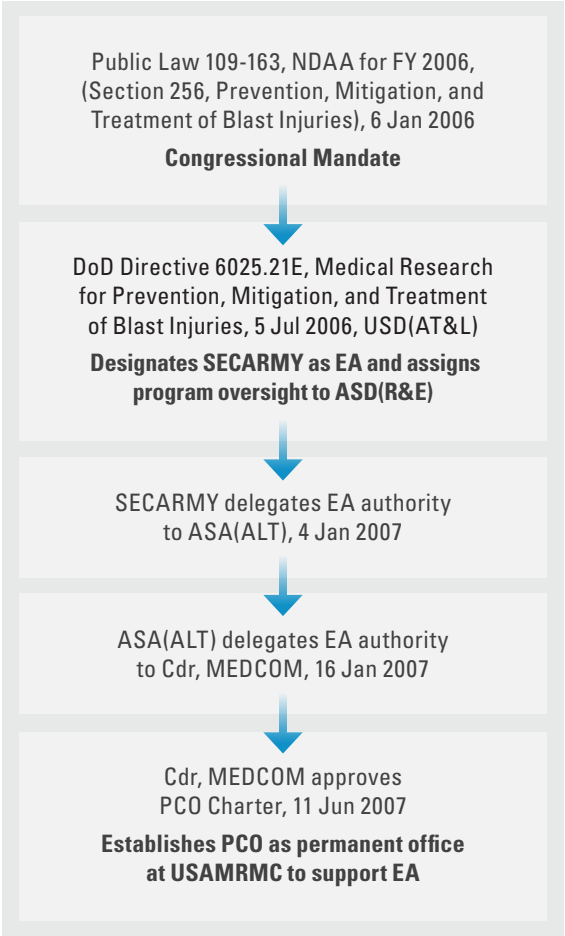
With the increased use of IEDs by terrorists and insurgents in Iraq and Afghanistan, blast injuries have emerged as one of the most pressing military medical challenges. Recent estimates indicate blasts were responsible for approximately 75 percent of US combat casualties in Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF).[2] The survival rate for those injured in OIF, OEF, and Operation New Dawn (OND) is much higher than in past wars in part due to advanced in-theater medical care, rapid evacuation, and improved PPE. For example, there were 7.5 wounded Service Members per fatality in Afghanistan and 7.2 in Iraq compared to 3.2 in Vietnam, 3.1 in Korea, 2.3 in World War II, and 3.8 in World War I.[3] As the survival rate increased, so too has the number of Service Members living with the life-long effects of their injuries.

The scope and impact of blast injuries are broad and complex. For example, 10–20 percent of OIF and OEF Service Members suffer from mTBI, the "signature injury" of operations in Afghanistan and Iraq.[4] Dizziness, vertigo, and ear damage are common ailments among those afflicted with blast-induced mTBI. Approximately 2.6 percent of those who fought in OIF and OEF suffered from traumatic limb loss. Blast injuries like these represent acute injuries with secondary comorbidities that can result in long-term healthcare challenges and costs. The US government continues to invest significant resources to improve the prevention, screening, diagnosis, treatment, and rehabilitation of Service Members who have experienced blast injuries.

In 2006, Congress passed legislation to address critical gaps associated with the blast injuries of Service Members. In Section 256 of Public Law 109-163, National Defense Authorization Act (NDAA) for FY06, Congress directed the Office of the Secretary of Defense (OSD) to designate an EA to coordinate DoD medical research efforts and programs relating to the prevention, mitigation, and treatment of blast injuries. In response to this direction, DoDD 6025.21E, Medical Research for Prevention, Mitigation, and Treatment of Blast Injuries, formally established the DoD Blast Injury Research Program on 5 July 2006 (see Appendix C).

DoDD 6025.21E assigned the Assistant Secretary of Defense for Research and Engineering (ASD(R&E)) with oversight of the Blast Injury Research Program and designated the SECARMY as the DoD EA (Figure 1-1).

FIGURE 1-1: Assignment of EA Authority*



* USD(AT&L)=Under Secretary of Defense for Acquisition, Technology, and Logistics.

Photo credit (opposite page): Specialist David Marshall/US Army

The SECARMY delegated authority and assigned responsibility to execute EA responsibilities to the Assistant Secretary of the Army for Acquisition, Logistics, and Technology (ASA(ALT)). The ASA(ALT) further delegated authority and assigned program responsibility to the Commander, MEDCOM. The Blast Injury Research PCO was established within MEDCOM at the USAMRMC, Fort Detrick, Maryland, to assist the Commander, MEDCOM, in fulfilling the EA's assigned responsibilities and functions.

To support the EA, the PCO coordinates relevant DoD medical research efforts and programs. Its role includes identifying blast injury knowledge gaps, shaping medical research programs to fill identified gaps, disseminating blast injury research information, facilitating collaboration, and promoting information sharing among DoD and non-DoD entities (Figure 1-2). Through these efforts, the PCO works to improve blast injury prevention, mitigation, and treatment strategies for Service Members and their Families.

Responsibilities and Functions

DoDD 6025.21E assigned key DoD components with specific responsibilities to coordinate and manage the medical research efforts and DoD programs related to the prevention, mitigation, and treatment of blast injuries. The following is a summary of the responsibilities assigned by the Directive. For a more inclusive description, please see Appendix C.

- **The ASD(R&E)** establishes procedures to ensure new technology developed under the DoDD is effectively transitioned and integrated into systems and transferred to DoD components; chairs the Armed Services Biomedical Research, Evaluation and Management (ASBREM) Community of Interest (COI), the immediate successor to the ASBREM Committee established under DoDD 6025.21E (ASBREM COI Charter, May 2014); oversees the functions of the DoD EA; and serves as the final approving authority for DoD blast injury research programs.
- **The ASD(HA)** assists in requirements development and needs assessments; conducts assessments of research efforts and coordination and planning to resolve capability gaps; approves MHS blast injury prevention, mitigation, and treatment standards; appoints representatives to DoD EA coordination boards and committees; and ensures the information systems capabilities of the MHS support the EA.
- **The SECARMY** is the DoD EA for Medical Research for Prevention, Mitigation, and Treatment of Blast Injuries who coordinates and manages DoD research efforts and programs. Under this role, the SECARMY gives full consideration to the RDT&E needs of the DoD components and the Director, Joint Improvised Explosive Device Defeat Organization (JIEDDO), now the Joint Improvised-Threat Defeat Agency (JIDA). The SECARMY addresses the following requirements:
  - Maintains a DoD technology base for medical research related to blast injuries
  - Performs programming and budgeting actions for all blast injury research
  - Programs and budgets actions for blast injury research based on analysis and prioritization of DoD component needs
  - Executes the approved DoD blast injury research program
  - Provides medical recommendations on MHS blast injury prevention, mitigation, and treatment standards
  - Ensures that blast injury research information is shared.
- **The Secretary of the Navy and the Secretary of the Air Force** assist in requirements development and needs assessment. They also coordinate all blast injury efforts and requirements through the EA.

- **The President of the Uniformed Services University of the Health Sciences (USUHS)** ensures that education relating to blast injury prevention, mitigation, and treatment is included in the USUHS medical education curriculum and programs. The president coordinates all blast injury efforts and requirements through the EA. This includes appointing representatives to any coordination boards, oversight, or assessment boards that the ASD(R&E) or the DoD EA establishes.
- **The Chairman of the Joint Chiefs of Staff (CJCS)** coordinates all blast injury efforts and requirements through the EA; appoints a senior member to the ASBREM COI; and appoints representatives to any coordination boards, oversight, or assessment boards that the ASD(R&E) or the DoD EA establishes.
- **The Commander, US Special Operations Command (USSOCOM)** establishes procedures for the coordination of Defense Major Force Program 11 activities with those of the EA; forwards that Command's approved blast injury R&E requirements to the DoD EA; and appoints representatives to the ASBREM COI and any other coordination, oversight, or assessment board that the ASD(R&E) or the DoD EA establishes.
- **The JIEDDO, now known as the JIDA,** supported the development, maintenance, and usage of a joint database on the efficacy of theater PPE and vehicular equipment designed to protect against blast injury by helping to establish the JTAPIC Program (see Chapter 2). The JTAPIC Program fulfills the intent of a "joint database" by providing a process that enables data sharing and analysis across communities. Other DoDD responsibilities include appointing representatives to the ASBREM COI and any other coordination, oversight, or assessment board the ASD(R&E) or the DoD EA establishes. JIDA also assists the DoD EA, the ASD(R&E), and the ASD(HA) in identifying related operational and research needs, assessing relevant research efforts, and coordinating planning to resolve capability gaps through focused research efforts.

FIGURE 1-2: Breadth of the PCO's Coordinating Responsibilities

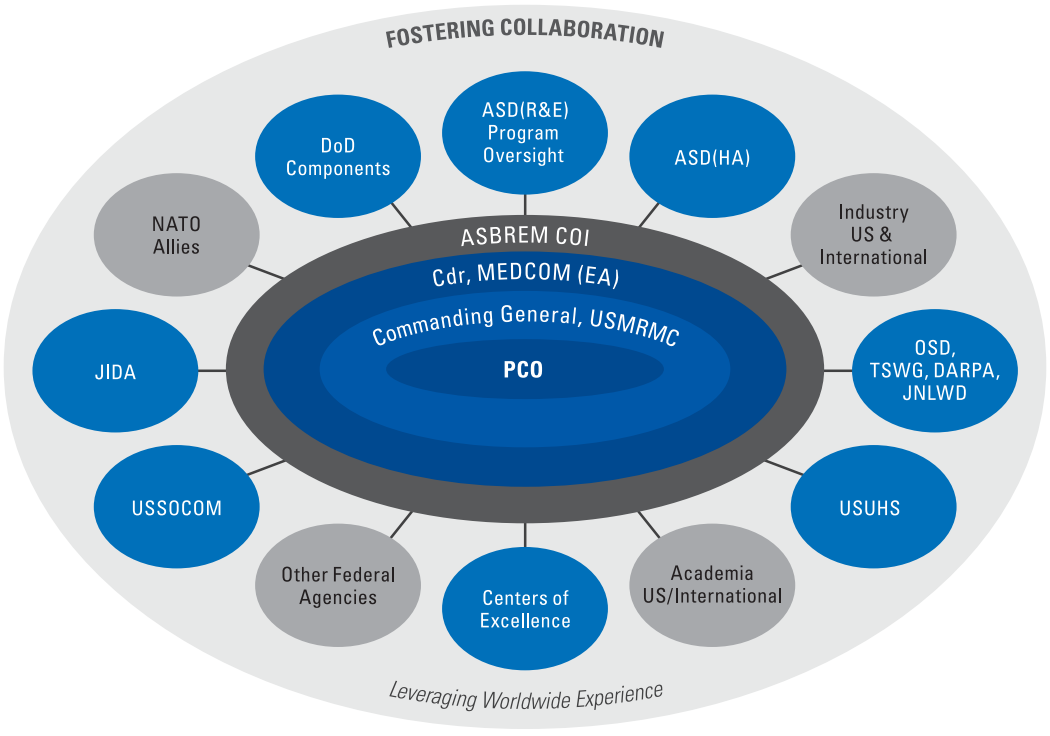


TABLE 1-1: Taxonomy of Injuries from Explosive Devices (from DoDD 6025.21E)

Injury Type	Description
Primary Blast Injuries: • Blast lung • Ear drum rupture and middle ear damage • Abdominal hemorrhage and perforation • Eye rupture • Non-impact induced mTBI	Primary blast injuries result from the high pressures created by the blast. These high pressures, known as blast overpressure, can crush the body and cause internal injuries. Primary blast injuries are the only category of blast injuries that are unique to blast.
Secondary Blast Injuries: • Penetrating ballistic (fragmentation or blunt injuries) • Eye penetration	Secondary blast injuries result when strong blast winds behind the pressure front propel fragments and debris against the body and cause blunt force and penetrating injuries.
Tertiary Blast Injuries: • Fracture and traumatic amputation • Closed and open brain injury • Blunt injuries • Crush injuries	Tertiary blast injuries result from strong winds and pressure gradients that can accelerate the body and cause the same types of blunt force injuries that would occur in a car crash, fall, or building collapse.
Quaternary Blast Injuries: • Burns • Injury or incapacitation from inhaled toxic fire gases	Quaternary blast injuries are the result of other explosive products (such as heat and light) and exposure to toxic substances from fuels, metals, and gases that can cause burns, blindness, and inhalation injuries.
Quinary Blast Injuries: • Illnesses, injuries, or disease caused by chemical, biological, or radiological substances (e.g., "dirty bombs")	Quinary blast injuries refer to the clinical consequences of "post-detonation environmental contaminants," including chemical, biological, and radiological (e.g., dirty bombs) substances.

DoD Framework for Characterizing Blast Injuries

The term "blast injury" includes the entire spectrum of injuries that can result from exposure to explosive weapons, ranging from nonimpact-induced mTBI and ear damage to penetrating wounds, heat and chemical burns, and/or loss of limbs. The DoD adopted the *Taxonomy of Injuries from Explosive Devices,* as defined in DoDD 6025.21E, to provide a common framework for characterizing the full spectrum of blast injuries. The *Taxonomy of Injuries from Explosive Devices* assigns blast injuries to five categories—Primary, Secondary, Tertiary, Quaternary, and Quinary—based on the mechanism of injury (see Table 1-1). The EA plays a key role in coordinating research and development for the entire spectrum of blast injury.

Blast Injury Research Program Areas

The DoD Blast Injury Research Program works to close knowledge gaps in the prevention, mitigation, and treatment of blast injuries. To address the gaps and capability requirements for the full spectrum of blast injuries, the program organizes current research efforts into three key research program areas: injury prevention, acute treatment, and reset (see Figure 1-3).

Injury Prevention

Injury prevention reduces the risk of blast injuries. This research program area provides medically-based design guidelines and performance standards for individual and combat platform occupant protection systems; comprehensive injury surveillance systems that link injury, operational, and protection system performance data; tools to identify individual susceptibility to injury; and individual resilience training to prevent or mitigate injuries.

FIGURE 1-3: Blast Injury Research Program Areas

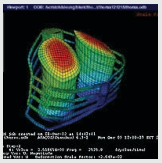
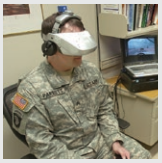
INJURY PREVENTION	ACUTE TREATMENT	RESET
 • Developing drugs to prevent and treat blast-related hearing loss	 • Developing diagnostics, treatments, and neuroprotectant drugs for TBI	 • Advancing tissue engineering and prosthetics
 • Analyzing combat injuries and PPE performance	 • Developing hemorrhage control and blood products	 • Improving recovery of function through virtual reality technologies and customized rehabilitative programs
 • Developing multi-effect blast injury models and evaluation tools to improve protective equipment	• Developing treatments for psychological trauma	• Developing return-to-duty standards
• Developing strategies that enhance psychological resilience and prevent PTSD and other psychological health problems	 • Developing medical procedures for burns, facial, hearing, visual, and extremity trauma	
	• Devising innovative strategies for improved pain management and wound infection mitigation	

Photo credits: Column 1—US Marine Corps, US Naval Research Laboratory, US Army; Column 2—US Army Medical Command, US Army Medical Research and Materiel Command, US Army; Column 3—US Air Force, Defense Advanced Research Projects Agency, Defense Centers of Excellence.

Acute Treatment

Acute treatment mitigates injury by providing immediate treatment across the spectrum of blast injuries. This research program area explores diagnostic tools, healthcare provider training, wound care, and medical treatment outcome analysis.

Reset

Reset mitigates disability by providing a biomedically-based performance assessment capability for return to duty and redeployment following injury; restoring full performance capabilities in redeployed individuals; and restoring function and ability to seriously injured Service Members with prosthetic devices. The term "reset" acknowledges a concept that extends beyond rehabilitation to include all activities necessary to return injured Service Members to duty or to productive civilian lives.

Coordination of Blast Injury Research Activities

DoD blast injury research efforts are requirements driven and fill knowledge gaps in preventing and treating injury, as well as restoring function. To address these gaps, researchers work with stakeholders from across the blast injury research community. Examples of programs and collaborative efforts supporting blast injury research follow.

DoD Component Services and Agency Research Programs

Each of the Services and the Defense Advanced Research Projects Agency (DARPA) has blast injury research programs primarily funded through the President's Budget. These programs sponsor research internally, within DoD laboratories and clinical centers, and externally through academic and industry partnerships. DoD blast injury research focus areas include injury surveillance, combat casualty care (CCC), wound infections, military operational medicine (MOM), and clinical and rehabilitative medicine (CRM).

TABLE 1-2: Joint Program Committees

JPC	DHA RDA Directorate Program Areas	Examples of Research Focus Areas
JPC-1	Medical Simulation and Information Sciences	• Medical Simulation • Health Information Technology and Informatics
JPC-2	Military Infectious Diseases	• Wound Infections (Prevention, Management, and Treatment) • Pathogen Detection
JPC-5	Military Operational Medicine	• Psychological Health and Resilience • Hearing Loss
JPC-6	Combat Casualty Care	• Damage Control Resuscitation • Mild, Moderate, Severe, and Penetrating TBI • Burn Injury • En Route Care
JPC-7	Radiation Health Effects	• Diagnostic Biodosimetry • Countermeasures (Protection and Treatment)
JPC-8	Clinical and Rehabilitative Medicine	• Neuromusculoskeletal Injury • Acute and Chronic Pain Management • Regenerative Medicine • Sensory Systems

Defense Health Agency Research, Development, and Acquisition (DHA RDA) Directorate

Established in FY10 by the Office of ASD(HA), the DHA RDA Directorate supports medical RDT&E programs related to the healthcare needs of Service Members. The DHA RDA Directorate manages the RDT&E funds of the Defense Health Program (DHP). Joint Program Committees (JPC), which consist of DoD and non-DoD technical experts, make funding recommendations for research and manage research programs under the DHA RDA Directorate in diverse military medical program areas, including those that directly address blast injuries (e.g., JPC-5, JPC-6, JPC-8) (see Table 1-2). These collaborative research programs rely on expertise and capabilities from across the Services, VA, US Department of Health and Human Services (HHS), academic centers, industry partners, and other scientific and technical communities. The current emphasis of the DHA RDA Directorate is on the Secretary of Defense's stated priorities: posttraumatic stress disorder (PTSD), TBI, prosthetic devices, restoration of eyesight and advancing eye care, and other conditions relevant to battlefield injuries and ailments that affect both Service Members and their Families. These focus areas closely align with several key research priorities for the DoD Blast Injury Research Program, including MOM, CCC, and CRM.

Congressionally Directed Medical Research Programs (CDMRP)

CDMRP is a global funding organization managing programs in cancer research, military medical research, and other disease- and injury-specific research. The CDMRP represents a unique partnership between the US Congress, the military, and public that uses congressionally directed dollars and core dollars (presidential budget appropriation) to fund groundbreaking, high-impact research awards. The CDMRP works collaboratively with the DHA RDA Directorate JPCs and other members of the DoD medical research community to support DHP and Army research program execution in several areas relevant to blast injury and military service: injury prevention, traumatic tissue injury, burns, hemorrhage and resuscitation, basic and applied psychological health, PTSD, TBI, neurotrauma, neuroplasticity, wound infections, infectious diseases, prosthetics, vision, hearing, balance, pain, and other rehabilitative and regenerative medicine efforts. Appendix D lists the CDMRP research programs that support blast injury research.

Centers of Excellence (CoE)

In response to congressional requirements within the NDAA, the DoD established several clinical CoEs. These centers seek to improve clinical care capabilities using new and updated clinical practice guidelines (CPG) and policy recommendations, understand injury and outcome trends, and inform research sponsors about the needs and requirements of the clinical communities. As a part of their mission, a number of CoEs address blast injury research: the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury (DCoE), National Intrepid Center of Excellence (NICoE), Pain Center of Excellence, Defense and Veterans Center for Integrative Pain Management (DVCIPM), Hearing Center of Excellence (HCE), as well as EACE and VCE whose efforts are highlighted in Chapters 5 and 6 of this report, respectively.

Research Forums, Consortia, and Programs Supporting Blast Injury Research

In addition to these research programs, numerous ongoing collaborative efforts (e.g., working groups, consortia, research programs) are investigating blast injuries and associated health outcomes. These collaborative efforts include the development of new blast injury protective or preventive measures, the development of new treatments for blast injury, and improvements in post-traumatic rehabilitation. For example, the Chronic Effects of Neurotrauma Consortium (CENC) targets mTBI (including blast-related mTBI) to address knowledge gaps in the basic science, determine its effects on late-life outcomes and neurodegeneration, identify Service Members most susceptible to these effects, and identify the most effective treatment strategies. Table 1-3 contains additional examples of collaborative research efforts.

Photo credit: Jennifer Brugman/US Air Force

Preview of this Report

The following chapters highlight research efforts to advance the DoD's ability to prevent, mitigate, and treat blast injury. Chapter 3 summarizes the PCO's participation in the NATO HFM-234 (RTG), and Chapter 4 focuses on the PCO's role in the BIPSR Process. Chapters 5–7 present the latest updates on DoD blast injury RDT&E supported by the DoD with more detailed discussions of the EACE and VCE. These chapters also present scientific advancements, improvements in standards of care, and the development of products to treat, diagnose, and prevent blast injuries. The report concludes with a discussion of the way forward for the Blast Injury Research Program in coordinating and supporting future advancements in blast injury research.

TABLE 1-3: Examples of DoD Research Forums, Consortia, and Programs Supporting Blast Injury Research

DoD Entity	Blast Related Efforts
Armed Forces Institute of Regenerative Medicine (AFIRM)	The multi-institutional, multi-disciplinary **AFIRM** collaborates across numerous agencies to accelerate the development of diagnostic products and therapies for severely wounded Service Members in need of reconstructive treatments. Currently, AFIRM represents 60 projects spread across 33 academic, corporate, and tri-service research institutions.
Auditory Fitness For Duty Working Group (AFFD WG)	One of the priorities of the **AFFD WG** is to assess occupations and identify hearing-critical tasks within the military. A hearing-critical task is defined as a task in which the detection of sound, understanding of speech, and/or localization of sound are essential for successful accomplishment of action. The AFFD WG also supports HCE's mission to heighten readiness and continuously improve the health and quality of life of Service Members and Veterans through advocacy and leadership in the development of initiatives focused on the prevention, diagnosis, mitigation, treatment, rehabilitation and research of hearing loss and auditory-vestibular injury.
Bridging Advanced Developments for Exceptional Rehabilitation (BADER) Consortium	The **BADER Consortium** works with military treatment facilities, VA centers, academia, and industry leaders to target orthopedic care after a blast injury. Special areas of interest include improving amputee gait, prosthetics, and quality of life issues following extremity injury.
Chronic Effects of Neurotrauma Consortium (CENC)	The **CENC** is a dedicated joint DoD and VA effort addressing the long term consequences of mTBI in Service Members and Veterans. It is conducted in response to the Presidential Executive Order 13625 and aligned to the National Research Action Plan for Improving Access to Mental Health Services for Veterans, Service Members, and Families. The CENC Coordinating Center is located at Virginia Commonwealth University and executes 10 studies and five integrated research cores across 30 participating institutions (https://cenc.rti.org). The majority of studies are focused on human subjects recruited from Veteran, Active Duty Service Members, Reserve, and National Guard populations. CENC studies examine chronic TBI and co-morbidities associated with mTBI; sensory deficits (visual, auditory, vestibular), movement disorders, pain (including headache), cognitive, and neuroendocrine deficits.
Pharmaceutical Intervention for Hearing Loss Working Group (PIHL)	The **PIHL Working Group** develops strategies for standardized analysis of potential systemic and local therapies for hearing loss prevention and rescue.
South Texas Research Organizational Network Guiding Studies on Trauma and Resilience (STRONG STAR)	**STRONG STAR** is a DoD-funded, multidisciplinary, and multi-institutional research consortium that develops and evaluates interventions for the detection, prevention, diagnosis, and treatment of combat-related PTSD and related conditions in active duty military personnel and recently discharged Veterans.
The INjury and TRaumatic STress Consortium (INTRuST)	The **INTRuST Consortium** was established to combine the research efforts of leading clinical researchers to bring to market novel treatments or interventions for those who suffer from PTSD and/or TBI. The INTRuST portfolio of clinical research and trials spans psychotherapeutics, pharmacotherapeutics, and devices.
The Consortium to Alleviate PTSD (CAP)	**CAP** is a joint VA and DoD effort to understand and treat PTSD and related conditions in active duty military Service Members and Veterans. The primary CAP objectives are to focus on the advancement of treatment strategies for PTSD and to identify and confirm clinically relevant biomarkers as diagnostic and prognostic indicators of PTSD and comorbid disorders.

DoD Entity	Blast Related Efforts
Federal Interagency Traumatic Brain Injury Research (FITBIR) Informatics System	The **FITBIR** was initiated as a collaborative effort supported by the DoD Combat Casualty Care Research Program (CCCRP) and the National Institute of Neurological Disorders and Stroke (NINDS) at the National Institutes of Health (NIH) as a secure, centralized informatics system developed to accelerate comparative effectiveness research in support of improved diagnosis and treatment for Service Members and civilians who have sustained a TBI. Data from, VA, DoD and/or NIH funded TBI research is required to be inputted into FITBIR. Benefits include 1) accelerating the testing of new hypotheses, 2) allowing multi-study data aggregation to increase the statistical power, and 3) providing existing comparator data and identifying patterns not easily extracted from a single study.
TBI Endpoints Development (TED)	The **TED** research consortium was initiated to establish a collaborative, multidisciplinary team to advance identification and validation of Clinical Outcome Assessments (COA) and blood-based and neuroimaging biomarkers to be submitted to the US Food and Drug Administration (FDA) Drug Development Tools (DDT) process or the Center for Devices and Radiological Health (CDRH) pilot qualification process. Decades of TBI research and trials had not yielded any drugs or devices capable of diagnosing or treating mild, moderate or severe TBI. The TED project team leverages DoD, NIH, and foundation-funded research networks and infrastructure, as well as several TBI study datasets containing thousands of TBI subjects to harmonize and curate data into a large Metadataset. The project will validate dataset of mild-moderate-severe TBI endpoints and enter into FDA qualification processes to become acceptable standard measures for clinical trials of TBI diagnostics or therapeutics and provide a clear path to market. Specifically the overarching objective is to leverage existing research and clinical infrastructure (TRACK-TBI, CENC, and the Concussion Research Consortium) to qualify COAs and biomarkers for FDA DTTs and CDRH pilot process. Working with the Clinical Data Interchange Standards Consortium (CDISC), the TED research consortium will identify and validate clinically relevant endpoints for diagnostic and therapeutic trials to conform TBI Common Data Elements (TBI-CDE version 2) to CDISC data standards for trials involving diagnosis and treatment of mild, moderate and severe TBI subject to FDA regulatory submission.
The NCAA-DoD Grand Alliance: Concussion Assessment, Research, and Education (CARE) Consortium	The **CARE Consortium** is aimed at specifically filling the gap in knowledge of the natural history of concussion and the effectiveness of concussion education at 30 colleges and the four Military Service Academies. Brain health/concussion is tracked for all NCAA students and cadets at the United States Military Academy and United States Air Force Academy, regardless of NCAA athletic status. This prospective, longitudinal, multi-center, multi-sport investigation that delineates the natural history of concussion in both men and women by incorporating a multi-dimensional assessment of standardized clinical measures of post-concussive symptomatology, performance-based testing (cognitive function, postural stability), genomic variability and risk factors, biomarkers of injury and trajectory of recovery, and psychological health.
Brain Trauma Evidence-based Consortium (B-TEC)	**B-TEC's** goals are to foster existing collaborations and new partnerships among TBI investigators in an effort to establish evidence-based principles and produce objective scientific advances in classification, diagnosis, and treatment of TBI. This project will deliver Guidelines on Concussion Diagnosis, Prognosis, Treatment, and Outcomes. B-TEC has two main objectives: 1. To use existing data sets of clinical TBI research to develop evidence-based guidelines that maximize diagnosis, prognosis, treatment, and outcomes 2. To establish an Evidence-based Clinical Research Coordinating and Training Center that integrates "best practice" of clinical research with evidence-based medicine, supporting new studies to answer key questions in TBI epidemiology, physiology, natural history, treatment, and outcomes

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CHAPTER 2:

DOD BLAST INJURY RESEARCH PROGRAM COORDINATING OFFICE

The DoD Blast Injury Research PCO supports the DoD EA by coordinating blast injury research investment within and outside of the DoD, both nationally and internationally, to support the delivery of timely and effective blast injury prevention, mitigation, and treatment solutions for Service Members. The PCO's activities help to identify and address knowledge gaps, share information broadly, and minimize duplication of effort. The PCO promotes collaboration among researchers across the DoD, other federal agencies, academia, industry, and international partners to solve complex challenges related to blast injury. It takes full advantage of the body of knowledge and expertise that resides both within and beyond the DoD.

MISSION

Support the DoD EA by:

- Coordinating DoD-sponsored biomedical research programs aimed at preventing, mitigating, and treating blast-related injuries;
- Identifying knowledge gaps and shaping research programs accordingly;
- Promoting information sharing among the operational, intelligence, medical, and materiel development communities; and
- Facilitating collaborative research among DoD laboratories and the laboratories of other federal agencies, academia, and industry to leverage resources and take full advantage of the body of knowledge that resides both within and outside of the DoD to accelerate the fielding of blast injury prevention and treatment strategies.

VISION

A fully coordinated DoD Blast Injury Research Program, as envisioned by Congress and directed by the Secretary of Defense, that delivers timely and effective blast injury prevention, mitigation, and treatment strategies to our Service Members today and in the future.

Key FY15 PCO Activities in Support of EA Mission Thrust Areas

In response to DoDD 6025.21E, Commander, MEDCOM established the PCO to assist in fulfilling EA responsibilities and functions and coordinating DoD blast injury research efforts and programs. The PCO executes its mission by supporting five key EA Mission Thrust Areas (see Figure 2-1). Below are examples of FY15 PCO activities supporting each of the five EA Mission Thrust Areas.

Facilitate Collaboration Within and Outside of the DoD

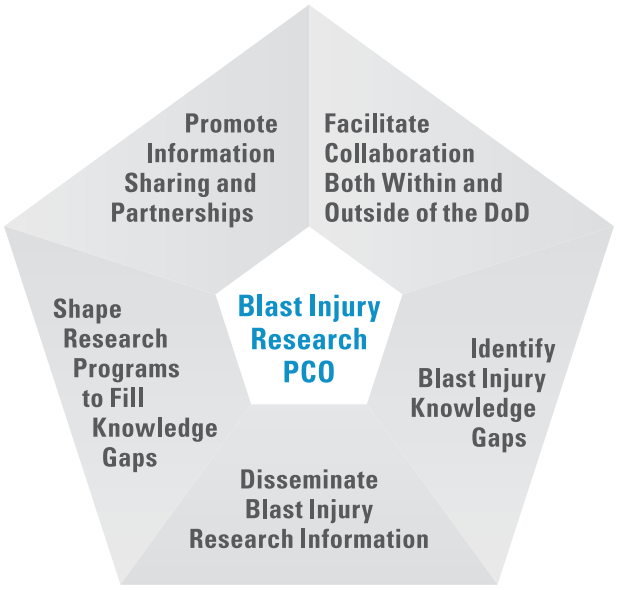
In support of the EA responsibility to promote collaboration on blast injury research topics, the PCO actively engages stakeholders within the DoD and across federal agencies, academia, and industry—both nationally and internationally. The following examples demonstrate the PCO's collaborative efforts with domestic and international partners.

US-India Collaboration

The PCO is a key player in the Defense Trade and Technology Initiative (DTTI), an international partnership organized by the Undersecretary of Defense for Acquisition, Technology, and Logistics and the Indian Ministry of Defence, Defence Research and Development Organization (DRDO). The first activity was the Indo-US Workshop on Cognitive Sciences/Autonomy held in New Delhi in September 2014, which resulted in a mutually agreeable list of potential topics for future collaboration. Following the workshop, the PCO participated in discussions sponsored by the Office of the ASD(R&E), Human Performance, Training, and Biosystems Directorate, to develop the US Science and Technology Strategic Plan for interacting with India in support of the DTTI. The group selected a proposal written by the PCO Deputy Director titled, "Experimental and computational studies of blast and blunt traumatic brain injury," as one of 11 potential collaborative projects with India. In April 2015, PCO leadership traveled to Delhi to jointly develop the proposal with leadership and research staff from the DRDO Institute of Nuclear Medicine & Allied Sciences (INMAS).

Photo credit (opposite page): Staff Sergeant Jamal D. Sutter/US Air Force

FIGURE 2-1: PCO Support of EA Mission Thrust Areas



They discussed project details including test methodologies, experimental design and procedures, data elements, collection of data, and methods/techniques for analyzing project data. This collaborative project supports the DTTI's objective to strengthen the important relationship between the US and India by leveraging an existing USAMRMC project to computationally model brain injury, which involves the Biotechnology High Performance Computing Software Applications Institute (BHSAI), New Jersey Institute of Technology (NJIT), WRAIR, and Naval Research Laboratory (NRL). Together with existing efforts at INMAS, the project aims to develop a fundamental understanding of the mechanism of brain injuries caused by blast and blunt impacts.

US-Israel Collaboration

Under the US/Israel Data Exchange Agreement (DEA) DEA-A-1977-IS-1230, "Military Medicine," information is exchanged on a broad array of medical research topic areas, including infectious diseases, CCC, physiological stress, PTSD and behavioral sciences, and chemical and biological defense. In support of the US/Israel DEA, the PCO Director traveled to Ramat Gan, Israel, in March 2015 to participate and present two briefings on key blast injury research topics at the 2015 Shoresh Conference on Military Medicine, the primary venue for the exchange of information under the agreement. The first briefing, "Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods, and Standards," highlighted the collaborative work and accomplishments of the NATO HFM-234 (RTG) (see Chapter 3). The second briefing, "Articulated Human Body Model for Computational Assessment of Explosion Blast Injury Loads, Body Responses, Personal Protection System Performance, and Casualty Assessment," focused on the development and demonstration of a computational analysis tool that can accurately simulate the effects of IED threats on human injury in both mounted and dismounted scenarios. A major outcome of the PCO's participation at the Shoresh Conference was the identification of several opportunities for collaboration between the PCO and the Israel Defense Forces (IDF). These opportunities include the sharing of historical blast injury research data, IDF participation in SoS meetings, and IDF participation in NATO HFM RTGs.

Identify Blast Injury Knowledge Gaps

Identifying knowledge gaps is critical to understanding the current state of the science on blast injury, the appropriateness of research efforts, and the direction of future efforts. In FY15, the PCO streamlined the BIPSR Process to be more effective and efficient at identifying gaps in available blast injury prevention standards; this process directly supports the key EA responsibility of recommending standards for ASD(HA) approval and DoD use.

Enhancing the BIPSR Process to Assess Blast Injury Prevention Standards

In collaboration with the MITRE Corporation, the PCO implemented significant efficiencies in the BIPSR Process that reduced the time required to review each injury type without sacrificing review quality. These efficiencies will have significant cost savings and will result in a process that is more responsive to the needs of Service Members. In FY15, BIPSR Process review of the lower extremity blast injury type was completed and a critical need for developing blast injury prevention standards in this area was identified. The PCO also initiated the BIPSR Process for spine and back, upper extremity, and auditory blast injury types; review of these injury types is expected to reach completion in 2016. For more information about FY15 BIPSR Process activities, please see Chapter 4.

Disseminate Blast Injury Research Information

Proper dissemination of blast injury research information ensures that all stakeholders along the RDT&E continuum, from laboratory to field, are equipped with the most timely, up-to-date information. Dissemination of this information occurs through multiple channels, including formal reporting mechanisms, direct requests for information (RFI) to the PCO, and stakeholder community briefings.

Annual Report to the EA

The PCO prepares an annual report to the EA covering science and technology efforts and programs focused on the prevention, mitigation, and treatment of blast injuries. Intended to inform senior DoD policymakers, fellow researchers, and a public audience, this report covers fiscal year blast injury research accomplishments across the DoD that address the full spectrum of blast injuries. The FY15 annual report is available on the PCO website (https://blastinjuryresearch.amedd.army.mil).

RFIs

The PCO plays an important role in connecting individuals and organizations with blast injury information and resources. For example, the PCO responded to a question from the Office of the Surgeon General (OTSG) about an article in USA Today, in which VA-sponsored researchers reported signs of early aging in the brains of OIF/OEF veterans who were exposed to blast. The PCO informed OTSG that within the scientific community, there is currently no consensus view on the relationship between brain injury and primary blast exposure (i.e., exposure to blast overpressure without subsequent head impact). The PCO suggested that a similar lack of consensus applies to the relationship between primary blast exposure and premature aging of the brain. To address knowledge gaps in the relationship between blast exposure and neurodegeneration, the PCO convened a meeting of experts on behalf of the DoD EA for blast injury research. The fifth International SoS Meeting was held in November 2015 to examine the evidence linking repeated blast exposures with neurodegeneration and the development and progression of CTE (see International SoS Meeting Series below).

Shape Research Programs to Fill Knowledge Gaps

The PCO helps to shape blast injury research programs by actively participating on research program planning, management, and advisory committees. Being an active participant ensures that key blast injury knowledge gaps are addressed, encourages collaborative research efforts, and identifies potentially duplicative research.

Shaping Research Through JPCs

The PCO continues to support the shaping of research programs through its work with the JPCs. In FY15, the PCO participated in the Joint DHP/VA Review and Analysis meetings for the CCC Research Program (CCCRP, JPC-6) and CRM Research Program (CRMRP, JPC-8).

These meetings provided a high-level snapshot of the key areas of each program's medical research investment and highlighted the importance of DoD/VA coordination and collaboration with researchers from other federal agencies, academia, and industry. The PCO's participation in Review and Analysis meetings and status as a voting member help to ensure that recognized blast injury knowledge gaps are being addressed in current and future medical research programs.

Computational Models for Blast-Induced TBI

To advance research on the mechanisms of blast-induced TBI, the PCO participated in an on-site kickoff meeting for a collaborative research project led by BHSAI, of the Telemedicine and Advanced Technology Research Center (TATRC), and USAMRMC. The objective of this project is to characterize and quantify the mechanisms that could cause blast-induced TBI. It is anticipated that the multidisciplinary team will develop and experimentally validate a whole-body computational model that is able to characterize the brain-tissue responses to direct and indirect mechanisms (and their combined effects) resulting from blast exposure. This will support the identification of correlates between predicted biomechanical responses and observed brain-tissue damage. Other collaborating organizations include the NJIT, WRAIR, the University of Utah, and the University of Maryland.

Quantifying the Physiological Effects of Blast Loads

Representing the EA for blast injury research across the DoD, the PCO took part in a science and technology program review titled "Blast Load Assessment: Sense and Test (BLAST) for Navy corpsman and other medical providers." This program, which is part of the Office of Naval Research (ONR) Force Health Protection Future Naval Capabilities Pillar, aims to develop technologies to quantify the physiological effects of blast loads on personnel in the field environment. It will replace the arbitrary stand-down times that compromise both operational and clinical goals. The enabling capabilities envisioned from this project include the following:

- **BLAST Sensor—**a field-ready, body-mounted sensor to record blast pressure, impulse, and acceleration for detecting and quantifying blast loads
- **Neuro-Functional Assessment Tool—** a forward-deployable screening tool to determine if a patient has experienced blast or other forceful exposures that may have caused a TBI
- **BLAST Algorithm—**an algorithm that incorporates physiological and neuro-functional data to provide a "Go/No Go" response to blast events.

It is envisioned that the resulting miniature "dosimeter" will have the capability to indicate if a given exposure presents a likelihood of injury and will be readable by a corpsman. The BLAST program is developing all three products in parallel and plans to transition the products to the Bureau of Medicine and Surgery (BUMED) by FY18.

Creating New Biomechanically-Based Auditory Standards

In February 2015, the PCO served as an advisor for the project, "Biomechanically-Based Auditory Standard," sponsored by the USAMRMC. The purpose of this three-year project, now in its final year, is to develop a valid, biomechanically based computational model of blast-related auditory injury that can serve as a replacement for Military Standard (MIL-STD) 1474D, "Design Criteria Standard, Noise Limits," which the Army medical community currently uses to assess auditory health risks associated with the use of weapon systems. The MIL-STD is widely recognized as overly conservative, and its application as a health risk criterion results in unnecessary restrictions on the use of weapon systems in training and combat.

The current project has made significant progress in developing a biomechanically based model by leveraging an extensive historical archive of human volunteer and animal data. These data have been used to refine and validate an existing auditory injury model known as the "Auditory Hazard Assessment Algorithm for Humans Model" (AHAAH) developed by the ARL. The next steps are to document and publish the new model and to engage the medical and weapons testing communities in discussions about its use in health risk assessment.

Preventing/Controlling Battle Infections

The PCO authored a Small Business Innovation Research (SBIR) Phase II topic titled "Antimicrobials Textiles" for which activities began in October 2014. The goal of the project is to identify a lightweight, durable, antimicrobial finish for integration into textiles to prevent and/or control infections—including those resulting from blast injuries—in military medical shelters and field hospitals. The project will characterize, develop, and optimize a catalytic antimicrobial system, and provide data on the extent of coating coverage, functional group density, coating adhesion, and antimicrobial activity. This novel technology could be extended to multiple fabric types to generate antimicrobial textiles for many military and civilian applications, including antimicrobial textiles, anti-infective wound dressings, hospital textiles, bedding, wipes, heating/ventilation/air conditioning filters, and various medical devices.

Promote Information Sharing and Partnership

Given the complex nature of blast injury, information sharing and partnership is critical to advancing blast injury RDT&E through coordinated efforts across stakeholder communities. In FY15, the PCO participated in several activities to promote information sharing and strengthen partnerships with key national and international organizations.

International Partnership through NATO HFM-234 (RTG)

The PCO's participation in NATO HFM RTGs promotes information sharing and partnerships across the international blast injury research community. The HFM-234 (RTG), chaired by the PCO Director, has developed tools and guidelines for conducting focused, multidisciplinary research that will lead to an understanding of the mechanisms of blast injuries necessary for developing effective prevention, mitigation, and treatment strategies. The team's efforts are guided by the approach used to solve classical toxicology problems wherein clear agreement on dose (blast dose), mechanism of delivery of the dosage, and dose-response endpoints are needed to understand the etiology of blast injury. See Chapter 3 to learn more about this effort.

Sharing Information with Academia

The PCO holds seminars to facilitate information sharing among blast injury research stakeholders within and outside the DoD. In November 2014, the PCO conducted a seminar for University of Maryland researchers to share their latest research efforts sponsored by the USAF Center for Sustainment of Trauma and Readiness Skills (CSTARS) program and the CDMRP. Participants included representatives from the CSTARS program, CDMRP, Military Operational Medicine Research Program (MOMRP), CCCRP, and PCO staff. The University of Maryland School of Medicine shared compelling evidence from two different TBI models. This evidence demonstrated that exposure to aeromedical evacuation-relevant hypobaria exacerbated both histologic and neurologic outcomes. The University of Maryland School of Engineering presented data on the effects of V-shaped hulls and thin-walled cylinders in the design of MRAP vehicles, which reduced vehicle damage after an underbody blast explosion and reduced the acceleration, impulse, and kinetic energies experienced by the frame.

These studies address knowledge gaps related to the mechanisms of injury and accelerate the development of tools to improve survivability after blast events.

US-Japan Information Sharing

In support of the EA's commitment to sharing information with international partners, the PCO, Japanese researchers, and DoD colleagues participated in a seminar in March 2015 that focused on new approaches to mTBI studies. The seminar, which was organized by the US Army Research, Development and Engineering Command (RDECOM) International Technology Center-Pacific (ITC-PAC) and the ARL Weapons and Materials Research Directorate, featured Japanese representatives from the Division of Biomedical Information Sciences, National Defense Medical College (NDMC) Research Institute. The research team from Saitama, Japan, presented studies that use laser-induced shock waves to understand the pathophysiology and mechanism of blast-related mTBI. To further US-Japan information sharing, the PCO, in collaboration with the NDMC, ITC-PAC, ONR Global, and the USAF Research Laboratory's Asian Office of Aerospace Research and Development, plans to organize a Japan-US Technical Information Exchange Forum on Blast Injury. See Chapter 8 for more information on this collaborative activity.

International SoS Meeting Series

The International SoS Meeting series has been a forum for knowledge sharing, collaboration, and communication across blast injury research communities since 2009. Each PCO-hosted meeting brings together the world's top researchers and experts from across the DoD, other federal agencies, academia, industry, and international partners to share expertise and cutting-edge research on a specific topic related to blast injury. Resulting recommendations shape future blast injury research priorities and facilitate the development of blast injury prevention, mitigation, and treatment strategies for the Service Member.

2014 International SoS Meeting on the Biomedical Basis for mTBI Environmental Sensor Threshold Values

The PCO organized the 2014 International SoS Meeting on the Biomedical Basis for mTBI Environmental Sensor Threshold Values to identify challenges associated with correlating environmental sensor threshold values to injury outcomes. Discussions and recommendations from the meeting will help guide the development of improved medical screening and assessment tools, as well as improvements in the design and development of PPE. The objectives of the meeting were as follows:

- Assess the current state of the science for the biomedical basis of environmental sensor threshold values and the relationship of these threshold values with the risk of the development of mTBI/concussion
- Identify gaps in the development and use of current environmental sensor injury threshold values
- Guide future research to gain understanding between varying blast forces and the development of TBI
- Improve protection, treatment, and mitigation for civilian and Service Member communities.

Literature Review

The meeting's literature review informed attendees on the current state of the science for mTBI/concussion thresholds associated with environmental sensors, with an emphasis on the neuropathology, mechanisms, computational modeling, environmental sensor technology, and evaluation of sensor technology, as well as the validation and correlation of environmental threshold values to mTBI/concussion.

Three main nonexclusive hypotheses exist for the mechanical mechanisms of blast-induced TBI: (1) thoracic pressure waves that transmit to the brain; (2) impact/head acceleration (both linear and rotational); and (3) direct cranial entry of blast waves. To determine the exact contribution of the thorax to structural changes in the brain following blast exposure, additional collaborative research efforts are needed. Flexion trauma appears to result in more serious injury than extension trauma, and additional research may contribute to the development of more effective protective equipment. Further research on the effects of blast waves on neuronal cells to aid in the development of novel biomarkers for blast exposure is needed.

Advancements in animal modeling and neuroimaging have allowed for more detailed investigation into the pathophysiological (e.g., neuroanatomical, cellular, molecular) outcomes of mTBI. Despite the challenges translating animal research outcomes to the human, investments in preclinical research have helped to inform clinical research, and inroads have been made regarding the outcomes and trajectory of TBI (blast and nonblast).

Advances in computational modeling allow the simultaneous simulation of the dynamic response of both fluids and solids to blast. Computer modeling may aid in elucidating the mechanisms of blast injury and identifying "regions of interest" for injury thresholds. The accuracy of computational modeling is limited by the ability to determine parameter values, which have varied over orders of magnitude in experiments.

Several environmental sensors have been deployed in the field. No reports, however, have been published linking data from fielded sensors to known injury. Product developers are conducting their own ad hoc tests on the sensors to determine accuracy. There is a need for independent standardized testing to validate sensory accuracy. Sensors currently under development align to one of three categories: packaged environmental sensors, raw pressure sensors, or burst sensors. Packaged environmental sensors can record pressure and acceleration (both linear and angular), along with vital signs such as electroencephalogram, heart rate, and oxygen saturation. Raw pressure sensors need further development before being packaged for fielding. Burst sensors are cheap, lightweight, and require no external power source; they, however, cannot report or accurately record environmental data.

Currently, there is no definitive experimental evidence that would permit the establishment of exposure thresholds for mTBI. Current blast injury tolerance curves for humans are obtained by scaling from animal models. Published reports on the identification of proposed mTBI thresholds from impact have come largely from the civilian sector, specifically professional and collegiate athletics.

November 2014 Meeting

The 2014 International SoS Meeting on the Biomedical Basis for mTBI Environmental Sensor Threshold Values took place from 4 to 6 November, 2014, in McLean, Virginia. The meeting's Planning Committee included clinical, research, and program representatives from the DoD, the National Institutes of Health (NIH), the National Football League (NFL), and the National Collegiate Athletic Association (NCAA). In addition to planning major aspects of the meeting, the committee identified a panel of six subject matter experts (SME) to serve as the Expert Panel. The Expert Panel was charged with chairing the focused working group sessions and identifying the major meeting findings and recommendations needed to advance the state of the science of environmental sensor threshold values.

More than 115 participants from the DoD, VA, NIH, athletic organizations, academia, medicine, industry, and international organizations attended the meeting.


4B-6
4B-6
4A-6

The agenda consisted of presentations with Expert Panel-facilitated discussions, a poster session, concurrent participant-focused working group sessions, and Expert Panel member reports summarizing the working group findings. Following the meeting, an executive panel session was held to review meeting data and formulate recommendations. The meeting presentations and poster abstracts can be found on the PCO website at https://blastinjuryresearch.amedd.army.mil/index.cfm?f=application.pco_sos_materials.

Expert Panel Findings

Leveraging the SoS literature review, meeting presentations, and outputs from the focused working group sessions held during the meeting, the Expert Panel concluded that biomedically valid sensor threshold values do not yet exist for blast-induced mTBI. Additional research is required to determine the relative contributions of linear acceleration, rotational acceleration, and blast overpressure to injury, as well as the individual factors (e.g., past exposure history, physique, gender) that contribute to mTBI risk. In addition, increased collaboration and access to existing blast and blast injury data are essential to develop product specifications and performance standards for sensor technologies.

The Expert Panel developed recommendations and a framework of suggested actions to advance the state of the science toward a biomedically valid environmental sensor threshold value for blast-induced mTBI. Based on the findings from the meeting, the Expert Panel recommended immediately establishing a fully funded and authoritative task force to facilitate the development of environmental sensor specifications that will ultimately correlate sensor data to medical outcomes. This multiagency, multidisciplinary task force will analyze existing data to identify the essential sensor data elements to be collected that will be most predictive of injury. The task force, in collaboration with the broader TBI community, will develop a consensus clinical definition/measure of mTBI against which sensor thresholds can be compared. Current mTBI assessment tools will be evaluated and the efficacy of potential screening tools, such as biomarkers, cognitive and/or motor tests, and neuroimaging tools, will be assessed. In addition, the task force will validate or invalidate existing preclinical models based on the best science available and will identify knowledge gaps to guide future research efforts. These activities will accelerate the development of a biomedically valid mTBI threshold value and will guide the development of improved screening tools and protective equipment.

2015 International SoS Meeting, "Does Repeated Blast-Related Trauma Contribute to the Development of CTE?"

In FY15, the PCO planned and executed the 2015 International SoS Meeting, which focused on the question, "Does Repeated Blast-Related Trauma Contribute to the Development of CTE?" The objectives of the meeting were as follows:

- Discuss the evidence linking repeated blast exposure to neurodegeneration
- Assess the pathophysiology, underlying mechanisms of injury, and progression of blast-induced neurodegeneration
- Identify specific features that can contribute to the characterization of CTE as a unique neurodegenerative disorder
- Examine relevant animal injury models for blast-induced CTE
- Discuss strategies for prevention, mitigation, early diagnosis, and treatment of blast-induced neurodegeneration
- Explore the link between blast-induced neurodegeneration and CTE
- Identify knowledge gaps that will inform future research directions.

Photo credit (opposite page): Jamie Hartman/US Naval Research Laboratory

Prior to the meeting, the PCO conducted an extensive literature review on CTE to inform meeting participants on the state of the science. The review, which is posted on the PCO website, focused on two research questions: 1) What is the current evidence describing the pathophysiological basis of CTE, and 2) What associations are known between the mechanism(s) of head injury (e.g., single or multiple exposures, impact or nonimpact injury) and the development of CTE? To address these, the report described the following areas of research related to CTE: neuropathology, exposure to head injury, epidemiology, clinical manifestations, animal models, biomarkers, and treatment and prevention strategies.

The meeting's Planning Committee included 26 representatives from the Services, DoD medical and nonmedical communities, other federal agencies, academia, the NFL, NCAA, and the private foundation, One Mind. The Planning Committee identified six SMEs to serve as the Expert Panel, whose role it was to lead discussions, ask tough questions, and challenge assumptions to tease out what is known and unknown in the field, as well as ways for moving the field forward.

The 2015 International SoS Meeting on the question, "Does Repeated Blast-Related Trauma Contribute to the Development of CTE?" was held from 3 to 5 November, 2015, in McLean, Virginia. 124 participants attended the meeting, including representatives from the DoD, NIH, VA, NFL, NCAA, industry, and academia. The meeting included plenary sessions with key topic and scientific presentations, poster sessions, and six working groups led by a member of the Expert Panel. The working groups discussed the following:

- Challenges to establishing definitive features of neurodegeneration from repeated blast-induced trauma; risk factors that are predictive of CTE
- Research needed to explore the putative progression from repeated blast exposure to CTE
- Challenges to identifying suitable biomarkers for the early detection and diagnosis of CTE
- Strategies to prevent, mitigate, or treat neurodegeneration following repeated blast exposure.

The working groups concluded that we do not have a complete understanding of CTE due to an inability to definitively establish the neuropathological characteristics unique to blast exposure; the lack of appropriate animal models; the need for large prospective studies that gather data on risk factors, potential fluid and imaging biomarkers, and brain tissue; and the lack of premortem diagnostic tests. Upon analyzing the findings of the working groups, the Expert Panel developing the following recommendations:

1. Initiate large prospective clinical studies that collect systematic data on candidate risk factors, potential fluid and imaging biomarkers, and tissues for neuropathological examination
2. Generate standardized assessments for capturing exposure histories that can be used to develop a clinical diagnosis
3. Create a brain bank repository accessible by the research community
4. Develop a strategy for the development of next-generation biospecimen and imaging biomarkers
5. Develop animal models clinically-relevant to blast injury and chronic neurodegeneration.

The PCO, with the help of the Expert Panel members, will synthesize the findings and recommendations from this meeting in a detailed report that will be distributed to the key stakeholders and made publicly available on the PCO website. A more detailed description of the meeting and its outcomes will be described in the FY16 EA Report.

JTAPIC Program

The JTAPIC Program was established at the USAMRMC in 2006 to assist the EA in fulfilling portions of its responsibilities under DoDD 6025.21E, in particular, the EA's responsibility to support the development, maintenance, and usage of a joint database for blast research-related information. The program's mission is to collect, integrate, analyze, and store operations, intelligence, materiel, and medical data to inform solutions that will prevent or mitigate injury during the full range of military operations, including blast injuries. The JTAPIC Program Management Office originally resided within the PCO, but it has since matured into a program of record. The JTAPIC Program Management Office is located at Fort Detrick, Maryland, with partners throughout the United States (see Table 2-1). It leverages the medical, intelligence, operational, and materiel expertise of these partnerships to support operational planning and the development of strategies to prevent or mitigate injuries during combat. The JTAPIC Program's key FY15 accomplishments are highlighted in Chapter 7.

