Science & Technology Efforts & Programs

PREVENTION, MITIGATION, AND TREATMENT OF BLAST INJURIES

FY14 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

On February 10, 2014, in Kabul, a vehicle-borne Improvised Explosive Device (IED) killed two civilian contractors who were working for the US-led international military coalition.[1] An IED killed a NATO soldier in the eastern part of Afghanistan just five days later.[2] In the southwest, 24-year-old Corporal Kyle Carpenter lost an eye and much of his jaw when he threw himself in front of a fellow Service Member to protect him from a grenade blast; the White House will award Corporal Carpenter with the Medal of Honor for his actions.[3] Enemy explosive attacks have a tremendous impact on Force operations and readiness, as well as the lives of Service Members who protect each other and the security of the American people. These stories of tragedy and heroism are reminders of the important role the Blast Injury Research Program and the Program Coordinating Office (PCO) play in supporting those Service Members by facilitating collaboration across stakeholder communities to accelerate the development of solutions that prevent, mitigate, and treat injuries from blast events.

Scientists and clinicians have made notable advancements in the field of blast injury research that are saving lives, reducing injury, and speeding the recovery and reintegration of Service Members into their military roles and civilian life. For example, a new software application enables earlier and more accurate detection of neurocognitive impairment from concussion. A novel anti-microbial skin substitute shows promise for treating the most common combat wound pathogens. A quadruple amputee who received a double arm transplant was featured on the front page of the Washington Post doing a pull-up. The rate at which soldiers can return to duty and maintain an active lifestyle is increasing with new and innovative advances in rehabilitation medicine.

This report to the Executive Agent (EA) describes the Fiscal Year 2014 (FY14) efforts of the Department of Defense (DoD) Blast Injury Research Program in addressing the entire spectrum of blast injuries. The report highlights significant accomplishments, addresses the challenges that remain, and proposes the way forward to close knowledge gaps and advance the state-of-the-science. By disseminating information on the Blast Injury Research Program to researchers, policymakers, military leaders, and the general public through the annual EA Report, we hope to demonstrate the power of collaboration and breadth of partnerships that exist within the diverse blast injury research community; we also want to build confidence in the DoD's commitment to preventing, mitigating, and treating the 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.

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Program Coordinating Office

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Assistant Secretary of the Army for Acquisition, Logistics and Technology (ASA[ALT])
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Marine Corps Systems Command (MCSC)
National Intrepid Center of Excellence (NICoE)
Naval Health Research Center (NHRC)
Naval Medical Research Center (NMRC)
Office of Naval Research (ONR)
Office of the US Air Force Surgeon General (OAFSG)
PEO Combat Support and Combat Service Support (CS&CSS)
PEO Project Manager Soldier Protection and Individual Equipment (PM SPIE)
Program Executive Office (PEO) Soldier
The MITRE Corporation
Uniformed Services University of Health Sciences (USUHS)
USAMRMC Armed Forces Institute of Regenerative Medicine (AFIRM)
USAMRMC Clinical and Rehabilitative Medicine Research Program (CRMRP)
USAMRMC Combat Casualty Care Research Program (CCCRP)
USAMRMC Military Infectious Diseases Research Program (MIDRP)
USAMRMC Military Operational Medicine Research Program (MOMRP)
USAMRMC Telemedicine & Advanced Technology Research Center (TATRC)
US Army Aeromedical Research Laboratory (USAARL)
US Army Medical Materiel Development Activity (USAMMDA)
US Army Medical Research and Materiel Command (USAMRMC)
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EXECUTIVE SUMMARY

Enemy use of explosive devices is on the rise, resulting in a high number of casualties with blast-related injuries. Fortunately, technological advancements are improving survivability from blast events, though Service Members are surviving attacks with blast-related injuries including hearing loss, amputation, and traumatic brain injury (TBI). Even relatively mild symptoms of blast-related injury (e.g., tinnitus, dizziness, and/or disorientation) can have major impacts on operational readiness and quality of life. Thus, the US Department of Defense (DoD) is investing significant resources on medical research for the prevention, mitigation, and treatment of blast injuries.

Formalizing the DoD's blast injury research efforts is DoD Directive (DoDD) 6025.21E (July 5, 2006), which established the DoD Blast Injury Research Program and assigned the Secretary of the Army (SECARMY) with Executive Agent (EA) responsibilities that include recommending DoD blast injury prevention and treatment standards; ensuring DoD-sponsored blast injury research programs are addressing the needs of the DoD components; and ensuring blast injury research information is shared among medical and nonmedical communities.

Following a series of delegations, the Commander, US Army Medical Command (Cdr, USAMEDCOM) assumed EA authority for the Blast Injury Research Program and established the Program Coordinating Office (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 critical knowledge gaps are filled, avoid costly and unnecessary duplication of effort, and accelerate the fielding of prevention and treatment strategies through collaboration and information sharing.

This report highlights several of the PCO's activities that support the Congressional intent for a coordinated DoD Blast Injury Research Program, and the EA's responsibilities. These activities include chairing the NATO Human Factors and Medicine (HFM) Research Task Group (RTG) on "Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods, and Standards" (HFM-234); developing and overseeing the Military Health System (MHS) Blast Injury Prevention Standards Recommendation (BIPSR) Process; and, implementing an International State-of-the-Science (SoS) Meeting Series with annual SoS meetings on key blast injury research topics.

The Congressional language that directed the establishment of a DoD EA for blast injury research encouraged collaboration with other countries on efforts for the prevention, mitigation, and treatment of blast injuries. The PCO Director chairs the NATO HFM-234 RTG that was established in July 2013. This RTG has 17 members representing nine NATO nations. Its objective is to develop guidelines and tools that will guide current and future blast injury research efforts, and accelerate the development and fielding of effective blast injury prevention, mitigation, and treatment strategies for Service Members. The specific deliverables of this RTG are a comprehensive dictionary of blast injury research terms that will facilitate communication and collaboration across research and operational communities, and 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 across the international blast injury research community, facilitate cross-study comparisons, and advance the state-of-the-science. In Fiscal Year 2014 (FY14), the RTG completed a final draft of its first product, the Blast Injury Epidemiological Study Guidelines. Plans are underway to finalize this draft document and publish it as an official NATO report for use by the international blast injury research community in FY15.

The EA is responsible for recommending blast injury prevention standards to the Assistant Secretary of Defense for Health Affairs (ASD[HA]) for approval as DoD standards and DoD-wide implementation. To support this key EA responsibility, the PCO developed the MHS BIPSR Process—the DoD's first unbiased, stakeholder-driven critical assessment methodology for recommending biomedically-valid MHS 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 FY14, the process matured and significant progress was made in the analysis of standards for preventing blast-related lower extremity (LE) injuries. Going forward, a more streamlined process embedded in a web-based collaboration environment will focus on standards for preventing spine/back injuries, upper extremity injuries, and auditory injuries.

Among the EA's key responsibilities are the responsibilities to identify blast injury knowledge gaps, and to facilitate collaboration among the world's blast injury research experts to help shape medical research programs that can fill the gaps and meet the needs of the DoD Components. To support these EA responsibilities, the PCO established the International SoS Meeting Series to address specific blast injury issues of importance to the DoD. These annual working meetings bring together research experts and stakeholders to determine what is known about specific blast injury issues, and to identify knowledge gaps that require additional medical research. In 2014, the PCO planned and executed its fourth SoS meeting. The topic of this meeting was the, "Biomedical Basis for mild Traumatic Brain Injury (mTBI) Environmental Sensor Threshold Values." The meeting's Expert Panel concluded that biomedically valid sensor threshold values do not yet exist for blast-induced mTBI. They recommended several specific actions that should be taken to develop valid thresholds. The meeting proceedings are posted on the PCO website (https://blastinjuryresearch.amedd.army.mil/).

In addition to providing a summary of key FY14 blast injury research accomplishments from across the DoD, this report also devotes separate chapters to two specific blast injury research topics of great concern to the DoD: hearing and balance disorders and hemorrhage control.

Hearing disorders, including peripheral hearing loss, central auditory processing deficits, tinnitus, and vestibular impairment, are the most common impairments associated with blast exposure. The Hearing Center of Excellence (HCE) coordinates with and draws from expertise across DoD and non-DoD organizations to identify solutions and best practices for hearing and balance disorders. Major FY14 accomplishments from HCE include the Joint Hearing Loss and Auditory System Injury Registry to track hearing loss and auditory and balance system injuries. The HCE also completed analyses of fieldable balance test instruments and auditory diagnostic tools for point-of-injury evaluation and potentially, early diagnosis of mTBI. The HCE is also collaborating with DoD organizations to increase Service Members' access to hearing protection devices.

The early control of hemorrhage within the first hour after injury, or the golden hour, is the most effective strategy for treating the leading cause of potentially preventable deaths on the battlefield. The USAMRMC Combat Casualty Care Research Program (CCCRP), coordinates all DoD efforts dedicated to developing and improving the products, drugs, devices, and capabilities needed for medical personnel to control traumatic hemorrhage and prevent secondary complications (resuscitation, shock, inflammation, and coagulopathy). The program focuses on medical interventions applied during the golden hour—from the point of injury through medical evacuation to a fixed treatment facility. The program also works to advance en-route care, advanced trauma life support, surgical stabilization, and definitive care in a US medical treatment facility.

Within CCCRP, the Hemorrhage and Resuscitation research portfolio works in close collaboration with the Forward Surgical and Intensive Critical Care portfolio to provide earlier intervention and care, regardless of location. The development of compressible and non-compressible hemorrhage control technologies that can be administered in the prehospital environment represent significant FY14 achievements in hemorrhage control.

To inform the EA of accomplishments throughout the blast injury research community, the PCO initiated a data call at the end of FY14 to DoD organizations and partners representing the medical research, test and evaluation (T&E), materiel development (MATDEV), and clinical care communities. The PCO received 168 data call responses from 27 organizations, and summarized those data call responses into 135 accomplishments that highlight advancements in the knowledge base for blast injury research, as well as tools and strategies for the prevention, mitigation, and treatment of blast injuries. For example, the US Army is supporting the development of the Enhanced Combat Helmet (ECH), which meets penetration probability requirements for fragments traveling 35% faster than the level required for the Advanced Combat Helmet, thereby providing better protection against secondary blast injuries.

Another example includes the use of virtual reality to elicit physiological responses associated with subthreshold Posttraumatic Stress Disorder (PTSD). This study by the Uniformed Services University of the Health Sciences (USUHS) supports the use of virtual reality in psychological assessments of Service Members returning from combat—in particular, Service Members with confirmed or suspected blast-related TBI, who often experience comorbid PTSD. The significant research accomplishments, initiatives, and activities highlighted in the FY14 annual report reflect the highly collaborative research efforts and knowledge sharing coordinated through the DoD Blast Injury Research PCO on behalf of the EA. These accomplishments 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 process.

CHAPTER 1:

INTRODUCTION

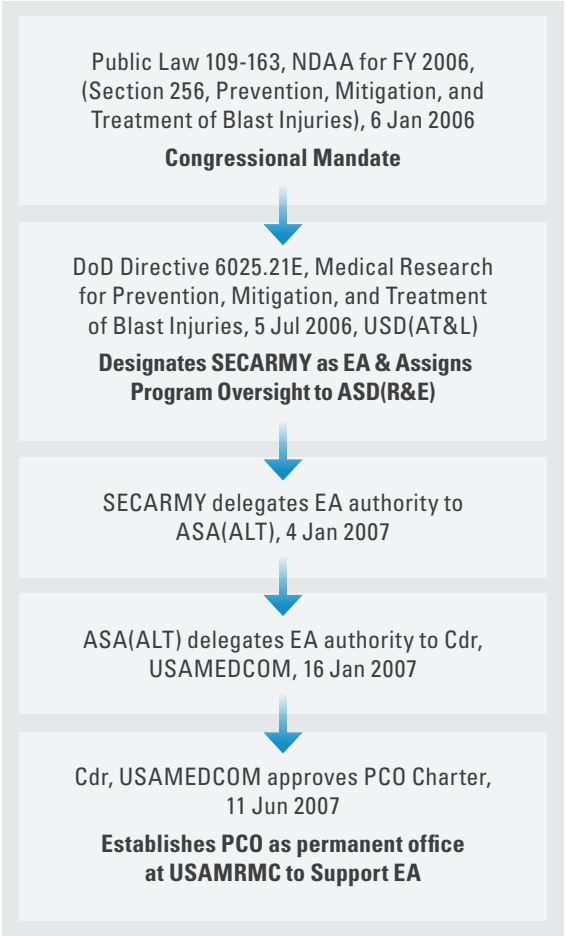
Blast injuries have emerged as the most pressing medical challenge in recent military conflicts due to the increased use of improvised explosive devices (IEDs) by terrorists and insurgent activities in Iraq and Afghanistan. Recent estimates indicate blasts are responsible for approximately 75% of US combat casualties in Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF).[4] The survival rate for those injured in OIF and OEF is much higher than in past wars due to advanced in-theater medical care, rapid evacuation, and improved personal protective equipment (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 WWII, and 3.8 in WWI.[5] As the survival rate from blast has increased, so too has the number of Service Members who have experienced blast-induced hearing loss, amputation, and traumatic brain injury (TBI).

The scope and impact of blast injuries is both broad and complex. For example, 10-20% of OIF and OEF Service Members suffer from mild TBI (mTBI), the "signature injury" of operations in Afghanistan and Iraq.[6] Dizziness, vertigo, and ear damage are also common symptoms among those afflicted with blast-induced mTBI. Consider as well that approximately 2.6% of Service Members who fought in OIF and OEF suffered from traumatic limb loss. Blast-induced injuries such as these represent acute injuries and secondary comorbidities that can result in significant long-term health care challenges and costs. Consequently, the US government is investing significant resources to improve prevention, screening, diagnosis, treatment, and rehabilitation of Service Members who have experienced blast-induced injuries.

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

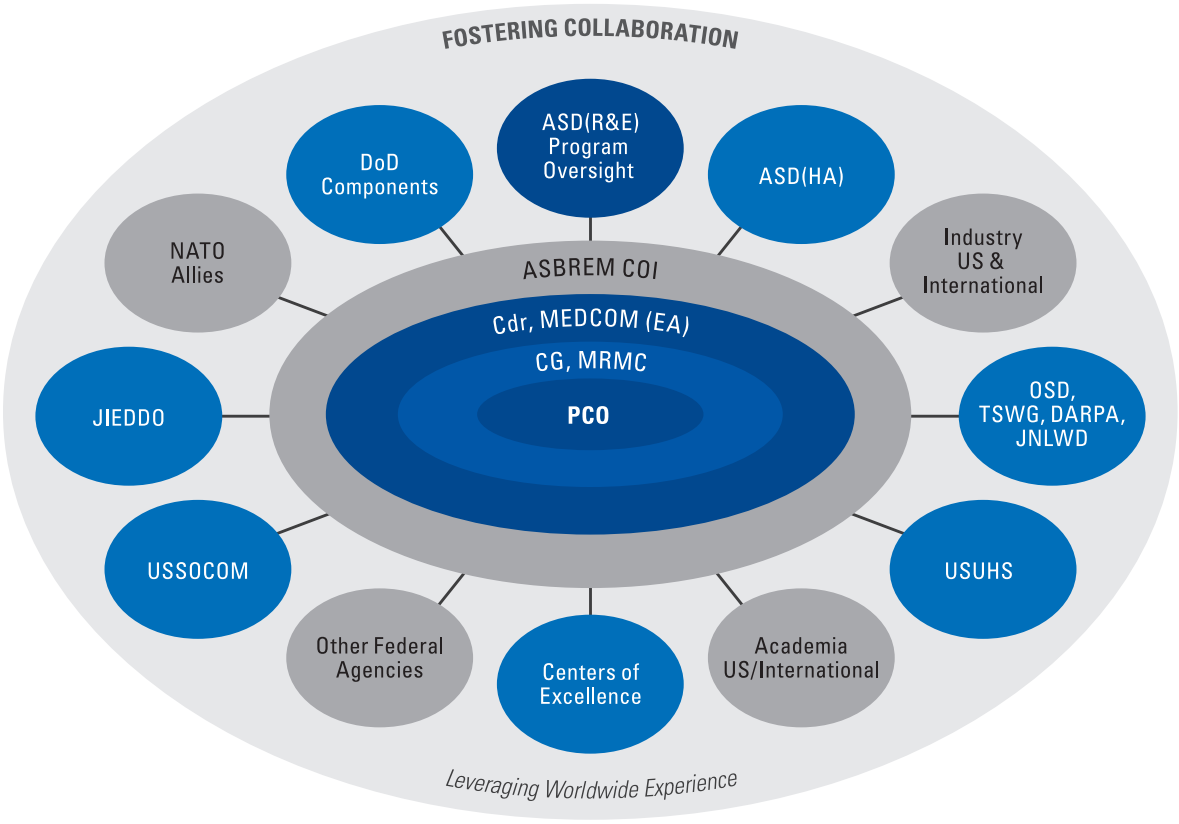
DoDD 6025.21E assigned oversight of the Blast Injury Research Program to the Assistant Secretary of Defense for Research and Engineering (ASD[R&E]) and designated the Secretary of the Army (SECARMY) as the DoD EA (Figure 1-1).

FIGURE 1-1: Assignment of EA Authority*



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

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



NATO=North Atlantic Treaty Organization; TSWG=Technical Support Working Group; DARPA=Defense Advanced Research Projects Agency; JNLWD=Joint Non-Lethal Weapons Directorate.

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 (Cdr), USAMEDCOM. The Blast Injury Research Program Coordinating Office (PCO) was established within USAMEDCOM at the USAMRMC, Fort Detrick, Maryland (MD), to assist the Cdr, USAMEDCOM, in fulfilling the EA's assigned responsibilities and functions.

In support of the EA, the PCO coordinates relevant DoD medical research efforts and programs by 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 hopes to improve blast-injury prevention, mitigation, and treatment standards for Service Members and their families.

Responsibilities and Functions

DoD assigned specific responsibilities and functions to key DoD components responsible for the coordination and management of medical research efforts and DoD programs related to prevention, mitigation, and treatment of blast injuries. Examples of key responsibilities and functions from the directive are listed below. For a more inclusive description, please see Appendix C.

- **Director of Defense Research and Engineering (DDR&E),** now known as 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 Armed Services Biomedical Research, Evaluation and Management (ASBREM) Community of Interest (COI) as the immediate successor to the ASBREM Committee established under DoDD 6025.21E (Armed Services Biomedical Research and Evaluation and Management Community of Interest Charter, May 2014), oversees the functions of the DoD EA, and serves as the final approving authority for DoD blast injury research programs.
- **Assistant Secretary of Defense for Health Affairs (ASD[HA])** assists in requirements development and needs assessments; assessment of research efforts and coordination and planning to resolve capability gaps; approves Military Health System (MHS) blast injury prevention, mitigation, and treatment standards; and appoints representatives to DoD EA coordination boards and committees; 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 responsible for coordinating and managing DoD research efforts and programs. Under this role the SECARMY gives full consideration to the Research and Engineering (R&E) needs of the DoD Components and the Director, Joint Improvised Explosive Device Defeat Organization (JIEDDO), by addressing 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 with regard to MHS blast injury prevention, mitigation, and treatment standards; executes the approved DoD Blast Injury Research Program; and ensure blast injury research information is shared.
- **The Secretary of the Navy (SECNAV) & the Secretary of the Air Force (SECAF)** assist in requirements development and needs assessment, and 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; and coordinates all blast injury efforts and requirements through the EA. The USUHS President also appoints representatives to any coordination boards, oversight, or assessment boards established by ASD(R&E) or the DoD EA.
- **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 established by ASD(R&E) or the DoD EA.
- **The Cdr, US Special Operations Command (USSOCOM)** establishes procedures for coordination of Defense Major Force Program 11 activities with those of the EA; forwards that command's approved blast injury R&E requirements for consideration and integration to the DoD EA; and appoints representatives to the ASBREM COI and any other coordination, oversight, or assessment board established by ASD(R&E) or the DoD EA.

TABLE 1-1: Types of Blast Injuries per DoDD 6025.21E

Injury Type	Mechanism of Injury
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.

- **The JIEDDO** supports 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 PPE and vehicular equipment designed to protect against blast injury; appoints representatives to the ASBREM COI and any other coordination, oversight or assessment board established by ASD(R&E) or the DoD EA; and assists the DoD EA, the ASD(R&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.

DoD Framework for Characterizing Blast Injuries

The term "blast injury," which is not limited to injuries resulting from a primary blast effect, includes the entire spectrum of injuries that can result from exposure to explosive weapons, ranging from non-impact induced mTBI and ear damage, to penetrating wounds, heat and chemical burns, and/or loss of limbs. DoD adopted the *Taxonomy of Injuries from Explosive Devices* as defined in DoDD 6025.21E in order to provide a common framework for characterizing the full spectrum of blast-related injuries; the EA is responsible for coordinating research and development for the entire spectrum. 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 (Table 1-1).

Blast Injury Research Program Areas

The DoD Blast Injury Research Program addresses defined capability requirements and aims to close identified knowledge gaps associated with the prevention, mitigation and treatment of blast injuries. To address the full spectrum of capability requirements and knowledge gaps, current research efforts are

FIGURE 1-3: Blast Injury Research Program Areas

organized along three key research program areas: injury prevention, acute treatment, and reset (Figure 1-3).

Injury Prevention

Injury prevention reduces the risk of blast injuries by providing 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.

Acute Treatment

Acute treatment mitigates injury by providing immediate treatment across the spectrum of blast-related injuries through improved diagnostic tools, health care 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 life.

Coordination of Blast Injury Research Activities

DoD blast injury research efforts are "requirements driven" and designed to fill knowledge gaps in preventing and treating injury as well as restoring function. In order to address the knowledge gaps, researchers work with a multitude of stakeholders who are invested in blast injury research. Examples of research programs and collaborative research efforts supporting blast injury research are described below.

TABLE 1-2: Joint Program Committees

JPC	DHA RDA Directorate Program Areas	Examples of Research Focus Areas
JPC-1	Medical Training and Health Information Sciences	• Electronic Health Records Applications • Surgical Simulation Technology
JPC-2	Military Infectious Diseases	• Wound Infections (Prevention, Management, and Treatment) • Pathogen Detection
JPC-5	MOM	• mTBI • Psychological Health and Resilience • Hearing Loss
JPC-6	CCC	• Damage Control Resuscitation • Moderate, Severe, and Penetrating TBI • Burn Injury
JPC-7	Radiation Health Effects	• Diagnostic Biodosimetry • Countermeasures (Protection and Treatment)
JPC-8	CRM	• Neuromusculoskeletal Injury • Acute and Chronic Pain Management • Regenerative Medicine • Sensory Systems

*Adapted from "Joint Program Committees," no date; and from "Defense Medical Research," 2012, p. 2–7.

DoD Component Services and Agency Research Programs

The Army, Navy, Air Force, and Defense Advanced Research Projects Agency (DARPA) have blast injury research programs that are primarily funded through the President's Budget (PB). These programs sponsor research both internally, within DoD laboratories and clinical centers, and externally, within academia and industry. 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).

Defense Health Agency Research, Development, and Acquisitions Directorate

Established in FY10 by the Office of ASD(HA), the Defense Health Agency Research, Development, and Acquisitions (DHA RDA) Directorate is a core DoD research program that supports medical research and development (R&D) programs with a focus on the needs of our Service Members. Aligned under the Defense Health Agency (DHA), the DHA RDA Directorate manages the research, development, test, and evaluation (RDT&E) funds of the Defense Health Program (DHP). A Joint Program Committee (JPC) consisting of DoD and non-DoD medical and military technical experts manages each of the research programs. These research programs are collaborative efforts that rely on expertise and capabilities from across the Services, Department of Veterans Affairs (VA), US Department of Health and Human Services (HHS), academic centers, industry partners, as well as various other scientific and technical communities. The JPCs provide guidance and funding recommendations for the DHA RDA Directorate research and manage research programs in diverse military medical program areas, including those that directly address blast injuries (e.g., JPC-5, JPC-6, and JPC-8) (Table 1-2).

The current emphasis of the DHA RDA Directorate is on the Secretary of Defense stated priorities of 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 Blast Injury Research Program including MOM, CCC, and CRM.

Congressionally Directed Medical Research Programs

The Congressionally Directed Medical Research Programs (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 among the US Congress, the military, and public in implementing the investment of congressionally directed dollars as well as 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 a number of areas relevant to blast injury and military service, including 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. For a listing of the CDMRP research programs that support blast injury research, please see Appendix D.

Centers of Excellence

In response to congressional requirements within the National Defense Authorization Act (NDAA), the DoD established a number of clinical Centers of Excellence (CoE). These centers seek to improve clinical care capabilities via new and updated clinical practice guidelines (CPG), policy recommendations, understanding injury and outcome trends, and informing 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 including the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury (DCoE), Extremity Trauma and Amputation Center of Excellence (EACE), Pain Center of Excellence, Defense and Veterans Center for Integrative Pain Management, VCE, and Hearing Center of Excellence (HCE).

Research Forums, Consortia, and Programs Supporting Blast Injury Research

In addition to the research programs noted above, there are numerous ongoing collaborative efforts (e.g., working groups, consortia, and research programs) investigating blast injuries and related 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 posttraumatic rehabilitation. For example, the Bridging Advanced Developments for Exceptional Rehabilitation (BADER) Consortium targets orthopedic care after a blast injury. Special areas of interest to the BADER Consortium include improving amputee gait, prosthetic devices, and quality of life issues following extremity injury. For additional examples of collaborative research efforts, please see Table 1-3.

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)	**CENC** is a collaborative effort leveraging collaborations among 18 participating institutions across academia, industry, DoD, and VA. The CENC is dedicated to establishing a comprehensive understanding of the chronic sequelae associated with neurotrauma, primarily focused on mTBI/concussion, and the relationship to neurodegeneration including common co-morbidities such as neurosensory system involvement (vision, balance, hearing, pain) and psychological dysfunction.
Mission Connect	**Mission Connect** is a collaborative neurotrauma research project focused on halting the progression of damage and restoring lost function in patients who have sustained a spinal cord injury, brain injury, or stroke.
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 multidisciplinary and multi-institutional research consortium funded by the DoD to develop and evaluate the most effective 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 co-occurring disorders.
Federal Interagency Traumatic Brain Injury Research Working Group (FITBIR)	**FITBIR** is a partnership between the National Institutes of Health and the DoD with the mission to enhance communication, coordination, and collaboration in the field of TBI across agencies.
TBI Endpoints Development (TED)	**The TED research team** is a unique collaborative partnership involving the DoD, NIH, FDA, industry, and academia to advance clinically validated endpoints which can support regulatory approvals for trials involving the diagnosis and treatment of mild to moderate TBI.
The NCAA-DoD Grand Alliance: Concussion Assessment, Research, and Education (CARE) Consortium	**The CARE Consortium** represents one of the most comprehensive investigations of sports-related concussion ever conducted and will involve symptomology assessments, performance-based testing, psychological health assessments, advanced imaging, and blood/serum/saliva biomarker collection.

*Adapted from DoD Blast Injury Research Program Coordinating Office, 2013, pp. 1-7, 1-9, 1-10, 2-5, 2-6; and "Psychological Health/Traumatic Brain Injury," 2014.

Preview of this Report

The following chapters highlight research efforts aimed at advancing DoD's capability to prevent, mitigate, and treat blast injury. Key initiatives in this report include a summary of the PCO's participation in the NATO Human Factors and Medicine (HFM) Research Task Group (RTG) (Chapter 3), and the PCO's role in the MHS Blast Injury Prevention Standards Recommendation (BIPSR) Process (Chapter 4). Chapters 5–7 present the latest updates on DoD blast injury research with a more detailed discussion of blast-induced Hearing and Balance Disorders (Chapter 5) and a summary of recent advances and new technologies for Hemorrhage Control (Chapter 6). Throughout these chapters, scientific advancements, improvements in standards of care, and the development of products to treat, diagnose, and prevent blast injuries are presented. Finally, the report concludes with a discussion of the way forward for the PCO in coordinating and supporting advancements in blast injury research.

02

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 external to 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 ensure that knowledge gaps are identified and addressed, information is broadly shared, and that duplication of effort is minimized. The PCO promotes collaboration among researchers across federal agencies, academia, and industry to solve complex challenges related to blast injury, taking 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 shape 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 warfighters today and in the future.

Key FY14 PCO Activities in Support of EA Mission Thrust Areas

In response to DoDD 6025.21E, Cdr, USAMEDCOM established the PCO to assist in fulfilling EA responsibilities and functions regarding the coordination of DoD blast injury research efforts and programs. The PCO executes its mission by supporting five key EA Mission Thrust Areas (Figure 2-1). Below are examples of FY14 PCO activities in support of each of the five EA Mission Thrust Areas.

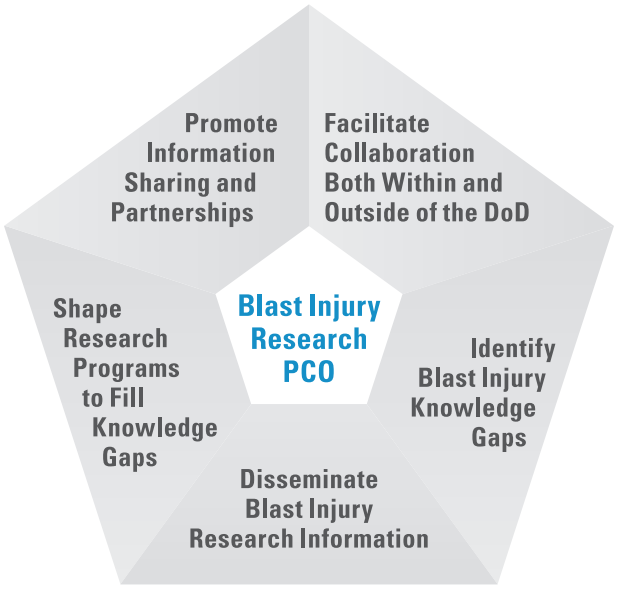
Identify Blast Injury Knowledge Gaps

The identification of blast injury knowledge gaps is critical to understanding the current state-of-the-science, appropriateness of research efforts, and direction of future efforts. In FY14, the PCO undertook several key activities in support of this EA responsibility which included participation in capability based assessments (CBA), the MHS BIPSR Process, and working group participation. Specific examples of PCO activities include, but are not limited to the following:

Medical Research CBA. The PCO participated in an ASD(HA)-sponsored Medical Research CBA to identify and address capability gaps in medical care for Service Members. In November 2013, the PCO advised ASD(HA) on recommended solutions to address operational gaps identified in the Medical Research CBA and improve the joint force's ability to sustain, improve, protect, and conserve the health and resilience of Service Members.

In January 2014, the PCO represented the EA in the subsequent CBA on medical R&D needed to support casualty care from point of injury through acute care, rehabilitation, and chronic care. This working meeting focused on the development of recommended approaches to close gaps identified in previous working meetings. Results from this CBA will be synthesized into an Initial Capabilities Document to the Joint Requirements Oversight Council for review and approval.

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



MHS BIPSR Process. In December 2013, the PCO hosted the second meeting of the BIPSR Lower Extremity (LE) Stakeholder Committee to review stakeholders' needs for specific LE Blast Injury Prevention Standards. The committee identified several specific needs for both mounted and dismounted personnel. The PCO coordinated with the US Army Medical Research Acquisition Activity (USAMRAA) to post a Request for Information (RFI) on LE Blast Injury Prevention Standards to solicit input related to existing or developing human LE blast injury criteria, thresholds, and models for consideration as potential DoD MHS Blast Injury Prevention Standards. The BIPSR LE Stakeholders assessed suitable candidate LE BIPSR standards and identified knowledge gaps associated with the LE injury criteria and testing methodologies currently used by DoD. The stakeholders agreed to convene an independent Subject Matter Expert (SME) panel to review and validate current findings. See Chapter 4 to learn more about the MHS BIPSR Process.

US Army Research Laboratory (USARL). In January 2014, the PCO participated in a workshop organized by the US Army Research Laboratory's (USARL) Weapons Material Research Directorate on Numerical Analysis of Human and Surrogate Response to Accelerative Loading. The workshop focused on available numerical analysis tools to simulate and investigate human and human-surrogate responses to blast events as experienced by vehicle occupants. The objectives of the workshop were to explore the scope of current research activities, document the capabilities of existing tools, extract knowledge and insights, and identify gaps and future needs. The workshop provided a forum for discussing the latest technologies regarding numerical analytic techniques for anthropomorphic test devices (ATD), multi-scale modeling, simulation of human tissue response to simulated blast loading conditions, and methods for analysis of ATD materials undergoing high-rate loading. This workshop was co-sponsored by the Warrior Injury Assessment Manikin (WIAMan) Program Management Office (PMO) and the Blast Protection for Platforms and Personnel Institute.

Disseminate Blast Injury Research Information

Proper dissemination of blast injury research information ensures that all stakeholders along the R&D continuum, from lab to field, are equipped with the most timely and up to date information. Given the complex nature of blast injuries, dissemination of this information must occur through multiple channels including formal reporting mechanisms, direct requests for information to the PCO and leadership, and stakeholder community briefings. Key FY14 examples of PCO activities in support of this EA responsibility are provided below:

Annual Report to the EA. The PCO prepares the annual report to the EA on the science and technology efforts and programs focused on the prevention, mitigation, and treatment of blast injuries. The report summarizes efforts across DoD Blast Injury Research Program, addressing the full spectrum of blast injury challenges and highlighting significant accomplishments.

In addition to informing the EA, this annual compilation of initiatives and accomplishments is a means for sharing blast research-related information. The FY13 Annual Report on Science and Technology Efforts and Programs Relating to the Prevention, Mitigation, and Treatment of Blast Injuries is available on the Blast Injury Research Program website (https://blastinjuryresearch.amedd.army.mil).

Responding to Requests for Information. The PCO plays an important role in connecting individuals and organizations with blast injury resources. For example, responding to a request via the PCO website, the PCO connected a Marine officer in Afghanistan to the Joint Trauma Analysis and Prevention of Injury in Combat (JTAPIC) PMO to obtain the necessary information regarding the reporting requirements for concussion injuries suffered during training. The PCO also coordinated a set of briefings between a Colonel of the Australian Defence Forces Medical Corps and several USAMRMC research components in response to a request for blast injury information related to an ongoing TBI research effort.

Informing Leadership. On behalf of the EA, the PCO briefs DoD leadership on the responsibilities and ongoing activities of the PCO. In October 2013, Mr. Leggieri, PCO Director, briefed the Director, Human Performance, Training, and BioSystems Directorate, Office of the Director, ASD(R&E) on the most recent accomplishments and initiatives of the PCO.

Shape Research Programs to Fill Knowledge Gaps

Blast-related research programs must be properly shaped so that research efforts can address identified knowledge gaps. The PCO helps to shape blast injury research programs by actively participating on research program planning, management, and advisory committees. As an active participant on these committees, the PCO ensures that key blast injury knowledge gaps are addressed, encourages collaborative research efforts, and identifies potentially duplicative research.

In FY14, PCO staff participated as voting members in JPC-2, JPC-5, and JPC-6 meetings, and in Integrating Integrated Product Teams (IIPT) meetings for the USAMRMC's MOM, CCC, and CRM Research Programs.

The PCO participated in other program planning and review activities that support shaping and guiding research programs to resolve identified knowledge gaps. Participation in program review activities included, but was not limited to the following:

CRM and Orthopedics Research Programs Portfolio Review and Analysis Meeting. In November 2013, the PCO participated in the DHP, VA, JPC-6, and JPC-8 CRM and Orthopedics Research Programs Portfolio Review & Analysis Meeting. Stakeholders formulated DHP and VA program sponsor objectives for research in CRM and orthopedics; reviewed and assessed the status of CRM and orthopedics programs; and made recommendations for next steps and program adjustments.

TBI, PTSD and Suicide Prevention Research Portfolios Review and Analysis Meeting. In February 2014, the PCO participated in the TBI, PTSD and Suicide Prevention Research Portfolios Review and Analysis meeting. The meeting included a review of the current status of agencies' research activities in the areas of TBI, PTSD, and suicide prevention; identification of potential research gaps; and identification of activities for meeting National Research Action Plan (NRAP) requirements.

Promote Information Sharing and Partnership

Information sharing and partnership of blast injury research activities is needed to support the advancement of blast injury research. Given the complex nature of blast injury, the PCO participated in numerous activities to promote information sharing and partnerships.

These activities include involvement with strategic planning efforts, invited speaker presentations, and engagement in NATO RTG activities. Highlights for several of these FY14 activities are summarized below:

Audiology and Speech Pathology Center (ASPC). In November 2013, the PCO participated in the Audiology and Speech-Language Pathology meeting hosted by the ASPC. The objective of this meeting was to review current clinical care and clinical research on audiology and speech-language pathology topics. Among these were blast injury topics of interest to the EA, including the physiology underlying blast injuries to the auditory system, as well as assessment and treatment approaches for Wounded Warriors with cognitive-communication impairment as a result of TBI.

DARPA Workshop. In November 2013, the PCO participated in a workshop sponsored by the DARPA Systems-Based Neurotechnology for Emerging Therapies (SUBNETS) program. The objective of the program is to deliver a platform technology for precise therapy in humans living with neuropsychiatric and neurologic disease, particularly Veterans and Service Members suffering from mental health issues. The program combines novel device development, complex computational modeling of behaving human neural systems, clinical neurology, and animal research to advance the understanding and translation of safe and effective neurotechnological therapies.

Allied NeuroSensory Warrior Related Research (ANSW2R). In FY14, the PCO collaborated with HCE and other organizations in the development of a new initiative to facilitate neurosensory polytrauma research among DoD CoEs, federal agencies, international agencies, and select academic institutions. In October, 2013, a strategic kick-off meeting was held to discuss the goals and objectives of this project, specifically the identification of clinical knowledge gaps, areas for collaboration, and the development of a research framework to comprehensively and comparatively examine injury treatment and rehabilitation across affected systems. The PCO continued its collaboration with ANSW2R by participating in three stakeholder meetings. The meetings focused on reviewing the current DoD neurosensory research investment and developing an operating model for ANSW2R based on best practices in government and business. These efforts culminated in an initial draft of the Business Case Analysis report.

Injury Modeling Information Sharing. In February 2014, the PCO hosted the Joint Non-Lethal Weapons Directorate (JNLWD)/ USAMRMC Injury Modeling Information Sharing Meeting. The purpose of this meeting was to identify opportunities for both JNLWD and USAMRMC to share injury and physiological modeling information and expertise, and to collaborate with the Biotechnology High Performance Computing Software Applications Institute to prevent unnecessary duplication of effort.

VA Office of Research and Development. In May 2014, the PCO participated in a DoD/VA-sponsored meeting on "Extremity and TBI Tracking using DoD and VA Databases" at the VA Office of Research and Development. The purpose of this meeting was to explore opportunities for linking relevant injury, treatment, and early clinical information from the DoD Trauma Registry to Veterans' current and long-term health issues, and to discuss current research initiatives on the assessment and long-term effects of TBI. Mr. Leggieri, PCO Director, presented the PCO-sponsored DoD Brain Injury Computational Modeling Expert Panel's efforts to develop a research roadmap to elucidate the underlying mechanisms of primary blast-induced mTBI.

Invited Lecture. In August 2014, Dr. Gupta, PCO Deputy Director, presented an invited keynote lecture titled "Multiscale modeling of blast-induced TBI: From whole body responses to brain microdamage" at the 11th World Congress on Computational Mechanics. The conclusion specified a need to link models of the primary blast event with the resulting brain tissue damage through a concerted collaborative effort between biophysicists, neurobiologists, mathematicians, and experimentalists to advance our current understanding of brain injury mechanisms and help in neurodiagnostics, treatment, and protection.

Personal Armour Systems Symposium 2014 (PASS2014). In September 2014, Mr. Leggieri, PCO Director, co-chaired the session on blast injury prevention at the PASS2014, a venue for international collaboration and information sharing on the development of personal protection systems designed to protect against blast and ballistic injuries. The blast injury prevention session included presentations on the performance of combat helmets in preventing blast-related brain injuries, the behavior of soft tissues under blast strain rates, the prevention of LE injuries from underbody blast, and the proper use of shock tubes in blast injury research.

Facilitate Collaboration Both Within and Outside of the DoD

In support of the EA responsibility to promote collaboration within and outside the DoD, the PCO engaged in various collaborative efforts. The four efforts highlighted below focus on enhancing the DoD's capabilities with respect to computational modeling of blast injury and also demonstrate the PCO's partnering efforts with the international community.

Small Business Innovation Research (SBIR). The PCO actively participated in the launch of new blast injury research projects using the SBIR support mechanism. In February 2014, the PCO initiated kick-off meetings for the "Human Body Model for Computational Assessment of Blast Injury and Protection" SBIR project. The objective of this SBIR Phase I project is to design a modeling framework integrating the anatomical data, geometric modeling tools for human body articulation, blast scene generation, and material property data needed for biodynamic and biomechanical simulations. Additionally, in September 2014, a project submitted by the PCO in response to a SBIR Phase II topic, "Antimicrobials Textiles" was awarded by USAMRAA. The ultimate goal of the project is to identify lightweight, durable, antimicrobial textile finishes that will prevent and/or control infections in military medical shelters and field hospitals, where blast injury infections were frequently encountered during recent military operations.

US India Science and Technology Collaboration. Dr. Gupta, PCO Deputy Director and Senior Science Advisor, participated in the Indo-US Workshop on Cognitive Sciences/Autonomy in September 2014 at the Defence Institute of Physiology and Allied Sciences in New Delhi, India. The meeting was organized by the Under Secretary of Defense for Acquisition, Technology, and Logistics (USD[AT&L]) and the Defence Research and Development Organization (DRDO), Ministry of Defence. The goals of this workshop were to share research ideas and data and identify collaboration opportunities. The US delegation was headed by Dr. Patrick Mason, Director, Human Performance, Training, and BioSystems Directorate, Office of the Assistant Secretary of Defense, Research and Engineering (ASD[R&E]). The outcome of the meeting was a mutually agreed upon list of topics for future collaborations, including a topic on "Experimental and Computational Studies of Blast and Blunt Traumatic Brain Injury."

NATO RTG (HFM-234) on "Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods, and Standards". NATO Technical Activity HFM-234, chaired by Mr. Leggieri, PCO Director, was established to develop 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 the classical toxicology problem wherein clear agreement on dose (blast dose), mechanism of delivery of the dosage, and dose-response endpoints are needed in order to understand the etiology of blast injury. The PCO's participation in NATO HFM-234 promotes information sharing and partnerships among the international blast injury research community. See Chapter 3 to learn more about this effort.

DoD Response to the Institute of Medicine Report

In March 2014, the DoD was invited by the VA to respond to the report "Gulf War and Health, Volume 9: Long-Term Effects of Blast Exposures," prepared by the Institute of Medicine (IOM) on behalf of the VA. The IOM was charged by the VA to conduct a comprehensive review of the medical and scientific literature to identify possible associations between specific long-term health outcomes and exposure to blast. This report represents the IOM's findings and describes the current evidence for the association of blast exposure with long-term health outcomes and the effectiveness of personal protective measures in mitigating blast injuries (https://www.iom.edu/Reports/2014/Gulf-War-and-Health-Volume-9-Long-Term-Effects-of-Blast-Exposures.aspx).

Although only two of the IOM's recommendations were specifically directed at the DoD, many of the conclusions and recommendations contained within the IOM report apply to the DoD, including development of CPGs; establishment of a blast injury literature clearinghouse; development of studies to identify blast injury biomarkers; effectiveness of PPE in mitigating primary, secondary, and tertiary blast injuries; and dissemination of knowledge through DoD sponsored State-of-the-Science (SoS) Meetings.

The PCO, on behalf of the EA, formulated a response to 27 of the IOM human health outcomes conclusions and 12 committee recommendations for future research. The PCO's responses were based on input from medical and non-medical organizations across the DoD to ensure a fully coordinated and representative DoD response. The responses addressed the level of scientific evidence cited for several health outcome conclusions based upon information from ongoing and/or completed DoD research efforts. The DoD response also included a brief overview of the DoD medical R&D infrastructure.

The PCO also responded to the IOM committee's recommendations for future research. These recommended research areas focus on efforts to improve our understanding of blast trauma and susceptibility to blast injury; support the development of screening tests for blast exposure; and increase the dissemination of knowledge from blast research to the members of the blast injury medical and scientific communities.

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

The PCO planned and organized the 2014 International SoS Meeting on the Biomedical Basis for mTBI Environmental Sensor Threshold Values. The meeting was designed to identify the challenges associated with correlating environmental sensor threshold values to injury outcomes and to develop recommendations for addressing knowledge gaps identified during the meeting.

