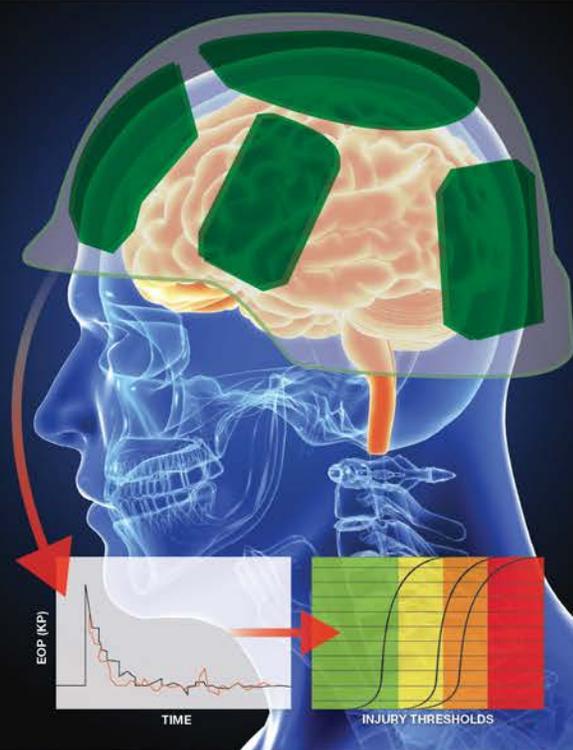


Biomedical Basis for Mild Traumatic Brain Injury (mTBI) Environmental Sensor Threshold Values

4-6 November 2014
McLean, VA



Summary of Meeting Proceedings, Key Findings, and Expert Panel Recommendations

**Department of Defense
Blast Injury Research Program Coordinating Office**

ATTN: MCMR-RTB
810 Schreider St.
Fort Detrick, Maryland
21702-5000

Phone:
301-619-9801

Email:
USArmy.Detrick.MEDCOM-USAMRMC.Other.Medical-Blast-Program@mail.mil

Website:
<https://blastinjuryresearch.amedd.army.mil/>

The opinions, interpretations, conclusions, and recommendations
contained herein are those of the authors and are not
necessarily endorsed by the Department of Defense or the US Army.

Preface

It is my pleasure to acknowledge the staff of the Department of Defense (DoD) Blast Injury Research Program Coordinating Office for its work on behalf of the DoD Executive Agent in planning and implementing the 2014 International State-of-the-Science Meeting on the Biomedical Basis for Mild Traumatic Brain Injury Environmental Sensor Threshold Values. This meeting brought together subject matter experts from around the world representing the DoD, other Federal agencies, academia, and industry to address the challenges associated with correlating environmental sensor threshold values to injury outcomes following a blast event.

I wish to commend the meeting planning committee, meeting presenters, expert panel members, and attendees for their excellent contributions, both in their presentations and discussions. Without their active participation, it would not have been possible to critically assess the state of scientific knowledge.

I thank all investigators whose research has supported the fielding of environmental sensors and the development of laboratory and computational models of blast injury. These efforts have advanced our knowledge of the underlying biological mechanisms of blast-related mild traumatic brain injury (mTBI). All of this work has led to a better understanding of the challenges facing Service Members and will help to focus future research efforts.

Further, I ask all of the meeting participants and the communities they represent to continue working together to solve the compelling research questions aimed at validating threshold values for mTBI which may guide the development of improved medical screening and assessment tools, and the design and development of enhanced protection equipment.

This document summarizes the proceedings of the meeting and serves to disseminate information regarding what is known and what still needs to be learned about the biomedical basis for mTBI environmental sensor threshold values. These proceedings will reach a broad audience that includes scientists, engineers, medical researchers, health care professionals, protection system development experts, and military leaders and decision makers at all levels. Thank you for your contributions that made this meeting a great success.

John F. Glenn, Ph.D.
Senior Executive Service
Principal Assistant for Research and Technology
US Army Medical Research and Materiel Command

Executive Summary

Despite research in the areas of mild traumatic brain injury (mTBI) and methods for detecting mTBI events, our understanding of the biomedical basis for mTBI environmental sensor threshold values is limited. In particular, our ability to quantify blast intensity and correlate that data to acute and chronic intracranial effects is limited.

To identify challenges associated with correlating environmental sensor threshold values to injury outcomes, the Department of Defense (DoD) Blast Injury Research Program Coordinating Office organized the 2014 International State-of-the-Science (SoS) Meeting on the Biomedical Basis for mTBI Environmental Sensor Threshold Values. This meeting brought together subject matter experts from across the DoD, other Federal agencies, academia, industry, and international organizations. Discussions and recommendations from the meeting will help guide the development of improved medical screening and assessment tools, as well as improvements in the design and development of personal protective equipment.

Leveraging the SoS literature review, meeting presentations, and outputs from the focused working group sessions held during the meeting, the Expert Panel concluded that:

Biomedically valid sensor threshold values do not yet exist for blast-induced mTBI

Additional research is required to determine the relative contributions of linear acceleration, rotational acceleration, and blast overpressure to injury as well as the individual factors (e.g., past exposure history, physique, gender) that contribute to mTBI risk. In addition, increased collaboration and access to existing blast and blast injury data is essential to develop product specifications and performance standards for sensor technologies.

The Expert Panel developed recommendations and a framework of suggested actions to advance the state-of-the-science toward a biomedically valid environmental sensor threshold value for blast-induced mTBI. Based on the findings from the meeting, the Expert Panel recommended to:

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

To fulfill this objective, the multiagency, multidisciplinary task force will analyze existing data to identify the essential sensor data elements to be collected that will be most predictive of injury. The task force, in collaboration with the broader TBI community, will develop a consensus clinical definition/measure of mTBI against which sensor thresholds can be compared. Current mTBI assessment tools will be evaluated and the efficacy of potential screening tools such as biomarkers, cognitive and/or motor tests, and neuroimaging tools will be assessed. In addition, the task force will validate or invalidate existing preclinical models based on the best science available and identify knowledge gaps to guide future research efforts. These activities will accelerate the development of a biomedically valid mTBI threshold value and will guide the development of improved screening tools and protective equipment.

Contents

1.0	Introduction.....	1
2.0	Background.....	2
2.1	Definition and Diagnosis of mTBI.....	2
2.2	Blast versus Impact Injuries	3
2.3	Mechanisms of Blast-Induced mTBI.....	3
2.4	Current Status of mTBI Biomedical Assessment Tools.....	3
2.5	Current Applications of Commercially Available Sensor Technologies.....	4
2.6	Key Background Concepts that Informed Meeting Discussions	5
3.0	Establishing a Shared Understanding of Sensor Threshold Requirements and Challenges.....	7
3.1	Key Messages from Keynote Speakers	7
3.2	Topic Presentations: Setting the Stage.....	8
3.3	Scientific Presentations: Defining the State of the Science	13
4.0	Focused Working Group Summary.....	21
4.1	Focused Working Group Question #1.....	22
4.2	Focused Working Group Question #2.....	23
4.3	Focused Working Group Question #3	24
4.4	Focused Working Group Question #4	25
5.0	SoS Expert Panel Findings and Recommendations	27
5.1	Expert Panel Findings.....	27
5.2	Expert Panel Recommendations	28
6.0	Conclusions	29
7.0	Appendices.....	30
	Appendix A. References	30
	Appendix B. Acronym List.....	31
	Appendix C. Table of Environmental Sensors.....	33
	Appendix D. Welcome Letter	34
	Appendix E. Meeting Agenda.....	35
	Appendix F. Poster Presentations.....	38
	Appendix G. Keynote Speaker Biographies.....	40
	Appendix H. Expert Panel Biographies.....	43
	Appendix I. Meeting Planning Committee Members	45
	Appendix J. Meeting Participants.....	46

Figures

Figure 1. Ideal single threshold curve (left panel) versus injury risk curve (right panel). The red dotted line represents a threshold for injury in the left panel, but represents a threshold for decision or action in the right panel.	6
Figure 2. Total number of DoD traumatic brain injuries diagnosed from 2000-2014. TBI cases have been separated by severity.....	8
Figure 3. Comparison of concussion outcomes. Data were obtained from the Known Events Tracker, a list of events that are potentially concussive as defined by the four criteria set by DoD.	11
Figure 4. Example of cost-benefit analysis that can be used to mathematically identify an optimal threshold.	12
Figure 5. Blast pressure transmittance in a human surrogate head model.....	14
Figure 6. mTBI risk curves based on logistic regression of HIT system data from the Virginia Tech collegiate football study.....	14
Figure 7. Contour lines from a logistic regression of concussion probability as a function of combined peak linear and peak rotational acceleration.....	15
Figure 8. Location and direction of impacts used to test the Stanford Mouthguard and HIT system against a reference sensor placed in a human surrogate neck and head equipped with a football helmet.....	15
Figure 9. Schematic injury risk curve showing boundaries that account for sensor measurement errors.....	16
Figure 10. Incident number and overpressure range for different blast categories in the PREVENT large animal study.....	17
Figure 11. Overpressure statistics for blast exposures recorded in the QBIS study.....	18
Figure 12. Definition of Helmet Mounted Sensor System (HMSS) sensor thresholds using injury risk curves from the JARI study of impacts on non-human primates.....	19
Figure 13. Reduction in linear and rotational acceleration provided by head protection during blunt impacts.....	19
Figure 14. Plots supporting the need to measure only linear acceleration.....	20

Tables

Table 1. Classification of TBI Severity.....	2
Table 2. Expert Panel Recommendations.....	28

1.0 Introduction

Blast-related mild traumatic brain injury (mTBI) is widely accepted as one of the “signature injuries” of Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) (Kovacs, Leonessa, & Ling, 2014). According to data from the Defense and Veterans Brain Injury Center (DVBIC), in the years between 2000 and the first half of 2014, over 300,000 Service Members sustained a traumatic brain injury (TBI); the vast majority (82.4%) of these injuries was classified as mTBI (DVBIC, 2014). Mild TBI affects a large number of Service Members, Veterans, and their families, as well as the operational readiness and resilience of our troops. The Department of Defense (DoD) defines mTBI as a traumatically-induced injury and/or physiological disruption of brain function as a result of an external force associated with at least one of the following: a) loss of consciousness for 0-30 minutes, b) alteration of consciousness for up to 24 hours, c) posttraumatic amnesia for up to 24 hours. Additionally, cases where a CT scan is performed, no intracranial lesion is found (US Department of Veterans Affairs & US Department of Defense, 2009) (Wilk, et al., 2010).

In response to the significant health concerns, several environmental sensors have been fielded to collect data on blast exposures and other potentially concussive events (PCEs), such as head impacts. Current environmental sensor research and development efforts are focused on devices that can notify Service Members and line leaders of exposure to a potentially concussive event so that Service Members can seek treatment and line leaders can better protect at-risk Service Members.

SoS Meeting Objectives

- Assess the current state-of-the-science for the biomedical basis of environmental sensor threshold values and the relationship between these threshold values and the risk of developing mTBI
- Identify gaps in the development and utilization of current environmental sensor injury threshold values
- Guide future research to gain understanding of the relationship between varying blast forces and the development of TBI
- Improve protection, treatment, and mitigation for both civilians and Service Members

To date, the detection of PCEs with an environmental sensor has remained limited largely due to the fact that there is not a biomedical basis for the sensor threshold values for identifying blast-induced mTBI. The DoD Blast Injury Research Program Coordinating Office (PCO) hosted the International State-of-the-Science Meeting on the Biomedical Basis for Mild Traumatic Brain Injury Environmental Sensor Threshold Values on 4 – 6 November 2014 in McLean, Virginia. This meeting brought together subject matter experts from across the DoD, other Federal agencies, academia, industry, and international organizations to assess the current state-of-the-science underlying the mTBI threshold values associated with environmental sensors.

The meeting planning committee included clinical, research, and program representatives from the DoD, the National Institutes of Health (NIH), the National Football League, and the National Collegiate Athletic Association (NCAA) (see Appendix D for the list of planning committee members). The committee identified a panel of six subject matter experts to serve as the Expert Panel (see Appendix H for Expert Panel Biographies). The Expert Panel was charged with chairing the focused working group sessions and identifying the major meeting findings and recommendations needed to advance the state-of-the-science of environmental sensor threshold values.

One hundred eighteen participants from the DoD, the US Department of Veterans Affairs (VA), NIH, athletic organizations, academia, medicine, industry, and international organizations attended the meeting (see Appendix J for the list of meeting participants). The agenda (see Appendix D) consisted of presentations with panel-facilitated discussions, a poster session, concurrent

participant focused working group sessions, and Expert Panel member report-outs summarizing the focused working group sessions. Following the meeting, an executive panel session was held to review meeting data and formulate recommendations. The meeting presentations and poster abstracts can be found on the PCO website at

https://blastinjuryresearch.amedd.army.mil/index.cfm?f=application.pco_sos_materials.

This meeting proceedings provides a summary of background information from a literature review prepared to inform meeting participants in advance of the meeting (see Section 2.0) and a summary of scientific topic presentations that served to elevate participant understanding of the current state of ongoing research efforts is presented in (see Section 3.0). The presentations that provided the context and objectives for meeting participants and the needs of the end user community are also summarized in Section 3.0.

A key element of the meeting was the opportunity for members of the scientific community to engage in rigorous dialogue regarding the knowledge gaps and requirements for advancing the state-of-the-science with respect to environmental sensor thresholds. The consolidated outputs from the six focused working group sessions are presented in Section 4.0. Finally, the Expert Panel findings and recommendations that were developed to guide further research efforts are detailed in Section 5.0.

2.0 Background

This section provides definitions and background information relevant to the focus of this State of the Science Meeting. In particular, the literature review findings summarized below highlight complexities associated with diagnosing and/or screening for mTBI, the status of currently available tools for biomedically evaluating mTBI, and the challenges associated with defining, interpreting, and applying environmental sensor threshold values. The literature review is available on the PCO website at

https://blastinjuryresearch.amedd.army.mil/index.cfm?f=application.pco_sos_materials.

2.1 Definition and Diagnosis of mTBI

The DoD defines TBI as the disruption of normal brain function resulting from a blow or a jolt to the head, and these injuries can be classified by severity as outlined in Table 1 (US Department of Veterans Affairs & US Department of Defense, 2009). Mild TBI can be more difficult to define and diagnose than the more easily visualized symptoms observed in moderate and severe TBI.

Table 1. Classification of TBI Severity

Criteria	Mild	Moderate	Severe
Structural Imaging	Normal	Normal or abnormal	Normal or abnormal
Loss of consciousness	0 to 30 minutes	> 30 minutes and < 24 hours	> 24 hours
Alteration of consciousness	Up to 24 hours	> 24 hours; Severity based on other criteria	
Posttraumatic amnesia	0 to 1 day	> 1 and < 7 days	> 7 days
Glasgow Coma Scale	13 to 15	9 to 12	< 9

Symptoms of mTBI may include confusion, inability to concentrate, memory loss, headache, nausea and vomiting, problems with balance and coordination, mood changes, and sleep disturbances. (Centers for Disease Control and Prevention, 2010; American Academy of Neurology, 2012). Despite the recognized symptoms, no objective criteria for assessing mTBI exist; rather, mTBI

remains a clinical diagnosis. A physician, often a neurologist, may use a combination of physical evaluations, Glasgow Coma Scale, questionnaires, cognitive tests, or brain imaging tools to establish mTBI diagnosis (American Academy of Neurology, 2012). Other assessment tools include the Military Acute Concussion Evaluation (MACE), which is a key diagnostic tool used in military settings, (French, McCrea, & Baggett, 2008) and the Standardized Assessment of Concussion (SAC), a rapid evaluation of memory, attention, and physical coordination used by sideline sports medicine personnel as a screening tool (The SPORT Foundation, 2014).

2.2 Blast versus Impact Injuries

Blast events cause a wide array of complex injuries, including penetrating ballistic wounds, burns, and inhalation injuries; the term “blast injury” may refer to any of these injuries. Blast-induced mTBI can result from the blast overpressure wave generated by an explosion and/or the rapid acceleration/deceleration of the head upon impact with blunt objects caused by the blast force. Within the meeting proceedings, the two types of blast-induced mTBI are referred to as *blast overpressure injury* and *impact injury*, respectively. Impact injuries also include non-blast-induced mTBI injuries such as those sustained in sports and automobile accidents.

2.3 Mechanisms of Blast-Induced mTBI

Blast-induced mTBI can result both from the overpressure wave associated with the blast event, or the impact, as defined above. Studies have suggested a number of mechanisms by which the overpressure wave can cause brain injury. These include linear and rotational acceleration of the head, skull flexure, structural cavitation, and the entry of overpressure waves directly through the cranium or indirectly through the thorax followed by transmission to the brain via the vasculature.

To date, the contributions of blast overpressure and rapid head acceleration/deceleration to mTBI remain unknown. Research indicates that head acceleration (both linear and rotational) is a major contributing factor to blast-induced mTBI. Current evidence suggests that flexion (forward bending) spinal trauma results in more serious injury than extension (backward bending) spinal trauma. Further research is needed to understand the differential contributions of blast overpressure and impact to mTBI and to determine which measurements are the most important in the application of environmental sensors in screening for mTBI. Understanding the mechanisms of mTBI may also lead to new advancements in personal protective equipment.

Key literature review findings

- The relative contributions of blast overpressure and rapid head acceleration/deceleration to mTBI are unknown
- The exact contribution of overpressure waves entering via the thorax to structural changes in the brain following blast exposure is unknown

2.4 Current Status of mTBI Biomedical Assessment Tools

Advances in animal modeling and neuroimaging have allowed for more detailed investigation of the pathophysiological (e.g., neuroanatomical, cellular, molecular) outcomes of mTBI (including blast- and non-blast-induced injuries). Neuroimaging tools such as functional magnetic resonance imaging (fMRI), diffusion tensor imaging (DTI), susceptibility weighted imaging (SWI), and quantitative susceptibility mapping (QSM) have provided imaging data demonstrating neuronal, axonal, and vascular changes which may be indicative of mTBI. Studies have indicated that these imaging tools may be sensitive to mTBI-related changes in brain structure and function, and

therefore able to detect mTBI; however, issues of data interpretation remain. For example, the rate of false positives can still be significant for these imaging techniques. Furthermore, some imaging techniques may require baseline data, which may be impractical. Before any imaging tools can become widely applicable for the diagnosis of mTBI, quantitative methods must account for hardware and software disparities, guidelines must be provided for how to interpret obtained data, and output values must be standardized.