TABLE 2-1: JTAPIC Program Partners

Intelligence and Operational Partners
National Ground Intelligence Center
Dismounted Incident Analysis Team
US Marine Corps Current Operations Analysis Support Team
Marine Corps Intelligence Activity
US Army Aeromedical Research Laboratory
Medical Partners
Armed Forces Medical Examiner System
Joint Trauma System
Naval Health Research Center
Materiel/Acquisition Partners
Project Manager, Soldier Protection Individual Equipment
Product Manager, Infantry Combat Equipment
US Army Research Laboratory

Way Forward

The Commander, MEDCOM established the PCO to coordinate research efforts on behalf of the EA to advance prevention, mitigation, and treatment solutions for Service Members. In support of the EA's five Mission Thrust Areas, the PCO will continue to provide critical information on knowledge gaps in blast injury research sourced from its collaborative efforts with scientists, clinicians, and engineers from across the domestic and international blast injury RDT&E communities. For information on PCO activities that will continue into FY16 and beyond, see Chapter 8.

03

CHAPTER 3:

NATO HUMAN FACTORS AND MEDICINE RESEARCH TASK GROUP

Blast injury has become a significant source of casualties in current NATO operations as NATO forces are increasingly subject to blast exposure from IEDs, land mines, and rocket-propelled grenades. Recent advances in PPE, in-theater medical care, and rapid evacuation are increasing the number of blast survivors. There is a direct correlation between the increased number of blast survivors and individuals suffering from TBI, neurosensory damage to eyes and ears, and extremity injuries resulting in amputation of the limb(s). NATO nations are responding to the increase in blast injuries that currently affect NATO forces by holding science and technology activities.

NATO science and technology activities are conducted through a dedicated NATO executive body operating under the NATO collaborative business model. Under the collaborative business model, NATO partner nations use member national resources within a NATO-provided forum to promote collaborative research and information exchange. The HFM technical panels are supported by RTGs or research symposiums (RSY). The mission of the HFM technical panels is to provide the scientific and technical basis for optimizing the health, safety, protection, wellbeing, and performance of the human in operational environments with a consideration of affordability.

The PCO supported collaborations between the United States and NATO member nations across several HFM activities between April 2008 and January 2013. The purpose of previous HFM activities related to blast injury (see inset) was to develop a greater understanding of the mechanisms of blast injury and translate scientific discoveries into prevention, mitigation, and treatment measures. The cumulative efforts of these activities serve as the foundation for current NATO efforts.

PREVIOUS NATO HFM ACTIVITIES RELATED TO BLAST INJURY

- HFM-090: Test Methodology for Protection of Vehicle Occupants against Anti-Vehicular Landmine Effects (2002–2006)
- HFM-175: Medically Unexplained Physical Symptoms in Military Health (2008–2012)
- HFM-193: Mild Traumatic Brain Injury in a Military Operational Setting (2009–2013)
- HFM-198: Injury Assessment Methods for Vehicle Active and Passive Protection Systems (2010–2013)
- HFM-207 Symposium: A Survey of Blast Injury across the Full Landscape of Military Science (2010–2012)

The present chapter describes the HFM-234 (RTG), *Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods, and Standards,* which stems from recommendations developed during the HFM-207 RSY, *A Survey of Blast Injury Across the Full Landscape of Military Science*. The PCO Director co-chaired the prior HFM-207 RSY. The Technical Evaluation Report generated from the HFM-207 RSY proposed the following recommendations: (1) establish a recurring technical exchange venue on blast injury and its mitigation; and (2) develop and implement a Technical Activity Proposal (TAP) exploring the toxicology of blast injury that focuses on models and methodologies for advancing translational research. In response to the recommendations of the HFM-207 RSY, a TAP, the *Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods and Standards,* was approved in October 2012. This TAP resulted in the establishment of a new NATO Science & Technology Organization (STO), HFM-234 (RTG), with the PCO Director as the chair. The activities of the HFM-234 (RTG) are ongoing and described in more detail in the following sections.

Photo credit (opposite page): Sergeant First Class Randall Jackson/US Army

FIGURE 3-1: HFM-234 (RTG) Participating Nations

Mr. Michael Leggieri, Chair
Dr. Raj Gupta, Secretary
US Army Medical Research and Materiel Command
UNITED STATES

Mr. Stephen Bjarnason
Defence Research and Development Canada, Suffield
Dr. Ibolja Cernak
University of Alberta, Canada
Dr. Lucie Martineau and Dr. Simon Ouellet
Defence Research and Development Canada, Valcartier
CANADA

Dr. Hans Orru
University of Tartu
ESTONIA

Dr. Jean-Claude Sarron
Direction Centrale du Service de Santé des Armées
FRANCE

Dr. Dan Bieler, Dr. Arnulf Willms, and Dr. Axel Franke
German Armed Forces Central Hospital, Koblenz
GERMANY

Mr. Mat Philippens
Nederlandse Organisatie voor Toegepast Natuurwetenschappelijk Onderzoek
THE NETHERLANDS

Mr. Stian Skriudalen and Mr. Jan Arild Teland
Norwegian Defense Research Establishment
NORWAY

Dr. Marten Risling
Karolinska Institutet
SWEDEN

Dr. Emrys Kirkman and Dr. Sarah Watts
Defence Science and Technology Laboratory
UNITED KINGDOM

OBJECTIVE:
To establish a framework for a new multidisciplinary research area on the environmental toxicology of blast that can be implemented across NATO nations, and provide validation guidelines for research models and standards for measurements.

HFM-234 (RTG): Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods, and Standards

The HFM-234 (RTG) is tasked with establishing a framework for a new interdisciplinary research area focusing on the environmental toxicology of blast exposure. Discussion from the HFM-207 RSY highlighted the analogous relationship between blast injury research and classical toxicology problems in that both require an understanding of dose, mechanism of dose delivery, and dose-dependent endpoint. With this analogy in mind, the purpose of the HFM-234 (RTG) is to address knowledge gaps by creating a systematic approach to better understand blast injuries. The HFM-234 (RTG) is focused on standardizing animal models of blast injury; creating common methods for establishing dose-response and route of exposure; generating computational models; specifying dose regimens relevant to human medical endpoints; and developing methods for translating basic research to medical products and/or improved PPE for Service Members.

The HFM-234 (RTG) consists of 17 members from nine NATO nations (see Figure 3-1). It established a regular meeting schedule, each meeting to be held in a different NATO member nation. The purpose of each meeting is to examine the state of the science and technology for blast injury toxicology, identify gaps, and discuss opportunities and methods to strategically address these gaps. Participating scientists, clinicians, and engineers from the international, military, academic, and industrial communities are asked to present their scientific, technical, clinical, and/or regulatory efforts and participate in working groups. Table 3-1 and Table 3-2 contain the TAP objectives and program of work for the HFM-234 (RTG). They reflect the HFM-234 (RTG)'s intention to develop four key products:

- A comprehensive dictionary of blast injury research terms
- Guidelines for conducting epidemiological studies of blast injury
- Guidelines for reproducing blast exposures in the laboratory
- Guidelines for using animal models in blast injury research.

Comprehensive Dictionary of Blast Injury Research Terms

Establishing reporting standards for collaborative blast injury research requires a common dictionary of terms and associated meanings. After the first HFM-234 (RTG) kickoff meeting in July 2013, a virtual core working group was assigned to create the comprehensive dictionary of blast injury research terms, which the working group will add to or update after each HFM-234 (RTG) meeting. The dictionary entries, or "elements," are expected to help professionals across disciplines (e.g., engineers, physicists, physicians, researchers) communicate using standardized blast injury terminology. Development of the dictionary is ongoing; the group aims to complete the dictionary by the end of the HFM-234 (RTG)'s term in July 2016. The finalized comprehensive dictionary of blast injury research terms will contain the first-ever standardized language guidelines to help those invested in blast injury research to improve information exchange and ultimately, form stronger collaborative research endeavors.

TABLE 3-1: Technical Activity Proposal Objectives

Objectives
The HFM-234 (RTG) will develop tools and guidelines for conducting blast injury research that will advance the state of the science, close knowledge gaps, and accelerate the delivery of solutions that protect Service Members from blast injury. These tools and guidelines include: • A comprehensive dictionary of blast injury research terms to support consistency in communication across research communities • Guidelines for conducting epidemiological studies of blast injury to establish common data elements and enable cross-study comparison • Guidelines for reproducing blast exposures in the laboratory to ensure relevant exposures and enable cross-study comparison • Guidelines for using animal models in blast injury research and a roadmap for the development of dose-dependent injury curves that will accelerate the development of valid human blast injury prediction tools.

TABLE 3-2: HFM-234 (RTG) Program of Work

Activity Workshop	Month/Year	Purpose	Host/Location
Meeting 1	1–2 Jul 2013	HFM-234 (RTG) Kick-off	STO (Paris)
Comprehensive Dictionary of Blast Injury Research Terms	Ongoing	Develop a dictionary of commonly used terms with definitions	Canada (Virtual)
Meeting 2	10–12 Dec 2013	Develop recommendations for collecting data necessary for conducting epidemiological studies	USA (Fort Detrick, Maryland)
Meeting 3	21–23 May 2014	Develop guidelines to reproduce blast exposure conditions in the laboratory	Canada (Medicine Hat, Alberta)
Meeting 4	7–9 Oct 2014	Synthesize workshops, discuss computational modeling, and review dictionary	Estonia (Tallinn)
Meeting 5	12–14 May 2015	Develop recommendations for standardized animal models and a roadmap for dose-dependent curves	Sweden (Stockholm)

Guidelines for Conducting Epidemiological Studies of Blast Injury

The importance of appropriate data collection and management in multisite epidemiological studies cannot be overemphasized. Using frameworks established by the Institute of Medicine as well as other well-documented epidemiological protocols, the HFM-234 (RTG) developed the Blast Injury Epidemiological Study Guidelines to standardize data collection, coding, and management, which will allow for cross-study comparisons and encourage greater international collaboration. The HFM-234 (RTG) finalized the guidelines in FY15. The group considered the parameters of interest to track initial exposure to blast; the data needed to link biological outcomes to blast exposure; the parameters of interest related to the use of sensors in blast studies; and the recommendations for optimizing existing databases for blast injury epidemiological studies. The guidelines underwent further revision following the October 2014 meeting in Estonia and in subsequent teleconferences. Now ready for publication, the guidelines detail critical elements of a blast injury epidemiological study: a well-defined research question; a focused hypothesis; a detailed study protocol; logical sampling methodology; identification of biases and limitations; definition of all variables and study size; standardized survey instruments and operational procedures; and an analysis plan. The study plan should include an ethics review and document any measures taken to ensure data quality. By standardizing data collection and analysis specific to blast injury epidemiological studies, these guidelines will enable international partners to share data, compare outcomes, and collaborate on future multinational studies. The HFM-234 (RTG) intends to publish the Blast Injury Epidemiological Study Guidelines as an official NATO document in FY16.

Photo credit: Staff Sergeant Patrick Mitchell/US Air Force

Photo credit: Randy Montoya/Sandia National Laboratories

Guidelines for Reproducing Blast Exposures in the Laboratory

As a part of the continuing effort to promote standardized study and data collection methodologies, the HFM-234 (RTG) is currently developing guidelines for reproducing blast exposure conditions in the laboratory. During the third meeting held in Canada in May 2014, the HFM-234 (RTG) decided to include the following key elements for inclusion in the laboratory guidelines: research rationale, blast exposure methodology, and target exposure characterization. The need for laboratory guidelines underscores the importance of establishing the comprehensive dictionary of blast injury research terms and the potential synergies that could be achieved by concurrently developing the laboratory guidelines and dictionary. Once finalized, the laboratory guidelines will enhance the reproducibility of research by reducing, if not eliminating, the variability of reported blast exposure information in the literature, standardizing experimental methodologies, and providing guidance on documenting experimental conditions.

Guidelines for Using Animal Models in Blast Injury Research

The intention of the fifth and most recent in-person meeting of the HFM-234 (RTG) was to develop recommendations for standardized animal models necessary for validating computational models of blast injury.

Invited guests from the University of Gothenburg (Sweden), the NDMC Research Institute (Saitama, Japan), and the NJIT gave presentations on the following topics: translational aspects of animal models; concepts for multiple models; animal model validation strategies; approaches to understanding systemic and immunological responses to blast; the use of animal model data to validate computational models; cutting-edge brain injury biomarkers; and the use of lasers to induce shock waves in animal models. Subsequent discussions led the team to conclude that a single animal model is not sufficient for the complex problem of blast-related brain injury. A more feasible solution may be to use a combination of models that, when taken together, will provide a more complete picture with relevance to humans. This approach will be articulated in guidelines the team will deliver by the end of its term in July 2016.

Way Forward

Advancements in blast injury treatment and care for Service Members require close collaboration across the domestic and international RDT&E, operational, and clinical care communities. By developing official NATO documents to standardize how data are collected, coded, and analyzed, the HFM-234 (RTG) is lifting the barriers to cross-study comparison and making international and multiorganizational collaboration more effective. The HFM-234 (RTG) will publish the guidelines for conducting epidemiological studies of blast injury in the beginning of FY16 and work toward publishing the comprehensive dictionary of blast injury research terms, guidelines for reproducing blast exposures in the laboratory, and guidelines for using animal models in blast injury research by the end of its term.

Photo credit (opposite page): Staff Sergeant Michael Behlin/US Army

04

CHAPTER 4:

MHS BLAST INJURY PREVENTION STANDARDS RECOMMENDATION PROCESS

Department of Defense Directive 6025.21E assigns to the EA the responsibility to "Provide medical recommendations with regard to blast-injury prevention, mitigation, and treatment standards to be approved by the Assistant Secretary of Defense for Health Affairs (ASD(HA))." Designed to address this requirement, the BIPSR Process is the DoD's first unbiased, inclusive, stakeholder-driven process designed to identify and assess the suitability and applicability of existing candidate standards and to recommend standards that meet stakeholder needs with a suitable level of validity, rigor, precision, and confidence. Candidate standards include injury thresholds, human injury probability curves, and injury prediction tools needed to generate the information for informed trade-off and risk acceptance decisions by appropriate decision makers in the RDT&E, medical, and operational stakeholder communities across the DoD Components. These standards support weapon system health hazard assessments, combat platform occupant survivability assessments, and protection system development and performance testing (Figure 4-1).

The BIPSR Process has two major objectives. The first is to identify existing candidate standards that can be used immediately to meet the needs of the DoD. The second is to inform the research community of gaps where no suitable candidate standards exist. The BIPSR Process is not a research program and does not develop new candidate standards. The process does not attempt to impose acceptability or survivability requirements on the stakeholder communities; rather, the process identifies and assesses the suitability of existing candidate standards and recommends standards that meet DoD stakeholder needs with a specified level of validity, rigor, precision, and confidence.

In 2012, the PCO developed and obtained ASBREM Committee approval to begin implementing the BIPSR Process, introducing the process via a series of stakeholder meetings. The Johns Hopkins University Applied Physics Laboratory (JHU/APL), a University Affiliated Research Center and DoD trusted agent, supported the PCO through the piloting of the BIPSR Process with an evaluation and analysis of the toxic gas inhalation blast injury type followed by the lower extremity blast injury type, resulting in recommendations to stakeholders. The BIPSR Process is guided by a larger BIPSR Process stakeholder group, representing interests across the DoD, while Focused Stakeholder Committee members participate in blast injury-specific BIPSR Process implementations, which lead to the medical recommendations to ASD(HA).

FIGURE 4-1: Blast Injury Prevention Standards Framework

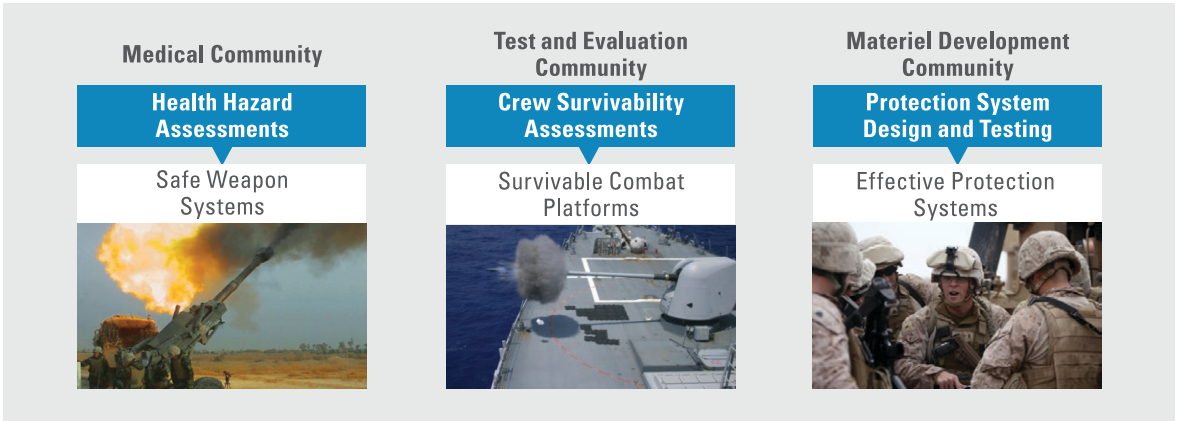


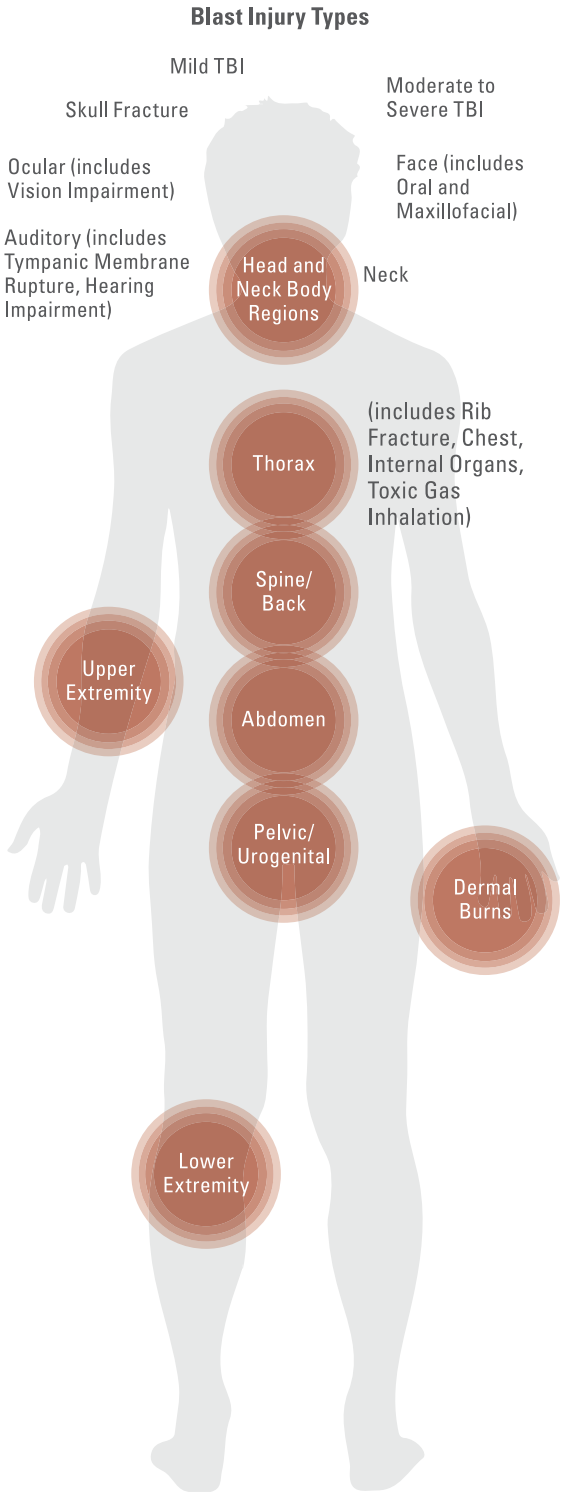
Photo credit (opposite page): Senior Master Sergeant Mike Hammond/US Air Force

In FY15, the MITRE Corporation, a DoD trusted agent that operates federally-funded research and development centers, supported PCO efforts in identifying and implementing efficiencies to a revised BIPSR Process resulting in a shorter timeline for each blast injury type without sacrificing the quality of the outcome. Using the BIPSR Process in conjunction with technology, the Interactive BIPSR (iBIPSR) capability adds the additional benefit of increased information sharing, collaboration, and transparency.

Having determined the 14 blast injury types (Figure 4-2) that will undergo the BIPSR Process, a mathematical model was used to establish a priority ranking across blast injury types to select the order in which the evaluations will occur. The prioritization outcomes received concurrence from the BIPSR Process Stakeholders at a January 2015 meeting, after which the PCO initiated the BIPSR Process for the spine and back, upper extremity, and auditory blast injury types.

The following sections of this chapter describe the activities and achievements of the BIPSR Process for FY15 including revisions to the BIPSR Process, development of the iBIPSR capability, conclusion of the lower extremity blast injury type, progress on implementing the revised BIPSR Process for the spine and back and the upper extremity blast injury types, and proving out the iBIPSR capability using the auditory blast injury type.

FIGURE 4-2: Categorization of Blast Injury Types by Body Region



BIPSR Process

BIPSR Process Revisions in FY15

Seeking to expedite the timeline required for evaluation of a blast injury type, the PCO developed the BIPSR Process simulation model using the Business Process Modeling Notation (BPMN) standard. This standardized business process modeling methodology is a way to graphically represent the BIPSR Process activities and facilitate quantitative and qualitative analysis via simulation of the overall process.

The BPMN model was populated with the actual timeline for the lower extremity BIPSR Process, resulting in confidence that the model is accurate. The PCO evaluated multiple scenarios for process improvements and recommended a revised BIPSR Process, which received concurrence in the January 2015 BIPSR Process Stakeholder meeting. These revisions are projected to accelerate the timeline for completion of all blast injury types by several years.

A key change in the revised BIPSR Process is reordering the sequence of preliminary activities. Specifically, performing a literature search and interviewing SMEs early on allows the PCO to develop an understanding of existing capabilities prior to defining stakeholder requirements. Understanding the existing research for a blast injury type earlier in the process ensures that a common context and terminology set are established prior to engagement of the stakeholders for requirements definition, effectively improving the efficiency of stakeholder interactions.

On the basis of BPMN analysis, a process step was also added to the BIPSR Process for cases in which a gap in standards is identified. The additional step allows for the definition of how to disseminate the gap information to the research community and close out the BIPSR Process upon declaration of a gap, rather than continue through the entire BIPSR Process.

In total, the process revisions to the BIPSR Process project a reduction in the time required to declare a gap for each blast injury type. This timeline is further accelerated through the implementation of the iBIPSR capability.

iBIPSR Capability

History and Background

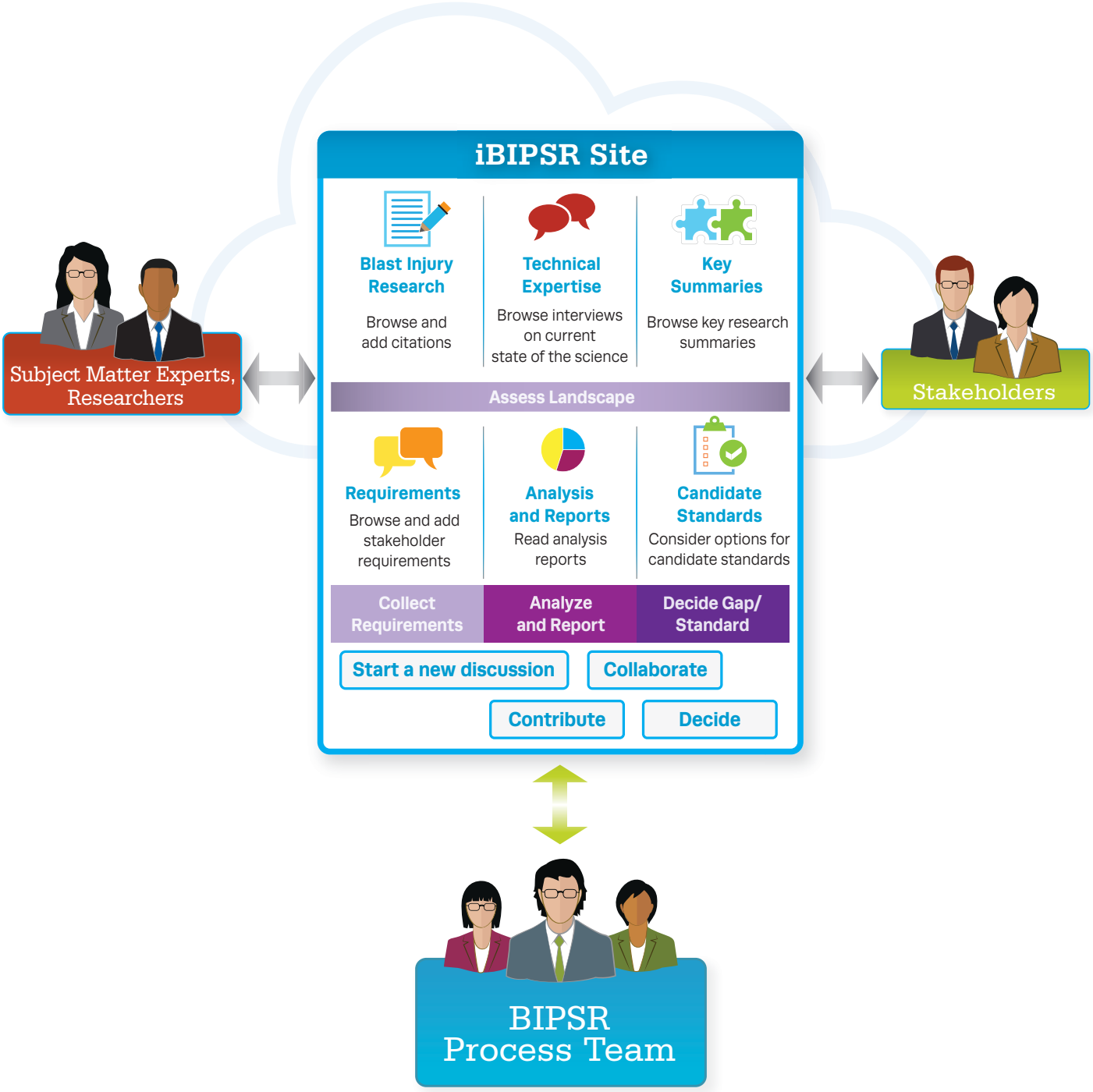
The PCO's EA support mission is to coordinate the DoD's medical blast injury research investment, on behalf of the EA, to ensure critical knowledge gaps are filled; to avoid costly and unnecessary duplication of effort; and to accelerate the fielding of prevention and treatment strategies by leveraging existing knowledge and fostering collaboration and information sharing among the world's blast injury experts. Development of the iBIPSR capability, a web-based collaboration environment, was recommended in the January 2015 BIPSR Process Stakeholder meeting.

The iBIPSR capability has foundations in collaborative semantic web technology, an information synthesis technology that is well suited to large collaborative multi-user information sharing and decision making efforts. The development of the iBIPSR site enhances information sharing among the world's blast injury experts and supports the PCO's EA mission to leverage existing knowledge and foster collaboration by removing obstacles to participation and allowing for a broader segment of the stakeholder community to engage in the process. It also provides opportunity for continuous collaboration, in contrast to discrete stakeholder meetings, throughout the BIPSR Process.

As shown in Figure 4-3, the iBIPSR capability website supports a variety of users with planned collaborative interactions between and among stakeholders, SMEs, and researchers. Additionally, the iBIPSR capability offers transparency into the BIPSR Process. For example, the iBIPSR site captures and maintains stakeholder requirements and facilitates research community understanding of the requirements. The iBIPSR site will also support interactive collaboration between stakeholders and SMEs, enabling greater community contributions to the identification of knowledge gaps and the development of standards recommendations. It enables individuals in the BIPSR Process community to engage, connect, and build relationships. This level of information sharing and collaboration accelerates the growth and development of the BIPSR Process community knowledge base.

The application of the iBIPSR capability could potentially be extended to support other areas of blast injury research.

FIGURE 4-3: BIPSR Process Supported by the iBIPSR Site



iBIPSR is an evolving capability, and the PCO recommended that the best injury type to use for evolving, finalizing, and proving out the iBIPSR capability would be one that has a high likelihood of requiring completion of the entire BIPSR Process. In the January 2015 BIPSR Process Stakeholder meeting, the stakeholders concurred with the PCO's recommendation that the auditory blast injury type, which has an existing military standard, is likely to have a candidate standard, making it ideal for building out and proving out the iBIPSR capability.

Power of iBIPSR

The iBIPSR interactive community-sourced capability represents a novel way to reduce the timeline of the BIPSR Process without sacrificing decision quality (Table 4-1). It is anticipated that the iBIPSR capability will expedite decisions by supporting continuous engagement and collaboration among SMEs, stakeholders, and researchers, and by supporting the simultaneous execution of the revised BIPSR Process for multiple blast injury types.

TABLE 4-1: The Power of the iBIPSR Site

Benefits of iBIPSR
The iBIPSR site is well-suited to large, collaborative, multi-user information sharing and decision making.
Leverages existing knowledge
Wiki technology fosters continuous collaboration
Removes obstacles to participation (e.g., travel and scheduling)
Allows for broad engagement in the process with access to information used in all stages of the BIPSR Process

Implementation of the BIPSR Process

Lower Extremity Blast Injury Type: Conclusion and Closeout of the BIPSR Process

The BIPSR Process for the lower extremity blast injury type was initiated in June 2013 through the establishment of the Lower Extremity Focused Stakeholder Committee. The committee included over twenty individuals from the RDT&E, medical, and operational communities representing the DoD, other federal organizations, academia, and industry. The Lower Extremity Focused Stakeholder Committee members collaborated to evaluate the state of lower extremity blast injury prevention standards over the course of meetings held July 2013, December 2013, July 2014, and April 2015, and ultimately the Lower Extremity Focused Stakeholder Committee concurred with the SME panel conclusions that no existing codified blast injury prevention standards address lower extremity blast injury requirements.

However, the BIPSR Process also found that there are methodologies used by some organizations in lieu of standards that could potentially serve as candidate lower extremity blast injury prevention standards. While these methodologies were determined to be the best available, the following gaps will be forwarded to the medical research community:

- Test methods that replicate both blast rate loading and duration
- Consensus on blast injury thresholds
- Inclusion of standing subjects with effective human weights for modeling dismounted Service Members
- More female specimens, a large enough age range to cover younger Service Members, and a statistically significant sample size
- More studies of soft tissue injuries, especially those that develop novel methods of modeling them, as soft tissue injuries may be better predictors of long-term outcome than bone fracture
- Experimentally validated lower extremity finite element models that can be used to accurately predict fracture patterns and locations, as well as the blast injury loads and blast loading rates.

It is important to note that current research is addressing some of the gaps and shortcomings. For example, the Warrior Injury Assessment Manikin (WIAMan) project will produce scientifically valid injury criteria for lower extremities (and other skeletal regions) for mounted Service Members who are subjected to accelerative loading caused by underbody blast.

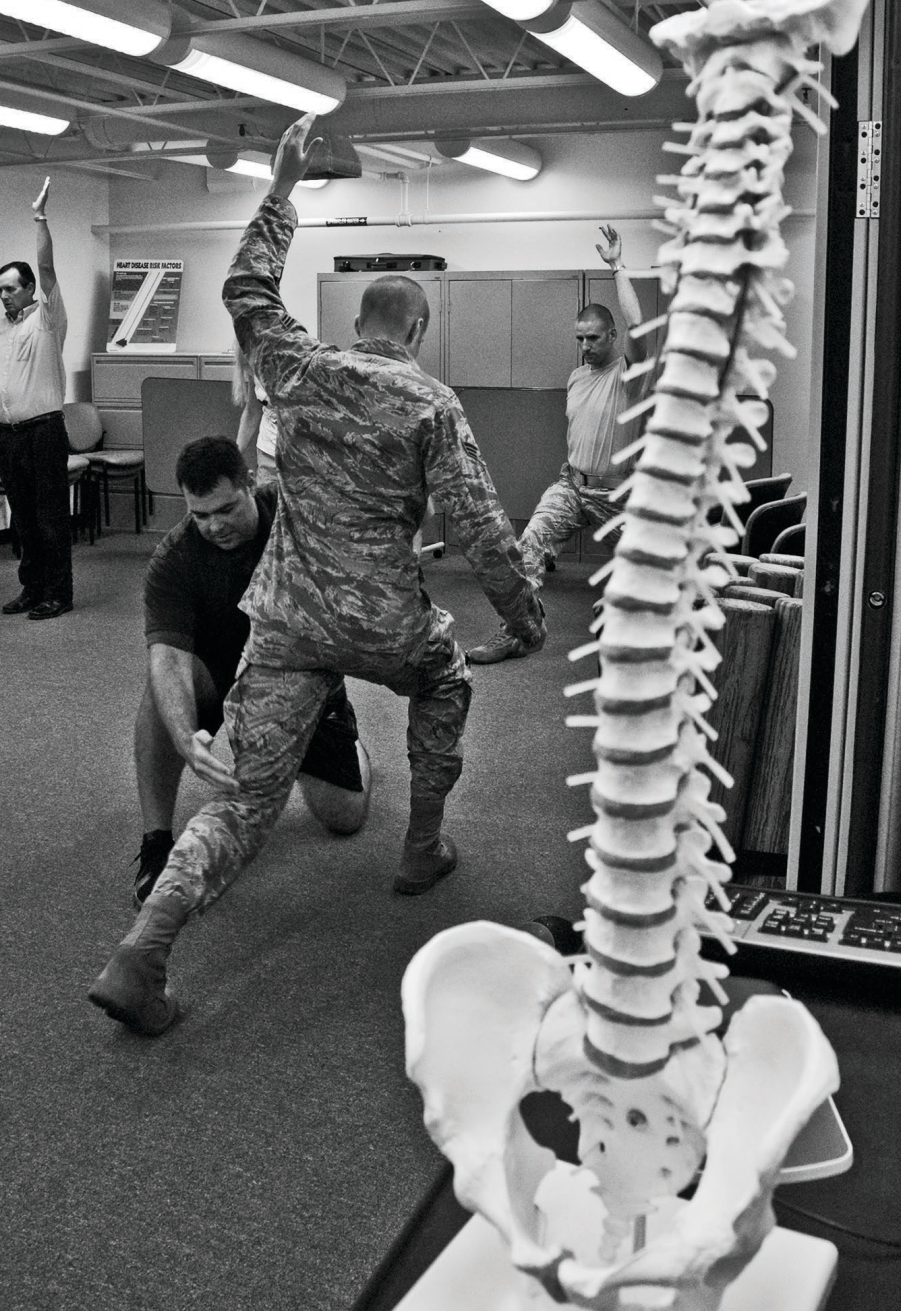


Photo credit: Randy Gon/US Air Force

Implementation of the BIPSR Process for Spine and Back Blast Injury Type

The spine and back blast injury type evaluation was initiated by the PCO following the January 2015 BIPSR Process stakeholder meeting. In FY15, following the initial steps of the BIPSR Process, the PCO evaluated the existing capabilities of the spine and back blast injury type through a literature survey, and by collecting information from a RFI on Federal Business Opportunities (FedBizOpps) and interviews of four SMEs from industry, academia, and government agencies. Through these activities, the PCO identified several standards for spine and back blast injury that are widely used in the automotive and aviation industries. The first Spine and Back Focused Stakeholder Committee meeting was held in June 2015 and was attended by nine Spine and Back Focused Stakeholder Committee members. Individuals represented the USAF, US Army, US Marine Corps (USMC), and US Navy and had interests spanning operations, medical, materiel development, and test and evaluation. At the meeting, the PCO presented the results of the initial existing capabilities review.

After the first Spine and Back Focused Stakeholder Committee meeting, the PCO initiated one-on-one interviews with stakeholders to gather requirements for a spine and back blast injury prevention standard. Ten stakeholders representing the RDT&E, medical, and operational communities completed the interview process. The PCO compiled the information gathered during the interviews and documented the requirement topics, followed by an initial analysis comparing stakeholder requirements against the existing capabilities that were discovered though the research activities, RFI submissions, SME interviews, and stakeholder feedback.

Next Steps

Having completed the initial analysis, the PCO will present their findings and recommendations in the second Spine and Back Focused Stakeholder Committee meeting, planned for early 2016. This meeting will review specifics of the stakeholder requirements interviews, details of the analysis process, and findings. Potential outcomes of this meeting include concurrence of analysis findings and recommendations, and recommendation of additional literature review or further investigation into existing standards.

Implementation of the BIPSR Process for the Upper Extremity Blast Injury Type

The upper extremity blast injury type began its BIPSR Process evaluation in FY15. Following the initial steps of the BIPSR Process, the PCO evaluated the existing capabilities of the upper extremity blast injury type through a literature survey, and by collecting information obtained by submissions following an RFI posted on FedBizOpps and interviews of six SMEs from industry, academia, and government agencies. The upper extremity findings for these activities included blast injury criteria of several different forms including force-at-failure values, numerical simulations of the upper extremity and upper extremity blast injuries, injury risk functions, injury risk thresholds, and findings on the validity of upper extremity anthropomorphic test devices (ATD).

The first meeting of the Upper Extremity Focused Stakeholder Committee took place in August 2015. The PCO presented the findings to date, including the two responses to the RFI, which included information related to impact and penetrating blast injury to the upper extremity. Following this first stakeholder committee meeting, the PCO interviewed additional SMEs, and initiated the interviews for stakeholder requirements for an upper extremity blast injury prevention standard.

Next Steps

Following the conclusion of the initial stakeholder interviews, the PCO plans to analyze the alignment between the stakeholder requirements and the existing capabilities discovered for the upper extremity blast injury type. The PCO anticipates presenting their findings, along with recommendations stemming from the analysis, at the second Upper Extremity Focused Stakeholder Committee meeting, which is being planned for Spring 2016. Potential outcomes of this meeting include concurrence of the analysis, findings, and recommendations, or recommendation of additional literature review and further investigation into existing standards.

Implementation of the BIPSR Process for the Auditory Blast Injury Type

At the January 2015 BIPSR Process Stakeholder meeting, the stakeholders elected to prove out the iBIPSR capability using the auditory blast injury type, as recommended by the PCO. As a result, the PCO has initiated the BIPSR Process for the auditory blast injury type. In accordance with the initial BIPSR Process step of reviewing existing capabilities, the PCO initiated a literature survey and is in the process of interviewing auditory blast injury SMEs from industry, academia, and government agencies, and an RFI was published on FedBizOpps. The literature search and discussion with SMEs so far has resulted in the identification of several auditory blast injury candidate standards. Benefits and limitations of each candidate standard for prevention of auditory blast injury are being examined. The team has populated the iBIPSR capability website with all the information gained from the initial capabilities review for auditory blast injury. The PCO is planning to implement the iBIPSR capability with the Auditory Focused Stakeholder Committee members at the upcoming meeting, planned for early 2016. The PCO is anticipating that the real-time access to citations, SME interview notes, and details of the RFI responses through the iBIPSR site will enhance information sharing and provide a collaborative, continuous-engagement environment for the stakeholders. In addition, access to real-time, ongoing discussion among stakeholders will provide the PCO with dynamic, valuable information as the team progresses through the evaluation of the auditory blast injury type. This broad engagement and collaboration throughout the BIPSR Process evaluation is anticipated to support both quality outcomes and the accelerated timeline.

KEY ACCOMPLISHMENTS

- Refined and improved the BIPSR Process through business process modeling; simulation of the process led to identification and implementation of improvements to the BIPSR Process which are expected to accelerate the completion date of all blast injury types
- Completed the BIPSR Process for the lower extremity blast injury type
- Initiated the spine and back blast injury type
- Initiated the upper extremity blast injury type
- Initiated the auditory blast injury type to prove out the iBIPSR capability

Next Steps

The first Auditory Focused Stakeholder Committee meeting is being planned for January 2016. At that time, the PCO plans to introduce the Auditory Focused Stakeholder Committee to the iBIPSR site and orient them to their role as part of the iterative refinement and development process for the iBIPSR capability. Feedback obtained will help shape features and capabilities, and will support development of a robust, user-friendly product. Following this first meeting, the PCO plans to engage the Focused Stakeholder Committee members in one-on-one interviews to generate requirements for an auditory blast injury prevention standard. After requirements collection, the PCO plans to analyze the initial capabilities review and requirements, and then present their draft findings and recommendations to the Auditory Focused Stakeholder Committee members at the next meeting.

Way Forward

In the coming year, the PCO plans to focus on finalizing the recommendations for the spine and back blast injury type and the upper extremity blast injury type, as well as proving out the iBIPSR capability for the auditory blast injury type. The PCO also plans to engage with BIPSR Process Stakeholders to ensure that the prioritization of the remaining blast injury types is aligned with the current needs of the DoD, and plans to initiate subsequent priority blast injury types as those currently under evaluation are concluded. Knowledge and technical gaps in the science identified by the BIPSR Process for completed blast injury types will be shared with the DoD research community to inform future blast injury prevention standards research.

The PCO anticipates moving forward with enhanced capability created by the increased use of the iBIPSR website, expanding participation following the pilot enrollment period. Ultimately, the recommendations developed through the BIPSR Process will better enable the DoD to apply the best available and scientifically sound standards aimed at protecting US Service Members from the entire spectrum of blast injuries.

Photo credit (opposite page): Staff Sergeant Robert Barnett/US Air Force

CHAPTER 5:

EXTREMITY TRAUMA AND AMPUTATION CENTER OF EXCELLENCE

Extremity injuries are the leading combat injury. Survivability from these complex wounds increased during recent conflicts due to the protection afforded by improved body armor; changes to combat tactics, techniques, and procedures (TTP); and systematic improvements in medical response to battlefield polytrauma[5]. Figure 5-1 reflects key conflict outcomes and compares them with earlier conflicts, beginning with the Civil War. Service Members suffering amputated and traumatic limb injuries in the US Central Command (CENTCOM) area of responsibility (AOR) had increased survival rates. These severely injured Wounded Warriors represent new and significant medical, surgical, and rehabilitation challenges.

FIGURE 5-1: Trends in amputee survival and prosthetic development

Civil War
21,000 amputations
Prosthetic development
Reintegration efforts

WWII
Approximately 15,000 amputations
5 US Army amputee centers
Multidisciplinary team
Inability to create prosthetics for young, active patients

OEF/OIF/OND
1,687 Service Members with amputations
Marked increase in multiple limb amputations
Higher survival rates with increased injury severity
Increased return to duty
Tremendous prosthetic advances

WWI
Over 4,000 amputations
Prosthetic manufacture in military hospitals
Rehabilitation and reintegration

Vietnam
Approximately 5,000 amputations
Improved surgical and rehabilitation techniques
Some prosthetic advances
Higher survival rates

Photo Credits: National Library of Medicine, US Army, US Air Force.

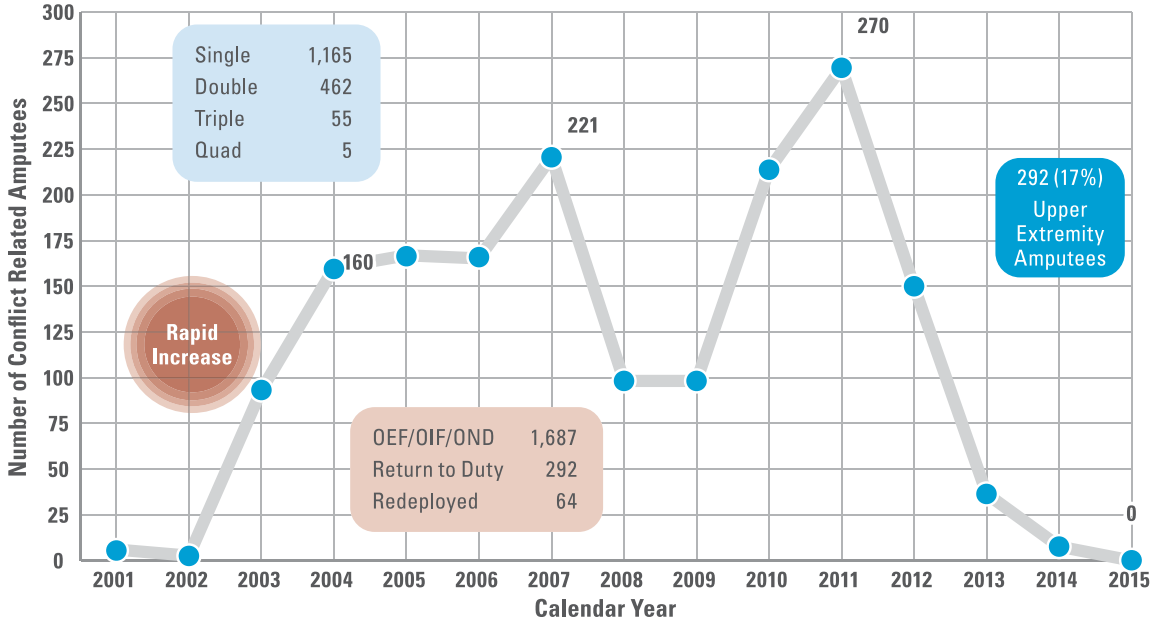
The predominant weapon employed during recent conflicts against US Services has been the IED.[6] Over ninety percent of combat-related amputees from 2001 to date are the result of IEDs and other types of blast injuries.[7] The enemy has used these simple, yet potent, devices throughout the CENTCOM AOR, often with overwhelming effect. Recent analysis of injuries in Afghanistan, where dismounted forces are deployed most often, demonstrates the dismounted Service Member in particular is at greater risk for severe, complex extremity injury and multiple amputations due to the effects of blasts.[8]

Blast wounds have a high infection rate, with extensive soft tissue damage, volumetric muscle loss, nerve damage, and complex scarring. Blast-related extremity injuries result in significant damage and often multiple amputations. Additionally, combat casualties from blast present with a host of complex comorbidities such as: multiple fractures/amputations, genitourinary injuries, traumatic brain and spinal cord injury (SCI), visual and hearing impairment, and psychosocial issues.[9]

As of 1 October 2015, 1,687 Wounded Warriors from OEF, OIF, and OND sustained traumatic or delayed amputation of one or more limbs, as depicted in Figure 5-2.[10] Approximately 13,000 Service Members sustained combat-related extremity trauma requiring care at a Role 3 military treatment facility.

Photo credit (opposite page): Technical Sergeant John Hughel/US Air National Guard)

FIGURE 5-2: Incidence of Service Members with traumatic or delayed amputation of one or more limbs



Data Source: EACE-R Amputee Database, 1 Oct 2015, including partial foot and hand amputations but excludes finger(s), thumb(s), and toe(s) amputations.

Extremity trauma injuries accounted for 70 percent of these total battle injuries from 2003 to 2015 (Figure 5-3).[11] Despite the development and use of advanced medical and surgical strategies, the severity of the injuries of many of these Wounded Warriors resulted in devastating and permanent loss of, or loss of function in, one or more limbs.

Management of Wounded Warriors with amputations or complex extremity injuries requires a comprehensive, coordinated, and multidisciplinary healthcare team throughout the continuum of care. This healthcare team provides the latest practices in medical/surgical interventions, prosthetic and orthotic technology, and rehabilitation management to enable injured Service Members to reach their highest level of function. This care, primarily provided at one of the three DoD Advanced Rehabilitation Centers (ARC), was developed during the recent conflicts to address the need for advanced, complex patient care and lengthy, complex rehabilitation (Figure 5-4). Initial response led to the US Army Amputee Care Program being organized at Walter Reed Army Medical Center (now the Walter Reed National Military Medical Center [WRNMMC]) in 2003. This formalized system of specialized care and its processes for amputation care, management, and transition are best defined in *The Care of the Combat Amputee, Textbooks of Military Medicine,* published in 2009 by the Borden Institute.[12]

Similarly, the VA enhanced their capabilities through development of its Polytrauma System of Care (PSC), an integrated network of specialized rehabilitation programs dedicated to serving Veterans and Service Members with both combat and civilian related TBI and polytrauma injuries, including limb loss.

FIGURE 5-3: Comparison of extremity battle injuries and all other battle injuries

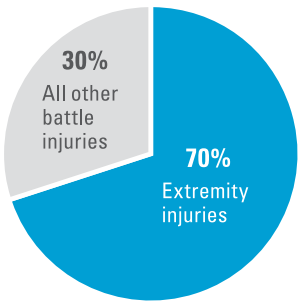


FIGURE 5-4: DoD Advanced Rehabilitation Centers; these centers address the need for advanced, complex patient care and lengthy, complex rehabilitation.

Military Advanced Training Center, Walter Reed National Military Medical Center
(Photo credit: Fred W. Baker III/DoD)

Center for the Intrepid, San Antonio Military Medical Center
(Photo credit: US Army)

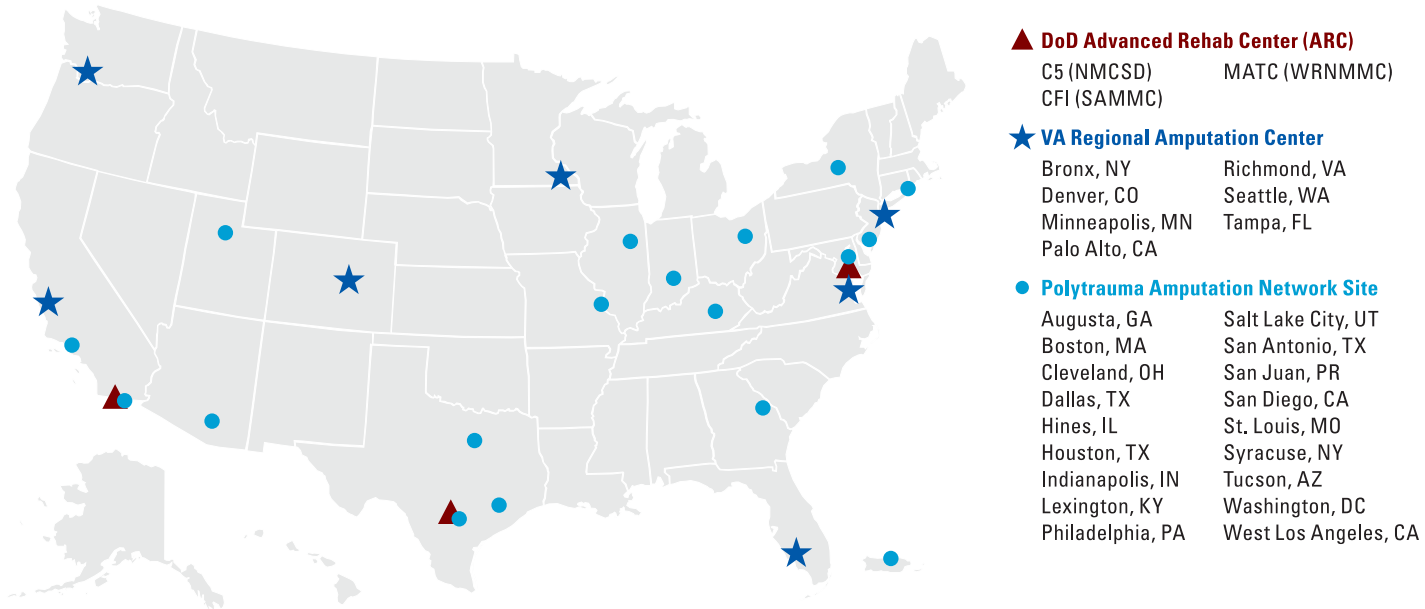
Comprehensive Combat and Complex Casualty Care Program, Naval Medical Center San Diego
(Photo credit: Mass Communication Specialist Third Class Jake Berenguer/US Navy)

In 2008, the VA expanded their efforts in amputation care, building upon the PSC with seven Regional Amputation Centers, 18 Polytrauma Amputation Network Sites, and 108 Amputation Care Teams making up the newly formed VA Amputation System of Care (ASoC). The ARCs, PSC, and the ASoC provide interdisciplinary evaluation and treatment, development of a comprehensive plan of care, case management, patient and family education and training, psychosocial support, and application of advanced rehabilitation treatments and prosthetic technologies.

Figure 5-5 depicts the major sites for federal amputee care. The DoD ARCs, VA Regional Amputation Centers, and VA polytrauma Amputation Network Sites are all identified on this map. The enduring mission to provide lifelong amputation care is shared between DoD and VA.

With persistent conflict and increased demand, efforts to care for the combat wounded expanded. The need for innovative new technologies and treatment strategies to assist in complex rehabilitation grew exponentially.

FIGURE 5-5: DoD and VA sites for federal amputee care



Existing programs, led by DoD's CDMRP and the Veterans Health Administration (VHA) Office of Rehabilitation Research and Development, broadened their research focus to include TBI, sensory loss, amputation, and polytrauma following blast injury, as well as the development of advanced prosthetics. DoD established the CDMRP in 2008 to further leverage and continue supporting efforts initiated by Congressional special interest. Multiple partnerships and collaborations across federal agencies, academia, and industry were created to expand research and address clinical gaps. Examples of such efforts include the Armed Forces Institute of Regenerative Medicine (AFIRM) and the Bridging Advanced Developments for Exceptional Rehabilitation (BADER) Consortium. Leveraging advanced technology, the DARPA Revolutionizing Prosthetics program addressed the development shortfall for advanced upper limb prosthetic technology.

DoD and VA research programs grew and strengthened clinical ties with the three DoD ARCs and VA polytrauma and amputation care facilities, to better identify research gaps, conduct research, and assess technological solutions. To advance the functional ability and quality of life of injured Service Members and Veterans, the DoD and VA targeted clinical and research collaboration at the point of care, which provided a means to develop knowledge and material products. This unique collaboration led to better limb reconstruction, more comprehensive rehabilitation, and cutting edge care. Additionally, it led Congress to direct joint DoD/VA establishment of a shared CoE, the EACE, which provides leadership, promulgates best practices, conducts research, and provides support and/or training for extremity trauma and amputation patients, their clinical care team, and the entire joint system of care.

The EACE

The increasing number of Service Members with devastating extremity trauma; the advances in, and expansion of, services and technologies; and the significant research efforts within the VA and DoD, drove the need for a comprehensive plan and strategy to advance all efforts for the mitigation, treatment, and rehabilitation of traumatic extremity injuries and amputations. In 2009, Congress enacted the establishment of the EACE, recognizing that DoD and VA share responsibility for the care of the nation's Service Members and Veterans. The EACE is the only Congressionally-mandated CoE that is jointly established between the DoD and VA. This joint organizational structure is designed to foster unprecedented collaboration and creates outstanding coordination for the benefit of wounded Service Members and Veterans. Governance is jointly provided by the Army Surgeon General as the DoD lead component and the VHA's Prosthetic and Sensory Aids Service on behalf of the VA. The EACE is the critical leadership hub for vetting new ideas, synchronizing competing interests, eliminating research redundancies, standardizing evidence-based practices, and deploying clinical recommendations. These imperatives, synchronized between the two departments, lead toward optimizing the quality of life for Service Members and Veterans throughout their lifetime.

The EACE provides DoD and VA the ability to collectively advance scientific knowledge and publish evidence-based practices. Collaborative efforts ensure a singular focus on mitigating disability, maximizing treatment, and optimizing rehabilitation for the nation's heroes. Research related to traumatic extremity injuries and amputations is now accomplished across DoD-VA multidisciplinary healthcare networks creating synergy across the continuum of care. The EACE provides a focal point for leadership to build on existing expertise to advance capabilities developed over the past 13 years. The EACE will help to retain these advances, set the course for future research, standardize clinical care advances, and ultimately increase readiness for the next conflict, when it comes.