A Planning Committee was established with representatives from across the stakeholder community including the ASD(R&E), ASD(HA), DARPA, Defense and Veterans Brain Injury Center (DVBIC), the National Institute of Neurological Disorders and Stroke (NINDS), WRNNMC, USAMRMC, Office of Naval Research (ONR), Air Force Office of Scientific Research, National Football League (NFL), and the National Collegiate Athletic Association (NCAA). The Planning Committee then identified six subject matter experts to serve as the Expert Panel.

The PCO conducted an extensive literature review on the biomedical basis of mTBI environmental sensor threshold values in order to inform meeting participants on the state-of-the-science. The literature review was provided to attendees as reference material in advance of the meeting. The review described six relevant areas of research including: mTBI, computational modeling of TBI, environmental sensors, evaluation of environmental sensors validation of blast environmental threshold values, and the correlation of blast environmental threshold values to injury.

The SoS Meeting on the "Biomedical Basis for Mild Traumatic Brain Injury (mTBI) Environmental Sensor Threshold Values" was held on 4–6 November 2014 in McLean, VA. The meeting proceedings titled "Biomedical Basis for Mild Traumatic Brain Injury (mTBI) Environmental Sensor Threshold Values" were published on the PCO website (https://blastinjuryresearch.amedd.army.mil/). Leveraging the literature review, meeting presentations, and working group sessions, the Expert Panel came to the following conclusions: (1) biomedically valid sensor threshold values do not yet exist for blast-induced mTBI; (2) the lack of coordination of sensor activities and gaps in information sharing have led to the fielding of sensors without valid thresholds or a clearly-defined purpose; and (3) there is no central authority for coordinating sensor activities or validating thresholds. The Expert Panel recommended the scientific community immediately establish a fully-funded and authoritative task force to facilitate the development of environmental sensor specifications that will ultimately correlate sensor data to medical outcomes. A more detailed report on the meeting and its conclusions will be presented in the FY15 Report to the EA.

JTAPIC Program

The JTAPIC Program was established at 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 JTAPIC 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-related injuries.

The JTAPIC PMO originally resided within the PCO, and has since matured into a program of record. In March 2013, the official JTAPIC Charter was signed, thus establishing the JTAPIC Program as an enduring program separate from the PCO. The JTAPIC PMO is located at Fort Detrick, MD, with partners throughout the US (Table 2-1). The JTAPIC Program 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.

TABLE 2-1: JTAPIC Program Partners

Intelligence and Operational Partners
National Ground Intelligence Center
Combat Incident Analysis Division
Dismounted Incident Analysis Team
US Marine Corps Current Operations Analysis Support Team
Marine Corps Intelligence Activity
US Army Aeromedical Research Laboratory (USAARL)
Medical Partners
Armed Forces Medical Examiner System
Joint Trauma System
Naval Health Research Center (NHRC)
Materiel/Acquisition Partners
Project Manager, Soldier Protection Individual Equipment (PM SPIE)
Product Manager, Infantry Combat Equipment (PdM ICE "US Marines")
USARL

Way Forward

The Cdr, USAMEDCOM established the PCO to coordinate research efforts on behalf of the EA in order to advance medical solutions associated with blast injuries. In support of the EA's five mission thrust areas, the PCO identified the following key objectives for FY15:

- **Establish the DoD Blast Injury Research Coordinating Board:** This board of representatives from DoD stakeholder organizations, chaired by the Director of the PCO on behalf of the EA, will identify blast injury research needs and foster information sharing and collaboration
- **Data Sharing Project:** The PCO is overseeing an effort to capture and make available data and information from 50 years of blast injury research conducted at the Albuquerque Blast Test Site, and provide a mechanism for sharing data from current and future DoD-sponsored blast injury research.
- **MHS BIPSR Process:** In FY15, the PCO will complete the BIPSR Process for LE injury and initiate reviews for spine/back injury and auditory injury.
- **NATO HFM-234 RTG, Environmental Toxicology of Blast Injury:** The nine-nation HFM-234 RTG will complete the first of several planned products. This product, "Guidelines for Conducting Epidemiological Studies of Blast Injuries," is discussed in further detail in Chapter 3.

In addition to these objectives, plans are underway for the 2015 SoS Meeting, publication of review articles and meeting proceedings, and an increase in international collaborations. The PCO will continue to provide critical information on knowledge gaps in blast injury research derived from the vast collaborations with scientists, clinicians, and engineers from across the blast injury research community.

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-related 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. In 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 RTG or research symposiums (RSY). The mission of the HFM panels is to provide the scientific and technical basis for optimizing health, safety, protection, wellbeing, and performance of the human in operational environments with consideration of affordability.

The PCO supported collaborations between the US and NATO member nations across several HFM RTG activities conducted between April 2008 and January 2013 (see call out box). The purpose of the previous HFM RTG and symposium activities 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 the original HFM activities serve as the foundation for current NATO efforts.

PREVIOUS NATO HFM RTGS RELATED TO BLAST INJURY

- HFM-175: Medically Unexplained Physical Symptoms in Military Health (April 2008–April 2012)
- HFM-193: Mild Traumatic Brain Injury in a Military Operational Setting (November 2009–January 2013)
- HFM-198: Injury Assessment Methods for Vehicle Active and Passive Protection Systems (January 2010–January 2013)
- HFM-207 Symposium: A Survey of Blast Injury across the Full Landscape of Military Science (October 2011)

The present chapter describes 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*. Mr. Leggieri, PCO Director, co-chaired the prior HFM-207 RSY. The Technical Evaluation Report generated from the HFM-207 RSY detailed the recommendations including: (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 to advance translational research. In response to the recommendations of the HFM-207 research symposium, a TAP on 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 Mr. Leggieri, PCO Director, as the Chair. The activities of HFM-234 RTG are ongoing and described in more detail in the following sections.

FIGURE 3-1: HFM-234 RTG Participating Nations

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

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 symposium highlighted the analogous relationship between blast injury research and classical toxicology problems in that both require understanding dose, mechanism of dose delivery, and dose-dependent endpoint. With this analogy in mind, the HFM-234 RTG's purpose is to close identified knowledge gaps by creating a systematic approach to better understand blast injuries. The HRM-234 RTG is focused on standardizing animal models of blast injury, common dose-response methods, route of exposure methods, computational models, dose regimens to human medical endpoints, and methods for translating basic research to medical products and/or improved PPE for Service Members.

The RTG is composed of 17 members from nine NATO nations (Figure 3-1). Through a series of meetings, the RTG convenes to identify gaps in research regarding the environmental toxicology of blast exposure and discusses opportunities and methods to strategically address these gaps.

HFM-234 RTG Meeting 1

In July 2013, the HFM-234 RTG kick-off meeting was held in Paris, France. Twelve RTG members representing nine NATO nations participated. The kick-off meeting reviewed the TAP objectives (Table 3-1), presented the guidelines for the upcoming three years of work, and established a program of work for the RTG (Table 3-2).

The RTG established a regular schedule of meetings during its term, each to be held in a different NATO member nation. Each meeting will examine the status of blast injury toxicology science and technology, with a specific focus as reflected in the program of work. 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, as appropriate.

Comprehensive Dictionary of Blast Injury Research Terms Update

Following the first HFM-234 RTG kick-off meeting, participants recognized that establishing reporting standards for collaborative blast injury research requires a common dictionary of terms and associated meanings. The Virtual-Core working group was assigned to collect terms and distribute the dictionary, with follow-on updates as needed until complete. 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 and will be updated after each HFM-234 RTG meeting. The goal is to complete a Comprehensive Dictionary of Blast Injury Research Terms by the end of the HFM-234 RTG's term in July 2016. The completion of the dictionary of terms will be the first-ever standardized language guidelines to help those invested in blast injury research improve information exchange and ultimately, form stronger collaborative research endeavors.

TABLE 3-1: Technical Activity Proposal Objectives

Objectives
The 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 warfighters 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 blast injury epidemiological studies to establish common data elements and enable cross-study comparison; • Guidelines for reproducing blast exposure conditions in the laboratory to ensure relevant exposures and enable cross-study comparison; • Guidelines for standardized blast injury animal models and a roadmap for the development of dose-dependent injury curves that will accelerate the development of valid human blast injury prediction tools.

HFM-234 RTG Meeting 2

In December 2013, the PCO hosted the second HFM-234 RTG meeting at Fort Detrick, MD. Ten RTG members representing seven NATO nations participated. The RTG meeting focused on developing Blast Injury Epidemiological Study Guidelines.

TABLE 3-2: HFM-234 Program of Work Activities

Activity Workshop	Month/Year	Purpose	Host/Location
Meeting 1	1–2 Jul 2013	HFM-234 RTG Kick-off	STO/CSO (Paris)
Comprehensive Dictionary of Blast Injury Research Terms	Ongoing	Develop a dictionary of commonly used terms with definitions (Virtual-Core working group to develop an initial list and distribute to RTG members)	Canada (Virtual)
Meeting 2	10–12 Dec 2013	Develop recommendations for collecting data necessary for conducting epidemiological studies	USA (Frederick, Fort Detrick, MD)
Meeting 3	21–23 May 2014	Develop guidelines to reproduce blast exposure conditions in the laboratory	Canada (Medicine Hat)
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)

To date, there are limited complete data sets and epidemiological guidelines for understanding the complex and multi-system injuries arising from blast exposure and data collection, and elements are not standardized. To address these issues, the discussions focused on four topics: (1) definition of parameters of interest for tracking initial blast exposure; (2) identification of types of data needed to link blast exposure to biological outcomes; (3) use of sensors; and (4) optimization of existing operational trauma databases for blast injury epidemiological studies.

The group identified three broad categories of parameters for characterizing blast exposure: characterizing the threat, capturing information related to the individual affected by the threat, and capturing scenarios and measurements related to the threat. Identifying the parameters of interest was the first step in establishing and building consensus on the type of data needed to accurately detect blast exposure and potentially predict a biological outcome. Table 3-3 provides a description of the key parameters of interest.

To understand the biological response to a blast event and its long-term effects, the RTG determined eight types of data required to link exposure with a biological outcome, and whether the categories represent data that are intrinsically dynamic or static. Dynamic data typically refer to an individual's response to an event, whereas static data refer to an individual's medical or work history. Dynamic and static data must be captured so that a link to a clinically relevant outcome is possible. The eight identified data types are summarized in Table 3-4.

The need for sensors to understand the actual exposure and the subsequent response of an individual linked to a blast event was evaluated. Table 3-5 summarizes the types of data that sensors can provide. For each parameter of interest, it is imperative to identify what the sensors are measuring and what the measurement means to the individual who experienced the blast event. Sensor measures need to be established and the interpretation of their output understood in order to be able to improve evaluations of Service Members blast exposure risk.

Recommendations for optimizing existing trauma databases for blast injury epidemiological studies were created (Table 3-6). Currently, there is a lack of necessary data in existing trauma registries, which limits the type of retrospective studies that can be performed. Meeting discussions addressed how to share information between nations given the differences in database structure and governmental regulations to which these databases are subjected. Optimizing information sharing between nations would enhance collaboration and accelerate research progress by allowing integration, reanalysis, and comparison of data between nations.

The product of this meeting was a draft comprehensive guidance document with the following key elements: (1) study design consideration and key elements; (2) recommendations for the data to be collected and sample data collection sheets; (3) blast injury data management recommendations, including optimization of databases and data sharing considerations. The importance of appropriate data collection and management in multi-site epidemiological studies cannot be over emphasized. Standardized data collection, coding, and management will facilitate advancement of blast injury research efforts and encourage greater collaboration between clinical studies. The Blast Injury Epidemiological Study Guidelines are being finalized and once completed, will be published as an official NATO document in FY15.

TABLE 3-3: Parameters of Interest to Track Initial Exposure to Blast

Category	Parameter
Threat	Characterize the threat in terms of its family (e.g., type of IED, mine, etc.), charge estimate, type of explosive (pure charge versus mixture of components), road and soil conditions, apparent crater dimensions, detonation method, etc.
	Characterize the threat environment (e.g., altitude, open air, explosion within or behind structures, ambient temperature, etc.).
	Estimate (measure) the distance between the warfighter and the threat as well as the body orientation.
Individual	Determine key demographics of individual (e.g., ID, sex, age, weight, relevant medical history (e.g., previous injuries), personality traits, Service (Army, Air Force, Marines, Navy, etc.), artillery or infantry or occupation).
	Determine body posture and extent of body exposure to threat.
	Determine type of PPE issued, items of PPE worn as well as their size (form and function).
	Assess for the presence of blunt impact and acceleration/deceleration, including linear and angular acceleration/deceleration of the entire body or body part, and contact pressure.
	Identify all types of injuries, medical conditions and relevant physiological status (e.g. dehydration, fatigue/exhaustion, etc.), and their effects on the body (including clinical, paraclinical, and biological). An indication of the injury data collection timeline must also be provided.
Scenario	Nature of operational context (operational, training, or other).
	Estimate body posture and extent of body exposure to threat.
	Identify vehicle crew seating positions and order of march for dismounted troops.
	Define the event timeline and location.
Measurements	Identify the sensor system used (e.g., the specifications and capabilities of the sensor).
	Describe the configuration of the suite of multiple sensors used (e.g., location and orientation of sensors with respect to a body coordinate system: aligned along 360 degrees).
	Determine relationship of pressure sensor to exposure source (distance is directly related to amplitude).
	Characterize the side on (static) and face on pressures (amplitude and duration) of the blast.

TABLE 3-4: Data Needed to Link Biological Outcome to Blast Exposure

Data	Type
Environment	Dynamic
Threat	Dynamic
Stressors (environmental, operational, psychosocial)	Dynamic
Medical data (static and dynamic) • Link medical data with incident data (includes data from trauma registries, medical records, and other sources) • Data collected at event	Static and dynamic
Psychosocial factors	Static
Personality traits of the individual	Static
Training and job history of the individual	Static
Identification of the cause of injury	N/A

TABLE 3-5: Parameters of Interest Related to the Use of Sensors in Blast Studies

Parameters of Interest
Sensors are needed to understand the real exposure
Types of data needed from sensors: • Physiological status of individual • Exposure level to stressors • Exposure level to threat
Sensors are crucial to being able to understand the response of an individual to a blast event
Sensors are not limited to the effects of blast exposure, but encompass thermal and other environmental stressors
Identification of the cause of injury

TABLE 3-6: Recommendations for Optimizing Existing Databases for Blast Injury Epidemiological Studies

Recommendations
Accurately reflect blast injuries in existing coding systems and databases • Include data from sensors • Include code for cause of injury or the threat (need mechanism of injury) • Include detailed wound mapping (e.g., entry and exit data, trajectory)
Share the lessons learned in designing the databases
Establish a NATO-level process for analyzing and sharing blast injury data that includes medical, intelligence, and operational information. Examples include the JTAPIC Program (US), CAPSAC (Canada), and Casualty Analysis (UK)
Maintain and continue to invest in all existing databases and data analysis processes
Expand existing databases to include information about injuries from occupational exposures to blast, including physical and mental health impairments

HFM-234 RTG Meeting 3

In May 2014, the third HFM-234 RTG meeting was hosted by the Defence Research and Development Canada (DRDC) in Ralston, Alberta. Eleven RTG members representing seven NATO nations participated. The objective of this meeting was to develop guidelines for reproducing blast exposure conditions in the laboratory.

Presentations from RTG members and invited speakers described laboratory practices for generating blast exposures. Speakers discussed a variety of laboratory approaches for blast wave simulation including free field, small shock tube, and large shock tube experiments. Presenters highlighted the importance of parameters such as loading, pressure, and reproducibility of exposure conditions, and noted the importance of distinguishing between static and dynamic pressures as well as total and reflected pressure.

Following the presentations, the development of guidelines for reproducing blast exposure in the laboratory was discussed and the following key elements were agreed upon for inclusion: (1) research rationale, (2) blast exposure methodology; and (3) target exposure characterization. The need for laboratory guidelines also highlighted the importance of establishing a 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, these guidelines will hopefully eliminate the variance in reported blast exposure information in the literature, standardize experimental methodologies, and provide guidance on documenting experimental conditions to enhance the reproducibility of the research.

HFM-234 RTG Meeting 4

Planning for HFM-234 meeting 4 was also completed in FY14. This meeting was held in Tallinn, Estonia in October 2015. The purpose of this meeting was to discuss computational modeling and review the Comprehensive Dictionary of Blast Injury Research Terms. A detailed description of the key activities and outcomes of this meeting will be included in the FY15 Report to the EA.

KEY ACCOMPLISHMENTS

HFM-234 RTG meeting series initiated and/or developed the following:

- Comprehensive Dictionary of Blast Injury Research Terms
- Blast Injury Epidemiological Study Guidelines
- Guidelines for reproducing blast exposure in the laboratory and recording key study characteristics in blast injury research
- Parameters of interest related to the use of sensors in blast studies

Way Forward

Advancements in blast injury treatment and care for Service Members require close collaboration between researchers, clinicians, engineers, and other stakeholders across countries. To date, there remains a lack of collaboration between those invested in blast injury research resulting in a lack of standardization in how data is collected and coded, which limits comparisons between studies. In addition, the scientific and technology community has a limited understanding of environmental sensor thresholds that can measure blast exposure and predict the subsequent biological response and damage in an individual. This gap in knowledge is further perpetuated by the lack of an animal model to successfully reproduce the complete spectrum of pathological changes observed after blast injury.

The tools being developed by the HFM-234 RTG meeting series (see key accomplishment box above) promote standardized study and data collection methodologies needed to move the field forward. A big step towards this goal is the development of the Blast Injury Epidemiological Study Guidelines, which will be published as an official NATO document in FY15 for use by the international blast injury research community. The Comprehensive Dictionary of Blast Injury Research Terms is planned to be completed by the end of the HFM-234 RTG in July 2016.

As a part of the continuing NATO effort, the HFM-234 RTG is currently developing guidelines for reproducing blast exposures in the laboratory, documenting key study characteristics in blast injury research, and identifying parameters of interest. The final HFM-234 RTG meeting will develop recommendations for standardized animal models necessary for validating computational models of blast injury; the meeting will also develop a roadmap for establishing dose-dependent curves. Dissemination of these guidelines via the NATO Science and Technology Organization and publication in peer reviewed journals will promote effective collaboration among research groups and enable valuable cross-study comparisons needed to catalyze technical advances to respond to blast injury needs and requirements.

CHAPTER 4:

MHS BLAST INJURY PREVENTION STANDARDS RECOMMENDATION PROCESS

DoDD 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 ASD(HA)." Designed to address this requirement, the MHS 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 T&E, MATDEV, 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 MHS 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 MHS 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.

The PCO obtained the support of the Johns Hopkins University Applied Physics Laboratory (JHU/APL), a University Affiliated Research Center and DoD trusted agent, to develop and implement the MHS BIPSR Process. The process was implemented through a series of stakeholder meetings that began in 2012. At that time, the PCO introduced the stakeholder communities to the MHS BIPSR Process approved by the ASBREM Committee.

The following sections of this chapter describe the activities and achievements of the MHS BIPSR Process for FY14, including the prioritization of blast injury types, assessment of the LE Blast Injury Type, and enhancements to the overall process.

FIGURE 4-1: MHS Blast Injury Prevention Standards Framework

MHS BIPSR Blast Injury Type Prioritization

The JHU/APL developed a methodology to establish a priority ranking across blast injury types as defined by consensus among BIPSR stakeholders. Shifting from an older classification of injury types that referred to individual organs and bones (as described in a 1989 Walter Reed Army Institute of Research [WRAIR] report[7]), BIPSR stakeholders classified blast injury types based on specific body regions that included a total of seven key body regions and a total of 14 blast injury types (Figure 4-2).

The Blast Injury Prioritization Methodology assessed the blast injury types against six Evaluation Factors defined in Table 4-1. These evaluation factors were developed and weighted on the basis of BIPSR stakeholder input. Subsequently, a Decision Support Analysis Tool (DSAT), a mathematical technique based on the principles of maximum information entropy, was applied to minimize unintended bias and to determine the final priority score for each Blast Injury Type based upon the Evaluation Factors and associated scores.

The initial implementation of the prioritization methodology in FY13 focused on the seven most prevalent blast injury types: mTBI, moderate to severe TBI, auditory, abdomen, cervical spine, LE, and upper extremity. Through this initial prioritization effort, the LE injury type was identified as the highest priority blast injury type to be evaluated using the MHS BIPSR Process.

As the MHS BIPSR Process for LE was initiated, a second iteration of the Blast Injury Prioritization Methodology was implemented in FY14 in order to complete the prioritization across all 14 Stakeholder-defined Blast Injury Types (Appendix E, Figure E-1). The LE Blast Injury Type remained the highest priority injury type at the conclusion of the second prioritization effort. The resulting prioritized ranking suggested the order in which the remaining 13 Blast Injury Types should be evaluated using the MHS BIPSR Process.

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

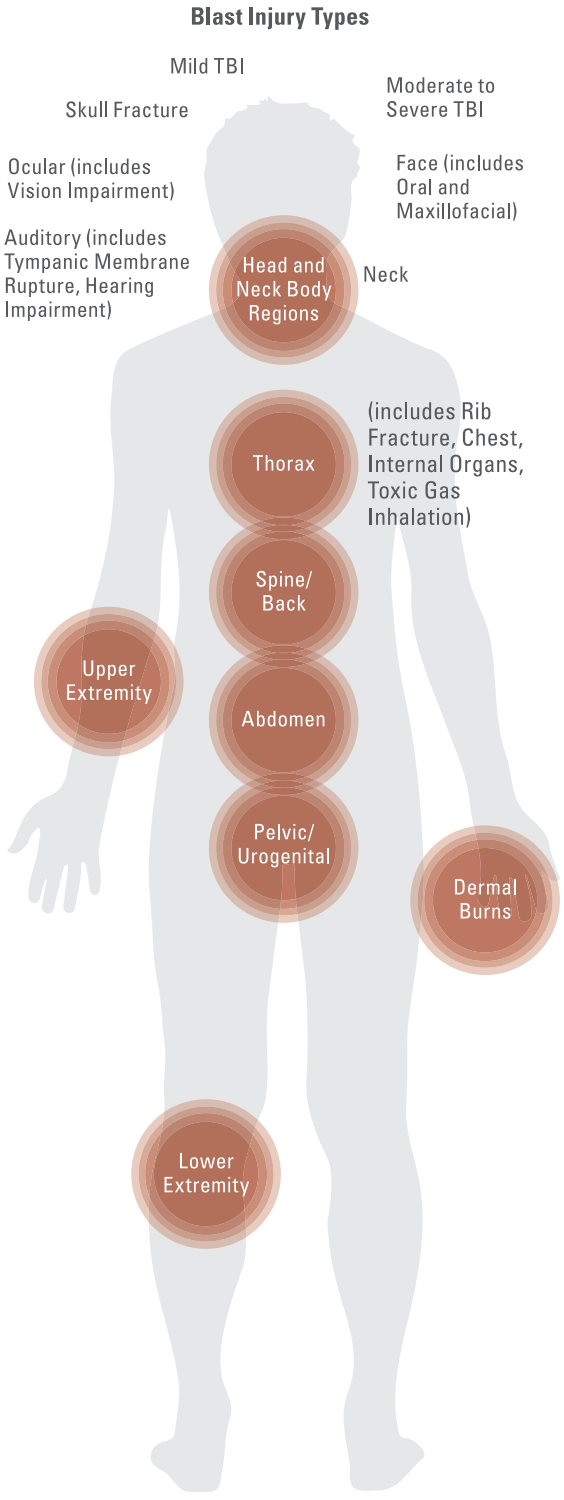


TABLE 4-1: Blast Injury Prioritization Evaluation Factors

Evaluation Factors	Description
Impact on Operational Readiness	The time for a Service Member to return to duty.
Blast Injury Prevalence Rate	The number of cases of a given Blast Injury Type expressed as a percentage of the total number of blast injuries.
Treatment Resources	Roles of medical treatment, which are the distribution of medical resources and capabilities to provide Service Member's medical care.
Maturity of the Science	Determined by the existence of established standards (e.g., MIL-STD-1474D Noise limits design criteria) or, in the absence of established standards, by the degree to which biomedically-valid injury mechanisms have been published in the peer-reviewed scientific literature, or by the development and application of assessment methodologies based on the established injury mechanisms to assess injury risks.
Rehabilitation Resources	Resources required to support a Service Member's rehabilitation beyond immediate treatment resources and may include therapy, pharmaceuticals, or devices needed to reset for quality of life
Disability Percentage	Designated percentage assigned to an injury type when calculating disability benefits.

Implementation of the MHS BIPSR Process for the LE Blast Injury Type

In order to initiate the MHS BIPSR Process for the LE Blast Injury Type, a LE-Focused Stakeholder Committee was established in June 2013. The committee included over twenty individuals from the T&E, MATDEV, medical, and operational communities representing the DoD, other federal organizations, academia, and industry. The LE Stakeholders collaborated to evaluate the state of LE Blast Injury Prevention Standards over the course of three meetings held in July 2013, December 2013, and July 2014.

July 2013 LE Stakeholder Meeting

The first MHS BIPSR LE-Focused Stakeholder Committee Meeting was held on July 22, 2013 during which the MHS BIPSR Process was introduced to the LE Stakeholders. The LE Stakeholders discussed the variations of LE blast injuries, defined the requirements for LE Blast Injury Prevention Standards, and provided insight on how these standards would be applied. Meeting participants could not identify formally codified LE standards, but made recommendations for key terms, phrases, and references for a literature review to find either established or candidate standards.

The LE-Focused Stakeholder Committee also agreed with the recommendation that one-on-one interviews with key LE Stakeholders, especially those not present at the meeting, be conducted to refine candidate LE Blast Injury Standard requirements, needs, intended uses, and literature search key words.
Following the meeting, 10 one-on-one interviews were conducted with individuals from the T&E, MATDEV, medical, and operational communities to refine the set of blast injury prevention standards needs and requirements. Through these interviews, the PCO was able to develop a comprehensive set of LE Blast Injury Prevention Standards needs and requirements, as well as a focused agenda for follow-on discovery tasks. These tasks include a review of the literature and the development of an RFI to solicit existing methods and tools, knowledge gaps, and other related R&D initiatives.

December 2013 LE Stakeholder Meeting

The second MHS BIPSR LE-Focused Stakeholder Committee Meeting, held in December 2013, focused around a discussion of LE Blast Injury Prevention Standards needs and requirements identified through one-on-one interviews.

The expanded set of needs and requirements were vetted and approved by the LE Stakeholder Committee. To extend the identification of candidate methods and techniques that could potentially serve as LE Blast Injury Preventions Standards, the Committee finalized the literature review approach and recommended the release of an RFI.

July 2014 LE Stakeholder Meeting

The third MHS BIPSR LE-Focused Stakeholder Committee Meeting was held on July 29, 2014. At the request of the LE Stakeholders, meeting participants were provided with an overview of the WIAMan Project which highlighted the project's focus on under-body blast (UBB) injuries to mounted Service Members in a seated position, and how results of the WIAMan project would inform aspects of the MHS BIPSR Process. During the meeting, the LE Stakeholders agreed that the WIAMan and MHS BIPSR projects were unique and identified ways that the results from the WIAMan could be leveraged to inform and advance the MHS BIPSR Process.

The results of the LE Blast Injury Prevention Standards literature review and RFI were also presented at the July 2014 meeting. The literature review and RFI identified no existing validated LE Blast Injury Prevention Standards. Published methodologies and criteria being used in lieu of standards were identified and their associated gaps and limitations were identified to inform potential LE standard development efforts. While the LE Stakeholders recognized these gaps and limitations, they continued to express a strong desire for LE Blast Injury Prevention Standards that ASD(HA) could approve. The LE Stakeholders also recommended that an LE SME Panel be established to review and verify the findings of the literature review and RFIs, as well as to identify any emergent research that could address shortcomings of existing methodologies. LE SME Panel members were identified based upon LE Stakeholder nominations and experts identified through the literature review. The LE SME Panel was a broad-based, non-advocacy panel whose members were drawn from industry, academia, and government. The SMEs were selected based upon LE Stakeholder nomination and relevant experience with the LE physiological and biomedical injury and performance responses associated with LE blast injury (e.g., dose-response curve, injury thresholds).

LE SME Panel Outcomes

The LE SME Panel critically evaluated the findings from the MHS BIPSR Process for the LE Blast Injury Type during the September 2014 meeting. The SME panel agreed that no codified LE Blast Injury Prevention Standards existed and acknowledged that the outcome of the WIAMan Project may address many of the needs and requirements for seated, mounted Soldiers subjected to vertical acceleration forces from underbody blast. Additionally, the LE SME Panel evaluated the methodologies and criteria identified as being used by organizations in the absence of ASD(HA)-approved standards. The SME panel evaluated the methodologies and criteria against the stakeholder needs and requirements to determine existing limitations and knowledge gaps to be addressed by future research activities. The identified limitations and knowledge gaps include the need for the following:

- More inclusive populations (e.g., both male and female specimens, greater age range) and larger sample size
- The use of test methods that replicate both blast rate loading and duration
- Incorporation of standing subjects with effective human weights for modeling dismounted Service Members

- Establishment of consensus-based blast injury thresholds
- Additional studies of soft tissue injuries, especially those that develop novel methods of modeling soft tissue injuries; soft tissue injuries may be better predictors of long-term outcome than bone fracture
- Experimentally validated LE Finite Element Models capable of accurately predicting the fracture patterns and locations, as well as the injury loads, at blast loading rates.

The next steps in the MHS BIPSR Process for LE are to report the SME Panel conclusions to the LE-Focused Stakeholder Committee and to finalize documentation of the LE BIPSR process findings.

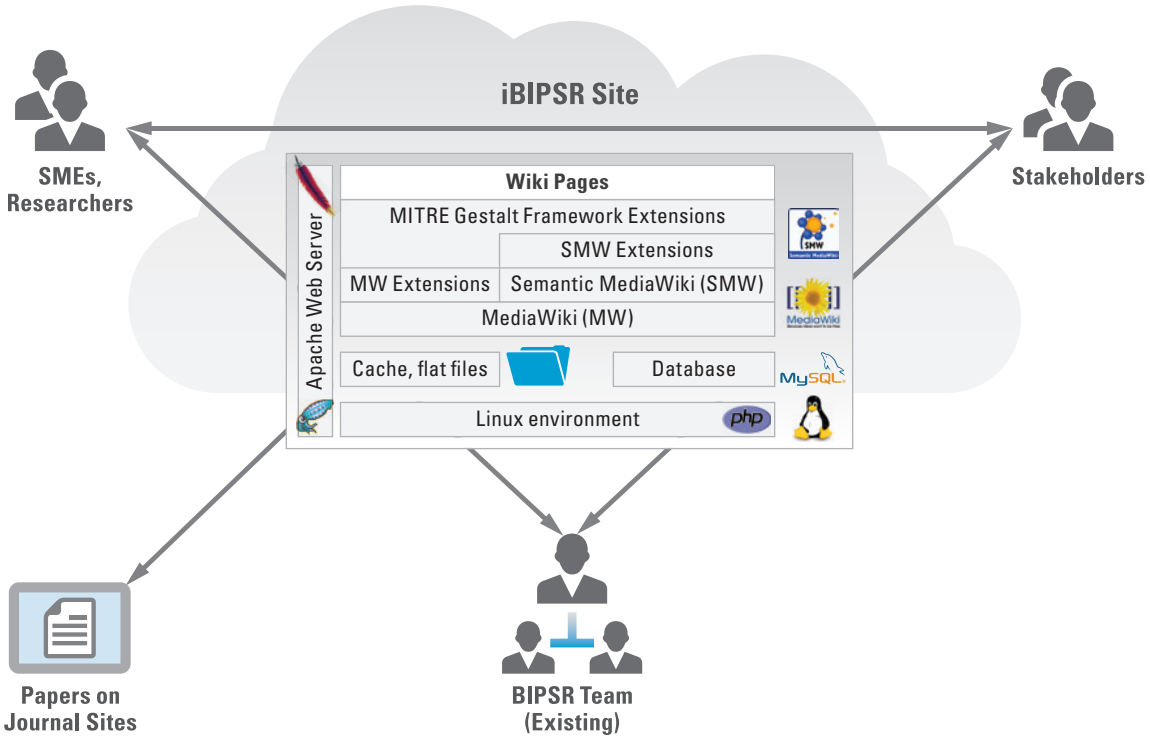
BIPSR Process Enhancement

The PCO collaborated with the MITRE Corporation, a not-for-profit organization that operates Federally Funded Research and Development Centers in the public interest, to initiate activities in FY14 to enhance the efficiency of the MHS BIPSR process without sacrificing the decision quality. These activities included streamlining the process based upon a business process review and analysis and the development of a new web-based collaboration environment known as Interactive Blast Injury Prevention Standards Recommendation (iBIPSR).

MHS BIPSR Process Revisions

Revisions to the MHS BIPSR Process began with an assessment of the process against the Business Process Modeling Notation (BPMN) standard. This standardized business process modeling methodology was used to graphically represent MHS BIPSR activities and facilitate quantitative and qualitative analysis of the overall process. Using the BPMN model, which was validated against the actual timeline for the LE BIPSR Process, the original MHS BIPSR Process was evaluated for opportunities to enhance efficiency without sacrificing decision quality.

FIGURE 4-3: Community Use of iBIPSR Site



KEY ACCOMPLISHMENTS

- Developed stakeholder-engaged methodology to identify, assess, and validate blast injury prevention standards for adoption by the community at large
- Completed prioritization methodology for all MHS BIPSR blast injury types
- Obtained lessons learned from the MHS BIPSR Process implementation of the LE Blast Injury Type; includes impacts of end-to-end stakeholder engagement; role of the WIAMan project in filling specific knowledge gaps pertaining to underbody blast; and understanding of knowledge gaps to inform the development of standards
- Streamlined MHS BIPSR process by reducing the estimated time for completion of reviews for all injury types to five years
- Initiated the development of community-sourced site, iBIPSR, to support sharing of blast injury knowledge; site facilitates contributions, and strengthens relationships across the blast injury research community

A key change in the revised MHS BIPSR Process was reordering the sequence of activities to review the research landscape and existing capabilities prior to defining stakeholder requirements. Defining the research landscape earlier in the process ensured a common context and terminology set were 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 added to the MHS 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. In total, the process revisions to the MHS BIPSR Process are projected to reduce the time per injury type to nine months and to enable completion of all injury types by 2024. This timeline is further accelerated through the implementation of the iBIPSR, described below.

iBIPSR Capability

In a continuing effort to improve the revised BIPSR Process efficiency and reduce timelines, development of the iBIPSR capability, a web-based collaboration environment, was initiated in FY14. The iBIPSR capability is being built on a collaborative semantic web technology; an information synthesis technology that is well-suited to large collaborative multi-user information sharing and decision making efforts such as the MHS BIPSR Process (see Appendix E, Figure E-2 for more information). The iBIPSR interactive community-sourced capability 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.

As shown in Figure 4-3, iBIPSR supports a variety of users that includes stakeholders, SMEs, and researchers and offers transparency into the MHS BIPSR Process. For example, the iBIPSR site captures and maintains stakeholder requirements and facilitates community understanding of the requirements. iBIPSR also supports interactive collaboration between stakeholders and SMEs, enabling greater community contributions to the identification of knowledge gaps and the development of standards recommendations. iBIPSR enables individuals in the larger Blast Injury Research community to engage, connect, and build relationships across the community. This level of information sharing and collaboration accelerates the growth and development of the MHS BIPSR community knowledge base, which facilitates a high-quality decision process. The application of the iBIPSR could potentially be extended to support other areas of blast injury research.

Power of iBIPSR

The development of the iBIPSR interactive community-sourced capability represents a novel way to reduce the timeline of the MHS BIPSR Process without sacrificing decision quality (Table 4-2). It is anticipated that iBIPSR will expedite decisions by supporting continuous engagement and collaboration among SMEs, stakeholders, and researchers

and by supporting the simultaneous execution of the revised MHS BIPSR Process for three different injury types. The iBIPSR capability is expected to enable the PCO to complete decisions on all injury types by the end of 2019; which is 15 years earlier than the estimated completion of the initial MHS BIPSR Process (Figure 4-4).

Way Forward

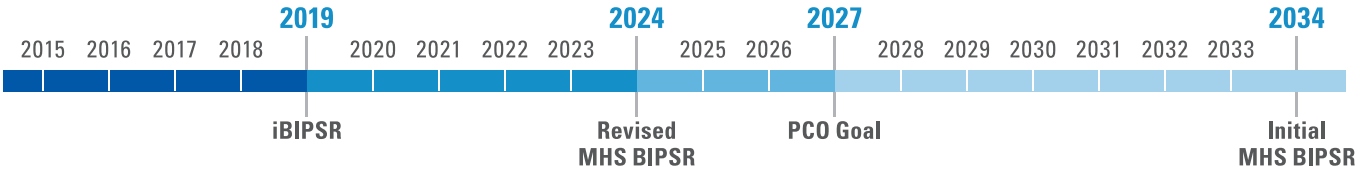
In the coming year, the PCO will focus on finalizing the recommendations from the MHS BIPSR Process for the LE injury type and piloting the revised MHS BIPSR Process and iBIPSR capabilities for additional blast injury types. Gaps in the science identified by the MHS BIPSR Process for LE will be shared with the medical research community to inform the development of future LE Blast Injury Prevention Standards. The revised MHS BIPSR Process, which is projected to take only nine month per Blast Injury Type, will be initiated and tested in FY15 for spine/back and upper extremity injury types. The iBIPSR-supported revised MHS BIPSR Process will be piloted using the auditory injury type, with finalized recommendations expected in FY16. Lessons learned from the next process iterations will be applied to further refine and enhance the MHS BIPSR Process.

TABLE 4-2: Power of the iBIPSR Capability

Benefits of iBIPSR
Eliminate down-time between meetings
Increase the community size and participation by everyone
Enable community members to contribute and share new knowledge in real-time
Collaborate transparently to support decision-making
Facilitate synthesis of information

The PCO anticipates moving forward with the iBIPSR Process and completing the recommendations for all blast injury types by 2019. Ultimately, the recommendations developed through the MHS BIPSR Process will better enable the DoD to apply the best available and scientifically sound standards during R&D efforts aimed at protecting US Service Members from the entire spectrum of blast injuries.

FIGURE 4-4: Anticipated Reduction in Timeline to Complete All Injury Types



CHAPTER 5:

HEARING AND BALANCE DISORDERS

Hearing injuries impede communication, reduce situational awareness, hinder threat detection, and ultimately impair safety and mission effectiveness. Noise is not unique to military service environments. Injurious noise is encountered in a variety of environments and can cause insidious or immediate damage. Unfortunately, auditory injuries—especially hearing loss and tinnitus—are highly prevalent among Service Members. According to the Veterans Benefits Administration, in FY13 tinnitus and hearing loss were the two most prevalent cumulative disabilities sustained during periods of conflict and peacetime. The prevalence of these auditory disabilities (Table 5-1) exceeded that of mental health (e.g., PTSD) and musculoskeletal (e.g., knee injuries, back strain) disabilities among all compensated Veterans.

Blast scenarios often result in multiple injuries (polytrauma), challenging the early detection and treatment of blast-related injuries to the auditory system. Peripheral hearing loss, central auditory processing deficits, tinnitus, and vestibular impairment are among the most common impairments associated with blast exposure. Even in relatively mild cases of blast-related auditory injury, initial symptoms of pain, tinnitus, hearing loss, dizziness, and/or disorientation can threaten individual and military unit effectiveness. Although these initial symptoms and deficits may dissipate over hours or days, blast overpressure can tear the tympanic membrane, fracture delicate middle ear ossicles, and disrupt the transduction and processing of sound by impacting the ear canal with blood, debris, or foreign bodies. Blast injury may also cause accumulation of fluid or blood behind the ear drum, perforations of the eardrum, separation of the small bones in the middle ear, and leakage of fluid from the inner ear that can lead to subsequent infection and inflammation. If left untreated, some blast-related injuries may lead to permanent impairment and even potentially fatal nervous system disease processes (e.g., meningitis).[8]

Diagnosis, treatment, and rehabilitation are especially challenging when hearing and balance injuries occur in combination with injuries to other brain and body systems. Evaluation and care of auditory and vestibular insults are often delayed due to triaged priority placed on more visible wounds of war, lack of diagnostic resources at the point of injury, and lack of awareness by initial care providers. Sensory injuries that are due to blast and/or head injury also can involve disruption of central neurosensory mechanisms and related processes that are crucial to the brain's ability to process, organize, and integrate sensory information. Where multiple injuries are involved, rehabilitative outcomes may be poorer for individuals who suffer sensory dysfunction.

There is a need for effective diagnostic methods for clinicians to directly inspect, assay, or image damage to the inner ear. All current methods are limited in their sensitivity; none can quantitatively identify progressive microscale damage. Hearing tests are behavioral measures that may fail to detect inner ear injury. Normal threshold sensitivity can mask ongoing and dramatic neural degeneration in noise-exposed ears.[9]

Lessons learned by military medical research and practice are critical for improving the care of Service Members and Veterans as well as advancing the care of civilians such as law enforcement and homeland security personnel who may suffer similar injuries from exposure to blast.

Hearing Center of Excellence

The HCE (www.hearing.health.mil) was established under the Duncan Hunter NDAA for FY09 (Public Law 110-417, Section 721). The purpose of HCE is to address the prevention, diagnosis, mitigation, treatment, and rehabilitation of hearing loss and auditory system injury, including the auditory-vestibular dysfunction often associated with TBI.

TABLE 5-1: Prevalent Disabilities of All Compensation Recipients

Disability	Body System	Male	%	Female	%	Total	%Total
Tinnitus	Auditory	1,056,443	7.4%	47,149	2.8%	1,121,709	7.0%
Hearing Loss	Auditory	823,134	5.8%	13,466	0.8%	854,855	5.3%
Post-traumatic stress disorder	Mental	600,193	4.2%	38,076	2.3%	648,992	4.0%
Lumbosacral or Cervical Strain	Musculoskeletal	519,957	3.7%	92,082	5.4%	616,937	3.8%
Scars, general	Skin	503,411	3.5%	59,455	3.5%	574,191	3.6%
Post-traumatic stress disorder	Mental	51,880	4.3%	5,708	2.9%	58,530	4.1%
Limitation of flexion, knee	Musculoskeletal	390,144	2.7%	60,650	3.6%	453,704	2.8%
Diabetes mellitus	Endocrine	383,916	2.7%	4,665	0.3%	398,480	2.5%
Paralysis of the sciatic nerve	Neurological	322,212	2.3%	18,517	1.1%	346,572	2.2%
Limitation of motion of the ankle	Musculoskeletal	303,079	2.1%	38,359	2.3%	343,834	2.1%
Degenerative arthritis of the spine	Musculoskeletal	293,540	2.1%	39,597	2.3%	335,692	2.1%
Total Most Prevalent Disabilities		**5,196,029**	**27%**	**412,016**	**24%**	**5,694,966**	**35%**
Total Number of Disabilities		**14,179,086**	**100%**	**1,691,759**	**100%**	**16,105,400**	**100%**

VA Annual Benefits Report 2013

MISSION

To heighten military readiness and to optimize quality of life through collaborative leadership and advocacy for hearing and balance health initiatives.

The NDAA also directed the Secretary of Defense to ensure collaboration with VA, institutes of higher education, other appropriate public and private entities, and international bodies to implement information exchange; coordinate research, care, and benefits; develop best practices; and enhance clinical education related to hearing and balance health.

The HCE is administered by the Air Force Medical Service and headquartered at the Wilford Hall Ambulatory Surgical Center, Joint Base San Antonio—Lackland, Texas. The HCE is organized into five interactive directorates: Operations/Global Outreach; Information Management, Prevention and Surveillance; Clinical Care, Rehabilitation, and Restoration; and Research Coordination. The HCE coordinates with and draws expertise from across DoD, VA, and other federal and non-federal mission-sensitive agencies and organizations to identify solutions that promote prevention, improve delivery and transition of care, and facilitate research. The HCE is currently working to reduce the high prevalence of auditory injuries in the military, correct the misperception that auditory injuries are functionally insignificant, specify military performance requirements (e.g., to communicate effectively in noisy military environments), improve our ability to prevent/mitigate injuries, support development and use of innovative protective solutions, design evaluation tools that are portable and rugged, identify new rehabilitative strategies, and advocate for research funding that is necessary to address critical knowledge and capability gaps.

