NORTH ATLANTIC TREATY ORGANIZATION

SCIENCE AND TECHNOLOGY ORGANIZATION

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STO TECHNICAL REPORT **TR-HFM-234**

Environmental Toxicology of Blast Exposures: Injury Metrics, Modelling, Methods and Standards

(Ecotoxicologie des expositions au souffle : indicateurs de blessures, modélisation, méthodes et normes)

This Report documents the findings and recommendations of the Task Group HFM-234.

Published December 2018

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The NATO Science and Technology Organization

Science & Technology (S&T) in the NATO context is defined as the selective and rigorous generation and application of state-of-the-art, validated knowledge for defence and security purposes. S&T activities embrace scientific research, technology development, transition, application and field-testing, experimentation and a range of related scientific activities that include systems engineering, operational research and analysis, synthesis, integration and validation of knowledge derived through the scientific method.

In NATO, S&T is addressed using different business models, namely a collaborative business model where NATO provides a forum where NATO Nations and partner Nations elect to use their national resources to define, conduct and promote cooperative research and information exchange, and secondly an in-house delivery business model where S&T activities are conducted in a NATO dedicated executive body, having its own personnel, capabilities and infrastructure.

The mission of the NATO Science & Technology Organization (STO) is to help position the Nations' and NATO's S&T investments as a strategic enabler of the knowledge and technology advantage for the defence and security posture of NATO Nations and partner Nations, by conducting and promoting S&T activities that augment and leverage the capabilities and programmes of the Alliance, of the NATO Nations and the partner Nations, in support of NATO's objectives, and contributing to NATO's ability to enable and influence security and defence related capability development and threat mitigation in NATO Nations and partner Nations, in accordance with NATO policies.

The total spectrum of this collaborative effort is addressed by six Technical Panels who manage a wide range of scientific research activities, a Group specialising in modelling and simulation, plus a Committee dedicated to supporting the information management needs of the organization.

- AVT Applied Vehicle Technology Panel
- HFM Human Factors and Medicine Panel
- IST Information Systems Technology Panel
- NMSG NATO Modelling and Simulation Group
- SAS System Analysis and Studies Panel
- SCI Systems Concepts and Integration Panel
- SET Sensors and Electronics Technology Panel

These Panels and Group are the power-house of the collaborative model and are made up of national representatives as well as recognised world-class scientists, engineers and information specialists. In addition to providing critical technical oversight, they also provide a communication link to military users and other NATO bodies.

The scientific and technological work is carried out by Technical Teams, created under one or more of these eight bodies, for specific research activities which have a defined duration. These research activities can take a variety of forms, including Task Groups, Workshops, Symposia, Specialists' Meetings, Lecture Series and Technical Courses.

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List of Abbreviations

ANS	Autonomous Nervous System
BBB	Blood–Brain Barrier
BINT	Blast-Induced Neurotrauma
BOP	Blast Overpressure
CBF	Cerebral Blood Flow
CSO	Collaboration Support Office
DoD	Department of Defense
DRDC	Defence Research and Development Canada
E	Epinephrine
HFM	Human Factors and Medicine
IED	Improvised Explosive Device
IOM	Institute of Medicine
mTBI	mild Traumatic Brain Injury
NATO	North Atlantic Treaty Organization
NE	Norepinephrine
PNS	Parasympathetic Nervous System
PoW	Program of Work
PPE	Personnel Protective Equipment
R&T	Research and Technology
RTG	Research Task Group
SNS	Sympathetic Nervous System
STO	Science and Technology Office
SYM	Symposium
TAP	Technical Activity Program
TBI	Traumatic Brain Injury
TT	Technical Team
US/USA	United States of America

HFM-234 Membership List

CHAIR

Mr. Michael LEGGIERI
US Army Medical Research and Materiel Command
UNITED STATES
Email: michael.j.leggieri.civ@mail.mil

MEMBERS

LtCol Dr. Dan BIELER
German Armed Forces
GERMANY
Email: dr.dan.bieler@t-online.de