EACE Lines of Effort

The EACE is composed of 41 general schedule (37 DoD and four VA) staff members, structured in five lines of effort: Clinical Care, Research and Surveillance, Clinical Informatics and Technology, Global Outreach, and Leadership, which is fostered at every level. The EACE lines of effort are focused on the following: improving clinical care for amputation and extremity trauma patients, conducting clinically relevant research, developing a health registry for extremity trauma and amputation tracking, and assisting foreign military partners in the care of their severely injured Service Members (Figure 5-6). EACE leaders and staff facilitate recurring DoD and VA collaboration, execute strategic planning functions, and create strategies that ensure success for all eligible patients and the system of care.

Clinical Affairs

The EACE Clinical Affairs staff is involved in the assessment and advisement for clinical care across the DoD and VA. The staff goal is to assist clinicians with guidelines and recommendations, education and training, and translation of current research into clinical practice. This line of effort is focused on developing strategies to improve collaboration, optimize system efficiencies, and enhance the continuum of care across the two federal healthcare systems. Education and training is an essential subset for this line of effort, as is a specific focus on prosthetic and orthotic support to the EACE population of interest. Clinical Affairs has ongoing efforts to facilitate improvement of clinical capabilities in DoD and VA extremity trauma and amputation care, such as the Rehabilitation of the Lower Limb Amputation and Management of Upper Extremity Amputation Rehabilitation CPGs.[13] The goals of these CPGs parallel those of the EACE Clinical Affairs program: reduce practice variance; enhance the standard of care; accelerate research translation into clinical practice; and improve health, quality of life, and patient satisfaction.

Prior to the formation of the EACE, DoD and VA clinical experts joined to develop the Rehabilitation of the Lower Limb Amputation CPG. Published in 2008, this CPG is scheduled for updating in FY16 by DoD and VA SMEs. The updated Lower Limb Amputation CPG will address potential gaps in blast injury management in the extremity trauma and amputation population, which will preserve lessons learned from recent conflicts. Seventeen percent of the combat related limb loss patients cared for within the ARCs involved the upper limb(s), compared to approximately three percent of the US limb loss population. Providers within DoD and VA noted variation in rehabilitative care, with inconsistent levels of expertise across disciplines. To address this, the EACE obtained authorization in FY12 for a DoD-VA Upper Extremity Amputation Rehabilitation CPG. This CPG, which specifically targeted rehabilitation of the upper limb amputation patient population, was completed and published for national and international utilization in November 2014 and can be accessed at: http://www.healthquality.va.gov/guidelines/Rehab/UEAR/.

The EACE recognized that clinical competencies in amputation care will degrade with the reduction in the number of new combat-wounded amputees.

FIGURE 5-6: EACE five lines of effort, focused on improving care, conducting research, registry development, and assisting foreign military partners in the care of their Service Members

Therefore, it is essential that these highly developed competencies, gained in over a decade of war, are defined, periodically updated, tracked, and reported.

In FY15, the EACE initiated an 18-month study to be conducted by the RAND Corporation for a formal compilation of core competencies for amputation care and rehabilitation. The study will identify, within the DoD, which services and clinical skills are integral to optimal amputation care. Identifying the requisite skills and knowledge will guide clinical training for both the DoD and VA. Should the DoD need to expand amputation care capability in the future, the documentation of requisite core competencies for amputation care will facilitate the preservation of exceptional levels of care for future incidents of traumatic limb loss.

The EACE is also developing knowledge products to sustain and enhance the lessons learned over the course of the current conflicts. Several current efforts were adapted from existing programs, to include in-person skills training known as the Federal Advanced Amputation Skills Training (FAAST) Symposium, Amputation Care Virtual Grand Rounds, and the Federal Amputation Care Interest Group. The exchange of knowledge across the federal healthcare systems regularly assists providers with updating their clinical practice.

The annual FAAST Symposium is co-sponsored by the EACE and VA ASoC and supported by the VA Employee Education System. The FAAST Symposium fosters interaction and knowledge sharing between DoD and VA clinicians and researchers. Attendees practice novel clinical skills to immediately use in their clinics and receive education on evolving, state-of-the-art clinical topics such as:

- **Independent Living with Assistive Technology:** Computer access and physical home modifications improve quality of life and are necessary tools in the rehabilitation of Service Members and Veterans with limb amputations.
- **Use of 3D Printing in Rehabilitation:** Rapid 3D printing prototyping is currently being used at WRNMMC. This cutting-edge capability is rendering new applications for wounded Service Members and Veterans in custom prosthetic design as well as surgical interventions.
- **Blood Flow Restricted Strength Training in Rehabilitation:** The Center for the Intrepid, Brooke Army Medical Center, is leading DoD research into clinical applications for blood flow restricted exercise in rehabilitation. Hands-on demonstration of the technique using lower loads during strengthening helped providers become familiar with the theory of achieving equal or greater gains than typical exercise allows.

The EACE partners with the VA ASoC to deliver bi-monthly Amputation Care Virtual Grand Rounds presentations to provide medical education for DoD and VA clinicians on relevant topics (Table 5-1).

TABLE 5-1: FY15 Grand Rounds Topics

Complication Management of the Persistently Symptomatic Patient with Limb Loss
Phantom Limb Pain: Theories and Therapies
Approach to Low Back Pain in Service Members and Veterans with Lower Extremity Amputations
Standardizing Outcome Measurement for Amputation Care
Complex Wound Care of Blast Injuries and Amputations
Extremity Trauma and Advancement of Osseointegrated Implants for Amputees in the VA System

The presentations are available for digital replay by those clinicians who are unable to attend the live session.

The EACE continues to promote training on highly advanced prosthetic technologies, such as advanced microprocessor powered knees and ankle prostheses. This ensures providers have the greatest range of tools and the very best technologies to optimize patient independence, maximize physical ability, and enhance quality of life.

The Advanced Orthotics Initiative is a comprehensive translational project initiative providing advanced, hands-on training. The program trained VA's senior orthotists to fabricate and fit advanced lower extremity orthoses, including the Intrepid Dynamic Exoskeleton Orthosis, which was developed at the Center for the Intrepid, Brooke Army Medical Center (Figure 5-7). Driving this training requirement was the significant number of Service Members and Veterans with functional loss following lower limb trauma that often followed limb saving procedures. Advanced orthotics leverage technology and provide great benefit to the population of extremity trauma patients.

Transplantation research is supported by DoD funding and the EACE assisted in policy development regarding transplantation for Service Members and Veterans with upper limb loss. One OIF Veteran who sustained loss of all four limbs received bilateral upper extremity transplants in December 2012. Ongoing coordination between the DoD and VA has been essential to ensure that this Veteran achieved the highest function and is receiving lifelong patient-centered care.

The VA and DoD continue development of a streamlined process for acquisition of lower extremity prosthetic components through partnership with the VA Denver Acquisition and Logistics Center. A centralized, depot-level, e-commerce purchasing initiative is in development to allow VA clinicians and authorized DoD clinicians to order prosthetic components through the Denver Acquisition and Logistics Center Remote Order Entry System. While VA is leading this effort, the EACE gained approval for a DoD "proof of concept" assisted acquisition led by NMCSD. This effort aims to simplify prosthetic procurement, reduce delivery times, decrease costs, and ultimately provide improved care for DoD and VA patients. The joint e-commerce project is anticipated to begin in FY16. If the initiative proves successful, DoD will work to expand the pilot program to additional locations.

FIGURE 5-7: Example of the Intrepid Dynamic Exoskeletal Orthosis

Photo credit: Meghan Portillo/US Army

Research and Surveillance

Over sixty percent of the EACE personnel (26 total) are in the Research and Surveillance Division. The EACE made a conscious organizational design decision to embed research staff at the point of care, to be colocated with clinicians and patients. The research staff configuration is based on a talent management model and is a blend of clinician and non-clinician researchers.

EACE researchers collaborate with clinicians to design and implement research studies aimed at addressing clinical gaps, priorities, and goals within the specific extremity trauma and amputation population. On-site collaboration between providers, patients, and researchers facilitates enhanced patient care, clinical training, and translational research. This configuration emphasizes development of timely and relevant key research initiatives in direct support of evolving clinical care goals. As scientific SMEs, EACE researchers are available as a resource to support healthcare staff through protocol development, data collection, data analysis, and knowledge dissemination.

EACE researchers have been successful in using funding to execute research from organizations like the BADER Consortium, Center for Rehabilitation Science Research, TATRC, USMRMC, ONR, BUMED, and NIH. Research and Surveillance Division leadership are also active participants in the JPCs. Key experts in the JPCs work through coordinated efforts to translate guidance into research and development needs. They also have key responsibilities for making funding recommendations and providing program management support.

The current clinical goals and research initiatives aligned with clinical and rehabilitation medicine gaps are depicted in Table 5-2.

Novel Rehabilitation Interventional Research

The area of novel rehabilitation interventional research is based within DoD and VA established programs aimed at: optimizing gait patterns for patients with amputations (Figure 5-8); safely returning patients to running, jumping, and agility activities following limb reconstruction; safely returning patients with amputation to high-level athletic activities; preventing and managing secondary health effects that can develop after primary neuromusculoskeletal injury; defining optimal treatment strategies and sequencing of progression throughout the rehabilitation process; and facilitating optimal reintegration into military or civilian communities. Findings from EACE research suggest that for high functioning Service Members with transtibial amputation, decreasing the metabolic demand of level surface walking may not be as imperative as previously thought.[14] Metabolic demand of higher-level activities in complex environments may be more advantageous to this population. This is the first study to report equivalent metabolic demand between Service Members with amputation and non-amputees. These results reflect the greater physical fitness of young Service Members with traumatic amputations and may serve to better guide outcome expectations in future clinical practice. However, further study is required to determine extrapolation to a larger population.

FIGURE 5-8: Service Members with amputations participate in extensive gait training to use their advanced prostheses

Photo credit: Terri Moon Cronk/DoD

TABLE 5-2: EACE current clinical goals and research initiatives aligned with clinical and rehabilitation medicine gaps

Clinical Goal	Key Research Initiative
Safely return patients with amputation to high-level athletic activities	Develop guidelines for safely returning amputee patients to high-level athletic/ sporting activities
Return patients to running, jumping, and agility activities following limb reconstruction	Provide alternatives to limb amputation by returning patients to running, jumping, and agility activities following limb reconstruction
Optimize gait patterns in patients with amputation	Optimize gait in patients with amputation with the goal to: decrease fall risk, improve endurance, prevent low back pain, and prevent osteoarthritis and other joint overuse conditions
Decrease pain in patients with amputation	Identify medical and therapeutic interventions that decrease phantom limb pain (PLP) in patients with amputation
Provide prosthetic solutions that encourage prosthetic use and improve function for patients with amputation	Assess advanced prosthetic technologies to determine efficacy within environments that include: 1) stairs, slopes, and uneven terrain; 2) running and other high-impact activities; 3) moisture, dust, limited ability to recharge device frequently Assess advanced prosthetic technologies to determine efficacy in improving upper extremity function and user satisfaction
Prevent and treat secondary health effects that can develop after primary neuromusculoskeletal injury	Identify medical and surgical interventions that decrease the occurrence of heterotopic ossification following amputation Assess medical and therapeutic interventions to enhance healing, decrease pain, and improve function for patients with posttraumatic osteoarthritis Identify prevention and treatment interventions that minimize risk for fragility fracture and other musculoskeletal overuse injuries Identify prevention and treatment interventions for health-related diseases associated with complex neuromusculoskeletal injury (i.e., cardiovascular disease, obesity) Identify prevention and treatment interventions for low back pain associated with neuromusculoskeletal injury
Define optimal treatment strategies and sequence of progression throughout the rehabilitation process	Determine the optimal combination, dose, and timing of rehabilitative techniques to minimize impairments
Implement standardized health and functional outcome assessments across the DoD and VA	Develop a health and functional outcome assessment toolkit that can be used to standardize short and long term outcomes measurements across the DoD and VA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Additional findings from EACE research suggest that transtibial amputees are at greater risk for falls when physically disrupted and are more likely to rely on their intact limb to maintain stability.[15] Gait training that integrates physical disruptions may help to prevent falls and lessen demand on the intact limb. This finding was translated into clinical rehabilitation treatment and gait training and will be included in the upcoming update to the CPG for the Rehabilitation of Lower Limb Amputation, which will be available at: http://www.healthquality.va.gov/amputation/amp_sum_508.pdf.

Advanced Prosthetic and Orthotic Technologies

Following the physical or functional loss of limbs, such as from a blast injury, Service Members and Veterans are often reliant on prosthetic and orthotic devices to return to activities of daily living, recreation, and occupation. The need to provide quality assistive devices to Service Members and Veterans is paramount, with prescription, fabrication, and fitting often conducted at the DoD ARCs and VA facilities. Therefore, EACE researchers are engaged in the study of advanced prosthetic/orthotic technologies with federal, academic, and industry partners. Advances in technology have led to the availability of novel devices, such as improved microprocessor-controlled prostheses, active power-producing prostheses, myoelectric-controlled prostheses, and exoskeletal orthoses.[16, 17, 18, 19]

Numerous studies are underway to test novel prosthetic and orthotic devices, as well as to optimize existing technologies. Additionally, studies are ongoing to determine optimal criteria for prosthetic and orthotic prescriptions individualized to the patient's goals. The underlying intent of these investigations is to determine if the technologies provide benefit to patient function across a variety of activities, including level-ground gait, slope, and stair ambulation, walking during destabilizing conditions, transitions from standing, and common activities of daily living. Combined, this research is aimed at maximizing the probability of optimizing outcomes through technology utilization and avoiding device abandonment.

Epidemiology

The EACE Research and Surveillance Division initiated a new epidemiologic research program in FY15 to comprehensively describe characteristics of the limb loss population. This area of research is necessary to longitudinally track long-term health outcomes and the impact of interventions that in turn support evidence-based clinical decision making. The epidemiologic research program uses existing data to conduct population-level research with the goal of decreasing morbidity and mortality while maximizing health and quality of life outcomes for patients with amputation.

In addition to studying the amputee population, significant efforts are ongoing to describe the population of wounded Service Members who sustained extremity trauma with permanent functional loss not resulting in amputation. The EACE epidemiology team is working to define this population, develop and validate a medical code algorithm, and identify prospective data on health outcomes of this group. Current epidemiology projects within these populations include:

- **Incidence and risk of long-term adverse health outcomes:** Study aims to identify significant independent risk and protective factors for various secondary health effect outcomes.
- **Factors associated with early return to duty:** Developing models that identify independent contribution of various characteristics (individual and rehabilitative) associated with successful return to duty after amputation.
- **Military outpatient and inpatient healthcare costs:** Epidemiological and economic analyses to quantify and estimate direct and indirect costs of inpatient and outpatient amputee care.

Photo credit (opposite page): Sergeant Ray Lewis/US Marine Corps

Photo credit: EJ Hersom/DoD

Instrumental to the aforementioned epidemiological efforts, EACE researchers are leveraging the Wounded Warrior Recovery Project (WWRP) based at NHRC. This project is an existing DoD-sponsored longitudinal biannual survey that assesses a myriad of outcomes, to include quality of life of injured Service Members. While in its infancy, it has the potential to impact the full spectrum of healthcare delivery to limb loss patients and to influence medical policy decision making.

Medical and Surgical Innovations

With its investment in personnel and assets, the EACE is building a capability to conduct research in medical/surgical innovations. This expansion of EACE research builds upon ongoing research efforts at WRNMMC and the USUHS in the area of regenerative medicine. For example, within the area of regenerative medicine/tissue engineering, efforts are ongoing to investigate effectiveness of next-generation therapeutics (e.g., biologic scaffold materials) to support enhanced tissue reconstruction following injury. In addition, efforts are ongoing to develop novel surgical care algorithms aimed at achieving stable, definitive wound coverage.[20]

Future areas of interest for EACE investigation or collaboration may include:

- Implantable myoelectric sensors
- Neural prostheses
- Regenerative medicine/tissue engineering
- Targeted muscle reinnervation
- Osseointegration
- Vascularized composite allotransplantation (e.g., limb transplant).

Clinical Informatics and Technology

The EACE is currently leading the MHS efforts to build a highly integrated registry to help track the extremity trauma and amputation population. In 2015, the MHS Clinical Management Portfolio Board approved the activation of an Integrated Project Team to develop the Defense and Veterans Extremity Trauma and Amputation Registry (DVEAR) functional requirements. The DVEAR will manage data and information reporting throughout DoD and will be designed for sharing of data between VA and DoD. The DVEAR will be a vital tool to capture and quantify the key demographic, socio-economic, and polymorbid characteristics of Service Members and Veterans affected by traumatic extremity injury and amputation. This is a known capability gap and this function is needed to support improved treatment strategies and mitigation of long-term disability. Functional limb loss and amputation data—from point of injury (POI) through lifetime care—will inform and improve care across patient populations and federal agencies.

Global Outreach

The EACE Global Outreach Program strengthens international relationships using clinical expertise, educational opportunities, on-site visits, and facilitating care under the DoD Secretarial Designee Program. The EACE serves as a resource for nations who would like to enhance their extremity trauma and amputation care capability (Figure 5-9). The EACE's total asset visibility of DoD amputation care and close relationship with the three ARCs ensures coherent and integrated delivery of outreach support to US Combatant Commanders around the world. The EACE has consistently demonstrated the ability to effectively share expertise with the larger community of academia, foreign militaries, industry, and other healthcare organizations.

FIGURE 5-9: Nations relying on EACE as a resource for enhancement of their extremity and amputation capability

Outreach efforts in the US are focused on facilitating community-based rehabilitation through the promotion and delivery of adaptive sports. One example is the 4th Annual "Heroes on the Hudson" adaptive maritime sports clinic in New York City, which was directed by EACE staff. More than one-third of the participants were New York area Veterans that are living with limb loss and received a full-day rehabilitation experience in their local community.

Leadership

The leadership of the EACE is fully engaged in developing collaborations at many levels to enhance Service Member care and support. The EACE reached full operating capability in 2014 and is currently able to meet its mandate to strategically plan to mitigate, treat, and rehabilitate extremity trauma and amputation patients.

The VA, DoD and the EACE must continue to prioritize the health of our Service Members and Veterans, providing amputee care that is dynamic, multi-faceted, and lifelong. Both Departments now provide the highest quality of clinical care ever for Wounded Warriors and Veterans who sustained an amputation injury as a result of their service. This world-class level of clinical care is achieved through an outstanding network of collaborations led by the EACE and many others. Wounded Warriors who sustained blast injuries resulting in amputation, benefit from care delivered by an integrated clinical team comprised of many clinical disciplines all working together to address the needs of these complex patients. Additionally, there is tremendous synergy achieved from the colocation of researchers, prosthetists and on-site family support directly in the clinical setting. Because this intensive rehabilitative care results in rapid advancements in technology and care practices, this unique expertise must not be lost during times of peace, as has been the case historically.

To sustain and advance the current state of amputee care in the future, the DoD and VA must continue to provide adequate resources that support partnerships with academic, health care, and civilian organizations; ensure sufficient training and education opportunities for health care professionals; engage in research on the long-term needs of amputees to inform preventive health care programs; and maintain the focus on rapid, translational research initiatives, which result in the implementation of new technologies and rehabilitation methodologies in the clinical setting.

06

CHAPTER 6:

BLAST-RELATED OCULAR AND VISION INJURIES

The incidence of ocular injuries as a percentage of combat injuries has marched upward over the last 150 years, from 0.5 to 0.65 percent during the US Civil War and the preceding Crimean War, to two to three percent in World Wars I and II, and Korea, to six to nine percent in the Yom Kippur and Vietnam conflicts, and 13 percent in Desert Shield/Desert Storm.[21] Rates for OEF/OIF are cited as six to 19 percent.[22, 23, 24, 25] At one point, eye injuries accounted for 23 percent of all theater evacuations.[23] In contrast to peacetime eye injuries, many combat eye injuries are bilateral and occur frequently in association with other head and neck or systemic polytrauma.[22, 27, 28, 29] The personal and societal costs of eye injuries are intuitive and significant. In Vietnam, 30 to 50 percent of penetrating eye injuries resulted in enucleation—only 25 percent of casualties were able to return to active duty, in contrast with 83 percent of all others surviving injuries.[21] A recent study corroborates the high likelihood of military discharge following eye injury.[29]

Multiple factors account for the disproportionately high number of eye injuries given the overall size of the eye and its representative proportion of total body surface area (<0.1 percent): the required preferential exposure of the eye, head and neck in combat in order to see and fight; better body armor that allows a greater chance of surviving previously lethal truncal wounds compared to relatively limited eye armor; the unique susceptibility of the eye to severe injury by small fragments that, striking elsewhere, would otherwise cause relatively innocuous or limited damage; and the changing nature of armaments and preferred weapons in modern conflicts, thereby shaping different injury patterns.

Regarding this last factor, one cannot escape the pervasive attention and interest devoted to the IED, known as the "signature weapon" of OEF/OIF. Indeed, current ocular injury statistics add further evidence to the destructive impact of IEDs as the principal wounding agent, in contrast with small ballistic fragments and gunshot wound injuries of prior wars and from the early stages of this one. More than 70 percent of severe ocular injuries during OIF were caused by explosions, followed by ballistic injuries.[22, 23, 24, 30, 31, 32] The shift of weaponry in this war caught many military medical personnel off guard and unprepared for the scale and degree of corporeal devastation. It is also driving rapid reevaluation of and adjustments to medical care[33] and a call for increased research. Interestingly, however, when considering the fundamental mechanism of injury—high-energy explosives, such as artillery shells and landmines detonating in close proximity to ground personnel, accompanied by a large debris burden—many striking similarities are found in the literature of World War I. Medical preparations for that war also focused on the historically familiar small arms injury; medical personnel were largely unprepared for the never-before-seen level of destruction of the newly introduced high explosives; the siege warfare that quickly set in, coupled with the artillery's newfound capability of long-range indirect fire, created a novel (but now familiar) and poorly understood injury type, the blast casualty.[34, 35] This casualty forced a similarly rapid reevaluation of medical tenets and practice and increases in research. Not surprisingly, a more thorough reading of that literature reveals conspicuously similar injuries.

COSTS OF MILITARY EYE INJURY

"Based on published data from 2000 to 2010, the total cost to the economy of all [military] ocular injury and vision impairment related to TBI is $25.107 billion…The present value of the projected costs to the remainder of the economy over the remaining lifetimes of the Service Members with eye injuries or vision impairment due to TBI is $24.286 billion. This last cost is not to the federal government but to the economy and society as a whole."

Frick K.D., Costs of Military Eye Injury, Vision Impairment, and Related Blindness and Vision Dysfunction Associated with Traumatic Brain Injury (TBI) without Eye Injury, www.eyeresearch.org, May 2012

Photo credit (opposite page): Staff Sergeant Robert Barnett/US Air Force

Photo credit: Master Sergeant Cohen A.Young/US Air Force

With respect to ocular injuries, too, the writings of that long-ago war accurately describe—often in frighteningly contemporary detail—almost every ocular injury encountered in this most current one, including blast-related, penetrating and open globe injuries, concussive and closed globe injuries, and visual disturbances we now ascribe to primary blast effects and TBI (referred to then as "shell shock," a concussive phenomenon) and PTSD (referred to then, initially, as "war shock," a psychiatric phenomenon distinct from "shell shock").

Types of Blast Eye Injuries

Much has been written about blast and blast effects on the body, yet little formal research has been focused on blast effects to the eye and to vision. It stands to reason that many of the mechanisms that cause significant organ and tissue injury elsewhere can be expected to have the same or even more profound effects on the eye. The eye is actually part of the brain, but it is the only part of the central nervous system that is exposed to the outside environment and provides the majority sensory input to the brain. It should come as no surprise that eye injury and visual dysfunction are frequent consequences of blast exposure. Furthermore, considering that the eye is a complex, multilaminar structure with multiple tissue and fluid interfaces of varying densities, elasticities, and adherence characteristics, with sinus air cavities surrounding an inelastic bony confine, it should be expected that recognized blast injury mechanisms would have a significant effect on the eye and ocular adnexa as well, and that most ocular injuries involve ocular polytrauma (usually requiring multiple subspecialists for proper care). Mechanisms—such as differential hydrostatic pressures; complex additive-, subtractive-, and focused-wave patterns; spallation; compression; and rarefaction—shear, implosion, and inertial effects should all be expected to have injurious short-term and long-term effects on the organ. Moreover, precisely because the eye is brain tissue, with limited regenerative capacity, even "slight" or subclinical injury carries a high risk of permanent loss of function. It is, quite literally, a TBI of a different sort.

Since the introduction and widespread use of high-energy explosives in World War I, the effect of blast on the eye in combat has been noted, including, presumptively, primary blast effects without overt evidence of external anatomic damage. As De Schweinitz noted in 1919, "...absence of outward signs is not necessarily an indication of lack of intraocular lesions, and moreover of extensive ones."[36]

Similar observations were made of blast injuries in World War II[37, 38] and have been once more corroborated in OEF/OIF.[27, 39, 40] Considering the increasing number of domestic terrorist bombings as well as the ever-present specter of industrial explosions such as the fertilizer plant explosion in West, Texas in 2013[41] or the more distant Halifax explosion of 1917,[42] the civil implications are equally clear.

All categories of blast injuries, from primary to quinary, can affect the visual system, and the resulting trauma is usually a combination of several different mechanisms. Table 6-1 lists a number of representative ocular injuries associated with both high-energy and low-energy blasts. Note that while many injuries listed are overt and will typically affect vision immediately, many other injuries may be less dramatic or conspicuous and may cause less immediate visual impact (if at all). For this reason, they may therefore be overlooked or discounted. In these cases, vision may be only minimally or transiently affected, although the eye may have suffered significant internal damage, which may lead to delayed recognition and a long-term risk of vision loss from conditions such as traumatic glaucoma, retinal detachment, photoreceptor dysfunction, and progressive visual field loss.[43]

The primary blast shock wave is characterized by high pressure, elevated temperature, and density moving at supersonic speed. The concussive energy wave propagates through the body and causes damage to the tissues (particularly at interfaces of differing tissue densities), including hemorrhage, edema, vasoconstriction, and induction of apoptosis.[44] Computational studies of primary blast on the eye using finite element modeling reveal that pressure differentials across different ocular tissues combined with the orbit's pyramidal shape cause pressure wave reflection and amplification inside the eye such that all locations posterior to the vitreous base suffer pressures significantly higher than those seen at the cornea.[45]

TABLE 6-1: Examples of Blast Ocular Injuries

Primary Blast Injury (Blast Overpressure)
Nonpenetrating blunt ocular injuries
Intraocular/intraorbital hemorrhage (hyphema, vitreous hemorrhage, retrobulbar hemorrhage, orbital compartment syndrome)
Corneal endothelial damage
Angle recession/iridodialysis/cyclodialysis
Lens dislocation
Retinal/choroidal detachment
Commotio Retinae/choroidal rupture
Photoreceptor and retinal ganglion cell dysfunction
Optic nerve avulsion or dysfunction
Globe rupture
Secondary Blast Injury (Blast Wind and Debris)
Penetrating ocular injuries
Superficial/intraocular/intraorbital foreign bodies
Traumatic optic neuropathy
Lid/lacrimal/adnexal laceration or avulsion
Orbital hemorrhage
Corneal abrasion
Orbital fracture
Tertiary Blast Injury (Translocation, Crush)
Orbital fracture
Orbital hemorrhage
Tissue crush/laceration/avulsion injuries
Quaternary Blast Injury (Burn/Toxins)
Lid/ocular burn
Toxic optic neuropathies
Traumatic Brain Injury
Convergence insufficiency
Photophobia
Ocular dysmotility
Visual field defects
Eye tracking disorder
Pupillary dysfunction

This phenomenon can explain lesions, multiple choroidal ruptures, subconjuctival and subretinal bleeding, and optic atrophy observed after blast in the absence of contact with flying debris.[26, 46] Another computational study using numerical modeling showed that longer duration and lower amplitude pressure waves also caused severe deformation, stretching, and strain damage, which could result in a separation of layered tissues, such as the choroid and retina.[47] Additional factors, such as peak overpressure, pressure rise-time and decay, the distance from explosion, and the alignment of the eyes vis-à-vis the shock wave may influence blast effects on the eye and may explain why persons in close proximity to each other can receive injuries of varying severity. The complex nature of the interaction of the blast wave with the body and the difficulty in separating the effects of primary blast from other blast categories on the battlefield make computational simulation studies of the blast invaluable in understanding the mechanisms of injury and in developing proper protection.

Secondary blast effect is the most common mechanism of ocular injury.[22] Impact from debris and flying objects can cause both open and closed globe injuries. Open globe injuries such as globe rupture and penetrating or perforating injuries constitute more than 75 percent of all serious eye blast trauma. Such injuries from blast, in marked contradistinction to small arms ballistic fragments, are often irreparable and require enucleation or evisceration with resulting blindness in one or both eyes.[27, 48] Extensive eye injuries with a high percentage of globe loss is a prominent feature of IED explosions; 57 percent of blast-associated perforations required enucleation in a group of patients with combat trauma seen at Walter Reed Army Medical Center (now WRNMMC) between 2003 and 2006.[32] Unfortunately, and unlike restorative prosthetics for extremity amputees, there are currently no options for vision restoration for patients who lose their eyes. The Horus Vision Restoration Project, a recent effort led by the USAMRMC and cosponsored by VCE, seeks to address this gap.

Closed globe injuries can be less obvious than open globe injuries and can be subsequently overlooked, especially because eye injuries are often accompanied by other more immediately life-threatening and extensive injuries, which require urgent attention. Yet, serious closed globe injuries may result in the loss of sight if not treated properly. These injuries include hyphema, traumatic cataract, vitreous hemorrhage, retinal detachment, choroidal rupture, and optic nerve injuries.[49]

Ocular surface injuries were found in 25 percent of blast-exposed Iraq and Afghanistan Veterans.[39] Unlike superficial corneal injuries from other causes, blast-related damage often results in permanent scarring and other abnormalities such as endothelial cell loss. Additionally, such superficial injuries are *prima facie* evidence of high-energy insult—in many instances despite the proper wear of ballistic eye protection—and could be a bellwether of more serious intraocular injury. In this context, a blast-related corneal injury may be much more ominous than a similar injury suffered in routine activity; it is not "just a corneal abrasion." The long-term significance of these findings is not clear and highlights the need for continued surveillance.

Another characteristic feature of blast eye injuries is the presence of multiple intraocular foreign bodies (IOFB), which typically require prompt removal.[32, 39, 48] Because of the possibility of ocular toxicity or metallosis, analysis of the chemical composition of removed fragments can be critical for clinical management. However, the very small size of IOFBs makes routine analysis challenging and therefore requires highly sensitive and specialized handling and analysis of the samples. VCE is collaborating with the DoD Joint Pathology Center in developing a pathway for streamlined submission of IOFBs for such sophisticated analysis.

Between 2000 and 2015 (first- to third-quarter), 339,462 Service Members were diagnosed with TBI.[50] While approximately 80 percent of TBI diagnoses among Service Members were non-deployment related, TBIs in theater are significantly more challenging to triage and treat. The DoD defines TBI as a traumatically induced structural injury or physiological disruption of brain function, as a result of an external force, that is indicated by new onset or worsening of at least one of the following clinical signs immediately following the event:

- Any alteration in mental status (e.g., confusion, disorientation, slowed thinking, etc.)
- Any loss of memory for events immediately before or after the injury
- Any period of loss of or a decreased level of consciousness, observed or self-reported.

For the full DoD definition of TBI, please see Appendix E. Of the Service Members diagnosed with TBI between 2000 and 2015, 279,898 were mTBI diagnoses.[50] More than 70 percent of mTBI patients report subjective visual symptoms.[46, 51, 52] Visual dysfunctions include light sensitivity, diplopia, convergence and accommodative insufficiency, visual field deficits, and reading problems,[46, 53, 54, 55] all of which can remain undetected and can substantially interfere with Service Member and Veteran reintegration to duty, postservice employment, and educational pursuits. Many patients have normal visual acuity and grossly normal ocular examinations and thus may require comprehensive assessments beyond the "routine" eye examination, as the pathology may lie in higher cortical areas responsible for sensory processing and integration. Further research effort is needed to elucidate the mechanisms of TBI-related visual dysfunctions and to identify both diagnostic markers and appropriate treatments and rehabilitative strategies.

In light of the above, the effects of blast on the eye—both obvious and subclinical—speak to the needs of increased awareness and continued focused research in this area. VCE, in partnership with research organizations like the USAMRMC and the DoD Blast Injury Research Program, actively tries to close these gaps.

Mission: To be a leader in the prevention, diagnosis, mitigation, treatment and rehabilitation of military vision and eye injuries

VCE

In response to recognized gaps in care for military ocular casualties—gaps highlighted by the increased number of eye and vision injuries sustained during the Global War on Terrorism—Congress directed the establishment of VCE. Historically recognized gaps included the coordination of care of ocular casualties across the care continuum from the POI through rehabilitation; the inability to follow patient progress and outcomes as they move through the healthcare system; and a paucity of research in ocular injury, treatment, and rehabilitation.

The NDAA for FY08 (Public Law 110-181, Title 16, Sec 1623) directed the Secretary of Defense to establish the center as a component of the Wounded Warrior Care program and to address the full scope of vision care including prevention, diagnosis, mitigation, treatment, and rehabilitation of military eye injuries and diseases, including visual dysfunctions related to TBI. The NDAA also required the implementation of a tracking registry to collect eye injury and vision dysfunction data, as well as surgical and therapeutic intervention data, from DoD and VA medical records and supporting systems "...for purposes of encouraging and facilitating the conduct of research, and the development of best practices and clinical education, on eye injuries incurred by members of the Armed Forces."

DEFENSE AND VETERANS EYE INJURY AND VISION REGISTRY

VCE, in collaboration with the DHA, led, developed, and implemented the Defense and Veterans Eye Injury and Vision Registry (DVEIVR) to collect and share eye injury and visual dysfunction data. This registry contains information pertaining to injury, medical and surgical treatments, and visual outcomes for Service Members and Veterans enrolled in the registry and who subsequently received treatment at DoD and/or VA medical facilities. Care may have been provided in theater, in DoD medical treatment facilities or in VA medical facilities. The analysis of DVEIVR data supports enhancements to readiness, formulation of evidence-based clinical recommendations, guides research, and informs policy.

VCE receives operational support from the Navy within the DoD and from the Office of Patient Care Services within VA. A memorandum of understanding between the ASD(HA) and the Under Secretary for Health for Veterans Affairs is in place to define the roles and responsibilities of the DoD and VA in establishing and operating VCE. VCE is jointly staffed, and the leadership team includes the Executive Director (DoD) and Deputy Director (VA), who are entrusted as the core decisional body of VCE who formulate VCE strategic direction and integrate with other stakeholder organizations across the DoD and VA. VCE is headquartered at the WRNMMC in Bethesda, Maryland.

Through its efforts to improve vision health and enhance the quality of life for Service Members and Veterans, VCE promotes collaboration, facilitates integration, and serves as an advocate for vision across the DoD and VA healthcare systems. Further collaborative efforts with other federal healthcare organizations, academia, and private sector organizations will enable VCE to enhance development of VCE program priorities for research and quality care initiatives. VCE strategic goals focus on research, clinical support, education and policy.

By fostering scientific and clinical investigation, research advances the state of understanding of visual dysfunction

Supporting Research and Reporting Efforts

VCE is a leader in identifying critical gaps in policy, resources, and vision-related military relevant research, such as ocular trauma and TBI-associated visual dysfunctions. In this capacity, the center works in collaboration with the USAMRMC CRMRP, MOMRP, Medical Simulation Research Program, and CCCRP, as well as TATRC, to identify emerging clinical needs and address them through directed research efforts.

Identifying Research Gaps

As a part of the Interagency Vision Research Scientific Steering Committee, VCE provides critical input in defining vision research priorities for the CDMRP Vision Research Program (VRP) portfolio. The program's research topics spans the discovery of better methods of protecting deployed individuals; improved battlefield treatments that will decrease the incidence of primary and secondary loss of vision; the development of long-term treatments for chronic visual dysfunctions; the need for better surveillance tools for as-yet-undetected problems; mathematical, computational, and physical modeling and simulation; and the development of valid approaches to the restoration of sight.

VCE works with government and private-sector partners to identify emerging clinical needs and to address them through directed research efforts:

- VCE participated in the development of the 2015 military vision research capability gaps as a part of CRMRP's Sensory System Scientific Working Group.
- VCE actively contributes to CRMRP Neurosensory Systems (JPC-8), CCCRP (JPC-6), and MOMRP (JPC-5) by participating in capabilities-based assessments, strategic planning, and scientific proposals reviews.

- There are currently 48 funded proposals with ten direct blast and eight TBI-related vision research projects funded in the joint CRMRP and VRP portfolio with additional proposals under consideration for funding.
- VCE played a pivotal role in the initiation of USAMRMC's Medical Technology Enterprise Consortium's Horus Vision Restoration Project. The goal of the project is to develop true artificial vision to restore sight to those with traumatic blindness.
- Glenn C. Cockerham, MD, Interim Deputy Director of VCE, is a co-investigator on a grant, "Visual Sensory Impairments and Progression Following Mild Traumatic Brain Injury," which the CENC awarded in 2015.

Also during FY15, VCE conducted a systematic review and analysis of blast-related ocular trauma literature and is currently developing a manuscript on the topic. The center also interviewed a sample of returning OEF/OIF ophthalmologists and optometrists to capture lessons learned in order to improve care and ensure readiness for future operational deployments; a report is under development. Finally, VCE fosters a continuous academic dialogue, including the following, to stay abreast of ongoing vision research and developing gaps:

- VCE publishes *Frontlines of Eye Care,* a quarterly research review newsletter that shares recent, noteworthy research findings from diverse fields within vision research.
- VCE maintains direct communications with international civilian and military academic researchers, such as the Hopkins Extreme Materials Institute at Johns Hopkins University, the Schepens Eye Research Institute and Massachusetts Eye and Ear Infirmary at Harvard University, Vanderbilt University, and the Royal Centre for Defence Medicine in Birmingham, United Kingdom, to communicate emerging needs in combat ocular casualty care.

VCE tracks VA and DoD vision-related publications, grants, and patents. More than 200 publications and more than 100 funded projects have been identified and catalogued.

Simulation

The VCE team continues to work to identify, validate, and address requirements for new DoD/VA ocular simulation capabilities. In FY15, VCE worked closely with the USAMRMC JPC-1 to update the 2012 Roadmap for Simulation in Eye Care report. A manuscript and an informative white paper are currently under development.

VCE is also a participant in a major study currently underway at the WRNMMC and the USUHS to validate an advanced ocular trauma simulator. Performance data are currently being collected on both expert and novice surgeons. Furthermore, the center is involved in evaluating a virtual reality direct ophthalmoscopy simulator for training primary care providers and medical students at Madigan Army Medical Center (MAMC). It is also directly involved in the design and development of an advanced ocular trauma manikin currently under development at Massachusetts General Hospital.

VCE worked closely with the Army Medical Department Center and School and RDECOM to develop the requirements for a canthotomy/cantholysis simulator to train a vision-sparing procedure. The requirement was selected as a 2015 US Army SBIR topic and is now in the Phase I award cycle.

VCE continues to actively advise the computational modeling and simulation communities in the development of advanced, high-fidelity ocular trauma models.

Sophisticated mathematical simulations of the eye and orbit will allow a greater understanding of blast phenomena and ocular interactions and effects, leading to more effective prevention, protection, and mitigation strategies. VCE expertise directly informed recent publications and presentations by researchers from Johns Hopkins University, the US Army Aeromedical Research Laboratory (USAARL), and the US Army Institute of Surgical Research.

Improving Clinical Impact

The sequential movement of a combat casualty through successive echelons of care, across long distances and multiple locations, and through the care of multiple providers creates an inherent lack of continuity of care, and an acknowledged gap in clinical feedback and follow-up. In such a system, it is challenging to provide uniform care, particularly when patients transit quickly, their providers rotate frequently, and the nature of the injury (most notably, blast injury) necessitates care by multiple specialists and subspecialists. This acknowledged gap has existed for more than 100 years.

To help address this deficit, VCE instituted a monthly worldwide ocular trauma video teleconference in 2011, bringing together providers from across the world to discuss combat eye casualty care. Now in its fifth year, the call has proven exceptionally valuable to deployed providers. International participants represent all echelons of care—from DoD, VA, and coalition partners; from theater to rehabilitation centers; and from academia and various organizations that influence CCC. In addition to providing clinicians with important clinical feedback, the call offers a forum for sharing best practices and lessons learned and for discussing and expertly vetting clinical recommendations. Additionally, the forum examines clinical cases for process improvement opportunities at both the clinical and systems level. To date, more than 48 percent of process improvement issues had been resolved. The monthly call also serves as a curriculum component for ongoing provider readiness education.

VCE also plays a direct role in the clinical care and support of Service Members and Veterans by driving improved coordination of complex ocular care between and among the DoD, VA, and civilian resources. Fostering improved coordination of care enhances the efficiency of patient care and ensures the highest quality and most compassionate vision care for our nation's Service Members and Veterans. VCE interacts with patients, care teams, and systems of care to evaluate and improve clinical outcomes and the quality of vision care and rehabilitation that Service Members and Veterans receive. The center identifies optimal pathways of ocular care and evidence-based best practices and provides the information to stakeholders to facilitate system-level improvements.

VCE provides direct clinical care coordination support through staff at the WRNMMC and MAMC. The objective of vision care coordination is to improve the efficiency with which patients with ocular injuries are transferred from overseas to stateside military health facilities and on to VA medical centers as necessary, as well as to improve the efficiency of care within a given facility. The VCE Vision Care Services Coordinator (VCSC) coordinates patient transfers to ensure that available ocular subspecialty capabilities at military treatment facilities and VA medical centers are matched to patients' clinical care needs. Additionally, the VCSC provides liaison between multidisciplinary services within a facility, such as trauma, ophthalmology, and rehabilitation services, as well as other care managers, thereby ensuring that special ocular needs are understood and met. During FY15, VCE reviewed existing military eye injury care coordination guidance to document best practices, identify gaps or needs, and formalize training and educational requirements.

Photo credit: Dr. Carmen Russoniello/Army Medicine

Understanding that the prevention of ocular injury is better than treatment and that the extent of an injury is best mitigated at the POI, VCE actively engages the prehospital and CCC communities. It participates in related conferences and symposia and actively communicates and collaborates with the Emergency Medical System and primary responder communities. For example, the center participates in the weekly DoD Joint Trauma System (JTS) worldwide trauma teleconference, maintains a close relationship with the Committee on Tactical Combat Casualty Care (CoTCCC), has provided educational material to the National Association of Emergency Medical System Physicians, and presented at several primary trauma conferences in FY15.

The development and dissemination of best practices, clinical recommendations, and clinical support tools can have a positive impact on the vision health of Service Members and Veterans across the DoD and VA. Ocular trauma and visual dysfunction have substantial impacts on patients, families, and the greater DoD, VA, and private sector communities. These impacts include, but are not limited to, loss of military personnel; increased VA and DoD management and operational costs from loss or impairment of personnel, as well as costs involved in training replacement personnel; and the challenges in training and reintegrating the injured Service Members and Veterans into the workforce. Clinical impact extends across the continuum of care: from predeployment, to POI, to treatment, to rehabilitation and reintegration.

To that end, VCE annually reviews and updates the JTS CPG, "Initial Care of Ocular and Adnexal Injuries at Role I, Role II, and Non-ophthalmic Role III Facilities." The companion Tactical Combat Casualty Care (TCCC) guidelines on combat ocular care are based on this CPG, and both resources are recognized by national emergency medical services as prehospital trauma care standards. The CPG underwent a major revision in FY15, and a manuscript version has been prepared for submission to a peer-reviewed medical journal.

During FY15, VCE developed a clinical recommendation, "Eye & Vision Care Following Blast Exposure and/or Possible Traumatic Brain Injury," which was approved by VA and endorsed by the DoD Tri-Service Specialty Care Advisory Board for distribution throughout both agency healthcare systems. Two other clinical recommendations that address vision issues associated with TBI are under development and are anticipated to be published in FY16.

Photo credit: Master Sergeant Kimberly A. Yearyean-Siers/US Air Force

Additionally, clinical recommendations for specialists rehabilitating persons with visual field loss and for the specialty care of oculomotor dysfunctions after TBI are nearing completion and will soon enter DoD and VA approval processes.

VCE also coordinated with the VA Blind Rehabilitation Service and the VA Polytrauma Nursing Field Advisory Committee to publish a fact sheet, "Caring for Patients Who are Blind or Visually Impaired: A Fact Sheet for the Outpatient Care Team." This fact sheet, along with a companion fact sheet for inpatient care teams developed in FY14, was distributed to all Veterans Integrated Service Networks, the three DoD TRICARE Regional Offices and Managed Care Support Contractors, and the TRICARE Beneficiary Education Communication Division. The fact sheets were also distributed at military medical treatment facilities and at the 2015 VA Blind Rehabilitation Service National Conference. An article on the fact sheets, "Vision Center of Excellence Opens Eyes on Best Care Practices," was published on Health.mil on 26 March 2015. The center also finalized development of a patient brochure on vision problems associated with TBI and fact sheets on visual field loss and oculomotor dysfunction associated with TBI. These products will be published and promoted during FY16.

VCE plays an active role in national patient clinical care and safety initiatives as well. Recognizing a clinical surgical capability shortfall, VCE authored an Army 2015 SBIR topic on a novel intraocular visualization tool to aid in delicate intraocular surgery through opacified ocular media, now in Phase I award. Additionally, VCE remains actively engaged in directing the progress of a previously awarded SBIR topic to develop a fully operational ophthalmic slit lamp on a smartphone base. This venture is now well into Phase II funding. Also in FY15, the center represented DoD ophthalmology as a charter member of the American Board of Ophthalmology and American Academy of Ophthalmology Joint Working Group on Patient Safety. The military's participation was specifically solicited for this long-term patient safety initiative.

VCE has continued collaboration and outreach with other Centers of Excellence, Veteran service organizations, and academia. In FY15, it partnered with the DoD HCE as sponsoring organizations for Salus University's Veterans Readiness Initiative: Multisensory Screening and Care for Post 9/11 Veterans. This program was conducted jointly by the optometry and audiology programs at the university, together with the Philadelphia VA Medical Center and the two largest community colleges in the Philadelphia area. The program provided Veterans with onsite screening for vision, hearing, and/or balance issues that may have the potential to interfere with academic and reintegration goals. The center also hosted a discussion forum that included members of the Blinded Veterans Association, providers, and industry partners concerning the growing need for and uses of computer-based and smart phone technologies by the visually impaired community.

Readiness

VCE actively supports the annual Tri-service Ocular Trauma Course for military ophthalmologists. As the only ocular trauma surgery readiness course in the country, it is essential to teaching and maintaining critical combat ocular trauma surgical skills. VCE is actively working to institutionalize the requirements and support for the course. The course forms the foundation of the military's ocular trauma curriculum.

Recognizing the educational opportunity inherent in the monthly worldwide ocular trauma video teleconference with respect to readiness, the call format was modified in 2015 to include a formal didactic component on trauma management principles. Continuing education credit is offered to physicians, nurses, and optometrists. The call now acts as an additional component of a broader provider readiness curriculum.

Facilitating Educational Opportunities and Resources

VCE designs, implements, and promotes traditional and new modalities for clinical training and education to ensure that our nation's medical force is ready to address military eye injuries and visual dysfunction associated with TBI. VCE also supports improved readiness for civil preparedness through educational offerings to promote ophthalmological preparedness for disaster or terror response.

In FY15, VCE and the CoTCCC coproduced an instructional video on the proper use of the rigid eye shield at the POI. The CoTCCC immediately incorporated the video into its national TCCC curriculum, and it is now an integral component of both the TCCC for Medical Providers and the more far-reaching TCCC for All Providers courses. VCE also collaborated with the CoTCCC and Defense Health Agency Medical Logistics to ensure that documentation of protective eye shield use was included on the newly approved DD Form 1380, TCCC card. In addition, the center was a key collaborator in efforts that resulted in the ASD(HA) directing the Services to update doctrine and training to include provision and use of rigid eye shields in DoD Individual and Joint First Aid Kits. The center also influenced development of a new eye shield embossed with instructions for use—this shield has received a federal stock number and is available as a commercial item.

Implementing innovative education and training initiatives to ensure ongoing knowledge transfer and promote new modalities for clinical training is another key part of VCE's mission.

Educational Products, Presentations, and Publications

VCE was an active participant in multiple national and international educational symposia. International podium presentations were delivered at the American Academy of Ophthalmology and the Association for Research in Vision and Ophthalmology annual scientific symposia; the University of Pittsburgh/Fox Eye Center's 5th International Conference on Regenerative Medicine; Virginia Commonwealth University's Symposium on Military and Veterans Health; and the DoD's MHS Research Symposium, where VCE presented two lectures and a poster. National presentations and webinars included talks at the American Optometric Association annual symposium and the MHS Speaker Series. Additionally, VCE finalized and released four new audio learning modules on the following topics: Antibiotic Resistance in Acute Postoperative Endophthalmitis, Vision Concerns Post Mild TBI, Visual System Biomarkers for Mild TBI, and Adult Onset Convergence Insufficiency.

It is anticipated that these audio learning modules will be released and promoted during FY16. Meanwhile, VCE continued to develop brief articles focused on blast injury for dissemination in a variety of high visibility newsletters with distribution across the DoD and VA, including the JTS and WRNMMC Trauma Newsletters. VCE personnel also actively participate in academic symposia and scientific forums, delivering various ocular injury presentations, also focused on blast eye injuries:

- "Combat Eye Injuries," presented at the American Optometric Association Scientific Symposium in Seattle, Washington, in June 2015
- "Caring for Wounded Warriors with Vision and Hearing Impairments—Impact on Rehabilitation," co-presented with HCE, USUHS, and the University of Pittsburgh at the USUHS State of the Science Quarterly Symposium
- "Combat Eye Injury and Visual Dysfunction—Association with TBI and Psychological Health," presented at the DCoE Summit on the Continuum of Care and Care Transitions in the MHS, in collaboration with WRNMMC Departments of Ophthalmology and Optometry
- "Co-morbidities of Visual Dysfunction and Psychological Health and Testing and Reliability of Afferent Visual Function in Blast Neurotrauma," a two-webinar series developed and delivered in conjunction with the VA Employee Education System.

Continuing its commitment to increase broader awareness of vision health topics and build relationships with military and Veteran health programs, VCE focused on key observances, such as Eye Injury Prevention Month (October) and Save Your Vision Month (March), and worked collaboratively with the HCE to support Vision and Hearing Month in May 2015. In July 2015, VCE launched the third in a series of Shields Save Sight advocacy campaigns to target increased use of eye protection and encourage proper response techniques to eye injuries. As part of this month-long targeted outreach effort, the center secured placements in military press and blogs; produced public service announcements that ran on the Armed Forces Network and on LCD screens at DoD installations; and further strengthened working relationships with stakeholder organizations, including the DHA, MHS, BUMED, Navy Installation Management Command, and Naval Safety Center, to expand access to target audiences. Finally, VCE strengthened its online presence with an enhanced website (http://vce.health.mil) to reflect contemporary functionality and a design to enhance the user experience and message retention. The user-friendly website includes VCE-developed educational audio learning modules on the following topics: applying eye shields; talking to patients about vision loss; concomitant cranial injury, TBI, and visual dysfunction; depression and vision loss; and keratoconus.

Institutionalizing Policies to Promote Visual Health

Every day, in a variety of settings across the federal and civil sectors, healthcare professionals make decisions with the potential to either mitigate vision loss or improve visual outcomes. VCE works to identify and communicate best practices to providers in all sectors and specialties, as well as to inform the DoD and VA when gaps in federal policies exist.

VCE Efforts: Eye Shields, Readiness, Eye Casualty Care

While VCE works actively to address gaps and needs in the short term, it realizes that true change requires institutionalization of improvements in the long term. Toward this goal, VCE also works closely with its partners to effect policy-level changes to ensure sustained system-level improvements.

A primary example is its collaborative work with the US Army Institute of Surgical Research, CoTCCC, and DHA, Readiness Division, to implement the aforementioned ASD(HA) policy on the addition of rigid eye shields to DoD Individual and Joint First Aid Kits and the revision of doctrine and training requirements for eye casualty care at the POI. Similarly, VCE is working to gain policy-level institutionalization of an ocular CCC system, which would include enhanced medical readiness training and improved care coordination.

Future Plans and Initiatives

As a primary resource for improving vision healthcare for Service Members and Veterans and for ensuring the readiness of providers, VCE must strategically plan at both the national and regional levels and must consider both federal (military and VA) and civil aspects. Specific considerations span from advocating for broad prevention measures, such as wearing proper eye protection in peacetime and training, as well as in combat; supporting the development of enhanced diagnostics; educating military and civil bystanders and first responders to proper eye injury care, i.e., use of rigid eye shields and not eye patches at the POI, thereby mitigating the extent of an injury; developing and disseminating evidence-based best treatment recommendations; supporting surgical readiness training; exploring new rehabilitation and vision restoration projects; and providing optimal ocular specialty care coordination. Critical efforts must include identification, retention, and dissemination of lessons learned from current and prior wars; institutionalization of hard-won improvements realized over the course of this conflict; and constant attention to provider readiness during peacetime. Such efforts are in line with VCE's mandate to enhance the prevention, diagnosis, mitigation, treatment, and rehabilitation of ocular injuries. Given

Policy drives the work of the DoD and VA, as well as the medical community in general. VCE works to support the development and implementation of policies that drive forward the mission of VCE.

the increase of blast-related terrorist and mass casualty incidents that are resulting in polytrauma casualties among innocent civilians and uniformed personnel, it is clear that these aspects are as apropos to our civilian colleagues as to the military. Because of this migration of combat-style injuries into civil populations, the increased medical and trauma-related research efforts of the past several years cannot be abandoned or diminished, even though military forces are decreasing and are less engaged in active combat. To this end, VCE is looking ahead to the future with highlights outlined below:

- Develop a comprehensive roadmap for study of blast-related eye injuries
- Organize and lead working group(s) to characterize and define the blast eye and associated best practices in clinical care and then publish and disseminate the findings
- Publish lessons learned and/or recommendations from reviews/analysis on blast-related eye injury and incorporate that information into readiness and injury response training for future conflicts
- Conduct, facilitate, and publish or present analyses using the Defense and Veterans Eye Injury and Vision Registry (DVEIVR) and other data sources on the diagnosis, treatment, or rehabilitation of eye and vision injuries to enhance the body of knowledge of combat eye injury diagnosis, treatment, and rehabilitation

- Document best practices and process improvements in vision care coordination and, based on findings, develop a plan to augment the number of VCSCs within the MHS and VA
- Support the development of advanced eye injury computational and surgical simulators, as well as readiness workshops, to develop and maintain surgical skills while reducing the use of animal models and increasing repetitions of critical ocular trauma surgical techniques
- Assess the need for, develop, host, and support educational workshops, e-learning or classroom-based clinical and readiness curricula for eye and vision injuries
- Expand communication of information on VCE programs, research, and publications with stakeholders
- Advocate for high-level policy changes to institutionalize improvements in readiness, care, and care coordination for the ocular combat casualty.