HCE Functions and Initiatives

Coordination and Collaboration

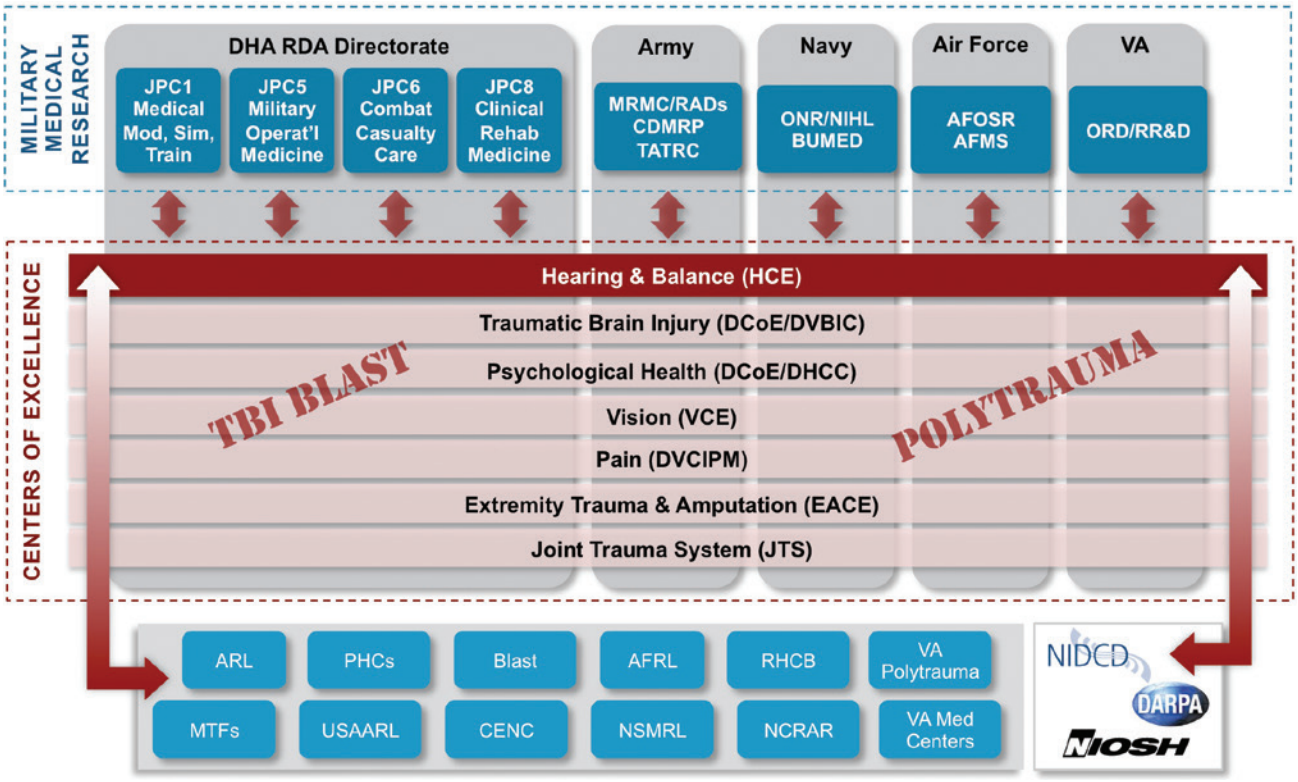
The HCE coordinates with researchers and organizations to develop and advocate for research objectives and outcomes, and to identify knowledge and capability gaps that require solutions to better serve the needs of injured Service Members and Veterans.

The HCE collaborates with research programs throughout DoD (Figure 5-1), including Army, Navy, and Air Force acoustic research laboratories; military treatment facilities (MTF); DHA RDA Directorate JPCs; the VA Office of Research and Development; and other federal funding agencies to support the identification and prioritization of research objectives that support military injury prevention and protection, restoration of capability, and enhancement of personal function and unit performance.

The HCE also coordinates closely with the VA Office of Research and Development and primary sites of clinical research within VA, and with other DoD CoEs, such as DCoE, VCE, the Defense and Veterans Center for Integrative Pain Management (DVCIPM), and EACE. Collectively, these CoEs address problems related to the study and treatment of polytrauma scenarios that commonly occur with blast exposure. In 2014, HCE initiated collaboration with the CENC to contribute guidance and expertise in the areas of hearing and balance to address the long-term effects of TBI.

The HCE also lends specialty expertise to the analysis and review of hearing-related Congressional appropriations, auditory and vestibular blast and noise analyses, and collaborative assessments with various academic partners in the development of CPGs. Examples include expert review and subject matter contributions to the IOM report on Long-Term Effects of Blast Exposure; collaboration with the DCoE for Psychological Health and TBI to develop guidelines for clinical care of dizziness; and working with the American Academy of Otolaryngology and Agency for Health Research Quality to develop clinical guidance and treatment review for tinnitus.

FIGURE 5-1: HCE Promotes Hearing and Balance Disorders Research Across the Federal R&D Landscape



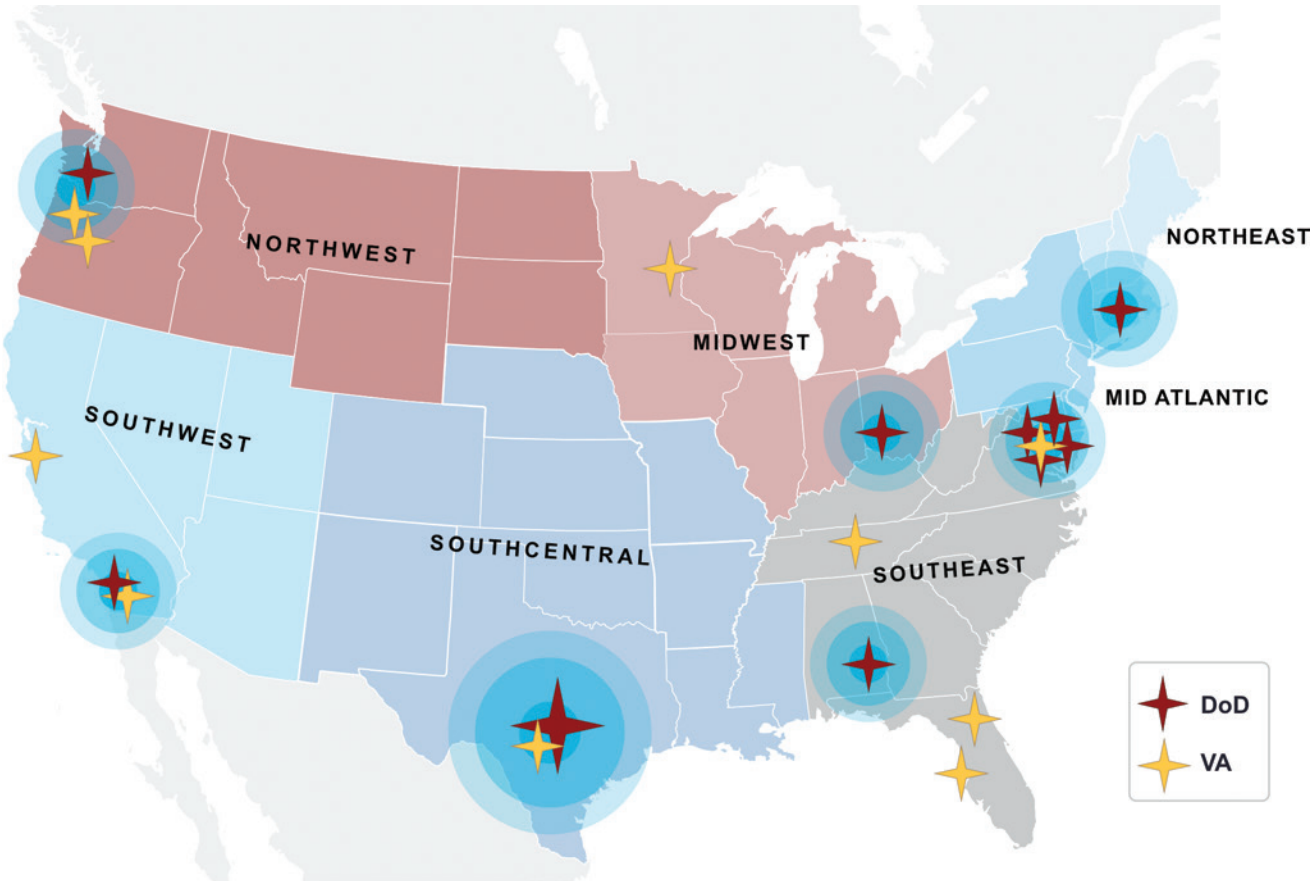
To promote execution of military and Veteran hearing and balance research initiatives, HCE supports a regionally based network of research administrators located at key military research facilities where they can promote information sharing and support investigators as they work to develop projects, multi-site grant awards, institutional review board (IRB) submissions, and technology transfer activities (Figure 5-2). The HCE established a centralized IRB within the USAMRMC IRB office, to facilitate multi-site research projects. The HCE has also developed a Research COoRDination Projects Database (ReCord) to track research proposals and awards, multi-site collaborations, output, and dissemination of research in hearing and balance across all activity levels, and to support assessment against remaining knowledge gaps and research priorities.

The HCE includes a consortium of experts, the Collaborative Auditory/Vestibular Research Network, whose membership now includes more than 150 SMEs representing 49 research laboratories, MTFs, public health offices, and other agencies across DoD, VA, National Institutes of Health (NIH), and seven countries. This collaborative network of experts assesses gaps and scientific innovations and has formalized working sub-groups to address PIHL, auditory fitness for duty (AFFD) policy, and assessment and integration of emerging technologies in auditory vestibular diagnosis, treatment, and rehabilitation.

Injury Surveillance

To identify and track every case of hearing loss and auditory and balance system injury in accordance with requirements under P.L. 110-417, HCE is working to develop a Joint Hearing Loss and Auditory System Injury Registry (JHASIR) within the Clinical Enterprise Intelligence Program of the DHA. The JHASIR will be a collaborative registry that interfaces with existing DoD and VA data systems to identify and gather pertinent clinical, demographic, and administrative data. This bi-directional data exchange mechanism will track hearing loss and auditory and balance system injuries; facilitate the conduct of research, development of best practices; and improve clinical education.

FIGURE 5-2: HCE Networks with Military Research Facilities that Support Hearing and Balance Initiatives



For example, the JHASIR will digitally capture clinical audiometric data gathered from all MTFs with those capabilities, including acute care metrics gathered from patients treated in the tertiary care theater evacuation and management system, as well as information about nature of the auditory injury. The JHASIR database will also incorporate hearing conservation program data from Defense Occupational and Environmental Health Readiness System for Hearing Conservation (DOEHRS-HC), and audiometric data from VA's National Hearing Loss Repository. Analysis of these data can then be used to inform data-driven design of CPGs and best practices, testing protocols, and care extension/telehealth applications. The HCE will also provide access to JHASIR data to enable researchers to investigate the incidence and prevalence of injury, the effectiveness of current clinical practices, and the longitudinal course and natural history of exposure. These analyses will include information about the recovery and/or progression of hearing injuries sustained by Service Members and Veterans, including their rehabilitation status and quality of life.

Prevention, Protection, and Service Member Readiness

The HCE's Comprehensive Health Hearing Program aims to prevent and mitigate auditory and vestibular system injuries by providing hearing health services to all Service Members; this includes education about hearing threats and protective measures, monitoring of hearing health and noise (steady state and blast) exposures, and prioritizing access to and proper fitting and use of hearing protection devices (HPD). Hearing health services are provided early in Basic Military Training, and are sustained throughout the military career life cycle to prevent hearing and balance problems and support early identification and timely mitigation of injuries.

All three of these components are essential to effect positive individual behavior, and organizational culture changes toward protection of hearing and balance as a life-long priority.

Because HPDs are essential to the prevention of hearing injuries, HCE is working with the DoD Hearing Conservation Working Group and representatives at DoD and VA logistics and contracting organizations to develop acquisition strategies for purchase of HPDs and Tactical Communication and Protective System (TCAPS) devices, and with the Army's Program Executive Office (PEO) Soldier to develop a Qualified Products List to ensure military organizations can procure and field HPDs that meet requirements for noise reduction, communication, and interoperability with military equipment.

Understanding that noise (steady state and impulse/blast) is not always avoidable, HCE has been involved with the ONR and participated with the High Noise Source Reduction working group to identify engineering solutions toward mitigating noise at the source. The HCE is working with the DoD Integrated Product Team for improving noise standards as well as with the Air and Space Interoperability Council standardizing international measures of noise and noise exposure.

Improving Clinical Care

The HCE works to optimize clinical care by codifying and disseminating lessons learned from war, new knowledge, techniques, and technologies to military and veteran health care providers that work directly with military patients and Veterans who have sustained hearing and balance injuries. In 2014, HCE partnered with AudiologyOnline to host a webinar focused on the clinical evaluation and care of blast-exposed patients.

The HCE in coordination with DoD and VA partners has helped to develop evidence-based best practice recommendations for vestibular evaluation, acoustic trauma, adult tinnitus management, and hearing aid selection and fitting.

The HCE is part of a DoD/VA working group to develop best practice recommendations for central auditory deficit evaluation and treatment, as well as hearing implant indications, techniques, and translation for the most severe cases of auditory injury. The HCE's evaluations of ruggedized auditory diagnostic tools for point-of-injury evaluation supported insertion of remote clinical (boothless) audiological evaluation into Afghanistan, with telehealth options for consultation and disposition guidance. The HCE has provided the USAMRMC CCCRP with an analysis of fieldable balance test instruments for potential use in the early diagnosis of mTBI. Additionally, HCE has sponsored the Military Vestibular Assessment and Rehabilitation seminar for hands-on training in vestibular rehabilitative care, is currently reviewing vestibular training modules developed by the James H. Quillen VA Auditory and Vestibular Research Enhancement and Award Program, and will lead a training session at the 2015 Joint Defense/Veterans Audiology Conference (JDVAC).

Research and Development

The HCE works closely with VA to identify solutions needed across the continuum of care and the military career life cycle (Figure 5-3). Research investment has been limited despite the high prevalence of auditory injuries in Service Members and Veterans and their impact on military operational performance. Thus, HCE advocates for additional R&D investment in hearing and balance, recognizing that knowledge gained from research will extend to improve the overall care, treatment, and "reset" of blast-injured Service Members. Examples of hearing and balance research efforts currently underway, advocated by HCE and supported by the DoD and VA, are found in Table 5-2. Please refer to Appendix F for summaries of these projects and their objectives.

Way Forward

The HCE will continue to draw on expertise from across federal and non-federal organizations to identify and develop solutions that promote readiness, health, optimal performance, and safety for Service Members and Veterans.

FIGURE 5-3: Research and Development Solutions are Needed Across the Continuum of Care

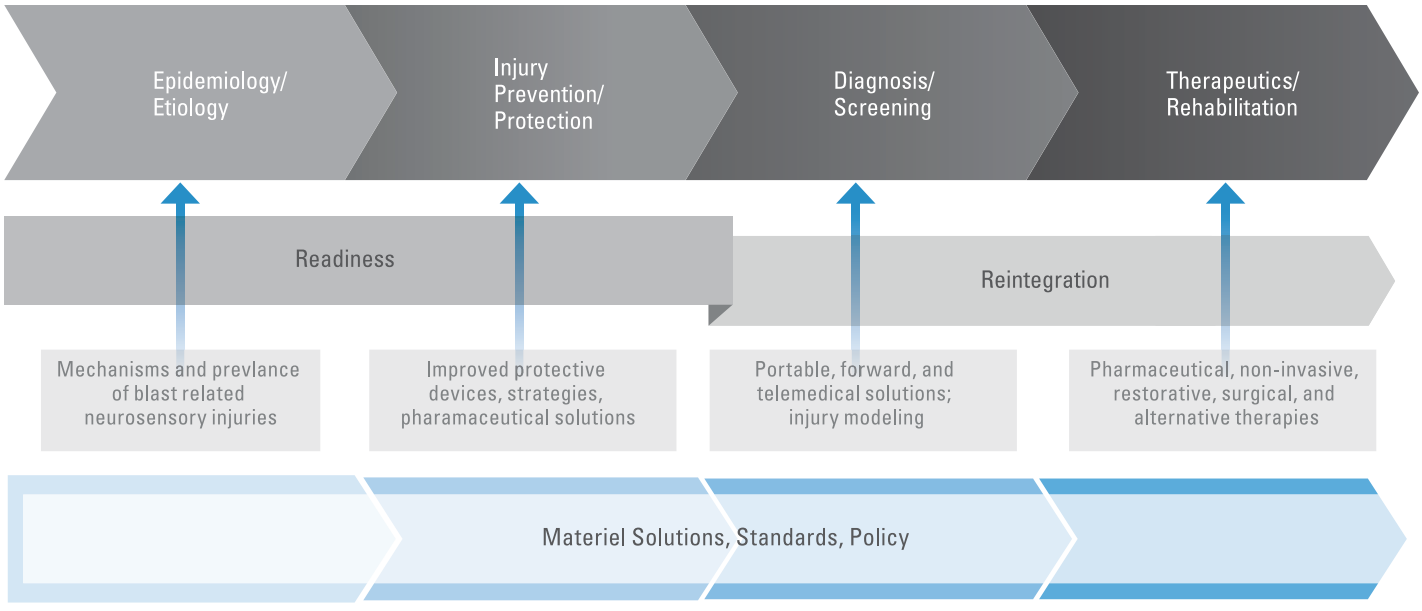


TABLE 5-2: Blast-related Auditory System Injury Research and Development

Research Projects	Research Organizations
Hearing Injuries	
Clinical Trials of D-Methionine to Reduce Noise Induced Hearing Loss and Tinnitus	Southern Illinois University
Antioxidant Therapeutic to Protect Against Hearing Loss	Hough Ear Institute
New "Hybrid" Approach to In-Ear Hearing Protection and Blast Noise Exposure Logging	Applied Research Associates, Inc. (ARA)
Diagnosis and Treatment of Blast-Induced Hearing Loss	Stanford University, Texas A&M University, Rice University, and Baylor College of Medicine
Auditory Rehabilitation after Mild Brain Injury	VA Medical Center, Tampa and VA Medical Center, Portland
Blast-related Auditory Injury Database (BRAID)	NHRC
Evaluation of Aurally-Aided Visual Search	National Military Audiology and Speech Center and National Intrepid Center of Excellence (NICoE)
Biomechanical Modeling and Measurement of Blast Injury and Protection Mechanisms	University of Oklahoma
Developing a Biomechanical Model-based Auditory Standard for Impulse Noise	L-3 Applied Technologies
Improvement and Extension of Auditory Hazard Models	ARA
Tinnitus	
Tinnitus Management and Epidemiology	National Center for Rehabilitative Auditory Research (NCRAR)
Central Auditory Processing Disorder	
Prevalence and Verification of Central Auditory Processing Disorders (CAPD)	Walter Reed National Military Center (WRNMMC), San Antonio Military Medical Center (SAMMC), and Navy Medical Center San Diego
Auditory Perception and Cognition Following TBI	VA Northern California Health Care System
Chronic Effects of Blast on Central Auditory Processing	National Center for Rehabilitative Auditory Research (NCRAR) and Oregon Health and Science University
Balance Injuries	
Vestibular Consequences of Blast-Related TBI	Mountain Home VA Medical Center (Tennessee) Vestibular/Balance Lab
New Solutions in Clinical Assessment	James H. Quillen VA Medical Center
Innovations in Vestibular Therapy	US Army Aeromedical Research Laboratory (USAARL)

Going forward, there is a critical need to improve prevention and protection from blast-related auditory and vestibular system injuries. Improvements in inner ear protection have lagged behind the development and acquisition of other personal protective gear. Other key focus areas for research include the need to better understand the mechanisms, effects, and processes of auditory and vestibular injuries; to identify opportunities and strategies for early, effective intervention and rehabilitation; to develop objective, sensitive measures of exposure capable of use in forward deployed settings; and to gain an improved understanding of central auditory processing of sound and balance, including diagnostic, therapeutic, and rehabilitative strategies for coping with dysfunction. Because blast injury scenarios often involve polytrauma, including TBI and CAPD, there is an additional need to improve our understanding of how injuries to multiple body systems interact to challenge effective treatment, recovery, rehabilitation, quality of life, and overall long-term health.

As part of its mission to facilitate research that addresses these and related knowledge and capability gaps, HCE will continue to encourage targeting of R&D resources to identify solutions that can meet these needs. Finally, HCE will advocate to support and encourage use of hearing protection by Service Members, and will encourage policy to maintain priority for acquisition of adequate hearing protection.

CHAPTER 6:

HEMORRHAGE CONTROL

Hemorrhage is the leading cause of potentially preventable death on the battlefield. Approximately 25% of these causalities could have been prevented if timely, more effective approaches to hemorrhage control were available closer to the point of injury. Early control of hemorrhage and the subsequent prevention of secondary complications (resuscitation, shock, inflammation, and coagulopathy) within the first hour after injury, or the golden hour, is the most effective strategy for treating preventable combat casualties due to bleeding. Hemorrhage control and resuscitation are also critical to avoiding severe hypotension and tissue hypoxia, two of the most important secondary injury factors that contribute to poor outcomes in TBI.

Efforts to control bleeding and manage the associated secondary effects during the golden hour have necessitated a shift from facility-based care to technology-based care. The traditional concept of the golden hour is based on movement of the injured Service Member to a fixed location within one hour. Emerging approaches to care involve delivering advanced resuscitative capability to the injured Service Member within one hour, regardless of location.[10]

The shift to providing effective care regardless of location within the golden hour represents a critical component of the CCCRP. CCC is a key research program within the USAMRMC whose mission is to reduce the mortality and morbidity resulting from battlefield injuries. The scope of the CCCRP includes caring for the injured Service Member from the point of injury, through prehospital care, en-route care, advanced trauma life support, surgical stabilization, and on to definitive care in a US medical treatment facility.

In particular, CCCRP's Hemorrhage and Resuscitation and the Forward Surgical and Intensive Critical Care research portfolios are dedicated to developing and improving hemorrhage control products, drugs, devices, and capabilities for medical personnel to provide earlier intervention and care in the prehospital environment (i.e., outside of a medical facility), with all efforts linked to requirements. The Hemorrhage and Resuscitation research portfolio collaborates across the Military Services, and with other federal organizations such as the National Heart, Lung, and Blood Institute (NHLBI), Biomedical Advanced Research and Development Authority (BARDA), DARPA, USSOCOM, and with academic and industry partners. The following sections provide a more in depth description of the Hemorrhage and Resuscitation research portfolio and the development of products, drugs, and devices to improve hemorrhage control and resuscitation.

Hemorrhage and Resuscitation Research Portfolio

The Hemorrhage and Resuscitation research portfolio encompasses the range from basic research through clinical development of US Food and Drug Administration (FDA) regulated products and includes clinical studies addressing important knowledge gaps in hemorrhage control, transfusion, and resuscitation.

The mission of the DoD Hemorrhage and Resuscitation research portfolio is to conduct a comprehensive, joint R&D program to provide medical capabilities for the treatment of battlefield casualties with traumatic hemorrhage. The program incorporates all DoD efforts in the areas of hemorrhage control, fluid resuscitation, blood products, transfusion, and the pathophysiologic responses to traumatic hemorrhage. The scope of the portfolio includes basic research through clinical development.

The vision of the DoD Hemorrhage and Resuscitation research portfolio is to deliver advanced medical capabilities to US troops to enable life-sustaining interventions for treatment of casualties with traumatic hemorrhage, anywhere on the battlefield for up to 72 hours before surgery. This is achieved in close collaboration with the Forward Surgical and Intensive Critical Care portfolio.

TABLE 6-1: Six Major Efforts of the Hemorrhage and Resuscitation Research Portfolio

Major Effort	Description of Major Effort
Improve Blood Products	Develop safer and more logistically supportable blood products for transfusion
Damage Control Resuscitation	Identify the best ways to use existing and newly developed blood products, drugs, and fluids (Including transfusion practices using existing products-CPGs)
Coagulopathy of Trauma	Elucidate mechanisms to identify diagnostic and therapeutic targets for the development of rapid diagnostics and drugs to prevent or treat coagulopathy of trauma
Immune/ Inflammatory Modulation	Evaluate promising approaches and identify key mechanisms leading to the long-term ability to modulate inflammatory responses of the patient
Metabolic and Tissue Stabilization	Evaluate promising approaches and identify key mechanisms leading to long-term ability to modulate/stabilize metabolic responses (Including oxygen delivery)
Hemostatic Devices	Evaluate/identify existing products and develop new products or procedures to control bleeding

The program also plans to deliver advanced blood product technologies that will enable transfusion wherever medically indicated on the battlefield or in transport. The capabilities provided under this program have the potential to reduce combat deaths by 25%.

Strategic Objectives

The program is focused on four strategic objectives, which will be achieved in three phases over time. The four overarching strategic objectives are:

- Provide technologies to control bleeding in the prehospital environment
- Provide safer, more effective, and more logistically supportable blood products
- Provide next generation resuscitation for prolonged prehospital management and casualty survivability
- Provide technologies and knowledge sets for improved damage control resuscitation

To meet the strategic objectives and aid in closing the capability gaps, the Hemorrhage and Resuscitation research portfolio is pursuing six major efforts outlined in Table 6-1. The six major efforts are executed to achieve the four strategic objectives in three broad phases over time (Figure 6-1).

Major Past Accomplishments

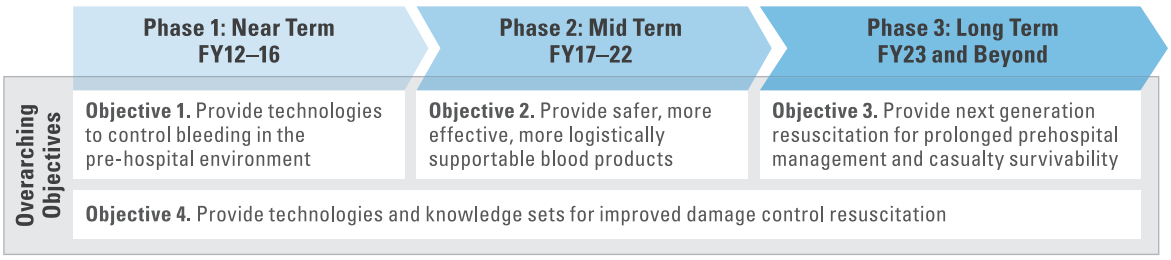
Since 2001, the DoD's R&D efforts in these areas have resulted in the development of advanced hemostatic dressings and improved tourniquets that have been fielded with all deployed US troops, used by allied nations, and adopted by the civilian sector.

Transfusion practices have also improved. Retrospective studies that examined outcomes of combat transfusions found that survival was increased when higher ratios of plasma to red blood cells were transfused. This led to changes in military clinical practice to use a 1:1:1 ratio of plasma to platelets to red blood cells. Since then, a higher ratio of plasma to red blood cells has been adopted by most civilian medical centers.

Current Activities

Even with the advances made to limb tourniquets, hemostatic dressings, and improved transfusion practices, there remain requirements for ongoing R&D of compressible and non-compressible hemorrhage control in an effort to continue to reduce combat death. The major efforts that have been undertaken to develop and/or improve hemorrhage control technologies are described in the section below.

FIGURE 6-1: Overarching Objectives Aligned with the Three Phases



Recent Advances to Control Compressible Hemorrhage

In the last five years, great advancements have been made across the DoD to address technological gaps in junctional hemorrhage (e.g., inguinal, axillary) control. Four devices were developed under DoD R&D programs: Combat Ready Clamp (CRoC™), SAM® Junctional Tourniquet, Junctional Emergency Treatment Tool (JETT™), and Abdominal Aortic Junctional Tourniquet (AAJT™). These commercially available devices address a critical capability gap in compressible junctional hemorrhage and are now undergoing the final stages of development to include limited fielding, systematic test and evaluation, and procurement planning.

CRoC™ is a vice-like focal tourniquet with FDA clearance for battlefield use in the treatment of amputations and pelvic fractures that are often the result of blast injury (Figure 6-2). The device compresses the femoral artery to control bleeding. CRoC™ has been fielded to medics in Afghanistan but there is limited information regarding its use. A preliminary case report published in the Journal of Special Operations Medicine described that CRoC™ was applied in 90 seconds by a medic in the battlefield to successfully control inguinal bleeding as a result of traumatic amputation.[11] CRoC™ is manufactured by Combat Medical Systems (Harrisburg, North Carolina).

FIGURE 6-2: CRoC™ Tourniquet

Credit: Steven Galvan/U.S. Army

SAM® Junctional Tourniquet is a circumferential tourniquet nylon pelvic binding belt with two inflatable bladders that are inflated to control difficult bleeds in the inguinal area and to immobilize pelvic fractures (Figure 6-3, panel A). The device can be correctly applied in under 25 seconds and can be modified for use in axillary hemorrhage. SAM® Junctional Tourniquet is FDA cleared for battlefield and trauma situations and is fielded in limited numbers. SAM® Junctional Tourniquet is also FDA cleared to stabilize pelvic fractures. SAM® Junctional Tourniquet is manufactured by SAM Medical Products (Wilsonville, Oregon).

JETT™ is a circumferential tourniquet nylon and plastic belt that includes two pressure pads which are positioned directly on an inguinal wound site and tightened with a screw mechanism to occlude blood flow (Figure 6-3, panel B). Since JETT™ uses a mechanical method rather than an air inflation to achieve compression, it can purportedly maintain steady pressure on the injury regardless of atmospheric pressure changes or evacuation from rugged terrains. JETT™ is FDA cleared to control acute bleeding in the groin and inguinal region and has been fielded in limited numbers. JETT™ is manufactured by North American Rescue, LLC (Greer, South Carolina).

AAJT™ is a circumferential tourniquet with an inflatable bladder wedge that was originally designed to compress the abdominal aorta at the lower abdomen to reduce blood flow (Figure 6-3, panel C). Usage has since been expanded to include axilla and inguinal junctional zones. The AAJT™ is FDA cleared for all junctional hemorrhage sites. This tourniquet can remain in place at junctional sites or on the abdomen for up to four hours. Similar to the other devices described here, the AAJT™ has been fielded by the DoD in limited numbers. AAJT™ is manufactured by Compression Works, LLC (Charlotte, North Carolina).

Strategies to Control Non-compressible Intracavitary Bleeding

Tourniquets, by definition, can only treat compressible injuries. Therefore, there is a critical need for improved prehospital strategies to treat severe non-compressible hemorrhage, which is often caused by injury-induced intracavitary bleeding from arteries and large veins. Current strategies to control non-compressible hemorrhage are described in more detail below.

FIGURE 6-3: Circumferential Tourniquets Capable of Treating Junctional Hemorrhage

Panel (A) SAM® Junctional Tourniquet (B) JETT™ (C) AAJT™. Credits: (A) http://www.popularairsoft.com/ (B) The University of Texas Medical School at Houston; U.S. Army; (C) John Croushorn/U.S. Army)

Platelet Derived Hemostatic Agent (PDHA). PDHA (dried platelet) is being developed as an acute intravenous (IV) hemostatic agent for the treatment of combat casualties with severe bleeding. Apheresis platelets have a very short shelf life (five days) due to risk of bacterial growth during room temperature storage, limiting their distribution and use in far-forward battlefield environments. To mitigate these issues, PDHA is under development as an adjunct to standard hemostatic measures and will be used when platelets are not available. It will have a longer shelf life and decreased logistical burden compared to apheresis platelets. In an interagency cooperative arrangement, BARDA is developing one PDHA while DoD is developing another, giving the US government a two-product strategy.

Prehospital Use of Tranexamic Acid (TXA) for Traumatic Hemorrhage. TXA is a FDA approved antifibrinolytic drug that improves hemostatic capacity in patients with hemophilia and prolonged uterine bleeding. Following publication of the Clinical Randomization of an Antifibrinolytic in Significant Hemorrhage 2 (CRASH-2) study and the positive experience of our allies, the US adopted the use of TXA for casualties with traumatic hemorrhage, under CPGs for Damage Control Resuscitation. Additional information is needed to optimize use. The DoD has sponsored three clinical studies on the use of TXA that focus on prehospital TXA for traumatic hemorrhage, prehospital TXA for TBI/Intracranial Hemorrhage (ICH), and the pharmacokinetics and mechanism of action of TXA in traumatic hemorrhage. These clinical studies aim to produce the most robust safety, efficacy, and pharmacokinetic data to address identified knowledge gaps and inform CPGs.[12] USAMRMC, DHP, and NHLBI are supporting these studies.

Wound Stasis System (WSS). WSS is an in-situ forming, polyurethane foam designed for prehospital use to treat non-compressible abdominal hemorrhage. The injected precursor liquid phases react to form a solid, expanding foam inside the body cavity, providing a local tamponade effect and direct pressure at the site of injury. This device is later removed by a surgeon at advanced levels of care. The company has submitted an application for device approval to the FDA in April 2015. Fielding is expected as early as FY16/17. This product was developed by DARPA and will be transitioned to Army-led Joint Advanced Development Program in August 2015.

ER-REBOA (Resuscitative Endovascular Balloon Occlusion of the Aorta). ER-REBOA is a vascular occlusion system that allows for endovascular aortic occlusion for non-compressible hemorrhage. It uses a small size catheter inflatable balloon to facilitate arterial access, and eliminates the potential need for fluoroscopy and x-ray imaging. This technology has the potential to close a capability gap as an innovative, rapid, and forward deployable hemorrhage control and resuscitative procedure for non-compressible torso hemorrhage. ER-REBOA has the potential to reduce blood loss, improve central hemodynamics, reduce the number of blood transfusions, and decrease time spent in a forward surgical facility, the operating room, or interventional angiography suite. The ER-REBOA is expected to receive FDA clearance by the end of 2015.

X-Stat Hemostatic Dressing (XSTAT). XSTAT is a syringe-like applicator of small, rapidly expanding mini sponges that expand on contact with blood to provide a tamponade effect at the site of injury (Figure 6 4). The sponges contain radiopaque markers for easy detection by X-ray and later removal. The device is intended to treat deep wound tract, non-compressible, or partially-compressible junctional injuries that are not normally accessible to tourniquets. XSTAT achieves hemostasis in a matter of minutes with a 90% survival rate in animal models. XSTAT is a *de novo* cleared FDA product for battlefield use only. Manufacturing development is underway by Revolutionary Medical Technologies™ (Wilsonville, OR). DoD is also seeking a label indication for civilian use. This program, initiated by USSOCOM, has recently transitioned to a joint medical advanced development program and has employed USSOCOM, Air Force, DHA, and Army funding.

FIGURE 6-4: XStat-30™ Applicator

Strategies for Resuscitation

Advanced approaches to resuscitation are needed to mitigate the pathophysiologic response to traumatic hemorrhage and are critical to improving survival in combat casualties. Progress has been made in identifying the best methods for blood transfusion and development of drugs to treat hemorrhagic shock.

Prehospital Use of Plasma for Traumatic Hemorrhage (PUPTH) Clinical Studies. The PUPTH clinical studies, sponsored by JPC-6 program office and funded by DHP, will provide the first ever randomized prospective clinical data on the potential beneficial or negative effects of prehospital plasma for traumatic hemorrhage. Three clinical studies were awarded, with a total of over 900 patients projected. The protocols have been harmonized to the greatest degree possible to optimize combined analyses.

Pragmatic, Randomized Optimal Platelet and Plasma Ratio Study (PROPPR). The PROPPR study was the first prospective randomized study of transfusion ratios. The secondary objective was to characterize the impact of trauma and resuscitation on coagulopathy. This multicenter study compared mortality and other parameters in civilian trauma patients requiring massive transfusion. Patients were randomized to receive transfusion ratios of 1:1:1 (plasma:platelet:red blood cells) versus 1:1:2 (plasma:platelet:red blood cells). The study was conducted through interagency partnering of NHLBI/Resuscitation Outcome consortium and DoD. The study has been completed and data are expected to be reported in FY15. This study was conducted with DHP funding under NHLBI management.

Valproic Acid (VPA). VPA is FDA approved for the treatment of seizures. The compound possesses histone deacetylase inhibition activity, which has been shown to activate pro-survival cell signaling pathways and protect cells during hypoxic events such as hemorrhagic shock. VPA is under investigation as a low-volume damage control resuscitant agent and is expected to be a key component of a multifunctional approach to next generation resuscitation. VPA is currently in Phase I clinical studies for low-volume pharmacologic resuscitation and planning is underway for Phase II clinical studies. Initial development of VPA was sponsored by ONR and is transitioning to a Navy-led joint medical advanced development program, with sponsorship from Navy and DHA.

Ethinyl Estradiol-3-Sulfate (EE3S). EE3S is also in development as a low volume damage control resuscitant. The agent is a water soluble estrogen capable of eliciting anti-inflammatory and cytoprotective activity. Evidence suggests EE3S may stabilize pathophysiologic responses to traumatic shock to improve casualty survivability during prolonged evacuation. Animal data show 6-hour survival in otherwise lethal hemorrhagic shock models. EE3S is in final preclinical testing before Investigational New Drug (IND) submission for low-volume pharmacologic resuscitation. EE3S is predicted to be a key component of a multifunctional approach to next generation resuscitation. The project is transitioning from DARPA to a Joint Development Program under guidance of a Joint Transition Working Group.

Improved Blood Products

For the foreseeable future, battlefield transfusion will be an essential part of combat casualty care. The DoD is fostering interagency collaboration with NHLBI, BARDA, and FDA among other organizations to identify ways to improve the safety and effectiveness of blood products, reduce logistical constraints, and enable distribution of blood products across the battlefield.[13] This will make it possible to transfuse blood products wherever medically needed on the battlefield or during transport. Several blood products are currently in development:

Cryo-Preserved Platelets (CPP). Platelets are a critical component of transfusion practice in combat trauma. Current liquid platelets are stored at room temperature and only have a five-day shelf life. This requires in-theater platelet collection and limits distribution of platelets on the battlefield. CPP capability will allow distribution, storage, and use of US-collected platelets for Role of Care 3. The product has completed a number of Phase I clinical trials and is preparing to enter Phase II clinical trials in FY15. FDA approval is expected in FY20. The US Army Office of the Surgeon General is the regulatory sponsor.

Improved Platelet Storage—Refrigeration. Platelets are a critical component of transfusions in combat trauma. Current liquid-stored platelets are stored at room temperature and have a five-day shelf life (seven days with bacterial testing). The short shelf life limits the distribution of platelets on the battlefield. Technology to store liquid platelets for 10–14 days will reduce logistical constraints, making platelets more consistently available. Refrigerated platelets are under development as a promising platelet storage method. Evidence suggests this method might improve the hemostatic potential of platelets through a pre-activation mechanism. Cold stored platelets show improved function at five days and sustained function through 10 days in vitro. Clinical studies are expected to begin in FY16.

Whole Blood Pathogen Reduction Device (WBPRD). The WBPRD is a new deployable device that will reduce the risk of pathogens (viruses, bacteria, parasites) in whole blood collected and transfused in combat environments. The Phase II clinical trial for the WBPRD is complete and the Phase III clinical trial will be initiated in FY15.

It is predicted that WBPRD will receive FDA approval in FY18. WBPRD is an Army-led advanced development program sponsored by Army and DHA and manufactured by Terumo BCT, Inc. (Lakewood, Colorado). A critical need exists for dried plasma as a capability for battlefield use and civilian preparedness. The US government therefore has initiated a coordinated three-pronged approach to develop dried plasma. Two distinct technological approaches are being developed by the DoD while a third is being developed by BARDA.

Freeze Dried Plasma (FDP). Freeze dried plasma is a product under development by the Army to provide a FDA-approved freeze dried plasma. Conducted under a cooperative R&D agreement with Vascular Solutions (Minneapolis, Minnesota), the plasma development program will deliver a single-donor, pathogen tested, freeze dried fresh frozen plasma that will reduce logistical constraints and enable plasma to be administered wherever medically needed from point of injury through all levels of evacuation and surgery. The second Phase I study is planned for FY15 and a Phase II clinical study is planned for FY16.

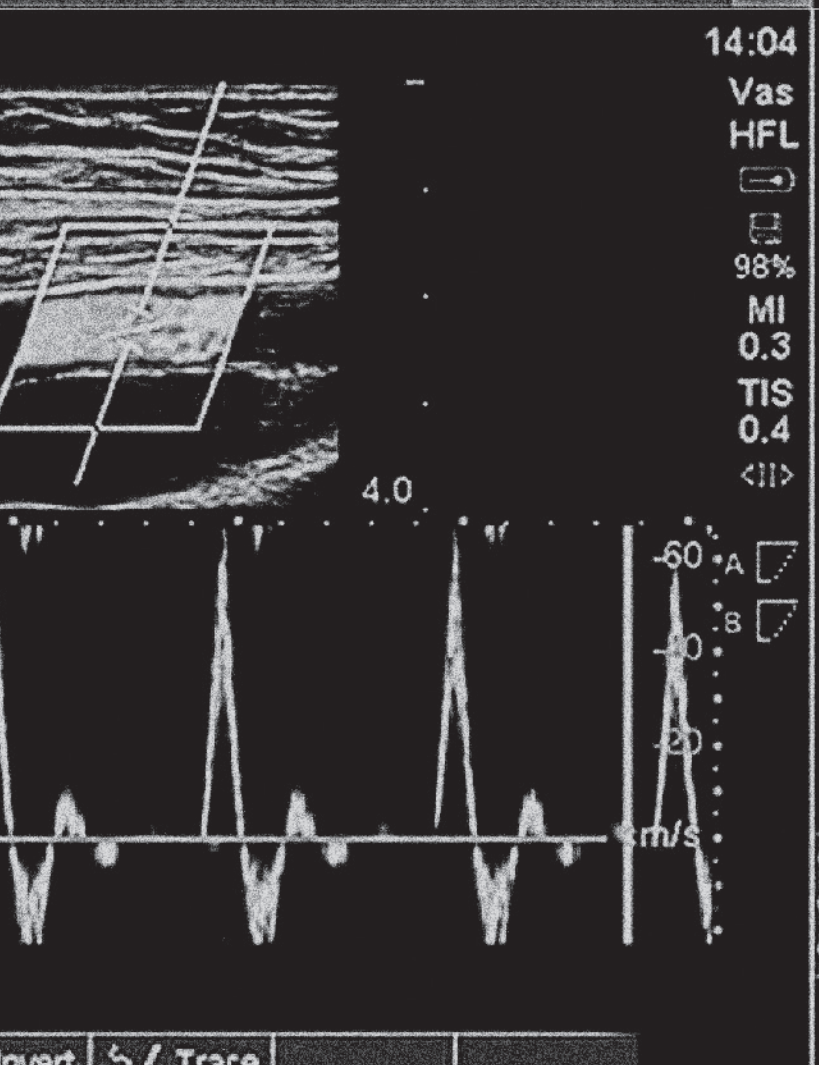
Solvent Detergent/Spray Dried Plasma (SD/SD Plasma). SD/SD Plasma is a pooled, pathogen-reduced, spray-dried plasma that will minimize logistical constraints and enable plasma to be administered wherever medically needed from point of injury thru all levels of evacuation and surgery. A Phase I clinical trial on SD/SD Plasma is complete and a Phase II trial will commence in FY15. This program was originally sponsored by ONR and has recently transitioned to a joint medical advanced development program sponsored by Navy and DHA. Entegrion, Inc. (Research Triangle Park, North Carolina) is the DoD development partner for this product.

Single-Donor Spray-Dried Plasma. BARDA is developing a single-donor, spray-dried plasma that can be produced locally by blood banks and stored at room temperature. This product is expected to reduce logistical burden and make it possible to deliver plasma wherever medically needed instead of only where freezers and thawing equipment are available. BARDA's development partner is Velico Medical, Inc. (Beverly, Massachusetts).

Development of Diagnostic Tools for Physiological and Hemodynamic Assessments Following Significant Blood Loss or Trauma

There is a lack of transportable, prehospital diagnostic tools available for physiological and hemodynamic assessments following hemorrhage or trauma. Currently available monitoring tools are often late to detect life-threatening cardiovascular collapse. They provide limited insight to first responder for prioritizing triage of bleeding Service Members on the battlefield. There is a need for prehospital assessment of unrecognized hemorrhage so that bleeding can be controlled as quickly as possible.