Mr. Stephen BJARNASON
DRDC Suffield
CANADA
Email: stephen.bjarnason@drdc-rddc.gc.ca

Prof. Dr. Ibolja CERNAK
University of Alberta
CANADA
Email: cernak@ualberta.ca

LtCol Dr. Axel FRANKE
German Armed Forces Central Hospital
GERMANY
Email: dr.axel.franke@t-online.de

Dr. Raj GUPTA
US Army Medical Research and Materiel Command
UNITED STATES
Email: raj.k.gupta.civ@mail.mil

Dr. Emrys KIRKMAN
Dstl Porton Down
UNITED KINGDOM
Email: ekirkman@dstl.gov.uk

Dr. Lucie MARTINEAU
DRDC Valcartier
CANADA
Email: lucie.martineau@drdc-rddc.gc.ca

Col Dr. Philippe MAY
Armed Forces Biomedical Research Institute
FRANCE
Email: philippe.may@intradef.gouv.fr

Dr. Hans ORRU
University of Tartu
ESTONIA
Email: hans.orru@ut.ee

Mr. Simon OUELLET
Defence R&D Canada
CANADA
Email: simon.ouellet@drdc-rddc.gc.ca

Mr. Mat PHILIPPENS
TNO – Netherlands Organisation for Applied Scientific Research
NETHERLANDS
Email: mat.philippens@tno.nl

Prof. Marten RISLING
Karolinska institutet
SWEDEN
Email: Marten.Risling@ki.se

Dr. Jean-Claude SARRON
Direction Centrale du Service de Santé des Armées
FRANCE
Email: jean-claude.sarron@intradef.gouv.fr

Mr. Stian SKRIUDALEN
Norwegian Defence Research Establishment (FFI)
NORWAY
Email: stian.skriudalen@ffi.no

Mr. Jan Arild TELAND
Norwegian Defence Research Establishment (FFI)
NORWAY
Email: jan.teland@ffi.no

Dr. Sarah WATTS
Dstl Porton Down
UNITED KINGDOM
Email: sawatts1@dstl.gov.uk

Maj Dr. Arnulf WILLMS
German Armed Forces Central Hospital
GERMANY
Email: arnulfwillms@gmx.de

PANEL/GROUP MENTOR

Dr. Patrick MASON
Department of Defense
UNITED STATES
Email: patrick.mason@navy.mil

Disclaimer:

The views expressed in HFM-234 (RTG) report, dictionary of terms and guidelines are those of the authors and may not necessarily be endorsed by the US Army or US Department of Defense.

Environmental Toxicology of Blast Exposures: Injury Metrics, Modelling, Methods and Standards

(STO-TR-HFM-234)

Executive Summary

Blast Injury is a significant source of casualties in current NATO operations and the spectrum of blast injuries and their consequences is broad. The HFM Research Symposium on Blast Injury (HFM-207) revealed a need for continuing NATO-wide research cooperation on the "environmental toxicology" of military personnel in blast exposure environments. Some of the scientific issues include a need for biomedically-valid computational models of primary blast injury that incorporate biomechanical and physiological responses, the establishment of common animal models of blast exposure and the resulting injuries, and an understanding of non-penetrating blast injuries to the brain which are manifest in a host of symptoms whose etiology is at best vague.

The primary objective of this Task Group was to consider the current knowledge gaps for blast injury research in the context of a toxicological approach to investigating blast effects on people. Additionally, the objective was to produce guidelines for blast injury research for each of the four Work Packages: Dictionary of Blast Injury Terms, Epidemiological Blast Injury Studies, Reproducing Blast Exposure in the Laboratory, and Animal Modeling for Blast Injury Research.

Dictionary of Blast Injury Terms is a consolidation of frequently used terms and definitions in both engineering and medical blast literature so that specialties can communicate effectively and results can easily be translated across the specialties.