VCE continues to press ahead in key strategic areas supporting improving vision health, optimizing operational readiness and enhancing quality of life for injured Service Members and Veterans.

Photo credit (opposite page): Senior Airman Zachary Hada/US Air Force

CHAPTER 7:

DOD BLAST INJURY RESEARCH PROGRAM ACCOMPLISHMENTS

The PCO's EA support mission is to coordinate DoD blast injury research investment and leverage expertise in order to develop strategies that prevent, mitigate, or treat blast injuries. To inform the EA of accomplishments throughout the blast injury research community, the PCO requested data from DoD organizations engaged in medical and nonmedical blast-related research at the end of FY15. The PCO received 140 responses from 31 organizations, summarized in the chapter that follows. These accomplishments are organized by the DoD Blast Injury Research Program's key program areas: Injury Prevention, Acute Treatment, and Reset. Each accomplishment adds to the knowledge base for blast injury research and refines the strategies that prevent blast injury or allow injured Service Members to return to duty and maintain an active lifestyle.

Program Area: Injury Prevention

Research on blast injury prevention considers the entire spectrum of potential injuries, from primary to quinary. The design of prevention systems requires an understanding of the mechanism of injury; thus, significant research efforts are focused on replicating blast exposure conditions in the laboratory and determining blast injury mechanisms using animal and computational models. Researchers are also collating clinical and theater data to analyze blast threats and assess PPE performance. These data are currently being used to establish safety thresholds for human exposure to blast, support the design of protection systems, strengthen guidelines for the safe use of weapon systems, and identify biomarkers and potential treatment targets. Findings are shared between the military and civilian research and development communities to encourage greater use and availability of protective measures against blast events in both sectors.

Blast Exposure Analysis

Blast Exposure from Shoulder-Mounted Rocket Launchers

Blast overpressure may cause deformations of the brain that could lead to TBI. Though much research has been devoted to understanding how explosive devices may engender unique kinds of brain damage, less work has been devoted to the overpressure created in the standard firing of military munitions. Artillery, rocket launchers, and other heavy-grade military weaponry can yield blast overpressures that affect operators and surrounding personnel. Shoulder-fired munitions can produce a blast overpressure greater than 36 psi. However, the blast events experience by operators of these weapons systems has not been systematically evaluated. In this study, investigators at the Defense and Veterans Brain Injury Center (DVBIC); NMCSD; Applied Research Associates; Black Box Biometrics; the Naval Hospital, Camp Pendleton; the Naval Surface Warfare Center (NSWC); and the USUHS examined the effect of shoulder-fired rocket and grenade launchers on military personnel. The researchers collected data from blast sensors positioned on the head, chest, and backs of 64 Service Members and instructors who participated in a combat training course. The Service Members fired five weapons systems in two-hour training blocks: the Carl Gustav 84 millimeter recoilless rifle, the Light Anti-Tank Weapon, the Rocket Propelled Grenade, the Mark-19 Automatic 40 millimeter Grenade Launcher, and fragmentation grenades. Each weapon was fired approximately the same number of times. Overpressure events above 2.5 psi were recorded. The sensors recorded 396 unique blast events, a median of five events per individual. On average blasts were 10 minutes apart.

Photo credit (opposite page): Army Research Laboratory

The average blast magnitude was 4.58 psi with 87 percent of the blasts having a psi above 4, the recommended safety threshold for blast exposure. The majority of blast events that exceeded the 2.5 psi threshold occurred with the Carl Gustav 84 millimeter recoilless rifle (56.1 percent), followed by the Light Anti-Tank Weapon (22.0 percent), then the Rocket Propelled Grenade (20.0 percent). The findings suggest that some shoulder-mounted weapon systems (like those above) consistently expose Service Members to blast overpressure above 4 psi. These events are above recommended safety threshold for blast exposure.

Underwater Explosion Quantity-Distance Working Group

The DoD Explosive Safety Board hosts a working group dedicated to establishing safety guidance for swimmers and divers in the presence of an underwater explosion. This working group is chaired by NSWC Indian Head Explosive Ordinance Disposal Technology Division personnel. Current safety standoff guidance is provided by the explosive ordinance disposal (EOD) community, Chief of Naval Operations, and US Army Technical Center for Explosives Safety—but no common DoD-level guidance is documented at this time. In FY15, this working group met nearly monthly and settled on objectives, which are to develop a good working shock propagation model in shallow water environments for low pressure shockwaves (a model already exists for deep water/high pressures); to review the metrics for physiological risks; and to develop equipment to mitigate the effects of an underwater blast. Gaps in capabilities are being tracked through a maturity chart. All four US DoD Services participate in this working group, as well as academia (Duke University), and foreign Navies (United Kingdom and Canada). The working group is tracking basic research, which is supported by ONR, the Environmental Security Technology Certification Program, and the Naval Submarine Medical Research Laboratory.

Massive Blast Characterization

JTAPIC supported testing of intelligence-based massive vehicle borne IED and the threat they pose to facilities and personnel. Ongoing tests at Dugway Proving Grounds consisted of controlled detonation of explosive devices with 5,000 pounds, 15,000 pounds, 30,000 pounds, and 60,000 pounds of non-military grade explosives. Numerous customers were invited to participate and deploy equipment and sensors in order to assess the damage such blasts would incur. PEO Soldier collected blast pressure on dismounted and mounted troops and evaluated several mitigation technologies. Additionally the Engineering and Research Development Center, which is part of the Army Corps of Engineers, evaluated technologies they are developing in support of an ASA(ALT) initiative on base protection. These tests were the largest controlled detonations since the 1960s and the data collected will greatly enhance the understanding and ability to model large blast events.

The Blast Exposure Accelerated Sensor Transition (BEAST) Program

The BEAST program at DARPA builds on progress made during the Blast Gauge program to enable a better understanding of blast-related injuries such as TBI and PTSD. Previous efforts to characterize blast injury effects have been primarily done in animal models, while human trials investigating the effects of real-world blast injury, especially in training, are limited to self-reporting. Studies to date do not have clear measurement of objective blast characteristics, such as the duration and intensity of blast overpressure, or the effects on interval between exposure and cumulative exposure over time. Previously, the Blast Gauge program resulted in production of a small, lightweight environmental dosimeter that monitors physical impacts of exposure to an explosive blast. The device is designed for flexible mounting; typically it is mounted on the nape pad of the combat helmet or the webbing of the outer tactical vest.

Photo credit (opposite page): US Army

During a blast event, the Blast Gauge device captures environmental data and available operational information in order to develop a three-dimensional recreation of the event and is used to help identify Service Members with significant exposures and to increase the knowledge base regarding conditions that cause injuries, including TBI. The BEAST program supports medical studies that utilize the Blast Gauge sensors to investigate the blast overpressure that Service Members sustain during heavy weapons training, and assess physiological and behavioral measures for any deficit following multiple sub-concussive blast exposures. Preliminary results suggest that some neurological effects, including temporary reduced performance on neuromotor, learning, and memory tasks, may result from repetitive low-level blast exposure. Clinical studies continue to refine experimental results and investigate physiological biomarkers that may be an early indicator of impairment.

Photo credit: US Army

Employing Environmental Sensors in Military Training for Measurement of Blast Overpressure

The Environmental Sensors in Training (ESiT) program is a US Army Training and Doctrine Command initiative that builds upon Army policy in 2007 for Service Member helmets to employ electronic sensor technologies to sense and record potentially concussive events in deployment environments, and upon Army policy in 2013 that provided guidance for management of potentially concussive events in garrison environments (Headquarters, Department of the Army Executive Order 165-13). ESiT is a holistic review of sensors for blast exposure and for blunt impact to the head. The purpose of ESiT is to inform the technical requirements for environmental sensors and the methodology for employment of those sensors in select training events. USAMRMC is administering the current ESiT effort, leveraging other programs and projects in related domains, particularly the Science & Technology Objective, "Brain in Combat," which demonstrates technologies to facilitate treatment, return to duty, and evacuation decisions for TBI. The effort under these conjugate programs provides opportunity for surveillance measurements of blast exposures in military training, as well as input to ongoing research on the association between blast exposures and neurophysiological effects. A report on ESiT pilot studies has been released via the Defense Technical Information Center and additional reporting from human subjects studies will be submitted in calendar year 2016 for peer-reviewed publication. Unlike training events that have the potential for blunt impact to the head and diagnosed concussion, training events with acute blast exposure are not known to result in concussion or other medical diagnosis. However, recent evidence suggests that cumulative blast exposure may be associated with negative neurophysiological outcomes. The ESiT program affords the DoD capability to evaluate and mitigate risk from chronic exposure to blast.

Characterizing Exposures Associated with the Light Armored Vehicle (LAV)-Assault Gun (AG)

The LAV is equipped with an AG that fires 90 millimeter cartridges filled with propellant that is ignited to produce a controlled combustion that propels a projectile toward a target. The chemical composition of propellants affect combustion rates, intensity of blast emitted from the gun muzzle during firing, and injury risk. During a test conducted in April 2015, blast test devices (BTD) and noise microphones served as proxy sensors and collected data at two crew positions inside the LAV: commander and driver. This test characterized exposures associated with the twenty-eight firing conditions involving different types of ammunition, round conditioning temperatures and main gun elevations. US Army Public Health Center (USAPHC) evaluators analyzed the sensor data using the Blast Overpressure-Health Hazard Assessment (BOP-HHA) version 2.0 software. This software employs an algorithm based upon experimental data collected from more than 1,000 specimens exposed over 20 years of testing. This software includes a biomechanical model that analyzes the time-pressure data captured by the BTD to calculate the amount of "push" or mechanical work imparted by the blast pressure wave to the thorax and transmitted to the lung. The calculated work value is used to estimate the risk of lung injury and serves as a predictor of injury since air-containing organs are more susceptible to blast injury. BOP-HHA is the primary methodology used by USAPHC to assess injury risk from the non-auditory component of blast. The results of the analysis were used to develop standard operating procedures that will reduce injury risks to Service Members and operators firing the 90 millimeter LAV-AG.

Characterizing Exposures Associated with the Multi-Role Anti-Armor/ Anti-Personnel Weapon System

The Multi-Role Anti-Armor/Anti-Personnel Weapon System uses ammunition that is filled with propellant that is ignited to produce a controlled combustion that propels a projectile toward a target. The chemical composition of propellants affect combustion rates, intensity of blast emitted from the both ends of the weapon during firing, and injury risk. In a test conducted by Aberdeen Test Center in August 2015, BTDs and noise microphones served as proxy sensors and collected data at two crew positions: gunner and assistant gunner. This test characterized exposures associated with the four firing conditions involving rounds conditioned to "hot" temperature and four different gunner firing postures: standing, kneeling, sitting and prone. USAPHC evaluators analyzed the sensor data using the BOP-HHA version 2.0 software. This software employs an algorithm based upon experimental data collected from more than 1,000 specimens exposed over 20 years of testing. The BOP-HHA software includes a biomechanical model that analyzes the time-pressure data captured by the BTD to calculate the amount of "push" or mechanical work imparted by the blast pressure wave to the thorax and transmitted to the lung. The calculated work value is used to estimate the risk of lung injury and serves as a predictor of injury since air-containing organs are more susceptible to blast injury. BOP-HHA is the primary methodology used by USAPHC to assess injury risk from the non-auditory component of blast. The results of this analysis were used to develop standard operating procedures that will reduce injury risks to Service Members/operators firing the Multi-Role Anti-Armor/Anti-Personnel Weapon System.

Characterizing Exposures Associated with M865 and M1002 120 millimeter Tank Training Cartridges

The purpose of this weapon test was to evaluate a new propellant for 120 millimeter tank training ammunition by characterizing blast exposures generated by this new propellant, Radford Propellant Development (RPD)-596, compared to the blast exposures generated by the current M14 propellant used in these cartridges. The M865 target practice, cone stabilized, discarding sabot with tracer (TPCSDS-T) and M1002 target practice, multi-purpose with tracer (TP-MP-T) cartridges were used in this testing.

M865 and M1002 120 millimeter tank training cartridges are filled with 596 propellant that is ignited to produce a controlled combustion that propels a projectile toward a target. The chemical composition of propellants affect combustion rates, intensity of blast emitted from the gun muzzle during firing, and injury risk. In a test conducted by Aberdeen Test Center in June 2015, BTDs and noise microphones served as proxy sensors and collected data at four crew positions inside of an M1A1 Abrams tank: commander, driver, gunner and loader. USAPHC evaluators analyzed the sensor data using the BOP-HHA version 2.0 software. This software employs an algorithm based upon experimental data collected from more than 1,000 specimens exposed over 20 years of testing. The BOP-HHA software includes a biomechanical model that analyzes the time-pressure data captured by the BTD to calculate the amount of "push" or mechanical work imparted by the blast pressure wave to the thorax and transmitted to the lung. The calculated work value is used to estimate the risk of lung injury and serves as a predictor of injury since air-containing organs are more susceptible to blast injury. BOP-HHA is the primary methodology used by USAPHC to assess injury risk from the non-auditory component of blast. The results of this analysis were used to develop standard operating procedures that will reduce injury risks to Service Members and operators firing from an Abrams M1A1 tank with M865 and M1002 120 millimeter tank training cartridges fueled by RPD-596 propellant.

Injury Models

Blast-Induced Acceleration in a Shock Tube: Distinguishing Primary and Tertiary Blast Injury Mechanisms in Rat TBI

Discerning biomechanical underpinnings is crucial for an understanding of the etiology and mitigation of blast-induced TBI. Scientists and engineers at WRAIR are examining the interplay of blast overpressure and accelerative forces using an Advanced Blast Simulator, which is capable of producing high fidelity IED-like blast waveforms in the laboratory. This undertaking involves understanding the role that parameters, like areal density (the mass of an object divided by its projected 2-dimentional area), play in the scaling of acceleration and displacement (blast throw) due to blast. Experiments to date on inanimate objects and laboratory rats indicate that acceleration is not a major contributor to blast-induced mTBI and, to the extent it occurs, acceleration is imparted during the shock diffraction phase and not during the loading phase of the blast, as traditionally thought, for objects that are less than the shock wavelength in diameter. Objects reach peak maximum acceleration within 0.6 milliseconds of the shock front arrival. For objects much smaller than the shock wavelength (less than 6 feet in diameter), the object's terminal velocity appears proportional to the peak total pressure of the blast and the areal density of the object and not the impulse (area under the blast pressure curve) of the shockwave. These characterizations are yielding great insight into scaling issues in laboratory experiments, as well as into the mechanisms that cause blast overpressure TBI.

Blast Exposure Causes Phosphorylation of Tau at Serine 396: A Potential Predisposition to Alzheimer's-Like Neuropathology

Blast-induced TBI is associated with acute and chronic neuropathological and neurobehavioral deficits. Tau protein, phosphorylated at serine 396, is rich in paired helical filaments that form neurofibrillary tangles (NFT) observed in the brains of patients with Alzheimer's disease. The number of NFTs is tightly linked to the degree of dementia, indicating that the formation of NFTs may underlie and contribute to neuronal dysfunction. Researchers at WRAIR evaluated brains of rats after exposure to single and closely coupled repeated blast overpressure and detected that phosphorylation of tau protein occurs preferentially at serine 396 in a severity-dependent, regionally selective manner. These results indicate that acute tau protein phosphorylation at serine 396 and chronic accumulation of amyloid precursor protein in the brain after blast exposure may predispose to Alzheimer's-like neuropathology.

Chemokine Ligand 2 (CCL2) Levels in Cerebrospinal Fluid (CSF) as an Early-Response Biomarker for Blast-Induced Neurotrauma

The neuroinflammatory response is an early pivotal immune process following brain injury. The inflammatory mediator CCL2, also known as monocyte chemotactic protein-1 (MCP-1), has been implicated in the pathogenesis of brain ischemia, Alzheimer's disease, and other neurodegenerative diseases. Using a rat model of single and repeated blast exposures in a shock tube, researchers at WRAIR investigated the time-course of changes in MCP-1/CCL2 levels in the cerebrospinal fluid and blood. Striking 40 fold elevations in MCP-1/CCL2 levels in CSF were detected at six hours and persisted for three days post-blast exposures in a severity-dependent manner and were accompanied by greatly increased CCL2 gene expression and protein overexpression in multiple brain regions. The result indicates that CSF CCL2 can be used as an early-response biomarker for diagnosis and prognosis after blast neurotrauma. Since cytokines, such as CCL2 are known to have both beneficial and detrimental effects in the milieu of the injured brain, and contribute to degenerative and regenerative processes, the timing of these responses is critical to their neurobiological importance.

Tissue Non-Specific Alkaline Phosphatase (TNAP) in the Etiology and Diagnosis of Tauopathy After Blast Exposure

CTE, a tau protein-linked neurodegenerative disorder observed in athletes with multiple concussions, shares clinical symptoms and neuropathological characteristics with those seen in victims of blast exposure. Prevention of tau phosphorylation and facilitation of the dephosphorylation of phospho-tau are critical to prevent tauopathy and preserve/restore neuronal microtubule assembly. TNAP serves this major role in the brain by dephosphorylating phospho-tau. Researchers at WRAIR have shown that the activity and expression of TNAP in the rat brain significantly decreased after blast exposure and was associated with increased phosphorylation of tau, revealing the potential role of TNAP in the development of tauopathy and CTE after blast exposure. The decreased activity/expression of TNAP in the brain was associated with a decreased TNAP activity in the plasma, pointing to the potential use of TNAP activity/level in the plasma or cerebrospinal fluid as a diagnostic marker of blast-induced tauopathy/CTE. A manuscript describing these results is in press (*Neuroscience Letters*) and a full patent application has been filed to claim that TNAP level/activity in the plasma can be used as a biomarker for the diagnosis and prognosis of tauopathy/CTE and intranasal delivery of TNAP can provide an effective treatment strategy against tauopathy/CTE phosphorylation of tau protein occurs preferentially at serine 396 in a severity-dependent, regionally selective manner.

Injury to the Retina and Brain Visual Centers by Primary Blast Waves

Exposure to blast shock waves is a leading cause of loss of vision in US Service Members. Blindness is a long-term disability that has a profound impact on the Service Member's quality of life. Researchers at WRAIR, with support from the USAMRMC TATRC Vision Research Program, have characterized the nature of blast wave injuries to the eyes (retina) and brain visual processing centers, and have explored therapies to halt the progression of neuronal cell degeneration. Using a rat model of whole-body exposure to blast over pressure in a shock tube, visual function is assessed by electroretinogram recordings, visual discrimination behavior testing, and eye and brain histopathology. Exposure to moderate pressure blast waves leads to marked visual system dysfunction that is associated with neuronal degeneration throughout the visual system (e.g., retina, optic tracts, and visual cortex). Novel drugs derived from omega (ω) -3 and -6 polyunsaturated fatty acids (PUFA), which are known to be potent pro-resolving lipid mediators of inflammation, i.e., lipoxins, neuroprotectins, and resolvins, are being evaluated for therapeutic efficacy.

Photo credit: Staff Sergeant Nick Wilson/US Air Force

Despite improvements in visual function, treatments have not impacted neuronal cell degeneration in the retina and brain, prompting targeted drug delivery using nanoparticle platforms to eliminate drug stability and tissue permeability issues.

Assessment of Cytokine Levels in Plasma, Brain, and Retina of a Rat Model of Blast-Induced mTBI, Using Immunoassay Arrays

Chemokines and cytokines play early pivotal roles in the inflammatory cascades underlying blast-induced injuries and are promising targets for therapeutic interventions. To effectively pursue this therapeutic avenue, the timing of the interplay among these responses must be characterized to identify the key participants and the optimal therapeutic windows for intervention. Cytokine levels in plasma, brain, and retina are being longitudinally screened by researchers at WRAIR at varied times after blast exposure using immunoassay arrays based on newly developed Luminex® bead technology. The arrays (Research & Development Systems Inc.) are used to precisely simultaneously quantify very small concentrations (pico-molar) of up to 17 rat specific cytokines across a single 96 sample well plate. Thus, this method is highly time and cost effective versus data yield. Analyses to date reveal marked increases (< 2-fold) in the pro-inflammatory cytokines CXCL3, ICAM-1, IL-1-α, IL-6, and TNF-α along with elevations in inflammation resolving cytokine TIMP-1 during three days post-insult. Based upon these response profiles, interventions with existing compounds targeting these mediators are likely to be most effective during subacute or acute phases of injury.

Characterization of a Rat Model of Blast-Induced mTBI: Pathophysiological Interplay of Primary and Tertiary Blast

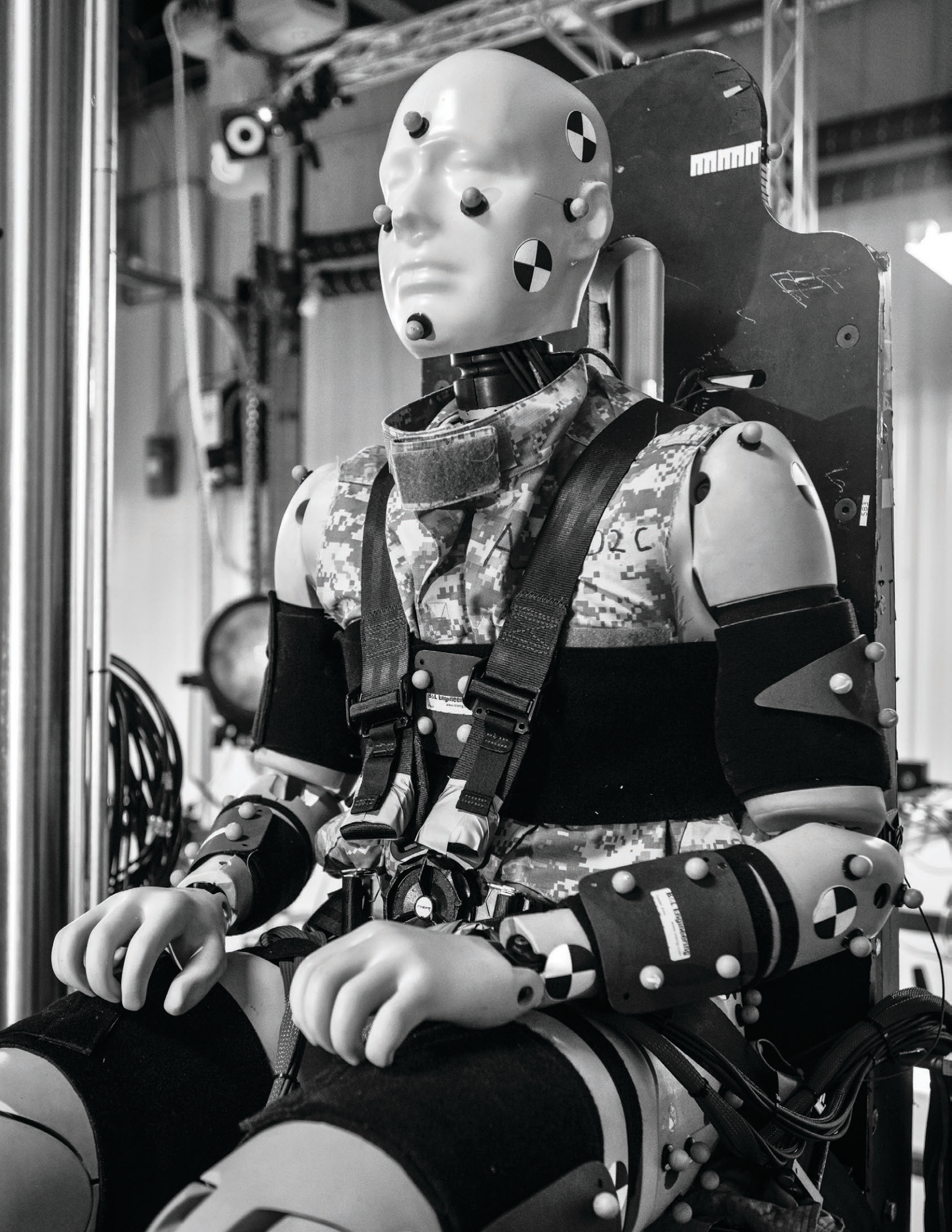
Many Service Members who sustain blast-induced TBI in combat are exposed to a brain insult resulting from a combination of both a shock wave (i.e., blast overpressure) and a biomechanical perturbation related to rapid acceleration and/or impact with a solid object. The TBI resulting from these combined insults is likely to be fundamentally different than that seen from either insult alone. By generating a closely associated insult to the brain (and other organs as well), blast overpressure may interactively compromise the brain's resilience to this additional insult and worsen the pathophysiological consequences that increase the likelihood of long-term deleterious outcome. Working collaboratively with researchers at Duke University and the USUHS, investigators at WRAIR are experimentally combining these biomechanical perturbations in rats to explore this interplay and to characterize the neurobehavioral and neuropathological changes resulting from blast overpressure exposures combined with impact/acceleration. Brain injury sequelae, including disrupted vestibulomotor function and spatial learning and memory, have been characterized and are accompanied by pathological features such as phosphorylated tau protein, which is a recognized hallmark of neurodegenerative disorders, such as CTE. Light microscopic and diffusion tensor imaging (DTI) analysis reveal striking exacerbation of disruptions following combined insults, with prominent microstructural disruptions and axonal injury. These results point to the utility of a "dual insult" model of blast-induced TBI as a valuable experimental tool to assist ongoing efforts to predict and mitigate the risks of blast-induced TBI in Service Members.

Sensitive Indicators and Risk Factors of Blast-Induced Neurodegeneration in Hippocampus

The pressure profile generated from shock tube devices does not match the profile produced by explosives (Chen and Constantini, 2013). To specifically study the effects of realistic blasts, a novel procedure was recently developed by researchers at ARL that generates reproducible shockwaves from a detonated explosive (Zander et al., 2015). The procedure uses a highly controlled construct of research department explosives (RDX), the major component of C-4 explosive and one of the most powerful military explosives. In order to examine the direct effects of explosives on brain tissue, the present study utilized in vitro slice cultures of the rat hippocampus. The hippocampus is the main focus of this study not only due to it being distinctly vulnerable to traumatic and excitotoxic injuries, but also because it is a region that is important for higher order brain functions, which expresses synaptic plasticity to compute diverse information and is involved in routing the encoded spatial, emotional, and reward information to other brain areas. Cultured hippocampal slices were placed in a specialized blast chamber in which defined assemblies of RDX were detonated outside the chamber to produce realistic and reproducible blast shockwaves. This is the first study using the in vitro blast paradigm to apply RDX detonations to intact brain tissue, and showed that multiple explosive blasts alter the levels of important synaptic markers: down-regulation of synaptophysin, synaptotagmin, and synapsin 2b and up-regulation of synapsin 2a. Thus, shockwaves from detonated RDX explosive appear to produce a unique type of pathology comprised of distinct reductions in synaptic proteins before cellular deterioration sets in. Identification of molecular indicators of blast-induced injury to neurons in sensitive brain areas could drive new therapeutic opportunities for mitigating the impacts of blasts to Service Members, independent of materiel solutions.

Development of Methods to Measure and Quantify the Response of Skulls to Blast and Impact Loading

Animal studies are conducted to understand the effect of impact and blast loading on the brain. To extend the understanding we obtain from animal studies to humans, ARL has strived to understand the mechanical response of the constituent materials of the head of animals and human. In ongoing research currently at ARL, skulls from 6-month-old Göttingen pigs were fabricated into specimens and subjected to quasi- static compressive loading while measuring load, far-field displacement, and local strain fields on the gage area of the specimen using optical digital image correlation method. In addition, the microstructure of each specimen was analyzed using a micro-computerized tomography (CT) scan before and after loading to quantify the skull structure. These measurements include porosity and bone volume fraction, structure thickness and separation, tissue mineral density, and anisotropy information (based on construction of the mean interceptor length fabric tensor). The anisotropy data (mean interceptor length fabric tensor) can be used to obtain the orthotropic elastic tensor that represents the complex stiffness of the skull. These experimental results are being used to develop an inverse computational-experimental methodology to estimate constitutive model parameters. In addition, an elasticity-morphology relationship from the literature was extended to represent the modulus variation in the functionally gradient skull structure (bone volume fraction) by calibrating the relationship with the experimentally-derived local moduli. The final goal of these experimental studies is to facilitate the development of a blast loading rate dependent, microstructurally inspired, homogenized material model for the minipig skull. These methods will also be used to develop similar models for human skull. Understanding the response of animal and human skulls will help ARL to understand how animal blast experimental results relate to injury in humans, thus helping develop better Service Member head protection devices to mitigate blast and impact loading to the head of the Service Member.



Evaluation of Prototype Body Sensor System for the Integrated Soldier Sensor System Program

Georgia Tech Research Institute (GTRI) and the Injury Biomechanics Division of USAARL collaborated on studies of GTRI's Body Sensor System, developed in support of the PM SPE Integrated Soldier Sensor System program. These efforts include development of Helmet Sensors, Body Sensor System, Physiological Status Monitor, Data Retrieval System, and Open Architecture. USAARL conducted shock tube testing of fixtures instrumented with GTRI pressure sensors and reference instrumentation, in order to obtain a direct comparison. Shock tube tests were performed at several target pressures and testing orientations, including testing of an instrumented Improved Outer Tactical Vest attached to the full upper torso of a Hybrid II Anthropometric Test Device.

The WIAMan Project

The cornerstone of the DoD's effort to prevent mounted Service Members from receiving skeletal injuries when subjected to the effects of under-body blast is the WIAMan project. The WIAMan project is investigating human response and tolerance to vertical accelerative loads that can produce tertiary blast injuries, and is using that knowledge to create a scientifically valid test capability for evaluating the survivability of ground vehicles during research, development and acquisition. Led by the WIAMan Engineering Office (WEO) of ARL, WIAMan was sponsored in 2010 by the Director for Operational Test and Evaluation (DOT&E) in the OSD to correct a shortcoming in the test technology used for Title 10 Live-Fire Test and Evaluation (LFT&E). The project is funded primarily by the Deputy Assistant Secretary of the Army for Research and Technology and by the Defense Health Program through the ASD(HA). DOT&E recognized a capability gap to assess skeletal injuries when mounted Soldiers are subjected to the rapid vertical acceleration that occurs when a vehicle is attacked by an under-body blast device such as an IED. ATDs are used to assess skeletal injury risk under such conditions. However the ATD currently in use, the Hybrid III, and the injury criteria used with it, were created for frontal automotive crash testing, and are inadequate for under-body blast conditions experienced by Service Members. To close this gap, the WIAMan project is conducting original biomechanics testing to characterize human response to vertical accelerative loading and to define human injury probability curves for skeletal injuries under these conditions. This information will be used to develop a new instrumented ATD that is purpose-built for use in the under-body blast LFT&E environment.

Biomechanics

Using theater injury data from the JTAPIC Program Management Office, and knowledge of the environment experienced by mounted Service Members, the WIAMan project is conducting a major biomechanics test program to gather required information on human response to underbody blast using postmortem human surrogates (PMHS). Testing and analysis is being performed at nine of the top biomechanics universities in the United States: JHU/APL, Medical College of Wisconsin, University of Michigan Transportation Research Institute, Wayne State University, The Ohio State University, University of Virginia, Virginia Tech, Duke University, and Wake Forest University. These efforts are yielding the biomechanics knowledge needed to guide the design of the ATD and to create the injury assessment criteria that will be used with it. The test program considers factors and parameters of interest for understanding initial exposure to blast-induced loading including seating position and posture, the use of PPE, and severity of the loading environment. The current WIAMan biomechanics focus is the development of biofidelity response corridors (BRCs) that are created by conducting sub-injurious testing with PMHS in order to evaluate and quantify biofidelity parameters, such as the time-dependent loading of the skeletal structure, and the resulting local and global deformation and kinematics. A BRC describes the distribution of biomechanic responses measured in PMHS.

Photo credit (opposite page): US Army Research, Development and Engineering Command (RDECOM) and Johns Hopkins University Applied Physics Laboratory (JHU/APL)

Photo credit: Army Research Laboratory

As of 2015, the WIAMan project has completed 14 BRC test series addressing the leg, lumbar spine, cervical spine, and pelvis regions, as well as the whole body. Six additional BRC series are currently in process. The BRCs will become performance requirements of the WIAMan ATD. When the ATD matches the relevant BRCs for a particular loading environment, it is considered to be biofidelic, a suitability requirement for making injury assessments. In addition to BRC tests, the project also conducted exploratory injury testing for the leg, pelvis, and cervical spine. The data are being used to validate that injuries produced in WIAMan testing match those experienced by Service Members in theater, and are also used to assess the validity of hypotheses that have been developed to guide the full human injury test program, which will begin in FY16. When possible, the new biomechanics information or capabilities will produce "spin outs" of knowledge that can be used to enhance the LFT&E injury assessment products prior to the fielding of the WIAMan system in FY21.

Instrumented ATD

In FY15, a technical data package for the WIAMan ATD concept was received through a contract with the Humanetics Innovative Solutions Corporation. Subsequently, a contract for fabrication of the first instrumented WIAMan ATDs was awarded to the Diversified Technical Systems (DTS) Incorporated, which will deliver the first WIAMan ATD technology demonstrator in December 2015. During FY15, DTS delivered parts of the ATD so component-level tests could be performed under the same conditions as PMHS testing (matched-pair testing). This testing provides data that can be used to evaluate biofidelity and refine the design and initial material selections. In addition, DTS has also been developing elements of the instrumentation and data acquisition system (DAS) that will be integrated with the ATD. The WIAMan ATD will use a distributed on-board DAS with a capability to acquire up to 148 channels of data. Load cells are being developed and acquired for use in the technology demonstrator ATD, and development of other elements of the instrumentation and DAS are progressing, including a six-degree-of-freedom accelerometer, the individual DAS units, and communication hubs.

Finite Element Analysis (FEA) Model

FEA is used to model the response and survivability of vehicles subjected to the effects of underbody blast, and an FEA description of the Hybrid III ATD is included in the simulation. However, the Hybrid III FEA model has limited validity for underbody blast loading conditions, and modelers make assessments of the risk of injury by applying the same injury criteria that have been judged to be inadequate for use in physical testing. The WIAMan project will produce an FEA model of the ATD that can support virtual prototyping of vehicle survivability; the WIAMan FEA model will be correlated against test data and suitable for comparison with the injury assessment tools that the project is creating for use with the physical ATD. However, this high-resolution model is not only an end-product, but is also an important tool during the development of the WIAMan ATD. The WIAMan FEA model enables the study of design options and material effects in order to develop an ATD that meets biofidelity and strength-of-design requirements in the fewest possible fabrication iterations.

In a joint FY15 effort among CORVID Inc, JHU/APL, Wake Forest University, and Virginia Tech, the project initiated an aggressive modeling effort and developed a baseline three-dimensional FEA model of the full WIAMan ATD that includes all sensors, and can be used in either the LS-DYNA or Velodyne solvers. As non-metallic materials were selected and fabricated, samples were tested and mechanical response models created which have been incorporated into the WIAMan FEA model. This 1.3 million element model is now in routine use for whole-body simulations, as well as simulation of component-level tests that are being performed for the cervical spine, lumbar spine, pelvis, and leg (including foot and ankle). FEA simulations have already provided extensive support to the project, enabling parametric sensitivity studies, strength-of-design studies for severe loading conditions, material optimization, and for pre-test predictions to guide physical testing of WIAMan ATD technology demonstrator hardware. Coordination meetings on the development of the WIAMan FEA model have been held with several DoD agencies, and several briefings on the effort will be presented at the 2nd Workshop on Accelerative Loading that will be held at ARL in January 2016.

Prolonged Hypobaria During Aeromedical Evacuation and the Effects on TBI

In response to concerns by USAF Critical Care Air Transport Team that prolonged flights during aeromedical evacuation of neurotrauma patients might worsen neurologic outcomes, the USAF sponsored research to investigate the effects of exposing rats to hypobaria at different times after mild or moderate TBI. Following either impact-induced moderate TBI or blast-induced mTBI, histologic and neurologic markers of injury were worsened by six hours hypobaria (=8000 feet altitude), initiated at six, 24, or 72 hours, after injury and six to seven days after injury. Brain injury was also worse when rats were exposed to 100 percent oxygen compared to 21 to 28 percent oxygen during hypobaria. Exposure to two flights at 24 hours and 72 hours caused more damage than one flight at either of these times following impact TBI but not blast-TBI. Following impact TBI, administration of CR8, an anti-inflammatory cell cyclin-dependent kinase inhibitor, improved behavioral and histologic outcomes.

Photo credit: Staff Sergeant Whitney Amstutz/US Air Force

TBI and subsequent hypobaria were accompanied by elevated levels of serum microparticles, which could contribute to systemic inflammation. Changes in gene expression in the brain following blast TBI and hypobaria suggest that drugs that trigger an increase in the expression of cytoprotective genes could be used to improve outcomes in these paradigms. These results support the hypothesis that exposure to aeromedical evacuation-relevant hypobaria within a few days after TBI can be dangerous. They also suggest that levels of inspired oxygen during aeromedical evacuation should not be greater than those necessary to maintain systemic normoxia. Although this study uses a rat model, it underscores the need for more work to be done to understand the human response to air evacuation. However it is important to note that the given the "perfect" time to transport a patient with a brain injury, there are many times when the operational environment and/or other injuries require rapid transport in any available platform.

Prevention of Blast-Related Injuries

This CDMRP-sponsored research project is designed to determine the cause of mTBI due to blast overpressure and, if possible, the human tolerance to blast overpressure. It consists of an experimental portion in which swine and postmortem human subjects are exposed to blast. The experimental effort is supplemented by a computer modeling section that can extend the results of the tests to blast scenarios not easily achievable experimentally. The investigators at Wayne State University have discovered that: The porcine brain is susceptible to blast overpressure and sustains both axonal and neuronal cell body injury when the pressure is high enough (above 400 kilopascal). The measured intracranial pressure (ICP) in the swine brain is generally lower than the incident overpressure with the parietal pressures being the highest and almost equal to the incident overpressure. Preliminary data from cadaver testing revealed that the ICP is also lower than the incident overpressure, even with pressurization of the brain with artificial CSF. Computer models of the swine and human brain in response to blast have been developed. They predict an ICP larger than the incident overpressure and they are looking for mechanisms that can lower the predicted ICP to match experimental observations. This study will result in a deeper understanding of the mechanisms of blast-related TBI and potentially identify human tolerance to blast, including the peak blast overpressure as a function of standoff distance for open field blasts, important in the prevention of blast-related injuries.

Improvement and Extension of Auditory Hazard Models

This work by a team from Applied Research Associates is leading to improved models of auditory injury after blast and other high-impulse noise. Auditory injury is a leading cause of medical referrals for Service Members, and additional work suggests that propagation of blast waves through the ear could exacerbate brain injury. Researchers have previously relied on models, such as the AHAAH model to predict the amount of auditory hazard after blast, however these models have limitations especially in large amplitude impulses. In the current proposal funded by CDMRP, the investigators are refining the AHAAH in multiple model systems to test which protective systems best mitigate auditory injury and protect. Performed at the University of Colorado Anschutz Medical Campus in Denver, Colorado, and the Brooke Army Medical Center in Fort Sam Houston, Texas, the majority of the work commenced in early 2015, and the investigators have already developed a new design for a blast wave emulator that allows for the delivery of high-amplitude acoustic stimuli to specimens in a controlled manner and improves the exposure level and frequency bandwidth of currently available devices. Using this new testing equipment, the investigators have completed testing on multiple postmortem samples and four different hearing protection devices. This preliminary data has led to refinements of the AHAAH model to take into account non-linear elements of hearing protection as some devices have amplitude-dependent responses.

Refinement of this model will aid the development of improved hearing protection devices for Service Members and mitigate the effects of auditory hazards.

Computational Modeling of Primary Blast Injury to the Eye

Researchers from the Johns Hopkins University Whiting School of Engineering are conducting research funded by a DHP grant through USAMRMC's CDMRP Vision Research Program to develop a validated computational model of the human eye globe to investigate injury mechanisms of a primary blast wave from an IED, which has accounted for 70 percent of the blast injuries in Iraq and Afghanistan. The model determines the stresses on and deformations to the eye globe and surrounding supporting structures to enable the development of more effective eye protection strategies. This application includes detailed anatomical and tissue features, and sophisticated mathematical techniques to model the movement of the blast wave and the transfer of energy when the blast wave hits the human face. The team is collaborating with scientists from the ARL to develop a geometric model of the head representing an average 21-year-old male, and models of spectacles and goggles currently approved for military applications. The model simulates the effectiveness of spectacles and goggles in reducing the blast pressure loading on the eye. The simulations reproduced the conditions of field blast in experiments performed by collaborators at the Army Test Center measuring blast pressure at the eye location of an instrumented FOCUS Head form model. Both spectacles and goggles dramatically reduced the peak pressure loading to the eye, but still allowed a small fraction of the blast wave to "under wash" through small gaps and reverberate between the surfaces of the goggles and the face. The goggles permitted a smaller amount of under wash, thus more effectively reducing the peak pressure loading compared to spectacles. The spectacles directed the flow along the lens and away from the eyes through the opening at the temples. However, the tighter fit of the goggles trapped the under wash in front of the eyes for a longer amount of time. As a result, the pressure loading on the eyes behind the goggles became higher than the pressure loading on the unprotected eyes and eyes behind the spectacles after 0.6 milliseconds post-impact from the blast wave.

Combined Effects of Primary and Tertiary Blast on Rat Brain: Characterization of a Model of Blast-Induced mTBI

In a study sponsored by the DoD's CDMRP, researchers at WRAIR acting through the Geneva Foundation have created an advanced blast simulator for the recreation of blast-like conditions in a rodent model of brain injury. Traditional methods of modeling blast utilize a cylindrical shock tube, which has inherent confounds with negative phase and recompression waves, reverberations, and secondary shock in the reverse direction. The advanced blast simulator eliminates these artifacts and creates positive pressure durations, which may better represent IED waveforms. Bad blast simulations have confounded much of the preclinical biomedical blast literature to date, and this newly developed research tool may help provide valuable preclinical insights. In studies with this tool, the research team has found significant increases in neuroinflammation (e.g., CCL2) and the accumulation of brain phospho-tau. Importantly, the enzyme primarily responsible for dephosphorylating phospho-tau, TNAP, was significantly decreased. This finding could provide a mechanistic explanation for increased phospho-tau following TBI and may suggest a target for therapeutic intervention in CTE.

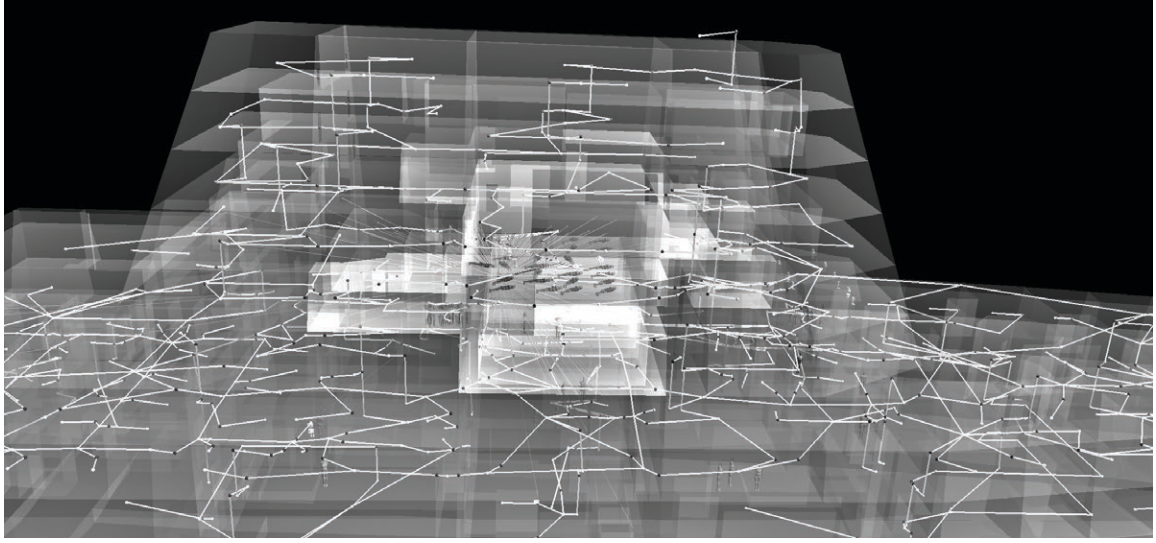
Untangling the Effect of Head Acceleration on Brain Response to Blast Waves

Several mechanisms have been postulated to contribute to blast-induced TBI, including wave propagation, skull flexure, cavitation (bubble formation and subsequent collapse), and head acceleration. Despite numerous experimental and computational studies that have examined how these mechanisms potentially contribute to blast-induced TBI, there is not yet a quantitative description of the specific contribution of each of these mechanisms.

Such a quantitative understanding could be key not only in understanding the etiology of blast-induced TBI, but also in guiding the development of equipment that will offer better protection to Service Members from explosive events. BHSAI, a subordinate organization of USAMRMC TATRC, has initiated computational investigations on the interaction of a blast wave with an animal head in order to determine the contribution of head acceleration to blast-induced TBI. BHSAI scientists developed a shock tube and two-dimensional rat head models and performed blast simulations to quantify the contribution of head acceleration to the biomechanical responses of brain tissues when exposed to blast waves in a shock tube. Biomechanical responses, such as pressure, stress, and strain, are correlated to brain tissue damage, and they provide valuable information on the response of the brain tissue to external mechanical loading, such as blast overpressure. By comparing pressure between the head model that captured all the mechanisms of blast-induced TBI (i.e., wave propagation, skull flexure, cavitation, and acceleration) to an acceleration-only model, BHSAI was able to calculate the relative contribution of head acceleration to blast-induced TBI. In addition, BHSAI investigated the response of the brain tissues to the different orientations of the blast wave. These simulations determined that head acceleration contributes 36 to 45 percent, depending on head orientation relative to the blast wave, of the maximum brain pressure at the coup region (area of the brain directly hit by the explosion), had a negligible effect on the pressure at the middle region, and was responsible for the low pressure at the contre-coup region (the region of the brain across from the coup region). These findings provide important guidance when performing blast-induced TBI experiments on small animals, as they demonstrate that the current practice of measuring rat brain pressure close to the center of the brain would record only two-thirds of the maximum pressure observed at the coup region. Therefore, it is recommended that in order to accurately capture the effects of acceleration in experiments, a pressure sensor be placed near the coup region, especially when investigating the acceleration mechanism using different experimental set-ups.

The Role of PP2A Methylation in Susceptibility and Resistance to TBI and Alzheimer's Disease-Induced Neurodegeneration

An award granted to the Taub Institute for Research on Alzheimer's Disease and the Aging Brain (Columbia University), managed through CDMRP's Peer Reviewed Alzheimer's Research Program, hypothesized that upstream regulators of tau phosphorylation status would be sensitive to the effects of blast. Two proteins that regulated the activity of tau phosphatase, PP2A, were investigated. Overexpression of PP2A methyltransferase, LCMT-1, was posited to result in decreased PP2A activity; while the PP2A methylesterase, PME-1, was expected to increase PP2A activity. Increases in PP2A activity were hypothesized to result in global dephosphorylation of tau, leading to cognitive impairments. Increases in LCMT activity were expected to beneficially maintain or increase tau phosphorylation status. Preliminary experiments showed that tau phosphorylation transiently (24-hour time frame) increased in response to blast in all mice including controls, leading the research team to conclude that tau phosphorylation had reached saturation using the experimental blast model. LCMT overexpression did not appear to overcome the effects of blast on tau phosphorylation. Soon after these preliminary experiments were completed, the research team also observed significant blast-related eye damage. The team posited that cognitive and behavioral results for this study may have been skewed by this damage, as many of these tests require visual cues. Shockwave exposure led to vitreous detachment, photoreceptor degeneration, pigmentary changes, and subretinal hemorrhage in 50 percent of eyes examined from shockwave-exposed mice. As such, an animal model using blast-naïve mice to control for blast-related eye injury was created.



The Human Injury and Treatment (HIT) model provides a comprehensive capability to forecast casualties potentially encountered during combat operations aboard ships—a crucial piece of information that assessments of Navy vessels historically have lacked. (Credit: Office of Naval Research)

Tau was extracted from shockwave-exposed mice and introduced via cannula into blast-naïve animals. Mice were infused shortly prior to testing on each day of a two-day radial arm water maze task with vehicle or tau purified from blast or sham mice. Infusion of tau from shockwave-exposed mice significantly impaired performance when compared to tau from sham-exposed animals. Tau from shockwave-exposed animals also impaired contextual fear conditioning when infused into wild type mice. Similar experiments were done in naïve LCMT and PME-overexpressing mice. The studies showed that LCMT overexpression was protective against the impairments, whereas PME exacerbated the impairment effects. The grant demonstrated that tau phosphorylation status is transiently altered after TBI, and that its status is closely modulated by its upstream regulators. The animal models may suggest new targets for modulating tau phosphorylation status, so that positive cognitive, behavioral and memory outcomes can be achieved after mTBI. It also illustrates that blast studies should account, and control for, blast-related eye damage. This damage can impede further cognitive and behavioral testing after blast which may rely on visual cues.

Human Injury and Treatment (HIT)

NHRC is evaluating the injury prediction capabilities of the ONR's Future Naval Capabilities FY10–FY15 HIT model. The HIT project was designed to support PEO Ship's LFT&E reporting requirements of the PMS-500's (DDG-1000) Damage Scenario Based Engineering Analysis, Littoral Combat Ship's Total Ship Survivability Tests. NHRC has developed a casualty modeling solution, independent of HIT's extant injury generating models. NHRC's medical response models account for abbreviated care, the effects of damage to shipboard medical capabilities, and multi-mechanistic anatomic injuries. This solution allows HIT to satisfy federally mandated testing and evaluation requirements, verify availability of adequately trained medical personnel, and ensure that an effective program is in place to facilitate medical response requirements. NHRC is currently conducting a discovery study to assess the spectrum of injuries output by HIT's extant injury generating models for various ship-weapon pairings and to identify solutions to rectify the injury gap. Improving HIT's capability to simulate realistic casualty streams for various ship-weapon type scenarios is critical to accurately assessing the residual crew capacity (ability to "fight the ship") and medical resource requirements for future US naval combat engagements. Improved injury generating models will pave the way for HIT's verification, validation, and accreditation process.

Operation Brain Trauma Therapy

Operation Brain Trauma Therapy was a unique multi-center, pre-clinical, drug screening and brain injury biomarker development consortium for the ultimate translation of the best potential drugs to clinical trials in TBI.

Operation Brain Trauma Therapy included investigators at the Safar Center for Resuscitation Research (University of Pittsburgh School of Medicine), the Miami Project to Cure Paralysis, (University of Miami School of Medicine), the Neuroprotection program at WRAIR, Virginia Commonwealth University and Banyan Biomarkers (University of Florida). Three rodent models (controlled cortical impact, parasagittal fluid percussion injury, and penetrating ballistic-like brain injury) were used in Pittsburgh, Miami, and WRAIR, respectively, for primary drug screening with the most promising candidate tested in a micropig model at Virginia Commonwealth University. Additional secondary screening of the most promising drugs was also carried out in more complex rodent models with polytrauma, hemorrhage, or advanced monitoring, as deemed appropriate. Operation Brain Trauma Therapy represented a unique resource for pre-clinical screening of new therapies for TBI and evaluation of serum brain injury biomarkers. The consortium was highly productive and valued having tested nine therapies across three rodent models in >1,200 rats with >5,000 biomarker assessments. They have identified levetiracetam as a promising therapy and moved it to testing in micropigs.

Triglyceride-Based, Ω-3 Long Chain Fatty Acid Emulsion for the Treatment of Blast-Induced TBI

The large incidence of blast-induced mTBI in combat casualties has prompted recognition of the need to establish the means to increase TBI resilience to hasten safe return to duty and minimize long-term and delayed TBI-related debilitations in returning Veterans. Using laboratory rats, investigators at WRAIR are establishing whether an ω-3 PUFA-deficient diet (mimicking a contemporary Western diet) promotes blast-induced TBI vulnerability and whether a concentrated ω-3 PUFA emulsion given intravenously immediately following blast-induced TBI serves as an effective countermeasure to blast-induced TBI. These investigators have established that consumption of a high-fat diet deficient in ω-3 PUFAs promotes an increased ω-6/ω-3 PUFA ratio resulting in a pro-inflammatory state following blast-induced TBI. The ω-6/ω-3 status is significantly reduced by a continuous intravenous infusion of the ω-3 enriched emulsion over five days following blast-induced TBI and is accompanied by significantly improved clinical outcome as measured by neurobehavioral testing. These researchers conclude that the intravenous infusion of a ω-3 enriched emulsion is an efficacious treatment for the management of blast-induced TBI in this rodent model and may represent a safe and effective therapy for blast-induced TBI in military Service Members.

Protective Equipment

Primary Blast Wave and Protective Eyewear Studies

Deployed Service Members are at particular risk of a spectrum of ocular injuries caused by blast. The spectrum includes penetrating and closed globe eye injuries, retinal detachment, eye rupture, intraocular hemorrhage, corneal lacerations, optic nerve damage, among others. To help protect Service Members from these injuries, the Authorized Protective Eyewear List was adopted in 2006 and incorporated acquisition guidelines for ballistic protection. However, there is growing laboratory evidence that the primary blast wave may cause significant ocular as well as higher visual system injuries. Researchers from USAARL evaluated the protection provided by current protective eyewear by evaluating pressure wave dynamics at the cornea in an instrumented headform. Eyewear protection coefficients were calculated using peak and integrated pressure readings. In general, goggles provided the greatest protection and eyeglasses were only slightly effective for frontal blasts. For oblique blast angles, eyeglasses actually potentiated the blast wave by creating higher pressures at the cornea. Oscillations in the time pressure recordings provided evidence of increased turbulence caused by some eyewear and this could lead to increased shear forces on ocular tissue. Computational modeling efforts led by BHSAI are confirming USAARL's findings.

The USAARL team's findings suggest that current eye protection, designed to reduce secondary and tertiary blast injuries, may provide insufficient protection against primary blast wave. Showing that foam inserts can reduce the energy impact on the eye may lead to optimized eye protection in the future.

Crew Turret Structural Modifications for Improved Service Member Survivability

Under the US Army M1A2SEPV3 program, the Product Manager, Abrams Tank System initiated an effort to improve crew survivability from underbody blast by making several seating, structural, and component mounting modifications to the crew turret area of the tank. These modifications were made to reduce the amount of shock transmission from underbody blast into the turret basket and seats, thereby increasing crew survivability during these types of events. Specifically, shock mounted seating systems to allow seats to move independently of the floor; stiffened structural components for increased turret basket support; modified supports to keep Service Members feet off of the turret basket floor to minimize lower leg injury; and removal, rerouting, and shock mounting of components under the turret to lessen transmitted loads from components into the turret basket were all incorporated into the overall survivability solution. Ballistic validation testing continues through early FY16. All changes are scheduled to be incorporated into the M1A2SEPV3 production beginning in FY17. All modifications scheduled for incorporation into the final design have demonstrated, via ballistic testing, to drastically reduce crew injury and turn previously unsurvivable underbody attacks into survivable events for the crew (results are classified).