Assessment of Internal Bleeding and Prediction of Shock. The Compensatory Reserve Index (CRI) is used as a tool to collect real-time physiologic data necessary for assessment of interventions during battlefield care of blast-injured casualties. The Forward Surgical and Intensive Critical Care portfolio has developed a method to assess the reserve to compensate for blood loss using a novel machine-learning algorithm to estimate the CRI based on analysis of the arterial wave form features obtained from photoplethysmographic recordings. This technology has been shown to reduce the time required by a first responder to recognize an unstable patient by more than 40%.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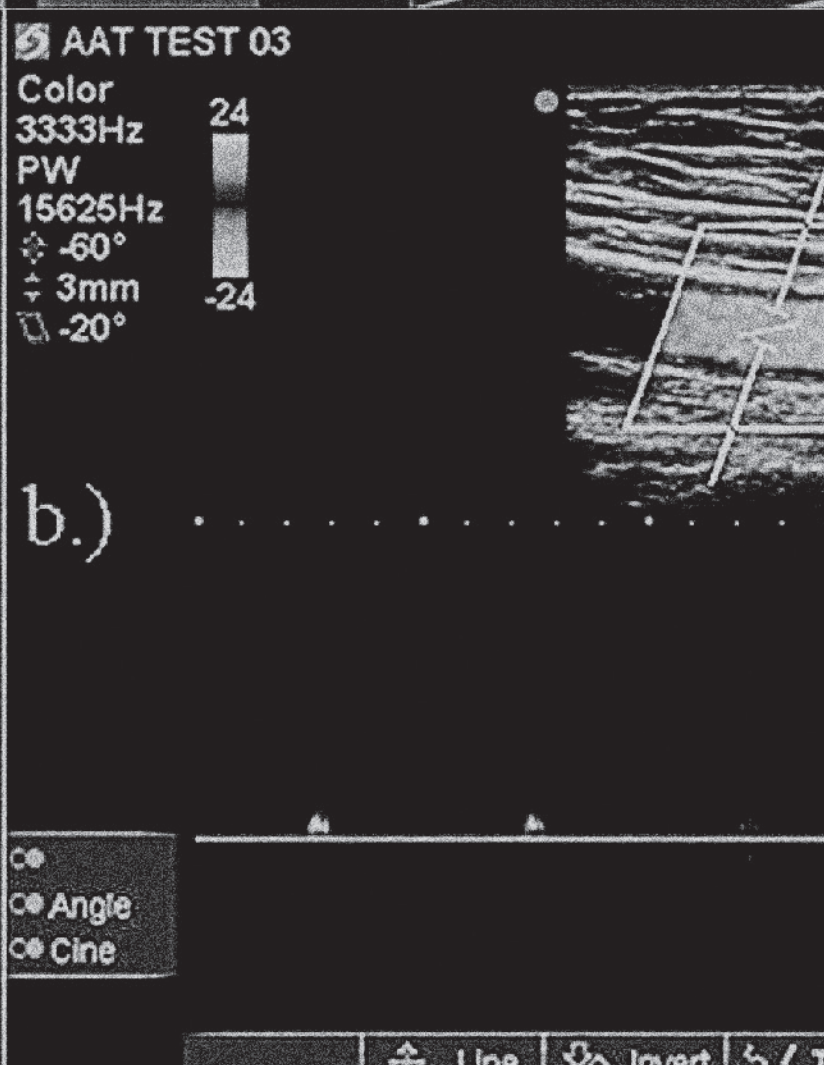
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Way Forward

Despite the many advances in hemorrhage control and resuscitation research, significant progress is needed to further enhance the DoD's ability to respond to combat injuries. To effectively reduce the number of combat deaths resulting from uncontrollable hemorrhage, research programs must develop solutions to provide advanced hemorrhage control and resuscitative capabilities for use as close as possible to the point of injury. Future research will focus on improving hemorrhage control and developing next generation resuscitation approaches to enable survival in prehospital environments up to 72 hours prior to reaching a medical facility. Prolonged survivability cannot not be achieved solely through the use of products that are expected to be available in the near-term. Next generation resuscitation approaches are required. Expanded capabilities will require identification of new uses for existing drugs such as VPA, a resuscitate agent, and the development of new drugs, devices and surgical techniques.

There is also a need to invest in additional research to identify the mechanism of trauma-induced coagulopathy so that diagnostic and therapeutic targets to rapidly detect or treat coagulopathy are possible in the prehospital setting. The first step will be to identify the pathophysiologic mechanisms associated with coagulopathy. To effectively advance the state-of-the-science and speed the development of specific diagnostics and therapeutics, DoD programs have partnered with the NHLBI through the Transagency Consortium in Trauma-Induced Coagulopathy (TACTIC). TACTIC brings together a significant NHLBI basic science effort and DoD's basic science and clinical studies programs to form a combined program to address the coagulopathy of trauma.[13]

In addition to the research efforts described, the Hemorrhage and Resuscitation program and the Forward Surgical and Intensive Critical Care program are expecting to develop capabilities in the following areas: (1) diagnostics and therapeutics for coagulopathy of trauma, (2) methods to modulate inflammatory response, (3) oxygen carrying solutions for prehospital resuscitation and stabilization, (4) next generation hemostatic devices, and others. Collectively, these R&D collaborative efforts hold promise for providing improved methods, drugs, and devices to stop bleeding, restore blood volume, and mitigate the consequences of hemorrhage.

07

CHAPTER 7:

KEY RESEARCH ACCOMPLISHMENTS

The goal of the PCO's EA support mission is to coordinate DoD blast injury research investment and leverage expertise to promote the development of strategies that prevent, mitigate, or treat blast injuries. To inform the EA of accomplishments throughout the blast injury research community, the PCO initiated a data call at the end of FY14 to DoD organizations engaged in blast-related research. The PCO received 168 data call responses from 27 organizations, and summarized those data call responses into the 135 accomplishments below. These accomplishments are organized into the Blast Injury Research Program's three focus areas: Injury Prevention, Acute Treatment, and Reset. Each accomplishment adds to the knowledge base for blast injury research and advances the delivery of effective strategies that prevent blast-related injury or allow injured Service Members to return to duty and maintain an active lifestyle.

Injury Prevention

Medical research to prevent blast injury considers the entire spectrum of potential injuries, ranging from eardrum rupture caused by the blast overpressure (Primary Injury) to illnesses or injuries caused by chemical, biological, or radiological substances (Quinary Injury). The design of prevention systems requires an understanding of the mechanism of injury; thus, significant research efforts are focused on identifying blast injury mechanisms and analyzing vulnerable areas of the body using animal and computational models. Researchers are also collating clinical and operational information in order to determine injury risk and assess PPE performance. Data from this area of research is currently being used to establish safety thresholds for human exposure to blast, enhance diagnostic capabilities, support the design of protection systems, and strengthen guidelines for the safe use of weapon systems. These findings are shared between the military and civilian research and development communities in order to encourage greater use and availability of protective measures against blast events in both sectors.

Mechanisms of Injury

Complications of Blast-related TBI

Researchers in the Naval Medical Research Center (NMRC), sponsored by US Navy Bureau of Medicine and Surgery (BUMED), are engaged in multiple investigations of TBI with or without other concurrent injury (polytrauma), with a particular focus on blast-induced TBI. One set of investigations is exploring the mechanisms by which blast exposure produces TBI, the levels of blast exposure (i.e., magnitude, number, and frequency) that affect the severity of injury, and potential interventions to mitigate the acute, subacute, and/or chronic neurological adverse effects of TBI. A second set of investigations is examining the potentially adverse effects of exposure to environmental stressors associated with aeromedical evacuation (e.g., hypobaria, vibration, noise) on TBI/polytrauma casualties. The third set of investigations, funded by JPC-5/DHP, is evaluating neurocognitive and vestibular data gathered from US military personnel previously exposed to IEDs. Researchers in the Neurotrauma Department at NMRC, in collaboration with clinical and scientific partners (including the WRAIR, USUHS, NINDS, National Institute of Nursing Research, the James J. Peters Department of Veterans Affairs Medical Center, the University of Virginia School of Medicine, and the NICoE) have also initiated a series of studies to develop occupational exposure standards for repeated exposure blast overpressure events. These studies will use both animal and human blast exposure and outcome data, and mathematical analysis of those data, to predict human safe blast exposure limits in terms of blast magnitude, number, frequency, and between-blast latency.

Information relevant to the clinician and researcher will be collected using a variety of neurocognitive, biomarker, and imaging modalities combined with new technologies to objectively measure blast overpressure. These data sets can be merged with health information obtained before and after exposure to provide more accurate pictures of long-term, chronic psychiatric, and comorbid health conditions that may develop following exposure to blast. Another multi-partner study with the Neurotrauma Department at NMRC is building on previous findings that blast overpressure waves may be transmitted into the skull via blood vessels. A rat model is being used to explore the potential role of damage to the cerebral vasculature incurred by either single or multiple blast exposures. Together, this large body of data will assist in the development of objective, clinically relevant cognitive and physical return to duty measures and help establish gold standards that can be used across military branches, assuring that improved methodology will be used to assess Service Members in the acute phase of a blast mTBI.

Estrogen Effects after a Crush Muscle Injury and Acute Exposure to Hypobaric Hypoxia in Warfighters with Blast-related Muscle Injury

A research study sponsored by the Office of the Air Force Surgeon General (OAFSG), the Air Force Medical Support Agency, and conducted in collaboration with University of Nevada, Las Vegas and the 59th Medical Wing, Lackland Air Force Base (AFB), investigated the ability of estrogen and estrogen-like substances to counteract enhanced inflammatory or altered genetic responses induced by hypobaric hypoxia during en-route care. The purpose of this study was to better understand the potential role of hypoxia and the inflammatory responses to crush injury, particularly during en-route care, in which the aeromedical platform maintains a cabin pressure equivalent to an altitude of 8,000 ft. This environment lacks supplemental oxygen systems, which may worsen a patient's injuries via low oxygen content and an enhanced inflammatory response. A novel, non-invasive mouse model of LE muscle crush injury and a hypobaric hypoxia model for LE crush injury at high altitude were developed and validated. These models were used to determine the relationship between pro-inflammatory and anti-inflammatory proteins at altitude in ovarian-intact female (IF), ovariectomized-estradiol-treated (OE) and ovariectomized-placebo treated control (OC) mice. As assessed by histological analysis, IF mice with muscle crush only (i.e., no hypobaric hypoxia) had large clusters of regenerating fibers in the gastrocnemius muscle 96 hours after injury. For IF, OE, and OC mice with hypobaric hypoxic gastrocnemius muscle, muscle regeneration began but inflammatory cells were still present in high numbers 96 hours after injury. At 192 hours after injury, fewer inflammatory cells were present and regenerating fibers were distinct in the muscle of IF and OE mice, but not as much in the muscle of OC mice. Estradiol treatment did not significantly affect the post-injury inflammatory response, but may help promote early muscle regeneration. Cytokine interleukin-1 beta (IL1-β) and cytokine IL-6 in skeletal muscle may have an important role in facilitating and activating the inflammation and regeneration process early after a crush injury. These findings advance our understanding of the impact of hypoxia and inflammatory responses after crush injury and may promote the development of new therapies, such as the administration of estrogen en-route, that expedite recovery after a crush muscle injury and reduce hypoxic effects at altitude.

Prolonged Hypobaria During Aeromedical Evacuation and the Effects on TBI

The University of Cincinnati Medical Center, with sponsorship from the Air Force Medical Service Support Agency and OAFSG, conducted a study of prolonged hypobaria exposure during aeromedical evacuation to determine the long-term effects of prolonged hypobaria on contusion- and explosion-induced TBI. Using a validated TBI rat model, animals were subjected to prolonged hypobaria at different time periods after induced TBI and outcomes were measured via histological, neurochemical, and behavioral assessments.

Rats exposed to six hours of hypobaria at elevations above 8000 ft. of altitude, at six, 24, or 72 hours after either a mild or moderate TBI had worse neurological or neuropathological outcomes than rats that were not exposed to hypobaria. These findings have important implications for operational treatment procedures during aeromedical evacuation. Future studies may investigate how and why hypobaria may worsen outcomes during aeromedical evacuation following TBI combined with hemorrhagic shock.

Application of High-Intensity Focused Ultrasound to the Study of mTBI

Researchers sponsored by the USUHS Center for Neuroscience and Regenerative Medicine (CNRM) used high-intensity focused ultrasound (HIFU) pulse trains as a model for blast exposure in rats to examine the brain's immune response to pressure changes. Though intrinsically of much higher frequency than open-field blast overpressures, HIFU pulse trains can be frequency modulated to produce a radiation pressure that has a similar form to blast overpressure. In this study, 1.5 millihertz HIFU pulse trains of one millisecond duration were applied to intact skulls of mice in vivo. Subsequent histological analyses revealed blood-brain barrier disruption and immune responses including astrocyte reactivity and microglial activation up to 24 hours after HIFU pulsing, patterns that are consistent with findings from other types of blast exposures. HIFU shows promise for the continued identification of some of the biological effects of blast-related, non-impact mTBI in animals.

Experimental TBI in Swine

Researchers from the Toxicology Evaluation Program, US Army Public Health Command (USAPHC), and ADVANCE LLC completed data analysis from a DARPA-sponsored study which examined blast-induced TBI in swine, including functional, behavioral, and pathological outcomes. Swine are good models for studying TBI in humans because the swine cerebral cortex is also gyrencephalic, or highly convoluted, and the ratio of white matter to gray matter is very similar in both species. Explosive detonation was used to produce realistic blast overpressure signatures equivalent to those in theatre. Experimental conditions were controlled to exclude all other injury mechanisms attributed to explosions other than primary blast overpressure. The entire body (including sensory organs) was blast-protected with the exception of the head. A neuropsychological automated test battery evaluated sensory/memory function while a kinematic motion analysis system examined the neurologic function in swine before and up to one week after exposure. The blast-exposed swine had significant memory loss and decreased neurologic function for the first two days following exposure, but function recovered after one week. Sleep disturbances were noted to be temporally similar to the observed functional decrements. Histopathological evidence of injury was mild, yet consistent, with no evidence of neuronal injury or death. The appearance of pathology after one week, when function is recovered, suggests that injured axons may not be a contributor to the observed functional impairments. The current study indicates that swine are a good model for detecting functional and behavioral deficits associated with mTBI, and suggests the need for future research to increase our understanding of the relationship between axonal injury and mTBI.

Rate-Dependent Fracture Modes in Human Femoral Cortical Bone

An accurate understanding of human bone fracture under complex loading scenarios is critical to predicting fracture risk. Cortical bone is subject to complex loading because of inherent multiaxial loading conditions, which are influenced by the anisotropy of the microstructure. However, when determining critical fracture parameters, bone is traditionally idealized as isotropic. In FY14, researchers at USARL, sponsored by the Army Materiel Command (AMC) and the Research, Development, and Engineering Command (RDECOM) investigated a method to examine rate-dependent mode mixity associated with cortical bone crack initiation.

Four-point bend experiments were conducted on cortical femoral bone samples from three human donors, and digital image correlation (DIC) was used to obtain full-field displacement maps at the crack tip during the experiments. An over-deterministic least squares method was used to evaluate Mode I (opening) and Mode II (shear) stress intensity factors (SIFs) for fracture initiation at low, intermediate, and high loading rates. Assuming material anisotropy under dynamic loading, the critical Mode I SIF was approximately 50% lower than fracture toughness. Additionally, critical Mode I and II SIFs had the lowest values at the highest loading rate examined, decreasing to one-third of their values under the low loading rate. Crack growth at the low and intermediate loading rates appeared to be Mode II dominant, and transitioned to mixed-mode at the high loading rate. This study suggests that the conventional assumption of isotropy is a conservative estimate at low and intermediate rates, but overestimates fracture strength at dynamic rates. This analysis will enable the design and evaluation of protection devices that mitigate bone fracture during blast and impact loading. A paper describing this study has been submitted to the *Journal of Fracture Mechanics*.

Temporal Progression of Visual Injury from Blast Exposure

Dr. Brittany Coats from the University of Utah's Department of Mechanical Engineering is conducting research funded by a DHP grant through USAMRMC's CRM Research Program (CRMRP) and a DHA grant through USAMRMC's CRMRP to investigate the temporal progression of eye injury from blast exposure and identify early predictors of visual dysfunction. Two studies comprise Coats' current work on the progression of visual system injury: (1) a retrospective and prospective analysis of Service Members exposed to a blast, and (2) an experimental study using a rat model to evaluate retinal and corneal damage as well as vitreous protein expression. Results from the second study using the rat model indicate that there is an immediate decrease in vision following a low-level blast exposure that remains steady until eight weeks post injury. The blast pressure alone resulted in corneal damage that was not observed until three weeks after exposure. The work from this project has resulted in collaboration with Dr. Barbara Wirostko, Chief Scientific Officer of Jade Therapeutics, Inc., who is also funded by USAMRMC to develop biodegradable biofilms that can be placed in the eye for drug delivery that will prevent or treat corneal damage resulting from blast exposure. The successful completion of these studies will expand our understanding of the time-dependent response of the visual system to blast, enhance current diagnostic capabilities, and lead to the development of time-dependent treatment strategies to mitigate the loss of vision in military personnel.

Effect of Body Orientation to Blast on Risk of Post Concussive Symptoms among Active Duty Service Members

Researchers from DVBIC, sponsored by the NICoE, investigated whether the postconcussive symptoms of active duty Service Members were affected by the body's orientation to a blast wave. Animal models of blast exposure have previously demonstrated that front (head-on) or top blast exposure increases overpressure through the brain more than left, right, or bottom exposure, resulting in greater intercranial pressure. This greater pressure may increase the likelihood of associated neuropathology and symptomatology following a TBI. Study participants were military Service Members with a reported history of one or more blast-related mTBI (n = 1,134); only the most recent mTBI was examined in the study. Participants were between one and 24 months post-injury and symptoms were measured with the Neurobehavioral Symptom Inventory. For individuals with no prior history of blast exposure, a front or top orientation to a blast that resulted in mTBI was associated with increased neurobehavioral symptoms. This study suggests that body orientation to blast may be an important characteristic to consider during clinical assessments to help understand neurobehavioral sequelae from blast-related mTBIs.

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

Researchers from WRNMMC and Madigan Army Medical Center, in conjunction with NIH, DVBIC, the Institutes of Nursing Research, USUHS CNRM, and the West Virginia University Health Sciences Center, investigated the mechanisms of persistent blast-related symptoms in a project sponsored by USUHS CNRM. Researchers examined the expression profiles of RNA transcripts across the genome to determine the role of gene activity in chronic symptoms following blast-TBI. Active duty military personnel with a medical history of blast TBI (n = 19) that occurred during deployment were compared to control participants without TBI (n = 17). Controls were matched to cases on demographic factors including age, gender, and race, and also in diagnoses of sleep disturbance, and symptoms of PTSD and depression. Using expression profiles of transcripts in microarray platforms of peripheral samples of whole blood, lists of significantly differentially expressed genes were generated. There were 34 transcripts in 29 genes that were differentially regulated in blast TBI participants compared to controls. Upregulated genes included epithelial cell transforming sequence and zinc finger proteins, which are necessary for astrocyte differentiation following injury. Tensin-1, which has been implicated in neuronal recovery in preclinical TBI models, was downregulated in blast-TBI participants. Protein ubiquitination genes, such as epidermal growth factor receptor, were also downregulated and identified as the central regulators in the gene network determined by interaction pathway analysis. This study identified a gene-expression pathway of delayed neuronal recovery in military personnel who experienced blast-TBI and/or chronic symptoms. Therapeutic agents that regulate these pathways may provide novel treatments for chronic blast-TBI-related symptoms.

Evaluating Brain Function in Warriors with Blast-related TBI

In a study sponsored by the DoD's CDMRP and CNRM, researchers at the Center for the Study of Traumatic Stress at USUHS conducted a longitudinal study using state-of-the-art measurements of brain structure and function to evaluate the effects of blast-related mTBI in Service Members at WRNMMC and Fort Belvoir Community Hospital. Event-related potentials (ERPs), measures of brain function with high temporal resolution, were obtained in Service Members (n = 137) at baseline and after blast injury. As assessed by ERP measurements, Service Members with mTBI had significant delays in the speed of auditory and visual processing. An unexpected finding was that blast-injured Service Members who screened negative for TBI showed similar processing delays as those diagnosed with TBI. These findings suggest that exposure to blast may lead to altered cerebral function not detected with current clinical assessment methods. Additional studies are needed to determine the implications of these findings on the diagnosis, treatment, and rehabilitation of injured Service Members.

Preliminary Findings of Cortical Thickness Abnormalities in Blast Injured Service Members and Their Relationship to Clinical Findings

Researchers at DVBIC and the SAMMC are using magnetic resonance imaging (MRI) to explore the effect of blast-related TBI on cortical thickness. A recent study included Service Members with blast-related TBI (n = 12) and neurologically healthy controls (n = 11). Anatomic 3 Tesla (3T) MRI scans of all participants were analyzed to produce cortical thickness maps and correlate cortical areas to functional roles. Between-group comparison demonstrated atrophy in several cortical regions of interest in brains exposed to blast TBI, including the superior temporal gyrus and superior frontal gyrus, which are associated with audition and language function, respectively. These results are the first to demonstrate anatomical differences between neurologically healthy brains and those exposed to blast-related TBI.

While cortical abnormalities have been observed in patients with moderate and severe TBI, no one has demonstrated such abnormalities in blast-related mTBI. Further work in larger sample sizes is required, but this research establishes the plausibility of using anatomical analysis to explore the effects of blast TBI. This result informs future studies seeking a more comprehensive understanding of the neurological effects of blast TBI and presents a potential methodology that could inform diagnostic development.

Blast-induced TBI Causes Specific Changes in Brain Circuitry that May Be Associated with PTSD

NICoE sponsored and conducted research to assess neurocircuitry with diffusion tensor imaging (DTI) in patients with blast-induced TBI. The most prominent injuries visualized by DTI in blast-injured brains occurred in fiber tracts of the frontal cortex. Specifically, neuroanatomical damage occurred in tracts connecting regions of the brain implicated in PTSD and other psychological health conditions. Depending on the orientation of the tracts within the brain, the tracts responded differently to either blast or non-blast TBI. These results suggest that PTSD and blast injury-induced alterations may have overlapping neurocircuitry mechanisms.

Connecting Combat-related mTBI with Posttraumatic Stress Disorder Symptoms through Brain Imaging

USUHS CNRM is sponsoring and conducting research to enhance understanding of the relationship between findings on structural and functional brain imaging and symptoms of PTSD. Researchers conducted a nested case-control analysis among a cohort of Service Members who did not meet criteria for PTSD but were willing to complete a comprehensive assessment within two months of returning from combat deployment. Data collection included DTI to assess injury-related white matter structural differences, resting state functional MRI (fMRI) to assess functional connectivity changes, and a range of psychological measures, including the Clinician-Administered PTSD Scale to assess PTSD symptoms. Data from these assessments were compared between Service Members with combat-related mTBI and age- and gender-matched controls. Individuals with mTBI had more degraded white matter integrity, a positive correlation between the white matter microstructure and default mode network (DMN) connectivity, and higher subthreshold PTSD symptoms than controls. Researchers have postulated that mTBI-related white matter structural changes that disrupt function of the DMN may influence the coordination of large scale brain networks during goal directed behavior, which could reinforce PTSD symptoms. These findings support this potential mechanism through which mTBI may alter brain function, and in turn, contribute to PTSD symptoms, and may ultimately enable distinction between symptoms presented by mTBI and PTSD.

Injury Models

Blast-Related Heterotopic Ossification: Animal Model of Combat Relevant Blast and Extremity Injury

Researchers from the Regenerative Medicine Department at NMRC and the Department of Surgery at USUHS have developed a combat-relevant rat model of heterotopic ossification (HO) that incorporates critical elements associated with combat-related blast injury: fracture/crush injury followed by traumatic amputation/repair that involves multi-system trauma, TBI, and the systemic inflammation seen in combat casualties. The development of an animal model of HO is critical to understanding how blast exposure contributes to this unique condition and to developing strategies to reduce the occurrence in the military population confronted with the increased use of IEDs on the battlefield. In addition to developing the blast HO animal model system, this research team has also demonstrated the possible contribution of wound infection, specifically of microbial bioburden (Acinetobacter baumannii and methicillin-resistant Staphylococcus aureus) to the development of HO.

The completion of this work effort and subsequent studies will enable the design and implementation of a future therapeutic clinical trial in which patients and specific tissue sites that are at high risk for HO are identified within 1 week after injury, and subjects will then be treated using targeted local therapies involving local injection or topical application of agents that can effectively prevent or inhibit HO with low associated risk.

Non-Human Primate *(Macaca mulatta)* Poly-trauma Model Development

Researchers sponsored by BUMED are working to develop a clinically translatable primate model of concurrent injury (polytrauma) that simulates multiple injury patterns (e.g. hemorrhagic shock, soft tissue injury, and musculoskeletal injury) and permits acute and long-term assessments of outcomes (e.g. metabolic insult, acute coagulopathy of trauma, and systemic inflammatory response). Because of the frequency of polytrauma, the causation of overall casualty death is multifaceted, and valid models of overall physiological insult are required not only to understand the pathologies to be treated, but also to evaluate potential therapeutic strategies. This results from this study will meet the objectives set forth by DHP's JPC-6 Combat Casualty Care Committee and ONR Force Health Protection Program of developing clinically translatable research models that will serve to identify novel targets for therapeutic interventions and provide a definitive final validation of concept prior to transitioning therapeutics into clinical trials.

Physical, Biological & Physiological Mechanisms of Injury Modeling

The Institute for Soldier Nanotechnologies (ISN), housed at Massachusetts Institute of Technology and sponsored by USARL, focuses on basic research that can lead to the development of new, lighter-weight materials for improved protection from blast, ballistic, and blunt trauma. Researchers also study material failure and human injury due to blast and other forms of mechanical energy to guide the design and formulation of novel protective materials for Service Members. Recent accomplishments include progress in developing validated models of the response of human brain tissue to blast waves and the assessment of the effectiveness and optimization of head protection equipment in mitigating blast-induced TBI. In FY14, researchers at ISN published a paper in the *Proceedings of the National Academy of Sciences* on the development of scaling laws for the effect of blast on animals and humans, concluding that mass scaling fails to capture the brain's mechanical response to blast in mammals, and that human brain vulnerability to blast is higher than in any other mammalian species. Significant progress has also been made in understanding the gel mechanics for synthetic polymer gels that can mimic the mechanical deformation of biological soft tissues optimized for mechanical energy dissipation under impact loading, with implications for protective and wearable materials. The work done by ISN will lead to improved protection for the Service Member against blast and ballistic threats.

Understanding Realistic Blast Impact on Neurons and Tissue Slices: Experimental and Modeling/Simulation Approaches

TBI is a major health issue that is hard to diagnose because it often occurs without signs of external injuries. Although it is known that shock wave exposure causes cell membrane damage, the mechanisms of injury and the role of certain physical parameters (e.g., shock wave velocity, shock pulse duration, or shock pulse shape) are unknown. Also, there is no well-characterized correlation between different physical shock loading mechanisms of injury and pathoanatomic injury, especially blast-induced mechanisms of brain injury. Researchers at USARL developed a novel in vitro indoor experimental system to study the effects of primary explosive blasts on dissociated neurons, using real military explosive charges to more accurately represent battlefield blast exposure. The study examined the effects of a series of pressure waves (30–500 psi) on neuroblastoma and glioma cell co-cultures. A computational model was used to help guide blast experiments.

Pressure traces were generated from the simulation to provide historical data that were otherwise inaccessible from the experiments. Preliminary analysis suggests increased membrane damage and the formation of reactive oxygen species in cells exposed to higher pressures. Furthermore, physical shock loading mechanisms may play a role in the complex biochemical and molecular mechanisms of primary blast-induced brain injury. Information from these ongoing experiments may inform the development of improved, novel in vitro models of mild primary blast-induced TBI, which could lead to better blast protective equipment, diagnosis, and therapy.

Non-uniform Strains in Kolsky Bar Tests on Soft Materials

Researchers at USARL used torsional Kolsky bar tests to perform detailed theoretical and computational studies on the high strain rate properties of soft materials that, similar to brain tissue, have an instantaneous elastic shear modulus on the order of 1–1000 kilopascals and density similar to water. One- and three-dimensional analyses and simulations were conducted to examine the stress and strain states that exist in these materials. These analyses highlighted limitations of previously published results, and demonstrated that correction factors need to be developed to account for inertial effects. This study will help provide better representations of biological soft tissue in computational models, which will improve the ability to predict and prevent blast injuries to the Warfighter.

Intervertebral Disc Model Improvements

Researchers at USARL implemented a transversely isotropic, hyperelastic, constitutive model in the Sandia National Laboratory code SIERRA/Solid Mechanics. This model enables the better representation of fibers in intervertebral discs of the human spine, and could have a critical role in predicting injuries due to burst fractures. Improved representation of the intervertebral discs in finite element (FE) models will enable more accurate modeling of the spine under blast loading conditions, and enhance the prediction of spinal injuries and the development of improved blast protection systems. This model may also potentially be applied to other biological tissues, such as brain tissue and skeletal muscles.

Quantitative Visualization of Human Cortical Bone Mechanical Response: Studies of the Anisotropic Compressive Response and Fracture Behavior as a Function of Loading Rate

Researchers at USARL, sponsored by AMC and RDECOM, studied the effect of loading rate and orientation on the compressive response of wet human femur cortical bone. Cortical bone compression specimens were extracted from three male donors (ages 36, 43, and 50) in the longitudinal and transverse directions, relative to the long axis of the femur. The compressive behavior of the cortical bone was studied at quasi-static, intermediate, and dynamic strain rates using a split-Hopkinson pressure bar to determine the strain rate dependency on the strength of bone. The failure strength of the human cortical bone in two directions was found to be positively correlated with strain rate. The cortical bone material was anisotropic and stronger in the longitudinal direction than the transverse direction, and was also rate dependent in both directions. This study will enable the design and evaluation of protection devices to mitigate bone deformation and injury during blast and impact loading.

Establishment of Lower Leg Collaboration with the Defence Science and Technology Laboratory (DSTL) under the Armor Technology Working Group (ATWG)

In FY14, a working collaboration was established between USARL and the United Kingdom's DSTL under the ATWG. As part of this effort, FE models of the lower legs used to predict injury have been exchanged between institutions, and complementary simulations are underway to establish critical features for accurate injury prediction. This accomplishment will provide additional resources for modeling LE injuries to the Warfighter, and will open a dialogue on the subject between scientists in the US and United Kingdom.

Sensitivity Study on the Finite Element Model of the Lower Leg

Over the past decade, the use of IEDs by enemy forces has increased exposure to UBB events among US combat vehicles and Service Members. Partly as a consequence of this, the lower extremities are one of the most commonly injured body regions among mounted Service Members in theater, necessitating the modeling of damage to the lower limbs to understand, prevent, and mitigate such occurrences. However, both human cadaver models and mechanical test devices have notable drawbacks. Numerical models such as FE models provide a potential solution. Researchers at USARL conducted 64 simulations on a lower leg FE model to understand the sensitivity of predicted injury relative to the choice of material parameters, and found that the prediction of injuries depends strongly on soft tissue properties. The results of this study provided critical feedback needed to make improvements to the FE model. An improved understanding of the importance of material characterization on the predicted response of the human body will help in the interpretation of modeling results and the prediction of injuries. These results will be used to develop improved protection technologies for both mounted and dismounted Warfighters.

Capturing Biological Variability for Injury Prediction in the Lower Leg

USARL has developed a computational framework to facilitate a functional modification of the FE model of the lower leg. This framework allows for key biological measurements to be specified (e.g., femur length, tibia length). A modified digital FE model can then be generated to meet the specified measurements. This approach will enable the development of injury corridors from a single FE model and the representation of multiple Service Members, thus better representing the full Warfighter spectrum. This technology will assist the development of improved blast protection capabilities for Warfighters.

Conversion of Lower Leg Finite Element Model to DYNA3D/ParaDyn

Researchers at USARL translated the SIERRA 3D geometry-based FE model of the lower right leg derived from Zygote medical scans into multiple formats for analysis. The leg was simulated in ParaDyn and DYNA3D to identify potential bone fracture mechanisms in UBB loading, and in LS-DYNA to benchmark against external research. Initial results were identical between ParaDyn and DYNA3D, but both were different from LS-DYNA. An exhaustive study of many computational options identified the element formulation as the major cause of this discrepancy, and once addressed, all solvers predicted the same results. A USARL technological report describing these findings is in progress. This will improve USARL's modeling capabilities by allowing models to be run on a high performance computing platform, which will in turn assist the development of improved blast protection capabilities.

Developing Robust, Predictive UBB Methodology for the Test and Evaluation Community

USARL, sponsored by the RDECOM UBB Program, participated in the development and evaluation of a fast-running model of the lower leg of an ATD. This model will be used in support of Live Fire Test and Evaluation (LFT&E) programs for all combat vehicles that have a requirement to provide UBB protection. USARL also supported an Army Analysis of Alternatives by assessing the vulnerability of current and conceptual combat vehicles to UBB, providing force-level modelers with data appropriate for evaluating alternative combat-vehicle designs with and without UBB protection within the context of a combat scenario. These efforts will aid in the design of combat vehicles with improved survivability for mounted Service Members exposed to UBB events. Additionally, these studies may reduce the overall cost of acquiring survivable vehicles by factoring in survivability early in the design phase, thereby decreasing the amount of testing required.

Matched-Pair Tests Identify Preliminary Injury Assessment Reference Curve for Foot and Ankle Fractures in Under-Body Blast Events

USARL is currently working with experts in injury biomechanics to simulate UBB in a laboratory setting to study LE musculoskeletal injuries resulting from high-rate blast loading. This collaboration is conducted via the ARL's WIAMan PMO and is sponsored by Director Operational Test and Evaluation (DOT&E), ASD(R&E), USAMRMC, and RDECOM. The current Live Fire foot-ankle criteria use post-mortem human surrogate fracture data, but lack the Hybrid III ATD matched-pair testing needed to appropriately assess risk of injury. Using the validated experimental pendulum and custom UBB vertical accelerator device at the Medical College of Wisconsin, USARL developed preliminary foot-ankle injury criteria for calcaneus and/or distal tibia fractures, which, concurrent with FE models, will inform the design of equipment to best prevent musculoskeletal injuries resulting from UBB events. Based on recent research on blast loading rates and Warfighter-specific anthropometry, the new foot-ankle criteria will allow ARL analysts and Service Evaluators to more precisely predict injury using the Hybrid III ATD and the WIAMan Blast ATD. It is anticipated that these capabilities (i.e., new blast-specific ATD and new injury assessment criteria associated with UBB loading rates) will allow vehicle developers to predict blast injuries and incorporate improved survivability features to protect Warfighters in military vehicles.

Blast-related LE Injuries

Researchers at the University of Virginia's Center for Applied Biomechanics and USAARL, sponsored by the DHA RDA Directorate, are conducting research into LE injuries resulting from UBB. To investigate injury and response of vehicle occupants subjected to simulated UBB loads, laboratory experiments were performed to recreate blast-induced intrusions, which included full visualization of the impact event, instrumentation of Post-Mortem-Human-Specimens, and ATDs. Results from these experiments include (1) a human injury risk function for lower extremities at UBB loading rates, (2) updated FE models of the Hybrid III ATD LE and human LE, and (3) the development of a transfer function for potential use with Hybrid III LE experimental results for determination of force levels in the human tibia. These findings suggest that loading rate plays a role in LE fracture location, and that fracture locations move distally as loading rate increases. This research program is helping the injury biomechanics community better understand the mechanisms of LE injury in the blast environment.

Instrumenting Under-Foot Blast Experiments

In collaboration with PEO Soldier and the Aberdeen Test Center, USARL developed and fabricated mannequins for evaluating pelvis protection for the Soldier Protection System (SPS). This new mannequin system has been used to evaluate candidate systems for SPS in under-foot blast experiments. In addition, USARL performed an injury analysis by using computer tomography (CT) scan data of the mannequins in conjunction with the Operational Requirement-based Casualty Assessment injury model to assess the potential of urogenital injuries. Overall, this technology could improve the ability to provide more effective blast protective systems by increasing the understanding of which types of under-foot threats that the SPS can protect against.

Pelvic Model with Multi-Sensory Data Acquisition

Quantitative modeling of sensor data allows researchers to understand the risk of injury following blast events, and contributes to the development of PPE to mitigate those risks. Researchers at Physical Optics Corporation (POC), sponsored by USAARL and USAMRMC, are developing a multisensory pelvic region ATD to predict potential blast injury to the pelvic, abdominal, and genital areas. POC has developed a prototype multi-sensory ATD that measures acceleration, pressure, strain, and temperature associated with blast. Quantitative modeling of the data is being used to refine the system design.

This research is intended to contribute to the development of PPE for the pelvic region against IEDs and dismounted complex blast injury.

Modeling of Head Protection System

Blast load transfer and mitigation for helmets or their foam pads is currently not well understood. The pads between the helmet and head can absorb energy, and the gap that the pad creates between the helmet and head helps prevent or delay contact between the helmet shell and the head during blast. Researchers at USARL are conducting coupled head/suspension/helmet modeling to gain insight on the load transfer to the head and potential injury mechanisms. A material model for composites made of Ultra High Molecular Weight Polyethylene (UHMWPE) was developed to study ballistic loading of the head. Flat plate ballistic limit and back face deformation and delamination characteristics were measured and used in model parameter development. The last two measures are critical in evaluating behind-helmet blunt trauma, an injury that results when the deformed helmet contacts the head. Additionally, a helmet and head model was exercised to investigate the role of pads in the load transfer to the brain, and a computational model for blast loading of head and helmet was developed. A set of material parameters was identified from the parametric/sensitivity analysis of the ballistic experiments. Further material tests can assist in establishing the estimated parameters and in improving the computational model. This investigation will help assess the role of protective equipment in mitigating ballistic load transfer to the head, and will lead to improved blast protection strategies.

Next Generation Under-Body Blast Injury Modeling and Simulation Assessment Capability

Historically, survivability LFT&Es have been conducted on tactical wheeled and combat vehicles using ATDs, injury biomechanics criteria, and data analysis standards developed by the automotive crash safety community. While the best technology available was used in these analyses, none of these tools were developed to assess the types of injuries experienced under the military conditions of UBB loading. OSD, through DOT&E, initiated a project to develop the next generation of injury assessment capability for UBB through the WIAMan PMO at USARL. ASD(R&E), USAMRMC, and RDECOM are also sponsors. The project includes biomechanics testing to assess human response, as well as injury modes and limits, which can be used to design and develop the injury assessment capability. This injury assessment capability will be applied to a new robust, biofidelic anthropomorphic test device (ATD). The WIAMan PMO is using modeling and simulation extensively to aid in the design of the new ATD. The modeling and simulation team is creating both component (e.g., leg, pelvis, lumbar, and head and neck) and full-body test predictions. The initial analysis has focused on highlighting ATD design strengths and risks, and assessing material selection sensitivities. Preliminary results from the component and full ATD simulations have already lead to design improvements in the WIAMan ATD tech demonstrator. The production WIAMan ATD (and the associated modeling and simulation capability) will allow vehicle developers to predict blast injuries and incorporate improved survivability features to protect Service Members in military vehicles.

Risk Assessment and Surveillance

Sensors to Detect Injurious Head Exposures

Researchers at the USAARL sponsored by the USAMRMC, are evaluating currently available environmental sensors for feasibility of use in military training environments. These sensors are designed to characterize potentially injurious head exposures, and were first tested in a controlled laboratory environment to (1) evaluate sensor performance in controlled laboratory exposures to blunt impact and indirect loading, and (2) quantify changes to impact protection, dynamic retention, or mass properties of the worn Advanced Combat Helmet (ACH). Laboratory testing is critical to understanding sensor capabilities and limitations prior to fielding. Environmental sensors were tested on a guided, free fall drop tower for blunt impacts and a custom mini-sled for inertial loading.

None of the environmental sensors degraded the blunt impact performance of the ACH. Only one sensor, which was mounted in the side of the helmet, provided usable data in the inertial loading tests, and the data correlated well with the reference acceleration data ($\varphi > 0.86$). This sensor was also one of only two sensors to provide time trace data during the blunt impact tests; again the side-mounted sensor data correlated well ($\varphi > 0.92$) with reference acceleration data. Five sensors were selected for further testing in military training environments.

The Blast Gauge to Record Overpressure

The US Army's PM SPIE Program Office is sponsoring and conducting R&D supporting the Blast Gauge, which is a set of small, lightweight sensors that record blast overpressure. Blast Gauge sensor technology is placed on the top of the non-firing shoulder, near the middle of the chest, and on the back of the helmet retention system. The goal of the Blast Gauge is to gather data to determine a correlation between blast overpressure and mTBI or other injuries. Overpressure data recorded by the Blast Gauge is categorized into one of three mTBI risk levels (i.e., green, amber or red) for potential referral for medical evaluation. Additionally, soldiers can check their overpressure exposure level at any time using a button press. Blast Gauge data are downloaded in theater and provided to the JTAPIC Program for analysis and correlation with Service Member medical records to determine the effect of blast overpressure on health outcomes.

Assessed Injury Risk from Blast Exposures for the XM104 Non-lethal Bursting Hand Grenade

Investigators at the USAPHC performed a quantitative risk assessment of the blast produced by the XM104 Non-Lethal Bursting Hand Grenade. The XM104 Grenade uses an explosive charge to produce a bright flash and loud report to disorient individuals to facilitate dispersal or easier apprehension, and is intended for use in confined spaces such as room clearing. Data collected during tests conducted by the US Navy at Naval Sea Systems Command Dahlgren were analyzed using Blast Overpressure-Health Hazard Assessment (BOP-HHA) v 2.0 software developed by USAMRMC. The BOP-HHA software helps characterize occupational exposures sustained by personnel firing weapons or detonating explosive devices and is the primary method used by the USAPHC to assess injury risk from the non-auditory component of blasts. This risk assessment of the grenades provided hazard severity and probability estimates for two firing conditions that helped the US Navy make evidence-based decisions about how this weapon should be employed. The results of this test will aid in developing a standard operating procedure for the use of the XM104 Non-Lethal Bursting Grenade that will reduce injury risk to the Warfighter/operator and to ancillary personnel in the vicinity when these weapons are deployed.

Developing an Improved Understanding of Blast Injuries Through Physiological and Behavioral Measures

The Blast Exposure Accelerated Sensor Transition (BEAST) program, a project performed at USUHS and sponsored by 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 carried out in animal models, while human data are generally limited to self-reporting and lack objective information about blast characteristics (e.g., intensity, duration) and effects following multiple, cumulative exposures. Previously, DARPA's Blast Gauge program resulted in the production of a small, lightweight environmental dosimeter device that monitors physical impacts of exposure to an explosive blast. The device is designed for flexible mounting on a combat helmet or tactical device. The Blast Gauge device captures environmental event data to develop a 3D recreation of the blast and potentially help identify Service Members with significant exposures. The BEAST program supports medical studies using Blast Gauge devices and has completed development of a web-based tool to store, organize, analyze, and visualize Blast Gauge recordings.

Researchers have also established a data collection plan for cognitive testing in clinical studies, and finalized approvals to commence clinical studies on physiological and behavioral measures correlated to blast exposure. This research will contribute to the TBI and PTSD knowledge base for improved treatment, and develop enhanced understanding of blast events to mitigate exposure and improve training procedures.

The Generation II Helmet Sensor (GEN II HS)

The US Army's PM SPIE program office is sponsoring and conducting research for development of the GEN II HS, which the program office began issuing to deployers in the first quarter of FY12. Mounted internally to existing combat helmets, the GEN II HS records and stores linear acceleration and angular rotation data for detection and quantification of exposure to blast impulses and impacts. Data gathered and downloaded in-theater by the GEN II HS will be analyzed by the JTAPIC Program to determine risk of TBI for potential medical evaluation referral and population-level analysis. The ultimate goal of GEN II HS R&D is to create a body of knowledge about kinetic events to support the Army medical community's research on mTBI. The GEN II HS program will aid the Army Medical Community in establishing a correlation between head motion and Service Member mTBI.

The Neuropsychological Symptom Inventory (NSI) is a Measure of Symptomatology and Accurately Validates Symptom Severity in the mTBI Population

Researchers at NICoE evaluated the efficacy of the NSI at assessing clinical changes in TBI patients participating in their intensive four-week interdisciplinary and holistic program. The NSI is used by the program to measure persistent symptoms associated with combat- and mission-related TBI and comorbid psychological health conditions. Prior to this study, the NSI had been used as an evaluative measure of a patient's condition at just one time point. In the current study, the NSI was a reliable indicator of response to treatment that could be used throughout the outpatient program to document changes in clinical symptoms in a military population. Additionally, NICoE validated the different NSI scoring modalities used when applying this assessment tool. Regardless of the modality used, the results were the same. These findings suggest that the NSI may be a valuable tool in objectively assessing benefits of treatment programs for patients with mTBI and comorbid psychological health conditions.