Guidelines for Conducting Epidemiological Studies of Blast Injury provides blast injury researchers and clinicians with a basic set of recommendations for blast injury epidemiological study design and data collection guidelines that need to be considered and described when conducting prospective longitudinal studies of blast trauma. These guidelines emphasize current and future threat environments and identify four broad themes of types of data needed to conduct epidemiological studies:

1) Defining parameters of interest to track initial exposure to blast;
2) Identifying the types of data needed to link biological outcome to blast exposure;
3) Using sensors; and
4) Optimizing existing operational databases for blast injury epidemiological studies.

Guidelines for Reproducing Blast Exposures in the Laboratory provides blast injury research laboratories with a fundamental set of characteristics that need to be collected and described when generating blast pressure waves, resulting in studies that allow for the comparisons of research between different laboratories.

Guidelines for Using Animal Models in Blast Injury Research provide guidelines that need to be considered when planning, executing and reporting animal experiments for blast trauma. Some consequences of blast-induced injuries may be difficult to study in animal models, however appropriately designed animal experiments will enhance the state of the science.

Finally, HFM-234 Research Task Group (RTG) initiated dissemination of four Work Packages to the medical and health sciences community via its sponsor, the NATO Human Factors and Medicine Panel.

Ecotoxicologie des expositions au souffle : indicateurs de blessures, modélisation, méthodes et normes

(STO-TR-HFM-234)

Synthèse

L'effet de souffle est à l'origine de nombreuses blessures dans les opérations actuelles de l'OTAN et le spectre de ces blessures et de leurs conséquences est large. Le colloque de recherche sur les blessures par effet de souffle (HFM-207) a révélé qu'il était nécessaire de poursuivre la coopération en matière de recherche à l'échelle de l'OTAN sur « l'écotoxicologie » du personnel militaire dans les environnements exposés à un effet de souffle. Les problèmes scientifiques rencontrés sont notamment la nécessité de modèles de calcul des blessures principales par effet de souffle, valables sur le plan biomédical, qui intègrent les réactions biomécaniques et physiologiques, l'établissement de modèles animaux communs d'exposition au souffle et des blessures qui en résultent, et une compréhension des blessures non pénétrantes au cerveau par effet de souffle, qui se manifestent par une foule de symptômes dont l'étiologie est au mieux vague.

Le principal objectif de ce groupe de travail était d'étudier les lacunes actuelles des recherches sur les blessures par effet de souffle, dans le contexte d'une approche toxicologique étudiant les effets du souffle sur les personnes. De plus, l'objectif était de produire des lignes directrices pour la recherche sur les blessures par effet de souffle dans chacun des quatre lots de travaux suivants : dictionnaire des termes relatifs aux blessures par effet de souffle, études épidémiologiques sur les blessures par effet de souffle, reproduction de l'exposition au souffle en laboratoire et modélisation animale pour la recherche sur les blessures par effet de souffle.

Le dictionnaire des termes relatifs aux blessures par effet de souffle est une compilation des termes fréquemment utilisés et de leur définition dans la littérature sur l'effet de souffle, en ingénierie et en médecine, afin que les spécialités puissent communiquer efficacement et que les résultats puissent être facilement traduits entre spécialités.

Les lignes directrices pour mener des études épidémiologiques sur les blessures par effet de souffle donnent aux chercheurs et cliniciens un ensemble basique de recommandations pour concevoir les études épidémiologiques et des lignes directrices de recueil des données à prendre en compte et à décrire dans les études longitudinales prospectives des traumatismes liés au souffle. Ces lignes directrices mettent l'accent sur les environnements de menace actuels et futurs et identifient quatre grands axes liés aux données nécessaires pour mener des études épidémiologiques :

1) Définir les paramètres intéressants pour suivre l'exposition initiale au souffle ;
2) Identifier les types de données nécessaires pour relier les résultats biologiques à l'exposition au souffle ;
3) Utiliser des capteurs ; et
4) Optimiser les bases de données opérationnelles existantes pour les études épidémiologiques sur les blessures par effet de souffle.

Les lignes directrices pour reproduire les blessures par effet de souffle en laboratoire fournissent aux laboratoires de recherche un ensemble de caractéristiques qui doivent être recueillies et décrites lorsque des

ondes de pression de souffle sont produites, ce qui permet de comparer les recherches entre différents laboratoires.