Parametric Optimization Study

Under the US Army's Future Fighting Vehicle (FFV) Program Bridge Extension Contract, General Dynamics Land Systems researchers performed a parametric optimization study on armor materials and thicknesses. The study was completed in mid-April 2015, and the results were briefed to Product Manager FFV on 29 April 2015. The study showed that by intelligently forming the underbody shape, aluminum, at the same areal density as steel, performed better due to the improved stiffness characteristics of a thicker material. Additional technical detail is available, but the information is competition-sensitive, and requests for it should be directed to Product Manager Armored Fighting Vehicle. This data was used to inform future designs for FFV. Under the FFV Phase 1 Science and Technology contract, all proposed designs now use an aluminum underbody.

Free Falling Heel Support Seat Base Side Mounted Foot and Leg Energy Absorbing Mechanism

US Marine Corps Systems Command Program Manager for the Light Armored Vehicle tasked the US Army Tank Automotive Research Development and Engineering Center (TARDEC) Center for Systems Integration to lead an effort to develop several kits that would improve the light armored vehicle's survivability and buoyancy. During this effort, the Center for Systems Integration team, in collaboration with ARL, developed a new concept breakthrough that has the potential to vastly improve the survivability of vehicles with regard to lower leg injury. The project team developed the Free Falling Heel Support Seat Base Side Mounted Foot and Leg Energy Absorbing Mechanism. Analysis on this concept has shown significant improvements, up to 75 percent lower compressive loading on the leg, over an energy-absorbing pad or typical foot rest. Unique to this design is the ability to allow the foot to slide out to prevent an excessive compressive loading on the leg, but still provide support so that the Service Member is comfortable. Implementing this unique design could significantly reduce Service Member lower leg injuries due to blasts.

Three-Dimensional Flail Zone Creation for Occupant Centric Platform Design

Occupant Centric Platform Technology Enabled Capability Demonstration tasked ARL to develop three-dimensional flail zones for head, arms, and legs, based on the two dimensional strike envelope information extracted from the Aircraft Crash Survival Design Guide (1989).

The strike envelope was based on the 95th percentile Army aviator, wearing restraints. Data was gathered using a 95th percentile ATD subjected to (-Gx) acceleration of 30G in a forward motion. This data was then extrapolated to create the expected lateral motion of an occupant. ARL utilized the Large Overall Male and Small Overall Female boundary manikins to bookend the central 90 percent of the Army Service Member population. The flail zones were exported for use in a computer-aided design to drive component placement inside of the occupant workspace, support space claim for energy absorbing materials, and visually show where impact hazards may exist. Implementing these unique flail zones could significantly protect the Service Member from contact injuries caused during vehicle impact and blast events.

Developing a New Analysis of Manikin Data (AMANDA) Model to Streamline and Improve Processes for Accelerative Injury Analyses for LFT&E Underbody Blast

During a LFT&E underbody blast event, biomechanical response data from acceleration is collected, processed, and analyzed. These data are used to assess injuries associated with the accelerative loading measured during the test, and to determine the cause of these injuries in order to ultimately identify vehicle design changes that prevent injury from underbody blast. Numerous tools and processes are required to generate the ARL's current and legacy accelerative injury analyses for LFT&E underbody blast. This suite of tools and processes are laborious and prone to introduce human error. Based on knowledge and experience in accelerative loading and associated underbody blast injury analyses, enhancements were made to the model and processes to streamline and improve the efficiency, accuracy, and timeliness of accelerative injury analyses by ARL's Survivability/Lethality Analysis Directorate. This directorate developed a single software package under one configuration-controlled model, AMANDA, for release in FY16. The new version of AMANDA has reduced the number of steps, tools, and cycle time by a minimum of 60 percent. The model has been designed to be easily extendable to support the forthcoming WIAMan manikin and associated injury criteria to enhance LFT&E practices ground vehicles for underbody blast threats. It has been transferred to the Blast Protection for Platforms and Personnel Institute for its use. While the previous process shortcomings did not negate the ability to perform analyses, addressing them improves quality and performance, ensures on-time delivery of accurate products, and reduces the number of steps, human error, time, and cost to produce a high-value product for program offices and evaluators for LFT&E.

Assessment of Soldier Protection System (SPS) Protective Undergarment (PUG) and Protective Overgarment (POG) Performance from Underfoot Blast Testing

This testing and analysis quantifies the effectiveness of various material solutions designed to protect the urogenital region from damage mechanisms produced from underfoot blasts. ARL designed and developed a customized pelvic protection manikin that is used to specifically evaluate PUG/POG systems. It was developed to evaluate ballistic protection to the area of coverage of PUG/POG systems and examine protection to dismounted Service Members from buried mines or IEDs. The pelvis component of the manikin is a bio-simulant to capture penetrating debris effects. Its composition agrees with the penetration mechanics of muscular-skeletal tissue. The design of this pelvis component allows for post-event injury analysis of the manikin. The report is being used by PEO Soldier to determine which protective solution to purchase. The methodology developed will be used for future acquisition decisions.

Engineering Analysis of Ground Vehicle Systems

ARL supported the MRAP program on multiple fronts in FY15. Title X LFT&E engineering involved ARL co-authoring test plans with the Live Fire Integrated Product Team. ARL assessed vehicle failures and crew injuries that were incurred in underbody blast testing and made mitigation recommendations to the Army Program Office MRAP, and the USMC Program Manager MRAP.

For FY15, the aforementioned pertains to Medium Mine Protected Vehicle Type I (RG-33L/Panther), Medium Mine Protected Vehicle Type II (RG-31), and the Navistar MaxxPro DASH Ambulance. ARL supported the USMC Cougar Seat Survivability Upgrade kit evaluation and procurement. ARL's engineering analyses and physiological evaluations of underbody blast tests validated the improvements made by the new energy attenuating crew seating design. Reductions in number and severity of lumbar injuries were recorded at "beyond objective level" threat sizes. ARL's damage assessment briefings, presented during Title X Live Fire Testing of the MRAP Cougar, serve as a foundation for the Cougar floor improvement/redesign. ARL's engineers and physiologists will assess the performance of the new floor designs when full-scale testing comes to fruition, providing data to the Program Manager for positive acquisition of a solution that meets their performance criteria. The new floor design is expected to raise the performance of the floor to that of the seat survivability upgrade so that the system performs acceptably, with reduced number and severity of lower leg and lumbar injuries, and beyond objective level threats as detailed in the design specification. The assessments will be used for future acquisition decisions and to support vehicle modifications to increase the survivability of the systems under test.

Affordable Protection from Objective Threats ManTech Program (Vehicle Underbody)

The ARL is executing an Affordable Protection from Objective Threats ManTech program developing manufacturing processes required to produce aluminum hulls capable of withstanding very large net explosive weight underbody blast threats. The manufacturing processes investigated include forging, forming, and advanced welding technologies. Lower hulls have been successfully fabricated using each of these manufacturing paths, and have been live-fire blast tested on a massive test fixture. One forged hull has been, and one formed hull will be, integrated into ballistic hull and turrets. Vehicles equipped with demonstrated technologies can withstand greater blast impacts than current systems with significantly less blast effects to vehicle occupants.

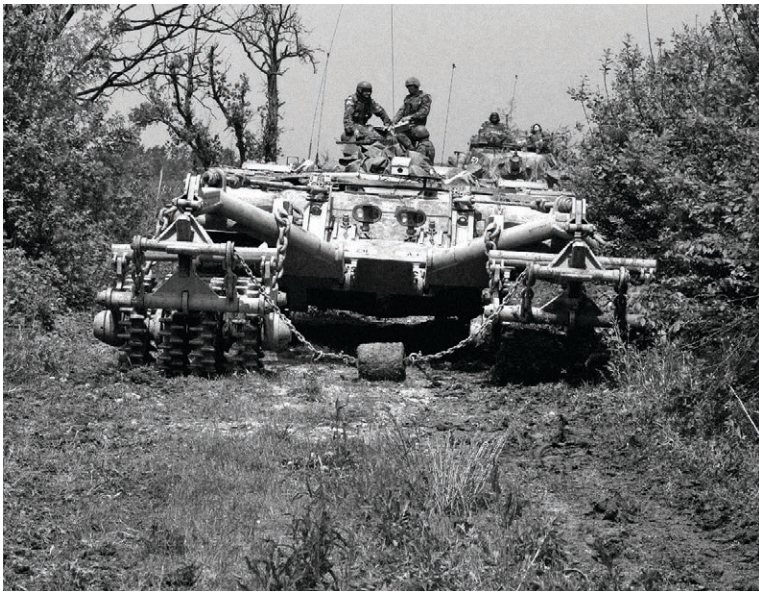


Photo credit: Staff Sergeant Jon Long/U.S. Army

Vehicle Occupant Protection

The following efforts were conducted to lighten the vehicle structure and reduce the probability of injury during underbody blast events.

Composite lightweight structure for blast energy mitigation: In FY15, ARL collaborated with the industry and completed various areas of investigation for vehicle occupant protection. Lightweight composite panels were developed and live-fire tested. The panel was designed to absorb blast energy and provide protection simultaneously. The test results were compared with steel and aluminum based vehicle structure materials. The hybrid composite structure can potentially reduce the weight and enhance ballistic performance.

New generation Dyneema composite for ballistic protection: A complete evaluation of the new generation polyethylene composite (Dyneema HB212 and X245) was conducted. The V50 ballistic performance of Dyneema panel was obtained using .22 and .30 fragment-simulating projectiles. This evaluation provides a foundation for new initiative of scale-up for manufacture, and the future Army application in personnel and vehicle protection.

Photo credit: Staff Sergeant Richard Andrade/US Army

Electromagnetic blast sensors: An electromagnetic sensor that can detect electric and magnetic fields generated by the detonation of explosive was developed and evaluated at ARL. The sensor development can provide a much-needed sensing capability for countermeasure.

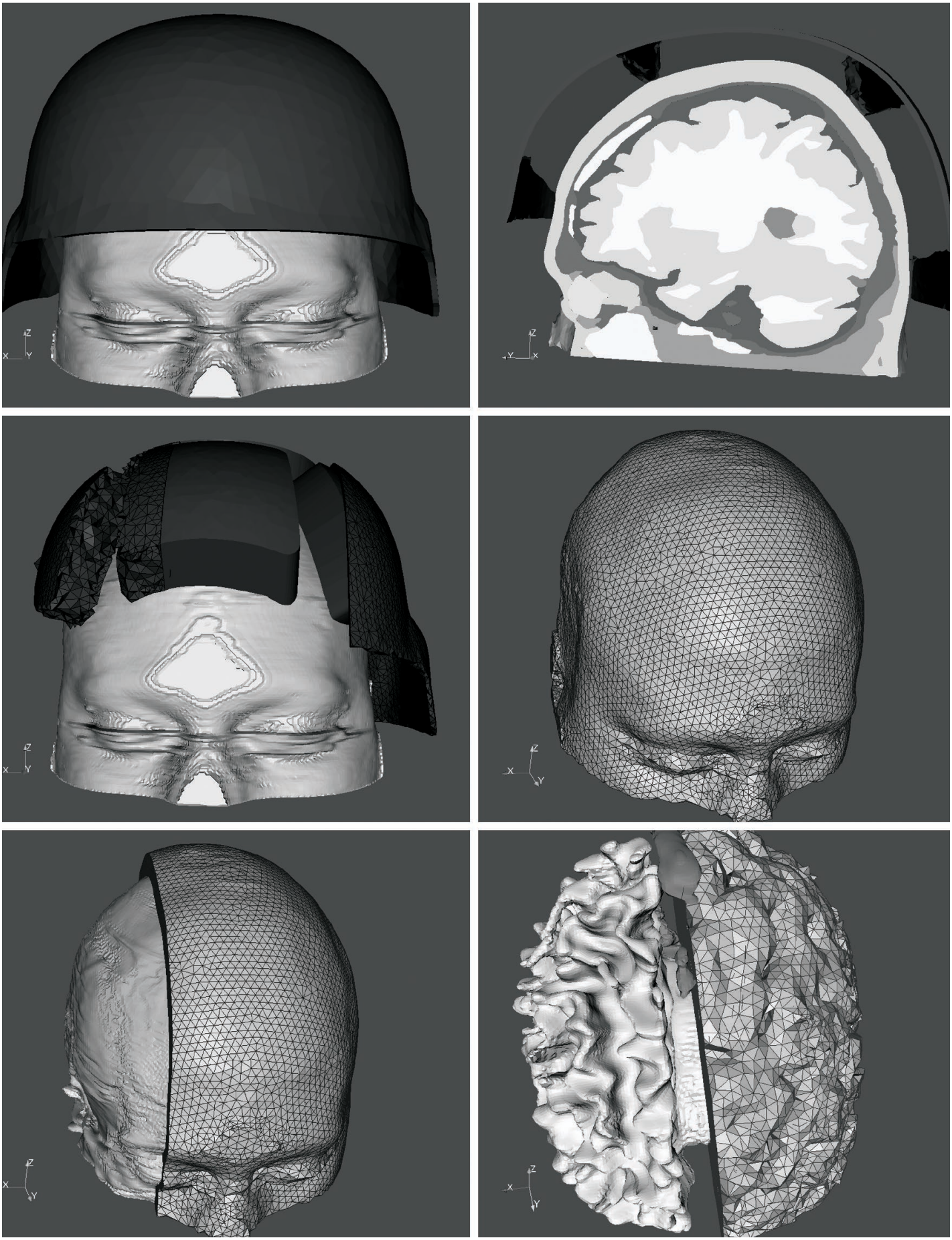
Dual-stage energy absorbing concept for vehicle occupant protection: A dual-stage energy absorbing concept was demonstrated for protecting vehicle occupants from underbody blast. The concept utilizes a novel shock-absorbing floor and seat mechanism to mitigate energy transmission to mounted Service Members. The protection scheme was integrated into a 30-ton surrogate ground vehicle structure and tested under elevated threat conditions. Test results proved the concept highly effective at reducing injury to the lower legs and spinal column of seated occupants at a high level of blast threat. The result confirms performance predictions obtained through computational modeling and simulated blast testing in a controlled laboratory environment.

Product Manager Soldier Protective Equipment (PM SPE) SPS Program

The PM SPE received a Milestone B approval 29 May 2013, for entrance of the SPS program into the engineering and manufacturing development phase. The SPS program is an Acquisition Category III program consisting of an integrated system of Torso and Extremity Protection, Vital Torso Protection, Integrated Head Protection System (IHPS)—which provides protection against multiple threats associated with blunt trauma, ballistic projectiles, fragmentation munitions, IEDs, and indirect fire—and the Integrated Soldier Sensor System. The SPS is designed to be worn by both mounted and dismounted Service Members during the full spectrum of combat operations. While developing an integrated modular, scalable, and mission-tailorable protective system with improvements over the Interceptor Body Armor, PM SPE will also be establishing and validating an enduring requirement to ensure Service Member protective capabilities are developed and sustained. Each subsystem is now its own program of record. Torso and Extremity Protection and Vital Torso Protection had their Milestone C reviews third-quarter FY15. IHPS is scheduled for its Milestone C first-quarter FY17, with Integrated Soldier Sensor System scheduled for the second-quarter FY17. The SPS will be the future system fielded to Service Members to protect against the user-identified threats, to include blast.

Pelvic Protection System (PPS)

The PPS is a two-tiered system designed to provide protection against ground-based IED blast events, and is provided to every Service Member deploying to Afghanistan. The PUG is worn next to the skin, and provides protection of the pelvis, femoral arteries, and lower abdominal organs in a blast or fragmentation event. The PUG also reduces the penetration of dirt and fine debris into a wound area to help prevent infections. The groin area of the PUG has enhanced ballistic protection that offers greater protection to reproductive organs, and the PUG has femoral ballistic inserts that are designed to protect against larger fragments. The POG is worn over the Army Combat Uniform trousers and provides fragmentation protection for the pelvis and lower abdominal organs. The POG provides the same level of overall fragmentation protection as the Improved Outer Tactical Vest. Previous field data clearly shows that the PPSs prevent serious injuries to the pelvic region and is saving lives.



Credit: Defense and Veterans Brain Injury Center/MIT Institute for Soldier Nanotechnology

PM SPE continues to leverage all Service Member input, feedback, and ongoing PPS assessments, along with working with industry to ensure the constant evolution and incremental improvements of pelvic protection and to improve the overall user acceptability and rate of wear by reducing the aerial density and weight, while striving to improve ballistic performance. These improvements have already influenced requirements for the next generation of pelvic protection, which is a component of the SPS.

Interceptor Body Armor Blast Injury Mitigation

The components of the Interceptor Body Armor system, to include the Soldier Plate Carrier System and the Improved Outer Tactical Vest, combined with the employment of hard armor protective inserts, have clearly demonstrated their benefit in mitigating blast injuries in theater. Research by Project Manager Soldier Protection and Individual Equipment (PM SPIE) Technical Management Division is underway to help understand the level to which a Service Member is protected by his body armor system when impacted by rifle and fragmentation threats. Sensor development and testing has been conducted to determine the direct measurements of the static and dynamic loading characteristics including force, pressure, and time responses, which is expected to more accurately correlate the ballistic performance of the system to actual injuries. Other ongoing research includes the measurement of forces found behind different types of personnel armor after a ballistic or fragmentation impact. PM SPIE directed and resourced Aberdeen Test Center to conduct numerous free field and shock tube blast overpressure tests during developmental testing of the vital torso protection subsystem of SPS.

Maxillofacial Protection for the Mitigation of Facial Injuries and Blast Wave Propagation

Researchers at the University of Nebraska at Lincoln, with support from PM SPE, have demonstrated that the addition of a maxillofacial system (mandible and visor) to a combat helmet not only provides increased ballistic and blunt impact protection to the face but also mitigates blast waves. The additional mass added by the maxillofacial system and its design mitigates the effect of blast waves to the head by disrupting its propagation and reducing the resulting pressure that is imparted on the head. This documentation allowed for the remaining maxillofacial systems (100) to be provided to a unit to conduct continental US training and to utilize when deployed outside the continental US. Feedback gathered from the unit refined the maxillofacial system and influenced requirements for the next generation of head protection—the IHPS, a subsystem of the SPS. Development of the IHPS also has provided technology that may be backwards compatible with the currently fielded Advanced Combat Helmet (ACH). PM SPE is exploring the operability of maxillofacial protection upgrade kits for the ACH. Preliminary data from an August 2015 user evaluation of ACH maxillofacial upgrade kits show that they meet user acceptability criteria.

IHPS for Mitigation of Facial Injuries, Blast Wave Propagation, and Blast Fragmentation

PM SPE is developing the IHPS with an integrated maxillofacial protection subsystem comprised of a removable mandible and visor. The IHPS maxillofacial protection subsystem protects mounted Service Members, such as turret gunners, from common blast fragments. The IHPS also leverages the lessons learned from research completed in conjunction with the University of Nebraska at Lincoln to effectively mitigate blast overpressure events under operationally relevant threat scenarios. In July 2015, PM SPE conducted limited live-fire blast testing of the IHPS maxillofacial protection subsystem at Dugway Proving Grounds in the turret of an RG-33 MRAP vehicle. These test results showed a peak overpressure reduction of 10 percent on the left side of the head (which was exposed to a greater reflective pressure hazard), 37 percent on the right side of the head, 55 percent on the top of the head, 38 percent on the back of the head, and 96 percent on the front of the head.

The IHPS will maintain the increased level of blast fragmentation protection provided by the Enhanced Combat Helmet (ECH). The IHPS will provide superior protection from a wider variety of explosive threats than any previously issued standard combat helmet. Milestone C is scheduled for first-quarter FY17.

Reduction and Prevention of Eye Injuries

In collaboration with USAPHC, PM SPE is preventing and reducing the severity of eye injuries through the issue and use of ballistic fragmentation protective eyewear through the Military Combat Eye Protection program. Every Service Member is provided with military combat eye protection that was evaluated, tested, and acquired by PM SPE. Since the implementation of Military Combat Eye Protection program in 2004, the number of eyewear injuries has decreased, while the number of attacks and blast events seen by the Service Member continued to increase. In addition, eyewear injuries seen from these events were less severe (reduced on the abbreviated injury score by one or more) than those who were not wearing eye protection. PM SPE continues to monitor Service Member feedback and injury data to improve the protection of the eyewear and reduce eyewear injuries. Information gathered directly influenced requirements for the next generation of eye protection: the Transition Combat Eye Protection, a subsystem of the SPS.

Helmet Coatings for Mitigating Blast Acceleration on Helmets

A series of test panels, based on combat helmet architecture, were provided by DuPont Corporation under an ONR-funded joint cooperative research and development agreement (CRADA) with NSWC Carderock Division for developing helmet technology to mitigate blast exposure to the brain. Use of panels was a lower cost alternative to testing full-size helmet shells used in previous work.

In the previous effort, two external helmet coatings, ST225 and Nanosonic's Hybridsil, were identified for mitigating injury levels. The focus of the effort using the panels was to identify alternate coatings that would indicate further improvements in lowering blast exposure. Based on levels of acceleration produced, two additional coatings with even further potential were identified, a polymer matrix containing hollow silicon carbide microspheres, designed by the NRL, and a sculpted design manufactured at the NSWC Carderock Division. Further efforts will include adding these coatings to helmets and testing their behavior with respect to blast mitigation.

Sensor-Based Stabilized Remotely Operated Vehicle—Waterborne IED Identification and Neutralization

The Sensor-Based Stabilized Remotely Operated Vehicle is a remotely operated vehicle is designed to mitigate underwater explosive threats to US warships and infrastructure using a stabilized vehicle and precision manipulator. Sensor-Based Stabilized Remotely Operated Vehicle will serve to enhance US Navy EOD Diver situational awareness, and allow EOD Divers to stay out of the blast zone and interrogate explosive threats from a safe distance. JIDA RDT&E support for the Stabilized Remotely Operated Vehicle culminated in a successful demonstration of its vision enhancement and its motion-stabilized interrogation capabilities at the Patuxent River ONR Demonstration in September 2015.

Micro-Tactical Ground Robot

The Micro-Tactical Ground Robot is a man-portable, counter-IED robot that can be used for the inspection and interrogation of explosive threats while allowing EOD personnel to maintain a safe standoff distance. In FY15, JIDA funded a repeater development effort that enables the Micro-Tactical Ground Robot to operate in radio frequency-restricted environments, such as tunnels and culverts. These repeaters extend Micro-Tactical Ground Robot's range far beyond line-of-sight operations and allow even further standoff from explosive threats than previously able.

Product Manager Heavy Tactical Vehicle (PdM HTV) Heavy Equipment Transporter (HET) Urban Survivability Kit (HUSK)

The M1070 HET is a military logistics vehicle used to transport, deploy, and evacuate heavy military vehicles. The M1070 HET and M1000 semitrailer, together, comprise the Heavy Equipment Transporter System (HETS).

Photo credit: Mass Communication Specialist Third Class Kristin L. Grover/US Navy

The HETS is capable of transporting and evacuating vehicles as large as the M1 series battle tank on highways, unimproved roads, trails, and level cross-country terrain. The M1070A1 Heavy Equipment Transporter (HETA1), unarmored, was approved for Type Classification Standard and Full Material Release on 9 May 2012. Production of the HETA1 ended August 2014 with a couple thousand produced. PdM-HTV strives to continually improve the HETA1 fleet's protection level. That improvement comes in the form of the HUSK. The HUSK is an armored replacement cab for the HETA1 that provides the Service Member MRAP-level protection. The HUSK will provide increased protection for the cab occupants by including the latest protection technologies. PdM HTV and TARDEC began the development of the HUSK in 2014. The project advanced through Preliminary Design Review and Critical Design Review, successfully demonstrating that performance and cost requirements would be achieved. Modeling and simulation was used extensively through the design process. It was completed third-quarter FY15 and determined that the design would meet the desired protection levels. A HUSK production contract is targeted for FY18. The plan is to produce enough HUSKs to protect the current fleet meeting the 2014 Tactical Wheeled Vehicle Strategy initiative.

Palletized Load System A1 Underbody Protection Kit

Building on the success of the HEMTTA4 Underbody Protection Kit and the similarities of the HEMTT4 and Palletized Load System cabs, automotive testing was conducted by PdM HTV to prove out the HEMTT Underbody Protection Kit on the Palletized Load System cabs. Testing began early FY15 and has been successful. Transportability lift testing is scheduled to be completed in early FY16. The successful completion of testing will ensure that Palletized Load System cabs adequately protect Service Members at an MRAP-level of protection.

M915A5 Underbody Protection Kit

PdM-HTV's Line Haul Fleet is also investigating improvements to crew protection. Over the last few years, PdM HTV worked with Rock Island Arsenal to design and create prototypes of kit, and now TARDEC has joined the effort to predict blast behavior via simulation. With the success of the modeling and simulation, changes to improve the kit are now being investigated. Further simulations will be conducted to verify design improvements. The work completed to date provides the confidence to support live-fire testing, and ultimately to provide the ability to protect Service Members at an MRAP-level of protection.

Investigation of Injuries to Armored Vehicle Personnel Subject to Blast: Preliminary Study with Emphasis on Lower Extremity Fractures

Severe lower extremity injuries are being reported from occupants of MRAP vehicles exposed to under-vehicular blasts. Both the etiology of these injuries and effective means to predict these injuries are not currently known or understood. This proposal is developed to study both the mechanisms of injury from these loads, as well as to develop lower extremity injury criteria that can be immediately implemented in vehicle design. This study sponsored by MOMRP aims to identify the mechanisms of injury sustained by MRAP vehicle occupants during under-vehicular blasts. By identifying the threshold levels of injury, an injury criterion will be developed allowing designers to predict injury in their designs before fielding. By creating this injury criterion, existing numerical models can predict injury at load rates seen in theater, and optimize systems of injury mitigation and prevention. This team has created an underbody blast simulator named ODYSSEY. The simulator has been used to test and improve the Finite Element Model of lower extremity fractures to be more accurate to military needs. This specific model has also developed tibia and fibula fracture thresholds for injury criterion. Several additional experimental tests were performed in this study: 1) a test of sub-calcaneal heel pad component testing; and 2) an evaluation of injury-mitigation materials using the Hybrid-III Finite Element Leg Model. The results of these studies have helped supplement the data produced by the WIAMan program and identify remaining research gaps that will provide better protective equipment.

Evaluation of PPE on Operator Movement and Performance (Survivability)

The Computer Assisted Rehabilitation Environment (CAREN), traditionally used for rehabilitation purposes, is being employed in a unique way at NHRC. Service Members are meeting opposing forces and hostile situations with greater loads as the emphasis on PPE continues to rise. These very same loads, when carried into battle, pose other risks of injury and performance deficits for US Marines and operators from other US military branches. The trade-off between surface-area protection by armor plates and the ability to move quickly and with agility translates directly to survivability. As a result, an inverse relationship is seen: As body armor increases adding more weight and gear, it is believed that mobility decreases, making it more difficult for the Service Member to maneuver efficiently and quickly, and vice versa. The Physiological and Cognitive Operational Research Environment team, within the Warfighter Performance Department at NHRC, is using the CAREN to measure survivability by comparing the effects of varying PPE on vision, range of motion, and performance on marksmanship tasks and other tasks relevant to the Service Member. Sponsored by the ONR and USSOCOM, equipment that is being tested ranges from that currently used by the different branches of the DoD, to novel designs that are being designed, including those from Product Manager Infantry Combat Equipment and the USSOCOM Tactical Assault Light Operator Suit program.

This gear is being designed to reduce Service Member injury both acutely (e.g., blast injury, etc.) and long term (e.g., lower back pain). The balance between maneuverability and PPE is not only integral to the success and safety of the individual Service Member but also has bearing on the overall success of a mission.

The goal of the gear being designed is to reduce Service Member injury both acutely and long term. The NHRC Physiological and Cognitive Operational Research Environment team is integral in the process of developing PPE that meets the many criteria required for both short- and long-term requirements.

Effectiveness of the Combat PPS in the Prevention of Genital and Urinary Tract Injuries: An Observational Study

Historically, the incidence of genital and urinary tract injuries in major conflicts has been approximately 5 percent. In a report by the US Army Medical Department, the rate of genital and urinary tract injuries increased to 12.7 percent in 2010 from 7.2 percent in 2009. The majority of these devastating lower extremity and pelvic injuries, including external genital injuries, stem from a blast when Service Members encounter IEDs on foot patrols. In response to the increasing incidence of genital injuries, and to mitigate the risk of blast injury to the external genitalia, the United States and United Kingdom issued protective overgarments and undergarments to troops deployed in support of OEF. These two systems combined constitute the PPS.

NHRC collaborated on this research in an attempt to evaluate if PPS use is associated with a reduction of genital and urinary tract injuries in subjects exposed to dismounted IED blasts. Two groups were identified for comparison: those who were confirmed to have worn the PPS at time of injury (n = 58) and a historical control group who were confirmed as not wearing the PPS (non-PPS; n = 61). Patients with any level of lower extremity amputation from a dismounted IED blast mechanism were included. Injury information for each of the patients was identified using NHRC's Expeditionary Medical Encounter Database (EMED), with the primary outcome measure as presence of a genital and urinary tract injury on admission. The study found that the mean injury severity score (ISS) was higher in the PPS versus the non-PPS group (26.1 versus 19.3, p = 0.0012). Overall, 31 percent of the patients in the PPS group sustained at least one genital and urinary tract injury versus 62.3 percent in the non-PPS group. The odds ratio of sustaining a genital and urinary tract injury in the PPS group as compared with the PPS group was 0.28 (31 percent versus 62.3 percent; 95 percent confidence interval, 0.62–0.12; p = 0.001). The most frequent injures were open scrotal/testes wounds, followed by open penis and open bladder/urethra injuries. The use of the PPS is associated with a decreased odds ratio of genital and urinary tract injury. Despite a 31 percent absolute reduction, future work should focus on improved efficiency.

In this observational study, the use of body armor that specifically addresses the perineal and groin area is associated with a decrease in the odds of genital and urinary tract injury. This conclusion, along with the body of literature from other studies that have shown inverse relationships between the use of body armor and penetrating injuries to protected body regions, provides strong support to the use of protective armor to mitigate injury. Injury mitigation and prevention is a primary objective for improving medical outcomes for the Service Member.

Polymer Coating for Protection Against TBI, Enhanced Ballistic Performance, and Helmet Testing against IEDs and Close-in Explosive Charges

ONR continues funding NSWC Carderock Division and its joint CRADA with DuPont Corporation. This effort focuses on the application of polyuria (a high strain rate, high pressure sensitive polymer) with and without special inclusions, applied as coatings on helmet shells supplied by DuPont.

A large series of close-in tests (54 separate cases) were performed on highly instrumented and helmeted manikins at the NSWC Carderock Division blast pit facility, and follow-on testing was completed at the NSWC Explosive Ordnance Disposal Technology Division against two large surrogate IEDs and an additional engineered IED configuration, which focused the blast energy more directly on the manikins. Test pressures for the IED tests were equivalent to those at the test pit, but the applied impulse was an order of magnitude higher.

The blast pressures were oriented to the conventional Bowen injury curves, but the detailed intracranial exposure is being studied from a power-intensity aspect, combining impulse and acceleration levels. This relationship derives from a postulate published by Arthur E. Hirsch (David Taylor Model Basin, 1966) with respect to blunt trauma injury. The intent is to also explore crossover between the blast and blunt trauma exposure conditions. The helmets produced from the shells, which are fabricated with advanced ballistic fabrics, are weight-neutral compared to the conventional ACH and ECH after the coating is applied. The coatings were applied by Nanosonics Corporation of Virginia (spray-on) and by the NRL. In addition to testing the blast and ballistic mitigation capabilities of these coatings, testing was conducted to examine the capability of these coatings to suppress penetration from sharp-edged flechette-type devices. This testing showed that these coatings exhibited significant defeat capability on helmet-configured panels for this purpose. This has illustrated an added potential benefit of the coatings for special operations type environments. Results were verified against actual IEDs and several close-in explosive tests and using acceptable intracranial exposure levels, impulse, and acceleration criteria. The proposed polymer coated helmet exceeds MIL-STD ballistic requirements, while satisfying all other MIL-STDs. In addition, the coating, while enhancing the helmet performance for protection against mTBI, ballistic, and weight requirements, offers at the same time protection against sharp-edged flechette-type devices.

Polymer Coating Protection against mTBI

ONR has continued funding researchers at the NRL to develop techniques for applying elastomeric polymer coatings with high strain rate sensitivity to combat helmets to improve on ballistic performance, and at the same time minimize mTBI. The NRL has been developing modifications of the ACH to address TBI that results from transfer of a blast wave through a helmeted head. The NRL has been substituting a portion of the resin used in the ACH with an active layer of material, comprised of a rate-sensitive polymer and hollow Silicon Carbide spheres. This active layer both dissipates the blast energy and disperses the blast wave. Tests were carried out over a range of blast pressures from moderate to severe (14–45 psi). The NRL designs attenuate the blast pressure transmitted through the helmet, providing reductions in acceleration of 41 percent and in velocity of 33 percent; commensurate decreases in displacement were also observed. These improvements were obtained with helmet (or equivalent panels) 10 percent lighter than the current ACH. Additionally, preliminary tests showed equivalent ballistic performance. mTBI injuries occur without skull fracture, potentially bruising the brain and damaging blood vessels and nerves. The damage mechanisms include acceleration (impact) and deformation (compression and shear) of the brain. However, the current detailed understanding, including subtleties in the coupling of the helmet, skull, and brain, is insufficient to allow correlation of brain injury to the characteristics of the blast wave. For this reason, it is necessary to focus our research on all measurable aspects of blast wave transmission through a helmet.

Improved Underbody Protection Design Excursion

Under the FFV Program, the Program Manager Armored Fighting Vehicles has requested that each contractor create a clean-sheet design for a new infantry fighting vehicle that can resist 5X underbody threats as the threshold level. This can be achieved through advanced materials, hull shaping, suspended floors, blast seats, or any other means available. Phase 1 Science and Technology contract period of performance began on 29 May 2015. The contractors have begun to bound the problem with concept designs. Currently, BAE Systems plans to form the underbody from 7020 Aluminum with an Al 5056 plate bolted on as a kit. General Dynamics Land Systems is investigating a four-inch aluminum trapezoidal shape in a welded structure. (Additional technical detail is available but competition-sensitive and requests for it should be directed to the Program Manager Armored Fighting Vehicles).

This design excursion is intended to push the state-of-the-art in underbody design. If the contractors can achieve more than double the required value in the capability development document, as this is, the program can look to increasing the minimum requirement on future vehicles. If the requirement cannot be achieved, it will provide valuable information to inform the requirement and the associated trade space.

Threat Analysis

Physical Evidence Recovery to Support Threat Assessments

The JTAPIC partnership enables a linkage between the medical and intelligence communities, which allows much more accurate assessments of threat capabilities and weapons proliferation. In this case, the National Ground Intelligence Center (NGIC) works routinely on site with the Armed Forces Medical Examiner reviewing threat munition components recovered from autopsies, explosive residue from clothing and other equipment, and threat weapon effects on personnel. This extremely effective relationship continued in FY15 when several unique munitions and threat weapon blast effects were identified. This process also enables a better understanding of the use of threat weapons by providing insight into the engagement ranges and tactics that threat forces employ. These data are shared with the RDT&E community in order to better design mitigation technologies. The ability to obtain this physical and medical evidence is just as important in military attack scene investigations and analysis as it is in law enforcement crime scene investigations. Every piece of the attack investigation can provide a wealth of information on not only the event and its outcome but it can help understand how to mitigate future similar events and threats. It also helps to understand how friendly TTPs can be adjusted or improved to protect Service Members, and it can provide early warning of an unknown or previously undetected threat, such as new ammunition, weapons and explosives.

Forensic Analysis of Recovered PPE

The PM SPIE Technical Management Directorate performs forensic analysis on recovered PPE in support of the JTAPIC project office. The Technical Management Directorate receives PPE from Service Members who have been killed in action from the Armed Forces Medical Examiner, and from Service Members who have been wounded in action from MEDCOM. In 2014, the Technical Management Directorate also agreed to analyze PPE recovered from Marines who were killed or wounded in action. PM SPIE analyzes events involving injury to dismounted Service Members to determine prevention and mitigation strategies, and also looks at the injury types and trends caused by particular weapons. The analyses are provided to Service materiel developers to influence protective equipment design and tactics, technique, and procedures.

Vehicle Modernization

JTAPIC provided answers to 13 RFIs in support of vehicle-upgrade programs. In FY15, the Army and other DoD agencies made significant decisions on the strategies for upgrading their vehicle fleets, including the US Army's Combat Vehicle Modernization Study. The Combat Vehicle Modernization Study was the number one priority for the US Army Training and Doctrine Command, and while not complete, the results from FY15 have laid the foundation and direction for this effort. Though the Combat Vehicle Modernization Study looks to the future, a critical aspect was identifying different threat environments and how well existing vehicles performed in them. As an example, the weapons used in an insurgency are very different from the ones that US Services would face in a maneuver warfare environment against a near peer opponent. While JTAPIC has been able to quantify the threat and effects posed to US Services over the last seven years, there are serious gaps in its understanding of different types of operations across the full spectrum of warfare.

To rectify this, JTAPIC began a major legacy data program to quantify different threat environments, including reaching out to allies who have operated against potential US enemies. In FY15, this effort added over 1,000 incidents and almost 3,000 casualties into the JTAPIC database. One example of this effort was a series of products in support of Stryker modernization, and in particular, how many Stryker Brigades would use the original Flat Bottom Hull design versus the Double V Hull developed to counter IEDs. This effort added an additional 89 events and 150 casualties to the joint database. Upgrading a brigade can potentially cost hundreds of millions of dollars, hence the customer needs to know not only what threat environments use IEDs and how likely the US would face them, but also the nature and severity of injuries that may result. Information was provided to the ASA(ALT), who decided on the final fleet mix. A similar project is underway for the Bradley Fighting Vehicle program office.

JTAPIC is supporting an ongoing effort to supply the WIAMan program with analytical products to aid in focusing the funding and biomedical research necessary to produce a manikin for ground vehicle testing. These RFIs aided WIAMan's ability to determine prevalent injuries and injury distribution analysis in blast events by providing number of injuries, location, severity, CT/X-ray images, and context. By identifying the mechanism of injury and providing associated radiology that is compared to the post-test manikin to verify similar facture patterns, these RFIs have enabled WIAMan testing to better simulate real-life events.

NGIC identified the specific events to support JTAPIC's summary of the most frequent visceral and skeletal injuries from underbody blast events in theater. The MOMRP was interested in these injuries for understanding the importance of developing non-bony tissue injury models versus strictly skeletal injury models.

NGIC aided in and led JTAPIC RFIs that addressed training effectiveness in regard to IED and other threat encounters for the Maneuver Center of Excellence and the Communications-Electronics Research, Development and Engineering Center. Maneuver Center of Excellence was interested in attacks by threat in order to evaluate the effectiveness of the Advanced Situational Awareness Training Course. The Communications-Electronics Research, Development and Engineering Center was looking for information to confirm or deny that there was a problem with the IED-detection capability gap (high IED casualty rate) with infantry and armor units conducting mounted patrols. The information helped to scope current science and technology initiatives.

Service Member Protection

During FY15, NGIC continued to partner with the JTAPIC program in answering 13 RFIs from multiple government organizations related to the efficacy of Service Member systems and protection, as well as dismounted TTPs, and base infrastructure designed to mitigate blast effects. These organizations included PEO Soldier, Product Manager Infantry Combat Equipment, Program Manager Special Operations Forces, DARPA, Maneuver Center of Excellence, Army Capabilities Integration Center, and Engineer Research and Development Center, among others. The studies included in-depth looks at historic indirect fire, dismounted IED, small-arms fire, and complex base attacks in Afghanistan, as well as current indirect fire attacks in Iraq and Ukraine, enabling threat analysis across the full spectrum of conflicts: asymmetric, hybrid, and near peer. By providing specific threat information, the RFI products not only enabled the requirements and development communities to address critical vulnerabilities, but also affected a holistic approach to considering the doctrine, organization, training, materiel, leadership and education, personnel, and facilities solutions in relation to the spectrum of most common and most stressing threats.

JTAPIC funded threat support to PEO Soldier's SPS development in the form of the System Threat Assessment Report, as well as significant input to the SPS LFT&E planning process, ensuring the future body armor mitigates relevant blast threats.

Throughout the fiscal year, the JTAPIC partnership also enabled significant participation from PEO Soldier, Product Manager Infantry Combat Equipment, and Program Manager Special Operations Forces in various threat live-fire and exploitation testing conducted by NGIC. These tests provided the program managers an opportunity to test current and future systems against specific threat weapons for the first time.

Another major success during FY15 was incorporating, with the support of JTAPIC, a day-long dismounted symposium during the annual Armor/Anti-Armor Coordinating Threat Coordinating Group that brought together a broad range of organizations representing dismounted capabilities and requirements, dismounted systems developers and program managers, and the intelligence and medical communities. The briefings and discussions synchronized future dismounted protection efforts while ensuring an understanding of the current and future threats.

Battlefield Vehicle Forensic Technicians Vehicle Survey Effort

JTAPIC continued its efforts to conduct surveys of battle-damaged vehicles in order to better understand the circumstances in which blast injuries and other weapon effects are occurring. An additional benefit of this effort is giving the intelligence community partners much clearer understanding of the employment and effect of threat weapons and an ability to characterize improvised devices. In FY15, the Battlefield Vehicle Forensic Technicians conducted 601 surveys, bringing the total number of surveys conducted to 8,534. This data represents a unique collection of information without which many of the successful vehicle upgrades would not have occurred. These surveys have also saved millions of dollars in the test and evaluation community by allowing more informed decisions to be made about the need or details for a given live-fire test.

JTAPIC Database

The JTAPIC Database, sponsored by the JTAPIC program and developed at the NGIC, continued to enhance the integration and sharing of information from DoD Services related to the efficacy of PPE (including body armor, helmets, and eyewear) and vehicular equipment designed to protect against blast injury. The JTAPIC Database is fed from the collection of ground combat incidents collected and analyzed by NGIC that, as a result of two minor releases and two patches during the FY15 development, not only includes attacks on vehicles but also now contains found and cleared events and attacks against dismounted personnel. Analyzed incident information on enemy weapons systems used, enemy TTPs, and the effects of weapon systems worldwide is integrated with structured Service Member injury data that represents the threat to life associated with the injury. Database development in FY15 extended the integrated dataset to support the addition of details associated with a Service Member's PPE at the time of the incident/injury. The FY15 JTAPIC Database enhancements and FY15 efforts to gather, analyze, and integrate over 1,186 legacy incidents and 2,731 casualties from calendar year 2003 and 2004 better support proactive, integrated all-source intelligence production and responses for program managers and senior decision makers that lead to modifications and upgrades to vehicle equipment/protection systems/PPE, and enhances ability to provide direct feedback to theater commanders and deploying units for improving Blue (TTPs) and battlefield situational awareness to protect against blast injury.

Surveillance of Battle from Blast-Related Causes During Operations in Afghanistan and Iraq, FY15

The Injury Prevention Program, USAPHC, conducted deployment injury surveillance for the Army during OEF (Afghanistan: October 2001 to December 2013) and OIF—New Dawn (Iraq: March 2003 to December 2011). This injury surveillance used a combination of medical, air evacuation, casualty, and safety data to identify and categorize the causes of battle and non-battle injuries among US Army Service Members.

Photo credit: US Army

The Injury Prevention Program has continued the same level of surveillance for the ongoing operation in Afghanistan since December 2014 (Operation Freedom's Sentinel). During FY15, there were 563 medical evacuations from Afghanistan. Of these, 37 (6.7 percent) were for battle injuries. According to the narrative patient histories in the medical evacuation records, 14 of these battle injuries were blast-related (38 percent of battle injuries). By comparison, during the period October 2001 to December 2014, a higher percentage of all medical evacuations were for battle injuries (n=11,987; 17.2 percent), and 73.3 percent of these battle injuries were blast-related (includes mortars, grenades, and IEDs). The deployment injury surveillance conducted at the USAPHC has informed senior Army leaders of the overall impact of battle and non-battle injuries that required medical evacuation (17 percent and 36 percent, respectively, of all medical evacuations) from the Army Central Command. By coding and reporting causes of battle and non-battle injuries that required medical evacuation, greater attention has been given to the leading causes of both battle and non-battle injuries among deployed Service Members.

Characterization and Comparison of Combat-Related Injuries in Women During OIF and OEF

To support gender-based research efforts in the military, researchers at NHRC critically examined what types of combat-related injuries military women sustained in recent conflicts. The researchers also investigated the likelihood of leaving active military duty after a deployment-related injury, as well as an examination of acute care medical resource usage in the severely injured female population. US Servicewomen who sustained combat-related injury in OIF or OEF between January 2003 and May 2014 were identified from NHRC's EMED. Injuries were then characterized using Abbreviated Injury Scale and International Classification of Diseases, 9th Revision codes. For study purposes, 844 combat-related injury episodes in women were utilized from EMED. Fifty-one percent (n = 433) were OIF injuries and 49 percent (n = 411) were OEF injuries. Blast events were responsible for 90 percent of injuries. The average ISS was 3, with no statistical difference in means between OIF and OEF. Of significance were increased head injuries in OEF compared with OIF (80 percent versus 48 percent; $p < 0.001$).

Although the majority of combat-related injuries suffered by women were mild, some women suffered life-threatening injuries, and nearly 65 percent of the injury episodes resulted in more than one injury. In-patient hospital days averaged 31.6 days post-injury in women with severe injuries (ISS > 9). At the time of this study, more than 65 percent of the injured women remained on active military status, either active duty, reserve, or National Guard. Future studies will investigate quality of life outcomes and gender differences in combat-related injuries.

Real-Time Casualty Injury Trending and Reporting for DoD Leadership

NHRC has been tracking each Service Member injured in overseas contingency operations since the beginning of OIF and OEF (October 2001). Over time, this capability has evolved into a database that includes all Service Members injured during deployment. This tri-Service capability, resident at NHRC, is named the EMED. Each casualty that occurs in overseas contingency operations is identified within seven days of injury, coded by diagnoses and ISS, and entered into the EMED for analysis. During FY15, NHRC continued to trend a number of sentinel injury types common during overseas contingency operations, including TBI, amputations, urogenital injury, facial injury, and complex blast injury. This report, which is produced quarterly, alerts DoD leadership to spikes in occurrence rates, indicating when a true state change in injury counts is occurring. This report is provided quarterly to the JTAPIC, Headquarters Marine Corps, Marine Corps System Command, BUMED, and the EACE. This capability allows the DoD to focus investigations on trends that represent a meaningful change in the running average of injury types over time. This saves precious resources and optimizes investigations about what is causing a rise in injury risk to our Service Members in theater. Furthermore, this report is used by the intelligence communities to track the evolution of the insurgency threat.

NHRC Data and Analysis Support to the JTAPIC Program

NHRC is intimately involved in supporting the JTAPIC program through the provision of the coded injury information that is associated with each combat event where a Service Member is injured. NHRC provides a weekly analysis of all combat casualties occurring in the previous seven days during overseas contingency operations to the JTAPIC Program Office. For each wounded Service Member, the medical data obtained from NHRC's EMED is thoroughly reviewed at NHRC, and a clinical profile is developed describing a casualty's injury characteristics. Each casualty's injuries are then coded on various diagnostic and injury severity taxonomies by registered nurses.

In addition to injury analyses conducted at NHRC, these detailed clinical profiles are then made available to the JTAPIC partnership for additional analysis where tactical data (such as weapon type, explosive weight, and strike point) are matched to the injury profiles. This mapping of medical to tactical data allows vehicle and personal protective equipment developers to design targeted modifications to improve vehicles and personal protective equipment, thereby reducing the frequency and severity of injury.

Because of the common requirement for medical data, NHRC participates in nearly every JTAPIC partnership analysis. In 2015, there were 28 JTAPIC products that used medical information provided by NHRC. In addition to supplying coded medical data, NHRC actively participates and produces medical analysis products for JTAPIC. During 2015, NHRC provided analysis for 10 products. The immediate availability of medical data and the provision of analysis allows the intelligence community to monitor the effectiveness of the insurgency threat's evolution. This permits rapid responses to identify and defeat new and emerging threats—directly reducing casualty rates. Because casualty medical data are mapped to tactical data, the DoD vehicle and PPE development communities can directly target materiel designs and enhancements to those threats and injury types producing the most serious and debilitating injuries.

This allows the minimum amount/weight of PPE to be worn because body coverage required is precisely targeted.

Establishing Large-Scale Data Repositories in a Military Healthcare Setting

The past decade of sustained combat operations has placed considerable stress on the MHS. As a result, researchers and medical providers have developed innovative healthcare strategies and techniques. Despite attempts to coordinate efforts, much innovation in military medicine occurs in a "stovepipe" fashion where similar efforts are replicated in parallel. Furthermore, much outcome data are either anecdotal or unpublished. The inability to share and monitor health outcomes can be costly to the Service Member and the MHS. Lastly, the MHS is facing patients with increasingly complex symptom presentations related to the homogeneous nature of combat injuries and related emotional injuries.

Efforts were made to design MHS electronic medical records, also known as the Armed Forces Health Longitudinal Technology Application (AHLTA), to allow for data extraction and analysis. However, much of these data are unusable, secondary to concerns regarding data accuracy and integrity. These concerns are often related to individual differences across medical providers in coding and notating patient history, treatment procedures, and diagnosis. These differences occur even between specialists in the same discipline and clinic. Despite these challenges, many clinics maintain databases for process improvement. While these efforts are noble, they are often hampered by poor information technology knowledge, ethical concerns (process improvement versus research and patient protection), and sustainability (time, resources, and frequent staff turnover).

To better understand the pathophysiology, disease progression, optimal diagnostic and evaluation, and associated outcome metrics in Service Members with TBIs and psychological health conditions, the Intrepid Spirit Concussion Recovery Center at the Naval Hospital Camp Lejeune initiated activities in FY15 to establish a clinical data registry. Data registries are organized systems (approved by an Institutional Review Board) that collect data for scientific, clinical, and/or policy purposes to elucidate the history of disease, determine effectiveness of healthcare services, measure or monitor safety, and/or measure quality. A registry allows sustainable and efficient exploration and publication of research findings and trends in clinical care. However, while a strong majority of clinicians value large scale data access and storage systems, a knowledge gap exists regarding how to leverage information technology and Institutional Review Board requirements for research purposes.

Development of Blast Overpressure Exposure Threshold Guidelines for Commanders

The Naval Medical Research Center (NMRC), with funding from the USAMRMC, is developing and testing environmental sensors for detecting blast overpressure intensities. Investigators led the effort to determine blast overpressure sensor requirements for the Army breacher, artillery, and mortar communities. Also resulting from this work is the characterization of the annual overpressure exposure profiles for M119 Artillery, M81 Mortar, and M120 Mortar crews. Continuing work will address the acute effects of blast exposure in military and law enforcement personnel. This program is designed to develop blast-exposure guidelines for DoD communities routinely exposed to blast events. These guidelines will be the first to provide decisional support to commanders in the form of thresholds that will inform them when Service Members have reached the safety limit of exposure that would put them at risk for long-term mTBI-related medical conditions.

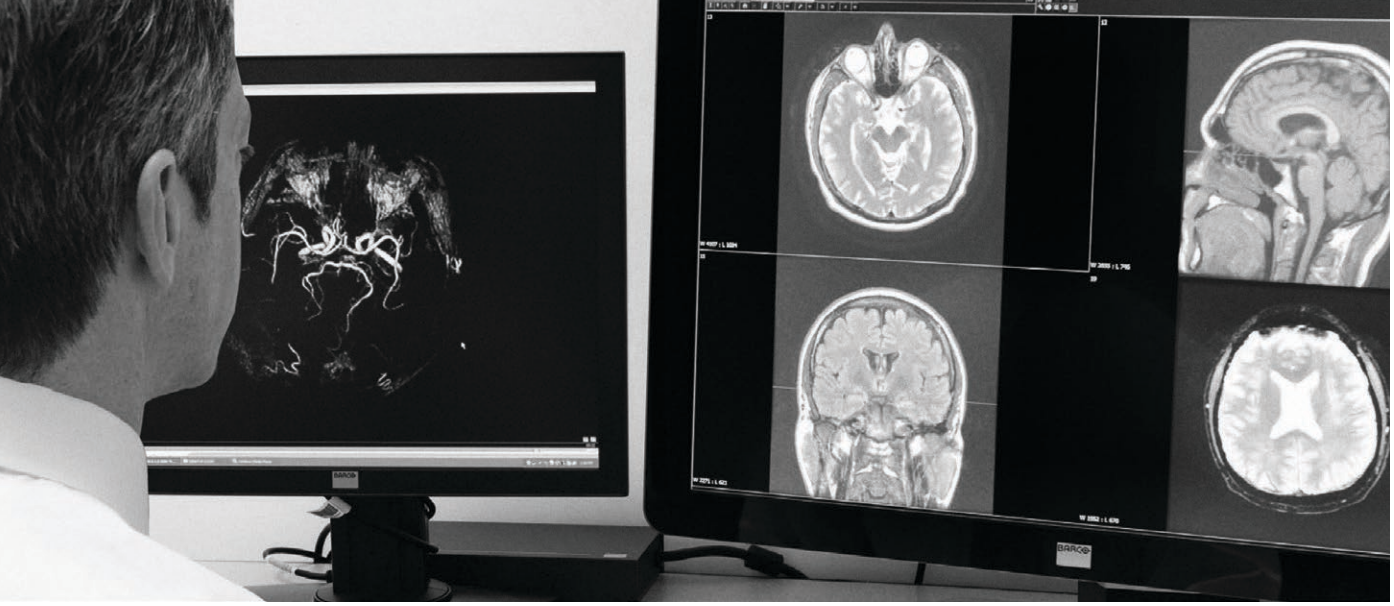


Photo credit: National Intrepid Center of Excellence

Program Area: Acute Treatment

Research in acute treatment is intended to improve survivability and mitigate long-term disability for Service Members with the full spectrum of injuries following blast events. Collaborations between DoD and partners in the US Food and Drug Administration (FDA), academia, and the private sector are investigating new diagnostic tools, therapies for TBI, hemorrhage control devices, strategies to mitigate wound infection, and interventions for facial, hearing, and visual injuries. This section demonstrates how the research community is employing novel neuroimaging techniques, evaluating clinical data, and experimenting in the laboratory to address the spectrum of blast injuries. The combined efforts of researchers in this area will lead to a greater understanding of the capabilities and limitations of current technologies, new tools and validated methods for injury mitigation in the prehospital setting, and improved diagnostics and clinical guidelines for the acute treatment of blast injuries.

Diagnostics

Advanced Magnetic Resonance Imaging (MRI) in Blast-Related TBI

A team at Washington University studied Service Members with acute TBI in two studies. The studies examined Service Members with TBIs and blast exposure in combat within one week of injury at two sites in Afghanistan and six to 12 months post-injury in the US. One of the most widely reported findings from the study was that the actual incidence of TBI from pure blast exposure was extremely low and that combat blast injuries were more closely associated with other post-blast related events (e.g., impact). A recent publication based on the second study found that Service Members with concussions demonstrated a greater magnitude of post-injury deficits (stress, depression, cognitive performance, headache, etc.). Additionally early signs of PTSD and related psychological symptoms more strongly predicted long-term disability (work, family, social activities, etc.) than post-concussive outcome measures.