Continued research into the neuropathology/pathophysiology of mTBI may also lead to the identification of biomarkers for use in diagnosing mTBI. Data obtained primarily from animal studies suggest the serum levels of certain biomolecules change in a dose-dependent manner following blast exposure. Post-mortem studies investigating chronic traumatic encephalopathy and a seminal study of Olympic boxers correlating particular protein levels in cerebrospinal fluid (CSF) with exposure to potential brain injury suggest the possibility of establishing potential CSF biomarkers for mTBI (Neselius S. B., 2012). Despite these advances in preclinical animal studies and in clinical research, the exact pathophysiological and clinical outcomes of blast and non-blast mTBI remain unknown.

Key literature review findings

Understanding of the underlying pathophysiology of mTBI remains limited despite advances in neuroimaging, biomarkers, and computational modeling

Computational modeling is another tool for studying the mechanism of blast-induced mTBI. Computer models can simulate the movement of both the head and brain in response to blasts, and recent advances in modeling allow the concurrent simulation of the dynamic responses of both fluids and solids to blast events. Such simulations can

estimate intracranial pressure, strain, stress, and acceleration experienced by the brain during blast exposure to elucidate mechanisms of blast-induced TBI. Computational modeling is a relatively low-cost approach, but the accuracy of computational modeling is limited by the ability to determine the appropriate values for the tissue material parameters and associated mechanical properties in the model, which have varied by orders of magnitude. Computational models do offer the advantage of enabling the investigation of phenomena and conditions not feasible in human studies or in laboratory experiments.

2.5 Current Applications of Commercially Available Sensor Technologies

There are a variety of commercially available environmental sensors designed to measure pressure as well as linear and rotational acceleration. Each of these commercially available sensors have various placement locations ranging from the back of the neck, in a mouth guard, skullcap, and within a helmet (see Appendix C for a Table of Environmental Sensors). Helmet-mounted blast sensors such as British Aerospace Systems' Headborne Energy Analysis and Diagnostic Systems™ (HEADS), Allen Vanguard's blast dosimeter, BlackBox Biometrics' Blast Gauge™, and Georgia Tech Research Institute's Integrated Blast Effect Sensor Suite™ (IBESS) have been deployed by the military, but no reports based on field data have been published. All of the noted sensors collect data on overpressure and acceleration experienced by the helmet with the exception of the Blast Gauge™. While many reports have been published on Simbex's Head Impact Telemetry (HIT) System, these have focused on sports injuries (e.g., concussions). No published studies have examined use of the HIT System in the military. The HIT System measures and estimates parameters related to linear and angular acceleration, duration and location of impact. Used alone, the HIT System cannot predict the presence of head injuries associated with overpressure.

Other sensors designed to detect sports-related impacts include Reebok's CHECKLIGHT™ and X2's xPatch™. CHECKLIGHT is currently available as a skull cap that displays a light to indicate the presence of a potential injury-causing impact, but does not transmit detailed recorded data. The xPatch is a wearable electronic device that can be taped behind the ear. The sensor has six-degree-of-freedom accelerometers, allowing xPatch to measure linear and rotational impacts and to determine impact location and direction using software algorithms. Information regarding these sensors is limited because there are no published studies determining standards for either CHECKLIGHT or xPatch. Like the HIT System, these sensors cannot predict injuries associated with overpressure.

Key literature review findings

- Reports linking data recorded from fielded sensors to observed brain injuries were not available
- Sensor accuracy validation tests are being performed ad hoc by the sensor developers
- Standards for sensor development or sensor parameters do not exist

2.6 Key Background Concepts that Informed Meeting Discussions

Single Threshold Values versus Injury Risk Curves

Ideally, the term “threshold” would refer to an exposure value obtained by a sensor that would predict injury when exceeded. In reality, measurement noise, differences between individuals, differences in events, and other factors eliminate the likelihood of single ideal threshold value, such that predicting injury becomes a probability-based assessment. That is, given an exposure or sensor value for a measured parameter (e.g., linear acceleration, rotational acceleration, overpressure), there is a probability of developing mTBI. The probability of injury as a function of exposure (or sensor) value is called an injury risk curve, which can only be obtained through the observation of a large number of events.

The concept of ideal single injury thresholds versus injury risk curves is demonstrated in Figure 1. An injury risk curve has a graded probability of injury between 0% and 100%, with greater probability corresponding to higher values of sensor output (Figure 1; right panel). A single injury threshold is simply a step-function injury risk curve that has 0% chance of developing mTBI below the threshold and 100% chance of developing mTBI above the threshold (Figure 1; left panel).

For the step-function risk curve, there is only one logical value for the placement of the threshold (red dotted line in the left panel of Figure 1). For the graded injury risk curve, there is no clear-cut placement of the threshold line. In this case, the threshold line is no longer an injury threshold (i.e., a single value that separates injury from no injury) but rather a decision threshold (i.e., a value that separates action from no action). Within a military context, actions may include medical evaluation, mandatory rest, or evacuation; all of which have implications for the health of our Service Members, associated costs, and impacts to operational readiness.

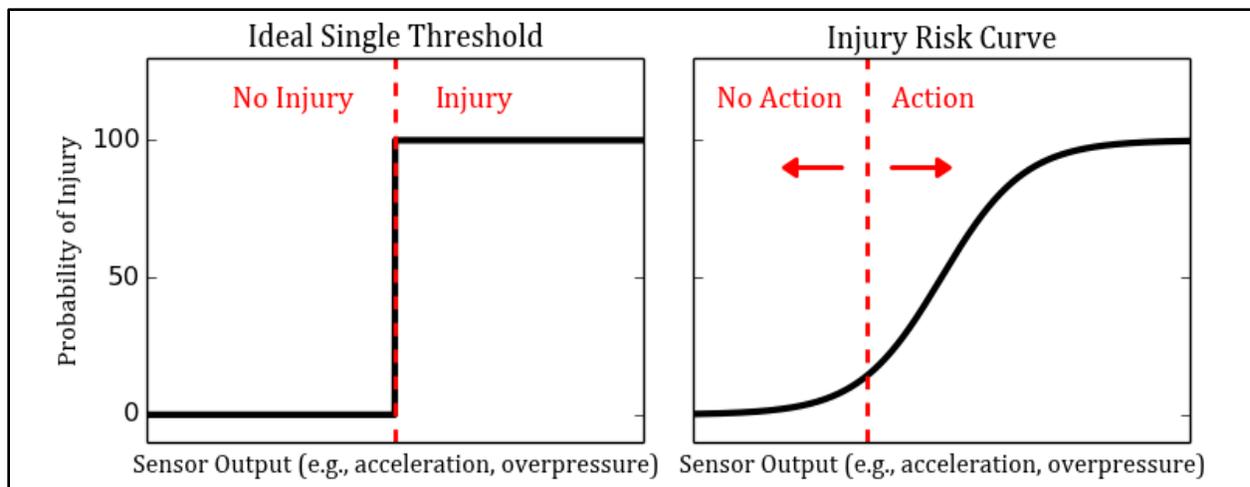


Figure 1. Ideal single threshold curve (left panel) versus injury risk curve (right panel). The red dotted line represents a threshold for injury in the left panel, but represents a threshold for decision or action in the right panel.

Placement of the decision threshold is a policy issue, one that decision makers and military leaders must set based on their risk tolerance. Setting the threshold too low will increase the likelihood of more false positives (i.e., incorrectly predicted cases of mTBI), whereas setting the threshold too high will favor more true negatives (i.e., unidentified cases of mTBI). Factors such as the distribution of exposure values, the cost of performing an action, and the cost of missing an individual requiring medical attention may enter into the calculation of risk tolerance.

Validation of Blast Environmental Threshold Values

The ability of environmental sensors to predict injury is complicated by background noise in sensor measurements, variations in types of blast event and locations of injury, and the heterogeneity of TBI. Additionally, difficulty lies in interpreting bodily responses from measurements taken on protective equipment (e. g., helmet acceleration vs head acceleration). These factors make it difficult to identify threshold values and ultimately, correlate threshold values with clinical outcomes. The existing sensor thresholds were defined using limited data from studies on animals, sports injuries, and breachers (i.e., people trained to use explosives to enter buildings). To date, no standardized method for validating these sensor threshold values has been established, and attempts to correlate the sensor data with clinical outcomes have been largely unsuccessful. Greater research investment is needed to improve sensor recordings and validate sensor measurements before these tools can be used to screen mTBI in the field.

Military policy based on risk tolerance levels is required for determining operational responses when threshold values are exceeded

Performance standards for validating sensor threshold values do not exist; attempts to correlate sensor data to clinical outcomes have been largely unsuccessful

3.0 Establishing a Shared Understanding of Sensor Threshold Requirements and Challenges

The meeting began with a series of presentations intended to orient and inform meeting participants on the user community needs, the depth and breadth of ongoing research efforts, and the challenges associated with development of validated environmental sensor threshold values to be used by Service Members and line leaders for determining when an individual may have been exposed to a PCE. The meeting presentations described below served to develop a shared understanding of the current application of the sensor readings, in both military and non-military settings, the status of sensor threshold and sensor development efforts, and the current associated knowledge gaps.

Note: The opinions and research findings described in the following sections are those of the presenters and not necessarily those of all meeting participants or Expert Panel members.

3.1 Key Messages from Keynote Speakers

The Biomedical Basis for Mild Traumatic Brain Injury Environmental Sensor Threshold Values meeting opened with three DoD keynote speakers. These speakers noted several critical research requirements blast injury sensors including: biomedically valid concussion thresholds, screening tools to reduce the number of unnecessary evacuations, concussion diagnostic tools, and injury criteria for improved combat helmets that protect against mTBI, informed treatment, injury classification, and return-to-duty guidelines. The keynote speakers emphasized the importance of diverse communities working together to accelerate scientific progress and fill critical knowledge gaps to support the development of improved protection and treatment strategies for Service Members.

Keynote Speakers
<ul style="list-style-type: none">• Major General Brian C. Lein - Commanding General, US Army Medical Research and Materiel Command and Fort Detrick; Deputy for Medical Systems to the Assistant Secretary of the Army for Acquisition, Logistics, and Technology• Rear Admiral Bruce A. Doll - Director of Research, Development, and Acquisition, Defense Health Agency; Deputy Commanding General, US Army Medical Research and Materiel Command• Dr. John F. Glenn - Principal Assistant for Research and Technology, US Army Medical Research and Materiel Command

“We’ve got a lot of data now - 15 years’ worth of data. None of that data is tied to treatment and none of that treatment is tied to outcomes... We’ve got to get after that, because if we don’t, we’re going to be in a lot of trouble... This group here, you’ve got years of work ahead of you and I need your commitment not just for the next two days, but next several years.”

- Maj. Gen. Brian C. Lein

3.2 Topic Presentations: Setting the Stage

Following the keynote presentations, speakers from government, athletic organizations, and industry presented information on key topics which set the stage for the focused technical presentations that followed. The overview topics discussed the prevalence of mTBI in Service Members, prevalence of mTBI in contact sports, helmet safety standards, and challenges in current sensor technology. These topic presentations provided broad context for the scientific presentations that followed.

3.2.1 mTBI in the DoD

DVBIC

Ms. Kathy Helmick, (DVBIC Deputy Director) presented data on the current incidence of mTBI within the DoD. From 2000 through the first half of 2014, the DoD reported 253,350 cases of mTBI, which represents 82.4% of all DoD TBI cases during that timeframe (see Figure 2). The number of TBI diagnoses has grown since 2006 when the DoD implemented specific policies to mandate evaluation for mTBI (i.e., the implementation of the policy itself resulted in a greater number of reported cases). After the policy became effective in 2010, approximately 16% of all PCEs, defined by any of the four events listed in the box below have led to a diagnosed mTBI. The leading causes of mTBI are associated with vehicular blast, collision, or rollover, which represents 9,266 out of 16,760 (55.3%) reported incidents and 1,524 out of 2,734 diagnosed (55.7%) concussions over the time period of August 2010 through June 2014. This is followed by blast exposure within 50 meters (m), which represents 6,548 of 16,760 (39.1%) reported incidents and 947 of 2,734 (34.6%) diagnosed concussions over the same time period.

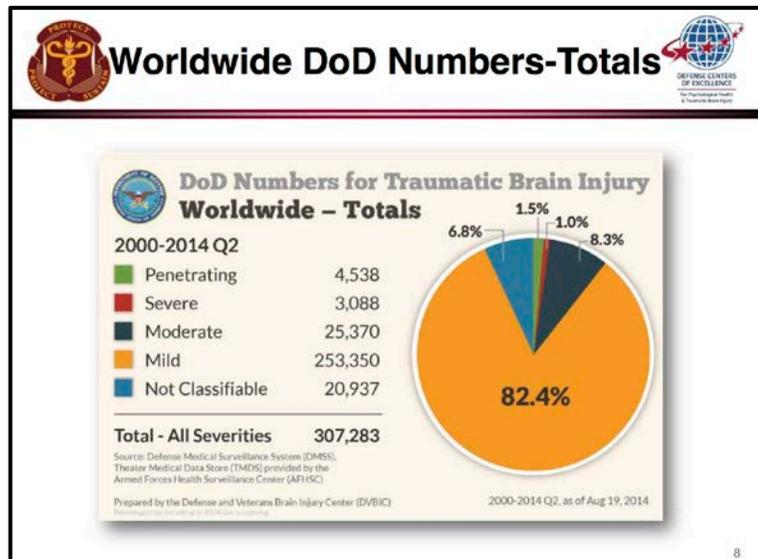


Figure 2. Total number of DoD traumatic brain injuries diagnosed from 2000-2014. TBI cases have been separated by severity.

Clinical evaluation has been the standard for diagnosing mTBI. The DoD is examining a number of potential diagnostic tools including pupil reaction, postural stability, visual tracking, biomarkers (in blood, saliva, or urine), near-infrared spectroscopy, electroencephalography (EEG) and event-related potentials. A combination of diagnostic tools will help address the multifaceted nature of mTBI.

RAND Corporation

Ms. Terri Tanielian from RAND Corporation presented the results of a 2007–2008 RAND study on psychological and cognitive injuries in the military, which included a component on mTBI (Tanielian & Jaycox, 2008). The study involved surveys of returning Service Members, a literature review, interviews with stakeholders

- | DoD-directed PCEs Mandating Concussion Evaluation |
|--|
| 1. Any Service Member in a vehicle associated with a blast event, collision, or rollover |
| 2. All Service Members within 50 m of a blast |
| 3. Anyone who sustains a direct blow to the head |
| 4. Service Members directed by their Command, including (but not limited to) those repeatedly exposed to blast |

and program officials, a cost model, and focus groups with Service Members and their spouses. The RAND study found that 23% of returned Service Members who participated in the study were “physically moved or knocked over by an explosion” and 18% received a “blow to the head from any accident or injury” during a prior deployment. Nineteen percent of returned service members met the criteria for a deployment related, probable TBI according to the Brief Traumatic Brain Injury Scale.

The RAND study also found that PTSD and major depressive disorder (MDD) affected roughly 1 in 5 returning Service Members surveyed in the study. Approximately the same proportion of returning Service Members surveyed reported experiencing a probable TBI; unfortunately, the proportion of mTBI could not be determined based upon the self-reported nature of the data. Exposure to combat trauma is the best predictor of reported probable TBI among this population. The results from this study highlight the need for researchers to elucidate mechanisms associated with TBI and develop better approaches to distinguish TBI from PTSD and MDD. The study also highlighted the potential long-term costs associated with untreated PTSD and MDD, and identified the importance of delivering high-quality care to reduce morbidity and societal costs.

3.2.2 mTBI in Contact Sports

DoD and NCAA joint venture

Dr. Steven Broglio from the University of Michigan presented a joint venture by the DoD and NCAA that is studying concussion in collegiate athletes, with a primary focus on football. Of the 38,000 college football players, an estimated 3,264–4,284 (4.8–6.3%) will suffer concussions; prevalence rates are comparable to other sports such as hockey, lacrosse, and soccer.

Looking across comparable sports between men and women (i.e., basketball, hockey, lacrosse, and soccer), women tend to have a higher incidence rate of concussions. The reasons behind this gender-based disparity are unknown; but may be due to differences in physiology (e.g., relative neck strength) or higher reporting rates.

The joint DoD/NCAA venture will study concussions across the entire spectrum of collegiate sports at participating universities, including the four Service academies. The study will include assessments of neurocognitive functioning, neurological status, postural stability, and symptomology. The study will also examine head impact sensors. Collegiate football will include impact monitoring from the Head Impact Telemetry (HIT) System, while football, hockey, lacrosse, and soccer will include monitoring from the X2 X-Patch system. In addition, the study will include neuroimaging, genotyping, and blood biomarkers.

Data collection for this study started in August 2014 with approximately 60 concussions captured to date. The study is expected to capture roughly 370 concussions total. The study data will eventually be made public.

National Operating Committee on Standards for Athletic Equipment (NOCSAE)

Dr. Robert Cantu from the National Operating Committee on Standards for Athletic Equipment (NOCSAE) presented NOCSAE’s current efforts to understand the role of helmets in sports-related concussions. Currently, the best data regarding concussion thresholds are statistical risk curves. Factors that affect concussion outcome are related to two broad categories: biomechanical and biological/clinical. Linear acceleration, rotational acceleration, duration of impact, location of impact, and tissue strain are all considered biomechanical factors. Concussion history (i.e., number, frequency, severity), impact anticipation, neck strength, age, gender, hydration, volume, and underreporting are some of the biological/clinical factors that affect susceptibility to concussion.

The HIT System has been the most frequently used monitoring system in research studies evaluating head impact in contact sports. Nevertheless, significant inaccuracy is associated with the HIT System measurements, especially when impacts are non-centric (i.e., relative to the center-of-mass) or involve the face mask. Additionally, deformations of the helmet can affect recordings. Some of the noise inherent in statistical risk curves may arise from these recording errors.