Influence of the Severity and Location of Bodily Injuries on Post-concussive and Combat Stress Symptom Reporting after Military-related Concurrent Mild Traumatic Brain Injuries and Polytrauma

Sponsored by NICoE, DVBIC researchers examined the influence of location and severity of bodily injuries on symptom reporting after mTBI to assess how bodily injuries might be associated with TBI symptoms. Participants were US military Service Members who sustained an uncomplicated mTBI with concurrent bodily injuries and were evaluated at two military medical centers (n = 579). Bodily injury severity was quantified using a modified Injury Severity Score (ISSmod). Participants completed the NSI and the PTSD Checklist-Civilian Version (PCL-C), on average, 2.5 months post-injury. There was a significant negative association between ISSmod scores and NSI and PCL-C total scores. Bodily injury severity was inversely related to TBI symptom reporting in this sample. Possible reasons for this include underreporting of symptoms, increased peer support, disruption of fear conditioning because of acute morphine use, or delayed expression of symptoms. These findings may help inform diagnostic procedures, particularly in individuals with significant bodily injury and delayed expression of TBI symptoms.

Factor Analysis of Persistent Post-Concussive Symptoms Within a Military Sample with Blast Exposure

Researchers at DVBIC at the Hunter Holmes McGuire VA Medical Center in Richmond, Virginia and Virginia Commonwealth University, sponsored by DVBIC, sought to determine the factor structure of persistent postconcussive syndrome (PCS) symptoms in a blast-exposed military sample.

Participants (*n* = 181) were Service Members and Veterans with at least one significant exposure to blast during deployment within the two years prior to study enrollment. Participants completed a battery of psychological tests and questionnaires: the Rivermead Postconcussion Questionnaire, PTSD Symptom Checklist-Civilian, Center for Epidemiological Studies Depression Scale, Sensory Organization Test, Paced Auditory Serial Addition Test, California Verbal Learning Test, and Delis-Kaplan Executive Function System subtests. Factor analysis was used to extract latent components in the data set, and demonstrated that PCS is characterized by four factors: emotional, cognitive, visual, and vestibular. All factors were associated with scores on the questionnaires and symptom inventories; visual and vestibular factors were also associated with balance performance. There was no significant association between the cognitive factor and neuropsychological performance or between a history of mTBI and factor scores. The analysis supports a four factor model of PCS symptomology, but does not necessarily relate the symptoms to mTBI. The study identifies four types of distress associated with a diagnosis of PCS. It also indicates that PCS development may be independent of factors associated with mTBI. This research contributes to a knowledge base that will inform how mTBI patients are triaged and cared for.

A Multisite Study of the Relationships Between Blast Exposures and Symptom Reporting in a Post-deployment Active Duty Military Population with mTBI

DVBIC researchers from SAMMC, WRNMMC, the National Medical Center San Antonio, Camp Pendleton, and DVBIC Headquarters sponsored by NICoE examined the effects of cumulative blast exposures (that did or did not result in TBI) on later postconcussive and posttraumatic symptom reporting after sustaining a mTBI. Service Members who sustained a mTBI (*n* = 573) were divided into four groups by number of blast exposures (1, 2, 3, and 4–10) and were compared to each other and to a non-blast control group. The NSI and PCL-C measured postconcussive and PTSD symptoms, respectively. Total NSI scores differed significantly, and the number of reported postconcussive symptoms increased with the number of blast exposures. Total NSI scores were significantly higher for the 3- and 4–10-blast groups than for the 1- and 2-blast groups, with effect sizes ranging from small to moderate. After controlling for PTSD symptoms using the PCL-C total score, NSI total score differences remained between the 4–10-blast group and the 1- and 2-blast groups, but were less pronounced. Analyses of NSI subscale scores using PCL-C scores as a covariate revealed significant between-blast group differences on cognitive, sensory, and somatic, but not affective symptoms. Regression analyses revealed that cumulative blast exposures accounted for a small but significant amount of the variance in total NSI scores (4.8%) and total PCL-C scores (2.3%). Among Service Members exposed to blast, postconcussion symptom reporting increased as a function of cumulative blast exposures. This work demonstrates that reports of postconcussive symptoms increase with cumulative blast exposures. These findings advance knowledge of the clinical implications of blast exposure and its effect on the manifestation of mTBI, and may help determine the relationship between cumulative blast exposures, symptom reporting, and neuropathological changes.

Factors Influencing Postconcussion and Posttraumatic Stress Symptom Reporting Following Military-related Concurrent Polytrauma and TBI

This study, sponsored by DoD and CNRM at USUHS, aimed to identify factors that predict or are associated with high endorsement of postconcussion and posttraumatic stress symptoms following military-related TBI. Participants were Service Members who sustained a mild to moderate TBI and had been evaluated by DVBIC at one of six military medical centers (*n* = 1,600). Twenty-two factors, including demographic, injury circumstances/severity, treatment/evaluation, and psychological/physical variables were examined.

Four factors were statistically and meaningfully associated with clinically elevated postconcussion symptoms: low bodily injury severity, posttraumatic stress, depression, and military operation where wounded. The combination of depression and posttraumatic stress symptoms accounted for the vast majority of unique variance (41.5%) and were strongly associated with, and predictive of, clinically elevated postconcussion symptoms. Five factors were statistically and meaningfully associated with clinically elevated posttraumatic stress symptoms: low bodily injury severity, depression, a longer time from injury to evaluation, military operation where wounded, and current auditory deficits. Depression alone accounted for the vast majority of unique variance (60.0%) and was strongly associated with, and predictive of, clinically elevated posttraumatic stress symptoms. There was a very clear, strong, and clinically meaningful association between depression, posttraumatic stress, and postconcussion symptoms in this sample. Brain injury severity, however, was not associated with symptom reporting following TBI. This study advances understanding of factors that are predictive of, or associated with postconcussion and posttraumatic stress symptoms and may help identify individuals who are at high risk for these conditions.

Predictors of Mental Health Outcomes of mTBI: DoD Concussion Clinics in Afghanistan

Sponsored by BUMED under the Wounded, Ill, and Injured (WII)/Psychological Health/TBI Program, NHRC examined acute symptoms reported after combat-related mTBI (e.g., loss of consciousness [LOC], altered mental status [AMS], amnesia, and headaches) and evaluated whether these acute symptoms are associated with long-term mental health outcomes such as PTSD and PCS. Medical records of Service Members who were diagnosed with combat-related mTBI and received treatment in concussion clinics in Afghanistan were reviewed using the Expeditionary Medical Encounter Database (EMED) and outpatient medical records. Medical records were reviewed for mTBI circumstances, characteristics, acute symptoms, and long-term mental diagnoses. Of the 1,089 Service Members assessed, 75% reported AMS, 46% reported LOC, and 43% reported amnesia. The most common symptoms reported were headache (84%) and nausea (43%), and 21% reported concurrent mental health symptoms. At final disposition, 25% of Service Members continued to report headaches. Within one year after injury, mental health diagnoses reported were PTSD (20%), PCS (12%), and depression (8%). After adjusting for mTBI symptoms, concurrent mental health symptoms were associated with PTSD, PCS, and depression, while retained headache was associated with PTSD and PCS. Initial poor concentration was associated with PTSD. A better understanding of acute symptoms after mTBI and whether these symptoms are associated with long-term mental health outcomes may lead to early identification of Service Members who require closer monitoring for the onset of these mental health outcomes. Future studies will include comparisons with non-concussion clinic cohorts on mental health and career performance outcomes.

Longitudinal Interactions of Pain and Posttraumatic Stress Disorder Symptoms in US Military Service Members Following Blast Exposure

Researchers at the Hunter Holmes McGuire Veterans Affairs Medical Center, DVBIC, and Virginia Commonwealth University conducted a longitudinal study to examine the interaction of PTSD and pain symptoms over time. Sponsored by DVBIC, this study recruited military personnel with combat-related blast exposure and co-occurring pain and PTSD symptoms (n = 209). Autoregressive cross-lagged analysis was used to examine longitudinal associations between self-reported pain and PTSD symptoms over a one-year period. PTSD symptoms had a particularly strong influence on subsequent pain symptoms. The best-fitting covariate model indicated that, across all points in the assessment period, pain and PTSD were significantly associated with one another.

The relationship between pain and PTSD symptoms was related to older age, race, and TBI characteristics. These findings further the understanding of complex injuries among military personnel and highlight the need for comprehensive assessment and rehabilitation efforts addressing the interdependence of pain and co-occurring mental health conditions. Further studies are needed to evaluate why these variables are connected and how they impact current models of care.

Predictors of Neurocognitive Syndromes in Combat Veterans

Researchers from USUHS's CNRM, NIH, and WRNMMC, with sponsorship from USUHS, conducted a prospective cohort study to identify Service Members at risk for developing disabling neurocognitive syndromes upon return from deployment. Service Members were evaluated at baseline and again at three, six, and 12 months after return from deployment to assess for new-onset PTSD, depression, or PCS. Analysis identified four baseline measurements that were associated with the development of PTSD or PCS in the year after returning from deployment: right superior longitudinal fasciculus tract volume on MRI; resting state connectivity between the right amygdala and left superior temporal gyrus (BA41/42) on fMRI; and single nucleotide polymorphisms in the genes coding myelin basic protein and brain derived neurotrophic factor. This study suggests that genetic markers and functional neuroimaging may help to identify Service Members at risk for developing disabling neurocognitive syndromes in the ensuing year. Further work is needed to define the value of these and other predictors, and to develop a risk stratification model that could enable targeted, timely intervention to prevent progression of symptoms.

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

In a study sponsored by NICoE, researchers at the TBI Clinic at WRNMMC examined the unique contributions of resilience, brain injury severity, and blast exposure on neuropsychological outcome following TBI. Participants were US Service Members who had sustained a mild to severe TBI (n = 60). When analyzed by TBI severity, there were medium effect sizes on 37.5% of neurocognitive and 41.0% of neurobehavioral measures. When analyzed by blast exposure (blast vs non-blast), there were medium effect sizes on 34.4% of neurocognitive and 25.6% of neurobehavioral measures. When analyzed by resilience (low vs high), there were medium to large effect sizes on 68.8% of neurocognitive measures, and medium to very large effect sizes on 89.7% of neurobehavioral measures. Using a series of linear regression analyses, resilience was a significant predictor for 53.8% of neurobehavioral measures (accounting for 10–63% of variance), and 34.4% of neurocognitive measures (8–15% of variance). These findings advance knowledge of specific risk factors for neuropsychological outcome following TBI. Blast and TBI severity were rarely significant predictors of outcome measures. Resilience was strongly associated with neuropsychological outcome following TBI, but blast exposure and TBI severity were not. More information on the role of resilience on outcome following TBI can inform its utility as an indicator for clinical care.

Army Study to Assess Risk and Resilience in Service Members (Army STARRS)

Researchers from USUHS, are working in collaboration with the University of California, San Diego (UCSD); Harvard Medical School; the University of Michigan; and scientists from the Army and the National Institute of Mental Health (NIMH) on the Army STARRS, the largest and most comprehensive study of military suicide ever undertaken. This study sponsored by the Army and NIMH, with Co-PIs at USUHS and UCSD, aims to enhance our understanding of the relationship between TBI and suicidality among Service Members. In FY14, major findings of the study were reported: there were high rates of self-reported mTBI in Army Personnel, with 75% of first TBI having occurred before entering the military; after adjusting for prior mental disorders, TBI increased the risk for developing several mental disorders;

TBI was associated with increased likelihood of suicidal ideation; and depression and suicidal ideation were associated with dysfunction in self-evaluative systems. Other findings relevant to TBI and blast injury included the observation that data collected in the first week of Army service can predict elevated risk for many outcomes such as violent crime perpetration and victimization, TBI, and suicidality in the next two to three years; the risk factors for suicide, accidents, and homicides are very similar; that nearly one in five Service Members reported sustaining a concussion while deployed to Afghanistan; and that TBI acquired during deployment is associated with more than a doubling of risk for PTSD post-redeployment. Army STARRS has helped to identify TBI-related risk factors for suicidality, which will assist in potentially decreasing suicide in Service Members returning from deployment.

TBI and Risk of Dementia in Older Veterans

DoD and CNRM at USUHS sponsored a retrospective cohort study to examine the association between TBI and risk of dementia in Veterans. Participants were US Veterans aged 55 years or older who had at least one inpatient or outpatient visit during both the baseline (2000–2003) and follow-up (2003–2012) periods and did not have a dementia diagnosis at baseline (n = 188,764). TBI and dementia diagnoses were determined using International Classification of Diseases, Ninth Revision (ICD-9) codes in electronic medical records. Fine-Gray proportional hazards models were used to determine whether TBI was associated with greater risk of incident dementia, accounting for the competing risk of death and adjusting for demographics, medical comorbidities, and psychiatric disorders. During the nine-year follow-up period, 16% of those with TBI and 10% of those without TBI developed dementia. There was evidence of an additive association between TBI and other conditions on risk of dementia. After accounting for competing risks and potential confounders, TBI in older Veterans was associated with a 60% increase in the risk of developing dementia over nine years. These findings suggest that TBI in older Veterans may predispose toward development of symptomatic dementia and raise concern about the potential long-term consequences of TBI in younger Veterans and civilians.

Characterization and Comparison of Combat-related Injuries in Women During Operation Iraqi Freedom and Operation Enduring Freedom

Researchers from NHRC, sponsored by BUMED, characterized combat-related injuries in 835 Service Women, comparing injury profiles between OIF and OEF and examining the likelihood of leaving active duty after injury. Women currently represent 15% of forces deployed in OIF and OEF. Although restricted from combat roles prior to 2013, women in the Armed Services have evolved from supportive occupations in previous conflicts to complex roles that now directly relate to combat operations. Detailed medical, injury profile, injury severity, and tactical data for each female casualty was obtained from NHRC's EMED. The women studied were nearly equally divided between OIF and OEF, the majority were in the Army (85%) and over 90% of the injuries were due to blasts. While the majority of the injuries were in the mild category, over half of the injured women had multiple injuries, which commonly occurs with blast exposure. The injury patterns did differ between OIF and OEF, with head and spine injuries more prevalent in OEF and open wounds more common in OIF. Seventy-eight percent of the injured women still remained in the military with active status. With women beginning to take a more active role in combat operations, it is important to examine injury patterns to determine if there are gender differences in combat injuries or if these injuries affect military women in unique ways. The results of this study and other planned work can inform and prepare health care providers to care for injured military women in ongoing and future conflicts.

Four-year Health Outcomes of Combat Amputee and Limb Salvage (LS) Patients

Combat amputee and LS patients injured in Iraq and Afghanistan conflicts present new challenges for DoD and VA providers. Researchers from NHRC, San Diego VA Healthcare System and UCSD, and the Naval Medical Center San Diego, with funding from the BUMED WII Program, tracked the health outcomes and medical care of combat amputee and LS patients over the first four years post-injury to assess the likelihood of these outcomes and provide preventative interventions. Records from NHRC's EMED were reviewed to identify patients with lower limb combat injuries sustained in Iraq and Afghanistan during the period 2001–2008. Health outcomes data were obtained from DoD and VA databases. The cohort consisted of 625 extremity-injured casualties and was followed for 48 months postinjury. The cohort comprised 440 early amputees (EA; < 90 days postinjury), 78 late amputees (LA; > 90 days postinjury), and 107 LS patients (no amputation). EAs had reduced likelihood of pain, musculoskeletal, osteoarthritis, mood disorders, substance abuse, PTSD, anxiety, and adjustment disorders than LA or LS patients, but had increased odds of osteoporosis. LAs had higher rates of osteoarthritis, lumbago, and late effects of injury diagnoses than EA or LS patients. The prevalence of PTSD generally increased after the first year postinjury. Obesity, substance abuse, or tobacco disorders were prevalent in 20–50% of all patients. Further, EAs had reduced prevalence of secondary complications and psychological disorders than LA or LS, particularly during the first several years. These findings may help inform treatment decisions and health care planning to reduce adverse outcomes associated with early amputation. Continuation studies are need to monitor the development of musculoskeletal disease and associated health care needs.

Surveillance and Epidemiologic Analysis of Injuries among Deployed and Non-deployed Soldiers

Investigators at the Injury Prevention Program, USAPHC, conduct injury surveillance for the Army across the Army Force Generation cycle. The surveillance function of the Injury Prevention Program includes the systematic collection, analysis, interpretation, and dissemination of injury data for the deployed and non-deployed Army populations. The Program's deployment injury surveillance activities use a combination of medical, air evacuation, casualty, and safety data to identify battle and non-battle injuries that result in death, in-theater hospitalization, or medical air evacuation from the theater. Annual surveillance reports describe injuries within the context of all medical encounters (both illness- and injury-related) to assess the overall impact of injuries in the Army. These reports also include the injury rates, trends, types, anatomic distributions, and causes for battle and non-battle injuries. Injuries that result from the effects of blast, such as TBI, urogenital injuries, and amputations, are included in these annual reports. The Injury Prevention Program also represented the USAPHC on USAMEDCOM's Complex Battle Injury Task Force and Council of Colonels, an effort which focused on identifying and implementing best practices to reduce the mortality and morbidity of blast-related injuries from IEDs. During FY14, the Injury Prevention Program provided updates to the Action Officer for the Complex Battle Injury Task Force at the Office of the Surgeon General on the number of battle-related amputations that were air evacuated from Central Command. A unique objective of the Program's deployment injury surveillance is to identify and classify the causes of non-battle injury that may be preventable; this is the only activity in DoD that routinely reports specific injury causes for non-battle injuries that did not require hospitalization.

Accomplishments from the Injury Prevention Program contribute to the identification of risk factors for injuries (both battle and non-battle injuries) and support programs to reduce the injury risk among Service Members.

Real-time Casualty Analysis, Trending, and Reporting for the Department of Defense Leadership

Researchers at NHRC have been tracking each casualty incurred in overseas contingency operations since the beginning of OIF and OEF in October 2001. Over time, this capability has evolved into the EMED, which includes all Service Members injured during deployment. Each casualty is identified within seven days of injury, coded by diagnoses and Injury Severity Score (ISS), and entered into the EMED for analysis. Based on the EMED, NHRC provides a weekly analysis of all combat casualties occurring during overseas contingency operations to the JTAPIC PMO. For each wounded Service Member, the medical data obtained from 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. These detailed clinical profiles are then made available to JTAPIC Program partners for additional analysis in which tactical data (e.g., weapon type, explosive weight, and strike point) are matched to the injury profiles. Since January 2014, NHRC has provided DoD with 2,290 detailed clinical profiles. NHRC also provides a trend report on sentinel injury types to the JTAPIC Program, the Headquarters Marine Corps, the US Marine Corps (USMC) System Command, BUMED, and EACE. In addition, 3,248 casualty medical records were reviewed by NHRC medical staff for compliance with directives associated with the BECIR for current theater operations. The availability of weekly data on combat casualties has allowed the intelligence community greater capability to monitor the evolution of insurgency threats. This permitted more rapid responses to identify and defeat new and emerging threats, directly reducing casualty rates. The trend reports have alerted DoD leadership to spikes in occurrence rates, allowing DoD to focus investigations on trends that represent a meaningful change in the running average of injury types over time. This has saved precious resources and has optimized investigations about what is causing a rise in injury risk to Service Members in theater. Additionally, the mapping of medical to tactical data allows developers to design targeted modifications to improve vehicles and PPE, thereby reducing the frequency and severity of injury. By precisely targeting the necessary body coverage, the minimum amount/weight of PPE is worn. Furthermore, recent enhancements in up-armoring of the Mine Resistant Ambush Protected (MRAP) and Stryker vehicle families have been implemented as a function of this reporting.

Protective Equipment

Understanding Blast-Mitigation Behavior of Materials

Researchers at USARL tested how different materials and the coupling of materials affects blast mitigation. Forty different materials were assessed, including fabric, rigid materials, and biological surrogates. A 1.5-pound pentolite sphere was used to ensure a repeatable blast environment, and a synthetic gelatin witness block captured the blast loading transferred through each material type. Preliminary results suggest that, in addition to traditional approaches for mitigating adverse shock waves with variations in mass, there might be other material designs and mechanisms that could be balanced with ballistic requirements to give more robust protection capability. Future work will focus on the directional response of material combinations exposed to blast and the feasibility of exploiting classical material impedance in the context of mass- and volume-efficient armor solutions. These results have the potential to enable more informed and explicit material design considerations for protective equipment as it relates to both ballistic and blast events.

Tensile Properties of Dyneema SK76 Single Fibers at Multiple Loading Rates Using a Direct Gripping Method

UHMWPE fibers such as Dyneema and Spectra are increasingly used in lightweight armor applications because they have higher tensile strength and lower density than aramid fibers, such as Kevlar and Twaron. UHMWPE fibers are difficult to grip using typical adhesive methods because of their low surface energy, and the ability to grip UHMWPE fibers is limited to small diameter fibers that are difficult to identify and extract from a yarn. Researchers at USARL, sponsored by AMC and RDECOM, used a direct gripping method to study multiple gauge lengths of Dyneema SK76 at three different strain rates (low, intermediate, and high strain) to better understand the effect of defect distribution along a fiber on its tensile response. The tensile strength of the Dyneema SK76 fiber increased as strain rate increased from low to intermediate, but did not increase further at the high strain rate. The failure strength of the fiber did not depend on the gauge length of the sample, indicating that the distribution of any critical defects in the fiber is at an effective spacing of less than five millimeters. These results can be used in single-fiber-based constitutive models for numerical simulation of impact events on soft armor. This study will enable the design of novel vehicle and soft armor with UHMWPE to protect against IED threats and novel bullets.

Tensile Response and the Associated Post-Yield Heating of Polycarbonate

Polycarbonate (PC) is a thermoplastic polymer that can be easily molded and thermoformed. The mechanical properties of polymers are dependent upon two key factors: the rate of deformation and the material temperature. Researchers from USARL, sponsored by AMC and RDECOM, studied the tensile behavior of PC as a function of strain rate. DIC was used to measure localized plastic strain concentration, and a thermal (infrared) camera was used to measure the temperature change in the specimen at quasi-static (~10-3/s) and intermediate (103/s) strain rates. The material experienced non-uniform heating as high as 50–70°C, and had a significant rate-sensitive mechanical response. As the specimens yielded and plastically deformed, temperature in the specimen increased due to plastic work, with the largest temperature increase concentrated in the necked region of the specimen. The results of this study will enable the design and evaluation of transparent protection shields to mitigate injury during blast and impact loading.

Reduction and Prevention of Eye Injuries

Researchers at the US Army Product Manager Soldier Protective Equipment (PM SPE) and USAPHC are studying prevention and reduction of eye injury through the issue and use of ballistic fragmentation protective eyewear as part of the Military Combat Eye Protection (MCEP) program. Injury data and Service Member feedback has been gathered and analyzed to improve the protection of the eyewear and reduce eye injuries since the implementation of MCEP in 2004. During this period, the number of eyewear injuries has decreased, while the number of attacks and blast events seen by the Warfighter continued to increase. Results also indicate that eyewear injuries seen from these events were less severe (reduced on the Abbreviated Injury Scale [AIS] by one or more) than those who were not wearing eye protection. These findings directly influenced requirements for the next generation of eye protection: the Transition Combat Eye Protection (CEP), a subsystem of the SPS.

Blast-related Eye Injuries

A growing body of laboratory evidence suggests that the primary blast wave may cause significant ocular as well as higher visual system injuries. Researchers from USAARL are engaged in two studies addressing blast-related eye injuries. In the first study, research performed and sponsored by USAARL evaluated the performance of currently available protective eyewear with respect to primary blast wave.

Pressure wave dynamics were measured at the cornea using an instrumented headform fitted with different protective eyewear. Eyewear protection coefficients were calculated using peak and integrated pressure readings. With respect to frontal blast, eyeglasses were slightly effective and goggles provided the greatest frontal blast protection. For oblique blast angles, eyeglasses potentiated the blast wave by creating higher pressures at the cornea. Furthermore, some eyewear produced oscillations in the time-pressure recordings indicative of increased turbulence that could lead to increased shear forces on ocular tissue. These findings suggest that current eye protection, designed to reduce secondary and tertiary blast injuries, may provide insufficient protection against primary blast waves.

In a second study, USAARL researchers sponsored by USAMRMC assessed the frequency and types of visual field (VF) defects seen at different testing stages following non-blast and blast-induced mTBI. The researchers performed a retrospective review of 500 electronic health records for military personnel sustaining mTBI during deployment. Of the records examined, 166 patients were tested with both confrontation VF and 30-2 Humphrey Matrix Frequency Doubling Technology (FDT) perimetry. Key study results were: (1) scatter defects (48%) were the most predominant deficits in both blast and non-blast mTBI injuries and over post-injury test timeframes; (2) confrontation VF was a poor qualitative predictor of VF defect; (3) a profound decrease in VF sensitivity was noted in comparison to previously reported FDT normative data, and (4) a significant trend of decreasing VF defects was seen over time, indicating the potential usage of FDT as a visual biomarker for monitoring mTBI recovery. These findings, described in a recently-accepted journal manuscript *(Military Medicine)*, highlight the importance of performing threshold perimeter testing in those who have suffered an mTBI or concussion-like event.

The Army Hearing Program (AHP), USAPHC: Updating Noise Standards

The AHP/USAPHC supported and engaged in a number of activities aimed at mitigating injury risk associated with impulse noise. The AHP undertook activities addressing MILSTD 1474D, the Military design standard and Army damage risk medical criterion for impulse noise, which is outdated and restricts Army acceptance of more powerful weaponry due to overly conservative impulse noise exposure limits. In one effort, the AHP participated in the DoD Working Group charged with updating MILSTD 1474D. The AHP also proposed a new, innovative, interim impulse noise damage risk medical criterion with the aim of developing a better medical risk assessment tool. The AHP developed and proposed a technique using Artificial Test Fixtures (manikins with built-in noise sensors) fitted with Army-approved hearing protection to measure actual exposure levels to weapon noise. 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.

The AHP USAPHC: Providing Safe Use Restrictions for Weapons, and Improving PPE for Impulse Noise Protection and Improving Data Taking Skills

To reduce the risk of noise-induced hearing loss for Service Members, the AHP provided safe use restrictions for new weapons and weapon systems introduced into the Army's arsenal. In FY14, the AHP conducted health hazard assessments for approximately 25 new materiel items and provided risk mitigation requirements, including PPE requirements and use restrictions, for safe use of the new materiel. The AHP 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 is 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 USARL's Human Research and Engineering Directorate to develop a new hearing protection module for the AHAAH model. This new 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 also consulted on several PPE projects that are characterizing requirements for impulse noise attenuation, speech intelligibility, and auditory situational awareness. The AHP consulted with the acquisition and auditory research community to define the hearing protection technology capabilities that best meet Service Members' needs; today's devices are significantly better than those of the previous generation and are more accepted for use by Service Members. Additionally, the AHP consulted with PEO Soldier to make the TCAPS of hearing protection a Program of Record in FY14. TCAPS is a device that offers hearing protection while maintaining situational awareness by attenuating loud sounds without attenuating quieter sounds. AHP is working to acquire a second radio-less version of the TCAPS.

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

Researchers at the University of Nebraska at Lincoln, sponsored by the US Army PM SPE, have demonstrated that the addition of a maxillofacial system, consisting of a mandible and visor, to a combat helmet increases ballistic and blunt impact protection and also mitigates blast waves. These results enabled the provision of 100 maxillofacial systems for Contiguous US (CONUS) training and potential Outside the CONUS utilization. Unit feedback was considered to refine the system and influence requirements for the next generation of head protection: the Integrated Head Protection System (IHPS), a subsystem of the SPS. Development of the IHPS also has provided technology that is potentially backwards compatible with the currently fielded ACH. Future work by PM SPE includes exploring the operability of maxillofacial protection upgrade kits for the ACH.

Advanced Combat Helmet and its Suspension System

Researchers at the University of Nebraska at Lincoln, with support from the US Army PM SPE, sought additional characterization of the ballistic, non-ballistic, and blast protection provided by the ACH and its pad suspension system. Researchers sought to better understand the correlation between material properties and dynamic impact response in order to develop an improved helmet suspension system capable of demonstrating increased protection. Results demonstrated that blast waves captured under the helmet were disrupted by the ACH suspension system pads in their approved configuration. Information gathered from this research has directly influenced requirements for the next generation of head protection, specifically the IHPS, which a subsystem of the SPS.

Enhanced Combat Helmet and its Suspension System

The US Army's PM SPIE Program Office has sponsored and conducted R&D supporting the Enhanced Combat Helmet (ECH) and its pad suspension system, which has been used in combat since 2014. The ECH represents a protective improvement over the ACH. The ECH meets penetration probability requirements for fragments traveling 35% faster than the level required for the ACH, which is an 83% increase in kinetic energy resistance with no increase in helmet weight. This improvement equips Service Members with enhanced fragmentation protection, thereby reducing blast-induced injuries. In addition, the ECH uses the same suspension system design as the ACH and thus retains the same blast-propagation disruption capabilities. The development of the ECH influenced requirements for the IHPS, a subsystem of the SPS. The IHPS base shell will provide the same level of blast-fragmentation protection as the ECH with a 5% reduction in helmet weight.

Advanced Honeycomb-core Helmet Pads for TBI Mitigation, Phase III

In FY14, TIAX, LLC, sponsored by the US Army Natick Soldier Research, Development, and Engineering Center (NSRDEC), advanced the development of an ACH pad system that uses thermoplastic elastomer materials formed into multi-layer honeycomb-like structures. This development of the improved ACH pad system was performed under a US Army Rapid Innovation Fund contract that followed up an earlier SBIR Phase II effort. The objective of the project was to reduce head injuries associated with tertiary blast by doubling the level of blunt impact protection provided by the current ACH pads. In this 18-month effort, a new helmet pad was designed, mechanically tested, and evaluated with users for acceptance. The design was optimized for a combination of comfort, weight, and blunt impact performance at 14 feet per second. The average and peak accelerations were significantly below those of the current-issue Team Wendy pad sets. However, as assessed by blunt impact tests, the system could not keep accelerations below 150 Gs for every impact location and every helmet size. Five hundred pad sets were fabricated for delivery to the Army for future evaluation. TIAX, LLC also explored large scale production processes for both low-rate and high-rate production, prepared a finalized cost evaluation and timeline for Army procurement, and identified a committed set of industrial manufacturing partners. Currently, TIAX, LLC has partnered with a prime vendor whose head-borne system is being tested and evaluated as a part of the SPS Program of Record managed by PEO Soldier. Should the prime vendor's design emerge as the winning solution, these improved helmet pads or an enhanced variant could be issued to Service Members as early as mid-FY16, increasing protection of Warfighters from blast-induced injury.

ONR Efforts on Blast Mitigation to Prevent mTBI

Reductions of intracranial pressures and accelerations following blast events will contribute to reductions in mTBI episodes. ONR is funding researchers at the Naval Surface Warfare Center Carderock Division (NSWCCD) on the use of special polymer coatings over advanced ballistic-fiber shells, which demonstrate capability for reducing intracranial pressures and accelerations in surrogate full-size, head-neck manikins. The polymer coatings also improve the ballistic resistance of the helmet shells, which are produced under a cooperative research and development agreement (CRADA) between the US Navy and DuPont Corporation, without increasing its weight over the baseline ACH. In parallel, researchers at the Naval Research Laboratory are developing new strategies for the deflection and attenuation of blast waves incident on helmets. Hollow (deformable) ceramic microspheres are dispersed in a rate-sensitive polymer matrix, which enables large reductions in bulk modulus of the polyurea composite with minimal changes in its shear modulus. Since brain tissue is weak in shear, the polymer composite affords protection, and due to its viscoelastic nature, the polymer response increases in efficiency with the severity of the blast impact. An irreversible energy dissipation mechanism is provided by the thin-walled spheres, to further attenuate the blast wave amplitude. Preliminary bomb tests show approximately 30% reductions in acceleration and deflection, while the ballistic performance of the helmet is maintained. Researchers from Clemson University are supporting these efforts with advanced finite element computer modeling and simulation. The results are closely aligned with the results from experimental testing, demonstrating a predictive capability that will assist in pinpointing the best areas and thicknesses to employ the polymer to protect specific vulnerable brain regions and help identify families of polymers and fillers for improved performance. Currently, DuPont has fabricated 32 helmets shells that will have different coating thicknesses and special fillers, based on three coating formulations. Further tests on the helmets will be performed in FY15 to reveal the most effective coating in reducing mTBI risk.

ONR Efforts on Blast Barriers to Protect the Warfighter against Internal Injury

Researchers at NSWCCD, funded by ONR, are developing blast barriers that would mitigate blast exposure in the 1000 to 3000 Hz range, which has been associated with greatly increased pulmonary injury. Blast suppression by targeting the most critical frequencies has not been considered along this line previously. A technology, using perforated plate suppressive shield technology as a base, was identified. The technology includes incorporation of different fabric components, emphasizing the use of cross-over points for strain reflections, for cost and availability. A Navy Invention disclosure was submitted, "Blast Frequency Control Barrier", Navy Case no. 102,194. This technology is useful for barriers and around check and inspection points for protecting against pulmonary and perhaps mTBI injury.

Pelvic Protection System (PPS)

The US Army's PM SPIE Program Office is sponsoring and conducting development of a PPS. The PPS is designed to provide protection against ground-based IED blast events. The PPS is a two-tier system, consisting of the Protective Under-Garment (PUG) and the Protective Outer-Garment (POG). The PUG is worn next to the skin, and provides protection of the pelvis, femoral arteries, and lower abdominal organs from blast or fragmentation events. 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 (IOTV). Ongoing PPS assessment and development by PM SPIE includes incorporation of Service Member feedback, and improving user acceptability and rate of wear. These efforts have informed requirements for the next generation SPS.

Soldier Protection System

The US Army's PM SPIE Program Office has secured approval for initiation of the SPS program into the Engineering and Manufacturing Development phase. The SPS program is developing an integrated suite of body armor systems (torso, extremity, head, and pelvic protection) against injury threats associated with blunt trauma, ballistic projectiles, fragmentation munitions, IEDs, and indirect fire. The SPS system will be an integrated, modular, scalable, and mission-tailorable protective system that improves upon the current Interceptor Body Armor (IBA).

Interceptor Body Armor Blast Injury Mitigation

The US Army's PM SPIE Technical Management Division is sponsoring and conducting research to study body armor protection to help understand the level to which Service Members are protected by body armor systems when impacted by rifle and fragmentation threats. Components of the IBA system, which include the Soldier Plate Carrier System and the IOTV combined with the employment of hard armor protective inserts, have demonstrated mitigation of blast injuries in theater. Research includes sensor development and testing to measure static and dynamic loading characteristics (e.g., force, pressure, and time response). These efforts could help characterize and correlate the ballistic performance of the system to actual injuries. PM SPIE has also directed and sponsored the Aberdeen Test Center to conduct free field and shock tube blast overpressure tests of the Soldier Protective System.

Forensic Analysis of Recovered Personnel Protective Equipment

The PM SPIE Technical Management Directorate (TMD) sponsors and performs forensic analysis on recovered personnel protective equipment in support of the JTAPIC PMO. PM SPIE TMD 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 USAMEDCOM. PM SPIE TMD analyzes PPE, events, and injuries to dismounted Warfighters to determine prevention and mitigation strategies. These analyses are provided to Service materiel developers to influence protective equipment design, tactics, techniques and procedures.

The analysis played significant role in terms of modification of PPE's performance specifications, which has resulted in better protection and survivability for soldiers in battle field.

Project Manager Mine Resistant Ambush Protected (MRAP) Supplemental Blast Kit

The development of the Supplemental Blast Kit was sponsored by the US Army, the Army MRAP Program Office and developed along with Navistar Defense to provide greater protection against IEDs for the MaxxPro family of MRAP vehicles. In 2007, the Base MaxxPro MRAP was developed and rapidly fielded to theater. The program had Live Fire oversight by the DOT&E and was tested at Aberdeen Test Center in Aberdeen, MD. Subsequent to that fielding, a MaxxPro Survivability Upgrade (MSU) was developed and installed in theater to further increase the under-body protection of the MaxxPro vehicles. In FY14, the MRAP Program Office took an additional step and developed and tested the Supplemental Blast Kit (SBK), which is an addition to the proven performance of the MSU kit. The purpose of the SBK is to strengthen the driver's and commander's floor as well as the sidewall of the vehicle against a hull breach from UBB. These R&D efforts will increase blast protection and survivability for Service Members.

Education and Research Resources

Guidance for Civilian First Responders

Recent mass shooting and IED incidents reveal that some traditional practices of first responders need to be realigned and enhanced to improve survivability of shooting victims and the safety of first responders caring for them. USARL served on the PPE subgroup of the White House Office of Science & Technology Policy IED working group, and co-authored the "First Responder Guidance for Managing Incidents with IEDs and/or Mass Shootings", which was published in FY14. This multidisciplinary, Federal first responder guidance translated evidence-based strategies from the US military's vast experience in responding to and managing casualties from IEDs and mass shootings, and its significant investment in combat casualty care research, into the civilian first responder environment. Additionally, civilian best practices and lessons learned from similar incidents, both in the US and abroad, were incorporated into this guidance. This work has potential to improve the survivability of the civilian population to terrorist events by better preparing first responders.

Worldwide Ocular Trauma Video-Teleconference

VCE hosts a monthly worldwide ocular trauma video-teleconference (VTC) which links theater ophthalmologists with subsequent providers across the full continuum of care, as well as with agencies and organizations that influence casualty care along that continuum. Presentations are made on active patient cases to provide real-time care coordination, leading to improved care. PEO Soldier and NSRDEC representatives participate in the monthly VTCs to address issues related to ocular injuries and approved CEP. While current anti-ballistic material is highly effective against fragments and shrapnel, its effectiveness against blast is less clear. As a result of this interaction, NSRDEC is more actively studying blast-protection characteristics of current CEP. One of the outcomes of the ongoing discussion on use of rigid eye shields (i.e., Fox shields) in the theater was an article co-authored by VCE personnel, "The use of rigid eye shields (Fox shields) at the point of injury for ocular trauma in Afghanistan," which was published in the *Journal of Trauma and Acute Care Surgery* in 2014. This retrospective observational study reviewed the DoD Trauma Registry and analyzed 157 eye injuries in Afghanistan from 2010–2012, and found that that only 39% applied eye shields, and that 80% of shields were applied incorrectly. The authors recommended that corrective efforts should include enhanced educational emphasis and increased shield availability. Improved care for wounded Service Members and improved CEP for use by Service Members in combat theater will lead to better outcomes and reduce the severity of injury.

Launch of Tissue Data Acquisition Protocol (BIOBANK)

In FY14, the Tissue and Data Acquisition Protocol (TDAP) developed by the Surgical Critical Care Initiative (SC2i) and sponsored by USUHS was launched at Emory University, and both Duke University and WRNMMC will follow suit in FY15. The annual expected enrollment is 500, across all sites. The TDAP is the standardized method for collecting all clinical data and biological specimens from properly identified patients and healthy volunteers in support of all research initiatives approved by the SC2i. General procedures covered under this protocol will include clinical sample acquisition, processing and storage, clinical data capture and storage, and the sharing of data and samples amongst SC2i partners. The protocol design recognizes that critical injury and illness, civilian or military, are frequently a multisystem event. A central, standardized means of enrolling patients that allows for post hoc analysis and sample distribution not only permits multiple observational trials to be served with the same patient population, but also, through standardized processes, allows for insights to be leveraged across observational platforms and for interdependent influences of various injury patterns to be recognized and clarified. TDAP will also reduce associated time and costs for repeating the protocol/institutional review board procedures with each SC2i project, maximize specimen retrieval, and standardize sampling and analysis procedures across the entire SC2i. Through the use of a standardized TDAP, the SC2i leverages resources in the most efficient use to maximize productivity for all critical care focus projects the program will model.

NICoE's Continuity Management Tool (NCMT) for Capturing TBI and Psychological Health Related Data

In FY14, researchers at NICoE completed the initial release of the NICoE's NCMT, a cutting-edge, large-scale informatics database that supports the collection, standardization, and analysis of TBI clinical data. The NCMT project leverages multiple existing DHA Health information technology (IT) assets to produce a cost-effective database system capable of collecting millions of clinical data points from various data sources. NICoE has also been working closely with USUHS to develop policies and procedures that will allow for the input of data from the NCMT to the CNRM database. CNRM's data can be shared with the Federal Interagency Traumatic Brain Injury Research (FITBIR) database and used by scientists and researchers across the country to accelerate work in the TBI/psychological health realm. This collaborative process of collecting data will produce a comprehensive database that will allow for external query and analysis. Additionally, the NCMT model has generated significant interest in DoD and has been noted as the model on which to implement IT solutions; HCE currently follows the NCMT model to design and develop their own tracking tools.

Acute Treatment

Research in the area of Acute Treatment is intended to improve survivability and mitigate long-term disability for Service Members suffering from the full spectrum of injuries following blast events. Collaborations between DoD and partners in the FDA, academia, and the private sector are developing new diagnostic tools, interventions for hemorrhage control and resuscitation, strategies to mitigate wound infection, and tools and guidelines for visual injuries. This section demonstrates how the research community is employing models and simulations, evaluating patient data, and building consensus among expert panels to address the spectrum of blast-related 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

Injury Treatment (Detection): Infrascanner

With sponsorship from Marine Corps Systems Command (MCSC) and ONR through SBIR, InfraScan Inc. has developed a hand-held screening device that uses near-infrared (NIR) technology to screen patients for intracranial bleeding. Three clinical studies were conducted to evaluate the performance of the NIR-based device. In the first clinical study, the device detected 90% of extra-axial, 88.9% of intra-axial and 93.3% of non-surgical hematomas (less than 25 milliliters [mL]). The NIR device correctly identified 88% of all participants in the second clinical study who had a clinically significant brain hematoma, and 90.7% of all participants who did not. In the third clinical study, the Infrascanner correctly identified 93% of children who did not have intracranial hemorrhage, and of all the negative identifications for clinically important TBI, none were false. These findings indicate that a NIR-based portable device can reliably screen for intracranial hematomas that are superficial and of a size likely to be of clinical importance. The NIR device cannot replace CT scanning in the diagnosis of TBI, but the device might be useful to supplement clinical information used to triage TBI patients, and in situations in which CT scanning is not readily available. MCSC is currently fielding the Infrascanner to the fleet.

Diffusion Tensor Imaging Reveals Acute Subcortical Changes After Mild Blast-induced TBI

Diagnosing mild blast-induced TBI poses special challenges due to overlapping symptomatology with other neuropsychiatric conditions and the lack of objective outcome measures. CNRM at USUHS is sponsoring and conducting preclinical research on rat models to investigate the potential of DTI to provide a clinically relevant differential diagnosis of mild blast-induced TBI. While no significant blast-related effects could be detected in brains fixed at 42 days after exposure to mild blast overpressures, significant blast-related effects were detected for several subcortical structures using samples fixed two hours after exposure. Significant differences between singly- and multiply-injured rats were identified in the thalamus, but not the hippocampus. These findings provide valuable information about the capabilities and limitations of DTI as tool to better understand the pathobiology associated with mild blast exposure.

Psychometric Investigation of the Abbreviated Concussion Symptom Inventory in a Sample of US Marines Returning from Combat

There is a lack of studies investigating the psychometric properties of the many screening tools that were rapidly developed to assess TBIs during OIF and OEF. This has a presented a challenge to properly screening for mTBI post-deployment. In a study published in *Applied Neuropsychology Adult,* researchers at Center for Rehabilitation Sciences Research (CRSR) at USUHS performed a psychometric investigation of the Abbreviated Concussion Symptom Inventory (ACSI)—a dichotomously scored, 11-item symptom checklist of postconcussive symptoms associated with mTBI. A total of 1,435 Marines took the ACSI within two to eight weeks of their return from combat deployments to Afghanistan; total scores were found to significantly differentiate between the different levels of head injury experienced by the Marines. Overall, the study supports the use of the ASCI in research settings requiring a psychometrically reliable measure of postconcussion symptoms.

New Technologies for Assessing Brain Injury (Science Technology Objectives Demonstration: Brain in Combat, Program Management)

Researchers at AnthroTronix, Inc. and BrainScope® Company, Inc., sponsored by Army and Navy through USAMRMC Military Operational Medicine Research Program (MOMRP), are developing technologies for the detection and assessment of brain injury.