Deficits in Visual System Functional Connectivity after Blast-Related mTBI are Associated with Injury Severity and Executive Dysfunction

Many Service Members returning from Afghanistan and Iraq sustain mTBI. A majority of these incidents are caused or associated with explosive blast. Visual and cognitive deficits are common complaints after TBI, but to date little research has explored how these symptoms may be related neurologically. In this study, investigators at DVBIC, Minneapolis; the Minneapolis VA Medical Center; the University of Minnesota; and the University of Iowa collaborated to study the relationship between cognitive and visual processing dysfunction after blast-related TBI. The study administered resting-state functional MRI scans to 131 Veterans of OEF/OIF. All participants completed the Minnesota Blast Exposure Screening Tool.

The resting-state data were processed and analyzed to determine the functional connectivity of four seeds in the brain's visual system: lateral geniculate nucleus, primary visual cortex, lateral occipital gyrus, and the fusiform gyrus. First, multiple regression analysis produced individual functional connectivity maps depicting each seed's correlation with every other voxel. Group-level analyses then regressed scores from the Minnesota Blast Exposure Screening Tool onto data from the functional connectivity maps. This analysis yielded F-statistic maps that identified brain areas where FC variance is related to blast severity. A Monte-Carlo-based thresholding procedure controlled for multiple comparisons. Data from voxel clusters that survived the procedure were correlated with cognitive (Stroop Color-Word, Trail-Making B) and visual test scores. The behavioral data available for this final analysis included 95 participants. The results demonstrate a negative correlation for blast severity and functional connectivity between the lateral geniculate nucleus seed and the medial frontal gyrus, lingual gyrus, and right thalamus; between the primary visual cortex seed and precuneus; between the lateral occipital gyrus seed and the middle frontal gyrus; and between the fusiform gyrus seed and the superior frontal gyrus, medial frontal gyrus, and left middle frontal gyrus. In addition, higher functional connectivity values between the seeds and fronto-cortical regions were correlated with better performance on Stroop and Trail-Making tests. This study demonstrates a deficit in connectivity between visual and frontal brain regions, which also negatively correlate with cognitive performance. An understanding of brain connectivity may be critical foundational information in diagnosing and treating TBI in the Service Member.

Neuropsychological Outcome and DTI in Complicated Versus Uncomplicated mTBI

Researchers at the NICoE investigated the relationship between neuroimaging abnormalities in individuals with mTBI and subacute outcomes. Participants were evaluated using cognitive testing, symptom reporting, and DTI, with these assessments occurring six to eight weeks after injury. Participants included 62 military Service Members with an mTBI, evenly divided into complicated or uncomplicated based on the presence of neuroimaging abnormalities. The presence of abnormalities was compared to cognitive outcomes. The results suggest that despite differences in the imaging results, there were no significant differences in cognitive performance between the two groups. Further, macrostructural neuroimaging changes following mTBI were associated with quantifiable changes in DTI signal Despite these structural differences, separating individuals into complicated or uncomplicated mTBI did not predict clinical outcome. This suggests that in addition to evaluation by neuroimaging, other assessments need to be performed.

Exploring Variations in Functional Connectivity of the Resting State Default Mode Network in mTBI

Researchers at the NICoE used functional MRI to investigate changes in the default mode network after a TBI. Resting state default mode network maps indicated an increase in spatial coactivity in mTBI patients in the cerebellum and the supplementary motor areas. However, these results were reported with low specificity and sensitivity. Participants included 27 military Service Members, 15 that sustained an mTBI and 12 controls. These results suggest that quantifying the default mode network following a TBI may facilitate identification of individuals who have experienced an mTBI, and provide insights into posttraumatic cognitive and emotional functioning.

DTI findings and Post-Concussion Symptom Reporting Six Weeks Following mTBI

Researchers at the NICoE investigated potential relationships between posttraumatic micro-architecture of the white matter and post-concussion symptom reporting. Participants were evaluated using DTI, neurocognitive testing and self-report assessments, with these assessments occurring six to eight weeks after injury.

Participants included 108 individuals who suffered an orthopedic injury, with 72 experiencing mTBI and 36 experiencing trauma. The latter group served as the control group. The mTBI group was further divided based on International Classification of Diseases-10 criteria for PCS— a PCS-absent and a PCS-present group. The results demonstrated no differences in cognitive function across the three groups, although the PCS-present group self-reported great anxiety and depression symptomatology. In the two mTBI groups, no differences were observed in the imaging data, although comparing the PCS-present group to the control group did reveal diffusivity differences. Therefore, individuals suspected of experiencing a TBI should be evaluated using different assessment modalities.

Olfactory Dysfunction as a Marker for TBI in US Troops

The objective of this study is to determine whether a structured and quantitative assessment of differential olfactory performance—recognized between a blast-injured TBI group and a demographically comparable blast-injured control group—can serve as a reliable antecedent marker for preclinical detection of intracranial neurotrauma. A collaborative research team from the WRNMMC, USUHS, and the NIH prospectively and consecutively enrolled 231 polytrauma inpatients, acutely injured from explosions during combat operations in either Afghanistan or Iraq and requiring immediate stateside evacuation and sequential admission to the tertiary care medical center over a two-and-a-half-year period. This study correlates olfactometric scores with both contemporaneous neuroimaging findings, as well as the clinical diagnosis of TBI, tabulates population-specific incidence data, and investigates return of olfactory function. Olfactometric score predicted abnormal neuroimaging significantly better than chance alone (area under the curve = 0.78, 95 percent confidence interval 0.70–0.87). Normosmia was present in all troops with mTBI (i.e., concussion) and all control subjects. Troops with radiographic evidence of frontal lobe injuries were three times more likely to have olfactory impairment than troops with injuries to other brain regions (relative risk 3.0, 95 percent confidence interval 0.98–9.14). Normalization of scores occurred in all anosmic troops available for follow-up testing.

These results indicate quantitative identification olfactometry has limited sensitivity but high specificity as a marker for detecting acute structural neuropathology from trauma. When considering whether to order advanced neuroimaging, a functional disturbance with central olfactory impairment should be regarded as an important tool to inform the decision process. The study was funded by the US Department of Defense Combat Casualty Care Medical Research and Development Program (DMRDP: ID-D10-I-AR-J6-626).[56]

Examination of the mTBI Atypical Symptom Scale and the Validity-10 Scale to Detect Symptom Exaggeration in US Military Service Members

Researchers at the DVBIC, WRNMMC, Center for Neuroscience and Regenerative Medicine, and USUHS examined the clinical utility of two validity scales intended for use with the Neurobehavioral Symptom Inventory (NSI) and the PTSD Checklist-Civilian version for potential use in assessing individuals with mTBI. The two validity scales, the Mild Brain Injury Atypical Symptoms scale and the Validity-10 scale, were administered to participants with mTBI. Participants were 63 military Service Members who experienced a TBI, and were divided into two groups receiving assessments. The results suggest strong support for the use of the Validity-10 as a tool to screen for symptom exaggeration on both the NSI and the PTSD Checklist-Civilian version. In contrast, the Mild Brain Injury Atypical Symptoms scale was not a reliable tool for screening, as it failed to identify the majority of people who exaggerated symptoms.[57]

Imaging Cerebral Microhemorrhages in Military Service Members with Chronic TBI

Researchers at the NICoE used susceptibility-weighted MRI to detect cerebral microhemorrhages in military Service Members suffering from chronic TBI.

After the imaging analysis, microhemorrhages were identified and characterized with key parameters being number, size, and magnetic susceptibility. Participants included 603 military Service Members who experienced a TBI, with cerebral microhemorrhages identified in 43 of those patients. Within those 43 patients, 585 microhemorrhages were identified. When follow-up assessments were performed, the number and qualitative assessment of the microhemorrhages improved over time. These results suggest that hemosiderin products undergo continued change after injury, during the chronic phase of TBI.

Therapy Development for TBI and Related Symptoms

Anti-Lysophosphatidic acid (LPA) Antibody Treatment for Protection Against Blast-Induced Polytrauma

LPA is a bioactive lysophospholipid released from activated platelets, astrocytes, choroidal plexus cells and microglia and is reported to play major roles promoting inflammatory processes through signaling events mediated through specific G-protein coupled LPA receptors. Investigators at WRAIR in collaboration with Lpath, Inc. (the manufacturer of anti-LPA antibodies, 504B3), are evaluating the role of 504B3 in ameliorating the deleterious effects of blast-induced neurotrauma. Although in initial experiments, intravenous administration of 504B3 did not appear to protect against the neurobehavioral or neuropathological abnormalities induced by blast exposure, it did greatly reduce retinal injury caused by these insults. The lack of efficacy in this model of blast TBI differs from positive findings seen with other brain injury models and is likely attributable to insufficient amounts of anti-LPA antibody reaching the brain after intravenous administration since immunoassays showed only trace amounts of anti-LPA antibody in brain and cerebrospinal fluid samples. To circumvent the blood-brain barrier, these investigators are currently testing the efficacy of intranasal administration as an alternative means to safely deliver therapeutic doses of anti-LPA antibody to the brain.

BrainScope's Ahead System

A project managed by CCCRP lead to the development of the Ahead System, a hand-held, point of care, non-invasive and non-radiation emitting medical device designed to improve early identification, staging, and optimization of treatment for patients who are suspected of TBI. The Ahead 100 and 200 systems received US FDA marketing clearance.

US Army HBO2 Clinical Trial

HBO2 clinical trials currently focus on treatment development using HBO2 for chronic PCS after mTBI in active duty Service Members. Many of the trial participants had deployment related mTBI due to blast. While HBO2 is approved by FDA for 13 conditions, the treatment of PCS is not a currently approved condition.

I. A pilot phase II study of HOPPS after mTBI using low dose HBO2 was completed and analyzed, and results were published in the Journal of the American Medical Association—Internal Medicine in January 2015, and the clinical study report was submitted to the FDA in June 2015. The HOPPS study was a DoD, multi-center, Phase II trial conducted at Fort Gordon, Georgia; Fort Carson, Colorado; Camp Lejeune, North Carolina; and Camp Pendleton, California, with assistance of research staff from the Denver VA Medical Center, Colorado, and Latter Day Saints Hospital, Salt Lake City, Utah. This study consisted of three arms with a total of 72 volunteer Service Members with PCS following mTBI. All subjects continued to receive routine local care. One arm received 1.5 ATA pressurization breathing 100 percent oxygen, one arm received 1.2 ATA pressurization breathing room air (21 percent oxygen), and one arm received no chamber procedures as a supplement to local care. From the standpoint of study design, the 100 percent oxygen breathing group (HBO2) was considered to be the treatment intervention. The room air breathing group was a comparative sham exposure and the routine care group was a non-chamber exposure control.

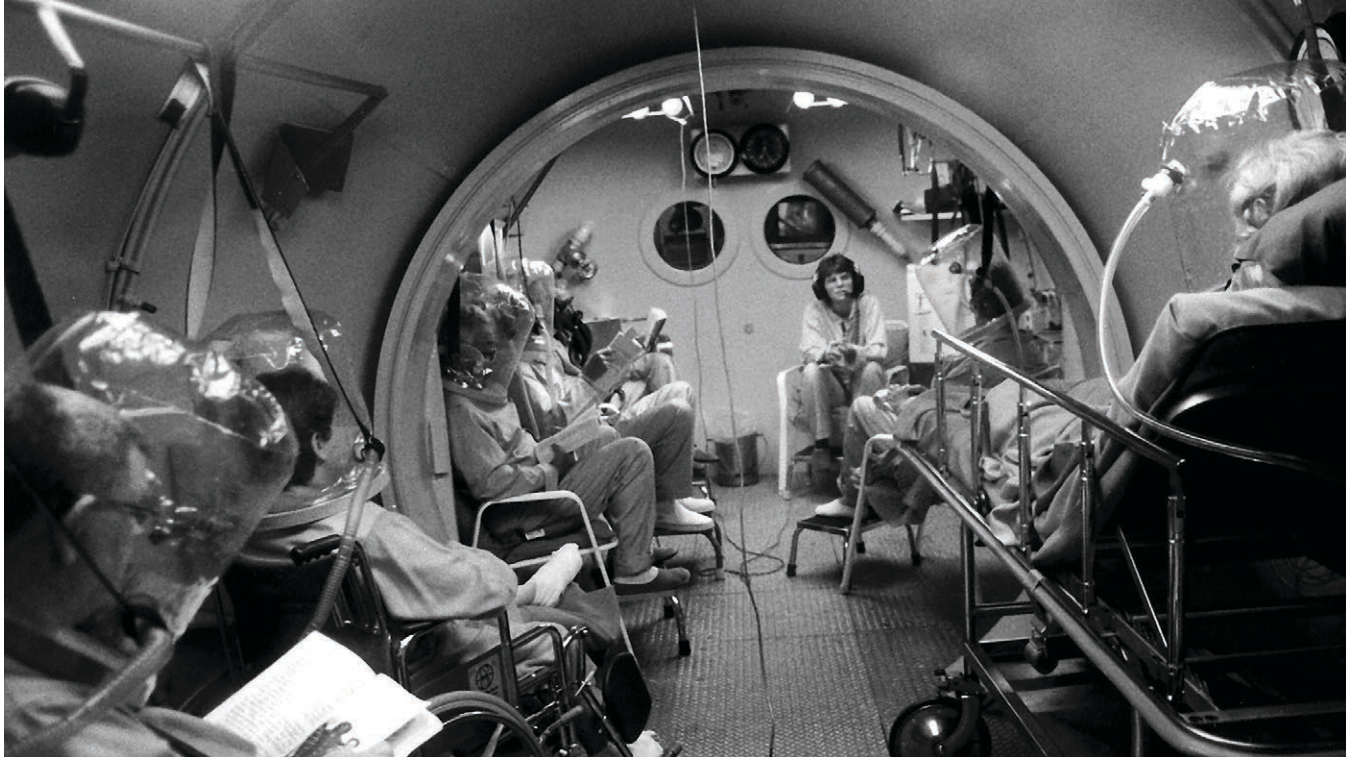


Photo credit: US Air Force

The focus was on the evaluation of PCS symptoms and neurocognitive improvement. The results of the study showed that HBO2 oxygen provided no differential benefit relative to room air breathing in terms of short-term relief (six weeks post-treatment) for PCS after mTBI. Researchers did note that some participants (20 to 30 percent) treated in the hyperbaric chambers with either HBO2 or room air (i.e. which is associated with no significant increase in body oxygen levels) did report short-term improvements in TBI symptoms compared to patients treated with TBI standard of care (control group; no chamber time). However, researchers believe the improvements were most likely due to placebo effects or participant expectations coupled with intensive involvement with the research team as part of the chamber procedures. The DoD-sponsored trials are the first ever placebo-controlled studies of HBO2 for PCS after mTBI. The DoD remains committed to researching and providing evidenced-based solutions for our wounded Service Members. The DoD is actively investigating a number of alternate potential treatments for wounded Service Members for the treatment of PCS and PTSD.

II. The HBO2 LTFU study was a single-survey, observational cohort research study of participants who participated in US Navy and Army interventional trials evaluating the efficacy of HBO2 therapy as a treatment for PCS after mTBI with or without PTSD. This research study, conducted from 2009 to 2010, was designed to provide follow-up at a single point in time, more than one year (HOPPS trials and DARPA-funded Virginia Commonwealth University) after intervention. The results showed no consistent trends to support the hypothesis that chamber exposure with either 1.5 ATA HBO2 or the study sham condition was associated with long-term improvement in PCS or PTSD symptoms. Within-group trends seen among LTFU participants from the Navy study (Cifu et al., 2014) were dissimilar to within-group trends seen among LTFU participants from the HOPPS study.

For the sham groups, modest improvement was seen in PCS and PTSD symptoms in Navy LTFU participants, but worsened in HOPPS LTFU participants. In the 1.5 ATA HBO2 groups, worsening from baseline was seen in PCS and PTSD symptoms in Navy LTFU participants while minor improvement in PCS and worsening in PTSD symptoms was seen in HOPPS LTFU participants. In a statistically invalid sample of three participants receiving 2.0 ATA HBO2, there was modest improvement of PTSD symptoms. The final report was disseminated to senior leadership at the USAMRMC in July 2015 and the study officially closed September 2015.

Progesterone for TBI, Experimental Clinical Treatment (ProTECT III) Trial

An effective medical treatment for TBI does not currently exist. Progesterone is inexpensive, safe, and early studies showed progesterone's potential to be an effective treatment for moderate and severe TBI. ProTECT III was a phase three, randomized, double-blind, placebo-controlled clinical trial that evaluated the utility and efficacy of intravenous progesterone in moderate and severe TBI when compared to placebo, using the six-month Glasgow Outcome Scale Extended as the primary outcome measure. The trial was funded by the National Institute of Neurological Disorders and Stroke (NINDS) and was conducted through the Neurological Emergencies Treatment Trials network. This network is made up of 17 civilian sites with affiliate hospitals. The only DoD site to participate in ProTECT III was the Wilford Hall Ambulatory Surgical Center, a USAF medical treatment facility (operated by the 59th Medical Wing) at San Antonio's Lackland Air Force Base. Results of the trial were published in the *New England Journal of Medicine* on 10 December, 2014 (Wright et al., 2014). ProTECT III did not show a benefit of progesterone over placebo in the improvement of outcomes in patients with acute TBI.

Mental Health Outcomes: Concussion Clinics in Afghanistan

mTBI continues to be a common injury in the current Iraq and Afghanistan conflicts and over 90 percent of mTBIs are blast related. In addition, these injuries are associated with long-term mental health outcomes such as PTSD and PCS. NHRC used the EMED to analyze records of 620 Service Members diagnosed with combat mTBI and who experienced a loss of consciousness. Of the 620 Service Members, 531 received care at a concussion clinic at a medical treatment facility in Afghanistan and 89 received standard concussion care at a medical treatment facility in Afghanistan. NHRC found the demographics of the two treatment cohorts were similar in terms of mean age, gender, military occupation, and branch of Service. A greater proportion of Service Members receiving concussion rehabilitation clinic care returned to duty after treatment (53.3 percent versus 29.5 percent), with fewer requiring light duty or evacuation (40.6 percent versus 57.9 percent and 6.0 percent versus 12.5 percent, respectively). Within one year post-injury, PTSD and PCS diagnoses were reported less frequently in Service Members who received concussion rehabilitation clinic care compared with Service Members who received standard care (20.7 percent versus 31.5 percent and 9.2 percent versus 32.6 percent, respectively). In this NHRC report, the type of in-theater concussion care may influence both return to duty and mental health outcomes in Service Members who have experienced a combat-related concussion. A higher proportion of return to duty dispositions and a lower proportion of evacuations from theater were seen in Service Members receiving concussion rehabilitation care in Afghanistan. In addition, a lower proportion of both PTSD and PCS diagnoses within one year post-injury were documented in Service Members receiving concussion rehabilitation care.

Healthcare Provider Training for Acute Treatment of Blast Exposure with Battle Field Acupuncture (BFA) to Help Manage Headache

The acute treatment of blast exposure can be complicated by many factors not typically experienced in the civilian healthcare arena. Some of the factors are: 1) The blast exposure can occur in an austere environment with limited medical resources and healthcare providers who are Navy corpsmen or their equivalents in other services- far away from a hospital with doctors, nurses, other healthcare professionals, and there are no imaging modalities such as CT or MRI available to help with diagnosis; 2) It may not be clear if the symptoms experienced by the patient are due to a TBI, a stress reaction to the blast exposure, or some other cause entirely; 3) There is a risk from pharmacological interventions that medication side effects, such as drowsiness, may make assessment of mental status difficult, or make it difficult for the individual to return to full duty after the blast exposure. BFA is an ideal treatment modality to add to the toolbox of providers involved in the acute treatment of blast exposure because the needles are easily transportable; virtually any healthcare provider can be trained in administrating BFA; there is no harm to the individual, though there is potential benefit if he/she is experiencing a headache due to causes other than blast exposure; and there is no risk of medication overdose or harmful side effects. Naval Hospital Camp Lejeune has hosted several BFA training sessions, and in May of 2015 trained two providers to be BFA instructors. In August 2015, Naval Hospital Camp Lejeune conducted its first class run completely by its own staff, training approximately 10 general medical officers and corpsmen in the use of BFA. It was well-received, and the tentative plan is to have quarterly BFA training. This training was provided to healthcare providers who are in the field, oftentimes attached to the Service Member's unit, enabling providers to administer BFA after a blast exposure. This gives providers another modality to treat the Service Member, potentially minimizing risk of pharmacological intervention and increasing the number of Service Members who can return to the fight sooner.

Hemorrhage Control and Resuscitation

Extracorporeal Membrane Oxygenation: Comprehensive Adult Extracorporeal Support Program

Extracorporeal membrane oxygenation represents a form of cardiopulmonary bypass that can be maintained outside the operating room and allows for the delivery of oxygenated blood to peripheral tissue beds over days to weeks, or even months. Early trials evaluating the potential benefits for adults in respiratory failure failed to show a benefit over standard therapy. However, subsequent improvements in gas exchange membranes, pump technology, cannulation catheters and techniques, and circuit management have made this previously cumbersome and complication-prone therapy rather more universally applicable. The purpose of this USAF-sponsored study is to prospectively collect data on critically ill adult patients referred for possible extracorporeal membrane oxygenation support in a standard registry. The data will be analyzed on a case-by-case basis for performance improvement and quality assurance. For those patients who actually require extracorporeal membrane oxygenation, data will be submitted to the Extracorporeal Life Support Organization for inclusion in their national registry. The project was moved to sustainment at the San Antonio Military Medical Center and has transitioned to a program.

Wound Stasis System (WSS)

DARPA funded the WSS program to address the need for an effective battlefield treatment of hemorrhage-inducing wounds to the abdomen that are inaccessible to combat medics for traditional treatments, such as direct compression. DARPA funded researchers to design an injectable polyurethane-based self-expanding foam that hardens inside the body cavity, providing a local tamponade effect and direct pressure at the site of injury.

This product, injected as a prehospital treatment, is later removed by a surgeon at advanced levels of care during definitive treatment. Researchers examined the dose dependence of survival using a lethal, closed-cavity, swine liver injury model. When used in this model, WSS improved survival from less than 10 percent in controls (fluid resuscitation only) to greater than 70 percent. To extrapolate this swine dose to a human dose, DARPA funded a novel multi-center translational research study. DARPA has transitioned WSS to USAMRMC where the researcher is under contract to conduct further development and run clinical trials supporting an FDA regulatory decision.

Control of Severe Intra-Abdominal Hemorrhage with Infusible Platelet-Derived Hemostatic Agents in a Non-Human Primate *(Macaca mulatta)* Model

Hemorrhage often accompanies blast injuries and is the most common cause of preventable death in American combat casualties. Researchers at Naval Medical Research Unit—San Antonio, sponsored by BUMED, have tested the efficacy and safety of a human platelet-derived hemostatic agent in a rhesus macaque *(Macaca mulatta)* model of uncontrolled hemorrhage. The work is now complete. Results reveal no difference in hemorrhage or survival in the post-deployment health assessment groups versus controls, allowing work to progress to other products that may prove more beneficial.

Evaluation of Ability of Infusion Therapeutic to Prolong Prehospital Survival and Permit Delayed Periods of Resuscitation Without Compromising Survival

Severe blood loss can decrease oxygen and nutrient delivery to critical tissues, leading to poor physiologic and neurologic outcomes. Prolonged evacuation after blast, polytrauma, and hemorrhage (four to six hours) in combat environments can compromise survival. Novel therapeutic agents, used commonly in cardiopulmonary bypass, can potentially extend these survival times without compromising outcomes. Researchers at Naval Medical Research Unit–San Antonio, sponsored by the USAF 59th Medical Wing, are evaluating the use of combined adenosine-Lidocaine-magnesium to stabilize patients in the setting of hemorrhagic shock and polytrauma, allowing prolonged evacuation times (prolonging the "golden hour") and allowing for best outcomes in modern and future areas of operation. This initiated project has the capacity to impact medevac options and survivability during transport following hemorrhagic blast injury.

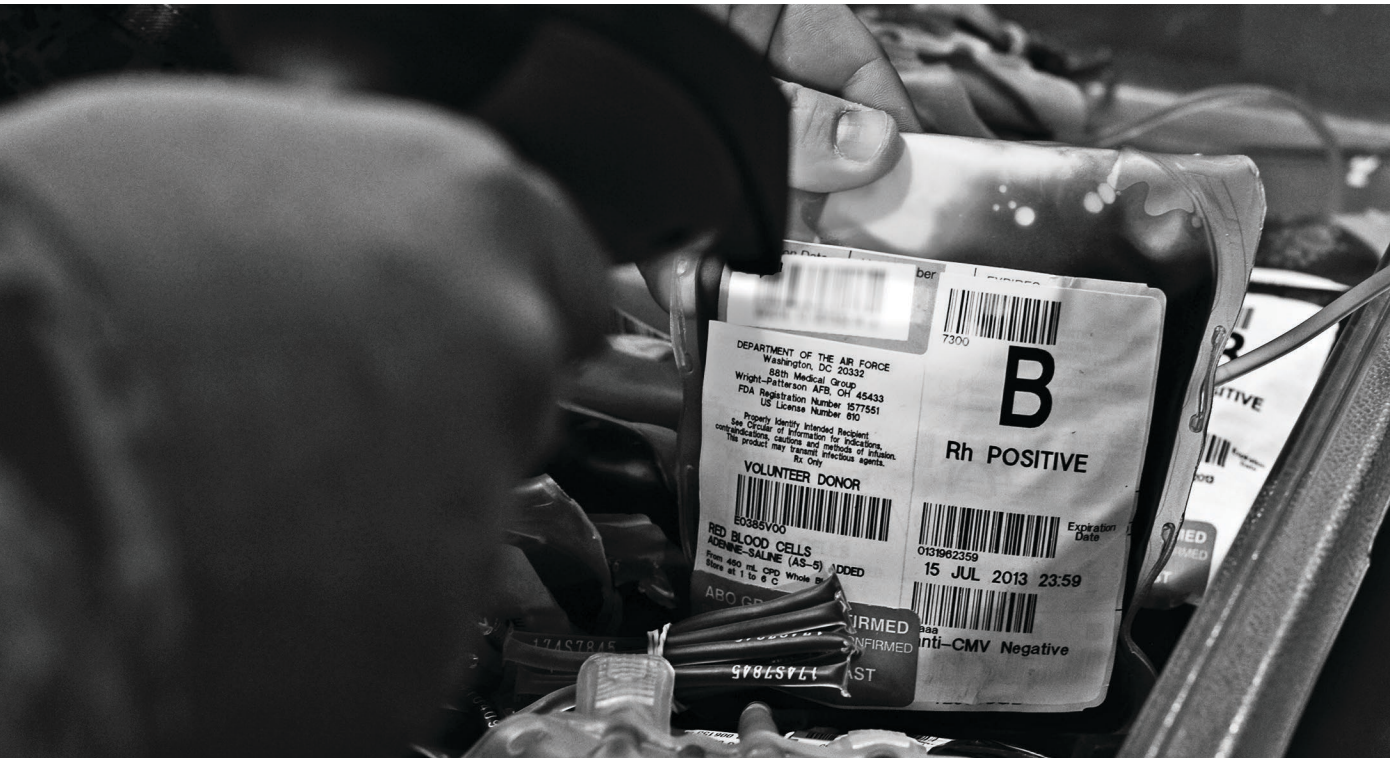
Evaluation of Junctional Hemorrhage Control Devices

Junctional hemorrhage control devices are critical for controlling hemorrhage in high-level traumatic injuries. As new junctional tourniquet designs emerge, it is critical to assess their safety and efficacy in environmental conditions that exist at the point of care and en route during patient transport. Researchers at the Naval Medical Research Unit–San Antonio, sponsored by the DHA RDA Directorate and the Marine Corps Systems Command, are evaluating the performance of four different commercially available, FDA-approved truncal/junctional hemorrhage control devices that aim to occlude blood flow at pressure points located near the torso, inguinal, and axilla regions. An initial phase of the study evaluated the performance of various junctional tourniquet designs during applications to a Multiple Amputation Trauma Trainer® during simulated operation conditions. Device stability during transfer and the effect of altitude on the devices (as some are pneumatic) were examined. Additional testing evaluating the tourniquets during extended application times and during simulated patient transport is underway using a SynDaver™ Synthetic Human, a human tissue equivalent manikin model with a circulatory system and heart pump. Performance metrics include application times, contact pressures, and most importantly, whether the device is able to achieve and maintain occlusion.

Evaluation of Extremity Tourniquets
Policy decisions implemented in 2005 to broaden tourniquet use by US military personnel in TCCC have led to a dramatic reduction in the number of deaths attributed to extremity hemorrhage in the last decade. Currently, several extremity tourniquets are on the market, and rigorous independent testing is imperative to ensure that the Service Member is equipped with the most effective, reliable, and operationally sound tourniquet designs. Researchers at Naval Medical Research Unit–San Antonio, sponsored by the US Army Medical Materiel Development Activity (USAMMDA) and the Marine Corps Systems Command, have evaluated extremity tourniquets for safety and efficacy using HapMed instrumented manikin limbs in different simulated field conditions, including limited visibility and soaked with a blood simulant. Thirteen tourniquet designs underwent initial testing to examine their performance and operational characteristics. Seven tourniquets performed at an acceptable level and are undergoing further evaluation using a SynDaver™ Synthetic Human and during self-applications. Performance metrics collected included application time and contact pressure, as well as end-user feedback.

The Safety of Early, Fresh Whole Blood (FWB) Transfusion Among Severely Battle Injured at US Marine Corps Forward Surgical Care Facilities in Afghanistan
In Afghanistan, care of the acutely injured trauma patient commonly occurred in facilities with limited blood banking capabilities. Apheresis platelets were often not available. Component therapy consisted of 1:1 packed red blood cells and fresh frozen plasma. FWB transfusion often augmented therapy in the severely injured patient. NHRC and NMCSD collaborated to analyze the safety of FWB use in a resource-limited setting. Using NHRC's comprehensive EMED, severely injured Service Members presenting to three US Marine Corps expeditionary surgical care facilities in Helmand Province, Afghanistan, between January 2010 and July 2012 were examined. Included in the review were patients with ISS of 15 or higher receiving blood transfusions. A total of 61 patients were identified; all were male Marines with a mean age of 23.5 years (standard deviation = 3.6), 89 percent were injured by blasts, and 74 percent suffered at least one traumatic amputation. The group receiving FWB was noted to have higher ISSs and lower blood pressure and base deficits on arrival, and all but one (25/26, 96 percent) were injured by blasts.

Photo credit: Senior Airman Bahja J. Jones/US Air Force



Results showed that traumatic coagulopathy was significantly less common in the group receiving FWB. Multivariable models found no other significant differences between the treatment groups. The early use of FWB in a resource-limited setting seemed to confer a benefit in reducing traumatic coagulopathy in this population. More research is needed to determine the overall safety of FWB use. In a resource-limited setting where TBIs are prevalent, the early use of FWB seems to confer a benefit in reducing traumatic coagulopathy. This finding is particularly noted when associated with procoagulant use. NHRC's findings contribute to a developing body of literature advocating for FWB use in appropriate settings. FWB is potentially a superior therapy for casualties requiring massive transfusion in facilities with limited blood-banking capabilities. The small sample size of the study precludes further statement on the overall safety of FWB use, and further research on the topic is needed. These findings may have significant implications to physicians developing contingency plans for trauma care delivery during times of natural or manmade disasters.

Pragmatic Randomized Optimal Platelet and Plasma Ratios (PROPPR) Trial: Design, Rationale and Implementation

Forty percent of in-hospital deaths among injured patients involve massive truncal hemorrhage. These deaths may be prevented with rapid hemorrhage control and improved resuscitation techniques. The PROPPR Trial was designed to determine if there is a difference in mortality between subjects who received different ratios of FDA approved blood products. Between August 2012 and December 2013, 680 patients were randomized. The overall median time from admission to randomization was 26 minutes. PROPPR is the largest randomized study to enroll severely bleeding patients. This study showed that rapidly enrolling and successfully providing randomized blood products to severely injured patients in an EFIC study is feasible. PROPPR was able to achieve these goals by utilizing a collaborative structure and developing successful procedures and design elements that can be part of future trauma studies.

Clinical Study of Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) for Severe Pelvic Fracture and Intra-Abdominal Hemorrhagic Shock

REBOA is a minimally invasive technique used by the trauma, critical care, and emergency medicine community to temporarily occlude large vessels using a balloon. REBOA results in reduced blood loss, improvement of central hemodynamics, fewer blood transfusions, and less time to the operating room or interventional angiography suite. REBOA was approved by FDA in January 2015. Pryor Medical has scheduled first delivery of its catheters in January 2016.

Wound Infection Mitigation

Antibiotic-Loaded Biopolymer Sponge for Prevention of Polymicrobial Wound Infection

Researchers from the University of Memphis have been working to combat infections in traumatic injuries using a scaled-up chitosan sponge delivery system to provide reliable, low-cost infection prevention that can be used in conjunction with surgical debridement and irrigation and systemic antibiotic regimens. In a murine model, the team demonstrated effectiveness of dual antibiotic (amikacin and vancomycin) loaded sponges against polymicrobial bacterial contamination *(Staphylococcus aureus* and *Pseudomonas aeruginosa)* and biofilm formation. Bionova Medical Inc., commercial licensing partner of the chitosan sponge technology and sub-award recipient, has made significant progress in the past year toward expansion and development of the technology into the marketplace. The chitosan technology was commercialized and officially launched as the Sentrex BioSponge in August 2014. Prior to launch, Bionova conducted a pilot study in goats to assess the degradation characteristics of the device in a clean injury, with both bony involvement and soft tissue injuries. Through this pilot study, it was determined that the device was biocompatible, with test subjects showing no adverse events related to sponge implantation.

Successful launch of the Sentrex BioSponge began with two large trauma centers—Regional One Health in Memphis, Tennessee, and University of Arkansas for Medical Sciences in Little Rock, Arkansas. The Sentrex BioSponge itself has been used to treat a variety of wounds, from surgical sites to open fractures, and even chronic, non-healing ulcers, and to date has been used over 800 times clinically in over 30 centers. The majority of use has been in orthopaedic trauma, although many uses have come on chronic non-healing wounds at surgical wound care centers. The Sentrex BioSponge was added to the Federal Supply Schedule on 1 April 2015. Transactions to VA and government hospitals are facilitated by the company Tryco. This study has resulted in a novel adjunctive therapy to prevent and treat infections associated with traumatic orthopaedic wounds, improving treatment outcomes for compound extremity fractures for both military and civilian populations. The cost-effective and time-saving treatment strategy can reduce the impact of these injuries on military healthcare resources.

Facial, Hearing, and Visual Injuries

Assessment and Treatment of Blast-Induced Auditory and Vestibular Injuries

Researchers at the WRAIR have developed complementary rodent models to characterize the effects of blast exposure on both the auditory and vestibular organs of the inner ear in conjunction with assessments of the disruptions in connections among the brain structures involved in auditory and vestibular signal processing. In collaboration with investigators at the National Institute for Deafness and Other Communicative Disorders and the Lieber Institute for Brain Development at the Johns Hopkins School of Medicine, these investigators are developing strategies for mitigating or reversing auditory/vestibular injury that originates from damage to mechanosensory hair cells and brain structures. The most common symptoms after blast exposure are headaches, hearing loss, balance problems, and dizziness, which strongly suggest impairment of blast waves to the structure of inner ear and neuronal encoding of sound. Using an advanced blast simulator that produces a high fidelity recreation of blast overpressure in the laboratory, rodents are exposed to shock waves to characterize the etiology of blast-induced hearing loss and balance disorders.

Photo credit: Lance Corporal Levi Schultz/US Marine Corps

Along with histopathological and neurochemical assessments, quantification and characterization of the auditory and vestibular injuries and efficacy of therapeutic interventions are judged by a battery of functional assessments, including auditory brainstem response, distortion product otoacoustic emission testing, vestibular sensory evoked potentials, and vestibulomotor functional measurements. Blast exposure causes dramatic disruptions in these functional parameters in association with progressively worsening hair cell loss and neuropathological changes in brain structures involved in central auditory and vestibular signal processing. These data indicate that both peripheral and central auditory systems are vulnerable to blast injury and also point to neuroinflammation as a pivotal contributor to the secondary neuronal damage underlying these debilitating injuries.

Standardization of Impulsive Auditory Hazards

Noise-induced hearing loss due to blast exposure reduces mission effectiveness, with associated healthcare costs to the VA reported to be $1.4 billion annually. Assessment and prediction of auditory hazards associated with blast injury has posed significant analytical challenges. ARL-sponsored research has shown that auditory hazard is not a simple function of summary waveform characteristics, such as waveform energy or peak pressure, and previous utilization of linear models are likely to have both over-predicted safe levels of exposure associated with the military's largest weapons systems, and under-predicted safe levels of exposure associated with rifles and other small-caliber weapons. These disparities are related to a non-linearity in the human auditory system that is captured in the AHAAH model. The AHAAH model, which is the result of over 40 years of experimental and analytical research and development, was recently incorporated in the newly published update to MIL-STD 1474(E), Design Criteria for Noise Limits (April 2015). It replaces previous standard hazard assessment models, making the AHAAH model the DoD criteria for evaluating compliance with impulsive noise limits, and providing materiel developers with improved and more accurate methods for assessing the risks of noise-induced injury to the Service Member in the technology development cycle. In the newly revised MIL-STD 1474 (E), AHAAH allows weapon developers to create more powerful weapons, because AHAAH accurately determines auditory risk, thereby eliminating the need for over-protection and the possibility of providing insufficient hazard assessment of the broad spectrum of blast-related impulsive noise exposures experienced by the Service Member.

Safe-Use Restrictions for Weapons and Improving PPE for Impulse Noise Protection

To reduce the risk of noise-induced hearing loss for Service Members, the Army Hearing Program (AHP) Noise Control Engineer provided safe-use restrictions for new weapons and weapon systems introduced into the Army's arsenal. In FY15, the AHP Noise Control Engineer conducted health hazard assessments for approximately 24 new materiel items and provided risk mitigation requirements, including PPE requirements and use restrictions, for safe use of the new materiel. The AHP Noise Control Engineer also prepared and instituted both Web-based and face-to-face programs to train industrial hygienists on the proper techniques for measuring and evaluating impulse noise, which are critical for properly assessing injury risk. The AHP also participated in several activities aimed at improving PPE for impulse noise protection. The AHP participated in a project with ARL Human Research and Engineering Directorate to continue developmental work on the hearing protection module for the AHAAH model. This capability enables the evaluation of impulse noise when hearing protection is worn using the AHAAH electroacoustic model of the ear and predicts the reduction of impulse noise at the ear afforded by all forms of hearing protection. The AHP consulted with PEO Soldier to make the Tactile Communication and Protective System non-radio hearing protection a Program of Record in FY15.

The Tactile Communication and Protective System is a device that offers hearing protection while maintaining situational awareness by attenuating loud sounds without attenuating quieter sounds.

MIL-STD 1474E (Design Criteria Standard—Noise Limits)

The AHP, USAPHC supported and engaged in a number of activities aimed at mitigating injury risk associated with impulse noise. The AHP participated in the DoD working group that was charged with updating MIL-STD 1474D, which was to be updated as MIL-STD 1474E. The new MIL-STD 1474E was published in April 2015. The AHP will continue working the MIL-STD as part of the Configuration Control Board established in FY15 to deal with implementation and updating matters. The AHP also proposed and implemented a new, innovative interim impulse noise damage risk medical criterion with the aim of developing a better medical risk assessment tool that addresses concerns from the medical community regarding portions of new MIL-STD. The AHP collaborated with the medical research community to focus research efforts on developing both short- and long-term tools for applying this new methodology.

Phase III Clinical Trials: D-Methionine to Reduce Noise-Induced Hearing Loss

Hearing loss can render a Service Member less able to detect and identify the enemy, less able to understand commands, particularly in background noise typical on the battlefield, and may permanently reduce quality of life. In some cases, hearing loss may preclude redeployment or result in less optimal job assignment. Currently, no FDA-approved pharmacologic prevention exists for noise-induced hearing loss. D-methionine is one of the more advanced pharmaceutical candidates to offer oto-protective ability after hazardous noise exposure. Investigators from Southern Illinois University have documented in animal studies that administration of D-methionine can reduce or prevent noise-induced hearing loss. The primary objective of the study was to determine the efficacy of D-methionine in preventing or reducing noise-induced hearing loss and tinnitus in a military population. The study population was a cohort of drill sergeant instructor trainees during, and 12 days after, their two-week weapons training that consisted of a minimum exposure to 1,100 rounds of M-16 weapons fire over a two-week period. By the end of 2015, 200 subjects will have completed the phase II trials at Fort Jackson, South Carolina. Preliminary results show a decrease in hearing loss from the trial participants. Further research and materiel development plans are being developed to achieve FDA approval.

Mechanisms and Mitigation of Hearing Loss from Blast Injury

Collaborating with groups from NMCSD, Applied Research Associates, and the University of Virginia in an investigation of blast-induced hearing loss from TBI, Cochlear Boulder, LLC has successfully developed a procedure to test whole cadaver heads using ARA's mobile shock tube, which is uniquely useful to this line of research and allows blast simulation to be safely performed near a medical research facility. Several forms of hearing protection were assessed, important to military protections, and they have shown that mitigation of ossicular displacements and intracochlear pressures secondary to blast and intense harmonic noise may be possible through stiffening/damping the ossicular chain, and that this may be achieved without adversely affecting auditory perception within the spectrum critical to speech perception. This research award has been completed and future studies are planned using actuators derived from Cochlear Boulder's MET to actively prevent injurious ossicular displacements. The actuator can be used in a fully implantable hearing system to remediate existing hearing loss, and at the same time, can be used to attenuate or block extreme ossicular displacements from blast exposure.

Effects of Blast Injury on Hearing in a Screened Military Population

Blast injury to the ear has emerged as one of the most common combat-related injuries among military personnel deployed during OEF and OIF, and may result in symptoms of tinnitus, hearing loss, and/or hearing shifts.

Photo credit: Sergeant Matthew C. Moeller/US Army

Exposure to hazardous noise, such as blasts, can compromise a Service Member's ability to hear and communicate, and thus, reduce situational awareness and operational readiness. mTBIs are also highly prevalent among those exposed to blasts and may pose a greater risk for future auditory impairments in blast-injured Service Members. To address this research gap, NHRC examined audiometric data from the comprehensive Blast-Related Auditory Injury Database of Navy and Marine Corps personnel who sustained a blast-related injury compared to those with a non-blast-related injury while deployed. Subjects included only those who had an audiogram within 12 months prior to and following injury. There were 661 Service Members with a blast-related injury and 913 with an non-blast-related injury identified by NHRC as having at least one audiogram within a year before and after injury (N = 1,574). Service Members in the blast-related injury group were more likely to be younger, infantry, sustain more injuries, and have higher ISS. Personnel who sustained a blast injury were significantly more likely than those with a non-blast-related injury to experience post-injury hearing loss and significant threshold shifts. An estimated 54 percent of risk for hearing loss in the blast-injured Service Members could be attributed to the blast-related injury event. A subgroup of 94 Navy and Marine Corps personnel with a provider-diagnosed, blast-related mTBI in NHRC's Theatre Concussion Clinic Neuroregistry and a pre- and post-injury audiogram were also examined to assess the association between initial mTBI symptoms and auditory outcomes. Results demonstrated that acute mTBI auditory symptoms are most related to auditory impairments within the first year after a blast-related mTBI. There were not any mTBI-specific acute symptoms that were related to auditory impairments. Future studies should compare blast and non-blast mTBI and its association with long-term auditory impairments. Auditory health and readiness are critical components of situational awareness and quality of life for the US military and combat Veterans. The results of NHRC's investigation about the hearing health status of deployed Service Members could provide decisive insight about operational readiness, injury prevention, and related medical problems. It is imperative to monitor the effects of blast injury on hearing outcomes, identify at-risk populations for early intervention and prevention, develop supportive policies and best practice guidelines, and allocate appropriate funds and resources.

Biomechanical Modeling and Measurement of Blast Injury and Hearing Protection Mechanisms

Funded by the DHA RDA Directorate, researchers at the University of Oklahoma are studying exposure to high-intensity sound or blast that directly results in hearing loss. Development of effective personal hearing protection devices for military Service Members has been a major focus for research in protection of blast injury. However, there is a profound lack of knowledge about how blast waves are transmitted through the ear and what specific changes occur in the ear structures following blast exposure. This research project investigates the biomechanical response of the middle and inner ear to noise/blast, using a combined modeling and experimental approach. A comprehensive finite element model of the human ear, including the three-dimensional components of the ear canal, middle ear, and cochlea, is further developed to simulate acoustic injury during blast exposure. Using human cadaver ears, researchers are quantifying the middle ear damage in relation to overpressure level and wave direction by simultaneously monitoring the pressure at the entrance of the ear canal (P0), near the eardrum in the canal (P1), and behind the eardrum in the middle ear cavity (P2), as well as the eardrum rupture threshold. Changes of dynamic properties of middle ear tissues after blast exposure are also determined. All these findings are employed to validate the finite element model. The peak pressure ratio P1/P0 predicted by the model is in the same value as that measured in human cadaver ears. Supplementing this research, a chinchilla model is being used to identifying middle ear protective mechanisms during blast exposure that rely on middle ear muscle activity. Electromyography of the stapedius muscle is measured from chinchillas during exposure and the results will be used for developing the active model of the human ear. The mass block attached to the stapes footplate and fixed on the bony wall through dash ports represents the cochlear load. The uniqueness of this research is that all ear components and hearing protection devices can be simulated in the finite element model for function analysis with anatomical, mechanical, and acoustic parameters. The project is directly relevant to provide a biomechanically validated three-dimensional model of the human ear so that a better understanding of prevention mechanisms of hearing loss in military operations can be obtained. The model will leverage the design and evaluation of both passive and active hearing protection devices for military applications.

Evaluation of Hearing Deficits in Blast-Exposed Listeners with Normal Audiometric Thresholds

Researchers at WRNMMC, Wilford Hall/Brooke Army Medical Center, NMCSD, and USAPHC are actively collecting data in a USAMRMC-funded study to evaluate the relationship between hearing acuity in complex listening tasks and deployment-related blast exposure in Service Members with normal or near-normal audiometric thresholds. The study is being conducted at hearing conservation sites where active duty Service Members are required to go once per year to get their surveillance audiograms. Service members who have H1 hearing profiles and are willing to participate in the study are asked to use a tablet-based computer to complete a short series of audio tests that were determined to be especially sensitive to the hearing deficits experienced by blast-exposed listeners in an earlier CDMRP-sponsored study at WRNMMC. This series of tests, which takes about 10 minutes to complete, is comprised of 1) a speech-in-noise test with a time-compressed target talker in the presence of spatially-separated, reverberant speech babble; 2) a binaural tone detection task; and 3) a short survey of subjective hearing systems. Preliminary results suggest that listeners with normal hearing who have been close to an explosive blast during a deployment are almost four times as likely as non-blast-exposed listeners to have abnormally poor scores on either the objective audio tests or the audio symptom questionnaire. This blast-related hearing impairment seems to be independent of and additive with the effects of mild hearing loss.

More than 1000 subjects were recruited into the study in FY15, and up to another 2000 are expected to be recruited in FY16.

Airway Management in Severe Combat Maxillofacial Trauma

Airway stabilization is critical in combat maxillofacial injury as normal anatomical landmarks can be obscured. The objective of this retrospective database analysis was to characterize the epidemiology of airway management in maxillofacial trauma from military treatment facilities in Iraq and Afghanistan and stateside tertiary care centers. In total, 1,345 military personnel with combat-related maxillofacial injuries sustained March 2004 to August 2010 were identified from the EMED using International Classification of Diseases, 9th Revision, Clinical Modification codes. This tri-Service capability, resident at NHRC, documents each casualty that occurs in overseas contingency operations within seven days of injury. The injuries contained in the EMED are coded with diagnoses and ISSs by trained nurse coders. A total of 239 severe maxillofacial injuries were identified. The most common mechanism of injury was improvised explosive devices (66 percent), followed by gunshot wounds (8 percent), mortars (5 percent), and landmines (4 percent). Of the subjects, 51.4 percent required intubation on their initial presentation. Of tracheostomies, 30.4 percent were performed on initial presentation. Of those who underwent bronchoscopy, 65.2 percent had airway inhalation injury. There was a significant relationship between the presence of head and neck burn and association with airway inhalation injury. There was also a significant relationship between the severity of facial injury and the need for intubation, as well as the presence of maxillofacial fracture and the need for tracheostomy. This unique study is a collaboration between Medical Modeling, Simulation & Mission Support (Department 161) NHRC and NMCSD. Results from this work highlight the important point that there is a high incidence of airway injury in combat maxillofacial trauma, which may be underestimated. Because of this, it is important for healthcare providers to assess this as part of maxillofacial trauma cases. This indicates that airway management in this population requires a high degree of suspicion and low threshold for airway stabilization.

Biomimetic Delivery of Biomolecules for Craniofacial Bone Regeneration

Recent improvements in body armor have reduced the rate of combat death but increased the rate of extremity and head and neck injury, burn, and limb loss in surviving casualties. Vascularized composite allotransplantation has recently emerged as a promising strategy for the repair or replacement of lost limbs and complex tissue loss. As vascularized composite allotransplantation is a burgeoning field, there are many fundamental elements relating to its biology and outcome that remain undefined, but have been well defined in standard transplantation. The principal objective of this project, managed by JPC-8 (CRM), is to hone vascularized composite allotransplantation into a useful therapeutic option for patients in need of advanced tissue reconstruction and replacement. The proposed studies include novel fundamental, translation, and clinical investigations specifically designed to inform data-driven clinical practice guidelines for this emerging option for reconstructive surgery. The results of this study will greatly aid decision making regarding ongoing and future cost-effective care of DoD casualties and Veterans with head and neck injuries and limb injury and loss, potentially leading to improved rehabilitation, psychological adjustment, deployability, and reintegration to the community. The ultimate goal is to expand the available options for individuals with combat-related injuries in need of complex tissue reconstruction by elevating vascularized composite allotransplantation to the level of an established therapy for use in appropriately selected personnel with severe traumatic tissue loss.

Visual Dysfunction at Different Stages Following Blast and Non-Blast mTBI

Researchers from USAARL assessed the frequency and types of visual defect seen at different testing stages following non-blast and blast-induced mTBI.

Data for the study were obtained from a comprehensive retrospective review of electronic health records of 500 US Service Members with a diagnosis of deployment-related mTBI who received eyecare at the Landstuhl Regional Medical Center. For analysis, the data were grouped by mechanism of injury and each group was further divided in three subgroups based on the number of days between injury and initial eye exam. The results showed a high incidence of visual symptoms and visual dysfunctions. However, the prevalence of visual symptoms and visual dysfunctions did not differ significantly between groupings by mechanism of injury and post-injury stage, except for eye pain and double vision. Among visual symptoms, binocular dysfunction was most common, including higher near vertical phorias, reduced negative fusional vergence breaks at near, receded near points of convergence, decreased stereoacuity, and reduced positive relative accommodation. The lack of difference in terms of visual sequelae between the blast and non-blast groups suggests that TBI research from the civilian (i.e., non-blast) environment is relevant to military personnel where combat injury results primarily from a blast event.

Effects of Repetitive Low-Level Blast Exposure on Visual Systems and Ocular Structures

Blast injuries to ocular structures and the visual system, particularly those that may be caused by the primary blast wave, are a significant concern due to the high prevalence of blast injuries seen over the past two decades of conflict in the Middle East. In a paper recently published in Military Medicine, sponsored by USAMRMC, USAARL researchers recruited seventeen USMC breacher instructors, assigned to Quantico, Virginia, who were assessed for signs of ocular damage as a result of exposure to repeated blast waves. The results from the study suggest that exposure to repetitive low-level primary blast may have detrimental effects on corneal endothelial cell density, near vertical phoria deviations, and general visual field sensitivity. Findings of the USAARL study highlight the importance of performing threshold perimeter testing in those who have suffered an mTBI or concussion-like events. Despite these findings, all test results in the experimental (cadre) group were within, or slightly lower (worse) than, normative value ranges defined for each test. These findings show that the current levels of blast exposure used in breacher training appear to be safe. However, health care providers should consider select ophthalmic tests in those individuals who have been exposed to repetitive blasts.

Program Area: Reset

The DoD Blast Injury Research Program is committed to reducing recovery time and improving the quality of life for Service Members who have experienced blast injuries. These efforts maximize the possibility of their return to duty and reintegration into the civilian community and workforce. Medical research in the area of Reset informs evidence-based clinical guidelines for procedures that restore critical function and improve disfigurement. It also forms the basis for rehabilitation programs for blast-related psychological disorders, amputations, and other injuries with long-term effects on quality of life. Reset strategies backed by extensive medical research enable the DoD and military medical community to retain the confidence and trust of Service Members, their Families, and the American public through measurable improvements to Service Member recovery.

Neurocognitive Function and Psychological Health

Assessing the Impact of mTBI on Multisensory Integration while Maneuvering on Foot

Researchers at WRNMMC and the NICoE have completed the first round of data collection in a USAMRMC and Psychological Health/Traumatic Brain Injury Research Program (PH/TBIRP)-funded study designed to examine how well active duty individuals with a history of blast exposure and mTBI can use auditory signals to visually acquire targets while standing and walking.

The study was designed around the CAREN, which is an immersive virtual environment located at the NICoE that allows participants to view images on a 180-degree video screen while standing or walking on an articulated treadmill. For the purposes of this study, a 64-speaker array was erected behind the projection screen to allow the presentation of spatialized audio sources originating from the same location as visual targets. All participants in the study (38 mTBI patients and 35 healthy controls) were tested in three conditions: 1) a baseline auditory localization task, which required participants to move a visual cursor to the perceived location of a sound source; 2) a baseline visual discrimination task, which required participants to identify a visual target presented from a known location; and 3) a "visual search" task, which required participants to identify a visual target presented at a random location in a field of 263 visual distractors. This visual search task was presented both as a visual only task with no audio signal, and as an aurally-aided visual search task where a spatialized audio cue was presented at the location of the visual target. Preliminary results show that performance was equivalent in the control and mTBI groups in the auditory localization task and the visual discrimination task, but that the mTBI listeners required significantly more time than the healthy controls to perform the visual-only and aurally-aided visual search tasks. The results also show that both the mTBI and control listeners were able to localize sounds faster, with no loss of accuracy, when they were walking on the treadmill than when they were standing. Both groups were also able to perform the aurally-aided visual search task more quickly when they were walking. This result illustrates the importance of evaluating complex multisensory tasks in order to determine the impacts that mTBI may have on sensory processing for blast-exposed individuals.