NOCSAE is currently adding sports helmet standards for rotational acceleration protection. The standard has tentatively been set at an inbound velocity for the linear impactor of 6 m per second (m/s) and a recording of no more than 6,000 radians per second squared (rad/s²). This is in addition to the linear drop test SI maximum of 1,200.

3.2.3 Current State of the Science and What's Next

NIH 2008 workshop on the SoS of mTBI recommended areas of interest
<ol style="list-style-type: none">1. The acute and long-term neurological effects of blast exposure; the need for clinical neuropathological data2. Potential clinical indicators of blast exposure, such as neurobehavioral assessments, imaging, and/or biochemical markers3. Standard approaches for performing blast exposure experimentation in animal models; validation of existing and new preclinical models4. Considerations for research concerned with civilian and military exposure to blast injury

NIH Involvement in mTBI Research and Data Sharing

Dr. Patrick Bellgowan from the NIH's National Institute of Neurological Disorders and Stroke (NINDS) presented NIH's perspective on the state-of-the-science of mTBI. While the NIH does not fund many blast research studies, the NIH funds a large number of mTBI studies and hosted a workshop on 10-11 April 2008 titled *Neurological Effects of Blast Injury*. The workshop led to identification of four areas of interest shown left.

The recommendations from the workshop were published in 2010 (Hicks, Fertig, Desrocher, Koroshetz, & Pancrazio, 2010). Based on these recommendations, the NIH has funded a number of research projects aimed at understanding neuropathology and neurodegeneration associated with chronic traumatic encephalopathy,

imaging methods such as DTI and MRI, machine learning classification methods to diagnose TBI, and head impact sensors such as HIT and mouthguard systems. NIH has also been supporting the development of common data elements to promote data sharing among researchers and the community at large. In conjunction with the DoD, the NIH currently hosts the Federal Interagency Traumatic Brain Injury Research (FITBIR) repository, where data can be shared and downloaded. FITBIR may serve as a data repository for the blast sensor community.

Blast Gauge Sensor Use in the Battlefield and in Research

CDR Josh Duckworth from the Defense Advanced Research Projects Agency/Uniformed Services University of the Health Sciences discussed his experiences with the Blast Gauge sensor in the field and in research. As a medical officer deployed to Afghanistan, CDR Duckworth found the gauges to be an invaluable, unbiased tool to help understand the history of Service Members' exposure to blast. Service Members presenting themselves to trauma units are usually unreliable sources of information as they are wounded and can often present false memories after losing consciousness. Having blast gauges provide context to medical personnel and can improve understanding of a patient's symptoms and injury. This understanding can in turn result in increased acceptance of an mTBI diagnosis by the patient and the unit and increased compliance with medical recommendations.

Considerations for Sensor Data Collection and Interpretation

Colonel Colin Greene, Director of the Joint Trauma Analysis and Prevention of Injury in Combat (JTAPIC) program, challenged participants to consider the goal of a sensor program and whether sensors were developed as field screening tests, research data gathering exercises, or device

calibration tests and to consider the downstream consequences of each of these sensor applications if applied inappropriately.

Colonel Greene asked the meeting participants to consider the critical issues and questions surrounding use and efficacy of environmental sensors. For example, sensors measure conditions at the helmet, not necessarily at the head (i.e., not the brain), and converting the helmet readings to head motion is challenging. Converting the data requires complex algorithms that can be a difficult to validate. Furthermore, response (risk) curves for the sensors have yet to be established. Other challenges to capturing accurate sensor data include software limitations such as date/time recording, unreadable waveforms, and issues with setting activation thresholds. Outputs from the sensor are not always readily interpretable. To ensure accurate sensor measurements, Service Members must be wearing the helmet when the blast exposure is measured, but empty helmets cannot always be detected and accounted for using algorithms. Finally, expectations for use and intended benefit of sensors are not clear, thus, more research and greater clarity is required to determine how collected blast injury data is to be used. The questions/issues above were not intended to dampen the pursuit of sensors as potential tools in the study of mTBI. Rather the questions/issues were intended to spur more critical examination of the purpose and applicability of sensors.

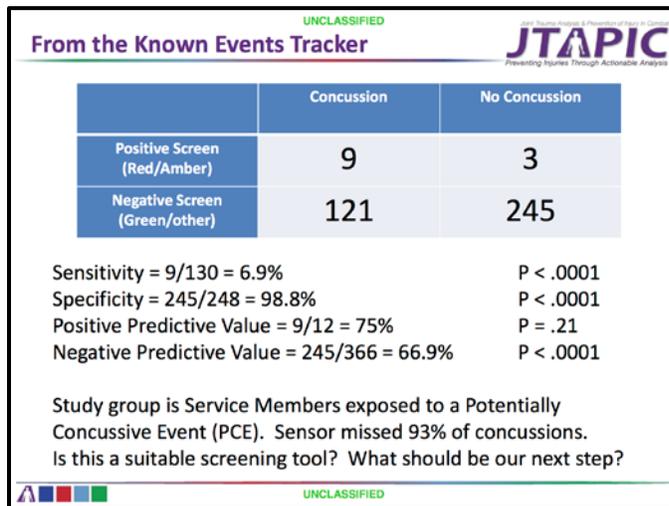


Figure 3. Comparison of concussion outcomes. Data were obtained from the Known Events Tracker, a list of events that are potentially concussive as defined by the four criteria set by DoD.

To highlight the current state of sensors as a potential screening tool for mTBI, Colonel Greene presented preliminary data from the Known Events Tracker (Figure 3), a list of PCEs defined by the four criteria set forth by the DoD. From this list of events, 378 occurred while the service member was outfitted with a sensor. Of these 378 events, sensors triggered a warning (defined as a red or amber light output) in 12 cases; 9 of the 12 warnings were eventually confirmed concussions, a positive predictive value of 75%. The sensors issued no warning (defined as a green light or no output) in 366 of the events, 121 of which were confirmed concussions. Therefore, the sensitivity of the sensor was 9/130 (6.9%, Figure 3). In other words, the sensors missed 93.1% of concussions amongst the potentially

concussive events. Further research into sensors and their relationship to mTBI is required for these sensors to be able to more accurately predict concussive events.

Challenges in Development of mTBI Thresholds

Dr. James Stuhmiller from L-3/Jaycor shared his thoughts on mTBI thresholds based on sensor-generated data and compared civilian and military environments. Dr. Stuhmiller noted three major challenges to developing thresholds for mTBI based on sensors: (1) determining dose-response relations (risk curves), (2) developing a reliable sensor for dose determination, and (3) selecting a threshold from a dose-response curve.

Determining Dose-response Relationships (Risk Curves)

Insufficient human data exist to develop dose-response relationships for blast. Controlled laboratory experiments with calibrated exposures can only be performed on animals, but interpreting animal studies relies on uncertain scaling laws and difficult mapping of behavioral changes to human cognitive outcomes. Nevertheless, ongoing research sponsored by US Army Medical Research and Materiel Command to determine the biomechanical, physiological, and neurological pathway of mTBI is resulting in a more fundamental understanding of the mechanisms of injury and promises to allow animal studies to be correctly used to set human tolerances. Early application of these concepts has had positive results in analyzing mTBI data from theatre.

Developing a Reliable Sensor for Dose Determination

Current sensors developed for sports environments are not robust enough for harsh military conditions. Military events tend to be far shorter in duration than in sporting events. Though a number of sensors for military purposes exist, these sensors were not developed using well-defined dose-response relationships. Limitations of current sensor technology include signal anomalies that arise from recording vibrations in the mounting surface and environmental noise, where these anomalies often outnumber real signals. Developing screening algorithms that filter out these anomalies is critical for successful sensor deployment. Additionally, translating sensor readings to the actual dose exposure is required in order to validate results. Finally, sensors frequently fail to capture the initial phase of an event because the sensors are event-triggered to save power due to their long deployment times. All of the above challenges require further research and development into sensor technologies in order to advance the development of sensor thresholds.

Selecting a Threshold from a Dose-response Curve

Once a dose-response relationship is established, criteria for selecting a threshold must be determined. The challenge in selecting a threshold lies in balancing the number of false positives with the number of true negatives. Setting the threshold high may keep the false positive rate low, but it may miss a large number of low dosage concussive events—since most events are low dosage, a large fraction of all concussive events may occur at low doses. On the other hand, setting the threshold too low may lead to an unacceptable rate of false positives. The choice of the threshold is situation dependent; occupational safety can use a low threshold with little cost from false positives, whereas dangerous military operations may require higher thresholds to offset costs associated with loss to operations from false positives.

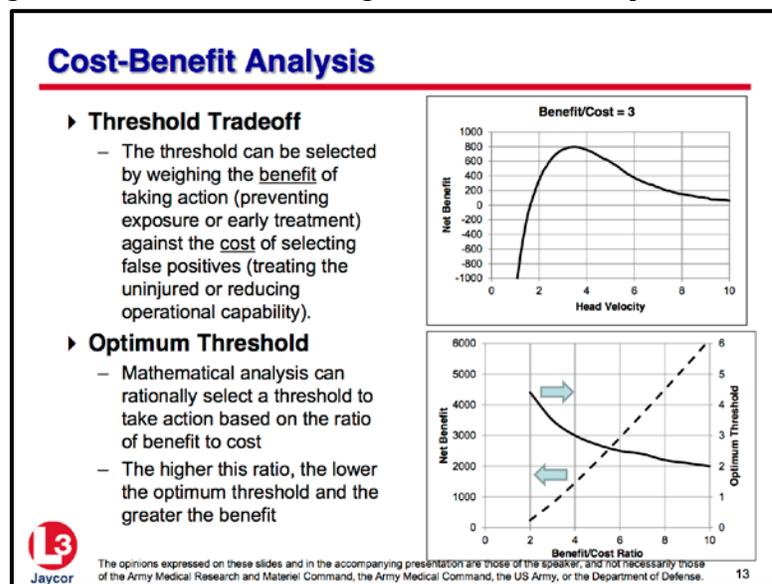


Figure 4. Example of cost-benefit analysis that can be used to mathematically identify an optimal threshold.

Dr. Stuhmiller suggested an approach based on cost-benefit analysis that maximizes net benefit given the cost of a false positive and the benefit of detecting and treating a true positive (Figure 4). This threshold changes when the ratio of benefit to cost changes—as the ratio increases, the threshold for action decreases—leading to a situation-dependent rational analysis of threshold

determination. Obstacles to developing such a curve include the evolution of risk curves due to scientific advances, the need for improvement in sensor technologies, and drastic changes to the cost/benefit ratio from changes in operational costs and benefits of treatment.

Nevertheless, using a cost-benefit analysis represents an objective approach towards determining the appropriate sensor threshold level.

3.3 Scientific Presentations: Defining the State of the Science

The presentations described above provided the broader context for the following scientific talks that focused on five key topics: (1) mechanisms of mTBI, (2) impact (acceleration) sensors in sports, (3) blast (acceleration and pressure) sensors in the military, (4) biomarkers of blast exposure, and (5) cognitive assessments of TBI.

In blast exposure, the brain experiences large linear and rotational accelerations and blast overpressure. Each of these mechanisms in isolation can lead to injury, however, the relative contributions of when all three occur simultaneously are unknown. Isolated blast overpressure injury has been observed in the laboratory, but field occurrences are exceedingly rare. Impact-only injuries are far more prevalent. While impact-only events can lead to mTBI, debate continues as to which aspect of blast, overpressure or acceleration, is the primary cause of injury in complex blast events. Understanding the biomechanical origins of blast injury can guide the development of sensors that are suitable for predicting events responsible for mTBI.

Animal Studies on Primary Blast and Rotational Acceleration Mechanisms

Dr. Marten Risling from the Karolinska Institutet presented ongoing research examining the isolated effects of two different mTBI mechanisms: (1) primary blast-only and (2) rotational acceleration. In isolated primary blast experiments with explosives in a blast tube, rodents were head-fixed and had their torsos protected while being exposed to blast waves. In this model, cell-death is very limited up to at least 500 kPa and white matter remained relatively intact. The duration of the primary peak is less than 0.5 ms, which may explain the limited degenerative changes. Brain stem nuclei such as the raphe nuclei and locus coeruleus may be the most vulnerable areas to primary blast and show significant changes in the monoaminergic systems; these results are preliminary and research is ongoing. In isolated rotational acceleration experiments, rodent heads are clamped to a rotating bar that is struck at high speeds to generate a head whipping motion. Axonal injuries and cell death were observed at peak rotational accelerations exceeding 1.1 megaradian/s²; scaled to humans, the threshold is estimated to be approximately 10,000 rad/s².

Human Head Models for mTBI Mechanism Research

Human surrogate models (i.e., mannequins and brain simulants) can complement animal studies as these models are configured for internal instrumentation, which allows for the direct measurement of environmental conditions inside the “head.”

Andrew Merkle from Johns Hopkins Applied Physics Laboratory presented research on three models of the human head: (1) human surrogate head model (HSHM), (2) post-mortem human surrogate (PMHS), and (3) in vitro head surrogate (hybrid model). The HSHM is a custom designed dummy head that is equipped with three intracranial pressure sensors, five surface pressure sensors, 3 linear and 3 rotational accelerometers, and 4 electromotive force sensors that measure brain displacement relative to the skull. Blast transmittance (i.e., the percentage of the surface overpressure that is converted to intracranial overpressure) can be examined using the HSHM. In the HSHM, sensors anterior to the blast measured approximately 42.5% transmittance; whereas sensors posterior to the blast measured approximately 16.8% transmittance (Figure 5).

Using the PMHS, beads imbedded into a post-mortem brain can be used to track relative brain motion using high-speed x-ray videography. Analysis of the subsequent brain motion can be used to validate computational models. Finally, the hybrid model embeds living cell cultures into brain and skull simulants. By exposing the hybrid model to blast, cell death quantification can be performed to determine the effects of blast exposure on cell integrity. Preliminary results suggest that blast overpressure alone, in the conditions tested, does not induce more cell death or changes in cell membrane permeability than control conditions. Research is underway to implant organotypic slices into brain and skull simulants to better mimic the stresses and strains experienced by an actual brain.

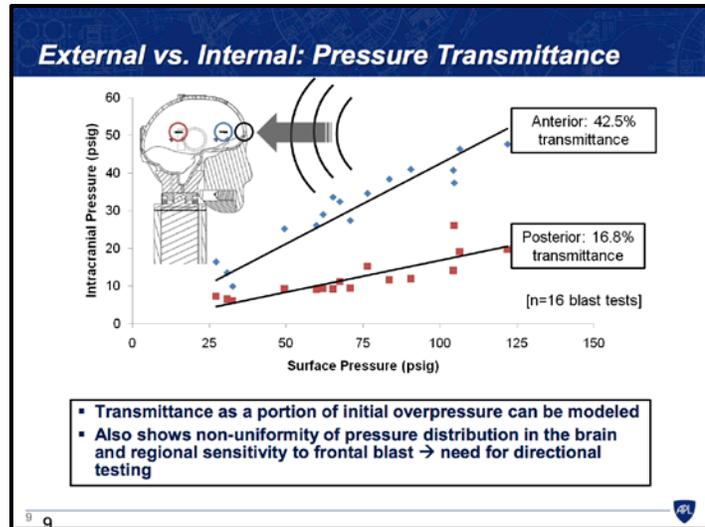


Figure 5. Blast pressure transmittance in a human surrogate head model

3.3.1 Impact Sensors and Concussion in Sports

HIT System Sensor Measurements for Football Concussions

A number of sensors that measure linear and rotational acceleration are commercially available (see Appendix C for a description of available sensors). Most of these sensors include an indicator light that notifies a user of exposure to a potential injury causing collision. Manufacturers often use proprietary algorithms to determine when an indicator light turns on. Other manufacturers allow the thresholds to be user-adjustable. A limited number of the sensors record data that can be downloaded for further analysis.

The most widely studied sensor is the Head Impact Telemetry (HIT) system. HIT records linear acceleration inside the helmet using 6 accelerometers and calculates rotational acceleration from linear acceleration. Data acquisition is triggered when any accelerometer registers acceleration above 10 g. Data is recorded wirelessly on a laptop computer for 40 ms at 1000 Hertz sampling frequency when triggered.

Professor Steve Rowson of Virginia Tech University reported an analysis of 286,636 impacts in collegiate football recorded using the HIT system. In all, 57 diagnosed concussions were recorded. From this data concussion risk curves can be constructed based on logistic regressions of peak linear acceleration,

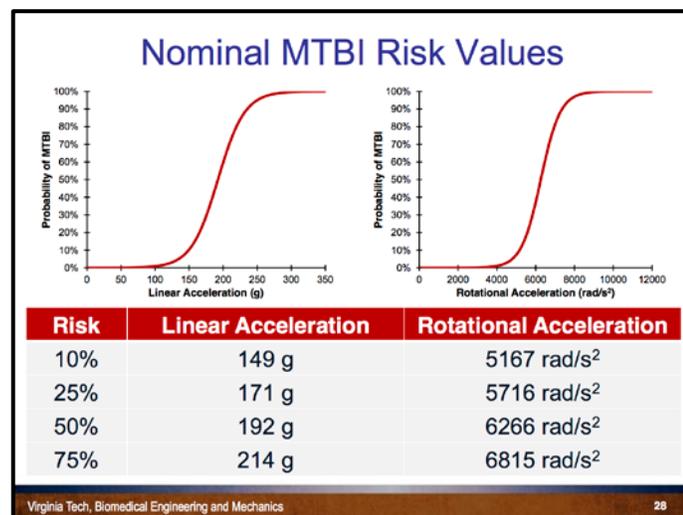


Figure 6. mTBI risk curves based on logistic regression of HIT system data from the Virginia Tech collegiate football study

peak rotational acceleration, and a combination of both. An impact with peak linear acceleration of 149 g is associated with a 10% risk of mTBI and 192 g is associated with a 50% risk. Similarly, an impact with peak rotational acceleration of 5,167 rad/s² is associated with a 10% risk of mTBI and 6,266 rad/s² with a 50% risk. Both risk curves can be seen in Figure 6.