The Defense Automated Neurobehavioral Assessment (DANA), AnthroTronix is a mobile software application that includes a comprehensive set of assessment tools designed to assist forward medics by enabling earlier and more accurate detection of neurocognitive impairment from concussion, combat-related psychological distress, and/or deployment-related exhaustion. The software also provides tools to aid psychologists and healthcare professionals in diagnosis. The Ahead® 100 device (BrainScope) uses a patient's electroencephalograph to provide an interpretation of the structural condition of the brain following head injury. Ahead® 100 is indicated for use as an adjunct to standard clinical practice to aid in the evaluation of patients who are being considered for a head CT scan. Both the DANA and the Ahead® 100 received FDA clearance in 2014 and are improving the detection and assessment of brain injury in the prehospital and hospital settings.

National Capital Consortium TBI Neuroimaging Core Project

NICoE is sponsoring the National Capital Consortium TBI Neuroimaging Core Project to develop a state-of-the-art imaging center for assessing TBI and to close existing knowledge gaps in the relationships between TBI imaging findings and clinical outcomes. To date, advanced neuroimaging data have been acquired from over 900 TBI patients and 50 controls. In a systematic review of the imaging data, punctuate T2 hyperintense regions were the most common brain lesion in patients with mTBI. Results suggest that high resolution 3T MRI may show lesions not detectable on routine clinical scans. Developing this large database may allow scans from a single individual to be compared to population-average templates derived from healthy controls to identify abnormalities and subcategories of disease. Findings from the MRI image analysis have informed the development of CPGs for imaging TBI in the military that were adopted by DCoE, DVBIC, and VA.

Magnetoencephalography (MEG) Provides Real-time Assessment of Neurologic Function and Stimulus Processing

NICoE is supporting and conducting research to identify characteristics unique to patients with mTBI. MEG measures magnetic fields generated by neuronal activity and is used to identify active areas of the brain. Unlike other imaging techniques, MEG provides very specific locations of brain activity in real time. Preliminary results identify a previously undescribed neural pathway involved in visual sensory processing; the activity of the pathway differed between patients with mTBI and comorbid PTSD and patients with mTBI only. The activity of this pathway observed by MEG could potentially provide an objective biomarker for comorbid PTSD. The study results also suggest a mechanism of action for certain PTSD symptoms and lay the groundwork for future research studies aimed at potential treatments to correct the underlying dysfunction, ultimately improving patient care.

The Community Balance and Mobility Scale: Detecting Impairments in Military Service Members with Comorbid Mild TBI and Psychological Health Conditions

Researchers at NICoE are examining the utility of the Community Balance and Mobility Scale (CB&M) for assessing the functional balance and mobility of active-duty Service Members with comorbid mTBI/psychological health conditions. In this sample, the CB&M was compared to other common measures such as gait speed, the Activities-specific Balance Confidence scale, and Functional Gait Assessment (FGA) to determine its appropriateness for identifying those with mTBI/psychological health conditions. The mTBI/psychological health conditions group (n = 8) performed significantly worse than the control group (n = 8) across all measures except the FGA. Diagnostic abilities of all objective measures ranged from fair to excellent for classifying participants with mTBI/psychological health conditions from healthy controls.

However, the largest group differences in effect size and the highest discriminate ability were observed with the CB&M. Thus, the CB&M may have slightly higher sensitivity and specificity than other measures of balance in Service Members with mTBI/psychological health conditions. This study is ongoing, and further answers may be apparent with a larger sample size.

Therapies for TBI-related Symptoms

Hyperbaric Oxygen for Blast-related Post-concussion Syndrome: Three-month Outcomes

Investigators at the Hunter Holmes McGuire Veterans Affairs Medical Center, including members of DVBIC, VA's Physical Medicine and Rehabilitation Programs, and Virginia Commonwealth University, conducted a randomized, double blind, sham-controlled study to test the efficacy of hyperbaric oxygen (HBO2) chamber treatment for PCS resulting from TBI. Marines with history of blast-related TBI and PCS were enrolled (*n* = 61). Participants received 40 compressions lasting 60-minute (min) over a 10 week-period in a HBO2 chamber under one of three conditions at 2.0 atmospheres absolute (ATA): (1) a surface air pressure equivalent of 10.5% oxygen (sham); (2) a 1.5 ATA oxygen exposure equivalent of 75% oxygen; and (3) a 2.0 ATA oxygen exposure equivalent of 100% oxygen. The primary outcome measure was the Rivermead Post-Concussion Questionnaire 16 (RPQ-16) score, collected before treatment and three months after compression. There was no interaction between performance on the RPQ-16, test time, and the intervention groups (sham, 1.5 ATA, 2.0 ATA). Performance on the RPQ-16 did not improve in participants who received the HBO2 treatment. The findings demonstrated that hyperbaric oxygen treatment does not have a clinical effect compared to sham controls on reducing symptomatic, cognitive, or behavioral sequelae associated with combat-related PCS up to three months post-compression.

Epigenetic Rescue of Injury Circuits in Brain Following Blast-induced TBI

Researchers at the USUHS Department of Anatomy, Physiology, and Genetics, sponsored by the Henry M. Jackson Foundation for Military Medicine, are investigating epigenetic changes induced by blast exposure. The researchers specifically studied whether epigenetic-regulated proinflammatory processes regulate the sensitivity of the amygdala and other parts of the frontolimbic circuit in the blast-exposed brain. Rats were subjected to blast injury and the following effects were measured: (1) epigenetic changes in the amygdala 24 hours after blast; (2) changes in the levels of a proinflammatory DNA-binding protein in activated immune cells in the amygdala; and (3) the ability of the histone deacetylase (HDAC) inhibitor suberanilohydroxamic acid (SAHA; also known as Vorinostat and marketed as Zolinza®) to reverse the clinical and molecular effects of blast exposure. Levels of HDAC two, four, and six significantly increased 24 hours after blast exposure. In the amygdala, levels of [pSer337]NFκB-p1-5/p50 and [pSER32/36] IκBα, both pro-inflammatory DNA binding proteins, significantly increased. Finally, SAHA treatment blocked HDAC activities in the brain, and pretreatment with SAHA reversed blast-induced sensory deficits 24 hours after blast. These findings support the possibility of using a safe, FDA-approved drug from the class of HDAC inhibitors to rescue cognitive impairment following blast exposure.

Hemorrhage Control and Resuscitation

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 (NAMRU-SA), sponsored by DHA's Research, Development, and Acquisitions Directorate and MCSC, are evaluating the performance of four different commercially available, FDA-approved truncal/junctional hemorrhage control devices which 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® in simulated operational conditions. Device stability during transfer and the effect of altitude on the devices (as some are pneumatic) were examined. The junctional tourniquets designs that employed pneumatic pressure applicators provided greater stability than the purely mechanical designs during simulated patient transfers; however, the amount of pressure exerted by the pneumatic devices varied with altitude. 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 mannequin model with a circulatory system and heat pump. Performance metrics include application times, contact pressures, and most importantly, whether the device is able to achieve and maintain occlusion. The results from this study will be used to inform decision-making to best equip the US Service Member.

Wound Stasis System (WSS) for Acute Treatment of Blast Injuries

To date, no effective battlefield treatment exists for hemorrhage-inducing wounds that are not accessible by combat medics for traditional treatments, like direct compression. As a result, rapid and uncontrolled blood loss often leads to death before transport from the battlefield to a surgical setting can occur. Working with Arsenal Medical, Inc., DARPA created the WSS program to pursue a stabilizing, non-compressible, intra-abdominal hemorrhage treatment that would keep injured Service Members alive until they could be transported to a surgical setting for definitive treatment. The program has developed a self-expanding, polyurethane-based foam technology to address this prehospital treatment challenge. DARPA examined the dose dependence of survival using a lethal, closed-cavity, swine liver injury model. An optimum dose of 100 mL (based on efficacy and safety), plus fluid resuscitation, resulted in a survival rate of 72% at three hours versus 8% for controls that received fluid resuscitation only. To translate this swine dose to a human dose, DARPA conducted a novel, multi-center, translational research study that demonstrated an optimal foam dose of 65 mL in humans. The WSS addresses the critical need to mitigate uncontrolled blood loss and has the potential to improve Service Member survivability.

Evaluation of Extremity Tourniquets

Policy decisions implemented in 2005 to broaden tourniquet use by US military personnel in tactical combat casualty care 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 US Warfighter is equipped with the most effective, reliable, and operationally sound tourniquet designs. Researchers at the NAMRU-SA sponsored by the US Army Medical Materiel Development Activity (USAMMDA) and MCSC, recently evaluated thirteen extremity tourniquet designs to examine their performance, safety, and operational characteristics. The tourniquets were first tested for basic physical parameters and to determine their compatibility with the individual first aid kit. The tourniquets also underwent safety and efficacy testing in the hands of non-medical participants using a HapMed instrumented mannequin limbs in simulated field conditions, including limited visibility and soaked with a blood simulant. Performance metrics included application time and contact pressure, as well as end-user feedback.

Of the thirteen designs tested, seven tourniquets met all initial performance criteria and will undergo further evaluations using a SynDaver™ Synthetic Human and during self-applications. The data generated in this controlled and repeatable test environment will assist in the selection of the most effective, reliable, and operationally sound tourniquet designs for use in combat casualty care.

Evaluation of Compression Bandages

Researchers at NAMRU-SA, sponsored by MCSC, evaluated the performance of compression bandages at ameliorating hemorrhage. Though often rudimentary in form, compression bandages are vital for hemorrhage control in battlefield trauma care, and can also protect the wound from contaminants that may cause infection or renew bleeding. A recent summit of medical experts and medical industry representatives established four consensus parameters on which to characterize and evaluate both simple and complex compression bandage systems: pressure, layers, components, and elastic properties. A range of compression bandages was evaluated based on the accepted parameters and during applications to two different mannequin systems, the HapMed and the SynDaver™ Synthetic Human. Compressional bandages with mechanical pressure applicators were more effective, without compromising blood flow to the rest of the extremity. The outcome of the study provided critical data regarding compression bandage use and efficacy. The results will aid the DoD selection process and improve quality of care in combat environments.

Launch of Massive Transfusion Protocol (Clinical Trial)

Massive transfusion in a short period of time has numerous potential complications. Determining whether a massive transfusion is required is often difficult for the bedside clinician. Doing so requires codification and at times, synthesis of many complex data points that vary over time. Because massive transfusions are resource-intensive and expensive, they require quick and accurate decision-making. Researchers sponsored by USUHS and supported by SC2i partners at Emory University began work in FY14 on a massive transfusion protocol (MTP) Smartphone application to prospectively evaluate accuracy in predicting the need for massive transfusion in critically injured patients. As such, this clinical scenario is uniquely suited for a Clinical Decisions Support (CDS) application, since accuracy and efficiency can result in improved patient outcomes and cost savings to the institution. The MTP Smartphone application allows for the accurate prediction of massive transfusion based on a sophisticated statistical model created using admission variables readily available to the clinician at the bedside. As part of a damage control resuscitation paradigm, MTPs have improved patient outcomes in multiple military and civilian series. The coordination of a MTP is a complex and multi-disciplinary effort that requires both significant oversight as well as the use of a large amount of human and blood bank resources. This protocol application has the potential to make this process less complex and more accurate, thereby improving outcomes for Service Members. Additionally, is estimated that the MTP app will reduce the number of patients receiving a massive transfusion by 15%, saving resources and time.

Wound Infection Mitigation

Deployment of Invasive Fungal Infection Clinical Decision Support Tool

With sponsorship from USUHS, a CDS tool for invasive fungal wound infections (IFI) was developed and validated collaboratively with the Infectious Disease Clinical Research Program—Trauma Infectious Disease Outcomes Study Group, and subsequently deployed within the Joint Trauma System for use in-theatre. This CDS tool can assist clinicians in controlling and preventing trauma-related IFIs in injured Service Members.

Cranial Implant Surface Modification to Reduce Infection Rates

Combat-related blast injuries to the head may require prosthetic reconstruction of the skull.

Electron beam melting is an additive manufacturing technique that is currently used to produce customized titanium-6 aluminum-4 vanadium (Ti6Al4V) cranial implants for wounded warfighters who require cranioplasty procedures. Titanium cranial implant devices often fail due to postoperative infections that require removal of the implant and additional cranioplasty procedures for treatment. Researchers at NAMRU-SA, with sponsorship from BUMED, are working to optimize the surface characteristics of EBM Ti6Al4V cranial implants to reduce the incidence of postoperative infection. Various surface modification procedures have been perfected for EBM Ti6Al4V and have led to the development of unique combinations of surface topography, roughness, surface chemistry, wettability, and surface energy. Studies to compare bacterial adherence and biofilm formation on the various electron beam melting Ti6Al4V surfaces are currently underway. It is hypothesized that, of the various modified surfaces, the mirror finish surface will exhibit a significant reduction in bacterial adhesion and biofilm growth. Modification of titanium cranial implant surfaces may reduce the need for replacing cranial implants and the negative sequelae that result from multiple surgeries.

Nano-fibrous Bioactive Wound Dressing

BUMED is sponsoring a research project developing an electrospun biomimetic bioactive wound healing dressing comprised of a nano-fibrous scaffold based on extracellular matrix morphology and composition. This innovative wound dressing could be used to as a physical barrier to keep wounds free of debris while actively improving the healing process. To fabricate this dressing, a nano-fibrous polymeric scaffold capable of sustained release of platelet-derived growth factor (PDGF) will be created. Bioactive PDGF stimulates chemotaxis, proliferation, and new gene expression in neutrophils, monocytes, macrophages, and fibroblasts, which are cell types that are essential for tissue repair. PDGF also inhibits the differentiation of fibroblasts into myofibroblasts, which may reduce scar formation. The development of this wound dressing could significantly improve wound healing rates and reduce operative trauma and complications. In FY14, NAMRU-SA successfully fabricated two composite nano-fibrous scaffolds containing Chitosan, Polyethylene oxide, and Fibrinogen. The scaffolds have an average fiber diameter < 500 nm, and have shown good antimicrobial properties. Additionally, the scaffolds demonstrated multi-phase degradation profiles, which make these scaffolds a prime candidate for loading PDGF. Studies are on-going to incorporate the growth factor into these composite scaffolds.

Cost-savings Analysis

Researchers sponsored by USUHS have estimated the cost-savings associated with using the SC2i-developed WounDx tool. WounDx, a validated CDS tool, is designed to guide the timing of wound closure in traumatic wounds as well as to establish criteria for both the number and frequency of wound debridement, on a wound-specific basis. Conclusions from the analysis suggest national cost-savings of $1.09 billion annually. Applied retrospectively to OIF and OEF, the cost-savings to MHS would have been around $470 million. A second analysis looking at the operational benefits of using a MTP during a conventional war scenario points to substantial logistical savings: ~30,000 red blood cell units, ~17,000 fresh-frozen plasma units, ~1,500 apheresis platelet units, ~12,000 cryoprecipitate units, as well as 34,500 gallons of aviation fuel (i.e. avoidable resupply missions). Additional analyses for SC2i-funded initiatives (e.g., Severe TBI, Monitoring of Physiologic Decompensation) will be developed and released in FY15. Employing CDS tools such as WounDx has the potential to bring spiraling costs under control through personalized, biology-driven care that provides the appropriate care at the appropriate time, rather than over-treating on the premise that more treatment itself will lead to better outcomes.

Visual Injuries

Acute Treatment—Publications and Presentations on Blast-Related Visual Injuries

VCE ophthalmologists, in collaboration with other civilian, military, and academic ophthalmologists, co-authored a paper, "Ocular Blast Injuries in Mass-Casualty Incidents: The Marathon Bombing in Boston, Massachusetts, and the Fertilizer Plant Explosion in West, Texas," published in *Ophthalmology*. Lessons learned from studying these two incidents included: the importance of staying away from windows during disasters; the benefit of rigid eye shields by first responders; the significance of reliable communications during disasters; deepening the ophthalmology call algorithm; the impact of visual incapacitation from loss of spectacles; the need to improve early detection of ocular injuries in emergency departments; and the importance of integrating ophthalmology services into trauma teams as well as maintaining a voice in hospital-wide and community-based disaster planning. VCE continues to provide expert guidance for the screening, assessment, referral, management and rehabilitation of eye and visual dysfunctions associated with blast exposure, concussion, and TBI and inform eye care providers in DoD and VA on best practices and cogent clinical decisions.

Fox Shield (Rigid Eye Shield) in the Improved First Aid Kit-II

Proper first aid following eye injury is critical, because applying pressure to a ruptured or perforated eye can cause further irreparable damage to the eye. The Fox rigid eye shield is a small a protective cover for an injured eye designed to curve away from the eye so no contact or pressure is applied, thus preventing further injury. The Fox rigid eye shield has now been included in the Improved First Aid Kit 2 (IFAK2), a personal first aid kit that is issued to every deployed Service Member since November 2013. In collaboration with VCE and USAPHC, the Tri-Service Vision Conservation and Readiness Program (TSVCR) supported efforts that reinforce proper use of the Fox rigid eye shield and promote awareness of its inclusion in the IFAK2. Materials developed by TSVCR included guidelines on use and informational articles published in the VCR quarterly newsletter, online and in the Army Times. Increased awareness of the Fox rigid eye shield and its proper use will result in improved first aid emergency care for Service Members who suffer traumatic eye injuries.

Reset

The Blast Injury Research Program is committed to reducing recovery time and improving the quality of life for Service Members who have experienced blast-related 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, are less invasive, and are less prone to complications such as infection. Research also forms the basis for rehabilitation programs for blast-related psychological disorders, amputations, disfigurement, and other long-term injuries. Reset strategies that are backed by extensive medical research allow the DoD and military medical community to retain the confidence and trust of Service Members, their families, and the American public through measureable improvements in Service Member recovery.

Neurocognitive Function and Psychological Health

Neurocognitive Eye Tracking Reveals Persistent Impairments after mTBI

The Laboratory for Neurocognitive Research at USUHS has developed advanced eye tracking technology to quickly and accurately assess neurocognitive function. Advanced clinical tools such as these may enable the detection of blast-related changes in brain function. In a case-control study, the Bethesda Eye & Attention Measure (BEAM) was uniquely sensitive to chronic postconcussion impairments in comparison to conventional cognitive tests. A greater number of mTBIs was associated with rapidly increasing risk for BEAM saccadic impairment. Examination of age effects on BEAM performance also suggest that mTBI is associated with heightened risk for age-related cognitive decline. Continued

R&D of the BEAM technology could be used to identify neurocognitive impairment and cumulative effects of blast-related neurotrauma in real-world clinical and operational environments. Additional research funded by USAMRMC Telemedicine and Advanced Technology (TATRC), is underway to cross-validate and extend these findings.

Analysis of Post-deployment Cognitive Performance and Symptom Recovery in US Marines

Computerized neurocognitive testing is proposed to be a useful screening tool for identifying post-deployment cognitive deficits; however, a study of the Automated Neurocognitive Assessment Metric (ANAM) demonstrated a need for additional methods for identifying Service Members requiring clinical follow-up post-concussion. A research team at the CRSR at USUHS assessed the clinical utility of ANAM testing post-injury/post-deployment, particularly as a measure of change in symptoms over time. In a longitudinal study published in *Public Library of Science One,* pre-deployment baseline ANAM tests were compared with two post-deployment ANAM tests in a group of Marines who experienced combat during deployment. Overall, there was a measurable deployment effect on cognitive performance, although this effect appears to resolve without lasting clinical sequelae in those without history of deployment-related concussion; however, the second simple reaction time component of the ANAM remained particularly impaired at an average of eight months post-deployment, and was the most consistent and sensitive indicator of the cognitive decrements. This study suggests that reliance solely upon computerized neurocognitive testing as a method for identifying Service Members requiring clinical follow-up post-concussion is not recommended, as cognitive functioning only slowly returned to baseline levels while clinical symptoms persisted. Instead, there is a need for a detailed clinical examination for Service Members with history of concussion and persistent clinical symptoms.

Glasgow Coma Scores, Early Opioids, and Posttraumatic Stress Disorder Among Combat Amputees

Two studies sponsored by BUMED under the WII program and conducted at NHRC investigated the association between the prevalence of PTSD and the use of IV morphine and fentanyl in combat amputees. The purpose of this research was to determine whether early post injury treatment with morphine (relative to fentanyl) could prevent the consolidation of traumatic memory and reduced risk for later PTSD. Combat casualty records from OIF and OEF from 2001–2008 were reviewed, which documented Glasgow Coma Scale (GCS) scores and/or morphine, fentanyl, or no opioid treatment within hours of injury. The psychological diagnoses of combat amputees were assessed at two years using military data (Study 1) and through four years post-injury using combined military and VA health data (Study 2). Results showed that IV morphine (relative to IV fentanyl only) administered within hours of injury reduced the risk of PTSD diagnoses over the first two years at military and/or VA facilities among amputees. The results of Study 2 showed increasing prevalence of PTSD between the first and second year after injury. These findings can inform screening and preventive programs for PTSD, particularly after the first year post-injury.

Psychophysiological Response to Virtual Reality and Subthreshold Posttraumatic Stress Disorder Symptoms in Recently Deployed Military

Subthreshold PTSD has garnered recent attention because of the significant distress and functional impairment associated with symptoms, as well as the increased risk of progression to full PTSD. However, the clinical presentation of subthreshold PTSD can vary widely and therefore is not clearly defined, nor is there an evidence-based treatment approach. Research performed and sponsored by CNRM at USUHS aims to further the understanding of subthreshold PTSD symptoms by studying the utility of a virtual combat environment in eliciting distinctive psychophysiological responses associated with PTSD symptoms.

In a novel procedure to assess subthreshold symptoms, heart rate (HR), skin conductance, electromyography (startle), respiratory rate, and blood pressure (BP) were monitored during three unique combat-related VR scenarios in a sample of 78 recently deployed US Service Members with subthreshold PTSD. The Clinician-Administered PTSD Scale was administered to assess PTSD symptoms, and linear regression analyses were used to investigate the relationship between symptom clusters and physiological variables. Of the range of psychophysiological measures studied, HR was most strongly associated with three Clinician-Administered PTSD Scale-based measures: hyperarousal, re-experiencing, and global PTSD symptoms. This study concludes that a VR environment can successfully elicit physiological responses associated with subthreshold PTSD symptoms, suggesting that the use of VR environments may prove useful in future experiments in the field.

A Study of Bilateral Prefrontal Transcranial Magnetic Stimulation (TMS) to Treat the Symptoms of mTBI and Comorbid Psychological Health Conditions

A study sponsored by NICoE investigated the feasibility and efficacy of TMS in rehabilitating Service Members with symptoms of mTBI and comorbid psychological health conditions. Study participants were patients at WRNMMC presenting with mTBI and comorbid psychological health conditions who received three or more repetitive TMS treatments per week. Patients were assessed at baseline and at the end of treatment for depression severity using the Periodic Health Questionnaire and/or the Quick Inventory of Depressive Symptomology. Based on a preliminary analysis, patients receiving TMS had improved outcomes. Patients with mild-to-moderate depression had significantly higher remission rates than patients with severe depression. The study results could impact guidelines for the treatment of Service Members with mTBI and comorbid psychological disorders and suggest that patients with mild-to-moderate depression should be considered for TMS treatment, as they may actually have an advantage with respect to depression remission.

Pain Management and Rehabilitation After Amputation

Investigation of Chronic Pain Following TBI

Sponsored by OAFSG and the Air Force Medical Support Agency, researchers from the 59th Medical Wing Scientist's Office, Lackland AFB successfully developed an experimental paradigm to support future studies of chronic pain in active duty Service Members, Veterans and civilians. This effort aimed to characterize the neural networks involved in posttraumatic pain using fMRI both in the resting state and during activation with a moderately painful stimulus. Based on a preliminary analysis of raw fMRI data, resting state and pain activation data were robust in individuals with chronic pain conditions. There was consistent to good activation in all of the regions of the pain network (i.e., primary and secondary somatosensory regions, insula, cingulate, primary motor regions, thalamus and cerebellum). Activation in participants with fibromyalgia was the most robust, followed by participants with chronic pain in TBI. Normal controls and those with migraine headaches had less robust activation patterns overall; the small study size limits the results to a general impression only. These findings indicate that this experimental paradigm can support future studies of chronic pain in active duty Service Members, Veterans and civilians. Future studies may contribute to an understanding of the changes in the brain that perpetuate pain in this population and other chronic pain conditions.

The Effect of Sedation on the Accuracy and Treatment Outcomes for Diagnostic Injections: A Randomized, Controlled, Crossover Study

In an effort to improve the accuracy and treatment outcomes for diagnostic injections for injured Service Members, researchers at CRSR at USUHS sought to determine the effect of sedation on the validity of diagnostic injections. In this randomized crossover study, 73 patients were allocated to receive a diagnostic sacroiliac joint or sympathetic nerve block performed either with or without sedation using midazolam and fentanyl.

Those who obtained equivocal relief, good relief lasting less than three months, or who were otherwise deemed good candidates for a repeat injection, received a subsequent crossover injection within three months (n = 46). Blocks performed with sedation had a significantly larger mean reduction in pain diary score than those done without sedation, significantly less procedure-related pain, and a significantly higher proportion of patients who obtained > 50% pain relief on their pain diaries. The improved pain reduction was not accompanied by increased satisfaction. No differences in outcomes were noted between the use and non-use of sedation at one-month follow-up. These findings indicate that the use of sedation during diagnostic injections has no effect on satisfaction or outcomes at one-month, and were published in *Pain Medicine*. This information may be used to inform clinical decisions for patients receiving sedation during diagnostic injections.

Epidural Adhesiolysis: An Evidence-based Review

Researchers at CRSR at USUHS published an extensive review article in the *Journal of Neurological Sciences* summarizing the benefits of the epidural lysis of adhesions (LOA) and a general overview of the process itself. Through the mechanical dissolution of epidural scar tissue, LOA may directly alleviate pain and facilitate the spread of analgesic substances to areas of pain generation. Although most commonly performed for failed back surgery syndrome (FBSS) in the lumbar region, a growing body of evidence that suggests LOA may be effective for spinal stenosis (SS) and radicular pain stemming from a herniated disc. There is preliminary evidence that LOA is more effective than conventional caudal epidural steroid injection (ESI) for FBSS and SS, and that LOA is more effective than sham adhesiolysis and conservative management for lumbosacral radiculopathy. For cervical disc herniation and SS, there is only anecdotal evidence suggesting effectiveness and safety. LOA may be more effective than traditional epidural steroid administration because of the high volume of corticosteroid administered, the use of hypertonic saline, and to a lesser extent the use of hyaluronidase and a navigable catheter to mechanically disrupt scar tissue and guide medication administration. Although LOA is widely considered a safe intervention, the complication rates are higher than those for conventional ESI. This review article suggests that larger randomized studies comparing epidural LOA to sham adhesiolyisis, conventional ESI, and conservative treatments are needed to confirm efficacy, and to identify those patients and conditions most likely to respond to treatment. With further development, LOA has the potential to be an effective solution for treating pain in injured Warfighters.

Epidural Lysis of Adhesions for Failed Back Surgery and Spinal Stenosis: Factors Associated With Treatment Outcome

A multicenter retrospective study headed by researchers at CRSR at USUHS investigated factors associated with outcomes following epidural LOA as a treatment for FBSS. The medical records of patients who underwent LOA for FBSS (n = 104) or SS (n = 11) between 2004 and 2007 were reviewed and 27 demographic, clinical, and procedural variables were extracted and correlated with outcome, which was defined as ~50% pain relief lasting approximately one month. Overall, 48.7% of patients had a positive outcome. As determined by univariable analysis, those who had a positive outcome were significantly older than those with a negative outcome (mean age: 64.1 years vs 57.2 years). Also, baseline Numeric Rating Scale (NRS) pain scores were significantly lower in those with a positive outcome (mean score: 6.7 vs 7.5). Use of hyaluronidase did not correlate with outcomes. As determined by multivariable logistic regression, age ~81 years, baseline NRS score of roughly nine, and patients on or seeking disability or worker's compensation were significantly more likely to experience a positive outcome. Results were published in *Anesthesia and Analgesia*. Selecting patients for epidural LOA based on demographic and clinical factors may help better select treatment candidates.

Procedural factors such as the use of hyaluronidase that increase risks and costs did not improve outcomes, so further research is needed before these become standard practice.

Can Changes in Vital Signs be Used to Predict the Response to Lumbar Facet Blocks and Radiofrequency Denervation? A Prospective, Correlational Study

A multicenter prospective study was conducted by CRSR at USUHS to determine whether objective measures such as changes in vital signs might be used to predict outcomes after facet joint radiofrequency (RF) ablation. Patients who underwent diagnostic lumbar medical branch blocks were recruited; a subset of these proceeded to RF denervation. For all participants, BP, HR, and pain scores were recorded before and after lumbar facet block. Overall, 56.1% of patients had a positive facet block. There were no significant correlations between changes in NRS scores and HR, systolic BP, diastolic BP (DBP), and mean arterial pressure. There were no significant associations between facet block outcomes and any vital sign. A decrease in DBP > 7.5 mmHg after facet block had 97.3% specificity, a Positive Predictive Value (PPV) of 85.7%, and Negative Predictive Value (NPV) of 58.3% for predicting outcomes at 3-months follow-up. These findings, which were published in *Regional Anesthesia and Pain Medicine,* indicate that changes in vital signs could potentially predict responses to RF denervation. Using an algorithm based on age, pain duration, baseline NRS score, and significant decrease in DBP, changes in vital signs could predict outcomes following RF denervation with 76.7% accuracy, but the low NPV precludes its use as a solitary screening tool.

Epidural Steroid Injections, Conservative Treatment, or Combination Treatment for Cervical Radicular Pain: A Multicenter, Randomized, Comparative-Effectiveness Study

Researchers at CRSR at USUHS conducted a comparative-effectiveness study to compare different types of non-surgical therapy for cervical radicular pain, which was published in *Anesthesiology.* A sample of 169 individuals with cervical radicular pain less than four years in duration received either nortriptyline and/or gabapentin plus physical therapies, up to three cervical ESIs, or combination treatment over six months. The primary outcome measure was average arm pain on a scale of 0–10 assessed one month after cessation of treatment. Mean pain scores were 3.5 in the combination group, 4.2 in ESI patients, and 4.3 in individuals treated conservatively. The mean reduction in arm pain score in the combination group was significantly greater than that in both the conservative and ESI groups and in ESI patients. For neck pain, the mean reduction of pain score in the combination group was significantly greater than that in both the conservative and ESI groups. Three months after treatment, 56.9% of patients treated with combination therapy experienced a positive outcome versus 26.8% in the conservative group and 36.7% in ESI patients. These findings indicate that combination therapy provided better improvement than stand-alone treatment on some measures, but not the primary outcome measure. Further studies on combination therapy will contribute to the development of non-surgical therapy options for individuals with cervical radicular pain.

Observation of Limb Movements Reduces Phantom Limb Pain in Bilateral Amputees

Mirror therapy has been shown to be an effective treatment for phantom limb pain (PLP) in unilateral amputees. In mirror therapy, a reflection of the intact limb provides a visual surrogate for the phantom limb and observations of movements of the limb reflection provide sensory feedback that facilitates the reduction of PLP. Mirror therapy is low-cost and non-invasive, but is not possible for bilateral amputees. In a study published in *Annals of Clinical and Translational Neurology,* researchers at CRSR at USUHS investigated whether a novel therapy in which bilateral amputees directly observe another person's limbs moving could be used to reduce PLP.

Twenty bilateral LE amputees were randomly assigned to either visual observation (n = 11) or mental visualization intervention groups (n = 9) and performed movements for 20 min daily for one month. In the visual observation groups, the study participants were asked to replicate the movements of a study investigator while directly observing the investigator's movements. In the mental visualization group, participants were asked to close their eyes and visualize the movements as prompted by investigators while trying to move the phantom limb. Before each daily session, the number of PLP episodes in the last 24 hours, the response to a 100-nm visual analog scale, and the response to the McGill Short-form Pain Questionnaire were recorded. Direct visualization significantly reduced PLP in both legs and may represent a novel low-cost, non-invasive therapy for PLP in bilateral amputees.

Virtual Reality Therapies for Phantom Limb Pain

Amputation may result in a variety of unintended side effects, including PLP. The perceived ability to move the phantom limb is related to pain severity; previous work using the illusion of an intact limb has resulted in reduced PLP. A research team at CRSR at USUHS presented four of their studies on VR therapies for PLP at the 8th Congress of the European Federation of the International Association for the Study of Pain Chapters in October 2013. The first study assessed the efficacy of combining "motor training" of the phantom limb with virtual feedback to alleviate PLP. After training twice a week for 8 weeks, five of eight participants reported > 30% pain reduction. The second study developed an immersive VR environment in which motions of an amputee's intact limb were tracked and transposed onto a computer-generated representation of the individual's phantom limb in the virtual environment. Four participants reported a tangible reduction in pain, two gained some control over their phantom limb's maneuverability, and one was even able to exercise some control over the residual limb, which had been paralyzed for over 12 years. The third study developed a novel variation on the mirror box treatment; motion data from a patient's residual limb were captured and transformed into goal-directed, virtual action enacted by an avatar in a VR environment. In a preliminary sample of 14 individuals (seven with arm and seven with leg amputations), 10 felt the virtual limb moved as their own and reported reductions in PLP that were greater than would be expected from the performance of a distraction task alone. The fourth study used the virtual integrated environment (VIE) developed by JHU/APL. Participants using the VIE were able to train and complete a full range of virtual arm motions over the course of twenty 30-min sessions. Five of the six participants reported that using the VIE alleviated PLP. Collectively, these studies use a variety of VR techniques for the treatment of PLP across diverse rehabilitation populations.

A Mechanism-based Classification of Phantom Limb Pain

Although PLP occurs in up to 85% of individuals with amputation, studies report characteristics that vary widely in PLP onset, duration, frequency, and overall description. This heterogeneity has led to widespread recognition among researchers that PLP likely has multiple causes. A research team at CRSR at USUHS conducted a meta-analysis, published in *Pain,* of randomized controlled trials of treatments for PLP published in the last decade. The researchers concluded that there may be many effective treatments for PLP that only work in specific subpopulations. Consequently, a mechanism-based classification of PLP was recommended, re-conceptualizing it as a cluster of pain disorders rather than as one single disorder. Future work should attempt to link subtypes of pain to a shared pathophysiological mechanism to generate clinically significant distinctions across patients that can be applied to PLP research. A mechanism-based classification system for PLP would allow future researchers to generate specific hypotheses and target a specific patient population according to the theorized mechanism of action of the treatment in question. Recognizing the complexity of the disorder while still seeking to create a system that allows for generalization across patients is critical to the progress of PLP treatment and research.

Bone Mineral Density Loss After Combat-related LE Amputation

Researchers at the CRSR at USUHS conducted a study to determine the incidence, severity, and associated risk factors for the development of low bone mineral density (BMD) after combat-related LE amputation. A retrospective case-control analysis was performed for 156 LE amputees (121 unilateral amputees, 35 bilateral amputees) for whom post-injury dual energy x-ray absorption (DEXA) BMD measurements were available. Proximal amputation level and delayed ambulation were significantly associated with low BMD after trauma-related amputation. These results, published in the *Journal of Orthopaedic Trauma,* suggest transfemoral amputees are at greater risk of BMD loss and that disuse atrophy is a primary factor in the development of low BMD. Furthermore, these results suggest that assessing calcium and vitamin D levels, supplementing appropriately, and focusing on early and aggressive weight bearing rehabilitation may lead to more efficient and successful rehabilitation of LE amputees.

Mediolateral Joint Powers at the Low Back Among Persons with Unilateral Transfemoral Amputation

Persons with unilateral transfemoral amputation walk with greater trunk lateral flexion than able-bodied individuals. Such movements may be a reactive adaptation to walking with a prosthesis, or an active trunk neuromuscular/movement strategy to compensate for weak (or missing) musculature in the residual limb. In a study published in *Archives of Physical Medicine and Rehabilitation,* researchers at the CRSR at USUHS conducted a retrospective analysis of mediolateral joint powers at the low back during gait among individuals with unilateral transfemoral amputation. The aim of this study was to better understand the functional contributions of tissues in and around the low back to altered lateral trunk movements in this population. In persons with transfemoral amputation, researchers found four distinctly larger positive phases of mediolateral joint power at the low back (lumbosacral joint) occurring before and after each heel strike. Mean total generation energies throughout the gait cycle were larger among persons with transfemoral amputation than among uninjured controls. Larger positive phases of joint power at the lumbosacral joint in the frontal plane support previous suggestions that persons with transfemoral amputation use a more active mediolateral trunk movement strategy. However, such an active, proximal (trunk) movement strategy may contribute to low back pain risk because trunk muscle activities directly influence spinal loads; several able-bodied individuals reported acute discomfort in the lower back when performing gait training aimed at increasing trunk lateral flexion. Also, concentric muscle activity is more energetically demanding than eccentric muscle activity, which may contribute to higher metabolic energy expenditures during gait in persons with lower-limb amputations. This study has the potential to improve rehabilitation time for Service Members with transfemoral amputations by providing evidence that a more active mediolateral trunk movement strategy may be advantageous.

More than the Final Score: Development, Application, and Future Research of Comprehensive High-level Activity Mobility Predictor

Researchers at the CRSR at USUHS developed the Comprehensive High-Level Activity Mobility Predictor (CHAMP), a performance-based assessment tool for measuring high-level mobility in individuals with lower limb amputation. Based on the existing literature, the most important factors influencing high-level mobility were determined to be balance, postural stability, coordination, power, speed, and agility. The Single Limb Stance, Edgren Side Step Test, T-Test, and Illinois Agility Test, which best capture these factors, were used to form the basis of CHAMP. Inter-rater and test-retest reliability results supported the CHAMP as a stable, repeatable measure of high-level mobility. Additionally, the construct convergent validity of the CHAMP was established using the six-minute Walk Test and Amputee Mobility Predictor (AMP).

These findings suggest that CHAMP is a stable and repeatable measure of high-level mobility in the clinical setting. Results of this study were published in the *Journal of Rehabilitation, Research, and Development*.

Rehabilitation of Multiple-limb Combat Amputees: Injuries and Functional Outcomes for a Small Case Series

Recent multiple-limb combat amputees present new challenges for rehabilitation care providers at military and VA facilities. Researchers sponsored by the BUMED WII Program conducted a comprehensive evaluation of the outpatient rehabilitation program at the Naval Medical Center, San Diego Comprehensive Combat and Complex Casualty Care (C5) facility. The researchers quantified injuries and functional outcomes for 29 multiple-limb amputees, all injured in 2010 and 2011 by blast weapons in the Afghanistan conflict; the sample reflected some of the most serious complex battle injury patients in this conflict. All patients completed the outpatient program at the C5 facility. At program discharge, most patients had improved scores on the Mayo-Portland Adaptability Inventory, 4th Revision (MPAI-4) for self-care, mobility, pain, recreation, and transportation. One-half or fewer of the patients had improved psychosocial and employment scores. This study provides rehabilitation professionals with detailed descriptions of the extensive injuries, including amputations and other injuries, of recent multiple-limb amputees returning from Afghanistan using established injury scales, namely the AIS. It also gives a careful description of novel rehabilitation approaches, including advanced prosthetics for the most complex blast injury patients from the recent Afghanistan conflict. Case reports of two triple amputees illustrated coordinated multispecialty care and contrasting prosthetic technologies. Military and VA providers can use this report as an initial resource to anticipate healthcare needs and improve their post-injury care programs for similar patients. Moreover, this project is one of the first to provide preliminary results which quantify changes in patient functioning following a novel outpatient rehabilitation program. The results also inform providers on healthcare needs for patients who sustain powerful blast injuries resulting in extensive injuries including multiple-limb amputations.

Orthotics and Prosthetics

The Influence of Ankle-foot Orthosis Stiffness on Walking Performance in Individuals with Lower-limb Impairments

Researchers at the CRSR at USUHS studied the influence of the stiffness of ankle-foot orthoses (AFOs) on gait performance improvement in patients with unilateral lower-limb neuromuscular and musculoskeletal impairments. Passive-dynamic AFOs utilize stiffness to improve gait performance through elastic energy storage and return. However, the influence of AFO stiffness on gait performance has not been systematically investigated, largely due to the difficulty of manufacturing devices with precisely controlled stiffness levels. Additive manufacturing techniques, such as selective laser sintering (SLS), were used to manufacture AFOs with controlled stiffness levels. Three-dimensional and electromyographic data were collected from each participant while walking overground with each of three orthoses of varying stiffness. As the AFO stiffness decreased, ankle range of motion and medial gastrocnemius activity increased while the knee became more extended throughout stance. Individuals effectively compensated for changes in AFO stiffness with altered activity of the gastrocnemius muscle, and the stiffness levels analyzed in this study had a minimal effect on overall walking performance. The study, published in *Clinical Biomechanics,* suggests that orthotists do not need to focus on identifying optimal orthotic stiffness for individuals who will primarily be using it for low-impact activities such as walking.

Selective Laser Sintered Versus Carbon Fiber Passive-Dynamic Ankle-foot Orthoses: A Comparison of Patient Walking Performance

In a study published in the *Journal of Mechanical Engineering,* researchers at CRSR at USUHS examined the degree to which biomechanical measures during gait differ between Carbon Fiber (CF) and stiffness-matched SLS passive-dynamic AFOs (PD-AFOs). Selective laser sintering is a well-suited additive manufacturing technique for generating subject-specific PD-AFOs. However, the mechanical properties of SLS PD-AFOs may differ from those of the more commonly prescribed CF PD-AFOs. Subject-specific SLS PD-AFOs were manufactured for 10 individuals with unilateral lower-limb impairments. Minimal differences in gait performance occurred when individuals used the SLS versus the CF PD-AFOs. These results support the use of SLS PD-AFOs to study the effects of altering design characteristics on gait performance. Using SLS can produce PD-AFOs that are tailored to individuals and their needs, greatly assisting in the rehabilitation of Service Members.

Biomechanics of Uphill Walking Using Custom Ankle-foot Orthoses of Three Different Stiffnesses

AFOs can provide support and improve walking ability in individuals with plantarflexor weakness. Passive-dynamic AFO stiffness can be optimized for over-ground walking. However, little research exists for uphill walking, when plantarflexor contributions are key. Researchers at CRSR at USUHS compared uphill walking biomechanics in dynamic AFO users with unilateral-limb salvage across different AFO stiffnesses to determine optimal AFO stiffness. AFO users experienced less ankle motion and power generation, lower knee extensor moments, and greater hip flexion and power generation than non-users during uphill walking at a 10° incline. Despite these deviations, they walked at equivalent self-selected velocities and stride lengths. Asymmetries were present at the ankle and knee with decreased ankle motion and power, and lower knee extensor moments on the AFO limb. Stiffer AFOs increased knee joint flexion, but a 40% range in AFO stiffness had few other effects on gait. Therefore, a wide range of clinically prescribed AFO stiffnesses may adequately assist uphill walking. A publication documenting this study is currently in press.

EACE Research Efforts in Evaluation of Orthotic Technologies

Researchers at EACE examined the Intrepid Dynamic Exoskeletal Orthosis (IDEO), a novel, customizable, AFO developed at the Center for the Intrepid (CFI) and designed to support and protect an extensive array of LE limb traumas. EACE researchers tested the IDEO at three different stiffness levels to determine whether a given stiffness could normalize gait mechanics (e.g., joint angles, moments, and powers) to the levels seen in non-injured control subjects. The study found that patients readily adapted to different dynamic AFO stiffnesses and demonstrated few biomechanical differences among conditions during walking. None of the stiffness conditions normalized gait to control levels. The IDEO is now being fitted at all three DoD Advanced Rehabilitation Centers. In FY14, VA clinicians were also trained in the techniques necessary to provide the IDEO. This enhanced availability of the IDEO is providing new options for Service Members and Veterans with severe LE trauma by increasing access to and minimizing wait times for orthoses, and by reducing the need for medical travel. Evaluation of orthotic technologies are critical to the expedited validation and acceptance of innovative technologies and rehabilitation programs available to Service Members, and their increased availability will aid in returning greater numbers of Wounded Warriors to duty.

IDEO and Accompanying Physical Therapy Regimen, "Return to Run Program (R2R)"

Researchers at CFI, SAMMC, sponsored by EACE studied the efficacy of the combination of a new orthotic device, the IDEO, with a novel physical therapy regimen, the R2R.