Vestibular Rehabilitation Using an Immersive Virtual Environment at NHRC

This project established novel rehabilitation therapies for patients with mTBI needing vestibular therapy as a result of blast or other injury under the sponsorship of BUMED. The therapies aim to accelerate recovery from mTBI and allow for faster return to duty or reintegration into society by using an immersive virtual environment, also known as CAREN, for vestibular therapy at NHRC. The project hosts one of the largest cohorts of vestibular patients that have participated in a single study at any of the US DoD CAREN sites. The novel rehabilitation program on the CAREN was compared with a program using traditional vestibular rehabilitation therapy in the clinical setting at NMCSD. 39 patients participated in the study. Patients were assigned to one of three groups and underwent 12 vestibular therapy sessions. Group 1 participated in six sessions in the traditional clinical setting and six sessions on the CAREN system, Group 2 participated in 12 sessions on the CAREN system, and Group 3 participated in twelve sessions of therapy in the traditional clinical setting. Preliminary results show that all groups significantly improved on standardized vestibular tests—such as the Activities-specific Balance Confidence Scale, Dizziness Handicap Inventory, Sensory Organization Test/Posturography, and the Functional Gait Assessment—over a six-week rehabilitation program. Walking speeds and weight shifting abilities of the patients participating in therapy on the CAREN were similar to those of an uninjured control population at six weeks. This work has shown the ability of physical and cognitive improvements to carry over to activities of daily life, demonstrating that training and rehabilitation in the CAREN environment is not only useful for CAREN-specific tasks but benefits the mTBI patient in daily living. Research findings suggest that the CAREN system can be an effective and challenging treatment modality for persons with vestibular dysfunction. Currently, similar therapy is being introduced to other subject populations such as those with vertigo and motion sickness.

Longitudinal Performance Change Related to Repeated Low-Level Blast Exposure

Exposure to blast is associated with reports of cognitive disruption. Even low-level exposure is hypothesized to yield effects, particularly cumulative effects. The hypothesized effects are reported to be cognitive deficit similar to head injury. "Breaching" (dynamic entry) involves repeated exposure to overpressure. In a study sponsored by MOMRP, 14 members of an elite breaching unit from New Zealand participated in longitudinal assessments that involved taking the Automated Neuropsychological Assessment Metrics multiple times over the course of several years. Many of these participants have data spanning five years of time. The repeated measure analysis of variance resulted in no significant effects for any of the subtest. However, there was a mean decrease of 135 milliseconds in the mathematical processing subtest from pre-exposure to post-exposure. Pre-test administration varied from two years to five years before the post. While not statistically significant, this data suggests the possibility of a longitudinal decrement. The lack of significance with a 135 millisecond decrement is probably a result of the high inter-subject variability. Additional analyses using change scores as well as looking at individual participants are underway and will be presented at the conference.

Brain Injury Biomarkers and Behavioral Characterization of mTBI in Service Members Following Repeated Low-Level Blast Exposure

The concern for negative effects from blast exposure is based on rates of operator self-reported headache, sleep disturbance, working memory impairment, and other concussion-like symptoms. A challenge in research on this topic has been the need for improved assessment tools to empirically evaluate the risk associated with repeated exposure to blast overpressure levels commonly considered to be too low in magnitude to cause acute injury. Evaluation of serum-based neurotrauma biomarkers provides an objective measure that is logistically feasible for use in field training environments. Among candidate biomarkers, ubiquitin carboxy-terminal hydrolase-L1 (UCH-L1) has some empirical support and was evaluated in a study by collaborators at WRAIR and NMRC. The team used daily blood draws to examine acute change in UCH-L1 among 108 healthy military personnel who were exposed to repeated low-level blast across a two-week period. The research volunteers also wore pressure sensors to record blast exposures and wrist actigraphs to monitor sleep patterns, and completed daily behavioral assessments of symptomology, postural stability, and neurocognitive function. UCH-L1 levels were elevated as a function of participating in the two-week training with explosives, but the correlation of UCH-L1 elevation and blast magnitude was weak and inconsistent. Also, UCH-L1 elevations did not correlate with deficits in behavioral measures. These results provide some support for including UCH-L1 as a measure of central nervous system effects from exposure to low-level blast. However, the weak relation observed suggests that additional indicators of blast effect are needed.

Assessment of Subtle Cognitive Changes Following Low Level Blast Exposure

The neurological deficits of mTBI can be subtle. This may be especially true in cases involving repeated sub-concussive events. Inferential statistics on neuropsychological scores may not be appropriate for detecting between-group differences in these scenarios. A sub-group of individuals with poor performance may be masked by others in the normal range. A more sensitive methodology may be calculating the reliable change interval (RCI) between pre- and post-test measurements, then determining whether individuals fall into this range. Researchers at DVBIC, the NMCSD, Space and Naval Warfare Systems Command, NSWC, and the USUHS investigated the RCI as a methodology for detecting neuropsychological deficits associated sub-concussive blast events. The researchers collected pre- and post-test neuropsychological measurements on learning (Hopkins Verbal Learning Test-Revised [HVLT-R]), delayed recall (HVLT-R DR), processing speed (Trail Making Test Part A), and executive function from Service Members who participated in a combat training course.

Participants fired shoulder-mounted munitions while sensors on their person recorded blast events above 2.5 psi. The researchers compared pre-training to post-training measures using three methods: inferential statistics (paired samples t-test), individual change with reliable RCI using a 90 percent confidence interval, and RCI with a correction for practice effects. Service Members experienced a median of five blast events above 2.5 psi in a one-hour period. The paired sample t-test showed no difference between pre- and post-test groups. The RCI methodology showed a larger than expected ($p < 0.001$) number of participants had lower scores on the learning (HVLT-R: 15.6 percent) and delayed memory tasks (HVLT-R DR: 20.3 percent). The RCI adjusted for practice effects did not appreciably change the number of participants with lower-than-normal scores. The study found that the paired t-test was unable to detect differences between pre- and post-test neuropsychological measures. However, the RCI methodology found that a higher-than-expected percentage of participants with low HVLT-R scores after combat training. The results suggest real cognitive deficits are associated with the repeated sub-concussive blast exposure. Specialized analysis of neuropsychological data may be necessary to detect this condition.

Examining the Internal Construct Validity of the NSI Using Rasch Model Analysis

The primary aim of this study is to assess the internal construct validity of the NSI (Cicerone & Kalmar, 1995), a 22-item self-report measure of post-concussive symptoms in a sample of OEF/OIF Veterans with a history deployment related TBI using Rasch model analysis. The NSI is the most widely used patient reported outcome measure of post-concussive symptoms among Veterans and military personnel. Psychometric analysis of the NSI has relied on traditional approaches, which are limited because they do not meet the fundamentals of measurement, e.g. unidimensionality of scale or hypothesized subscales are not explicitly tested, summation of raw ordinal scores are erroneously treated as interval data, and all items are given the same weight. Evaluation of NSI using modern psychometric approaches is crucial to attaining conjoint measurement, a prerequisite for calculating change scores. Collaborators of the Program include the Department of the Army, Department of the Navy (Marine Corps), Department of the Air Force, and VA. The study was a retrospective analysis of NSI data collected from the VA National Comprehensive TBI Evaluation database for FY08 and FY09. Cases were included that met one of the America Congress of Rehabilitation Medicine criteria for mTBI. Included cases were randomly assigned to either an evaluation or validation sample. Analyses were conducted on 9,679 cases from the evaluation sample. The study examined the dimensionality of the NSI using both factor and Rasch analysis. The Rasch measurement properties of NSI symptom domains were also examined for model fit, person separation and reliability, dimensionality, item hierarchy, rating scale structure, and item invariance by gender and PTSD. The initial Rasch analysis with all 22 items of the NSI (9,679 OEF/OIF Veterans; 94.2 percent males; mean age= 30.7 years) indicated that the NSI is multidimensional (first contrast eigenvalue = 3.1; exceeds the criteria of < 2). Principal Component Analysis of Rasch residuals for symptom domains confirmed unidimensionality of vestibular-sensory, cognitive and mood-behavioral symptoms scales but not the cognitive symptoms scale (1st contrast eigenvalue = 2.1). Examination of contrasts revealed that cognitive symptoms were clustered together providing more support for this three-factor solution. In conclusion, the NSI Total Score is not valid and should not be used as a clinical outcome. However, a three-factor solution comprised of vestibular-sensory, cognitive and mood-behavioral symptoms appears to represent unidimensional domains and acceptable Rasch properties. Hearing loss demonstrated significant differential item functioning by gender (on average much harder to endorse for women). There was no differential item functioning for items in any of the symptom domains compared by PTSD status.

Balad/Bagram Longitudinal Assessment of the Symptoms of TBI/PTSD

The lack of collaboration between neurologist and psychologists has been one of the greatest shortcomings of this area of research, and is a large part of the rationale behind this study sponsored by the USAF and performed by the University of Texas Health Science Center at San Antonio. The study was separated into three different phases: Phase I—Retrospective Study of Archival Clinical Data: Conduct retrospective evaluation of TBI/PTSD clinical assessment data already collected on 700 Blast patients at Balad; Phase II—Prospective Study: Convene experts to analyze data to disentangle symptoms of TBI/PTSD assessment battery and conduct prospective study of the assessment battery in Afghanistan; Phase III—Follow-up assessment study: Conduct 12-month follow-up evaluations of study participants; reconvene the panel of experts to develop a recommended decision tree for treating patients with TBI/PTSD. Recruitment for Phase II was halted due to the on-site neuropsychologist being transferred to another location. A replacement neuropsychologist was not provided, thus recruitment for the patients who suffer from TBI was forced to be closed, three months earlier than planned. Other factors that contributed to the limited number of participants that were recruited include a lull in the fighting season during the winter and a reduction in military personnel due to the upcoming withdrawal of troops from Afghanistan. It was determined that the recruitment goal for this study would not be met; however, the University of Texas Health Science Center at San Antonio continued follow-ups with enrollees. A final report was submitted for the in-theater Phase II protocol in June. In April 2014 the Cooperative Agreement provided a No-Cost Extension to May 2015. The final report for Phase I is in preparation.

No Significant Acute and Subacute Differences Between Blast and Blunt Concussions Across Multiple Neurocognitive Measures and Symptoms in Deployed Service Members

Researchers at the NICoE examined the effect of blast or blunt trauma on neurocognitive function. Assessments were conducted within 72 hours of injury using the Military Acute Concussion Evaluation, the Automated Neuropsychological Assessment Metrics, traditional neuropsychological tests and health status questionnaires. Participants included 50 military Service Members who experienced a TBI. Of the 50 participants, 34 had blast-related injuries and 16 had blunt-trauma injuries. These results demonstrate no differences between blast injury and blunt injury participants on any of the psychological assessments, or in any demographic parameters. Multiple neurocognitive assessments administered to personnel who have suffered either blast or blunt trauma did not detect any differences between the two injury types. This suggests that models derived from sports or mechanical events may be equally effective in developing sensors, protective gear, and treatments, as using blast injury models.

A Multi-Site Study of the Relationships between Blast Exposures and Symptom Reporting in a Post-Deployment Active Duty Military Population with mTBI

Cumulative blast exposures result in greater impairment, suggesting the need to develop more effective means of monitoring the exposure of military personnel to blasts. Additionally, studies investigating cumulative or repeated blasts should ensure that a sufficient number of blasts are applied under experimental conditions to appropriately mimic the neuropathological changes. Researchers at the NICoE examined the influence of previous cumulative blast exposures on symptom reporting after mTBI. Post-concussion symptom reporting was completed using NSI and the PTSD Checklist—Civilian version.

Participants included 573 military Service Members with mTBI, who were divided into four groups based on the number of blast exposures (1, 2, 3 and 4–10 exposures), along with a non-blast control group. Results showed greater impairment in individuals with three to ten blast exposures compared to the one and two blast exposure groups. These results suggest the need for further investigation into relationships between cumulative blast exposures, symptom reporting, and neuropathological changes.

The Neuropsychological Outcome from Military-Related TBI: Preliminary Analyses of the Role of Resilience, TBI Severity, and Blast Exposure

Several factors may affect outcomes after TBI. Patient resilience is a currently less understood, but potentially important variable. Resilience is multi-dimensional in nature and may involve a patient's outlook, openness to experience, and motivation to meet challenges. In short, resilience is how well a patient is able to cope psychologically and behaviorally with a trauma. Understanding why some are better able to adapt than others may inform TBI treatment and rehabilitation strategies. Investigators at DVBIC, WRNMMC, and the NICoE researched the effect of resilience on outcomes after TBI. The researchers administered a test battery consisting of neurocognitive and neurobehavioral measures to 60 Service Members who had sustained mild to severe TBIs. Analysis involved calculating the effect sizes for different divisions in the data: TBI severity (uncomplicated mTBI versus complicated mTBI-severe), blast (blast versus non-blast), and resilience (high versus low). Comparing groups based on TBI severity and blast resulted in medium effect sizes on both neurocognitive and neurobehavioral measures. Comparing groups based resilience resulted in medium to very large effect sizes for neurocognitive (68.8 percent) and neurobehavioral (89.7 percent) measures. These results indicate resilience is more strongly associated with neuropsychological outcome than either TBI severity or blast. This suggests that resilience is an important factor in TBI recovery. Further research is necessary to fully understand the impact of resilience and appropriate ways to measure the trait. Understanding resilience may inform the design of TBI rehabilitation programs, ultimately affording better care to the injured Service Member.

Novel Motor-Skill Therapy Improves Attention and Memory in Blast-Related TBI

Interactive metronome (IM) therapy is an operant conditioning program that develops precision motor timing and coordination. The therapy could be of service to TBI patients by improving efficiency in cerebellar connections. The ultimate result of this therapy may be an improvement in memory and attention among those afflicted with post-concussive symptoms. Investigators with DVBIC, Fort Carson; the Evans Army Community Hospital, Fort Carson; General Dynamics Information Technology; US Public Health Service; Chenega Corporation; and the University of Washington researched the effect of IM therapy on patients with blast-related TBI. The researchers recruited 48 active duty Service Members with a documented history of mild to moderate blast-related TBI. Patients were randomly assigned to standard rehabilitation care (SRC) or standard rehabilitation care with the addition of 15 sessions of IM therapy (IM+SRC). Outcome measures were assessed using the Repeatable Battery for Neuropsychological Status (RBANS), administered at three time points (T1, T2, and T3). Data were analyzed using a one-way, between-groups analysis of covariance with RBANS index scores as the independent variable, treatment as the dependent variable, baseline scores, and loss of consciousness as covariates. The IM+SRC group showed a significant 20 percent increase in RBANS delayed memory scores throughout the course of the treatment. In contrast, the SRC group showed no difference in delayed memory with therapy. The IM+SRC group showed significantly better RBANS immediate memory scores at T2 and significantly better RBANS attention scores at T3. IM therapy resulted in significant improvements in memory and attention among blast-related TBI patients.

Photo credit: Mass Communication Specialist Second Class Jeff Troutman/US Navy

This improvement was greater than SRC alone. Recent research suggests the cerebellum is functional in memory and attention in addition to motor control (Koziol et al., 2013). These findings suggest there is transference from practicing precision motor tasks to cognitive performance. Operant training of precision motor skills may improve cognitive abilities by strengthening neural networks in the cerebellum. More research is necessary to evaluate the benefits and limitations of this therapy. It could represent an effective way of treating both Service Members and civilians after sustaining a mild or moderate TBI.

Predicting Return to Duty Status in an mTBI Military Population

mTBI in combat settings may result from blast exposure. A survey of 2,525 US Army Service Members returning from Iraq reported that 72 to 79 percent of head injuries were caused by blast (Hoge et al., 2008). At present there are no tests that accurately predict whether mTBI patients will return to duty or will proceed to a military medical board for further evaluation. Investigators at the DVBIC/Intrepid Spirit at Camp Lejeune, North Carolina, performed a study to identify variables that differentiate TBI patients sent to the medical board and those healthy enough to return to duty. The researchers searched the AHLTA database, acquired, and de-identified the records of 350 patients seen at the Naval Hospital at Camp Lejeune, North Carolina. Relevant variables included blast injury history, brain injury history, loss of consciousness, health risk factors/comorbidities, clinical exam results, medical evaluation board status, laboratory test values, neuropsychological status, self-report measures, and CT, MRI, and positron emission tomography scans. Between-group testing indicated that there is no statistical difference between the medical board and return to duty patients on any laboratory tests (i.e., blood count, comprehensive metabolic panel, erythrocyte sedimentation rate). There were, however, significant differences between the medical board and return to duty patients on neuropsychological variables. Therefore, understanding what factors are most prognostic in patients with TBI is critical in designing effective long-term treatment plans.

This study provides evidence that neuropsychological testing is a significant factor in determining whether mTBI patients return to duty or receive further medical treatment. The results indicate that for mTBI patients, neuropsychological testing is perhaps the best indicator of referral to the medical board. These findings could inform clinical strategy in how the military employs and cares for injured Service Members.

Predicting Return to Duty Status in a Blast Exposed mTBI Military Population

This DCoE-sponsored study was done in conjunction with the University of Pennsylvania and Children's Hospital of Philadelphia and examine lab, imaging, and neuropsychological tests of 318 blast exposed Service Members with mTBI. The purpose of the study was to develop a predictive model through the use of clinical tools of those blast exposed Service Members who are more likely to return to duty as opposed to being referred for a medical board. An initial review of lab and imaging data, as well as self-report measures, including the PTSD Checklist, Alcohol Use Disorders Identification Test, Neurobehavioral Symptom Inventory, Pittsburgh Sleep Quality Index, and Patient Health Questionnaire-9 were sectioned by individuals who proceeded to a medical board and those who returned to full duty suggested no differences between these two groups. However, on a cognitive screen using the RBANS, there was a statistically significant difference between the medical board group and returned to full duty group, with the medical board group scoring significantly lower ($p < .01$). The fact the RBANS scores were significantly lower in the group that proceeded to the medical board suggests that the RBANS may be helpful as a prognostic indicator of individuals who are likely to return to duty and deserves further study. By identifying those individuals most likely to return to full duty early in the recovery process, Service Members can be provided with a more hopeful prognosis related to their ability to return to their military career.

A Prospective, Longitudinal Study of the Predictive Validity of the Military Functional Assessment Program (MFAP) for Predicting Successful Return to Duty

High rates of neurosensory injury from combat operations directly impact the health and well-being of both individual Service Members and troop readiness; thus, it is imperative to evaluate the psychometrics of assessments guiding return to duty decisions. The MFAP is a military-relevant assessment using multidisciplinary sources to verify Service Member cognitive and physical fitness. Researchers from the USAARL evaluated the relationship between clinical assessments and MFAP scores, and the predictive validity of MFAP scores on successful return to duty (or reintegration to civilian life). Active duty male and female Service Members (18 to 45) with a history of at least one concussive event were administered a clinical screening battery prior to treatment and rehabilitation. This battery includes core cognitive, psychological, vestibular, and occupational assessments. Other data include demographics, MFAP scores, and return to duty determinations. Follow-up data were collected at six and 12 months post-MFAP to include online self-report clinical assessments and structured phone interviews of occupational/cognitive performance. The six tasks most highly related to MFAP performance require judgment and decision-making skills as well as the ability to work well under pressure. The study was instrumental in evaluating the usefulness of the MFAP in assessing Service Member readiness to return to duty after mTBI (blast or non-blast). An ongoing study is correlating MFAP scores with actual Service Member job performance after returning to duty.

Dual-Task Assessment Using the CAREN: Implications for Service Members with Co-Morbid mTBI and PTSD

Given the overlapping symptoms of mTBI and PTSD, the evaluation of dual-task skills is important because deficits can have a negative impact on decision making and the Service Member's ability to perform mission essential tasks.

The NICoE's study seeks to determine whether the CAREN can be effectively utilized to assess dual-task performance in Service Members with comorbid mTBI and PTSD. Outcome measures will be obtained from a conventional dual-task performance assessment, the Walking and Remembering Test, and compared to those obtained through use of the CAREN Walking and Remembering Test and Dual-Task Rank Insignia applications. In the past, cognitive visual tasks had been ruled out when developing dual-task assessments because of the difficulty in implementing visual task components during gait; however, use of the CAREN allows visual tasks to be incorporated on the screen as Service Members simultaneously walk on the system's treadmill. The CAREN Dual-Task Rank Insignia application may be more appropriate for evaluating this patient population and could provide clinicians with further insight into deficits identified. To date, 25 impaired and 12 control participants have completed the protocol. Preliminary analyses, of the results collected to date, indicate that there are trends emerging in the data but that a greater sample is needed to determine significance. Hence, the researchers are still recruiting healthy controls.

Influence of the Severity and Location of Bodily Injuries on Post-Concussive and Combat Stress Symptom Reporting after Military-Related Concurrent mTBIs and Polytrauma

Researchers at the NICoE reported that injuries to three bodily regions, the face, abdomen, or extremities, were significant predictors of the total score on a NSI. Two regions, the face and extremities, were predictors of the total score on the civilian form of the PTSD Checklist—Civilian version. Participants included 579 military Service Members with an uncomplicated mTBI with concurrent bodily injuries. Assessments were collected within 2.5 months of the injury, on average. These results suggest an inverse relation between bodily injury severity and symptom reporting, which may be due to underreporting of symptoms, increased peer support, disruption of fear conditioning due to pharmaceutical intervention, or delayed symptom expression. Additional studies are needed to better understand the correlation of injuries with neurobehavioral symptom inventory. Assessments of injured personnel based on self-report symptom reporting should be interpreted with caution due to possible underreporting, pharmaceutical intervention, delayed expression of symptoms, or disruption of fear conditioning.

Military Personnel with Chronic Symptoms Following Blast TBI have Differential Expression of Neuronal Recovery and Epidermal Growth Factor Receptor Genes

Researchers at the NICoE investigated the mechanisms of persistent blast-related symptoms, focusing on the gene expression profiles likely to be involved in chronic symptomatology after blast injury. Thirty-four transcripts were identified in 29 genes that were differentially regulated after blast TBI in comparison to control participants. Upregulated genes included epithelial cells transforming sequence and zinc finger proteins. Down-regulated genes included tensin-1 and protein ubiquination genes. Participants included 36 military Service Members, with 19 individuals with a history of blast-TBI matched to 17 individuals based on age, gender, race, and diagnoses of sleep disturbance, PTSD, and depression. Transcripts were identified by microarray analysis of peripheral samples of whole blood. These results suggest the existence of a gene-expression pathway of delayed neuronal recovery in military personnel who have suffered a blast-TBI and experience chronic symptoms. A more complete understanding of these genetic changes could lead to more effective treatments of chronic posttraumatic symptoms.

Health Outcomes and Long-Term Care Following Extremity Injury

Amputation Injuries in Deployed Female Veterans from Operation Iraqi Freedom and Operation Enduring Freedom

Prior to the lifting of the combat restriction rule for women in 2013, female military members still suffered from combat-related injury due to the asymmetric and irregular nature of the conflicts in Iraq and Afghanistan. Due to the type of injury mechanisms in these conflicts, women also suffered traumatic amputations. Researchers at NHRC identified from the EMED that 21 US Servicewomen sustained combat-related major limb amputations in Iraq and Afghanistan between March 2004 and December 2013. Injuries were characterized using Abbreviated Injury Scale and International Classification of Diseases, 9th Revision codes. To compare gender differences in the combat-related amputee population, a matched cohort of 21 men who had also suffered combat-related amputations were identified. Matching strategies used by the researchers resulted in pairs of female and male patients who had identical amputation injuries, had the same ISS, and were close in age. In the case of a complex injury profile, such as a patient who suffered a traumatic amputation plus open liver laceration or burns, the additional injuries were also matched to maintain similar injury profiles between the groups of women and men. After the two matched cohorts were ascertained, data on post-injury acute care utilization and current military status were collected. The median age of women and men was 25, with an average ISS of 16. Amputations originally identified in the female group were predominately in the lower extremities (81 percent). Blast events were responsible for all of the injuries. A median number of three acute care hospitalizations in the first year post-injury were seen in both genders. Although women averaged more acute care bed days in the first year post-injury than men (49.2 versus 44.5), and averaged less intensive care unit days (2.8 versus 4.1), no statistical differences were found, which possibly may be attributed to the small sample sizes. To date, 10 percent of the women remain on active duty compared with 24 percent of the men. Future studies will identify complications that arise in these severely injured populations, as well as investigating gender differences in mental health issues and quality-of-life outcomes after suffering combat-related injury. New and continued research in this area can inform the advancement of military medicine by identifying interventions and remedies of potential benefit to all Service Members.

Photo credit: Airman First Class Collin Schmidt/US Air Force

By recognizing gender differences in medical care usage and return to duty rates in the seriously injured Service Member, military leaders and medical planners can forecast care requirements throughout the continuum of medical care. This insight will promote individualized care, ensuring optimal outcomes for all combat-injured Service Members.

Increased Prevalence of Metabolic Syndrome Among Combat Veterans with Lower Limb Amputation

Studies of World War II Veterans found relatively high rates of cardiovascular disease, including long-term mortality following combat-related amputations. However, little research has described risk factors for cardiovascular disease, including metabolic syndrome among US Service Members who sustained lower limb amputations in the Iraq and Afghanistan conflicts. Approximately 90 percent of these combat amputations were caused by blast injuries. This study described cardiovascular disease risk factors, including metabolic syndrome for patients with lower limb amputations and those with serious lower extremity injuries without amputation. Researchers at NHRC and the San Diego VA, with funding from the BUMED Wounded, Ill and Injured program, identified study patients and injury-specific data in NHRC's EMED. Patients were injured in Iraq and Afghanistan between 2001 and 2008 and had serious lower limb injury without amputation (n = 162), unilateral (n = 380), or bilateral (n = 134) lower limb amputations. VA national data sources provided cardiovascular disease measures over an average of five years post-injury. These measures included blood pressure, body mass index (BMI), high- and low-density lipoprotein cholesterol, and metabolic syndrome. Researchers found significantly increased likelihood of cardiovascular disease risk factors, particularly following bilateral amputation compared to no amputation. These elevated risk factors included high-density lipoprotein cholesterol and metabolic syndrome. Importantly, the team found that the association between amputation and increased metabolic syndrome was significant only for patients with high BMI (>28 kg/m^2). For patients with high BMI, the prevalence of metabolic syndrome was 11.5 percent among Veterans without amputation versus 25.9 percent and 32.7 percent for Veterans with unilateral or bilateral amputation, respectively.

The present study indicates that lower limb amputation, and particularly bilateral lower limb amputation, is associated with increased cardiovascular disease risk.

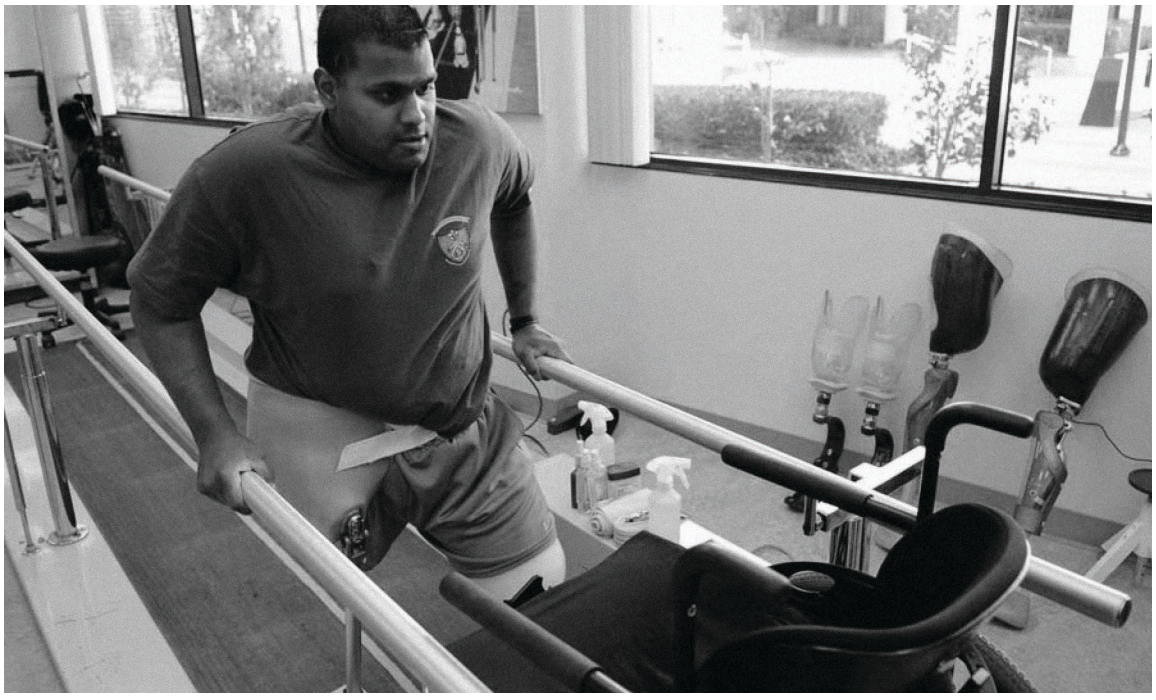


Photo credit: Mass Communication Specialist Third Class Jessica L. Tounzen/Navy Medicine

The study identifies an important modifiable variable, namely bodyweight or BMI, which is associated with increased likelihood of metabolic syndrome for patients with lower limb amputations. The results support the need for primary care and lifestyle interventions to manage weight and lipid levels, particularly following combat-related amputations.

TRICARE Comprehensive Outpatient Medical Utilization and Cost in Extremity Combat Amputee and Limb Salvage Patients

The clinical impact of combat-related amputations is substantial, with adverse effects on health and quality of life for affected Service Members. Approximately 90 percent of these amputations were caused by blast injuries. Less is known about the outpatient costs following upper and lower extremity amputation and limb salvage injuries. This study describes the outpatient medical utilization and procedure costs for extremity combat amputees and limb salvage patients. Researchers at NHRC and NMCSD, with funding from the BUMED Wounded, Ill and Injured program, identified study patients and injury-specific data in NHRC's EMED. Researchers conducted analysis of patients injured in Iraq and Afghanistan between 2001 and 2014. One-year post-injury outpatient encounter medical and billing data were queried for 1,560 patients from the TRICARE administrative direct care ambulatory medical database. The total direct cost for all 1,560 patients for one year of post-injury follow-up time was $177 million. The estimated costs of durable medical equipment, including limb prosthetics and repairs, were approximately $51 million. There were 584,748 outpatient encounter records for all patients in one year. For upper extremity amputations, researchers found an average of 197 outpatient encounters, and patients had a median of $47,400 in medical costs. For lower extremity amputations, researchers found an average of 275 encounters, and patients had a median of $87,600 in medical costs. For patients with upper and lower extremity amputations, researchers found an average of 338 encounters, and patients had a median of $108,900 in medical costs. For limb salvage patients, researchers found an average of 92 encounters, and patients had a median of $18,000 in medical costs. Even though prosthetics accounted for only 7 percent of the total number of outpatient procedures, those prosthetic procedures account for 29 percent of the total reported costs. This study shows the substantial outpatient healthcare costs and resource utilization requirements following combat-related extremity amputations. Understanding patterns of injury and resource utilization will support medical planning, optimize resource allocation, and improve rehabilitation of patients with serious extremity injuries.

Photo credit: Stan Jones/Navy Medicine

Five-Year Health Outcomes Following Upper Limb Combat Amputations

US Service Members who sustained combat amputations to the upper limbs in the Iraq and Afghanistan conflicts present new challenges for military and VA providers. Approximately 90 percent these amputations were caused by blast injuries. Little research has tracked their health outcomes beyond the short term due to the difficulty of integrating military and VA health data. This study described the physical and psychological outcomes for US Service Members during the first five years following upper-limb amputations sustained in Iraq and Afghanistan, 2001–2008.

The research team from NHRC, NMCSD, and San Diego VA, with funding from the BUMED Wounded, Ill and Injured program, compared clinical diagnoses for patients with upper-limb amputations to individuals with serious upper-limb injuries without amputation. The team identified study patients and injury-specific data in NHRC's EMED. Researchers conducted a retrospective review of military and VA health databases for patients who sustained unilateral upper-limb amputation (n = 141) or serious upper-limb injury without amputation (n = 85) in the Iraq and Afghanistan conflicts, 2001–2008. Military and VA health diagnoses were followed for five years post-injury for all patients. The team found that patients with above-elbow amputations had significantly higher ISSs than patients with below-elbow amputations or no amputation. The above-elbow group had significantly higher prevalence of anemia, pulmonary embolism, osteomyelitis, and eye disorders compared with below-elbow amputation patients and/or upper-limb injury without amputation. By contrast, neuroma was significantly more likely following below-elbow than above-elbow amputation or no amputation. The prevalence of heterotopic ossification was 11 to 21 percent and highest following above-elbow amputation. All groups had similar relatively high incidence of lumbago and/or limb pain (40 to 60 percent), hypertension (15 to 20 percent), and obesity diagnoses (12 to 19 percent). The five-year incidence of osteoarthritis ranged between 8 percent and 15 percent with no significant differences between groups. Nearly 90 percent of all groups had at least one psychological disorder. The prevalence of PTSD increased significantly after the first year for the amputation groups, while diagnoses of mood, anxiety, and adjustment disorders declined over the first five years post-injury for all groups.

This is one of the first studies to integrate military and VA health records for five years after combat amputations to the upper limbs. It is also one of the first to describe how physical and mental health outcomes following upper-limb amputation may be unique by comparison to patients with serious upper-extremity injury without amputation. These results can help refine existing treatment strategies to prevent early wound complications and other physical and psychological health complications. The results can also guide development of post-injury treatment pathways for patients with upper-limb amputation versus other serious upper-extremity trauma.

Incidence and Clinical Correlates of Venous Thromboembolism After Combat-Related Amputation

DVT and pulmonary embolism are potentially life-threatening complications that have not been well-studied after traumatic limb amputations caused by combat injury. This is particularly true for US Service Members who sustained severe blast injuries causing high-level and often multiple limb amputations during the recent Afghanistan conflicts, 2009–2011. The research team's objective was to determine the incidence, post-injury timing, and risk factors for DVT and pulmonary embolism following combat-related amputations.

Researchers at NHRC and NMCSD, with funding from the BUMED Wounded, Ill and Injured program, reviewed casualty records in NHRC's EMED. Injuries and treatments documented by providers at Role 2 or 3 facilities in Iraq or Afghanistan were reviewed for 366 patients who sustained traumatic limb amputation proximal to the wrist or ankle. Researchers recorded the ISS, number of blood transfusions during the initial 24 hours, duration of mechanical ventilation, and intensive care unit length of stay. Researchers also recorded the primary outcome, diagnoses of DVT or pulmonary embolism, through 12 months post-injury. The team found that 28 percent of patients had DVT and/or pulmonary embolism diagnoses, including 16 percent who had a pulmonary embolism. Approximately two-thirds of DVT/pulmonary embolism cases occurred within 10 days of injury and nearly 90 percent occurred during the first 60 days post-injury. Increased number of ventilator days and units of blood transfused were significantly associated with increased likelihood of DVT.

Increasing units of fresh frozen plasma transfused was significantly associated with increased likelihood of pulmonary embolism. Prophylactic medication significantly decreased the likelihood of DVT and pulmonary embolism. The present study helps providers identify early treatment factors that increase patient risk for the life-threatening complications of DVT and pulmonary embolism. The prevalence of pulmonary embolism and DVT was relatively high after traumatic amputation. Therefore, post-injury surveillance and use of prophylactic medication is indicated for this population. Identifying risk factors for DVT and pulmonary embolism helps focus acute care resources on patients who are most likely to develop these complications.

Biological Approaches to Improve Functional Recovery After Compartment Syndrome

Compartment syndrome leading to non-healed fractures, volumetric muscle loss, or amputation are potentially devastating complications of severe extremity injury to the Service Member. Researchers at Wake Forest University, with funding from USAMRMC, are investigating improved treatments for extremity injury and compartment syndrome using human muscle progenitor cell therapy (hMPC) to regenerate limb tissues, along with an adjunctive pharmacologic approach to inhibit fibrosis and scarring. In FY15, researchers demonstrated in a rodent model of extremity injury and compartment syndrome that treatment with an angiotensin receptor blocker (losartan)—used to treat hypertension and heart failure—showed significant improvement in muscle regeneration and decreased scarring. In a muscle injury model in immunocompromised rats, three preparations of hMPCs were injected into injured muscle, with promising results. A human study of losartan is expected in the next one to two years. This line of investigation offers a promising adjunctive approach to improve outcomes in extremity trauma complicated by compartment syndrome, a leading cause of morbidity among wounded Service Members.

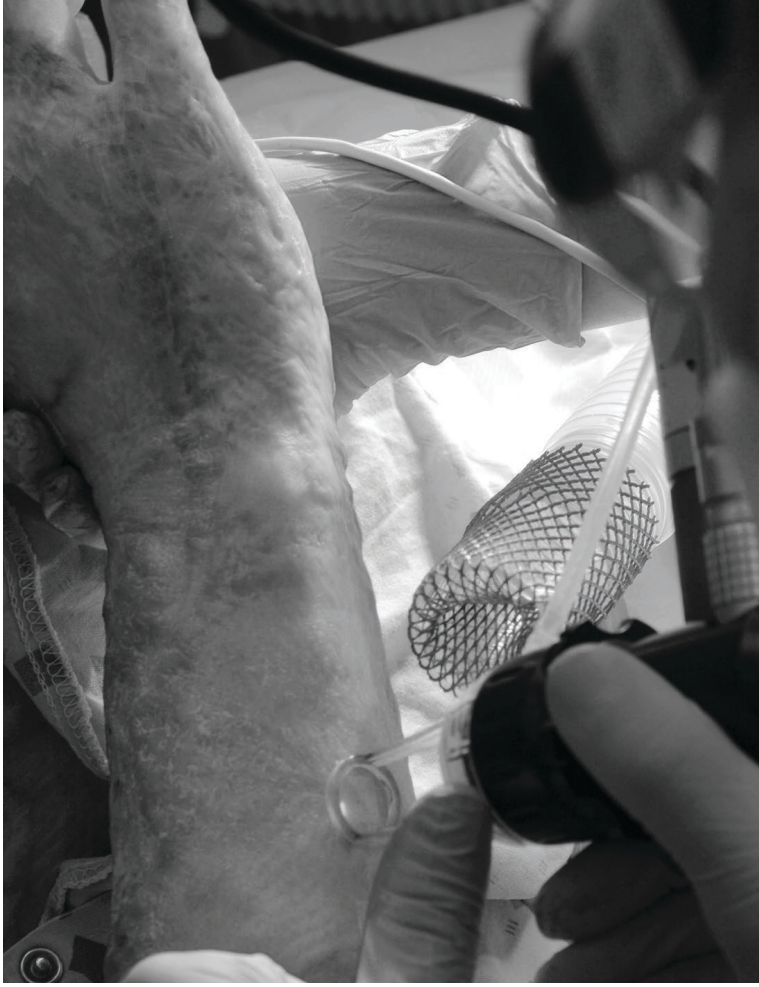


Photo credit: Staff Sergeant Robert Barnett/US Air Force

Compartment Syndrome Treated with Autologous Bone Marrow

Compartment syndrome leading to non-healed fractures, volumetric muscle loss, or amputation are potentially devastating complications of severe extremity injury to the Service Member. Researchers at Oregon Health and Science University are developing a treatment of severe traumatic lower extremity injury complicated by compartment syndrome using autologous bone marrow mono-nuclear cells to regenerate limb tissues, with the goal of reducing disability and improving functional recovery. Pre-clinical studies of anterior tibialis compartment syndrome in large animals showed safety, long-term functional engraftment of bone marrow cells, and statistically significant improved muscle strength and gait. A clinical trial is expected in the next one to two years. This line of investigation offers a promising adjunctive approach to improve outcomes in extremity trauma complicated by compartment syndrome, a leading cause of morbidity among wounded Service Members.

Nociceptin/Orphanin FQ Peptide Receptor (NOP)-Related Agonists as Analgesics in Primates

Blast injuries invariably result in pain. Opioids, such as morphine, that bind to the mu opioid receptor are the most efficacious agents for the treatment of moderate to severe pain. However, morphine-like drugs have side effects, including respiratory depression, physical dependence, and abuse liability that reduce their usefulness in some situations and for some individuals with pain. Previous studies have shown that NOP-receptor agonists may have morphine-comparable analgesic effects without morphine-associated side effects in primates. However, pharmacological data derived from the NOP agonists in primates are limited, because only one non-peptidic NOP agonist has been studied in the primate models. Initiated with funding from the Peer Reviewed Medical Research Program, and with continued support from the Joint Warfighter Medical Research Program, researchers from Wake Forest University Health Sciences are determining the relative antinociceptive effectiveness, safety, and abuse potential of various NOP-related agonists in different primate pain models. Evidence suggests that in non-human primates, the selected NOP-related agonists produced antinociceptive effects comparable to morphine, with a wider therapeutic window, and without the induction of respiratory depression or itch-scratching behavior, suggesting that these agonists are effective and safe analgesics in primates. Moreover, the selected agonists did not produce reinforcing effects as compared to mu opioid agonists. Thus, these agonists have promising therapeutic profiles as analgesics to be further developed for use in the treatment of blast and other battlefield injuries.

Pain relief is an essential component of CCC. For injured Service Members, analgesia can enhance comfort, allowing them to remain quiet when noise discipline is at a premium, and enhance mobility so that they might either carry on their mission, or remove themselves from dangerous areas. Although NOP agonists, such as morphine and fentanyl, can provide all of these benefits, and could be used effectively by the Service Member in the field for self-medication, these drugs have some limiting side effects. Among the most dangerous are respiratory depression/arrest, the risk that Service Members given access to large quantities of NOP agonists might abuse these drugs, and the risk that Service Members might develop physical dependence following chronic administration. Many combat Service Members were heavy users of widely available and relatively pure heroin and/or prescription opioids. These young men and women are at a vulnerable age and in high-stress situations that greatly increase the risk of recreational use of opioids if they were made available for emergency pain relief. Research to identify potential analgesics with fewer side effects and more importantly, with reduced abuse liability and physical dependence, is pivotal to advances in healthcare of all individuals, but most critically, military personnel.

Transplants and Burn Injury Treatment

Hand Transplantation with Reduced Immunosuppression

For Service Members who have suffered catastrophic limb loss, transplantation offers the potential of improved function with less disability. The central challenge for the field of transplantation is to develop novel strategies to regulate the host's immune system. The USAMMDA Tissue Injury and Regenerative Medicine (TIRM) Project Management Office is managing several studies of novel immunomodulatory strategies in hand transplantation. The studies are being conducted at five centers, including the Johns Hopkins University, University of Pittsburgh, Duke University, University of Louisville, and the Brigham and Women's Hospital. As of FY15, 12 hand transplants have been performed with DoD funding (two performed in FY15).

Investigators at the collaborating centers focused their FY15 efforts on tolerance induction using chimeric donor-host derived cells, bone marrow-derived stem cells, with particular preclinical success in transplants containing vascularized bone, immunomodulation using regulatory T-cells, and stromal-derived factor cells from adipose tissue, in an effort to discover new methods to lower the risk for rejection. Hand transplantation offers an alternative to prosthetics, and the potential of improved function with less disability, for Service Members who have suffered catastrophic limb loss.

Face Transplants to Address Catastrophic Tissue Loss in the Face

Brigham and Women's Hospital performed the fifth and sixth face transplants under the Biomedical Translational Initiative contract, and Cleveland Clinic performed the first face transplant under the AFIRM I cooperative agreement. Face transplants offer the possibility of restored function—chewing, swallowing, nasal breathing, oral competence, intelligible speech—and appearance, which could not be accomplished with conventional reconstructive surgery, to those wounded Service Members who have suffered catastrophic facial injuries.

Improved Cutaneous Coverage following Severe Burn Injury

Extensive burn injuries, particularly full-thickness burns, result in significant and life-changing morbidity. While autografting from donor sites remains standard of care, StrataGraft® offers a promising alternative for skin coverage after extensive burns, reducing the need for autografting. StrataGraft is a human skin substitute with many of the structural and biological properties of normal human skin. In late 2014, Stratatech Corporation completed enrollment in a multicenter clinical trial, which included US Army Institute of Surgical Research as a clinical site, to assess the safety, tolerability, and efficacy of StrataGraft skin tissue compared to autografts in deep partial-thickness burns. Data from that trial suggests that StrataGraft facilitates wound closure and is replaced by the patient's own cells as the wound heals. The investigators are preparing follow-on studies, and anticipate trial initiation in the next one to two years.

This product offers a promising alternative for skin coverage after extensive burn injuries.

Photo credit: Staff Sergeant Robert Barnett/US Air Force

KeraStat® Burn Gel and Halofuginone to Prevent Scar Contracture After Burn Injuries

No currently available burn product has shown efficacy in substantially decreasing wound healing time and preventing scar formation. The goals of this project are to expand on the results obtained in the Phase I study that showed that (1) halofuginone inhibited collagen-mediated contracture in dermal fibroblasts and (2) the presence of the keratin in the KeraStat burn product results in an attenuation of the cellular injury response following UVB irradiation. Investigators from Wake Forest University are testing two potential solutions (KeraStat and Halogel), in partnership with the manufacturer Keranetics, to determine their comparative efficacy in reducing time to wound closure and decreasing scarring in a porcine burn healing and scarring model. Following in vivo animal efficacy testing, they plan to test the efficacy of KeraStat in reducing time to wound closure and in scar prevention in an investigator-initiated 60 patient human clinical trial in partial-thickness burn patients. A follow-on clinical trial is anticipated in the next one to three years.

Treatment to Limit Burn Injury Progression

Burn injuries often become larger in the two to three days following injury, resulting in a higher risk of scarring, contractures, infection, disability, and possibly mortality from more serious wounds. Currently there is no treatment to stop this process. With funding from USAMMDA and AFIRM, investigators at Synedgen Inc. are developing and evaluating a treatment to prevent burn injury progression. Synedgen's product has been demonstrated in vivo and in vitro to reduce inflammation and increase healing in dermal wounds. In a porcine burn model, the treatment reduced inflammation and fibrosis. In the current effort, Synedgen aims to improve the healing rate and to reduce inflammation and fibrotic scar formation in burns. The investigators are completing preclinical studies necessary to support an Investigational New Drug application to the FDA. A clinical trial is expected in the next two to three years.

Quality of Life

Long-Term Quality of Life Outcomes in Injured Tri-Service US Service Members: The WWRP

The long-term effects of blast-related injuries and diagnoses are not well understood. To better understand the consequences of these combat injuries on Service Members' long-term health and readiness, NHRC in San Diego, California, is longitudinally assessing clinical, rehabilitative, and quality-of-life outcomes in injured US Service Members. This project, named the WWRP, is being conducted with funding support from the Navy BUMED under the Wounded, Ill, and Injured program and the EACE. Each of the more than 55,000 Service Members in injured in Iraq and Afghanistan beginning in October 2001 are currently being contacted and invited to participate in the WWRP. The WWRP is a 15-year, longitudinal, prospective, population-based survey study of injured Service Members, with surveys being administered every six months to gauge physical health, mental health, and quality-of-life outcomes. To date, 3,711 injured Service Members have provided informed consent and enrolled in the study and over 910,000 survey responses have been collected. Approximately 79 percent of respondents were injured in a blast event. In all respondents, injuries to the head and spine are associated with worsened psychosocial outcomes. Future follow-up surveys will integrate more specific measures of interest, including pain and social support, and prosthetic use/satisfaction in the amputee population. These discrete measures may provide insight into the nexus between quality-of-life and specific target areas of concern as well as focus on severe blast injuries. This study is being conducted predominantly online, with supplemental telephone and paper surveys for those Service Members who cannot respond online. The public-facing website can be viewed at: http://www.wwrecoveryproject. WWRP is the first and only initiative to longitudinally study injured Service Members and examine their long-term physical health, mental health, and quality-of-life outcomes after combat injury.

By assessing long-term QOL outcomes, NHRC, EACE, DoD, and the VA can evaluate those clinical treatments, rehabilitative programs, and prosthetics/orthotics that are actually moving the QOL meter for injured Service Members and those that are not. This not only results in immediate and real improvement in the quality of care delivered, but also in immense cost savings now and throughout the lifetime of care that many of these Service Members will require. The WWRP continues to produce manuscripts, presentations, technical reports, and recommendations.

Conclusion

It is an honor for the PCO to share so many accomplishments from across the blast injury research community in FY15. The breadth of research topics and outcomes is truly astounding, and it should inspire confidence among Service Members, their Families, and the general public that major advances are being made to protect each Service Member from potential blast injuries, as well as support the injured throughout their treatment and recovery processes. Collaboration across the community—both domestically and internationally—continues to enhance the knowledge base on the spectrum of blast injuries and leads to evidence-based clinical guidelines, programs, and products for blast injury prevention, mitigation, and treatment. The PCO will continue to support the mission of the EA in coordinating medical research that forms the foundation for the programs and products that target blast injuries. By disseminating information on FY15 accomplishments, the PCO encourages collaboration among the research community and builds confidence in the efforts of the Blast Injury Research Program and its domestic and international partners.

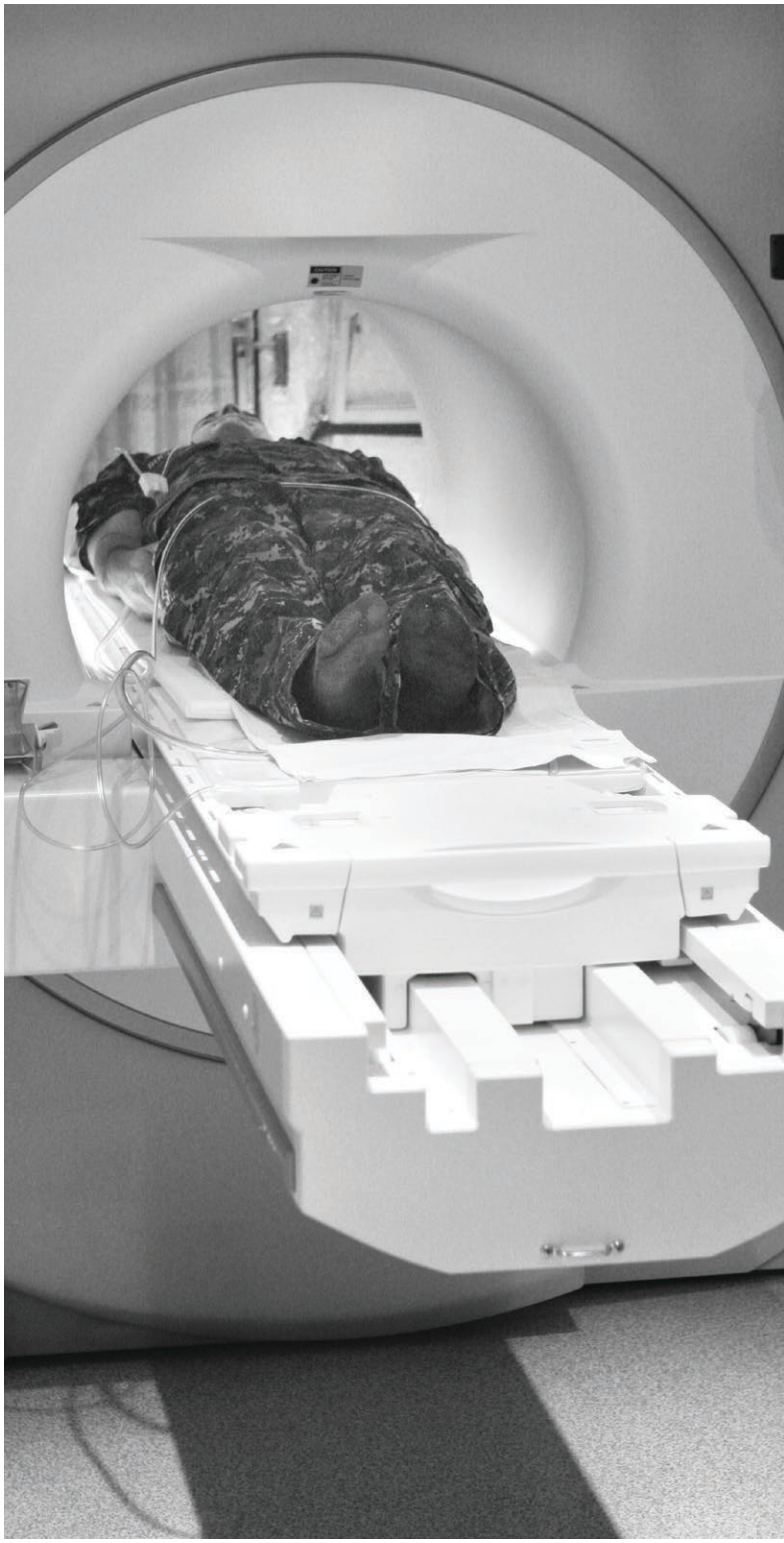


Photo credit: Lance Corporal Jonathan G. Wright/US Marine Corps

08

CHAPTER 8:

WAY FORWARD

This report to the EA covers key accomplishments of the blast injury research community and the PCO in FY15. In FY16 and beyond, the Blast Injury Research Program will continue to pursue strategies for blast injury prevention, mitigation, and treatment. This chapter covers continuing initiatives that will further research and development objectives; foster collaboration and information sharing between research communities; disseminate critical information; and shape future research priorities to fill knowledge gaps across the entire spectrum of blast injury.

Ongoing PCO Initiatives in FY15

DoD Blast Injury Research Coordinating Board

The PCO plans to establish a standing DoD Blast Injury Research Coordinating Board with representatives from all DoD stakeholder organizations to serve as the venue for identifying blast injury research needs and sharing plans for future blast injury research. It is anticipated that the coordinating board will provide a forum for cross service coordination and an oversight mechanism for facilitating collaborations and partnerships across the Services and within the various RDT&E communities; and to be a vehicle for wide dissemination of research knowledge related to blast injury across the various medical, operational, testing and evaluation, and materiel communities across the DoD. The specific objectives include:

- Advise EA on requirements, research gaps, and future research investment;
- Coordinate and integrate research efforts in order to understand the mechanism of blast injury and accelerate the translation of research acquired knowledge to development of prevention and treatment strategies;
- Address current and future blast injury challenges, such as:
  - Understanding the mechanisms of blast-related brain injuries in order to guide protection and treatment strategies
  - Ensuring access to historical blast injury research data to the widest possible community in order to support research on current and future blast injury challenges
  - Identifying blast injury prevention standards to support the development of effective blast protection systems for both the dismounted and mounted Service Member
  - Facilitating information sharing that encourages collaboration, prevents duplication of effort, and fulfills the objective of the Congressional mandate for a coordinated DoD Blast Injury Research Program.

DoD Human Injury Modeling Working Group

The PCO is in the process of establishing a DoD Human Injury Modeling Working Group to encourage collaboration and facilitate cooperative RDT&E programs across the DoD related to human injury models of Warfighters. It is envisioned that this working group will coordinate and provide policy and guidance across the DoD for a framework that will ultimately result in a robust high performing model of the Warfighter, to be used by engineers, that will be able to accurately predict injuries and functional incapacitation across all military hazard stimuli and will allow for the creation of protective systems and medical response planning. The working group will include representatives from all DoD stakeholder organizations. The specific goals include:

Photo credit (opposite page): Staff Sergeant Kenny Holston/US Air Force

- Develop a policy for an architectural framework that will result in the creation of a comprehensive model of the Warfighter for use across the DoD that will accurately predict injuries, functional incapacitation, and long term disability
- Promote the common goal of creating a comprehensive model of the Warfighter
- Critically assess the current state of the art in modeling of humans
- Identify knowledge and technology gaps to be filled by ongoing and future programs
- Promote coordination, collaboration, and resource sharing across the DoD for modeling of Warfighter injuries.