The logistic regression combining both peak linear and peak rotational acceleration suggests that the effects of linear and rotational acceleration may simply be additive; that is, Figure 7 shows that the regression demonstrates only a small interaction between linear and rotational acceleration. Using a receiver operating characteristic (ROC) analysis, the regression analysis also suggests that linear acceleration is more predictive of injury than rotational acceleration; the area under the curve (AUC), a measure of the predictive ability of the regression analysis, shows that the AUC is significantly higher for peak linear acceleration alone than for peak rotational acceleration alone ($p < 0.015$). One caution, however, must be noted: HIT uses the linear accelerometers to compute rotational acceleration; therefore, the two sets of data are therefore not independent.

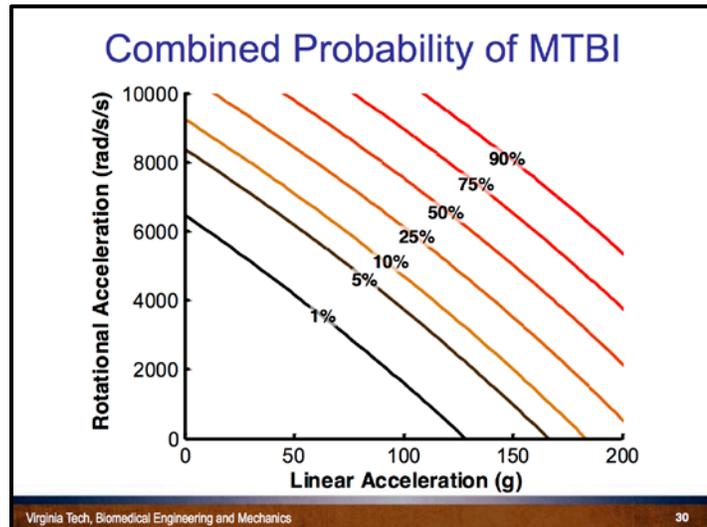


Figure 7. Contour lines from a logistic regression of concussion probability as a function of combined peak linear and peak rotational acceleration

Comparison of Stanford Mouthguard, X2 xPatch, and Skullcap Sensor Measurement of Simulated Head Collisions

Professor David Camarillo from Stanford University presented a new sensor that is incorporated into a mouth guard. The Stanford Mouthguard houses three linear accelerometers and three rotational accelerometers and relays data to a laptop located on the sideline. The accuracy of the Mouthguard was tested by performing measurements against a reference sensor placed in a human surrogate neck and head equipped with a football helmet. The Mouthguard measurements tracked the reference sensor closely for most impact sites, but tended to underestimate peak linear and peak rotational acceleration for side impacts (Site C in Figure 8).

The Stanford Mouthguard, X2 xPatch, and sensor mounted to a skullcap (to mimic the Reebok CHECKLIGHT which does not output time series) were simultaneously tested in vivo against a reference ear canal accelerometer, which is known to have very little

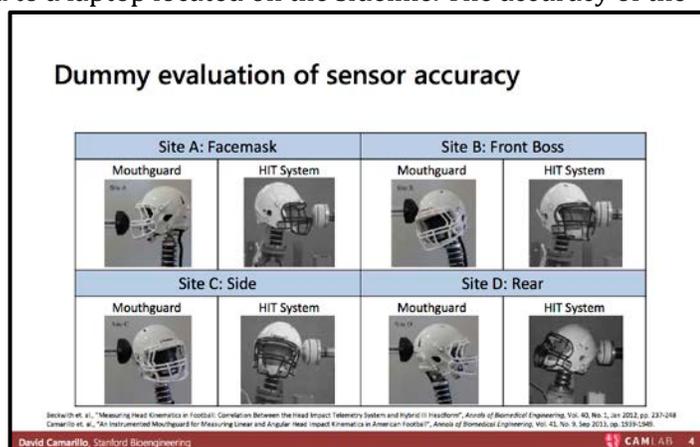


Figure 8. Location and direction of impacts used to test the Stanford Mouthguard and HIT system against a reference sensor place in a human surrogate neck and head equipped with a football helmet.

motion relative to the head when placed deep enough into the ear canal. Of the three sensors, the Mouthguard sensor showed the least amount of motion relative to the ear canal sensor during a single head collision with a soccer ball. Moreover, both the X2 xPatch and skull cap showed overestimation of peaks due to rebound motion.

The Mouthguard sensor has recorded two impacts associated with clinically confirmed concussions. Head Injury Criterion (HIC) was a poor predictor of injury. Hence, a finite element method model was used to estimate brain motion during impact loading. Using the model, peak strain at the corpus callosum was observed to be the best predictor of injury.

3.3.2 Comparison of HIT System and gForce Tracker™ Measurement of Head Impact

Professor Kristy Arbogast from Children’s Hospital of Philadelphia/University of Pennsylvania also presented results on the accuracy of helmet sensors. Her lab measured the HIT system and gForce Tracker™ (GFT) against a Hybrid III 50th percentile male head and neck dummy. The dummy was fitted with a hockey helmet that was struck with a pneumatic linear impactor. The relationship between the HIT system measurements and Hybrid III reference sensor values was nonlinear for both peak linear and peak rotational accelerations. A power law fit showed that the HIT system had an exponent of 0.93 ($R^2 = 0.98$) for peak linear acceleration and 1.14 ($R^2 = 0.92$) for peak rotational acceleration during side impacts. The exponents were higher in oblique back impacts, changing to 1.49 ($R^2 = 0.92$) and 1.99 ($R^2 = 0.84$) for peak linear and peak rotational acceleration respectively. Fit exponents were not reported for the GFT but are contained in a recently published paper by Arbogast’s group (Allison, Kang, Maltese, Bolte 4th, & Arbogast, 2014).

Looking at the error of the recorded peak linear and peak rotational acceleration, HIT had an average absolute error ranging from 18–31%, depending on impact direction, for peak linear acceleration and had an average absolute error ranging from 35–64% for peak rotational acceleration. Using a power law conversion of the HIT values, the error ranges could be reduced to 7–18% and 12–45% for peak linear and peak rotational acceleration respectively. In general, side impacts and back impacts were more accurate than oblique back impacts.

Looking at the HIT system’s ability to categorize direction of impact, HIT was 100% correct in categorizing front and back impacts, but 79% correct in categorizing oblique back impacts. The helmet-head interface was found to influence the accuracy of sensors. Three different interface types were tested: nylon cap, dry wig, and wet wig. The greatest difference in peak linear acceleration between HIT system measurements and the reference sensor values was observed with the dry wig, whereas the nylon cap exhibited the smallest difference, however, all surface interfaces demonstrated good precision ($R^2 = 0.96-0.97$).

The GFT sensor, which has accelerometers and gyroscopes to measure linear and rotational velocity directly, was also tested. After empirically converting raw

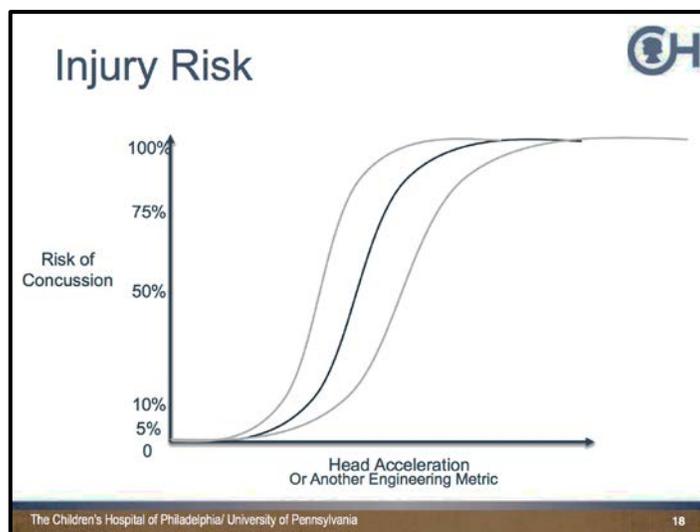


Figure 9. Schematic injury risk curve showing boundaries that account for sensor measurement errors.

data via a power law, the average sensor error for peak linear acceleration ranged from 4.8–21.5% when placed inside the helmet, depending upon impact direction and helmet manufacturer, and ranged from 4.8–22.0% when placed outside the helmet. The average error for peak rotational velocity ranged from 2.3–13.7% and 2.3–10.1% for inside and outside placement respectively.

While both of these sensors systems showed strong correlation with the reference acceleration, due to the many sources of error inherent in sensor measurements, Professor Arbogast suggested that the community account for and characterize the noise as much as possible, especially when considering injury risk curves. Specifically, injury risk curves could demonstrate their uncertainty due to measurement error, as schematized in Figure 9.

3.3.3 Blast Sensors and mTBI in the Military

Several blast sensors have been fielded in the military (see Appendix C for a description of available sensors). The sensors measure blast overpressure and some combination of linear and rotational acceleration and/or velocity. Despite the lack of a validated biomedical threshold, the sensors are equipped with indicator lights that can alert a user to the presences of an environmental exposure that potentially requires further evaluation. Current sensor thresholds are based on a combination of breacher training and animal studies. Further research, however, is needed to link sensor outputs with injury outcomes.

Ms. Lee Ann Young of Applied Research Associates, Inc. presented the basis for the threshold levels that were programmed into BlackBox Biometrics’ Blast Gauge™ system. Blast Gauge is deployed as a trio of sensors: on the back of the neck, on the chest, and on the shoulder of the non-shooting arm. Blast Gauge measures both overpressure and linear acceleration, but lights are triggered based on overpressure alone. Peak overpressure exposure levels up to 4 pounds per square inch (psi) trigger a green light, 4–16 psi trigger a yellow light, and 16 psi or greater trigger a red light. The green light is a status check indicator. The yellow and red lights indicate moderate to high levels of exposure. The gauges are designed so that the ranges for these colors can be modified based upon data and clinical experience.

PREVENT program is studying blast in a large animal model (Yorkshire pig) under three conditions: blast tube (simulated free-field), high mobility multipurpose wheeled vehicle, and buildings. The current testing conditions are shown in Figure 10. The study is examining EEG, electrocardiography, gait, physiological measures, histochemical and immunohistochemical stains, and reverse capture protein arrays. Thus far, 14 subjects have been identified as having mTBI; the blast pressure ranges for these subjects were 19–42 psi.

Blast Environment	Number of Blasts	Blast Range (Peak OP, psi)
Blast Tube (Simulated Free-field)	12	19 to 33
	30	37 to 53
	5	70 to 91
HMMWV	3	29 to 37
	12	40 to 85
	2	139 to 171
Building (4 walls, one entrance, no roof)	3	23 to 26
	19	38 to 130

Figure 10. Incident number and overpressure range for different blast categories in the PREVENT large animal study.

The objective of the Quantico Breacher Injury Study (QBIS) is “to determine whether repeated low level blast exposures cause measurable abnormalities in human neurological anatomy, physiology, and function.” QBIS looked at a two-week standard breacher training course at US Marine Corps

Weapons Training Battalion Dynamic Entry School. Forty volunteers (7 controls, 28 students, 5 instructors) were enrolled. Test subjects were exposed to approximately 40 blasts each. Blast exposure conditions are shown in Figure 11. The study performed neurobehavioral testing, neuroimaging, auditory/ vestibular assessments, and blood toxin screening. The study had no clinically confirmed cases of mTBI due to a recorded maximum peak overpressure exposure of 13 psi.

PREVENT indicates that peak overpressure thresholds (in pigs) are in the vicinity of 20 psi, while QBIS suggested that a peak overpressure exposure of 16 psi (in humans) does not cause injury nor any appreciable neurological changes. Therefore, 16 psi was chosen as a conservative value for the red light threshold.

Dr. David Borkholder of BlackBox Biometrics elaborated on the choice of thresholds in his presentation. Säljö et al. (2008) showed that swine exposed to multiple blasts at 3.3 psi (50 cal, 3X) had subdural hemorrhage and parenchymal and subarachnoidal bleeding (Säljö, Arrhén, Bolouri, Mayorga, & Hamberger, 2008). Though 3.3 psi is a lower value than the 4 psi threshold used in the Blast Gauge, the fact that Säljö et al. used swine and multiple blast exposures suggests that 4 psi is a reasonable threshold for humans at single exposure levels. Nevertheless, Dr. Borkholder cautions that the effect of multiple blast exposures are still unknown, which should serve as a caution against interpreting green lights as indicating no injury. Regarding the second threshold, Lu et al. (2012) showed that single exposure to a 12 psi free-field blast exhibited no detectable histopathological changes in subhuman primate brains; the result suggests that the threshold in humans should be higher than 12 psi (Lu, et al., 2012).

Dr. Borkholder also proposed widening the scope of how sensors should be deployed. That is, sensors should be thought of not only as field screening tools, but also as research data gathering tools. Data collected from the field is unique and not replicable in the lab; therefore, analyzing existing field data should be a goal of any sensor program.

Mr. Gregory Rule from Applied Research Associates, Inc. outlined how overpressure recordings from Blast Gauge (or any pressure sensor) could be used to reconstruct blast exposure conditions. Blast conditions (e.g., reflective surface, shielded by body, free-field) influence the shape of overpressure traces recorded by sensors. By comparing pressure traces from deployed sensors with traces taken from known situations, it may be possible to estimate blast parameters such as charge size and standoff distance. The parameters could then be used to calculate pressure conditions experienced by Service Members. Exposure levels could then be correlated with injury risk curves.

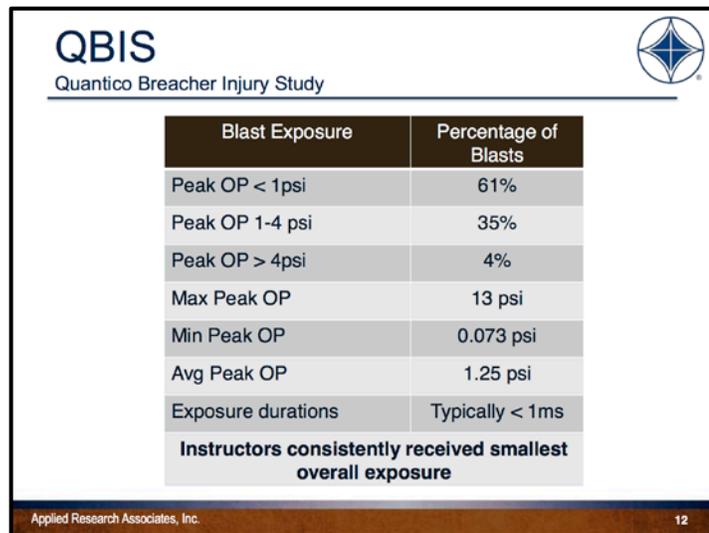


Figure 11. Overpressure statistics for blast exposures recorded in the QBIS study.

Dr. Paul Rigby of L-3 Applied Technologies presented the current status of the Helmet Mounted Sensor System (HMSS) manufactured by BAE Systems. The sensor is mounted inside the crown of an Advanced Combat Helmet (ACH) or Enhanced Combat Helmet (ECH). The sensor records linear acceleration, rotational velocity, and overpressure. The sensor records 102 ms of data triggered when linear acceleration is greater than 80 g. The sensor can store 2,000 events and data can be downloaded via USB.

HMSS has three lights (green, amber and red) that indicate environmental conditions predictive of concussion. Thresholds are based on the Japanese Automobile

Research Institute (JARI) study of impacts on non-human primates. L-3 Applied

Technologies developed a concussion risk curve through regression analysis of concussion probability versus maximum head velocity (i.e., head velocity is estimated using a simplified lumped mass model that translates sensor motion to head center of gravity motion). This was done for three different concussion types, defined by the number of symptoms observed: loss of corneal reflex, apnea, and bradycardia for at least 20 seconds. The amber light threshold was set as the lower 90% confidence bound for a 50% risk of any type of concussion (grade 1, 2, or 3). The red threshold was set as the lower 90% confidence bound for 50% risk of concussion at grade 2 or 3. The threshold for the green light was not discussed, however, green does not mean no risk for concussion; instead, it indicates a less than 35% probability of having a grade 1 concussion, (Figure 12). The light thresholds will be updated as human data becomes available.

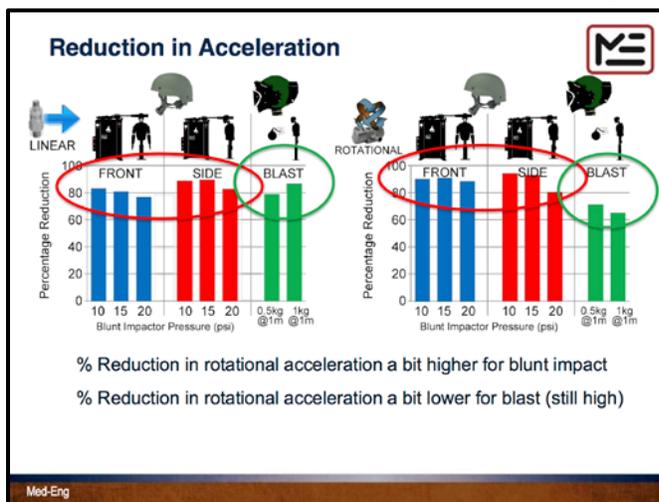


Figure 13. Reduction in linear and rotational acceleration provided by head protection during blunt impacts.

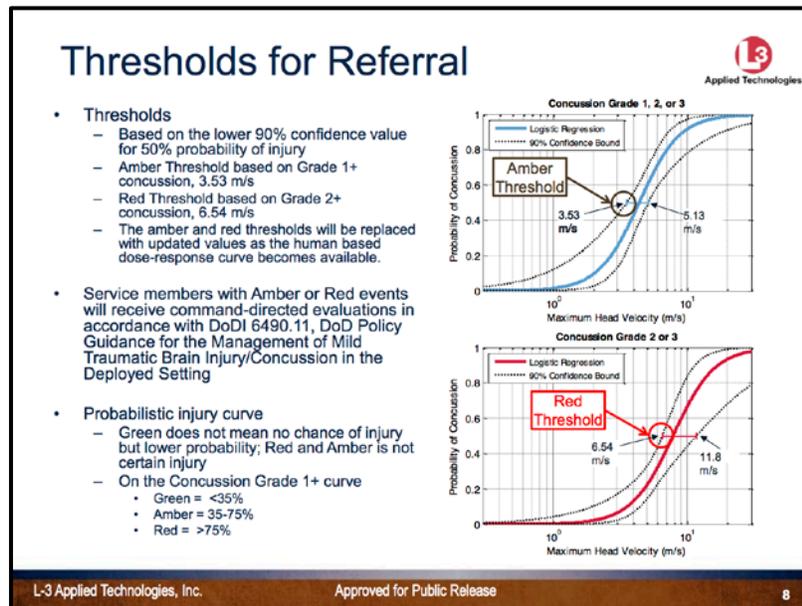


Figure 12. Definition of Helmet Mounted Sensor System (HMSS) sensor thresholds using injury risk curves from the JARI study of impacts on non-human primates.