The IDEO has quantified advantages over existing braces and orthoses in patient comfort and performance because it can accommodate early changes during rehabilitation, including improvements in strength and motion. R2R is an aggressive physical rehabilitation program that focuses on strength, plyometrics, power, and agility training. Active duty Service Members participating in the integrated orthotic and rehabilitation initiative after an LE injury have a higher rate of return to duty than those in previous reports, and the return to duty rate is significantly higher than that of the IDEO alone. Efforts are underway to determine whether the R2R clinical pathway with the IDEO can be successfully implemented in other military health centers. This effort provides Service Members with access to state-of-the-art orthoses and physical therapy programs to help them return to duty or reintegrate into civilian life.

EACE Research Efforts in Fall Prevention

Researchers at EACE published a number of scholarly works in FY14 on the prevention of falls in individuals with amputations and limb injury. These efforts focused on those with transtibial amputations, a population with decreased walking stability. Safely walking on uneven surfaces at varying speeds is critical to preventing falls and is a major safety concern in prosthetic use. Recent data suggest that the use of a prosthesis with adaptive ankle motion (the Proprio) may assist with walking on slight downhill slopes, while a powered prosthesis provided no distinct advantage over a passive prosthesis in maintaining dynamic balance during stair walking. Additional work is needed to determine the advantages and disadvantages of different types of prosthetics. Preliminary clinical data indicate that multiple rehabilitative strategies utilizing a VR environment (e.g., CAREN) can uniquely train individuals in rapid response techniques to unexpected perturbations (defined as a deviation of a system, moving object, or process from its regular or normal state of path, caused by an outside influence) during ambulation. Additionally, individuals with transtibial amputations were given task-specific fall training on a microprocessor-controlled treadmill. These training exercises have significantly increased confidence and provided a perceived decrease in fall risk for individuals who have sustained an amputation. All these capabilities are critical to a Warfighter's return to duty status and ability for high level activities, while minimizing the risk of secondary injuries.

A Case Series of Initial Fit with the PowerKnee™

Researchers at CRSR at USUHS conducted a case study on use of the PowerKnee™ (PK), the first motor-powered, artificially intelligent prosthesis for individuals with above-the-knee amputation. Four Service Members with unilateral transfemoral amputation were fitted with the PK immediately following surgical closure and clearance for prosthetic fitting and training. These patients all suffered combat-related limb loss, but no significant neuromuscular deficits existed for their contralateral intact lower limb. Each individual was fit by the same prosthetist and was provided minimal training on the device, including instructions to ambulate normally. All four Service Members had ambulation timelines that were faster than those of the average Service Member equipped with a traditional passive prosthesis, including achieving step-over-step stair ascent and descent within one to three weeks of initial fitting. Patients reported mixed feedback on the PK, with one patient abandoning the device in favor of a variable cadence microprocessor knee. Over-ground gait analyses revealed similar outcomes between the C-Leg and the PK, although intact knee and hip joint powers tended to be lower than those in the group using the PK. The PK may be a viable choice for the initial prosthetic fitting of individuals with transfemoral amputation in order to rapidly progress through early rehabilitation, with no apparent adverse effects on gait outcomes. A paper discussing this study has been submitted to the *Journal of Rehabilitation, Research, and Development*.

Further research is needed to better understand the potential advantages or disadvantages of this technology, including defining patient selection criteria and optimal timing of prosthetic fitting. Future studies will also investigate biomechanical outcomes in more demanding tasks where additional power may be beneficial.

EACE Research Effort in Gait Optimization

Researchers at EACE authored six publications in peer-reviewed journals on gait optimization in individuals with transtibial and transfemoral lower limb amputation. In the journal *Gait Posture,* the researchers examined the upper extremity kinematics of bilateral transtibial amputee (BTA) gait, finding that BTAs display greater lateral trunk flexion range-of-movement and shoulder abduction than able-bodied individuals when walking at similar speeds. A study published in *Clinical Orthopaedics and Related Research* concluded that residual femur length has less of an effect on transfemoral amputee gait efficiency and energy requirements than previously thought. In a paper published in *Clinical Orthopaedics and Related Research,* the authors suggested that there is an increased risk for early onset and progression of arthritis in the intact limb, especially in individuals with transfemoral limb loss. In a second article published in *Gait Posture,* EACE researchers reported the relationship between pelvis-trunk coordination and lower back pain in individuals with transfemoral amputations, and suggested that lower back pain may result from altered gait mechanics associated with use of prosthetic devices. In the *Journal of Prosthetics and Orthotics,* the authors presented a case study of a patient with bilateral amputations (right transtibial, left transfemoral), and found that a powered prosthetic system may offer increased mechanical efficiency and decreased lower-limb loading than a passive prosthetic system. Additionally, a literature review published in *Work: A Journal of Prevention, Assessment and Rehabilitation* concluded that the CAREN is a capable tool for both assessment and rehabilitation, but more research is needed to evaluate its effectiveness as a rehabilitation tool. Collectively, the biomechanical, prosthetic, and rehabilitation research conducted by EACE is critical to improving the understanding of increasingly complex prosthetic and orthotic devices and ensuring that they are properly prescribed and utilized.

EACE Research Efforts in Comorbidities and Secondary Health Effects of the Amputation Population

Researchers at EACE authored three major publications in FY14 on the comorbidities and secondary health effects associated with amputation. Comorbidities and secondary health effects are of great concern to Service Members and Veterans impacted by limb amputation. Research findings suggest an increased risk for early onset and progression of arthritis in the intact limb, especially in those with transfemoral limb loss. Preliminary work indicates that manual therapy may increase knee movement in amputees with knee osteoarthritis. There is also evidence that persons with lower limb amputations use an unnatural trunk movement strategy that may contribute to the risk of developing medical issues in the lower back and spine. A pilot study was conducted to determine whether bone bridge surgeries, as opposed to the traditional method, result in better outcomes; the results were inconclusive due to the small sample size, but indicate that preservation of residual limb length is crucial. In addition, there is a need for future work to assess the risk of overuse injuries with carried loads in the transtibial amputation population. Improving understanding of comorbidities and secondary health effects in the amputation population is critical for optimal prescription of prosthesis and physical activities, the health and well-being of the Warfighter, and the overall management of amputation and extremity injuries. This effort will ultimately prevent and/or mitigate disability in our Warfighters.

Transplants and Grafts

Face Transplants to Address Catastrophic Tissue Loss in the Face

Managed by the Tissue Injury and Regenerative Medicine (TIRM) Program Management Office and sponsored by the US Army Medical Materiel Development Activity (USAMMDA), investigators from the Cleveland Clinic Foundation and Brigham and Women's Hospital (BWH) are conducting clinical trials of face transplantation to offer Wounded Warriors with severe facial disfigurement and dysfunction a new treatment option if standard reconstructive surgeries are inadequate. In FY14, BWH performed the fifth and sixth face transplants under the Biomedical Translation Initiative contract. Both patients are doing well with expected challenges following transplantation. Also in FY14, Cleveland Clinic performed the first face transplant under the AFIRM I cooperative agreement. The patient is doing well. The advancement of the facial transplant procedure offers the possibility of restored function (e.g., chewing, swallowing, nasal breathing, oral competence, intelligible speech) and appearance to who have suffered catastrophic facial injuries.

Hand Transplants with Reduced Immunosuppression

For Service Members who have suffered catastrophic limb loss, hand transplantation offers an alternative to prosthetics, and the potential of improved function with less disability. The University of Louisville, in conjunction with USAMMDA, performed the first hand transplant under the AFIRM II award in November 2014. The graft was removed on postoperative day four for intractable swelling, the cause of which is under investigation. Retired US Army sergeant, Brendan Marrocco, a quadruple amputee who received a double arm transplant at Johns Hopkins University in December 2012, was featured on the front page of the Washington Post on 30 June 2014 doing a pull-up.

Vascular Grafts to Address Vascular Trauma and Replacement

A group of investigators managed by the TIRM PMO and sponsored by USAMMDA are conducting research to mitigate vascular injuries sustained in theater. Researchers at Johns Hopkins University, funded through AFIRM and collaborating with Humacyte, a company funded by DoD, are developing an off-the-shelf human tissue engineered vascular prosthesis. This decellularized human collagen-based vascular tissue technology has performed well in both canine and baboon studies, and will enter Phase 1 clinical trials in 2015 to support a trauma indication. New technology in vascular grafts, which improves long term patency and durability of the grafts while reducing complications from infection, may reduce limb loss and long term disability for Service Members.

Burn Injury Treatment

Treating Combat Wounds with a Biologically Active Advanced Antimicrobial Human Skin Substitute

With funding from USAMRMC and Military Infectious Diseases Research Program MIDRP, Stratatech Corporation has developed a human skin substitute for use in burn and trauma patients. The human skin substitute also performed as an autograft in preclinical effectiveness and safety testing. FDA awarded Stratatech's human skin substitute orphan drug status in 2012. Microbial infections, however, still remain a concern in burn and trauma patients. With MIDRP funding, Stratatech is developing a genetically enhanced human skin substitute that has sustained expression of cathelicidin—a naturally occurring, human-produced defense peptide with broad-spectrum antimicrobial properties that demonstrates effectiveness against multidrug-resistant bacteria and fungi. Initial preclinical studies have demonstrated effective antibacterial activity against multidrug-resistant Acinetobacter baumannii, one of the most common pathogens associated with combat wounds. This product could help prevent microbial infections in burn and trauma patients requiring skin grafts. More preclinical efficacy and toxicity studies are underway in preparation for an IND submission proposed for the fourth quarter of FY15.

Improved Cutaneous Coverage Following Severe Burn Injury

Researchers at Wake Forest University, funded through AFIRM, are collaborating with researchers at USAMMDA, US Army Institute of Surgical Research, and Stratatech Corporation to conduct a multicenter clinical trial to assess the safety, tolerability, and efficacy of prolonged exposure to increasing amounts of a single application of StrataGraft skin tissue (compared to autografts) in deep partial-thickness burns. StrataGraft is a living, meshable, suturable human skin substitute that reproduces many of the structural and biological properties of normal human skin. Data obtained from the first clinical trial cohort suggested StrataGraft works to facilitate wound closure and is replaced as the patient's own cells close the wound. Two additional cohorts completed follow-up in 2014, one of which doubles the area of burn treated with StrataGraft, and the other, which looks at the use of cryopreserved material; data analysis is underway. Stratech is preparing to initiate a Phase 3 clinical trial in 2015. StrataGraft is a promising alternative approach for cutaneous skin coverage after extensive burn injuries.

Treatment to Limit Burn Injury Progression

Burn injuries often become larger or deeper in the two to three days following injury, which may result in a higher risk of scarring, contractures, infection, disability, and possibly mortality, from serious burn wounds. Currently there is no treatment to stop this process. With funding from USAMMDA and AFIRM, investigators at Stony Brook University are developing a treatment to prevent burn injury progression. A single IV infusion of P12, a novel molecule derived from fibronectin, attenuated burn injury progression in both rodents and pigs, even under hypoxic conditions. The investigators are completing preclinical studies necessary to support an IND application to 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 Military Personnel: The Wounded Warrior Recovery Project (WWRP)

Conducted by NHRC, with funding from BUMED under the WII program and EACE, 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. The goal of the project is to discover the long-term effects of combat injury on the health and quality of life of Service Members. Participants from all branches of the US military who have been injured during combat in Iraq and Afghanistan beginning in October 2001 are currently being contacted and invited to fill out an online survey every six months, and will be followed for 15 years after enrollment. The survey collects data about the recovery process, physical and mental health, and quality of life. These data can be used to develop evidence-based solutions to many types of injury-related problems. To date, 3,600 injured Service Members have provided informed consent and enrolled in the study and over 571,000 survey responses have been collected. By assessing long-term quality of life outcomes, DoD and VA can evaluate those clinical treatments, rehabilitative programs, and prosthetics/orthotics that are actually moving the quality of life meter for injured Service Members and those that are not. This results in not only an immediate and real improvement in the quality of care delivered, but also in immense cost savings now and throughout the lifetime that many of these members will be requiring care. WWRP was recently been invited to discuss the progress of the program by IOM, which endorsed WWRP and indicated that it fills a long standing gap in casualty care. Preliminary results, in this as yet relatively small sample size, suggest that long term quality of life outcomes for injured US Service Members is lower than their civilian trauma injured counterparts, controlling for injury severity.

Again, controlling for injury severity, the incidence of moderate to severe depression and PTSD were higher than expected. The public facing web site can be viewed at: www.wwrecoveryproject.org.

Real-time Amputation Injury Quality of Life Outcomes Analysis and Reporting for Department of Defense Leadership

NHRC, in conjunction with EACE and with sponsorship from BUMED, was tasked by the Office of the US Army CSA with providing a report covering long-term outcomes of tri-service US military Service Members who sustained single or multiple amputations and those sustaining non-amputation injuries. This capability is built upon NHRC's EMED, which includes all Service Members injured during deployment since the beginning of OIF and OEF (October 2001). In addition, the EMED includes WWRP, a long-term, prospective survey study measuring quality of life outcomes in injured personnel. To date, 3,600 injured Service Members have provided informed consent and enrolled in the study, and enrollment is ongoing. With over 55,000 injured Service Members eligible to participate, it is the largest DoD effort to date to provide follow-up metrics and quality of life outcomes data in this population. Based on a preliminary analysis, amputees reported significantly lower quality of life than non-amputee injury groups, even after controlling for injury severity. However, their depression and PTSD status did not seem to be worse than other combat-injured groups. Looking more closely at amputee subgroups, multiple amputees had significantly lower quality of life scores than single amputees. This study is providing DoD and VA with a crucial understanding of the long-term physical, mental health, and quality of life outcomes of this population. Measuring the impact of these injuries on quality of life can inform strategies to optimize operational capacity, military health policy, allocation of resources, the development of strategic plans, and assessment of the effectiveness of the treatment and rehabilitation programs throughout DoD and VA. Current and future efforts of EACE and NHRC are focused on developing tailored instruments to assess long-term use and satisfaction with the prosthetics and orthotics prescribed to this population. These instruments will be targeted specifically to the WWRP participants with extremity and amputation injury.

Clinical Skills Sustainment for Extremity Trauma and Amputation Care Providers

The Performance Optimization Warrior Enhanced Rehabilitation (POWER) Program at CFI aims to return injured Service Members, regardless of injury or disability, to full duty and the highest possible quality of life using three interlinked parts: activity, nutrition, and health psychology. The POWER program takes a multidisciplinary approach that incorporates current, optimal, evidence-based practice into patient care to provide Service Members with the necessary tools to effectively and autonomously impact stamina, strength, and resilience. This sports medicine-based program is similar to civilian programs that cater to professional athletes. The interdisciplinary CFI team's clinical successes and collaborative work in maximizing the effectiveness of rehabilitation to return patients to military or civilian life resulted in receipt of the Army Surgeon General's Wolf Pack Award, a quarterly award created by the Army Surgeon General and the Chief of the Army Medical Department Civilian Corps to recognize exceptional teamwork by an integrated group of military and civilian team members focused on excellence in support of Army Medicine.

Education and Clinical Tools

Defense and Veterans Eye Injury and Vision Registry (DVEIVR)

VCE facilitated the collaboration between DoD and VA to develop a registry of military eye and vision injuries, including those associated with blasts. The DVEIVR will provide the DoD and VA vision care communities with the capability of analyzing longitudinal outcomes of Service Members and Veterans with vision trauma and disorders, in order to promote enhancements to clinical practice, guide research, and inform policies pertaining to vision care.

Eye care providers, other clinical care practitioners, and researchers will have a tool that allows them to access the information needed to develop strategies, that when implemented, will enhance and improve patient (Service Member and Veteran) care and outcomes over that patient's lifetime.

Federal Advanced Amputation Skills Training (FAAST) Symposium

The first FAAST Symposium was held July 8–10, 2014 at the Veterans Health Administration (VHA) National Conference Center in Arlington, Virginia. The theme was "Care for the Individual with Multiple-limb Amputation." The FAAST Symposium was supported by EACE, Veterans Affairs Amputation System of Care (ASoC), VHA Employee Education System, VHA Office of Prosthetics and Rehabilitation, and DoD, and was planned by a joint VA and DoD committee. More than 90 clinicians and researchers from both VA and DoD attended the symposium, which fostered interaction and knowledge sharing between clinical experts and researchers from multiple institutions. Attendees were provided with hands-on clinical skills for the immediate enhancement of Service Member and Veteran care. Clinicians in attendance also received education on evolving state-of-the-art clinical topics such as hand transplant, targeted muscle reinnervation, and osseointegration. The success of this joint collaboration effort was confirmed by the balanced number of presenters and attendees from both agencies, as well as a 95% response rate of overall satisfaction with the training. Approximately 90% of respondents stated they had gained new knowledge and would be able to apply that knowledge in the clinical setting.

Development of the First VA/DoD CPG for the Management of Upper Extremity Amputation Rehabilitation

The Management of Upper Extremity Amputation Rehabilitation Working Group, with support from The Veterans Affairs Office of Quality, Safety and Value and the USAMEDCOM Office of Evidence Based Practice, and with sponsorship from EACE, developed the first clinical pathway/guideline for care of patients with upper extremity amputation. This CPG is a culmination of more than a decade of research, unprecedented clinical experience, and funding of new technologies by VA and DoD SMEs. The CPG is an evidenced-based guide for upper limb amputation rehabilitation and clinical care and will assist in identifying priorities for research efforts and allocation of resources. The goals of this CPG are to reduce practice variance, enhance clinical practice, accelerate research translation into clinical practice, and ultimately lead to improved health, quality of life, and satisfaction for patients with upper limb amputations. The development of this CPG will help to optimize the patient's health status, function, independence, and quality of life.

EACE/ASoC Rehabilitation Virtual Grand Rounds

EACE partnered with VA's ASoC to deliver the first Virtual Grand Rounds presentation in FY14. Virtual Grand Rounds is a venue to rapidly translate key research findings and new rehabilitative strategies and techniques to clinical staff. This program benefits Service Members and Veterans by reducing the time for new clinical and rehabilitation findings to be implemented by healthcare providers. Virtual Grand Rounds is conducted bimonthly and provides continuing medical education (CME) to both DoD and VA providers on current topics relating to limb loss and extremity trauma rehabilitation care. This program averages 120 attendees per session and is also available for digital replay on VA's Content Distribution Network and MilSuite (DoD). VA's Employee Education System supports the Virtual Grand Rounds program by providing CME for both VA and DoD attendees of the live sessions, hosting the virtual room in Adobe Connect, and recording sessions for digital replay. Overall satisfaction for the Virtual Grand Rounds training is 88%, with more than 90% of the respondents reporting that they obtained new knowledge from the training which they will apply in the clinical setting.

EACE Global Outreach Efforts

Global Outreach efforts provide an avenue to share the EACE lessons learned, capabilities, and outcomes with coalition partners. During FY14, EACE facilitated site visits to Singapore and the Republic of Georgia. The purpose of the visit to Singapore was to assess a sailor in the Singaporean Navy who sustained a triple limb amputation. A clinical team from WRNMMC provided on-site evaluation of the patient and engaged in SME consultation with Singaporean providers to develop an appropriate rehabilitation plan for this critically injured sailor. The purpose of the visit to Tbilisi, Republic of Georgia, was to evaluate the progress being made in the establishment of an amputation care system that had begun with initial team visits in 2011 and 2012. A clinical team from WRNMMC visited the rehabilitation hospital, physical therapy clinic, and prosthetic fabrication lab. These efforts result in direct health care benefits to those receiving assistance as well as skill sustainment for participating US health care team members.

Injury Prevention—Reset—Vision Trauma Research

VCE's work addresses effective solutions for the mitigation, diagnosis, and treatment of mTBI in Service Members and the potential development of vision restorationffidevices for Service Members who have sustained eye injuries. Additionally, VCE works towards both the better mitigation and treatment of traumatic eye injuries sustained by Service Members as well as better rehabilitation and reintegration strategies for Service Members with eye and vision dysfunction. Researchers at VCE work in collaboration with a wide variety of government and private sector partners to identify emerging clinical needs and address them through directed research efforts. VCE maintains its lead role in the development of the DoD vision research portfolio by chairing and participating in the USAMRMC CDMRP Vision Research Program Steering Committee activities, including identifying and updating vision research gaps, developing research program announcements, and reviewing proposals. In FY14, VCE chaired an expert working group in collaboration with the CCCRP to identify studies that support the potential uses of eye-movement techniques and technologies for the assessment of mTBI and concussion. Results were documented in a report, "Traumatic Brain Injury Detection using Oculomotor and Eye Movement Tracking—A Technical Working Group Critical Review." This report will be used to inform an IIPT at USAMRMC and will contribute to the selection and development process of effective solutions for mTBI in Service Members. VCE has also completed a manuscript of this report that will be submitted for publication in a peer-reviewed journal.

Assessment of Sexual Health and Intimacy in TBI and Psychological Health Patients

The team of Licensed Clinical Social Workers who interact closely with patients at NICoE throughout their course of care identified the need for a more formalized program that would help Service Members and their families understand the impact of TBI/psychological health symptoms on their intimacy and sexual functioning. Clinicians at NICoE, in collaboration with the WRNMMC Sexual Health and Intimacy working group, are implementing educational offerings and couples intimacy assessments for patients and their significant others during their stay at NICoE. Since this collaborative program began, approximately 20% of all Service Members seen at NICoE have requested individual or couple intimacy assessments. Those who participated in the assessment have shared their appreciation for the NICoE staff who candidly and professionally addressed a topic that is oftentimes overlooked in a traditional medical model of care.

Validation of Efficacy of NICoE's Four-week Interdisciplinary Program for TBI Patients

NICoE recently conducted an internal study of their four-week interdisciplinary program for TBI patients who have not improved with standard medical care. In FY14, NICoE focused on taking their already developed and practiced interdisciplinary model and employing it in an Integrated Practice Unit (IPU) setting.

As an IPU, NICoE organizes its practices around the needs of the customer and the patient population. In healthcare, that requires a shift from organizations that are divided by medical specialty to ones that structure interdisciplinary teams around the patient's medical condition. In this IPU, NICoE personnel work together as an interdisciplinary team toward a common goal: maximizing the patient's overall outcome as efficiently as possible. Patients and their families receive more than 100 provider encounters throughout the course of their treatment, benefiting from specialized imaging and clinical equipment; patients also participate in individual, group, and family programs. To evaluate patient care, researchers and clinicians at NICoE collected a variety of standardized rating scales on over 400 patients. There were significant decreases in symptom severity across a variety of neurological and behavioral health parameters during the patients' stay at NICoE. Service Members responded positively, supporting the need for an interdisciplinary care model and improved classification of TBI and psychological health patients. In the NICoE program, Service Members identified skills and activities associated with recovery, including yoga, acupuncture, biofeedback, and other treatment options. Using validated rating scales to document the program's effectiveness is consistent with recommendations from the IOM's report on PTSD care within DoD and VA systems.

A Comprehensive Review of TBI: A Focus on the US Military Population

The use of explosive armaments in OEF and OIF has contributed to approximately 15% of the 313,816 diagnosed cases of TBI in the military since 2000. Rehabilitation from TBI remains challenging due to polytrauma and treatment strategies must be developed on a per patient basis. In response to these concerns, the DoD has issued guidelines to (1) standardize TBI diagnosis criteria, (2) classify TBI based on injury mechanism and severity, (3) categorize symptoms in somatic, psychological, and cognitive groupings and (4) standardize the care received by Service Members during the acute and chronic/rehabilitation stages of treatment. However, a thorough review of the literature conducted by the CRSR at USUHS indicates that the vast majority of cases in the DoD consist of mTBI, a condition in which traditional biomarkers are unavailable and diagnostic findings remain inconsistent. Results to date indicate that in order to optimize rehabilitation clinicians and investigators must further evaluate long-term mTBI care for resilience and readiness training. This review manuscript is currently under review with the *Journal of Public Health*.

Conclusion

It is an honor for the PCO to receive so many submissions from across the blast injury research community detailing their accomplishments in FY14. The breadth of research topics and outcomes is truly astounding, and 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 process. 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-related injuries. By disseminating information on FY14 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.

08

CHAPTER 8:

WAY FORWARD

This report to the EA covers all the major accomplishments reported by the blast injury research community and the PCO in FY14. In FY15 and the coming years, the PCO will continue to support the EA's responsibility to coordinate medical research efforts across the DoD aimed at advancing strategies for blast injury prevention, mitigation, and treatment. This chapter covers four PCO initiatives that will continue into FY15 to foster collaboration and information sharing between research communities, disseminate critical information, and shape research priorities to fill knowledge gaps on the entire spectrum of blast injury.

PCO Initiatives in FY15

Preservation and Dissemination of DoD Historical Blast Bioeffects Injury Data

Comparison across datasets, particularly historical and contemporary datasets, is the gateway to a greater understanding of scientific phenomena such as the bioeffect of blast exposure. Providing researchers ready access to valuable historical data enables the blast injury research community to fill gaps in the existing knowledge base, validate models and hypotheses, compare findings, and minimize duplication of effort. In support of the EA's responsibility to promote information sharing and dissemination, the PCO has launched an effort to make DoD historical and contemporary blast injury data available to the research community. In FY15, the PCO aims to preserve and make available data for programmatic guidance and research use. The Blast Injury Research Program currently has access to hard copy records that include over 500 technical reports and investigator notes detailing blast experiments conducted between 1951 and 1996 at the Blast Test Site (BTS) on Kirtland Air Force Base. These include studies on the biological effects of occupational and operational exposures to blast funded by USAMRMC from 1978 to 1996. Many of these experiments are no longer possible due to enhanced restrictions on use of animals in laboratory research and a constrained fiscal environment—making historical data all the more valuable. Through this effort, the PCO can also serve as a clearinghouse for vetting all data, models, and hypotheses, and provide guidance on behalf of the EA for medical injury prediction algorithms and protective strategies for blast-related injuries.

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

Advances in blast injury treatment for Service Members in the US and allied Armed Forces require close collaboration between researchers, clinicians, engineers, and other stakeholders across disciplines and international boundaries. The PCO continues to play a critical role in fostering collaborations between the US and NATO member nations, as well as the international research communities. The tools being developed by the HFM-234 RTG (detailed in Chapter 3) promote standardized study and data collection methodologies needed to advance the field of blast injury research. A big step towards this goal is the completion of the Blast Injury Epidemiological Study Guidelines in FY15, and the creation of the Comprehensive Dictionary of Blast Injury Research Terms, which will be completed by July 2016. 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, thereby facilitating international collaboration to improve the prevention, treatment, and mitigation of blast injuries for our Service Members and our partners in these efforts. The HFM-234 RTG is also developing guidelines for reproducing blast exposures in the laboratory, to include documenting key study characteristics in blast injury research and identifying parameters of interest.

The final HFM-234 RTG meeting will develop recommendations for standardized manimal models necessary for validating computational models of blast injury; the meeting will also develop a roadmap for establishing dose-dependent curves. Dissemination of these guidelines via the NATO Science and Technology Organization and publication in peer reviewed journals will promote effective collaboration among research groups and enable valuable cross-study comparisons needed to catalyze technical advances to respond to blast injury needs and requirements.

SoS Meeting Series

The International SoS Meeting series hosted by the PCO has been a forum for knowledge sharing, collaboration, and communication across blast injury research communities since 2009. Each meeting focuses on a specific topic related to blast injury, and brings together the world's top researchers and luminaries from the DoD, other Federal agencies, academia, industry, and international partners to share expertise and cutting-edge research. Recommendations that result from the SoS Meetings help to shape future blast injury research priorities and facilitate the development of blast injury prevention, mitigation, and treatment strategies for the Service Member. The next SoS Meeting is scheduled for November 2015 in the National Capital Region.

As a continually refined process, the PCO is implementing new strategies for the planning and execution of the next SoS Meeting. For example, a major enhancement in FY15 will be the topics selection and voting process. The SoS meeting topic selection process is an open forum whereby the PCO solicits recommendations from diverse organizations across the DoD with a vested interest in blast injury research. To maximize the diversity of input and make the process more inclusive, the PCO distributes a list of potential topics to a range of stakeholders within the DoD, including the research, acquisition, operational, and materiel communities, the Centers of Excellence, and USUHS. These stakeholders rank their top three topics in order of priority and have the option of submitting write-in topics to be included in the list for 2016. Using a weighted scoring system, the PCO selects the topic with the highest score, thereby selecting a topic that represents the interests of a diverse DoD voting community. Topics not selected for the 2015 meeting will be considered for the meeting in 2016.

Similar to the 2014 meeting, the PCO will establish a Planning Committee comprised of representatives from the DoD, other Federal agencies, academia, industry, and international organizations who will help guide the development of the 2015 meeting agenda and key activities. The Planning Committee will identify an Expert Panel of leading authorities on the selected topic who will guide discussions and lead focused Working Groups that will address specific questions. Through an executive session at the close of the meeting, the Expert Panel and the PCO will work together to synthesize meeting findings, articulate key knowledge gaps, and formulate specific actionable recommendations for addressing these gaps in the coming year. Meeting findings and resulting recommendations will be shared with military and civilian communities to reduce the barriers to successful medical research and accelerate the development of blast injury prevention and treatment solutions.

BIPSR Process Enhancements

In the coming year, the PCO will focus on finalizing recommendations from the MHS BIPSR Process for LE and piloting the revised MHS BIPSR Process and iBIPSR capabilities for additional bast injury types. The gaps in the science identified by the MHS BIPSR Process for LE will be shared with the medical research community to inform the development of future LE standards. The revised MHS BIPSR Process, which is projected to take only nine months per blast injury type, will be initiated and tested in FY15 for spine/back and upper extremity injury types. The iBIPSR-supported revised MHS BIPSR Process will be piloted using the auditory injury type, with finalized recommendations expected in FY16. The lessons learned from the next process iterations will be applied to further refine and enhance the MHS BIPSR Process. The PCO anticipates moving forward with the iBIPSR Process and completing the recommendations for all blast injury types by 2019. Ultimately, the recommendations developed through the MHS BIPSR Process will better enable the DoD to apply the best available and scientifically sound standards during R&D efforts aimed at protecting Service Members from the entire spectrum of blast injuries.

APPENDIX A:

ACRONYMS

#

3D	Three-dimensional
3T	3 Tesla

A

AAJT™	Abdominal Aortic Junctional Tourniquet
AAVS	Aurally Aided Visual Search
ACH	Advanced Combat Helmet
ACSI	Abbreviated Concussion Symptom Inventory
AFB	Air Force Base
AFFD WG	Auditory Fitness For Duty Working Group
AFIRM	Armed Forces Institute of Regenerative Medicine
AFO	Ankle-foot Orthosis
AHAAH	Auditory Hazard Assessment Algorithm for Humans
AHP	Army Hearing Program
AIS	Abbreviated Injury Score
AMC	Army Materiel Command
AMS	Altered Mental Status
ANAM	Automated Neurocognitive Assessment Metric
ANSW2R	Allied NeuroSensory Warrior Related Research
ARA	Applied Research Associates, Inc.
Army STARRS	Army Study to Assess Risk and Resilience in Service Members
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
ASoC	Amputation System of Care
ASPC	Audiology and Speech Pathology Center
ATA	Atmosphere Absolute
ATD	Anthropomorphic Test Devices
ATF	Acoustical Test Fixture
ATWG	Armor Technology Working Group

B

BADER	Bridging Advanced Developments for Exceptional Rehabilitation
BARDA	Biomedical Advanced Research and Development Authority
BEAM	Bethesda Eye & Attention Measure
BEAST	Blast Exposure Accelerated Sensor Transition
BFP	Brain Fitness Program
BIPSR	Blast Injury Prevention Standards Recommendation
BMD	Bone Mineral Density
BOP-HHA	Blast Overpressure-Health Hazard Assessment
BRAID	Blast-related Auditory Injury Database
BTA	Bilateral Transtibial Amputee
BUMED	US Navy Bureau of Medicine and Surgery
BWH	Brigham and Women's Hospital

C

C5	Comprehensive Combat and Complex Casualty Care
CAPD	Central Auditory Processing Disorders
CAREN	Computer Assisted Rehabilitation Environment
CBA	Capabilities Based Assessment
CB&M	Community Balance and Mobility Scale
CCC	Combat Casualty Care
CCCRP	Combat Casualty Care Research Program
CDMRP	Congressionally Directed Medical Research Programs
Cdr	Commander
CDS	Clinical Decision Support
CENC	Chronic Effects of Neurotrauma Consortium
CEP	Combat Eye Protection
CF	Carbon Fiber
CFI	Center for the Intrepid
CHAMP	Comprehensive High-Level Activity Mobility Predictor
CME	Continuing Medical Education
CNRM	Center for Neuroscience and Regenerative Medicine
CoE	Center of Excellence
COI	Community of Interest
CONUS	Contiguous United States
CPG	Clinical Practice Guideline
CPP	Cryo-Preserved Platelets
CRADA	Cooperative Research and Development Agreement
CRASH-2	Clinical Randomization of an Antifibrinolytic in Significant Hemorrhage 2
CRI	Compensatory Reserve Index

CRoC™	Combat Ready Clamp
CRMRP	Clinical and Rehabilitative Medicine Research Program
CRoC™	Combat Ready Clamp
CRSR	Center for Rehabilitation Sciences Research
CT	Computed Tomography
cVEMP	Cervical Vestibular Evoked Myogenic Potentials

D

DANA	Defense Automated Neurobehavioral Assessment
DARPA	Defense Advanced Research Projects Agency
DBP	Diastolic Blood Pressure
DCoE	Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury
DDR&E	Director of Defense Research and Engineering
DHA	Defense Health Agency
DHA RDA	Defense Health Agency Research, Development, and Acquisitions
DHP	Defense Health Program
DIC	Digital Image Correlation
DMN	Default Mode Network
DNA	Deoxyribonucleic Acid
DoD	Department of Defense
DoDD	Department of Defense Directive
DOEHRS-HC	Defense Occupational and Environmental Health Readiness System for Hearing Conservation
DOT&E	Director, Operational Test and Evaluation
DSTL	Defence Science and Technology Laboratory
DTI	Diffusion Tensor Imaging
DVBIC	Defense and Veterans Brain Injury Center
DVCIPM	Defense and Veterans Center for Integrative Pain Management
DVEIVR	Defense and Veterans Eye Injury and Visions Registry

E

EA	Executive Agent
EACE	Extremity Trauma and Amputation Center of Excellence
ECH	Enhanced Combat Helmet
EE3S	Ethinyl Estradiol-3-Sulfate
EMED	Expeditionary Medical Encounter Database
ERP	Event-related potentials
ER-REBOA	Resuscitative Endovascular Balloon Occlusion of the Aorta
ESI	Epidural Steroid Injection
EVPOME	Ex Vivo Produced Oral Mucosa Equivalent

F

FAAST	Federal Advanced Amputation Skills Training
FBSS	Failed Back Surgery Syndrome
FDA	US Food and Drug Administration
FDT	Frequency Doubling Technology
FE	Finite Element
FGA	Functional Gait Assessment
FHP	Force Health Protection
FM	Frequency Modulation
fMRI	Functional Magnetic Resonance Imaging
FY	Fiscal Year

G

g	Grams
GEN II HS	Generation II Helmet Sensor

H

HBO2	Hyperbaric Oxygen
HCE	Hearing Center of Excellence
HDAC	Histone Deacetylase
HFM	Human Factors and Medicine
HHP	Hybrid Hearing Protection
HO	Heterotopic Ossification
HPD	Hearing Protection Device
HPN-07	2,4-Disulfonyl α-Phenyl Tertiary Butyl Nitrone
HR	Heart Rate

I

IBA	Interceptor Body Armor
iBIPSR	Interactive Blast Injury Prevention Standards Recommendation
ICH	Intracranial Hemorrhage
IDEO	Intrepid Dynamic Exoskeletal Orthosis
IED	Improvised Explosive Device
IFAK2	Improvised First Aid Kit2
IFI	Invasive Fungal Wound Infection
IHPS	Integrated Head Protection System
IND	Investigational New Drug
IOTV	Improved Outer Tactical Vest
IIPT	Integrating Integrated Product Teams
IOM	Institute of Medicine
IPU	Integrated Practice Unit
IRB	Institutional Review Board
ISN	Institute for Soldier Technologies
ISS	Injury Severity Score
ISSmod	Modified Injury Severity Score
IT	Information Technology
IV	Intravenous

J

JDVAC	Joint Defense/Veterans Audiology Conference
JETT™	Junctional Emergency Treatment Tool
JPC	Joint Program Committee
JHASIR	Joint Hearing Loss and Auditory System Injury Registry
JHU/APL	Johns Hopkins University Applied Physics Laboratory
JIEDDO	Joint Improvised Explosive Device Defeat Organization
JTAPIC	Joint Trauma Analysis and Prevention of Injury in Combat

L

LE	Lower Extremity
LFT&E	Navy Live Fire Test and Evaluation
LOA	Lysis of Adhesions
LS	Limb Salvage

M

MCEP	Military Combat Eye Protection
MCSC	Marine Corps System Command
MEG	Magnetoencephalography
MHS	Military Health System
MIDRP	Military Infectious Disease Research Program
min	Minute
mL	Milliliters
MOM	Military Operational Medicine
MOMRP	Military Operational Medicine Research Program
MRE	Magnetic Resonance Elastography
MRAP	Mine Resistant Ambush Protected
MRF	Multi-functional Resuscitation Fluid
MRI	Magnetic Resonance Imaging
MSU	MaxxPro Survivability Upgrade
mTBI	mild Traumatic Brain Injury
MTF	Military Treatment Facilities
MTP	Massive Transfusion Protocol

N

NAC	N-acetylcysteine
NAMRU-SA	Naval Medical Research Unit-San Antonio
NATO	North Atlantic Treaty Organization
NCMT	National Intrepid Center of Excellence Continuity Management Tool
NCRAR	National Center for Rehabilitative Auditory Research
NDAA	National Defense Authorization Act
NHLBI	National Heart, Lung, and Blood Institute
NICoE	National Intrepid Center of Excellence
NHRC	Naval Health Research Center
NIH	National Institutes of Health
NIMH	National Institute of Mental Health
NIR	Near-infrared
NMRC	Naval Medical Research Center
NPV	Negative Predicative Value

NRS	Numeric Rating Scale
NSI	Neurobehavioral Symptom Inventory
NSRDEC	US Army Natick Soldier Research, Development, and Engineering Center
NSWCCD	Naval Surface Warfare Center Carderock Division

O

OAFSG	Office of the Air Force Surgeon General
OC	Ovariectomized-placebo treated Control
OE	Ovariectomized-Estradiol-treated
OEF	Operation Enduring Freedom
OIF	Operation Iraqi Freedom
ONR	Office of Naval Research
OSD	Office of the Secretary of Defense

P

PCL-C	Posttraumatic Stress Disorder Checklist—Civilian Version
PCO	Blast Injury Research Program Coordinating Office
PCS	Postconcussive Syndrome
PD-AFO	Passive-dynamic Ankle-foot Orthosis
PDGF	Platelet-derived Growth Factor
PDHA	Platelet-derived Hemostatic Agent
PEO	Program Executive Office
PIHL	Pharmaceutical Interventions for Hearing Loss
PK	PowerKnee™
PLP	Phantom Limb Pain
PMO	Program Management Office
PM MRAP	Project Manager Mine Resistant Ambush Protected
PM SPE	Product Manager Soldier Protective Equipment
PM SPIE	Project Manager Soldier Protection and Individual Equipment
POG	Protective Outer-Garment
POWER	Performance Optimization Warrior Enhanced Rehabilitation
PPE	Personal Protective Equipment
PPS	Pelvic Protection System
PROPPR	Pragmatic, Randomized Optimal Platelet and Plasma Ratio Study
PRORP	Peer Reviewed Orthopaedic Research Program
PTM	Progressive Tinnitus Management
PTSD	Posttraumatic Stress Disorder
PUG	Protective Under-Garment
PUPTH	Prehospital Use of Plasma for Traumatic Hemorrhage

R

R&D	Research and Development
RDECOM	Research, Development, and Engineering Command
ReCord	Research COoRDination Projects Database
RF	Radiofrequency
RFI	Request for Information
RPQ-16	Rivermead Postconcussion Questionnaire 16
RSY	Research Symposium
RTG	Research Task Group

S

SAHA	Suberanilohydroxamic Acid
SAMMC	San Antonio Military Medical Center
SBIR	Small Business Innovation Research
SBK	Supplemental Blast Kit
SC2i	Surgical Critical Care Initiative
SD/SD Plasma	Solvent Detergent/Spray Dried Plasma
SECARMY	Secretary of the Army
SIF	Stress Intensity Factor
SLS	Selective Laser Sintered
SME	Subject Matter Expert
SoS	State-of-the-Science
SPS	Soldier Protection System
SS	Spinal Stenosis
STRONG STAR	South Texas Research Organizational Network Guiding Studies on Trauma and Resilience

T

TACTIC	Transagency Consortium in Trauma-Induced Coagulopathy
TATRC	Telemedicine and Advanced Technology
TBI	Traumatic Brain Injury
TCAPS	Tactical Communications and Protective System
TDAP	Tissue and Data Acquisition Protocol
T&E	Testing and Evaluation
TIRM	Tissue Injury and Regenerative Medicine
TMD	Technical Management Directorate
TSVCR	Tre-Service Vision Conservation and Readiness Program
TXA	Tranexamic Acid

U

UBB	Under-body Blast
UCSD	University of California, San Diego
US	United States
UHMWPE	Ultra High Molecular Weight Polyethylene
USAARL	United States Army Aeromedical Research Laboratory
USAMEDCOM	United States Army Medical Command
USAMMDA	United States Army Medical Material Development Activity
USAMRAA	United States Army Medical Research Acquisition Activity
USAMRMC	United States Army Medical Research and Materiel Command
USAPHC	United States Army Public Health Command
USARL	United States Army Research Laboratory
USMC	United States Marine Corps
USSOCOM	United States Special Operations Command
USUHS	Uniformed Services University of the Health Sciences

V

VA	Department of Veterans Affairs
VCE	Vision Center of Excellence
VF	Visual Field
VHA	Veterans Health Administration
vHIT	Video Head Impulse Test
VIE	Virtual Integrated Environment
VOR	Vestibulo-ocular Reflex
VPA	Valproic Acid
VTC	Video-teleconference
WBPRD	Whole Blood Pathogen Reduction Device

W

WIAMan	Warrior Injury Assessment Manikin
WII	Wounded, Ill, and Injured
WRAIR	Walter Reed Army Institute of Research
WRNMMC	Walter Reed National Military Medical Center
WSS	Wound Stasis System
WWRP	Wounded Warrior Recovery Program

X

XSTAT	X-Stat Hemostatic Dressing

APPENDIX B:

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APPENDIX C:

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Department of Defense
DIRECTIVE

NUMBER 6025.21E
July 5, 2006

USD(AT&L)

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

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(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

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://www.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

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 (PH) 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 TB • Development of field-ready diagnostic devices for PTSD and TBI
Spinal Cord Injury Research Program (SCIRP)	The SCIRP funds collaborative research to advance the treatment and rehabilitation of spinal cord injuries (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 post-traumatic 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:

SUPPLEMENTAL: MHS BLAST INJURY PREVENTION STANDARDS RECOMMENDATION PROCESS

As implementation of the BIPSR Process for LE was initiated, the Blast Injury Prioritization Methodology mentioned earlier was revisited to complete the prioritization of all 14 Blast Injury Types and to determine the next Blast Injury Type to go through the BIPSR Process. After assimilating stakeholder feedback and updating the values of the Evaluation Factor levels (Maturity of Science, etc.), the DSAT tool was applied to calculate priorities for all of the stakeholder defined blast injury types. The results are shown in Figure E-1 as a plot of percentile (based on a probability density function consistent with currently available blast injury information) versus weighted stakeholder score.