Japan-US Technical Information Exchange Forum on Blast Injury

The PCO, in collaboration with the NDMC (an organization of the Ministry of Defense, Japan), RDECOM's ITC-PAC, ONR Global, and the USAF Research Laboratory's Asian Office of Aerospace Research and Development, plans to organize a Japan-US Technical Information Exchange Forum on Blast Injury, followed by a Japan-US Technical Information Exchange meeting. The purpose of the Forum is to bring together blast injury researchers and clinicians from the US and Japan to share expertise, experience, and approaches to solving blast injury problems of mutual interest; to identify knowledge gaps; and to identify collaborative research opportunities that will lead to improvements in prevention, clinical diagnosis, and treatment of blast-related brain, lung, and auditory injuries.

US-India Medical Strategic Initiatives Working Group

The PCO plans to provide EA oversight for the US–India Medical Strategic Initiatives Working Group within the ASBREM COI. The Medical Strategic Initiatives Working Group was established by the Chair of the ASBREM COI to provide guidance, encourage collaboration, and facilitate cooperative medical RDT&E projects between the United States and India. The collaborative efforts will be conducted under the umbrella of the Memorandum of Agreement between the US DoD and the Ministry of Defence of the Republic of India for Research, Development, Testing and Evaluation Projects. The formation of this Working Group serves to represent the combined medical RDT&E interests of the India-US Joint Technology Group with the goal of promoting partnership and coordination between the US DoD and India's Ministry of Defense. The Medical Strategic Working Group in coordination with the Defense Threat Reduction Agency, the Office of the ASD(R&E), and DRDO, Indian Ministry of Defence, is helping to organize the joint US–India medical and chemical/biological workshops in the Fall of 2016.

US-India Collaboration on Experimental and Computational Studies of Blast and Blunt TBI

Under the US-India DTTI, the PCO in collaboration with MOMRP developed, received approval, and secured OSD matching funds for the project titled, "Experimental and Computational Studies of Blast and Blunt Traumatic Brain Injury." The outcome of this effort will support the rapid design, prototyping, and testing of novel protective and therapeutic concepts that will lead to faster introduction of enhanced protective and treatment strategies. The lead collaborative organizations are the USAMRMC and DRDO INMAS (an organization of the Ministry of Defence, India). Other participants include BHSAI, NJIT, NRL, WRAIR, the Indian Defense Institute of Psychological Research, and the Indian Terminal Ballistics Research Laboratory. The specific objectives of the project include:

- Develop and validate a blast injury animal model for mTBI using imaging, histological, cognitive, and behavioral analyses
- Develop, validate, and cross-validate a computational model for blast and blunt injury
- Develop anatomically accurate head/brain models for blast/blunt injuries from clinical and experimental data
- Compare the blunt and blast data to develop a scaling ratio.

US-India Collaboration on Injury Mechanisms in Blast and Blunt TBI—A Comparative Study Based on Clinical Data and Numerical Analysis

The PCO plans to continue jointly sponsoring the collaborative project, "Injury Mechanisms in Blast and Blunt TBI—A Comparative Study Based on Clinical Data and Numerical Analysis," with RDECOM's ITC-PAC and ONR Global. Performed by team of researchers from the All India Institute of Medical Sciences, Indian Institute of Technology-Delhi, and NJIT, this project will explore the hypothesis that the mechanism of injury is different between blast and blunt neurotrauma.

Preservation and Dissemination of DoD Historical Blast Bioeffects Injury Data

In support of the EA's responsibility to promote information sharing and dissemination, the PCO initiated an effort focused on recovering historical blast-effect data collected from four decades of experimental research at the Albuquerque Blast Test Site. Blast-effect data have been generated from a range of experiments, including nuclear and underwater explosion, airburst, and shock tube experiments on laboratory animals that varied in size and body mass. Knowledge gained from these data can be used to improve soldier protection, survivability, and warfighting capabilities. The goal of this project is to make the data available to the DoD program managers, researchers, and decision makers as well as civilian researchers engaged in understanding blast-induced injuries and developing protection technologies.

NATO HFM-234 (RTG)—Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods, and Standards

The tools that the HFM-234 (RTG) is developing (detailed in Chapter 3) promote standardized study and data collection methodologies needed to advance the field of blast injury research. The HFM-234 (RTG) technical team plans to complete its deliverables, which include a final report and four key products:

- A comprehensive dictionary of blast injury research terms
- Guidelines for conducting epidemiological studies of blast injury
- Guidelines for reproducing blast exposures in the laboratory
- Guidelines for using animal models in blast injury research.

It is not the intention of the HFM-234 (RTG) to prescribe how to conduct blast injury research; rather, these documents provide an awareness of parameters that need to be considered during the design of blast injury studies. The main objectives of these documents include the following:

- Raise awareness with regards to the complexities and pitfalls of blast research
- Standardize and promote good practices
- Help the community to generate valid and comparable results
- Increase the quality of publications in this field of research.

By promoting standardization in experimental methods, data collection, and reporting, the outcomes of HFM-234 (RTG) will help to eliminate obstacles that hinder collective research efforts and will facilitate international collaboration to improve the prevention, treatment, and mitigation of blast injuries for our Service Members and our partner nations.

BIPSR Process

In the coming year, the PCO plans to finalize recommendations from the BIPSR Process for the spine and back and upper extremity blast injury types. The science and technology knowledge gaps identified for these blast injury types, as well as the lower extremity blast injury type, will be shared with the medical research community to inform the development of future blast injury prevention, mitigation, and treatment standards. In continuation of efforts to enhance BIPSR Process capabilities, the PCO plans to initiate a pilot project, "the iBIPSR capability," using the iBIPSR site for the auditory blast injury type. The PCO expects to provide initial iBIPSR site access to the Auditory Focused Stakeholders, with their feedback driving improvements as they engage with the site. The PCO anticipates moving forward with the iBIPSR capability on future BIPSR Process evaluations, and plans to provide access to relevant Stakeholder communities. The PCO also plans to initiate a reprioritization of the remaining blast injury types with the participation of BIPSR Process Stakeholders. Lessons learned from each blast injury type evaluation will be applied to refine and enhance the BIPSR Process. Ultimately, the knowledge gaps discovered and the recommendations developed through the BIPSR Process will enable the DoD to apply blast injury prevention standards that support weapon system health hazard assessments, combat platform occupant survivability assessments, and protection system development and performance testing.

Ongoing Activities Across the DoD Blast Injury Research Program

The prevention, mitigation, and treatment of blast injuries cannot be addressed without the cooperative RDT&E efforts of organizations across the DoD, other Federal agencies, academia, industry, and international partners. The following are examples of initiatives that will continue to address the challenges of blast injuries in FY16 and beyond.

Stop the Bleed

A person who is bleeding can die from blood loss within five minutes. The "Stop the Bleed" campaign, sponsored by the CCCRP, aims to teach everyday citizens basic techniques in hemorrhage control so that an injured person has a greater chance of living long enough to reach a doctor's care at the hospital. The campaign is based on the success of the US military in reducing combat deaths during recent conflicts in Afghanistan and Iraq. Since most combat fatalities occurred on the battlefield prior to reaching a hospital and the majority of potentially preventable deaths occurred due to hemorrhage, bleeding control is now a cornerstone of the improved survival techniques used by the Services.

Bioengineered Vascular Grafts for Extremity Reconstruction

Vascular injury is occurring at a much higher rate in modern combat than in prior conflicts, highlighting the unmet need for a readily available, universal, off-the-shelf vascular graft. Current treatment options are limited by the absence of donor sites for autologous grafting, and the dual issues of infection and patency for synthetic grafts. Supported collaboratively by USAMMDA's TIRM Project Management Office and the Combat Casualty Care Research Program, surgeons at Johns Hopkins University are investigating a bioengineered, de-cellularized vascular graft manufactured by Humacyte, Inc. for the treatment of severe vascular injury. The graft is composed entirely of human proteins in an effort to achieve a superior biologic response compared to currently available engineered grafts. A clinical trial is expected to begin enrollment in the next one to two years.

Growth Hormone Treatment for Severe Burn Injury Patients

When someone suffers from burn injury, their muscles decrease in size, and they cannot exercise as long as they did before they were burned. During the recovery phases following burn injury, persistent loss of lean muscle mass impairs patient function and delays independence and rehabilitation. Hormone levels (e.g., human growth hormone) are reported to be depressed for more than two years following severe burns and are associated with loss of lean muscle mass. Researchers at the University of Texas, who are funded by CRMRP, are administering human growth hormone to severely burned patients in clinical trials to examine its effect on the loss of lean body mass and bone mineral content, rehabilitation, and speed of reintegration. The goal is to spend less time in the hospital, spend less time recovering, be able to get their strength back more quickly, and have less stress on their bodies during this process.

Major Extremity Trauma Research Consortium (METRC)

METRC was established in September 2009 with funding from the CCCRP. It consists of a network of clinical centers and one data-coordinating center that work together with the DoD to conduct multi-center clinical research studies relevant to the treatment and outcomes of orthopaedic trauma sustained in the military. METRC is a collaboration of 22 Core Civilian Trauma Centers, four Military Treatment Facilities, and 30 Satellite Centers throughout the US, unified to identify and address critical issues challenging the recovery of combat and civilian trauma patients. The goal of the Consortium is to establish evidence-based treatment guidelines for the optimal care of the wounded Service Member and improve the clinical, functional, and quality of life outcomes of both Service Members and civilians who sustain high energy trauma to the extremities.

"TBI Detection via Protein Biomarkers" Study

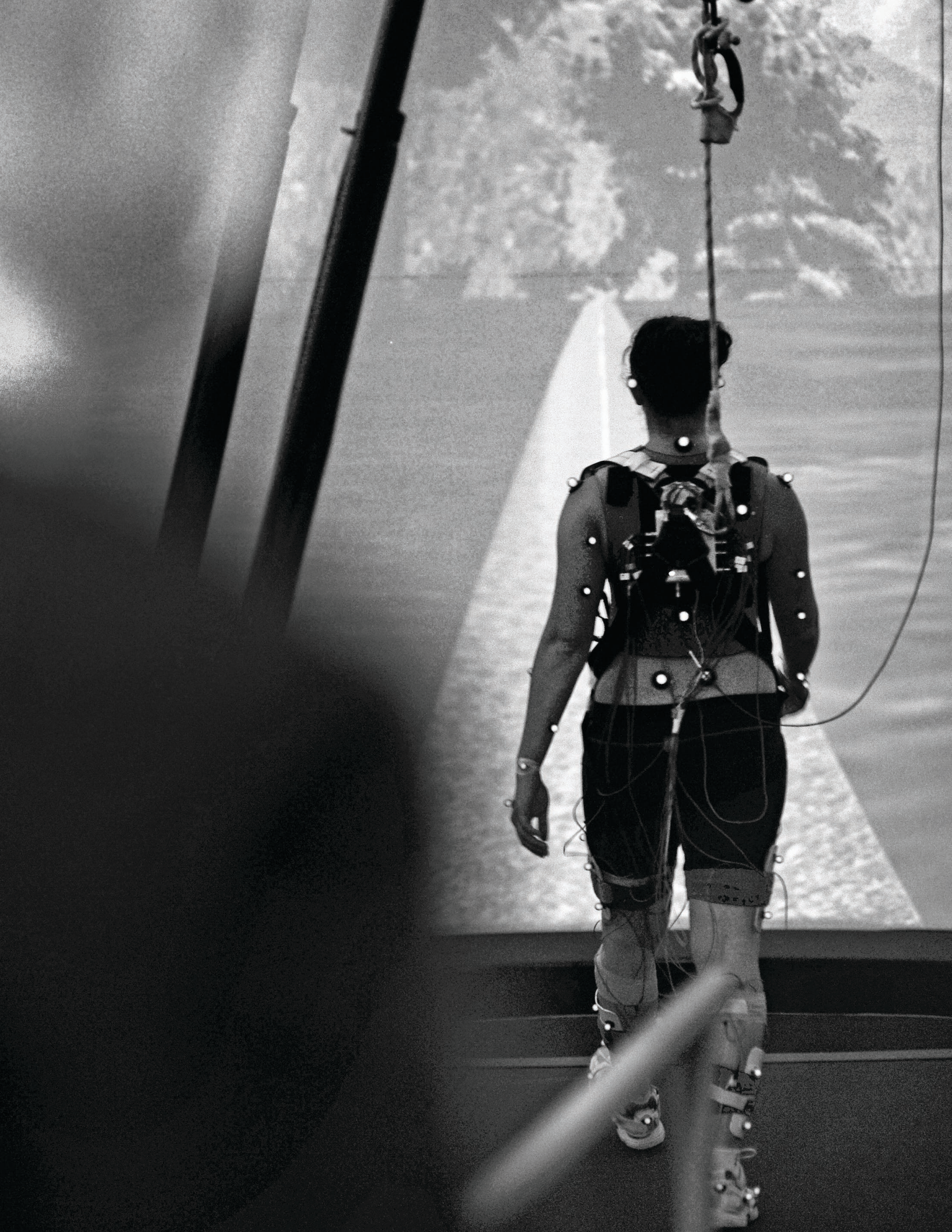
With support from the CCCRP, Banyan Biomarkers is developing two biomarkers with the aim to develop a benchtop assay able to aid in diagnosis of mTBI.

Treatment for TBI using NNZ-2566

NNZ-2566 is a synthetic analog of the naturally- occurring neuroprotective tripeptide IGF-1(1-3) that Neuren Pharmaceuticals is developing as a treatment for TBI. Based on positive preclinical efficacy data and an excellent safety/tolerability profile, the CCCRP is sponsoring two Phase II clinical trials for NNZ-2566. The moderate to severe TBI clinical trial of the intravenous formulation of NNZ-2566 is anticipated to be completed by first-quarter FY16 and Tier 1 analysis is expected to be completed by the end of second-quarter FY16. The mTBI clinical trial of the oral formulation of NNZ-2566 is being conducted at Fort Bragg; it began enrolling subjects during October FY15.

Virtual Reality Rehabilitation of Cognition and Driving Abilities after TBI

Cognitive impairments resulting from blast-related TBI may impact a wide range of everyday activities, including the ability to operate a motor vehicle. Motor vehicle accidents are the leading cause of injury and death in the post-deployment period. However, existing forms of cognitive rehabilitation have not been shown to improve real-world functional abilities such as driving. In collaboration with investigators at the University of Virginia, a research team at USUHS has developed a therapy that uses virtual reality as a safe environment in which to rehabilitate critical cognitive and driving skills. This intervention, "Neurocognitive Driving Rehabilitation in Virtual Environments (NeuroDRIVE)," will be evaluated in a randomized controlled trial funded by the Center for Neuroscience and Regenerative Medicine.



Cognitive performance, driving abilities, post-concussive symptoms, and functional neuroimaging will be compared between TBI participants receiving NeuroDRIVE and wait-list controls. Participating sites include USUHS and the NIH. Recruitment of participants with TBI (all severities) began in early 2015. Successful validation of NeuroDRIVE would pave the way for dissemination of the NeuroDRIVE intervention to reduce morbidity associated with TBI.[58]

Daily Diary Assessment of Posttraumatic Stress Symptoms in US Service Members (a.k.a.: Daily Diary Study)

The Daily Diary Study, funded by the Center for the Study of Traumatic Stress at USUHS, uses an ecological momentary assessment methodology to monitor in real time posttraumatic stress symptoms of current and former military Service Members. Stress symptoms, collected four times daily over a 15-day period, will be compared with psychiatric disorders (e.g., PTSD, depression), sleep, pain, health risk behaviors (e.g., alcohol and tobacco use), and other areas of health and functioning. In phase I of the study, Service Members complete daily assessments on paper questionnaires. In phase II, Service Members complete assessments using electronic tablets programmed with a sophisticated application developed through the collaboration of the Center for the Study of Traumatic Stress and the National Center for Telehealth and Technology. TBI-related assessment measures include the DVBIC TBI Screening Tool, also called The Brief Traumatic Brain Injury Screen, the Brief Symptom Inventory (Somatization and Hostility subscales), and individual assessment items that relate to specific TBI symptoms such as trouble with memory, concentration, irritability, and changes in mood. This important study will increase our understanding of the relationship between daily variability in posttraumatic stress symptoms and mental health conditions as well as inform future use of technology in psychiatric assessment, treatment, and research.

Wearable Noise Dosimetry for Tactical Environments

In theater, exposure to hazardous noise levels is a known threat to Service Members; however, it is difficult to obtain individualized characterizations of such exposure in tactical environments. To address the lack of data, the Bioengineering Systems & Technologies Group at the Massachusetts Institute of Technology (MIT) Lincoln Laboratory successfully fielded prototype helmet-mounted and modified commercial off-the-shelf acoustic sensors in August 2013 through collaborations with the Marine Expeditionary Rifle Squad and the US Army Research Institute of Environmental Medicine. The sensor was designed specifically to collect high decibel-level noise and was hardened for tactical collection during USMC dismounted operations out of Patrol Base Boldak, Afghanistan. To maintain operational security, speech content was removed from the recorded data, while the relevant noise exposure information was preserved. The 274 hours of combat audio data collected in Afghanistan by 19 Marine volunteers captured their exposure to vehicle noise and weapons fire. Analysis of the data by MIT Lincoln Laboratory in FY14 revealed that the majority of the Marine volunteers were exposed to noise conditions exceeding 85 A-weighted decibels, the safety threshold set by the National Institute for Occupational Safety and Health, over the course of a two-day collection period, and that several Marines were exposed to noise conditions that greatly exceeded the 500 auditory risk unit (ARU) impulse noise limit set by MIL-STD 1474E. During one firefight that occurred during the data collection period, one Marine's exposure even exceed 2500 ARUs.

Photo credit (opposite page): US Air Force Technical Sergeant Jacob N. Bailey/DoD


SEATEC

In FY15, development started on a second-generation prototype wearable device funded by the Marine Expeditionary Rifle Squad and the US Army Natick Soldier Research, Development & Engineering Center. The new device incorporates improvements such as a higher sampling rate, expanded dynamic range, onboard processing to provide real-time exposure metrics, global positioning system, and wireless connectivity. Validation testing of the second-generation prototype is expected to begin in March 2016. A potential late-FY16 fielding is under discussion to support an existing USMC/Navy study of hearing injury sustained during Marine rifle training exercises. The ongoing work to collect individualized exposure data will help to more accurately quantify its complex relationship with hearing injury. This will enable the development of more accurate exposure limits and hearing protection criteria for combat environments, which could help reduce the risk of hearing loss and increase hearing protection usage compliance.

EOD Diver/Safe Swimmer Standoff Project

In FY14, live fire field data were collected by NSWC Indian Head Explosive Ordinance Disposal Technology Division in partnership with the Canadian Navy on underwater explosions. In FY15, the data were used to validate propagation models which will expand our understanding of the effects of underwater explosions on human physiology. Analysis is ongoing; results are expected in FY16.

The WIAMan Project

In preparation for the future acquisition, deployment, operation and sustainment of the WIAMan injury assessment test capability, the Army determined the WIAMan project should transition to a program-of-record at Milestone B, which is projected to occur in FY18. At that time, RDECOM will transition leadership of the WIAMan project to the PEO for Simulation, Training, and Instrumentation (STRI). To ensure the injury biomechanics, ATD expertise, and Live-Fire testing experience of the WIAMan Engineering Office remains a part of the project post-transition, RDECOM and PEO STRI will sign a memorandum of agreement to establish the roles and responsibilities of their respective offices for the remainder of the project. In preparation for the program-of-record, the Army developed a transition plan and Program Office Estimate, and began an effort to create a Test Capability Requirements Document (TCRD) for the WIAMan system. The TCRD documents the key performance parameters and key system attributes required to progress through its acquisition milestones. This document will be signed by DOT&E, RDECOM, and the US Army Test and Evaluation Command. As the Army prepares for the formal acquisition program, RDECOM, through the WIAMan Engineering Office will continue to execute the Science & Technology program to develop biomechanics knowledge and new instrumented ATD technology that will be transitioned to the program-of-record in FY18. In the next year, the project will greatly expand the knowledge of human biomechanics and will test the technology demonstrator ATD, perfect the design, and initiate fabrication of first generation prototypes.

Photo credit (opposite page): Technical Sergeant Samuel King Jr./US Air Force

APPENDIX A:

ACRONYMS

#

1LT	First Lieutenant

A

Aβ	Amyloid Beta
ACH	Advanced Combat Helmet
AFFD WG	Auditory Fitness for Duty Working Group
AFIRM	Armed Forces Institute of Regenerative Medicine
AG	Assault Gun
AHP	Army Hearing Program
AHAAH	Auditory Hazard Assessment Algorithm for Humans
AHLTA	Armed Forces Health Longitudinal Technology Application
AMANDA	Analysis of Manikin Data
AOR	Area of Responsibility
ARC	Advanced Rehabilitation Center
ARL	Army Research Laboratory
ARU	Auditory Risk Unit
ASoC	Amputation System of Care
ATA	Atmospheres Absolute
ASA(ALT)	Assistant Secretary of the Army for Acquisition, Logistics, and Technology
ASBREM	Armed Services Biomedical Research, Evaluation, and Management
ASD(HA)	Assistant Secretary of Defense for Health Affairs
ASD(R&E)	Assistant Secretary of Defense for Research and Engineering
ATD	Anthropomorphic Test Device

B

BADER	Bridging Advanced Developments for Exceptional Rehabilitation
BEAST	Blast Exposure Accelerated Sensor Transition
BFA	Battle Field Acupuncture
BHSAI	Biotechnology High Performance Computing Software Applications Institute
BIPSR	Blast Injury Prevention Standards Recommendation
BLAST	Blast Load Assessment: Sense and Test
BMI	Body Mass Index
BPMN	Business Process Modeling Notation
BRC	Biofidelity response corridors
BOP-HHA	Blast Overpressure-Health Hazard Assessment
BTD	Blast Test Device
B-TEC	Brain Trauma Evidence-based Consortium
BUMED	Bureau of Medicine and Surgery

C

CARE	Concussion Assessment, Research, and Education
CAREN	Computer Assisted Rehabilitation Environment
CBRN	Medical and Chemical, Biological, Radiation, and Nuclear
CCC	Combat Casualty Care
CCCRP	Combat Casualty Care Research Program
CCL2	Chemokine Ligand 2
CDMRP	Congressionally Directed Medical Research Programs
CDRH	Center for Devices and Radiological Health
CDISC	Clinical Data Interchange Standards Consortium
CENC	Chronic Effects of Neurotrauma Consortium
CENTCOM	US Central Command
CJCS	Chairman of the Joint Chiefs of Staff
COA	Clinical Outcome Assessment
CoE	Center of Excellence
COI	Community of Interest
CoTCCC	Committee on Combat Casualty Care
CPG	Clinical Practice Guidelines
CRADA	Cooperative Research and Development Agreement
CRM	Clinical and Rehabilitative Medicine

Photo credit (opposite page): Corporal Ian Ferro/US Marine Corps

CRMRP	Clinical and Rehabilitative Medicine Research Program
CSF	Cerebrospinal fluid
CSTARS	Center for Sustainment of Trauma and Readiness Skills
CT	Computerized Tomography
CTE	Chronic Traumatic Encephalopathy
CXCL-3	Chemokine (C-X-C motif) Ligand-3

D

DARPA	Defense Advanced Research Projects Agency
DAS	Data Acquisition System
DCoE	Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury
DDR&E	Director of Defense Research and Engineering
DDT	Drug Development Tool
DEA	Data Exchange Agreement
DHA	Defense Health Agency
DHP	Defense Health Program
DoD	Department of Defense
DoDD	Department of Defense Directive
DOT&E	Director for Operational Test and Evaluation
DRDO	Defence Research and Development Organization
DTI	Diffusion Tensor Imaging
DTS	Diversified Technical Systems
DTTI	Defense Trade and Technology Initiative
DVBIC	Defense and Veterans Brain Injury Center
DVCIPM	Defense and Veterans Center for Integrative Pain Management
DVEAR	Defense and Veterans Extremity Trauma and Amputation Registry
DVEIVR	Defense and Veterans Eye Injury and Vision Registry
DVT	Deep Vein Thrombosis

E

EA	Executive Agent
EACE	Extremity Trauma and Amputation Center of Excellence
ECH	Enhanced Combat Helmet
EMED	Expeditionary Medical Encounter Database
EOD	Explosive Ordinance Disposal
ESiT	Environmental Sensors in Training

F

FAAST	Federal Advanced Amputation Skills Training
FDA	US Food and Drug Administration
FEA	Finite Element Analysis
FedBizOpps	Federal Business Opportunities
FITBIR	Federal Interagency Traumatic Brain Injury Research Working Group
FFV	Future Fighting Vehicle
FWB	Fresh Whole Blood
FY	Fiscal Year

G

GTRI	Georgia Tech Research Institute

H

HBO2	Hyperbaric Oxygen Therapy
HCE	Hearing Center of Excellence
HET	Heavy Equipment Transporter
HETA1	M1070A1 Heavy Equipment Transporter
HETS	Heavy Equipment Transporter System
HFM	Human Factors and Medicine
HHS	Health and Human Services
HIT	Human Injury and Treatment
hMPC	Human Muscle Progenitor Cell Therapy
HOPPS	Hyperbaric Oxygen for Persistent Post-concussive Symptoms
HUSK	Heavy Equipment Transporter Urban Survivability Kit

HVLT-R	Hopkins Verbal Learning Test—Revised
HVLT-R DR	Hopkins Verbal Learning Test—Revised Delayed Recall

I

iBIPSR	Interactive Blast Injury Prevention Standards Recommendation
ICAM-1	Intercellular Adhesion Molecule-1
ICP	Intracranial Pressure
IDF	Israel Defense Forces
IED	Improvised Explosive Device
IHPS	Integrated Head Protection System
IL-1-α	Interleukin-1-alpha
IL-6	Interleukin-6
IM	Interactive Metronome
INMAS	Institute of Nuclear Medicine & Allied Sciences
INTRuST	The Injury and Traumatic Stress Consortium
IOFB	Intraocular Foreign Bodies
ISS	Injury Severity Score
ITC-PAC	International Technology Center—Pacific

J

JPC	Joint Program Committee
JHU/APL	Johns Hopkins University Applied Physics Laboratory
JIDA	Joint Improvised-Threat Defeat Agency
JIEDDO	Joint Improvised Explosive Device Defeat Organization
JNLWD	Joint Non-Lethal Weapons Directorate
JTAPIC	Joint Trauma Analysis and Prevention of Injury in Combat
JTG	Joint Technology Group
JTS	Joint Trauma System
JWMRP	Joint Warfighter Medical Research Program

L

LAV	Light Armored Vehicle
LCMT1	Leucine Carboxyl Methyltransferase 1
LFT&E	Live Fire Test and Evaluation
LPA	Lysophosphatidic Acid
LTFU	Long Term Follow Up

M

MAMC	Madigan Army Medical Center
MCP-1	Monocyte Chemotactic Protein-1
MEDCOM	United States Army Medical Command
METRC	Major Extremity Trauma Research Consortium
MFAP	Military Functional Assessment Program
MHS	Military Health System
MIL-STD	Military Standard
MIT	Massachusetts Institute of Technology
MOM	Military Operational Medicine
MOMRP	Military Operational Medicine Research Program
MRAP	Mine Resistant Ambush Protected
MRI	Magnetic Resonance Imaging
mTBI	Mild Traumatic Brain Injury

N

NATO	North Atlantic Treaty Organization
NCAA	National Collegiate Athletic Association
NDAA	National Defense Authorization Act
NDMC	National Defense Medical College
NeuroDRIVE	Neurocognitive Driving Rehabilitation in Virtual Environments
NFL	National Football League
NFT	Neurofibrillary Tangle
NGIC	National Ground Intelligence Center

NHRC	Naval Health Research Center
NICoE	National Intrepid Center of Excellence
NIH	National Institutes of Health
NINDS	National Institute of Neurological Disorders and Stroke
NJIT	New Jersey Institute of Technology
NMCSD	Naval Medical Center San Diego
NMRC	Naval Medical Research Center
NOP	Nociceptin/Orphanin FQ Peptide Receptor
NRL	Naval Research Laboratory
NSI	Neurobehavioral Symptom Inventory
NSWC	Naval Surface Warfare Center

O

OEF	Operation Enduring Freedom
OIF	Operation Iraqi Freedom
ω-3	Omega-3
OND	Operation New Dawn
ONR	Office of Naval Research
OPORP	Orthotics and Prosthetics Outcomes Research Program
OSD	Office of the Secretary of Defense
OTSG	Office of the Surgeon General

P

PCO	Blast Injury Research Program Coordinating Office
PCS	Post-Concussive Syndrome
PdM HTV	Product Manager Heavy Tactical Vehicle
PEO	Program Executive Office
PH/TBIRP	Psychological Health/Traumatic Brain Injury Research Program
PIHL	Pharmaceutical Interventions for Hearing Loss
PME-1	Protein Phosphatase Methylesterase-1
PMHS	Postmortem Human Surrogates
PM SPE	Product Manager Soldier Protective Equipment
PM SPIE	Project Manager Soldier Protection and Individual Equipment
POG	Protective Overgarment
POI	Point of Injury
PP2A	Protein Phosphatase 2A
PPE	Personal Protective Equipment
PPS	Pelvic Protection System
PRMRP	Peer Reviewed Medical Research Program
PROPPR	Pragmatic Randomized Optimal Platelet and Plasma Ratios
ProTECT III	Progesterone for Traumatic Brain Injury, Experimental Clinical Treatment
PSC	Polytrauma System of Care
psi	Pounds Per Square Inch
PTSD	Posttraumatic Stress Disorder
PUFA	Polyunsaturated Fatty Acid
PUG	Protective Undergarment

R

R&E	Research & Engineering
RBANS	Repeatable Battery for Neuropsychological Status
RCI	Reliable Change Interval
RDA	Research, Development, and Acquisition
RDECOM	Research, Development, and Engineering Command
RDT&E	Research, Development, Testing, and Evaluation
RDX	Research Department Explosives
REBOA	Resuscitative Endovascular Balloon Occlusion of the Aorta
RFI	Request for Information
RPD	Radford Propellant Development
RSY	Research Symposium
RTG	Research Task Group

S

SAMMC	San Antonio Military Medical Center
SBIR	Small Business Innovation Research

SCI	Spinal Cord Injury
SCIRP	Spinal Cord Injury Research Program
SECARMY	Secretary of the Army
SME	Subject Matter Expert
SoS	State-of-the-Science
SPS	Soldier Protection System
SRC	Standard Rehabilitation Care
SSG	Staff Sergeant
STO	Science and Technology Organization
STRI	Simulation, Training, and Instrumentation
STRONG STAR	South Texas Research Organizational Network Guiding Studies on Trauma and Resilience

T

TAP	Technical Activity Proposal
TARDEC	United States Army Tank Automotive Research Development and Engineering Center
TATRC	Telemedicine and Advanced Technology Research Center
TBI	Traumatic Brain Injury
TBI-CDE	TBI Common Data Elements
TCCC	Tactical Combat Casualty Care
TCRD	Test Capability Requirements Document
TED	Traumatic Brain Injury Endpoints Development
TIRM	Tissue Injury and Regenerative Medicine
TNAP	Tissue Non-specific Alkaline Phosphatase
TP-MP-T	Target Practice, Multi-Purpose with Tracer
TPCSDS-T	Target Practice, Cone Stabilized, Discarding Sabot with Tracer
TSWG	Technical Support Working Group
TTP	Tactics, Techniques, and Procedures

U

UCH-L1	Ubiquitin Carboxy-Terminal Hydrolase-L1
US	United States
USAARL	US Army Aeromedical Research Laboratory
USAF	United States Air Force
USAMMDA	United States Army Medical Materiel Development Activity
USAMRMC	United States Army Medical Research and Materiel Command
USAPHC	United States Army Public Health Center
USD(AT&L)	Under Secretary of Defense for Acquisition, Technology, and Logistics
USD(P&R)	Under Secretary of Defense for Personnel and Readiness
USMC	United States Marine Corps
USSOCOM	United States Special Operations Command
USUHS	Uniformed Services University of the Health Sciences

V

VA	United States Department of Veterans Affairs
VCE	Vision Center of Excellence
VCSC	Vision Care Services Coordinator
VHA	Veterans Health Administration

W

WIAMan	Warrior Injury Assessment Manikin
WRAIR	Walter Reed Army Institute of Research
WRNMMC	Walter Reed National Military Medical Center
WSS	Wound Stasis System
WWRP	Wounded Warrior Recovery Project

APPENDIX B:

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APPENDIX C:

DODD 6025.21E

Department of Defense
DIRECTIVE

NUMBER 6025.21E
July 5, 2006

USD(AT&L)

SUBJECT: Medical Research for Prevention, Mitigation, and Treatment of Blast Injuries

References: (a) Section 256 of Public Law 109-163, "National Defense Authorization Act for Fiscal Year 2006" [1]
(b) DoD Directive 5101.1, "DoD Executive Agent," September 3, 2002
(c) DoD Directive 5134.3, "Director of Defense Research and Engineering (DDR&E),"November 3, 2003
(d) DoD Directive 5025.1, "DoD Directives System," March 2005
(e) through (g), see Enclosure 1

1. PURPOSE

This Directive:

1.1. Implements Reference (a) by establishing policy and assigning responsibilities governing coordination and management of medical research efforts and DoD programs related to prevention, mitigation, and treatment of blast injuries.

1.2. Designates the Secretary of the Army, in compliance with Reference (a) and consistent with Reference (b), as the DoD Executive Agent (DoD EA) for Medical Research for Prevention, Mitigation, and Treatment of Blast Injuries according to Reference (b).

1.3. Establishes the Armed Services Biomedical Research Evaluation and Management (ASBREM) Committee. The ASBREM Committee serves to facilitate coordination and prevent unnecessary duplication of effort within DoD biomedical research and development and associated enabling research areas, to include serving as the forum for implementation of subsections (d) and (g) of Reference (a).

1 Federal legislative information is available through the Library of Congress THOMAS site, http://thomas.loc.gov. DoDD 6025.21E, July 5, 2006

Photo credit (opposite page): Corporal Paul S. Martinez/US Marine Corps

2. APPLICABILITY

This Directive applies to:

2.1. The Office of the Secretary of Defense, the Military Departments, the Chairman of the Joint Chiefs of Staff, the Combatant Commands, the Office of the Inspector General of the Department of Defense, the Defense Agencies, the DoD Field Activities, and all other organizational entities in the Department of Defense (hereafter collectively referred to as the "DoD Components").

2.2. Medical and associated enabling research supported by any DoD Component for prevention, mitigation, and treatment of blast injuries.

3. DEFINITIONS

As used in this Directive, the following terms are defined as follows:

3.1. Blast Injury. Injury that occurs as the result of the detonation of high explosives, including vehicle-borne and person-borne explosive devices, rocket-propelled grenades, and improvised explosive devices. The blast injury taxonomy is provided at Enclosure 2.

3.2. Research. Any systematic investigation, including research, development, testing, and evaluation (RDT&E), designed to develop or contribute to general knowledge.

4. POLICY

It is DoD policy that:

4.1. DoD research related to blast injury prevention, mitigation, and treatment will be coordinated and managed by a DoD EA to meet the requirements, objectives, and standards of the DoD Military Health System as identified by the Under Secretary of Defense for Personnel and Readiness (USD(P&R)) and the unique combat casualty care requirements of the DoD Components.

4.2. Relevant research shall take maximum advantage of the scientific and technical capabilities of industry, academia, DoD Components, and other Federal Agencies.

4.3. The ASBREM Committee will be the venue for joint and cross-Service coordination specified by Reference (a).

4.4. DoD Components will gather and share medical information related to the efficacy of personal protective equipment and of vehicular equipment designed to protect against blast injury.

5. RESPONSIBILITIES AND FUNCTIONS

5.1. The Director of Defense Research and Engineering (DDR&E), under the Under Secretary of Defense for Acquisition, Technology and Logistics, according to DoD Directive 5134.3 (Reference (c)), shall:

5.1.1. Plan, program, and execute the functions and reports mandated for the DDR&E by Reference (a).

5.1.2. Have the authority to publish DoD Issuances consistent with Reference (d) for implementation of this Directive.

5.1.3. Establish, as needed, procedures to ensure that new technology developed under this Directive is effectively transitioned and integrated into systems and subsystems and transferred to and firmly under the control of the DoD Components.

5.1.4. Chair the ASBREM Committee to coordinate DoD biomedical research (see Enclosure 3 for additional detail), and employ that entity to facilitate the DoD EA's coordination and oversight of blast-injury research as specified in Reference (a).

5.1.5. Serve as the final approving authority for DoD blast-injury research programs.

5.1.6. Oversee the functions of the DoD EA and conduct/report on related periodic assessments (per Reference (a)).

5.2. The Assistant Secretary of Defense for Health Affairs (ASD(HA)), under the USD(P&R), shall:

5.2.1. Assist the DDR&E, the DoD EA, and the Director, Joint Improvised Explosive Devices Defeat Organization (JIEDDO), with identification of related operational and research needs, assessment of relevant research efforts, and coordination of planning to resolve capability gaps through focused research efforts.

5.2.2. Be the approving authority for Military Health System prevention and treatment standards developed and proposed by the DoD EA.

5.2.3. Appoint appropriate representatives to related coordinating boards or committees established by the DoD EA.

5.2.4. Ensure that the information systems capabilities of the Military Health System support the DoD EA and the functions specified by this Directive.

5.2.5. Serve as Co-chair of the ASBREM Committee. (See Enclosure 3 for additional detail.)

5.3. The Secretary of the Army is hereby designated as the DoD EA for Medical Research for Prevention, Mitigation, and Treatment of Blast Injuries, consistent with Reference (a), to coordinate and manage relevant DoD research efforts and programs, and in that role shall:

5.3.1. Give full consideration to the Research and Engineering (R&E) needs of the DoD Components and the Director, JIEDDO, addressing those needs/requirements by:

5.3.1.1. Maintaining a DoD technology base for medical research related to blast injuries and based on the DDR&E-approved program for the DoD Components.

5.3.1.2. Performing programming and budgeting actions for all blast-injury research to maintain the R&E programs based on DDR&E-approved priorities of the DoD Components.

5.3.1.3. Programming and budgeting for blast-injury research based on analysis and prioritization of needs of the DoD Components, consistent with paragraph 5.1 of this Directive.

5.3.1.4. Executing the approved DoD blast-injury research program consistent with DoD guidance and availability of annual congressional appropriations.

5.3.2. Provide medical recommendations with regard to blast-injury prevention, mitigation, and treatment standards to be approved by the ASD(HA).

5.3.3. Coordinate DoD blast-injury-research issues with the staffs of the DDR&E, the ASD(HA), and the Director, JIEDDO.

5.3.4. Support the development, maintenance, and usage of a joint database for collection, analysis, and sharing of information gathered or developed by the DoD Components related to the efficacy of theater personal protective equipment (including body armor, helmets, and eyewear) and vehicular equipment designed to protect against blast injury.

5.3.5. Appoint a medical general or flag officer representative to the ASBREM Committee.

5.3.6. Ensure that information is shared as broadly as possible except where limited by law, policy, or security classification and that data assets produced as a result of the assigned responsibilities are visible, accessible, and understandable to the rest of the Department as appropriate and in accordance with Reference (e).

5.4. The Secretaries of the Navy and the Air Force shall:

5.4.1. Forward their respective approved blast-injury medical R&E requirements to the DoD EA for consideration and integration.

5.4.2. Appoint medical general or flag officer representatives to the ASBREM Committee and appoint representatives to any other coordination, oversight, or assessment board established by DDR&E or the DoD EA.

5.4.3. Coordinate with other DoD Components on the assignment of Joint Technical Staff Officers to Army medical research entities, research and acquisition organizations, or installations for coordination of research programming and execution needs pertaining to their Component.

5.4.4. Provide an appropriate system for identification, verification, prioritization, and headquarters-level approval of their respective blast-injury R&E requirements before submission to the DoD EA.

5.5. The President of the Uniformed Services University of the Health Sciences (USUHS), under the ASD(HA) and USD(P&R), shall:

5.5.1. Ensure that education relating to blast-injury prevention, mitigation, and treatment is included in the USUHS medical and continuing education curriculum and programs.

5.5.2. Appoint a representative to any coordination, oversight, or assessment board established by DDR&E or the DoD EA.

5.6. The Chairman of the Joint Chiefs of Staff shall:

5.6.1. Coordinate input to the DoD EA and ensure integration of the requirements processes of the Joint Capabilities Integration and Development System [2] with the processes employed under this Directive.

5.6.2. Appoint a relevant senior representative to the ASBREM Committee.

5.6.3. Appoint representatives to organizational entities of the ASBREM Committee and to any other coordination, oversight, or assessment board established by DDR&E or the DoD EA.

5.7. The Commander, US Special Operations Command shall establish procedures and processes for coordination of relevant Defense Major Force Program 11 activities with those planned, programmed, and executed by the DoD EA and shall also:

5.7.1. Forward that command's approved blast-injury R&E requirements for consideration and integration to the DoD EA.

5.7.2. Appoint representatives to organizational entities of the ASBREM Committee, as appropriate, and to any other coordination, oversight, or assessment board established by DDR&E or the DoD EA.

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2 8CJCSI 3170.01E, "Joint Capabilities Integration and Development System," May 11, 2005, is available at http://.dtic.mil/cjcs_directives/cjcs/instructions.htm.

5.7.3. Coordinate with the command on the assignment of Joint Technical Staff Officers to Army medical research entities, research and acquisition organizations, or installations for coordination of research programming and execution needs.

5.7.4. Provide an appropriate system for identification, verification, and headquarters-level approval of that command's blast-injury R&E requirements before submission to the DoD EA.

5.8. The Director, JIEDDO, consistent with Reference (f), shall:

5.8.1. Support development, maintenance, and usage of a joint database for collection, analysis, and sharing of information gathered or developed by DoD Components related to the efficacy of theater personal protective equipment (e.g., body armor, helmets, and eyewear) and vehicular equipment designed to protect against blast-injury.

5.8.2. Appoint representatives to organizational entities of the ASBREM Committee, as appropriate, and to any other coordination, oversight, or assessment board established by DDR&E or the DoD EA.

5.8.3. Assist the DoD EA, the DDR&E, and the ASD(HA) with identification of related operational and research needs, assessment of relevant research efforts, and coordination of planning to resolve capability gaps through focused research efforts.

6. AUTHORITY

The DoD EA identified by this Directive is hereby delegated authority to do the following:

6.1. Obtain reports and information, consistent with the policies and criteria of DoD Directive 8910.1 (Reference (g)), as necessary, to carry out assigned responsibilities and functions.

6.2. Communicate directly with the Heads of the DoD Components, as necessary, to carry out assigned functions, including the transmission of requests for advice and assistance. Communications to the Military Departments shall be transmitted through the Secretaries of the Military Departments, their designees, or as otherwise provided in law or directed by the Secretary of Defense in other DoD issuances. Communications to the Commanders of the Combatant Commands shall normally be transmitted through the Chairman of the Joint Chiefs of Staff.

6.3. Communicate with other Federal Agencies, representatives of the Legislative Branch, members of the public, and representatives of foreign governments, as appropriate, in carrying out assigned responsibilities and functions. Communications with representatives of the Legislative Branch shall be coordinated with the Assistant Secretary of Defense for Legislative Affairs and the Under Secretary of Defense (Comptroller)/Chief Financial Officer, as appropriate, and be consistent with the DoD Legislative Program.

7. EFFECTIVE DATE

This Directive is effective immediately.

Gordon England

E1. ENCLOSURE 1

REFERENCES, continued

(e) DoD Directive 8320.2, "Data Sharing in a Net-Centric Department of Defense," December 2, 2004
(f) DoD Directive 2000.19E, "Joint Improved Explosive Device Defeat Organization (JIEDDO)," February 14, 2006
(g) DoD Directive 8910.1, "Management and Control of Information Requirements," June 11, 1993

E2. ENCLOSURE 2

TAXONOMY OF INJURIES FROM EXPLOSIVE DEVICES

E2.1.1. Primary. Blast overpressure injury resulting in direct tissue damage from the shock wave coupling into the body.

E2.1.2. Secondary. Injury produced by primary fragments originating from the exploding device (preformed and natural (unformed) casing fragments, and other projectiles deliberately introduced into the device to enhance the fragment threat); and secondary fragments, which are projectiles from the environment (debris, vehicular metal, etc.).

E2.1.3. Tertiary. Displacement of the body or part of body by the blast overpressure causing acceleration/deceleration to the body or its parts, which may subsequently strike hard objects causing typical blunt injury (translational injury), avulsion (separation) of limbs, stripping of soft tissues, skin speckling with explosive product residue and building structural collapse with crush and blunt injuries, and crush syndrome development.

E2.1.4. Quaternary. Other "explosive products" effects—heat (radiant and convective), and toxic, toxidromes from fuel, metals, etc.—causing burn and inhalation injury.

E2.1.5. Quinary. Clinical consequences of "post detonation environmental contaminants" including bacteria (deliberate and commensal, with or without sepsis), radiation (dirty bombs), tissue reactions to fuel, metals, etc.

APPENDIX D:

SUPPLEMENTAL TABLES

TABLE D-1: FY15 CDMRP Congressionally Directed Research Programs with Blast Injury-Related Research Activities

CDMRP Research Program	Program Focus
Joint Warfighter Medical Research Program (JWMRP)	The JWMRP funds mature research projects close to yielding tangible benefits to military medicine. The JWMRP focuses on six program areas: Medical Simulation and Information Sciences, Military Infectious Diseases, MOM, CCC, Radiation Health Effects, and CRM. Example focus areas relevant to blast injury: • Simulation technology and medical training • Prophylactics and novel therapeutics to treat multi-drug resistant organisms in combat wound infections, countermeasures that prevent and mitigate Service Member injury • Development and validation of effective evidenced-based prevention, screening and assessment strategies, as well as treatment and rehabilitation interventions for concussion/mild traumatic brain injury • Identification and development of medical techniques and materiel (medical devices, drugs, and biologics) for early intervention in life-threatening battle injuries • Neuromusculoskeletal injury (including amputees), sensory systems (including balance, vision, and hearing), acute and chronic pain, and regenerative medicine
Orthotics and Prosthetics Outcomes Research Program (OPORP)	The OPORP funds research that evaluates the comparative effectiveness of orthotic and prosthetic clinical interventions and/or their associated rehabilitation interventions, using patient-centric outcomes for Service Members and Veterans who have undergone limb impairment or limb amputation. Example focus areas relevant to blast injury: • Determination of optimal timing for prosthetic/orthotic intervention and selection of optimal device • Evaluation of comparative effectiveness of different orthotic devices as well as prevention of secondary adverse consequences from prosthetic/orthotic use • Application of specific rehabilitation interventions to accelerate the time, course, or extent of functional outcomes
Peer Reviewed Medical Research Program (PRMRP)	The PRMRP funds research across the entire spectrum of medical research toward improving the health and well-being of Service Members, Veterans, and their Families. Example focus areas relevant to blast injury: • Posttraumatic headache • DNA vaccine technology for postexposure prophylaxis • Neuroprosthetics • Posttraumatic osteoarthritis • Tinnitus

Photo credit (opposite page): Jamie Hartman/US Naval Research Laboratory

CDMRP Research Program	Program Focus
Peer Reviewed Orthopaedic Research Program (PRORP)	The PRORP funds research to advance the treatment of and rehabilitation from musculoskeletal injuries sustained in combat. The PRORP seeks to optimize recovery and restoration of function following orthopaedic injuries. Example focus areas relevant to blast injury: • Decreasing secondary health effects of reduced mobility following non-spinal cord traumatic neuromusculoskeletal injury • Comparative evaluation of physical/occupational therapy regimens to achieve optimal rehabilitation • Prevention of surgical site/amputation site neuromas • Development of novel materials and technologies to improve performance of prosthetics and orthotics • Development of osseointegration for upper extremity prostheses • Techniques for healing blast-related segmental bone injuries, in which large pieces of bone are lost
Psychological Health and TBI Research Program	The Psychological Health/TBI Research Program funds research efforts aimed at improving prevention, detection, and treatment of psychological health disorders and TBIs. Research funded by Physiological Health/TBI spans the translation research spectrum from basic research to clinical trials. Example focus areas relevant to blast injury: • Investigations of blast physics for improved understanding of mechanism and for enhanced design of personal protective equipment • Comparison of behavioral and neural pathologies in blast-induced and mechanically-induced TBI • Evaluation of rehabilitative therapies for TBI injury, including telerehabilitation and virtual reality • Evaluation of neuroprotective and/or therapeutic compounds to treat TBI • Development of field-ready diagnostic devices for PTSD and TBI
SCI Research Program (SCIRP)	The SCIRP funds collaborative research to advance the treatment and rehabilitation of SCI. Example focus areas relevant to blast injury: • Management of acute SCI care (pre-hospital, en route care, and early hospital management) • Best practices for rehabilitation and adjustment to SCI • Research towards the development of spinal regeneration • Secondary health effects and complications following SCI • Investigation and improvement of functional deficits

CDMRP Research Program	Program Focus
Vision Research Program (VRP)	The VRP funds research efforts to improve and transform the care of military personnel affected by diseases and injuries of the eye. The program focuses on funding innovative, military-relevant research that addresses unmet clinical needs. Example focus areas relevant to blast injury: • Mitigation and treatment of traumatic ocular and visual system injuries • Treatment of TBI-induced visual dysfunction, including that caused by direct blast injury • Strategies for the protection, prevention, and rehabilitation of eye injuries • Epidemiological studies of military eye trauma, including TBI-induced visual dysfunction
Epilepsy Research Program (ERP)	The ERP funds research to develop an understanding of the magnitude of posttraumatic epilepsy (PTE) within the military and to expand research into the basic mechanisms by which traumatic brain injury (TBI) produces epilepsy. Example focus areas relevant to blast injury: • Epidemiological characterization and identification of risk factors for developing PTE following TBI • Identifying markers or mechanisms that address PTE • Development of new models or better characterization of existing models for PTE, including repetitive TBI
Military Burn Research Program (MBRP)	The MBRP funds projects that support a broad research portfolio in the treatment of burns and the trauma associated with burn injuries sustained during combat or combat-related activities. Example focus areas relevant to blast injury: • Investigation of the impact of various fluid resuscitation techniques on clinically relevant outcomes during acute burn resuscitation • Studies sepsis or on single or multiple organ failure in the burn/trauma patient • Evaluation of factors involved in burn wound healing and optimization of strategies for treatment • Impact of prolonged field care and delayed evacuation on patient outcomes
Reconstructive Transplant Research (RTR) Program	The RTR Program funds innovative research that will foster new directions for, and address neglected issues in, the field of reconstructive transplantation, specifically for vascularized composite allotransplantation (VCA)-focused research. Example focus areas relevant to blast injury: • Immune system regulation • Improved access to reconstructive transplantation • Reconstructive transplantation rehabilitation • Graft surveillance—clinical monitoring • Psychosocial issues associated with VCA

APPENDIX E:

DOD DEFINITION OF TRAUMATIC BRAIN INJURY

A traumatically induced structural injury or physiological disruption of brain function, as a result of an external force, that is indicated by new onset or worsening of at least one of the following clinical signs immediately following the event:

- Any alteration in mental status (e.g., confusion, disorientation, slowed thinking, etc.)
- Any loss of memory for events immediately before or after the injury.
- Any period of loss of or a decreased level of consciousness, observed or self-reported.

External forces may include any of the following events: the head being struck by an object, the head striking an object, the brain undergoing an acceleration/deceleration movement without direct external trauma to the head, or forces generated from events such as a blast or explosion, including penetrating injuries.

The above criteria define a TBI. Sequelae of TBI may resolve quickly, within minutes to hours after the neurological event, or they may persist. Some sequelae of TBI may be permanent. Most signs and symptoms will manifest immediately following the event. However, other signs and symptoms may be delayed from days to months (e.g., headaches, subdural hematoma, seizures, hydrocephalus, spasticity, etc.). Signs and symptoms may occur alone or in varying combinations, and may result in a functional impairment. These signs and symptoms are not better explained by pre-existing conditions or other acute medical, neurological, or psychological causes, but may be a case of an exacerbation of a pre-existing condition. The signs and symptoms generally fall into one or more of the following three categories:

- **Physical:** Headache, nausea, vomiting, dizziness, sleep disturbance, weakness, paresis/plegia, sensory loss including hearing loss, visual loss, loss/alteration of taste or smell, tinnitus, spasticity, aphasia, dysphagia, dysarthria, balance disorders, disorders of coordination, seizure disorder.
- **Cognitive:** Deficits in attention, concentration, memory, speed of processing, new learning, planning, reasoning, judgment, executive control, self-awareness, language, abstract thinking.
- **Behavioral/emotional:** Feelings of depression or anxiety, agitation, irritability, impulsivity, aggression.

Note: The signs and symptoms listed above are typical of each category but are not an exhaustive list of all possible signs and symptoms.

Severity of Brain Injury Stratification:

Not all individuals exposed to an external force will sustain a TBI. TBI varies in severity, traditionally described as concussion/mild, moderate, or severe. These categories are based on the presence and duration of the immediate, injury-induced alteration of consciousness; loss of consciousness; or posttraumatic amnesia.

Injury severity (i.e., concussion/mild, moderate, severe) is determined at the time of the injury, but this severity level, while having some prognostic value, does not necessarily reflect the patient's ultimate level of functioning. It is recognized that serial assessments of the patient's cognitive, emotional, behavioral, and social functioning are required. Current anatomic and functional imaging technology is only an adjunct to the diagnosis of TBI.

Photo credit (opposite page): US Navy

- TBI is classified as concussion/mild, moderate, or severe if it meets any of the criteria below within a particular severity level. If a patient meets criteria in more than one category of severity, the higher severity level is assigned. The trauma may cause structural damage and intracranial hemorrhage requiring immediate surgical intervention, or may produce subtle, non-structural damage indicated by altered brain function and a normal Computed Tomography (CT) scan.
- If it is not clinically possible to determine the level of severity because of medical interventions (e.g., sedation, pharmacologic paralysis, etc.), other severity markers may be required, such as a CT scan.
- It is emphasized that the majority (more than 80 percent) of those with a concussion, which is the most common type of TBI, will have a full, spontaneous recovery within a few days or weeks. Guidance on concussion evaluation and treatment can be found in the Concussion Management Algorithms located on the Defense and Veterans Brain Injury Center (DVBIC) website (http://www.dcoe.mil/content/Navigation/Documents/DCoE_Concussion_Management_Algorithm_Cards.pdf).

TABLE E-1: TBI Stratification

Mild/Concussion	Moderate	Severe
A CT scan is not indicated for most patients with a concussion.*	Normal or abnormal structural imaging	Normal or abnormal structural imaging
LOC = 0–30 minutes**	LOC > 30 minutes and < 24 hours	LOC > 24 hours
AOC = a moment up to 24 hours	AOC > 24 hours. Severity based on other criteria	
PTA = 0–1 day	PTA > 1 and < 7 days	PTA > 7 days

AOC: Alteration of consciousness/mental state; LOC: Loss of consciousness; PTA: Posttraumatic amnesia
*If obtained, the CT scan is normal.

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