The light thresholds will be updated as human data becomes available.

Dr. Jean-Philippe Dionne from Med-Eng – The Safariland Group presented research that examined differences between linear and rotational acceleration during blunt impact and blast. In tests comparing dummies with unprotected and protected heads (i.e., ACH for blunt and Explosive Ordnance Disposal [EOD] helmet for blast), head protection reduced peak linear acceleration by approximately 85% for both blunt impact and blast, whereas peak rotational acceleration was reduced by approximately 90% for blunt impact and 70% for blast, see Figure 13.

This finding appears to contradict a study by King et al. (2003), which found that football helmets provide substantial reduction for peak linear acceleration (~25%) but NOT for peak rotational acceleration (~3%) in blunt impacts. The studies, however, operated in different regimes of linear acceleration; the current study operated around 700 g and 200,000 radians/s², whereas King et al. operated around 150 g and 10,000 radians/s². Also, ACH and the EOD helmet are far stiffer than football helmets.

Furthermore, Dionne argued that there is a high degree of redundancy in capturing both peak linear and peak rotational acceleration ($R^2 = 0.93$ for impact and blast combined). When looking at various injury criteria, rotational motion leads to contradictory results based on the protected and unprotected impact and blast scenarios, see Figure 14. Head Impact Power (HIP), which is based on change of linear and rotational energy, is more consistent with the data. HIP, however, correlates very strongly with HIC ($R^2 = 0.88$), which is based on linear acceleration only. Therefore, according to Dionne, rotational acceleration may offer limited independent information from linear acceleration when trying to determine injury thresholds. Dionne's finding complements results presented by Steve Rowan, who found that rotational acceleration was less predictive of injury than linear acceleration in collegiate football.

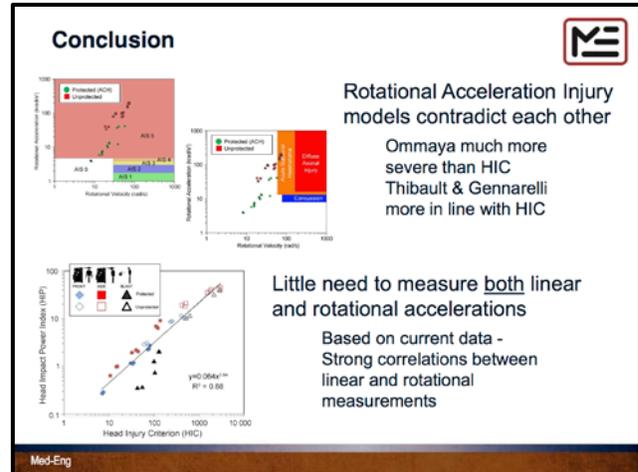


Figure 14. Plots supporting the need to measure only linear acceleration.

3.3.4 Biomarkers of Blast Exposure

Exposure to blast induces a cascade of biochemical changes in the body. Cell membrane integrity is affected by blast, leading to the release of intracellular components from the brain and peripheral organs into CSF and blood. Intracellular component release is dependent upon blast exposure dosage. Therefore, measuring CSF and blood serum levels of these biomarkers has the potential to serve as blast dosimeters. Known biomarkers, however, reach peak measurable levels within 24 hours, which may be difficult to assess for Service Members in deployment situations. In addition, the detection of biomarkers requires equipment and personnel that may be unavailable to deployed medical personnel. Finally, neither animal nor human studies have been proven to be conclusive as yet; therefore, biomarkers currently have limited applicability as a deployable screening tool.

Dr. Peethambaran Arun from the Walter Reed Army Institute of Research (WRAIR) presented a number of potential biomarkers that may be indicative of blast exposure. Tissue enzymes, cell-free DNA (CFD), and cytokine levels were tested in rats exposed to blast using shock tube. Levels of enzymes such as aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, creatine kinase, and myeloperoxidase are elevated in rats exposed to blast in an overpressure dose related manner. Average enzyme levels can increase from 2-fold to 131-fold relative to sham controls over a period of 4–6 hours after exposure to blast; average enzyme levels return to baseline at 24 hours of exposure. Torso protection can negate or buffer the average level of enzyme increase. Mean levels of CFD are higher in blast-exposed rats relative to sham, with approximately a 5-fold increase at 2 hours and a 3-fold increase at 6 hours; mean CFD levels return to sham levels at 24 hours post-exposure.

Major Walter Carr from the WRAIR presented research looking into ubiquitin carboxy-terminal hydrolase L1 (UCH-L1) as a potential biomarker of blast exposure. The study examined humans who were enrolled in military training that included explosive breaching. Subjects were exposed to multiple sub-concussive blasts throughout the course of training and were equipped with sensors to monitor blast exposure. No injuries were reported in the study. Subjects, however, reported an elevated concussion-like symptomology such as headache, dizziness, and concentration difficulty following the largest blast. Daily blood draw showed levels of UCH-L1 were weakly correlated with peak blast exposure, but results are preliminary and require further investigation.

3.3.5 Cognitive Assessment of mTBI

One goal of the environmental sensor program is to determine whether an individual is ready to return to duty after impact or blast exposure. Sensor readings could aid in identifying individuals who require further screening based on acceleration and/or overpressure exposure levels correlated to injury. Current screening methods for mTBI employ a combination of cognitive and motor tests. The development of reliable, portable, non-invasive, and low-cost methods to screen for mTBI could complement sensor technology as a screening tool for mTBI.

Dr. Christopher Rhea from University of North Carolina at Greensboro presented the development of a portable gait analysis tool with the potential to be used for mTBI evaluation. The test is a walking-in-place task where an Android-based cell phone acts as an accelerometer. When compared against a research grade accelerometer, the cell phone accelerometer performs very accurately in the X- and Y-directions ($R^2 = 0.88$ and $R^2 = 0.74$, respectively) but not in the Z-direction ($R^2 = 0.33$). The military is currently testing the gait analysis protocol on a cohort of Navy SEALs ($N = 91$). Analysis of data is ongoing.

Dr. Mark Tommerdahl of Cortical Metrics presented another device that has the potential to screen for concussion. Rather than analyzing gait, Cortical Metrics has developed a somatosensory testing device, roughly the size of a computer mouse, equipped with two stimulators that can provide vibrations independently to two different fingers. One advantage of Cortical Metrics testing protocol is that it is not dependent upon having baseline data for subjects. For example, in a temporal order judgment task, where subjects have to determine which finger was stimulated first, non-concussed individuals perform significantly worse in the presence of a background “illusory” vibration than without it (statistics not reported). Concussed (and autistic) individuals perform about the same under both illusory and non-illusory conditions and outperform non-injured subjects in the illusory condition (statistics not reported). A similar pattern holds for several other tasks, including amplitude discrimination, in which illusory conditioning has little or no impact on concussed individuals. All of the task designs were based on specific neurophysiological mechanisms identified in non-human primate studies, and combining scores from the different tasks creates an individual CNS profile. Profiles of concussed individuals are differentiated from those of non-concussed individuals with 99% confidence levels.

4.0 Focused Working Group Summary

On the second and third day of the meeting, participants divided into six focused working groups; with each group chaired by an Expert Panel member. Each group was charged with discussing and answering the same set of four specific questions based on their expertise and information provided in the literature review. Following the focused working group discussions, participants reconvened and each Expert Panel member presented the conclusions of his or her focused

working group. Recommendations and highlights from the focused working groups are detailed below.

4.1 Focused Working Group Question #1

Are the existing environmental sensor threshold values suitable for predicting the development of mTBI? Proposed topics for discussion included:

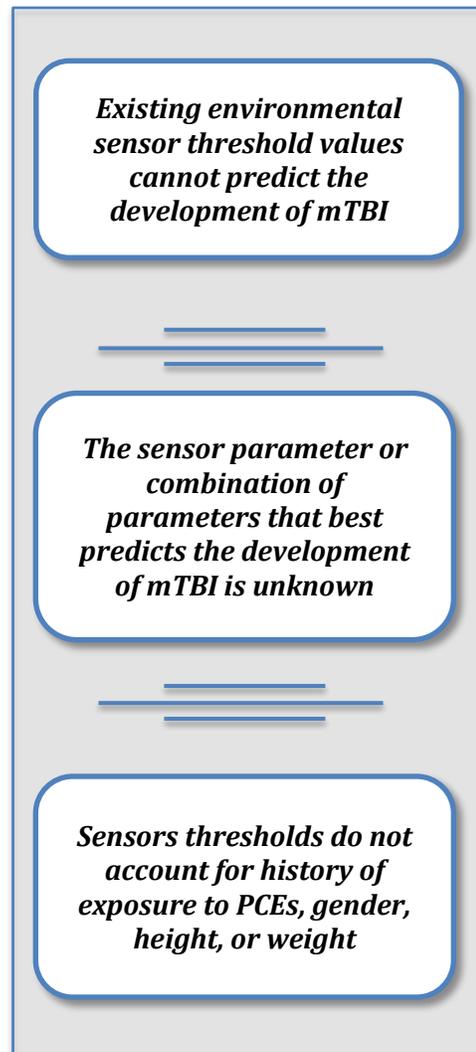
- Ways that sensor threshold values have been validated
- Ways in which current sensor threshold values can be enhanced or refined

All working groups agreed that current environmental sensor threshold values were not suitable for predicting the development of mTBI. Current environmental sensor thresholds include: blast gauges (4 psi/16 psi), HIC (700), angular acceleration (6,000 rads/sec² [football]), linear acceleration (150 g [football]), and velocity (3.5 m/sec). Current thresholds are based on the best science available, however research is needed to correlate sensor outputs with injury outcomes.

The working groups noted several factors that could contribute to enhancement or validation of sensor threshold values. These include 1) capture of blast overpressure parameters, 2) capture and correlation of linear and rotational acceleration and velocity, 3) individualization of sensors, 4) increased access to data from fielded sensors, and 5) better definition of mTBI injury.

Current sensor technology captures blast overpressure and some combination of linear and rotational acceleration or velocity. Indicator lights on the sensors are triggered based on one of these variables. Currently, it is unknown which variable is the most predictive of injury, and whether that variable will be different for blast overpressure exposure events versus impact events. It is also unknown whether combining variables will lead to improved sensor thresholds. Further research is needed to understand which variables that sensors should be capturing and how the variables can be combined to better predict injury.

Enhancement to current sensor thresholds may require development of individualized thresholds. Current sensor thresholds do not account for individual characteristics such as height, weight, gender, and history of injury and exposure. More research is needed to understand how these factors influence injury risk and the prediction of injury from sensor outputs. Understanding the influence of injury and exposure over time requires the collection of baseline (pre-deployment) behavioral and cognitive data from Service Members to elucidate how cumulative blast exposure may affect performance.



Refinement of sensor thresholds requires evaluation of data collected from fielded sensors. To date, data recorded from fielded sensors have not been available to all researchers. Analyzing existing data may support the development of stronger correlations of sensor outputs to injury outcomes which may also lead to insights for current sensor technology and methods to improve current thresholds.

Lack of access to available data for military fielded sensor technologies limits correlation of data outputs to injury outcomes

4.2 Focused Working Group Question #2

What are the challenges for developing biomedically valid, standardized thresholds that accurately capture mTBI events? Proposed topics for discussion included:

- Repeat exposures to sub-concussive events might affect the development of these sensor thresholds

In considering the challenges for developing biomedically valid thresholds for accurate capture of mTBI events, the working groups stated that the fundamental challenge was the lack of a clear purpose for the application of sensor technology as research, screening, or diagnostic tools. A clearly stated purpose is important for understanding where to set sensor thresholds. The original intent for some of the fielded sensors was to collect data on PCEs and was not meant to be used as a predictor of injury.

The effect of repeated exposures to sub-concussive events on injury thresholds is currently unknown. As noted in the response to Question #1, other factors may also impact thresholds including blast and/or impact direction, past injury history, gender, age, genetics, weight, and height. Demographic and medical history factors should be investigated to understand their influence on injury thresholds. To capture patient histories, baseline information should be collected from all Service Members. Information should be collected pre-deployment and tracked throughout a Service Member's career and eventually by the Veterans Health Administration.

Current sensor development efforts should analyze currently available blast injury data. Significant issues with this data exist, particularly with respect to the collection (e.g., fidelity and quality), the analysis, and the availability (e.g., access/sharing) of the data. While blast injury data exist, much of this data has not been correlated to blast injuries. Researchers need to define the relevant data elements to collect and then conduct the appropriate analyses.

Furthermore, a lack of standardization in blast injury terminology, experimental methodology, clinical definition of mTBI, and reporting methods hinders communication and collaboration across stakeholders and impedes sensor development efforts. The absence of standard animal and computational models complicates efforts to translate research into human outcomes. Even when

Sensors are being developed and deployed without a clearly-defined purpose

Greater access to demographic information and medical histories is needed to assess the impact of repeated exposure to PCEs

Existing blast injury data should be made available to researchers

terminology, clinical definitions, and reporting method standards are developed, there is no central authority for implementation of the standards. Addressing the lack of standards and designating an authority to ensure their adoption are critical prerequisites for advancing environmental sensor research.

In addition to the challenges previously described, a lack of Service Member compliance with sensor guidelines, ethical concerns with gathering human data in a controlled environment, incomplete exposure and injury history of individuals, and an inability to successfully translate data from animals to human are challenges in the development of biomedically valid thresholds. Lastly, the mechanisms of mTBI and the relative contributions of different environmental exposure types (overpressure, linear acceleration, and rotational acceleration) are currently unknown.

In summary, to address the challenges discussed above, the development of standardized thresholds that accurately capture mTBI events will require a multidisciplinary approach that includes clinicians, engineers and biologists in order to better understand the biomechanical forces and physiological effects between blast events and injuries.

No central authority for the development and adoption of standards has been established

A multidisciplinary approach is required to elucidate the relationship between sensor data and biological and clinical outcomes

4.3 Focused Working Group Question #3

What are the appropriate parameters (e.g., linear/rotational acceleration, pressure, event duration) for which sensor threshold values need to be established? Proposed topics for discussion included:

- Customized threshold value parameters for sensor placement on different parts of the body

As noted earlier, the sensor parameters or combination of sensor parameters most predictive of mTBI are not currently known. Understanding the biomechanics of mTBI and the relative contributions of different exposure types to injury may help elucidate the appropriate parameters for which the sensor threshold values should be established. It may be necessary to have multiple thresholds for each parameter type. To date, the most relevant measurements (e.g., peak value, impulse value) for predicting injury are unknown.

At present, thresholds surrounding impact events are better established due to the sports and automotive safety literature. How blast overpressure may interact with those injury thresholds and whether blast overpressure alone can cause mTBI are unknown. Understanding the relationship between overpressure and impact will require a multifaceted research approach, including analysis of existing sensor field data, animal and human surrogate studies, and computational modeling.

The optimal placement of sensors on helmets and uniforms has not been established. Ideally, acceleration sensors should be placed as close as possible to the center of rotation and on the most rigid part of the head, reducing environmental noise. If the sensor cannot be placed on the head, it should be

Accurate data collection requires establishing optimal placement of helmet and body blast sensors to be able to predict injury outcomes

placed on the helmet or other head mount. When capturing overpressure data, sensors should be placed in three independent directions, and a solid surface is necessary for the sensor to measure pressure accurately. Sensors, if possible, should capture blast direction. Nevertheless, when placing sensors, researchers must consider usability and the potential for sensors to hinder human performance. The main challenge is to develop protective gear into which the sensor can be incorporated. The sensor has to be useful and incentivized for the Service Member to wear it (e.g., wearing the equipment will give better protection or tactical advantage). Helmet-mounted sensors have been developed but validated algorithms to translate data recorded by these sensors into conditions experienced by the head and brain do not exist.

4.4 Focused Working Group Question #4

What are the existing knowledge gaps that require additional research? Proposed topics for discussion included:

- The need for additional biomedical research to develop predictive models (e.g., computational models, animal models) for association of sensor threshold values and development of mTBI

Fundamental knowledge gaps related to 1) objective injury measurements; 2) the relative contributions of blast overpressure to injury; 3) translation of data from computational and animal models to human outcomes; and 4) the effects of demographics, individual history, and repeated exposure on injury risk curves must be addressed prior to focusing on the development of predictive injury models.

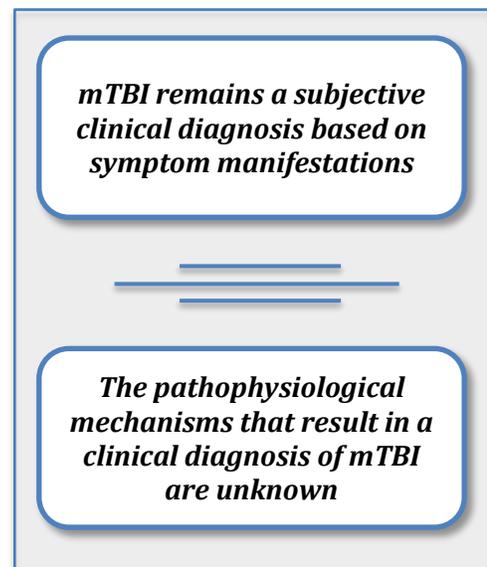
Objective injury measurements

As noted above, the focused working groups agreed that a clinically quantifiable, validated, and accepted definition of mTBI must be elucidated before an environmental sensor threshold can be established. Currently, mTBI is determined through a subjective clinical diagnosis. The physiological, pathological, and behavioral based definition of mTBI is needed for researchers to develop sensors that measure blast event variables and accurately predict the degree of exposure.