FIGURE E-1: Plot of DSAT Results of 14 Blast Injury Type Priorities

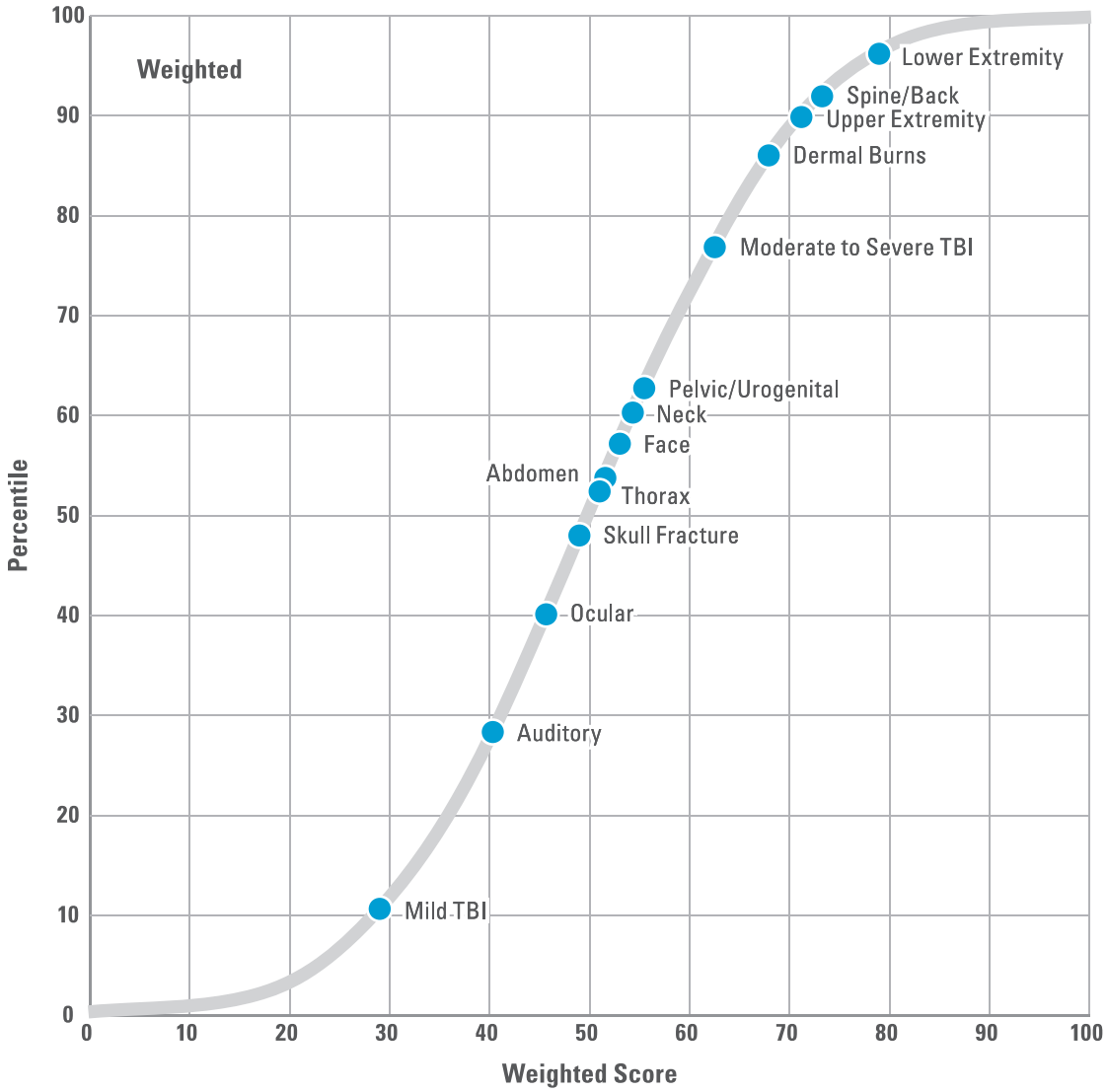
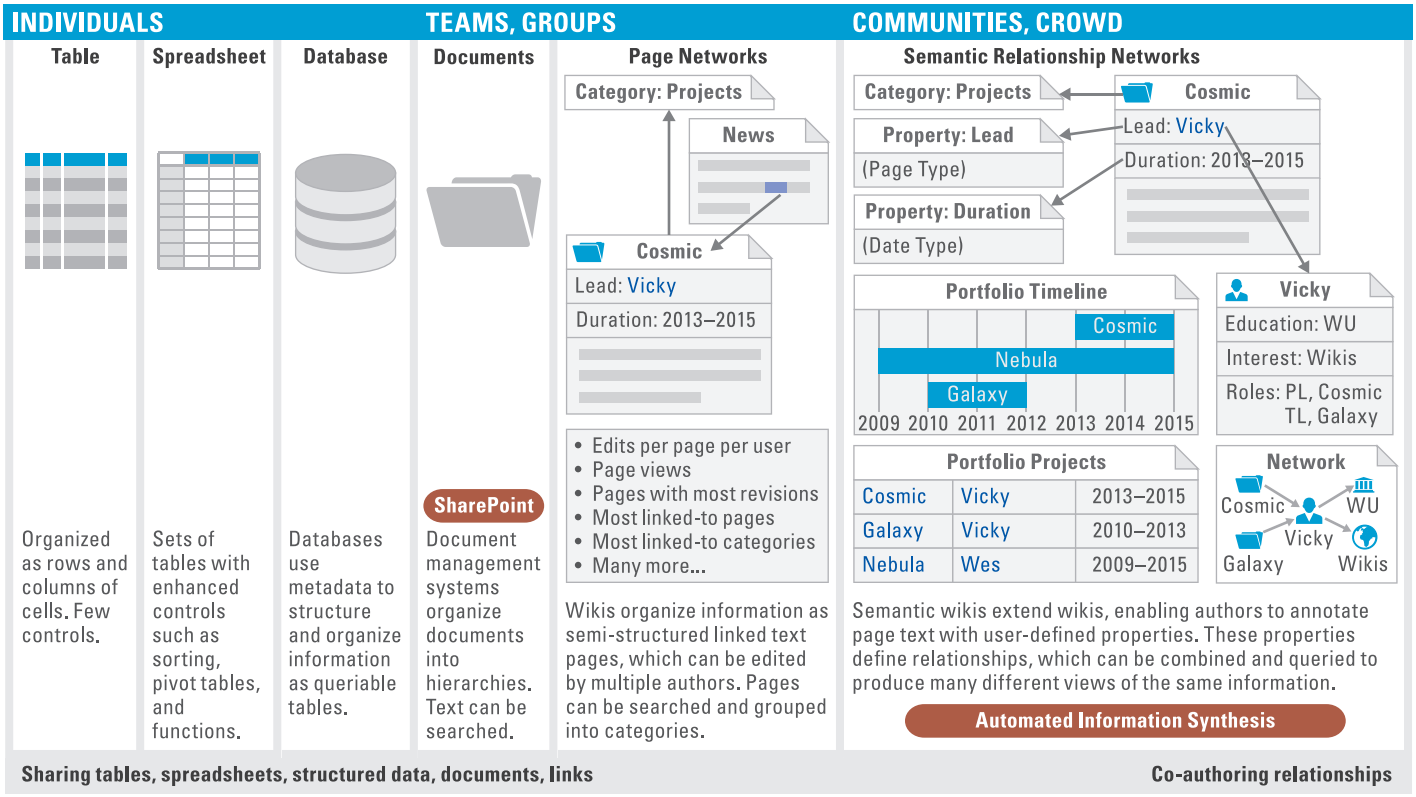


FIGURE E-2: Information Sharing & Collaboration Technology Spectrum: Cells to Semantics



Semantic Web Information Sharing Technology

Semantic web technologies are state-of-the art technology for information synthesis. Information storage and retrieval technologies have matured over the last two decades starting with from tables, spreadsheets, and databases to the SharePoint technology, which is now used to store and retrieve documents (see Figure E-2 for more details). Taking it one step further, Wiki technologies capture information on Wikipedia-like text pages; the information is organized on semi-structured linked text pages, which can be edited by multiple authors.

Semantic wikis augment wiki technology by enabling authors to annotate page text to add additional user-defined data elements.

Relationships between the user-defined data elements can be used to customize how the captured data is represented and can be used to automate information synthesis. Web-based semantic wikis facilitate community-sourced information synthesis and are an ideal technology for supporting the type of large collaborative multi-user information sharing and decision making that form the core of the MHS BIPSR recommendation process.

APPENDIX F:

SUPPLEMENTAL: HEARING AND BALANCE RESEARCH AND DEVELOPMENT

Hearing Injuries

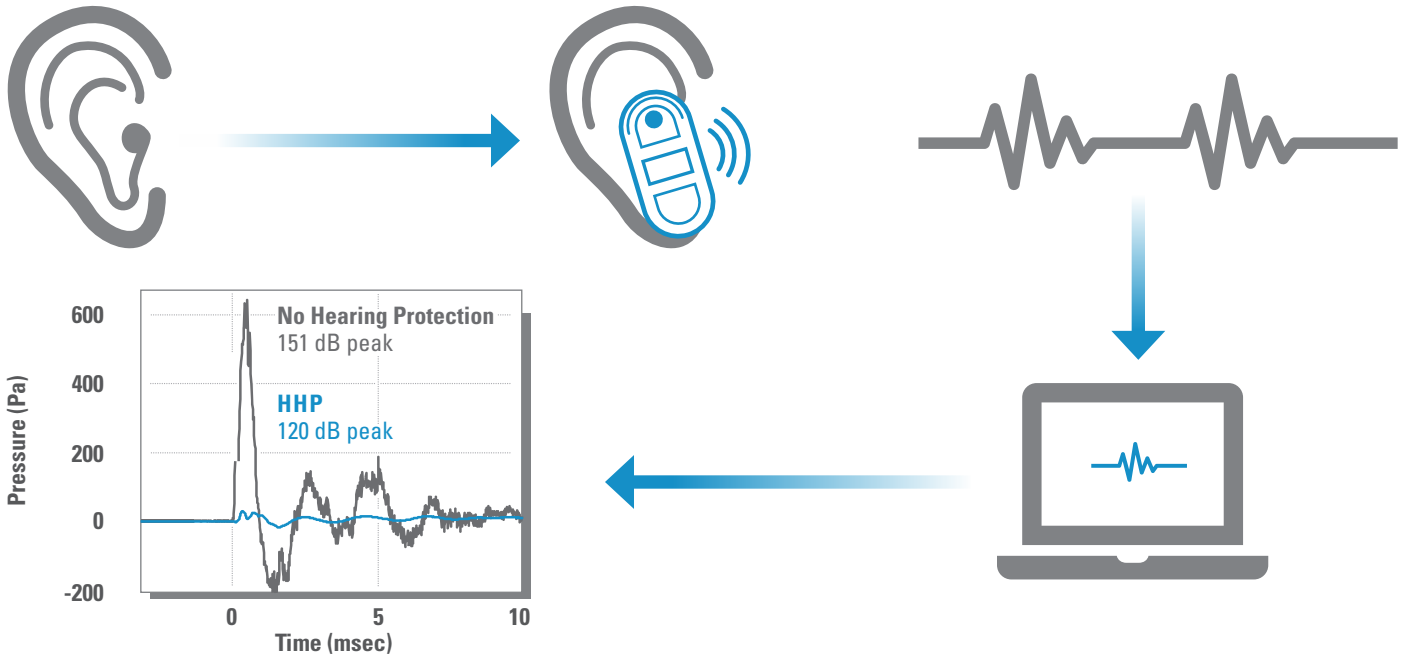
Phase II Clinical Trials: Testing D-Methionine to Reduce Noise-Induced Hearing Loss and Tinnitus

Novel pharmaceutical interventions have the potential to support early mitigation and treatment of hearing loss before it becomes permanent. Researchers at Southern Illinois University School of Medicine are working to develop the first FDA approved drug to prevent noise-induced hearing loss and tinnitus. D-methionine has shown over the last 20 years that it has the ability to protect cochlear hair cells from the side effects of pharmaceuticals containing cisplatin and aminoglycosides, which are known to be ototoxic, and over the last decade has also shown potential to reduce the effects of noise-induced hearing loss. Funded by the USAMRMC Military Operational Medicine Research Program, the SIU research team is now working to quantify D-methionine's effectiveness in preserving hearing when military personnel, while wearing required hearing protection, are subjected to 500 rounds of M-16 weapons fire at the Drill Sergeant Instructor Training School at Fort Jackson, South Carolina. The Phase II clinical trial reached full-scale data collection in January 2014. If successful, this research would help provide a much needed supplemental hearing protection capability for the military.

Antioxidant Therapeutic to Protect Against Hearing Loss

Funded by the US Department of the Navy, ONR, researchers at the Hough Ear Institute (Oklahoma City) are conducting a Phase I clinical trial to determine the safety, tolerability, and pharmacokinetic parameters of a combination oral therapeutic that in preclinical study has been shown to substantially reduce blast-induced hearing loss, brain injury, and tinnitus. The combination consists of two antioxidant compounds, n-acetylcysteine (NAC) and 2,4-disulfonyl-phenyl tertiary butyl nitrone (HPN-07). Relative to control rats, treatment with NAC and HPN-07 after blast exposure significantly reduced measures of hearing loss and cochlear hair cell loss, suggesting a reduction in damage to both the mechanical and neural components of the auditory system after blast exposure.[14] The same treatment also reduced several biomarkers associated with brain injury, indicating a promising therapeutic approach for simultaneously reducing or eliminating primary auditory injury as well as blast-induced hippocampal neurodegeneration and posttraumatic dementia in both civilian patients and military personnel. Follow-on preclinical studies are now under way with additional blast studies to determine if the treatment will reduce blast-induced tinnitus as it has already been shown to reduce noise-induced tinnitus. Future studies are envisioned and funding is being sought to determine if the treatment combination will reduce behavioral and MRI evidence of blast-induced TBI. The concept is that combatants would carry the oral therapeutic on their person and take it by mouth shortly after exposure to a loud noise or blast injury, to reduce permanent hearing loss, brain injury, and tinnitus. If additional studies prove successful this treatment would be unique as the only known therapeutic to address the triad of blast-induced hearing loss, tinnitus, and brain injury in rodent. To date, no safety or tolerability issues have been discovered at the highest oral doses; a multiple dose study is funded and planned to start this year. If additional preclinical and human safety studies prove favorable, this technology could transition to the clinic.

FIGURE F-1: Hybrid Hearing Protection Technology



The HHP provides normal hearing at low levels and protection at high levels of noise including blast. Optional exposure logger counts and stores impulsive noise events that exceed 150 dB, 160 dB, and 170 dB.

In-Ear Active Hearing Protection: Achieving Natural Hearing, Preventing Hearing Damage, and Encouraging Use

Funded by the DHA RDA Directorate, researchers at ARA have developed a novel approach to hearing protection that combines key features of passive and active hearing protection technologies.

The technology provides passive protection through a nonlinear acoustical element (to provide blast protection) integrated within a high-fidelity resonator to achieve flat frequency-response similar to a musician's quality HPD. Due to the volume-dependent response, lower-volume sounds pass through the passive filter with limited insertion loss, but high-volume impulsive noises are attenuated much more strongly. Active hearing restoration and protection is achieved by a simple, inexpensive, low-power electronic amplifier that counteracts the insertion loss from the passive elements and restores natural hearing at lower sound pressure levels. Thus, the new "Hybrid Hearing Protection" (HHP) technology merges simplicity and low cost with high sound quality and situational awareness (Figure F-1). This device also optionally integrates a noise exposure logger that counts and characterizes loud impulsive noises such as gunshot and blast.

Human testing has demonstrated that the new hybrid approach achieves performance similar to the most sophisticated electronic HPDs but at a much-reduced cost and with increased battery life. The HHP eliminates the need for electronics that would otherwise be necessary to protect against blast events with rapid rise times. The exposure logger attaches to the in-ear HHP with additional electronics housed behind the ear to quantify impulsive noise events that exceed certain thresholds; the logger stores this information in memory that is accessible through a micro-USB connector and software. This project is scheduled for completion in 2015.

Diagnosis and Treatment of Blast-Induced Hearing Loss

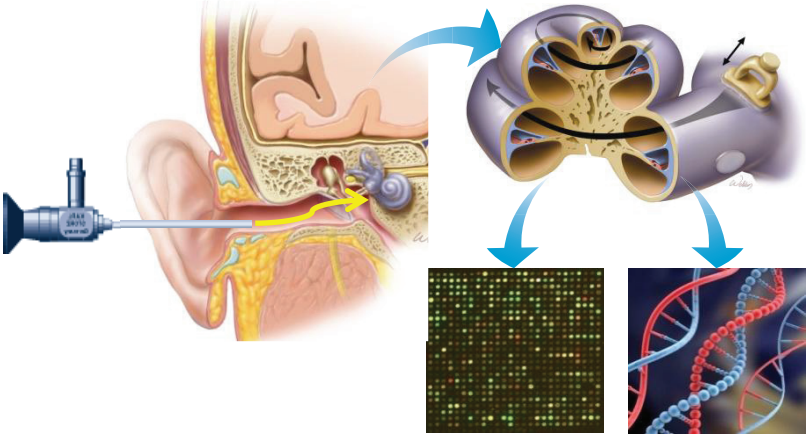
Protective and therapeutic interventions for hearing loss are currently limited by a lack of pathophysiological descriptions of anatomic, molecular, and genetic changes that occur after blast injury, and by the inability to directly visualize cellular and tissue damage to the ear.

Funded by the USAMRMC CRMRP and DHP, researchers at Stanford University along with their collaborators at Texas A&M University, Rice University, and Baylor College of Medicine have developed an endoscope that can image the ear at very high resolution; their objective is to produce a safe, non-invasive, portable device to improve diagnosis and treatment of blast-induced hearing loss. The device is now being tested in human temporal bone to characterize cellular changes that occur within the first 24 hours after blast injury (Figure F-2).

The Stanford research has also developed and validated a blast-injury model that can be used to test possible treatments. By defining the relationship between the blast wave characteristics and resultant damage and progressive injury to the ear, this research is helping to identify molecular changes in the injured tissue that may be drug targets to prevent or reduce damage immediately post-blast. Results from this research to date include several published papers,[15–22] a patent application, and four additional grant awards: two NIH R01 grants, and two grants that will support first-in-human clinical trials.

FIGURE F-2: Imaging Blast-related Damage to the Ear

1) Novel device to image the ear after blast injury at high resolution



2) Cellular, molecular, and genetic characterization studies to identify novel therapeutic agents

Auditory Rehabilitation after Mild Brain Injury

Researchers at the VA Medical Centers in Tampa and Portland have completed clinical trials to examine intervention approaches for Veterans who have significant complaints of difficulty hearing after mTBI despite clinically normal hearing (normal/near-normal auditory sensitivity). Such patients commonly report difficulty understanding speech in noisy environments and/or when people speak rapidly. In a between-subjects randomized controlled clinical trial, blast-exposed patients who had mTBI received rehabilitation via (1) the use of personal miniaturized frequency modulation (FM) systems which increase the loudness of speech signal relative to that of unwanted noise, and/or (2) the provision of auditory training with Posit Science Brain Fitness Program (BFP) which improves listening ability by exploiting neural plasticity. In this study Veterans were randomly selected to receive one of four treatments: (1) FM use alone, (2) BFP training alone, (3) FM+BFP training combined, or (4) informational counseling.

Outcomes were measured subjectively through self-report of auditory competence and objectively through auditory processing evaluation. Results of the study will help to determine whether or not FM systems or auditory training, either alone or combined, are effective as interventions for blast-exposed Veterans with reported functional hearing difficulties and normal/near-normal auditory sensitivity. Initial findings have been submitted to the VA Office of Rehabilitation Research & Development.

Blast-related Auditory Injury Database (BRAID)

The NHRC has developed a database of nearly 17,000 blast and non-blast injured Navy and Marine Corps personnel whose demographic, tactical event, point-of-injury, medical outcome, and pre- and post- audiometric screening data can be used to address key research questions about blast-related hearing loss. Service Members represented in the BRAID database are predominantly male, 28 years older or younger at time of injury, Marine Corps enlisted rank personnel. Thirty-nine percent (39%) of those in the BRAID experienced a hearing loss (> 25 dB) for at least one frequency on an audiogram.

Uniquely, the new database also documents specific blast event characteristics for each injury scenario such as injury severity, mounted versus dismounted posture, distance from blast, and the relative size of munitions involved. The BRAID will allow researchers to address key questions about blast-related hearing loss while for the first time controlling for variables that could affect the severity of the injury.

For example, the NHRC database can be used to support determination and analysis of the prevalence of hearing loss in personnel who are exposed to blast, and identify risk factors and exposures related to specific types of injuries and impairments such as blast-related hearing loss/dysfunction, tinnitus, tympanic membrane perforation, and otalgia. Reliable audiometric data associated with deployment injury will improve the determination of event-related hearing shift and the impact of blast-related injury on human auditory systems. The database will also enable researchers to follow long-term outcomes and examine audiometric configurations at various time points following exposure to blast. It is hoped these findings can provide decisive input about operational readiness and support hearing loss prevention strategies and program policies for affected Service Members and military commands.

Evaluation of Aurally-Aided Visual Search

To effectively communicate, move, and shoot in the combat environment, Service Members must integrate information from their auditory, visual, and vestibular sensory systems. However, most clinical tests can only address the function of a single sensory system in isolation. This makes it difficult to predict how blast/TBI exposed individuals who perform at the bottom end of the normal range in more than one sensory modality might perform on an integrated task that requires use of visual, vestibular, and auditory systems simultaneously. To address this issue, researchers at the National Military Audiology and Speech Center and NICoE are studying how normal and blast-exposed Service Members perform in an Aurally Aided Visual Search (AAVS) task that requires them to use auditory localization cues to locate and identify a visual target presented in a cluttered background of similar visual distracters. This study utilizes the Computer-Assisted Rehabilitation Environment (CAREN) system which allows the AAVS task to be performed in both stationary and walking conditions. Preliminary results collected from 18 blast-exposed participants and 13 normal participants show no significant difference in an auditory discrimination task (using a head-slaved crosshair to the location of the noise) or in a visual discrimination task (accurately identifying the number of dots on a visual target presented at a known location). However for the AAVS task, there were significant differences between the normal and blast-exposed participants and between the stationary and walking conditions. Both groups responded more quickly when walking than when stationary, but with no loss in accuracy. One possible explanation is that walking activates neural processes that are beneficial for AAVS tasks. The results also show that the blast-exposed participants had greater difficultly than the normal participants in both the walking and stationary conditions. This suggests that blast-exposed individuals could be experiencing multisensory integration deficits that may not be apparent in traditional, single modality clinical tests of sensory function. This work was partially supported by a grant from the Congressionally Directed Medical Research Programs, the Department of Clinical Investigation Award W81XWH-12-2-0068, and the Audiology and Speech Pathology Center, Walter Reed National Military Medical Center.

Biomechanical Modeling and Measurement of Blast Injury and Protection Mechanisms

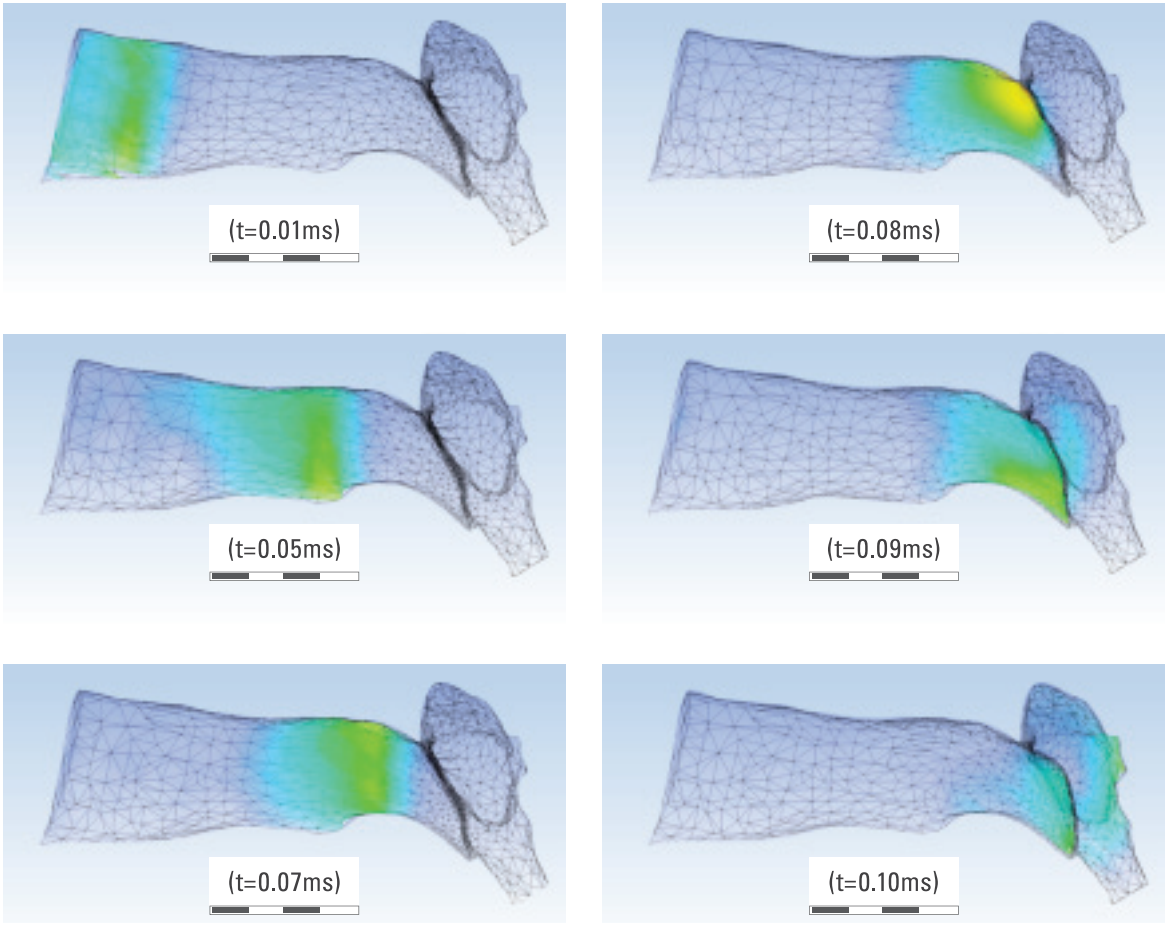
Funded by DHA RDA Directorate, researchers at the University of Oklahoma are studying exposure to high-intensity sound or blast that directly results in hearing loss. Currently, there is a profound lack of knowledge about how high intensity sound waves are transmitted through the ear and what specific changes occur in the ear structures following blast exposure.

This project hypothesizes that the biomechanical response of the middle and inner ear to noise/blast can be characterized in a comprehensive model, using a combined modeling and experimental approach. The research objectives are to determine middle ear protective mechanisms in the conductive path of impulse noise/blast into the cochlea, and to develop a finite element model of the human ear for simulation of acoustic injury. Using human cadaver ears, researchers are attempting to quantify middle ear injury in relation to blast overpressure level and wave direction, and to determine changes of dynamic properties of middle ear tissues after high impulse noise/blast exposure. Supplementing this research, a chinchilla model is being used to identify middle ear protective mechanisms during blast exposure that rely on muscle activity. Biomechanical measurements from the experimental studies will be used to validate a 3-dimensional finite element model of the human ear to predict pressure propagation fields from the ear canal entrance to the middle ear cavity (Figure F-3).

Developing a Biomechanical Model-based Auditory Standard for Impulse Noise

The current impulse noise standard (MIL-STD-1474D) is overly conservative and does not incorporate an objective measure of hearing protection. Funded by the DHA RDA Directorate, researchers at L-3 Applied Technologies are developing a new biomechanically based auditory standard using the improved Auditory Hazard Assessment Algorithm for the Human (AHAAH) model to mathematically simulate traumatic response of the auditory system to impulse noise. The AHAAH model is a physics-based computer model of the human inner, middle, and outer ear electro-acoustically connected to allow the propagation of external noise to the cochlea.

FIGURE F-3: Pressure Propagation in the Human Ear



Time-history plots of the pressure propagation in human ear with an impulse pressure of 28kPa or 182 dB SPL at the entrance of the ear canal.

It has been modified with improved material properties and parameters to produce monotonic dose-response with increasing exposure level, validated against historical large weapon and rifle noise data, with and without hearing protectors, respectively.
The AHAAH model has been converted to MATLAB/Simulink codes for verification of parameters, modifications, and improvements based on the latest published literature data.
To account for effects of hearing protection, a new testing method using acoustical head forms (acoustical test fixture, ATF) is used to collect eardrum pressures under hearing protectors for model input (Figure F-4).
This method was established by field blast tests using ATFs with comparison to human data.
Investigators have identified the integrated cochlear energy as the best damage risk correlate to establish the dose-response curve for determining the injury threshold (TTS > 25dB) based on human data comparison.
Going forward, the intention is to challenge the testing community to adopt the new model-based standard and make recommendations for research needed to address modern data operational needs.

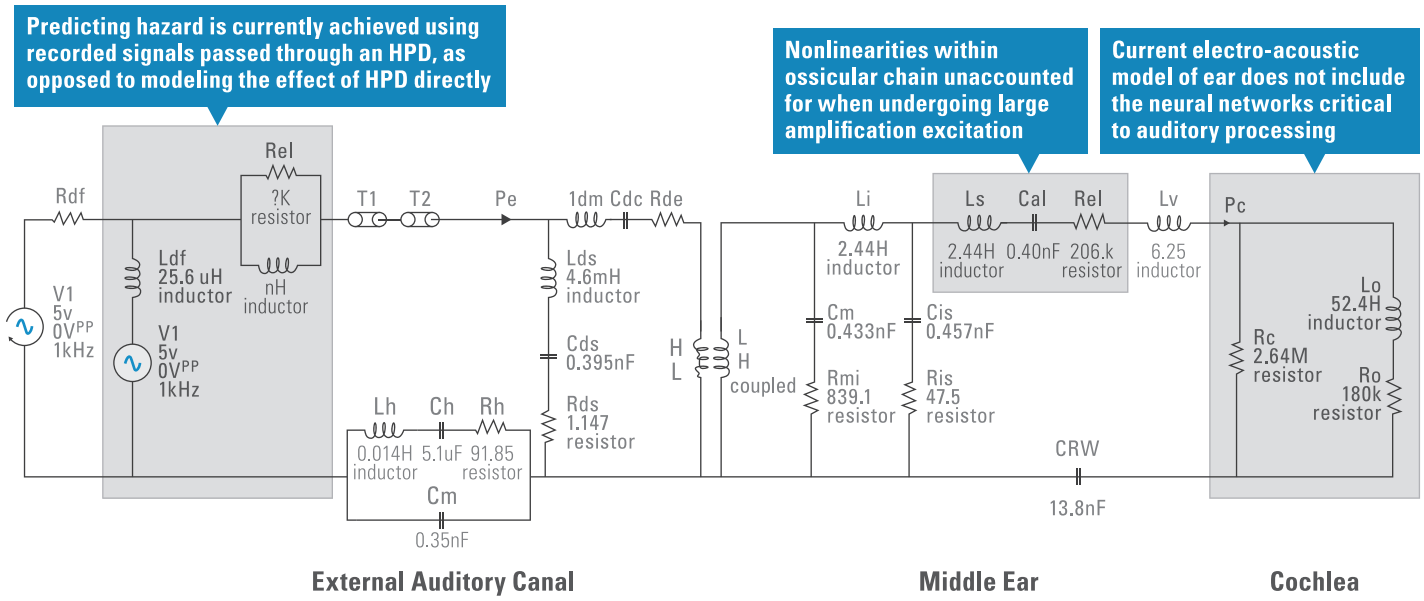
FIGURE F-4: Field Testing ATF Exposure to Mortar Blast

Field test to collect ATF eardrum data for exposure to mortar blast

Improvement and Extension of Auditory Hazard Models

The DHA RDA Directorate has funded Applied Research Associates, Inc. to improve and extend the biomechanical understanding of auditory injury from blast and noise. This project addresses limitations of current auditory risk models that are inaccurate when applied to extreme conditions typical of the modern military service environment.
The AHAAH is a mechano-electro-acoustic circuit analog of the human auditory system designed to predict threshold shifts (Figure F-5). However, the AHAAH model is limited by its oversimplification of the complex ossicular behavior during blast events and lack of validation by animal electrophysiological and behavioral data.
A study designed to address these limitations will test post-mortem human surrogates to quantify the pressures in the external auditory canal and skull exposed to various levels of blast, with and without hearing protection.
The study will also quantify the motion of the bones of the middle ear in the post-mortem surrogate and in a chinchilla model using laser Doppler vibrometry. Findings from these tests will be applied to increase the fidelity of the nonlinear parameters in the AHAAH model representing the stapes and annular ligament, and will establish transfer functions that relate human to animal auditory mechanisms and physiological responses to blast events.
The AHAAH model will also be extended to include the response of the auditory nerve. By extending the AHAAH model into the brain's neural networks, it is possible to gain a better understanding of the effect of blast on auditory neuro-functional pathways. Improvements to the existing model will make it possible to predict hearing loss likelihood in individuals who have sustained blast injury with or without hearing protection.

FIGURE F-5: AHAAH Model of Ossicular Behavior during Blast



Tinnitus

Tinnitus Management and Epidemiology

The VHA has provided ongoing support for research performed at the NCRAR to evaluate and develop the Progressive Tinnitus Management (PTM) program, a cross-disciplinary (mental health and audiology) counseling/self-management approach shown to reduce symptoms and improve life satisfaction for tinnitus sufferers.

PTM is utilized across VA and military hospitals and can be delivered via in-home telehealth technology, which greatly expands access. PTM online training has been developed for VA clinicians, and is currently under development for military clinicians, which will increase its utilization as clinicians complete the training. The VHA Polytrauma and Blast-Related Injuries (PT/BRI) Quality Enhancement Research Initiative is currently supporting a PTM "pre-implementation" project, which will lead to greater access to tinnitus clinical services for Veterans with TBI/polytrauma.

CDMRP provided funding to the NCRAR for related research now underway to address the etiology, prevalence, and effects of tinnitus and hearing loss among newly-discharged Veterans. This research will include cross-sectional analyses to address the relationships between military noise and solvent exposures, blast-related injuries, and auditory disorders. The HCE has been approved to expand this research to include active duty military personnel at the SAMMC. Subsequent longitudinal research is planned to identify measures needed for the assessment of military injuries and to inform future practice guidelines.

Central Auditory Processing Disorder

Prevalence and Verification of CAPD

Clinicians and researchers who work in DoD and VA health care communities observe that even when blast-exposed individuals present with normal audiometric thresholds and no severe neurological problems, they experience difficulty understanding speech in complex listening environments. This may be evidence of blast-related damage to peripheral and central auditory structures. One of the most challenging problems facing DoD and VA audiologists is to diagnose and treat such patients. Researchers at WRNMMC, SAMMC, and the Navy Medical Center San Diego are conducting a three-year multi-center study to identify specific behavioral tests and self-report measures that are sensitive to hearing difficulties experienced by blast-exposed individuals.

The objective of the study is to address the prevalence of central auditory processing dysfunction, and to develop evidence-based protocols for its diagnosis. In the first phase of the study, active-duty Service Members are being tested in routine hearing conservation screenings to determine the proportions of blast-exposed and non-blast-exposed Service Members with normal audiometric thresholds who report difficulty hearing in complex listening environments or who perform more poorly than expected on difficult speech-in-noise tests. In the second phase of the study, Service Members with listening difficulties will be evaluated and compared against non-blast-exposed control subjects for their performance on a battery of central auditory and cognitive communication processing tests. Researchers at WRNMMC are also working to develop functional measures of hearing performance that may be useful to evaluate patients who have normal audiograms but find it difficult to understand speech in complex auditory environments. Participants with normal or near-normal audiometric thresholds were identified and recruited to blast-exposed (experimental) and non-blast-exposed (control) groups and tested for their performance in complex listening tasks designed to mimic the acoustic cues likely to be encountered in real-world environments. The test battery was designed to examine various aspects of functional hearing ability, including speech perception in the presence of noise, speech and babble maskers, audiovisual speech perception, perception of fast speech in reverberant environments, spatial release from masking, and sound localization. A significantly larger number of blast-exposed individuals performed in the bottom range of normal, pointing specifically to difficulties in spatial perception and in the understanding of fast speech in reverberant environments.

Auditory Perception and Cognition Following TBI

Blast-related TBI is often accompanied by hearing loss and/or tinnitus due to damage to the cochlea and central auditory system. Although audiologic screening of TBI patients is not routine, previous studies have found hearing abnormalities in more than 50% of patients with blast-related TBI.[23] Hearing disorders may explain other TBI-related deficits as hearing loss has been shown to disrupt speech comprehension[24] and working memory.[25] Although there is research to indicate that other types of hearing loss (e.g., age-related hearing loss) can affect memory and cognition,[26,27] relatively little research has been done to address these impairments for TBI-related hearing loss.

To better understand cognitive impairment as may be associated with TBI-related hearing loss, researchers at the VA Northern California Health Care System are studying auditory perception and cognition in Veterans with TBI. Veterans who have sustained TBI are being assessed for changes in hearing, speech perception, and memory as may relate to abnormalities in brain structure and functional brain activation.

Early results of this research indicate that a decline in hearing due to TBI, even when still within normal range, can impair memory ability. The reverse also holds true: deficits in concentration and executive function due to TBI can adversely affect Veterans' ability to understand speech in noisy environments. Findings from patients' brain scans reveal that abnormalities in frontal brain regions correspond to greater memory deficits, while abnormalities in temporal brain regions correspond to greater hearing deficits.

An anticipated benefit of this research is to facilitate the development of rehabilitation strategies more specifically targeted to underlying structural damage and neurological dysfunction. It is particularly useful to examine the incidence of hearing and phonological processing deficits in TBI populations because audiological rehabilitation with hearing aids and perceptual training can significantly improve speech comprehension and, ultimately, memory and concentration. It is necessary first to identify patients who are likely to benefit from hearing-based versus memory-based rehabilitation. Analysis of brain structural abnormalities will also improve our understanding of the structural basis of TBI-related cognitive deficits.

Chronic Effects of Blast on Central Auditory Processing

A 2014 IOM report concluded that blast exposure can adversely affect both peripheral and central auditory nervous systems, but found inadequate evidence in the literature to conclude that blast effects on central auditory processing persist beyond six months after exposure. To address this question, researchers at the NCRAR and Oregon Health and Science University have conducted research to determine if blast exposure has negative long-term implications for the central auditory system. Dysfunction in central auditory processing typically manifests as poor performance in tasks that require temporal pattern perception, auditory temporal resolution, binaural processing, and dichotic listening. Electrophysiological measures of auditory cortical function may also indicate slower, diminished responses. All of these changes can occur even when peripheral hearing function is within the normal range.[28] Investigators at VA administered behavioral tests to evaluate temporal acuity (detection of brief silent intervals in ongoing noise), dichotic listening (auditory selective attention), temporal pattern perception, and binaural processing (binaural signal detection) to Veterans whose previous most serious exposure(s) to blast had occurred, on average, more than seven years earlier. The researchers found that 83% of blast-exposed individuals had abnormal results on at least one test (versus 19% of non-blast-exposed control subjects) and that for every measure, the blast group performed more poorly on average. Notably, some blast-exposed Veterans did not have difficulties with any of the tests; few performed poorly on more than three tests. This suggests that blast exposure produces a range of chronic effects and there is a need for test strategies that can capture a wide range of potential dysfunction while avoiding fatigue. These findings have direct clinical implications for military audiologists and other clinicians treating Service Members and Veterans who have been exposed to blast. Audiograms are insufficient to evaluate the problems these individuals may experience. Further, difficulties processing auditory information may hinder effective care if deficits are not recognized by caregivers.

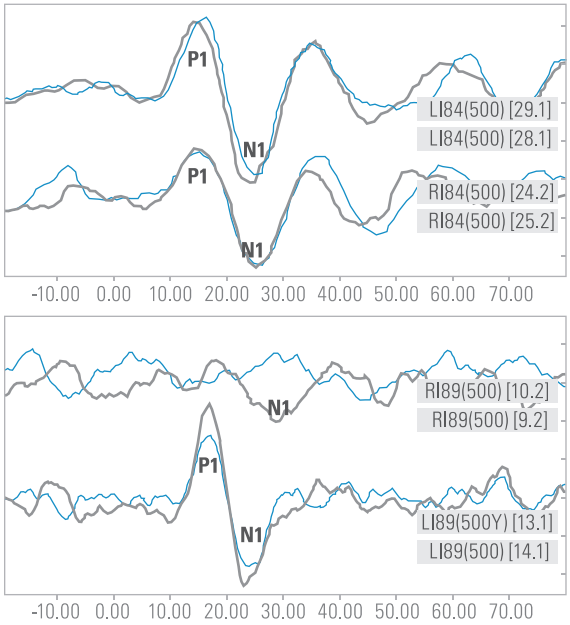
Balance Injuries

Vestibular Consequences of Blast-Related TBI

Researchers at the Mountain Home VA Medical Center (Tennessee) Vestibular/Balance Lab have recently completed a case-controlled study of OEF/OIF Veterans to identify effects of mTBI and blast exposure on central and peripheral vestibular function, postural stability, and dizziness-related quality of life. Individuals with a history of blast exposure and/or mTBI and symptoms of dizziness were compared with age-matched controls (non-blast/TBI, no dizziness) based on a battery of tests, including brain imaging (MRI, DTI, MR spectroscopy), vestibular function tests, and balance and gait testing, and questionnaires regarding symptoms, tinnitus, and posttraumatic stress.

Preliminary brain imaging data reveal abnormal susceptibility weighted imaging (vascular damage) in 20% of patients with TBI and/or blast exposure with blast exposure.

FIGURE F-6: Cervical Vestibular Evoked Myogenic Potentials Following TBI/Blast



cVEMP comparison of control (upper) and blast-exposed (lower) subjects. The blast-exposed subject has no repeatable cVEMP on the right side.

Almost all (98%) of the individuals in the mTBI/blast group also reported tinnitus (versus 14% of controls). Preliminary findings of the VA study indicate that absent or abnormal cervical vestibular evoked myogenic potentials (cVEMPs) were the most common clinical findings following TBI/blast, and that in fact the otolith organs may be relatively more susceptible to TBI/blast injury than the horizontal semicircular canal (Figure F-6). These findings are consistent with other observations that the saccule may be especially susceptible to blast- or acute noise-related damage,[29–31] and suggest that current comprehensive vestibular testing may be missing important otolith impairments in patients exposed to blast. Preliminary data from the VA study also demonstrate that balance performance on the sensory organization test may be impacted by loss of saccular function, a result consistent with previous research demonstrating that impaired otolith function may be associated with increased postural sway and increased fall risk. Pilot data have been published,[32] and full report manuscripts are now in preparation.

FIGURE F-7: Horizontal Video Head Impulse Test

Clinician and patient positions during the horizontal video head impulse test (vHIT)

New Solutions in Clinical Assessment

There is a need for rapid, portable, and easily administered tests to assess balance function after injuries such as TBI and blast exposure. Early identification of balance disorder can indicate the presence of mTBI that may otherwise be difficult to diagnose. However, current "gold standard" balance function tests are relatively expensive, slow, and non-portable. They are rarely used in military field settings because they require advanced training to administer, and are ill-suited for transport and use in austere environments. Researchers at the James H. Quillen VA Medical Center are now investigating a new test, the video head impulse test (vHIT) that uses a high-speed digital video camera to record head and eye movement during and after brief, high-acceleration, passive head rotations in the horizontal and vertical planes (Figure F-7). The vHIT detects and records abnormal eye movement and calculates the gain of the vestibulo-ocular reflex to identify unilateral and bilateral vestibular dysfunction. It assesses the vestibular system using a stimulus that is physiologically relevant and representative of head movements (e.g., rapid head turns while moving) that typically occur during military activities and daily living. Compared to other tests, the vHIT is also less costly, relatively fast (5–10 minutes) to administer, more portable, and more comfortable for patients. It consists of a laptop computer and either video goggles or an external camera, and can be administered by corpsman-level medical personnel. Software provides results and employs automated response detection and analysis algorithms. The study will examine the precision and accuracy of the vHIT for consideration of its potential use in-theater and to determine the role of the vHIT in the vestibular test battery.

Innovations in Vestibular Therapy

Researchers at the USAARL are developing a tactile sway feedback strategy to augment physical therapy for patients with balance disorders, which are common among victims of concussion or blast. Touch cues are very helpful to balance. Even when contact force is inadequate to provide physical support, holding one's finger on a stable reference bar can reduce sway as effectively as visual cues. For individuals who have lost their eyesight, the light touch of a cane is as effective as forceful contact to reduce postural sway. Recent studies suggest that vibrotactile sway cueing may also be helpful to improve stability of people with vestibular or balance problems.

The device developed by USAARL is a sensitive detector of body sway, measured via center-of-pressure changes across a floor-based platform, and indicates to the user which direction the sway has occurred (Figure F-8).The user receives haptic feedback through a belt (worn around the torso) that houses eight vibrotactors. A prototype version of the device is now being tested on civilian balance patients and military personnel who experience balance problems following MTBI/concussion, to determine if tactile sway feedback fosters more rapid or complete recovery of balance after vestibular rehabilitation therapy. The system is already portable enough for easy relocation within or between clinical settings; efforts are underway to make it wearable for ambulatory use.

FIGURE F-8: Tactile Sway Feedback System

The tactile sway feedback system is designed to aid patient evaluation and rehabilitation, and foster more rapid return to duty

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