Fundamental knowledge gaps of blast overpressure injury mechanisms preclude developing predictive models of mTBI. Tissue damage, bleeding, and diffuse axonal injury are associated with non-blast TBI but blast-induced injury does not have a known pathophysiological mechanism. The extent to which blast overpressure alone causes brain injury and the injury mechanism is unknown.

A standard definition of mTBI will allow for independent sensor evaluation across manufacturers. In addition, capturing greater granularity on injury, rather than just a binary injured or not-injured outcome may be helpful in understanding injury thresholds.

Additional knowledge gaps associated with the development of environmental sensors are presented below.



Knowledge gaps that need to be addressed in future research
Mechanism of injury in mTBI
Contributions of different environmental exposure types on mTBI
Biomechanics of mTBI
Correlation of existing data from fielded sensors to injury
Physical scaling law to translate blast conditions from animal models to humans
An understanding of the parameters (e.g., linear acceleration, rotational acceleration, blast overpressure) and features (e.g., peak value, impulse value) that are most predictive of injury
Characterization of the interaction between different parameter types
Effect of overpressure on impact and whether overpressure-only injury exists
Effects of demographic, medical history, and exposure history on injury thresholds
Effect of sensor placement and algorithms to transfer sensor outputs with conditions experienced at the head and brain

Relative contributions of blast overpressure to injury

As noted in Section 4.1, the variable most predictive of injury, and whether that variable will be different for blast overpressure exposure events versus impact events is unknown. It is also unknown whether using a combination of variables will lead to improved sensor thresholds. Research is needed to understand the key variables that sensors should be capturing and how variables can be combined to better predict injury.

Translation of data from computational and animal models to human outcomes

The pathophysiological mechanism of blast-induced mTBI may be addressed through a combination of animal and human surrogate studies, computational modeling, and analysis of existing sensor data. To date, there is no accepted animal model of blast injury or standardized method of translating animal data into human outcomes. If a standard set of biomarkers and/or cognitive performance metrics could be determined, then a level of consistency in interpreting results across different preclinical studies may be established. Improvement and standardization of computational models is also needed. In particular, improved models of fluid-solid interactions and more accurate measurements of physical parameters (e.g., elasticity modulus of biological tissue) are needed.

There is no accepted animal blast injury model or method for predicting human outcomes based on animal data

Effects of demographics, individual history, and repeated exposure on injury risk curves

As noted in Section 4.2, understanding the relationship between demographic variables, medical history, and exposure history is needed to develop predictive models for determining useful sensor thresholds.

In conclusion, the findings and recommendations described above were developed by the International SoS Meeting on the Biomedical Basis for mTBI Environmental Sensor Threshold Values meeting participants. The understanding of the state-of-the-science developed during the focused working group sessions and throughout the meeting forms the basis of the SoS Expert Panel findings and recommendations described below.

5.0 SoS Expert Panel Findings and Recommendations

Following the focused working group sessions, the Expert Panel convened to identify major themes that emerged from the meeting and formulate recommendations. The identified themes encapsulate the major discussion points that recurred throughout the keynote, topic and scientific presentations, the poster sessions, and the focused working group sessions. The Expert Panel identified eight key findings from the meeting that capture the major scientific and technological issues that need to be addressed in order for sensor threshold values to be established.

5.1 Expert Panel Findings

A standard definition of mTBI needs to be established for use in establishing environmental sensor thresholds. Mild TBI is currently a clinical diagnosis guided by a number of different assessment tools (e.g., Acute Concussion Assessment, MACE, SAC, and Sport Concussion Assessment Tool). To ensure that risk curves and thresholds are comparable across sensor manufacturers, a standard definition of mTBI must be adopted.

Mild TBI outcomes should be reported using a graded, not binary, response. Injury data are usually reported simply as the presence or lack of an injury. This response measure may obscure a more nuanced concussion diagnosis. Outcome data should include as much detail as possible regarding injury and symptom descriptions.

Correlations between existing environmental sensor data and medical outcomes need to be established. The DoD has deployed sensors both in theater and in training. Though the sensors have recorded many blast events, analysis and reporting of the existing data have been limited. Research that links current sensor data with known medical outcomes needs to be assessed.

Data sharing and access need to be improved. The DoD possesses a large database of blast events with known medical outcomes linked to the events. At this time, researchers are unable to access the data for further analysis. The data need to be anonymized and cleansed of classified information to facilitate sharing with the scientific community. Moreover, a central repository that houses all data related to concussion (e.g., sports science, automotive safety studies, and military blast events) should be established and utilized.

Injury risk curves for blast-induced mTBI currently do not exist. Injury risk curves do not yet exist for blast-induced mTBI, but could be developed from field and training sensor data or scaled from animal model studies. Sports, automotive safety, and blast injury research have developed injury risk curves for humans based on scaling from animal studies and human surrogate models.

Scaling laws for animal models need to be established. Animal models represent the only opportunity to study blast exposure in vivo under controlled laboratory conditions. There needs to be a standardized method of blast environment (i.e., tube) and test methodology that can simulate field-relevant PCEs. The DOD needs to establish such a standard so that the results from different animal models can be compared and validated. Additional challenges currently hinder the interpretation of animal studies. Factors that indicate mTBI concussion in animals may not correspond to the same disease in humans, moreover, environmental conditions such as acceleration and overpressure need to be scaled to humans. A consensus on scaling laws has yet to be reached; scaling laws need to be established and validated to generate injury risk curves applicable to humans.

Personalized sensor threshold values are needed that incorporate physical attributes (e.g., history of previous TBIs [number and severity], age, gender, weight, height). Injury risk curves are typically defined with respect to a single variable (i.e., exposure level). Other risk factors such as age, gender, weight, and height are usually ignored. Understanding the link between physical and demographic attributes may aid in improved individualized prediction of injury risk. Such factors can be integrated into a single variable, as is commonly done in blunt injury research.

Biomechanical mechanisms of blast-induced mTBI need to be understood. The precise mechanisms of blast-induced mTBI are unknown. Further research into the relative contributions of overpressure and acceleration to injury and the mechanisms of transmission to the brain will help identify the most relevant environmental variables to setting injury thresholds.

5.2 Expert Panel Recommendations

As the findings described above were defined, the Expert Panel developed a set of recommendations for advancing the state-of-the-science for mTBI sensor thresholds. The recommendations do not specify studies required for establishing environmental sensor thresholds; rather, these recommendations outline a set of actions that will facilitate discovery and communication in blast and environmental sensor research. Table describes the Expert Panel recommendations and proposed timeline for addressing the knowledge gaps discussed in these proceedings. The timeframe for these recommendations spans from immediate to near-term and long-term goals for understanding the biological mechanisms of mTBI and developing validated sensor threshold values.

Table 2. Expert Panel Recommendations

Recommendation	Timeframe	Components
1. Establish a fully-funded and authoritative task force to correlate sensor data to medical outcomes	Year: 0-1	<ul style="list-style-type: none"> Identify and invite committee members that represent a multidisciplinary cross-section of researchers and stakeholders Form charter that establishes the scope and authority of the task force Identify existing data (e.g., pressure, acceleration, PCE) that could be used in support of correlating environmental conditions and medical outcomes
	Year: 1-2	<ul style="list-style-type: none"> Identify the relevant elements from the data for establishing a link between sensor readings and medical outcomes Analyze data to establish any correlations between sensor data to medical outcomes Identify data that need to be captured in the future Identify risk factors for blast-induced mTBI based on the analysis
	Year: 3-5	<ul style="list-style-type: none"> Publish results of the analysis Publish lessons-learned and standards to be adopted by sensor manufacturers and researchers
2. Establish or utilize current databases for blast and sports injury data so that researchers can	Year: 0-1	<ul style="list-style-type: none"> Collect and organize data that already exists and is currently accessible (e.g., NIH, NCAA, DoD) Make existing data publicly accessible Mandate government funded projects to make data publicly available (i.e., FITBIR)

Recommendation	Timeframe	Components
analyze and correlate data to help identify thresholds	Year: 1-2	<ul style="list-style-type: none"> Identify additional data elements that need to be collected moving forward Establish common data elements for standardization of future data
	Year: 3-	<ul style="list-style-type: none"> Share and analyze publicly available data
3. Establish a consensus clinical definition/measure of concussion against which sensor thresholds can be developed and compared	Year: 1-2	<ul style="list-style-type: none"> Compare and evaluate current concussion assessment tools (e.g., MACE, ACE, SAC)
	Year: 3-	<ul style="list-style-type: none"> Determine efficacy of potential screening tools such as biomarkers, cognitive/motor tests, electrophysiology, and neuroimaging Publish consensus report that establishes a definition/measure of concussion for sensor manufacturers and researchers
4. Improve preclinical models (e.g., animal, computational, in vitro, human nerve pathology, ex vivo) to establish mTBI thresholds and identify mechanisms	Year: 0-1	<ul style="list-style-type: none"> Establish interdisciplinary task force of researchers to serve as reviewers for the current state-of-the-science
	Year: 1-2	<ul style="list-style-type: none"> Assess existing data/models and inventory to determine current consensus knowledge and gaps Validate/invalidate current models based on best science available
	Year: 3-	<ul style="list-style-type: none"> Determine biological mechanisms of mTBI Publish lessons learned and summary of findings
5. Create a consensus on nomenclature for mTBI, including sub-concussive events	Year: 0-1	<ul style="list-style-type: none"> Identify major terms that need clarification
	Year: 1-2	<ul style="list-style-type: none"> Identify all usages of ambiguous terms
	Year: 3-	<ul style="list-style-type: none"> Establish and publish a set of guidelines for terminology

6.0 Conclusions

The goal of the 2014 International State-of-the-Science Meeting on the Biomedical Basis for mTBI Environmental Sensor Threshold Values was to survey the current state-of-the-science for the biomedical basis of environmental sensor threshold values and the relationship between these threshold values and the risk of developing mTBI. Gaps in the development and utilization of current environmental sensor injury threshold values were identified to guide future research. Through three days of active discussion, participants shared advances in the field of sensor development and grappled with the fundamental questions on the state-of-the-science and areas where additional research is needed to close knowledge gaps. In the end, the Expert Panel developed a set of recommendations that will serve as the basis for greater coordination of research activities and information sharing among mTBI sensor programs sponsored by the DoD. The recommendations that resulted from this meeting could translate into enhanced protection, treatment, and mitigation of traumatic brain injury by providing improved methods and tools for assessing the impact and potential health outcomes of the blast exposures experienced by Service Members.

7.0 Appendices

Appendix A. References

- Allison, M. A., Kang, Y. S., Maltese, M. R., Bolte 4th, J. H., & Arbogast, K. B. (2014). Measurement of Hybrid III Head Impact Kinematics Using an Accelerometer and Gyroscope System in Ice Hockey Helmets. *Annals of Biomedical Engineering*, Epub ahead of print. doi:10.1007/s10439-014-1197-z
- American Academy of Neurology. (2012). *Understanding Concussion*. Retrieved from <https://www.aan.com/practice/patient-education-brochures/>
- Blast Injury Research Program Coordinating Office. (2014). *Biomedical Basis for MTBI Environmental Sensor Threshold Values Literature Review*. Retrieved from https://blastinjuryresearch.amedd.army.mil/index.cfm?f=application.pco_sos_material
- Centers for Disease Control and Prevention. (2010). *What are the Signs and Symptoms of Concussion?* Retrieved from http://www.cdc.gov/concussion/signs_symptoms.html
- DVBIC. (2014). *DoD Worldwide Numbers for TBI*. Retrieved from <http://dvbic.dcoe.mil/dod-worldwide-numbers-tbi>
- French, L., McCrea, M., & Baggett, M. R. (2008). The Military Acute Concussion Evaluation. *Journal of Special Operations Medicine*, 8(1), 68-77.
- Hicks, R. R., Fertig, S. J., Desrocher, R. E., Koroshetz, W. J., & Pancrazio, J. J. (2010). Neurological Effects of Blast Injury. *The Journal of Trauma*, 1257-1263. doi:10.1097/TA.0b013e3181d8956d
- Kovacs, S. K., Leonessa, F., & Ling, G. S. (2014). Blast TBI Models, Neuropathology, and Implications for Seizure Risk. *Frontiers in Neurology*, 5(47). doi:10.3389/fneur.2014.00047
- Lu, J., Ng, K. C., Ling, G., Wu, J., Poon, D. J., Kan, E. M., . . . Ling, E.-A. (2012). Effect of blast exposure on the brain structure and cognition in Macaca fascicularis. *Journal of Neurotrauma*, 1434-1454. doi:10.1089/neu.2010.1591
- Neselius, S., Brisby, H., Marcusson, J., Zetterberg, H., Blennow, K., & Karlsson, T. (2012). CSF-Biomarkers in Olympic Boxing: Diagnosis and Effects of Repetitive Head Trauma. *PLOS One*, 7(4), e33606. doi:10.1371/journal.pone.0033606
- Säljö, A., Arrhén, F., Bolouri, H., Mayorga, M., & Hamberger, A. (2008). Neuropathology and pressure in the pig brain resulting from low-impulse noise exposure. *Journal of Neurotrauma*, 25, 1397-1406. doi:10.1089/neu.2008.0602
- Tanielian, T., & Jaycox, L. H. (Eds.). (2008). *Invisible wounds of war: Psychological and cognitive injuries, their consequences, and services to assist recovery* (Vol. 1). Rand Corporation.
- The SPORT Foundation. (2014). *Standardized Assessment of Concussion*. Retrieved from <http://sportfoundation.org/concussion-clinic/standardized-assessment-of-concussion-sac>
- US Department of Veterans Affairs & US Department of Defense. (2009). *Clinical Practice Guideline for Management of Concussion/mild Traumatic Brain Injury*. Retrieved from http://www.healthquality.va.gov/guidelines/Rehab/mTBI/concussion_mtbi/sum_1_0.pdf
- Wilk, J. E., Thomas, J. L., McGurk, D. M., Riviere, L. A., Castro, C. A., & Hoge, C. W. (2010). Mild traumatic brain injury (concussion) during combat: lack of association of blast mechanism with persistent postconcussive symptoms. *The Journal of Head Trauma Rehabilitation*, 25(1), 9-14. doi:10.1097/HTR.0b013e3181bd090f

Appendix B. Acronym List

Acronym or Abbreviation	Full Name
ACH	Advanced Combat Helmet
AUC	Area Under the ROC Curve
CFD	Cell-Free DNA
CSF	Cerebrospinal Fluid
DARPA	Defense Advanced Research Projects Agency
DNA	Deoxyribonucleic Acid
DoD	Department of Defense
DTI	Diffusion Tensor Imaging
DVBIC	Defense and Veterans Brain Injury Center
ECH	Enhanced Combat Helmet
EEG	Electroencephalography
EOD	Explosive Ordnance Disposal
FITBIR	Federal Interagency Traumatic Brain Injury Research
fMRI	Functional Magnetic Resonance Imaging
GFT	gForce Tracker™
HEADS	Headborne Energy Analysis and Diagnostic Systems™
HIC	Head Injury Criterion
HIP	Head Impact Power Index
HIT	Head Impact Telemetry
HITS	Head Impact Telemetry System
HMSS	Helmet-Mounted Sensor System
HSHM	Human Surrogate Head Model
IBESS	Integrated Blast Effect Sensor Suite™
JARI	Japanese Automobile Research Institute
JTAPIC	Joint Trauma Analysis and Prevention of Injury in Combat
kPa	Kilopascal
m	Meters
MACE	Military Acute Concussion Evaluation
MDD	Major Depressive Disorder
MRI	Magnetic Resonance Imaging
ms	Milliseconds
mTBI	Mild Traumatic Brain Injury
NCAA	National Collegiate Athletic Association
NIH	National Institutes of Health
NOCSAE	National Operating Committee on Standards for Athletic Equipment
PMHS	Post-Mortem Human Subject
PCE	Potentially Concussive Event
PCO	Blast Injury Research Program Coordinating Office
psi	Pound Per Square Inch

Acronym or Abbreviation	Full Name
PTSD	Posttraumatic Stress Disorder
QBIS	Quantico Breacher Injury Studies
rad	Radians
SAC	Standard Assessment of Concussion
SoS	State-of-the-Science
UCH-L1	Ubiquitin Carboxy-terminal Hydrolase L1
USUHS	Uniformed Services University of the Health Sciences
TBI	Traumatic Brain Injury
VA	Department of Veterans Affairs
WRAIR	Walter Reed Army Institute of Research

Appendix C. Table of Environmental Sensors

Sensor Name	Manufacturer	Linear Acceleration	Rotational Acceleration	Pressure	Placement	Indicator	Notes
Blast Gauge	BlackBox Biometrics	Yes	No	Yes	Back of neck, off-arm, & chest	Green, Yellow, Red (0/4/16 psi)	
Brain Sentry	Brain Sentry	Indicator	No	No	Back of helmet	LCD counter/LED light	Multiple proprietary algorithms
Checklight	Reebok	Indicator	Indicator	No	Skullcap	Green, Yellow, Red (proprietary algorithm)	Does not capture time series data.
gForce Tracker	Gforcetracker Inc.	Yes	No	No	Inside or outside helmet	Alarm & flashing LED (programmable in g-level)	
Hammerhead Mouthguard	i1 Biometrics	Yes	Yes	No	Mouth guard	Laptop or mobile app	
HMSS	BAE Systems	Yes	Velocity	Yes	Helmet crown	Green, Amber, Red (0/3.53/6.54 m/s)	Triggers on linear acceleration
HIT	Riddell/Simbex	Yes	Computed	No	Helmet lining	Offline	Estimates impact location
Impact Indicator	Battle Sports Science	Indicator	Indicator	No	Chin strap	Green, Red (0/240 HIC)	Does not capture time series data
SafeBrain	SafeBrain Systems	Yes	No	No	Back of helmet	Flashing light (programmable in g-level)	Data log point also adjustable
ShockBox	Impakt Protective	No	No	No	Top or inside helmet	Bluetooth to cellphone (events > 50 g)	Binary force switch
Soldier Body Unit	Georgia Tech Research Institute	Yes	?	Yes	Chest and back	Offline	Part of I-BESS
xPatch	X2 Biosystems	Yes	Yes	No	Behind ear	Offline	Estimates impact location

Note: Additional sensor technologies discussed in these proceedings may not be included in this table if the specifications were not publicly available.

Appendix D. Welcome Letter

Dear Colleague:

On behalf of the DoD Executive Agent for Medical Research for Prevention, Mitigation and Treatment of Blast Injury, welcome to the International State-of-the-Science Meeting on the Biomedical Basis for Mild Traumatic Brain Injury (mTBI) Environmental Sensor Threshold Values. Approximately 140 subject matter experts have volunteered to participate in this meeting, and I look forward to the important work that we will accomplish. Scientific information gained from this meeting will be used to shape and guide future medical science and technology strategy.

Traumatic brain injury is a major health issue in both military and civilian communities. According to the Defense and Veterans Brain Injury Center, approximately 295,000 Service Members sustained a TBI between 2000 and 2013, and it has been called the “signature injury” of the wars in Afghanistan and Iraq. Additionally, the Centers for Disease Control reports that an estimated 1.5 million Americans experience a TBI annually, and approximately 50,000 deaths occur each year as a result of TBI. Despite extensive research in the areas of mTBI/concussion and methods of detecting concussion events, medically validated threshold values for detecting mTBI have not been established yet.

During the meeting, experts from the scientific, medical, and operational communities will present their work and participate in working groups. Your active participation will help to achieve the objectives of the meeting:

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

Over the next three days, I encourage you to take advantage of opportunities to engage with your colleagues and actively participate in working group discussions. I’m especially looking forward to the dialogue during the working group sessions, as we seek to answer these questions:

1. Are the existing environmental sensor threshold values suitable for predicting the development of mTBI/concussion?
2. What are the challenges for developing biomedically valid, standardized thresholds that accurately capture mTBI/concussion events?
3. What are the appropriate parameters (e.g., linear/rotational acceleration, pressure, event duration) for which sensor threshold values need to be established?
4. What biomedical research is needed to develop predictive models (e.g., computational models, animal models) for association of sensor threshold values and development of mTBI/concussion?

Please accept my gratitude for your active participation in this meeting.

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

Appendix E. Meeting Agenda

Tuesday, 11/4		
7.30am	Expert Panel Introductions/ Orientation	Mr. Michael Leggieri, DoD Blast Injury Research Program Coordinating Office
8.00am	Registration	
8.30am	Housekeeping/Introduction	Dr. Nick Tountas, DoD Blast Injury Research Program Coordinating Office
8.35am	Welcome & Keynote Introductions	Mr. Michael Leggieri
8.55am	MG Brian C. Lein, Commanding General, US Army Medical Research and Materiel Command and Fort Detrick / Deputy for Medical Systems to the Assistant Secretary of the Army for Acquisition, Logistics, and Technology	
	RADM Bruce A. Doll, Director of Research, Development, and Acquisition, Defense Health Agency / Deputy Commanding General, US Army Medical Research and Materiel Command at Fort Detrick	
	Dr. John F. Glenn, Principal Assistant for Research and Technology, US Army Medical Research and Materiel Command	
9.40am	Topic Introduction: Define Problem & Requirements	Mr. Michael Leggieri
	Department of Defense Traumatic Brain Injury (TBI) Overview	Ms. Kathy Helmick, Defense and Veterans Brain Injury Center (DVBIC)
	The concussion problem: the NCAA's perspective	Dr. Steven P. Broglio, National Collegiate Athletic Association (NCAA) / University of Michigan
	Q&A for all speakers	
10.35am	AM BREAK	
10.50am	Topic Introduction: Current State of the Science & What's Next?	Dr. Raj Gupta, DoD Blast Injury Research Program Coordinating Office
	DARPA perspective on current state of the science	CDR Josh Duckworth, Defense Advanced Research Projects Agency (DARPA) / Uniformed Services University of the Health Sciences (USUHS)
	NIH perspective on current state of the science	Dr. Patrick Bellgowan, National Institutes of Health (NIH), National Institute of Neurological Disorders and Stroke (NINDS)
	What NOCSAE and I have learned from 40 years of concussion research and helmet testing	Dr. Robert C. Cantu, National Operating Committee on Standards for Athletic Equipment (NOCSAE)
	Q&A for all speakers	
12.15pm	LUNCH	
1.15pm	PM Topic Speaker Introductions	Dr. Raj Gupta
1.20pm	Define Problem & Requirements: Invisible Wounds of War: Psychological and Cognitive Injuries, Their Consequences, and Services to Assist Recovery	Ms. Terri Tanielian, RAND
1.40pm	What is the Goal of a Sensor Program? A Primary Care and Public Health Point of View	COL Colin Greene, Joint Trauma Analysis and Prevention of Injury in Combat (JTAPIC), US Army Medical Research and Materiel Command
2.00pm	Thresholds of mTBI Based on Sensor-Generated Data	Dr. James Stuhmiller, L-3 / Jaycor

International State-of-the-Science Meeting Proceedings Draft

Biomedical Basis for mTBI Environmental Sensor Threshold Values

Tuesday, 11/4		
	Q&A for all speakers	
2.40pm	PM Break	
2.55pm	Scientific Presentation Introductions	Mr. Michael Leggieri
3.00pm	Blast Gauge Threshold Settings for Detecting Risk of Blast-induced Neurotrauma	Ms. Lee Ann Young, Applied Research Associates, Inc.
	Helmet Mounted Sensor System State of the Science	Dr. Paul Rigby, L-3 Applied Technologies, Inc.
	Helmet-based Accelerometer Sensors: Importance of Sensor Accuracy	Dr. Kristy Arbogast, Children's Hospital of Philadelphia / University of Pennsylvania
4.00pm	Daily Wrap-Up	Dr. Nick Tountas
4.05pm	ADJOURN	

Wednesday, 11/5		
8.00am	Registration	
8.30am	Housekeeping	Dr. Nick Tountas
8.35am	Welcome & AM Scientific Presentation Introductions	Dr. Raj Gupta
8.45am	Six Degree Of Freedom Measurements of Human Mild Traumatic Brain Injury	Dr. David Camarillo, Department of Bioengineering, Stanford University
	Blast and Impact Induced Linear and Rotational Head Acceleration	Dr. Jean-Philippe Dionne and Aris Makris, Med-Eng - The Safariland Group
	Biomechanically Characterizing Mild Traumatic Brain Injury using Helmet Instrumentation	Professor Steve Rowson, Biomedical Engineering, Virginia Tech
	The Blast Gauge™ System Overpressure Thresholds – Present and Future	Dr. David Borkholder, BlackBox Biometrics, Inc.
	Finding Real Meaning in Chaos, Interpretation of Personnel-Mounted Blast Sensor Data	Mr. Gregory Rule, Applied Research Associates, Inc.
10.25am	AM Break	
10.40am	Late AM Scientific Presentation Introductions	Dr. Raj Gupta
10.50am	Biological Dosimeters of Blast Exposure	Dr. Peethambaran Arun, Walter Reed Army Institute of Research
	UCH-L1 As A Serum Biomarker Of Exposure To Occupational Low Level Blast	MAJ Walter Carr, Walter Reed Army Institute of Research
	Neurosensory Assessments of Concussion	Dr. Mark Tommerdahl, Cortical Metrics
	TBI Assessment of Readiness Using a Gait Evaluation Test (Target): Development of a Portable mTBI Screening Evaluation	Dr. Christopher Rhea, University of North Carolina at Greensboro
	Physical and Pathological characterisation of 3 models for blast TBI	Professor Marten Risling, Karolinska Institutet
12.30pm	LUNCH & Poster Session	Poster presenters

International State-of-the-Science Meeting Proceedings Draft

Biomedical Basis for mTBI Environmental Sensor Threshold Values

Wednesday, 11/5		
2.00pm	PM Scientific Presentation Introduction	Mr. Michael Leggieri
2.05pm	Seeking a Biomedical Basis for mTBI Exposure Level: Consideration of Synthetic, Post-mortem, and live cell surrogates	Mr. Andrew Merkle, Johns Hopkins Applied Physics Laboratory
2.25pm	Roles/Responsibilities of Working Groups	Mr. Michael Leggieri
2.35pm	Working Groups*	A: Dr. Namas Chandra (Room 2002) B: Dr. Donald Marion (Room 2011) C: Mr. Dave Ritzel (Room 2032) D: Dr. Douglas Smith (Room 2010) E: Dr. Liying Zhang (Room 2014) F: Dr. James Zheng (Room 2005)
5.00pm	ADJOURN directly from Working Groups	

*Breaks were determined within each Working Group.

Thursday, 11/6		
8.00am	Registration	
8.30am	Working Groups*	A: Dr. Namas Chandra (Room 2001A) B: Dr. Donald Marion (Room 2011) C: Mr. Dave Ritzel (Room 2001B) D: Dr. Douglas Smith (Room 2010) E: Dr. Liying Zhang (Room 2014) F: Dr. James Zheng (Room 2001C)
11.30am	LUNCH & Poster Session	Poster presenters
1.00pm	Working Groups*	Expert Panelists/Working Groups
2.00pm	Working Groups Report Out	Working Group Chairs/Expert Panelists
4.00pm	Closing	Mr. Michael Leggieri
4.20pm	ADJOURN	

*Breaks were determined within each Working Group

Appendix F. Poster Presentations

Title	Presenter
<i>Primary Blast Injury Impairs Learning in Rat Organotypic Hippocampal Slices</i>	Dr. Barclay Morrison Columbia University
<i>Cavitation-Induced Structural and Neuronal Damage in Brain Tissue and Surrogates: Relevance to TBI</i>	Professor Ghatu Subhash University of Florida
<i>An End-To-End mTBI Model That Translates Measureable External Quantities to Clinical Outcomes</i>	Dr. Laurel Ng L-3/ATI
<i>Understanding the Realistic Blast Impacts on Neurons and Cultured Slices of Rat Hippocampus: In Vitro Experimental and Simulation Approach</i>	Dr. Thuvan Piehler US Army Research Laboratory
<i>Brain PET Scanning with Florbetapir and T807 In The Diagnosis Of Chronic Traumatic Encephalopathies</i>	Professor Sam Gandy Icahn School of Medicine at Mount Sinai and the James J Peters VA Med Center
<i>Physical- Versus Blast-Traumatic Brain Injury: Commonalities in Cognitive Dysfunction And Hippocampal Gene Transcriptome in Mice</i>	Professor Chaim Pick Tel-Aviv University
<i>Investigating the Effects of Mild Blast Injury on TBI Symptoms and Tau Pathology</i>	Dr. John Lloyd James A Haley VA Hospital
<i>Biomechanical Evaluation of Helmet Protection against Concussion and TBI</i>	Dr. John Lloyd BRAINS, Inc.
<i>Human Injury Criteria for Blast - Issues and Results</i>	Dr. Karin Rafaels US Army Research Laboratory
<i>Imaging-Based Classifier As Synthetic Biomarker For TBI Patients</i>	Dr. Benjamin Odry Siemens Corporation, Corporate Technology
<i>Laboratory and Field Validation of the Blast Gauge™ sensor system (BG) in Selected Operational Overpressure (OP) Scenarios</i>	LT Uade da Silva Naval Medical Research Center
<i>Brain Pathological and Biochemical Responses Following Repeated Blast Exposures in Rats</i>	Dr. Ying Wang Walter Reed Army Institute of Research
<i>Role of Transcranial Doppler Ultrasound in the Management of Wartime Traumatic Brain Injury</i>	Dr. Alexander Razumovsky Sentient NeuroCare Services, Inc.
<i>Transcranial Doppler Ultrasound as a Quantitative Biomarker in Evaluation of Patients with Traumatic Brain Injury</i>	Dr. Alexander Razumovsky Sentient NeuroCare Services, Inc.
<i>An Experimental Model for Traumatic Axonal Injury Based on Cytoskeletal Evolution</i>	Dr. Adam Fournier US Army Aberdeen Test Center
<i>Blast-Induced Motion And Scaling For Model Assessments Of Blast TBI</i>	Mr. Stephen Van Albert Walter Reed Army Institute of Research
<i>In Vitro Studies of Primary Explosive Blast Loading on Neurons</i>	Dr. Nicole Zander US Army Research Laboratory

Title	Presenter
<i>Purinergic Signaling: Therapeutic Approaches to Improve Acute and Chronic TBI Outcomes</i>	Dr. Theresa Lusardi RS Dow Neurobiology Laboratories, Legacy Research Institute
<i>Traumatic Brain Injury Due to Blast Exposure in Women Deployed to a Combat Theater</i>	Ms. Joyce Wagner Intrepid Spirit Concussion Recovery Center Naval Hospital Camp Lejeune
<i>Considerations for Acceleration-based Environmental Sensors in Military Environments</i>	Mr. Tyler Rooks US Army Aeromedical Research Laboratory
<i>Biomechanics of Head Injury under Blast and Blunt Impacts: The Influence of Directionality of Impact and Protective Headgears</i>	Professor Ghodrat Karami North Dakota State University
<i>Star Wars in Medicine is Here!</i>	Lt Gen Paul K. Carlton Jr. Retired US Air Force
<i>Could the iPhone have aided Alexis Carrel's World War I Surgical Techniques to Prevent Wound Disinfection?</i>	Dr. Bruce Capehart Duke University

Appendix G. Keynote Speaker Biographies

MG Brian C. Lein

Commanding General, US Army Medical Research and Materiel Command and Fort Detrick / Deputy for Medical Systems to the Assistant Secretary of the Army for Acquisition, Logistics, and Technology



MG Brian Lein grew up in New York and attended the United States Military Academy. He graduated in 1984 as a Distinguished Military Cadet with a Bachelor of Science, and was commissioned a Second Lieutenant in the Medical Service Corps. He then attended Temple University School of Medicine in Philadelphia. He graduated in 1988 as an Alpha Omega Alpha Scholar with an MD degree. He completed his Internship in General Surgery at Madigan Army Medical Center in 1989. He completed his Residency in General Surgery at Abington Memorial Hospital in 1993. He is board certified in general surgery.

MG Lein's military education includes graduation from the AMEDD Officer Basic and Advanced Courses, the US Army Command and General Staff College, the US Army War College and the US Army Airborne School.

Following commissioning in the Regular Army, MG Lein served as a General Surgeon in 2d General Hospital/Landstuhl Army Regional Medical Center. During this assignment he was assigned to the 67th Forward Surgical Team (Airborne) and deployed to Bosnia-Herzegovina in support of Operation Joint Endeavor. His next assignment was as Chief of General Surgery, William Beaumont Army Medical Center. There he was PROFIS to the 31st Combat Support Hospital (Caretaker) as the Chief of Surgery. During this time he was also assigned to Joint Special Operations Command as a general surgeon. His next assignment was as the Division Surgeon, 4th Infantry Division (Mechanized). He served on the Army Surgeon General Panel for Objective Force Redesign for Medical Force Structure. In 2003, he graduated from the US Army War College. He then served as Commander, Evans Army Community Hospital, Fort Carson, Colorado. His next assignment was Command Surgeon, Coalition Forces Land Component Command/US Army Central/Third Army. He then served as Commander, Landstuhl Regional Medical Center. He also served as Command Surgeon, US Army Forces. During this assignment, MG Lein deployed in support of Operation Enduring Freedom as Command Surgeon, ISAF Joint Command, from February to May 2012. His most recent assignment was as the Deputy Surgeon General and Deputy Commanding General, Operations, US Army Medical Command.

MG Lein's awards and decorations include the Legion of Merit (2OLC), Bronze Star Medal, Defense Meritorious Service Medal, Meritorious Service Medal (2OLC), the Army Commendation Medal (2OLC), the Joint Service Achievement Medal, Army Achievement Medal, GWOTEM and GWOTSM, Overseas Ribbon, NATO Medal, the Army Parachutist Badge, the Joint Superior Unit Award, the Army Superior Unit Award, the Order of Military Medical Merit and the German Sports Badge (Gold).

RADM Bruce A. Doll

Director of Research, Development and Acquisition, Defense Health Agency / Deputy Commanding General, US Army Medical Research and Materiel Command at Fort Detrick



A graduate of Colgate University, Rear Adm. Doll began his Navy service when he was competitively selected for the 1925I program and was commissioned as an ensign in the US Navy Reserve. Upon graduation from the State University of New York at Buffalo, School of Dentistry with a Doctor of Dental Surgery in 1981, he was commissioned a lieutenant. Doll attended the Naval Dental School and received a certificate in periodontology in 1989. He was reassigned as Periodontics department head and training officer at the dental clinic, U. S. Naval Academy (USNA), Annapolis, Md. He also qualified as an offshore sailing captain for the USNA midshipmen sailing program. In September 2007, he deployed as the commanding officer, Navy Expeditionary Medical Unit. The unit participated in joint support of Landstuhl Regional Medical Center, Germany during OEF/OIF. Upon his return in October 2008, Doll served as the deputy commander, Navy Medicine East and deputy chief, Navy Reserve Dental Corps. Doll also served as

chief operating officer, Rutgers University/Cleveland Clinic research consortium focusing on regenerative medicine for the wounded warrior until August 2010. From 2010 to 2012, Doll was dual-hatted as the medical advisor at NATO, ACT and the command surgeon at US Joint Forces Command in Norfolk, Va. From 2012 to 2014, Doll served as Deputy Chief, Navy Medicine Research and Development, Bureau of Medicine and Surgery (M2), Special Assistant for DoN Office of Research Protections, BUMED Commander, Naval Medical Research and Development Command. Between 2008 and 2013, Doll also served as Deputy Chief, Navy Reserve Dental Corps.

In his current position, Doll serves as the Director of the Research, Development and Acquisition Directorate within the Defense Health Agency in Falls Church, VA as well as the Deputy Commanding General of the US Army Medical Research and Materiel Command, Fort Detrick, MD. Doll is a member of many professional societies and a diplomate of the American Board of Periodontology. He is also a grantee of the National Institutes of Health. He has received fellowships from Omicron Kappa Upsilon, the International and American College of Dentists. Doll's decorations include the Defense Superior Service Medal, Legion of Merit (2 awards), Meritorious Service Medal (2 awards), Navy and Marine Corps Commendation Medal (2 awards), Navy and Marine Corps Achievement Medal, Meritorious Unit Commendation (3 awards), Fleet Marine Force Ribbon, Arctic Service Ribbon and other awards.

Dr. John F. Glenn, SES

Principal Assistant for Research and Technology, US Army Medical Research and Materiel Command



Dr. John Frazier Glenn was selected to the Senior Executive Service in November 2005. He serves as the Principal Assistant for Research & Technology at the US Army Medical Research and Materiel Command at Fort Detrick, Maryland where he exercises scientific oversight and direction of the Command's Science and Technology programs (\$1.7 billion in FY10) in Military Infectious Diseases, Military Operational Medicine, Combat Casualty Care, Clinical and Rehabilitative Medicine, Advanced Technology, Medical Chemical and Biological Defense, and Congressional Directed Special Interest Research Programs, as well as in oversight of the Command's worldwide laboratory system of laboratories, six in the continental United States and three outside the continental United States.

Prior to his current appointment, Dr. Glenn was the Technical Director, Headquarters, US Army Medical Research and Materiel Command from 2004 to 2005. Before retiring at the rank of Colonel with 30 years of military service, he served as the Deputy for Research and Development from 2000 to 2004 and Director, Plans Programs, Analysis, and Evaluation from 1998 to 2000 at Headquarters, US Army Medical Research and Materiel Command. Prior to these positions, Dr. Glenn also served as the Director, Medical Systems Integration Office from 1996 to 1998 and the Executive Assistant to the Commanding General from 1992 to 1996 at Headquarters, US Army Medical Research and Materiel Command. Dr. Glenn was also the Deputy Commander, Headquarters, US Army Research Institute of Environmental Medicine, Natick, MA from 1989 to 1992. Prior to this assignment, he was the Senior Army Technology Staff Officer for Medical Research, Office of the Assistant Secretary of the Army for Research, Development and Acquisition, Washington, DC from 1988 to 1989 and the Liaison Officer, Office of the Program Executive Officer for Combat Medical Systems, US Army Medical Materiel Development Activity with duty at the Pentagon Office of the Assistant Secretary of the Army for Research, Development & Acquisition, Washington, DC from 1987 to 1988. Dr. Glenn also served as the Senior Staff Officer, Medical Chemical Defense Research Program, Headquarters, US Army Medical Research and Materiel Command, Fort Detrick, MD from 1986 to 1987 and the Chief, Neurotoxicology Branch, US Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, MD from 1982 to 1986. Prior to these assignments, he also was the Deputy Chief, Neurotoxicology and Experimental Therapeutics Branch from 1981 to 1982 and a Research Psychologist, Physiology and Neurotoxicology and Experimental Therapeutics Branches from 1980 to 1981 at the US Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, MD. He also was a Research Psychologist, Behavioral Research Directorate, US Army Human Engineering Laboratory, Aberdeen Area, Aberdeen Proving Ground, MD from 1975 to 1979.

Appendix H. Expert Panel Biographies

Dr. Namas Chandra, *New Jersey Institute of Technology*



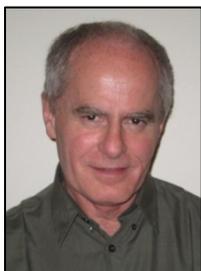
Dr. Namas Chandra is a Professor of Biomedical Engineering and the Director of Center for Injury Bio-mechanics, Materials, and Medicine at New Jersey Institute of Technology. He was the founder director of a \$5.8 M UNL-Army Center for Trauma Mechanics. Dr. Chandra has about 28 years of academic experience (NJIT, FSU, and UNL) and about 9 years of industrial experience. He was a university distinguished research professor at FSU and Associate Dean for Research at UNL. His blast facility was recognized as the top 10 laboratory in the country by Popular Science. He has published over 206 articles including 106 in archival journals, cited 2450 times, edited four books, two book chapters, and delivered 65 colloquiums, 6 workshops. He has been funded to the tune of \$26 M as PI and co-PI from private and federal agencies. He has also supervised MS, Ph.D., and post-doctoral students totaling 52 in number. Dr. Chandra is serving as the Chair of the Expert Panel.

Dr. Donald Marion, *Defense and Veterans Brain Injury Center (DVBIC)*



Dr. Donald Marion is an academic neurosurgeon who has focused on the clinical pathophysiology and treatment of TBI for more than 25 years. He published the first clinical report to show the benefit of therapeutic moderate hypothermia for TBI (The New England Journal of Medicine, 1997). He is the editor of a book entitled "Traumatic Brain Injury," and he has authored or co-authored more than 200 journal articles and book chapters, mostly related to TBI. Dr. Marion's previous positions have included professor and chair of the Department of Neurosurgery, The Boston University School of Medicine; professor and vice-chair, Department of Neurosurgery, The University of Pittsburgh School of Medicine; and director of the Brain Trauma Research Center at the University of Pittsburgh. He is past president of the National Association of Injury Control and Research Centers; and past chair of the Neurosurgery Subsection, the Committee on Trauma of the American College of Surgeons.

Mr. Dave Ritzel, *Dyn-FX Consulting Ltd.*



Mr. Dave Ritzel holds a B.Sc (With Distinction) in Mechanical Engineering and M.A.Sc. in Aerospace Sciences. He began his career in blast research in 1978 with Defence R&D Canada (DRDC) at Suffield, Alberta, covering the theory, computational modelling, and experimental study of blast phenomenology, effects on structures/materials, and personal vulnerability. Mr. Ritzel became Head of Explosives Effects Group at DRDC Suffield in 1989; in 1995, he accepted a position with the Defence Science and Technology Organisation (DSTO), Australia where he became Head of Weapons Terminal Effects Group. In 2000, he formed his own consulting company addressing blast threats including analyses of blast injury and blast protection of soldiers and civilians. Mr. Ritzel has authored or co-authored over 60 reports on blast/shock research, was co-editor of NATO AEP-25 "*Blast and Thermal Test Methods and Procedures*", and developer of the Advanced Blast Simulator; he has received numerous international awards and distinctions.

Dr. Douglas Smith, *University of Pennsylvania*



Dr. Douglas Smith serves as Director of the Center for Brain Injury and Repair (CBIR) and is the Robert A. Groff Endowed Professor and Vice Chairman for Research and Education in Neurosurgery at the University of Pennsylvania. Dr. Smith is also director of National Institutes of Health (NIH) and Department of Defense grants on concussion. His laboratory studies the effects of mechanical stretch of nerve fibers called “axons” during traumatic brain injury. They have found that proteins accumulate in axons after injury, which can lead to neurodegenerative changes similar to those found in Alzheimer’s disease. Moreover, Dr. Smith’s laboratory has also recently discovered that slow continuous stretching of axon tracts in culture can stimulate enormous growth, creating transplantable living nervous tissue constructs that can repair large lesions in the nervous system. These collective efforts have resulted in over 170 published scientific reports. These efforts have also earned scientific awards, including the recent Dorothy Russell Medal.

Dr. Liying Zhang, *Wayne State University*



Dr. Liying Zhang is an Associate Professor of the Biomedical Engineering Department at Wayne State University. Her areas of expertise include injury biomechanics, mechanisms and thresholds of traumatic brain injury in blunt impact and blast wave, helmet performance, and computational modeling of human and animal head/body models using finite element techniques. Her research efforts focus on the prediction, mitigation, and prevention of trauma in automotive, military, and sports applications. Dr. Zhang is the PI of the head model center of excellence of the Global Human Body Models Consortium, a global endeavor to create an advanced standard finite element model of the human body for trauma prediction. She has served on the US Department of Defense expert panel on Brain Injury Computational Modeling. She is on the helmet standard technical committee of American Society for Testing and Materials.

Dr. James Zheng, *Program Executive Office – Soldier (PEO Soldier)*



Dr. James Zheng is the Director of Technical Management Directorate, and Chief Scientist for Project Manager – Soldier Protection & Individual Equipment, Program Executive Office – Soldier, US Army. Dr. Zheng obtained his Bachelor’s degree in Chemistry and Master’s Degree in Physics from the University of Science and Technology of China. He earned his Ph.D. degree in Physical Chemistry from Purdue University in 1991. Dr. Zheng holds three patents and published more than 50 scientific papers. He was one of the recipients of the US Army’s AMC Greatest Invention Award in 2002 for developing the current DOD standard body armor system – The Interceptor Multiple Threat Body Armor. He received the US Army “Superior Civilian Service Medal” Award in 2008 for “exceptional meritorious and superior technical achievement”. In 2009, he received the “Program Manager of the year” award from Office of Secretary Defense – Comparative Testing Office. He is one of the recipients of 2013 Office of Secretary Defense – Manufacturing Technology Achievement award.

Appendix I. Meeting Planning Committee Members

Meeting Planning Committee Members	
<p>Mr. Michael Leggieri <i>Planning Committee Chair</i> DoD Blast Injury Research Program Coordinating Office</p>	<p>Dr. Raj Gupta <i>Planning Committee Co-Chair</i> DoD Blast Injury Research Program Coordinating Office</p>
<p>LTC Chessley R. Atchison Environmental Sensors in Training Assessment US Army Medical Research and Materiel Command</p>	<p>Dr. Richard Ellenbogen National Football League</p>
<p>Dr. Patrick Bellgowan / Dr. Ramona Hicks National Institute of Neurological Disorders and Stroke National Institutes of Health</p>	<p>Dr. Brian Hainline National Collegiate Athletic Association</p>
<p>COL Dallas Hack Brain Health Program US Army Medical Research and Materiel Command</p>	<p>Dr. Lina Kubli Walter Reed National Military Medical Center National Military Audiology and Speech Pathology Center</p>
<p>Dr. Crystal Hill-Pryor Combat Casualty Care Research Program US Army Medical Research and Materiel Command</p>	<p>Dr. Donald Marion Defense and Veterans Brain Injury Center</p>
<p>Dr. Faris Bandak Defense Advanced Research Projects Agency</p>	<p>Dr. Frederick J. Pearce Office of the Secretary of Defense Assistant Secretary of Defense for Research and Engineering</p>
<p>CAPT Sean Biggerstaff Health Affairs, Defense Health Program Defense Health Agency</p>	<p>Dr. Richard Shoge Military Operational Medicine Research Program US Army Medical Research and Materiel Command</p>

Appendix J. Meeting Participants

Meeting Participants		
Dr. Yil Agimi Defense and Veterans Brain Injury Center	Dr. Kristy Arbogast Children's Hospital of Philadelphia University of Pennsylvania	Dr. Peethambaran Arun Walter Reed Army Institute of Research
LTC Chessley Atchison Environmental Sensors in Training Assessment US Army Medical Research and Materiel Command	Dr. Amit Bagchi Naval Research Laboratory	Dr. Thomas Balkin Walter Reed Army Institute of Research
Dr. Faris Bandak Defense Advanced Research Projects Agency	Dr. Rohan Banton US Army Research Laboratory	Dr. Adam Bartsch Cleveland Head, Neck & Spine Research Laboratory
Dr. Patrick Bellgowan National Institute of Neurological Disorders and Stroke National Institutes of Health	Dr. Ronald Benjamin US Army Medical Materiel Development Activity	Dr. Timothy Bentley Force Health Protection and Readiness, Office of the Deputy Assistant Secretary of Defense
Dr. David Borkholder BlackBox Biometrics, Inc.	Dr. Steven P. Broglio University of Michigan National Collegiate Athletic Association	Lt Col Kathy Brown Product Manager Soldier Protection Equipment
Dr. David Camarillo Department of Bioengineering, Stanford University	Dr. Robert C. Cantu National Operating Committee on Standards for Athletic Equipment	Dr. Bruce Capehart Duke University
Lt Gen Paul K. Carlton Jr. Retired US Air Force	MAJ Walter Carr Walter Reed Army Institute of Research	Dr. Namas Chandra New Jersey Institute of Technology
Mr. Raymond Chen Technical Management Directorate, Soldier Protection and Individual Equipment, PEO Soldier	Dr. Paul Ciminera Office of Public Health Department of Veterans Affairs	Dr. Jeffrey Colombe MITRE
MAJ Aaron Cronin Womack Army Medical Center US Army Medical Command	LT Uade da Silva Naval Medical Research Center	Dr. Douglas DeWitt University of Texas Medical Branch
Dr. Ann Mae DiLeonardi US Army Research Laboratory	Dr. Jean-Philippe Dionne Med-Eng - The Safariland Group	RADM Bruce Doll Defense Health Agency Research, Development, and Acquisition Directorate US Army Medical Research and Materiel Command
CDR Josh Duckworth Defense Advanced Research Projects Agency Uniformed Services University of the Health Sciences	Professor Stefan Duma Virginia Tech	Dr. Adam Fournier US Army Aberdeen Test Center
Ms. Elizabeth Fudge Defense Health Agency / Health Care Operations	Mr. Eleuterio Galvez Joint Trauma Analysis and Prevention of Injury in Combat US Army Medical Research and Materiel Command	Dr. John F. Glenn US Army Medical Research and Materiel Command

Meeting Participants		
COL Colin Greene Joint Trauma Analysis and Prevention of Injury in Combat US Army Medical Research and Materiel Command	Dr. Frederick Gregory US Army Research Office	Dr. Raj Gupta DoD Blast Injury Research Program Coordinating Office
COL Dallas Hack Brain Health Program US Army Medical Research and Materiel Command	Ms. Virginia Halls PEO Soldier	Dr. Scott Hartley BAE Systems Protection Systems
Ms. Kathy Helmick Defense and Veterans Brain Injury Center	Dr. Stuart Hoffman US Department of Veterans Affairs	Mr. Erick Ishii US Department of Veterans Affairs
Professor Ghodrat Karami North Dakota State University	Mr. Kevin Kelley Defense Health Agency	Dr. Michael Kleinberger US Army Research Laboratory
Ms. Jennifer Kraszewski US Navy Office of Naval Research	Dr. Lina Kubli National Military Audiology and Speech Pathology Center Walter Reed National Military Medical Center	Dr. Robert Labutta US Army Medical Materiel Development Activity
Mr. Kevin Lambing Trifecta Solutions LLC	Mr. Michael Leggieri DoD Blast Injury Research Program Coordinating Office	MG Brian Lein US Army Medical Research and Materiel Command
Dr. Charles Linden Jr. X2 Biosystems, Inc.	Dr. John Lloyd James A Haley VA Hospital / BRAINS, Inc.	Dr. Joseph Long Walter Reed Army Institute of Research
CPT Matt Lopresti Walter Reed Army Institute of Research	Dr. Theresa Lusardi RS Dow Neurobiology Laboratories, Legacy Research Institute	Mr. Michael Maffeo US Army Natick Soldier Research, Development & Engineering Center
Dr. Aris Makris Department of Research & Development, Med-Eng, The Safariland Group	Dr. Haojie Mao Biotechnology HPC Software Applications Institute	Dr. Donald Marion Defense and Veterans Brain Injury Center
Dr. Peter Matic Naval Research Laboratory	Dr. Stephanie Maxfield Panker US Army Office of the Surgeon General	Dr. Joseph McCabe Uniformed Services University of the Health Sciences
Mr. Joe McEntire US Army Aeromedical Research Laboratory	Dr. David Meaney University of Pennsylvania	Mr. Andrew Meloni US Army Natick Soldier Research, Development & Engineering Center
Mr. Andrew Merkle Johns Hopkins Applied Physics Laboratory	Dr. Edward Mlinek X2Biosystems	Dr. Barclay Morrison Columbia University
Dr. Laurel Ng L-3 Communications/ ATI	Dr. Savita Nigam Combat Casualty Care Research Program US Army Medical Research and Materiel Command	MAJ Brent Odom PEO Soldier, Soldier Protective Equipment
Ms. Jessica Oribabor Defense and Veterans Brain Injury Center	Dr. Thomas O'Shaughnessy Naval Research Laboratory	MAJ Elaine Paszkowski Environmental Sensors in Training Assessment US Army Medical Research and Materiel Command

Meeting Participants		
Dr. Assiminia Pelegri Rutgers University	Ir. Mathieu Philippens TNO Defence Security & Safety	Professor Chaim Pick Tel-Aviv University
Ms. Linda Picon Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury	Dr. Thuvan Piehler US Army Research Laboratory	Dr. Siddiq Qidwai US Naval Research Laboratory
Dr. Karin Rafaels US Army Research Laboratory	Dr. Vineet Rakesh Biotechnology HPC Software Applications Institute Telemedicine and Advanced Technology Research Center	Dr. Alexander Razumovsky Sentient NeuroCare Service, Inc.
Dr. Jaques Reifman Biotechnology HPC Software Applications Institute Telemedicine and Advanced Technology Research Center	Dr. Patricio Reyes Phoenix VA Medical Center	Dr. Christopher Rhea University of North Carolina at Greensboro
Dr. Paul Rigby L-3 Applied Technologies, Inc.	Professor Marten Risling Karolinska Institutet	Mr. Dave Ritzel Dyn-FX Consulting Ltd.
Mr. Tyler Rooks US Army Aeromedical Research Laboratory	Professor Steve Rowson Biomedical Engineering, Virginia Tech	Mr. Gregory Rule Applied Research Associates, Inc.
Dr. Thomas Sawyer Defence R&D Canada, Suffield Research Center	Dr. Richard Shoge Military Operational Medicine Research Program US Army Medical Research and Materiel Command	SGM Kyle Sims US Army Special Operations Command
Dr. Douglas Smith University of Pennsylvania	Dr. David Stepp US Army Research Office	Dr. James Stuhmiller L-3 / Jaycor
Professor Ghatu Subhash University of Florida	Ms. Terri Tanielian RAND	Dr. Mark Tommerdahl Cortical Metrics
Dr. Valerie Trabosh US Army Medical Research and Materiel Command	Dr. Ginu Unnikrishnan Biotechnology HPC Software Applications Institute	Mr. Stephen Van Albert Walter Reed Army Institute of Research
Dr. Roy Vigneulle Military Operational Medicine Research Program US Army Medical Research and Materiel Command	Dr. Ying Wang Walter Reed Army Institute of Research	Dr. Tusit Weerasooriya US Army Research Laboratory
Dr. Brock Wester Johns Hopkins University Applied Physics Laboratory	Ms. Lee Ann Young Applied Research Associates, Inc.	Dr. Laila Zai Applied Research Associates
Dr. Nicole Zander US Army Research Laboratory	Dr. Liying Zhang Wayne State University	Dr. James Zheng PEO Soldier, US Army
Dr. Mariusz Ziejewski North Dakota State University		