Les lignes directrices d'utilisation des modèles animaux dans la recherche sur les blessures par effet de souffle fournissent des principes à étudier au moment de la planification, l'exécution et le compte rendu des expériences de traumatisme lié au souffle chez l'animal. Certaines conséquences de blessures dues à l'effet de souffle peuvent être difficiles à étudier sur des modèles animaux. Cependant, des expériences sur l'animal conçues de manière adéquate amélioreront l'état de la science.

Enfin, le groupe de recherche HFM-234 a commencé à diffuser quatre lots de travaux auprès de la communauté médicale et des sciences de la santé par le biais de son promoteur, la Commission sur les facteurs humains et la médecine de l'OTAN.

Chapter 1 − INTRODUCTION

1.1 BACKGROUND

Explosions are one of the most significant sources of casualties in recent North Atlantic Treaty Organization (NATO) operations. Consequently, the primary focus of blast injury research is on the prevention, treatment, rehabilitation, and continuum of care for the injured from acute treatment to the return of duty.

For the purpose of this discussion, the term "blast injury" refers to the entire spectrum of injuries that can result from exposure to an explosion. The taxonomy of blast injuries are defined in Table 1-1 based on the type of injury: primary, secondary, tertiary, quaternary, and quinary.

Table 1-1: Taxonomy of Injuries from Explosive Devices Adapted from DoD Directive (DoDD) 6025.21E [3].

Taxonomy of Blast Injuries	
Primary	Blast Overpressure (BOP) injury resulting in direct tissue damage from the shock wave coupling into the body.
Secondary	Injury produced by primary fragments originating from the exploding device (preformed and natural (unformed) casing fragments, and other projectiles deliberately introduced into the device to enhance the fragment threat); and secondary fragments, which are projectiles from the environment (debris, vehicular metal, etc.).
Tertiary	Displacement of the body or part of body by the BOP causing acceleration/ deceleration to the body or its parts, which may subsequently strike hard objects causing typical blunt injury (translational injury), avulsion (separation) of limbs, stripping of soft tissues, skin speckling with explosive product residue and building structural collapse with crush and blunt injuries, and crush syndrome development.
Quaternary	Other "explosive products" effects − heat (radiant and convective), and toxic, toxidromes from fuel, metals, etc. − causing burn and inhalation injury.
Quinary	Clinical consequences of "post detonation environmental contaminants" including bacteria (deliberate and commensal, with or without sepsis), radiation (dirty bombs), tissue reactions to fuel, metals, etc.

NATO forces regularly sustain attacks from blasts by Improvised Explosive Devices (IEDs), land mines, and rocket-propelled grenades. The United States (US) Department of Defense (DoD) reports that the use of IEDs and other explosive devices have led to an injury landscape different from that in previous wars [1]. The complexity of physical trauma resulting from direct or indirect exposure to an explosion has challenged medical practitioners across the spectrum of disciplines from surgery to mental health. Especially challenging are blast injuries to the brain where neither injury pathophysiology nor medical diagnosis are well understood. Moreover, the number of casualties incurred in NATO operations brings urgency to the blast injury research community to use medical information in the design of better protection technologies and the development of new treatment strategies for service members [2].

Blast injuries are often caused by more than one mechanism, do not occur in isolation, and typically elicit a secondary multisystem response. Research efforts often do not separate blast injuries caused by blast waves from those caused by blunt force trauma and other mechanisms. To add more complexity to elucidating blast injury pathophysiology, symptoms are often not immediately recognized or noticeable by a blast-exposed individual, especially when the individual is exposed to the blast waves but do not sustain blunt force trauma [2]. Currently, limited data and evidence-based guidelines exist regarding complex, multisystem injuries associated with blast exposure. Epidemiological studies are critical for obtaining the necessary data to understand the mechanisms of injury caused by explosions, the response of an individual to a blast event as well as long-term effects of blast exposure. Data elements required to evaluate an individual's response to blast exposure are summarized in Figure 1-1.

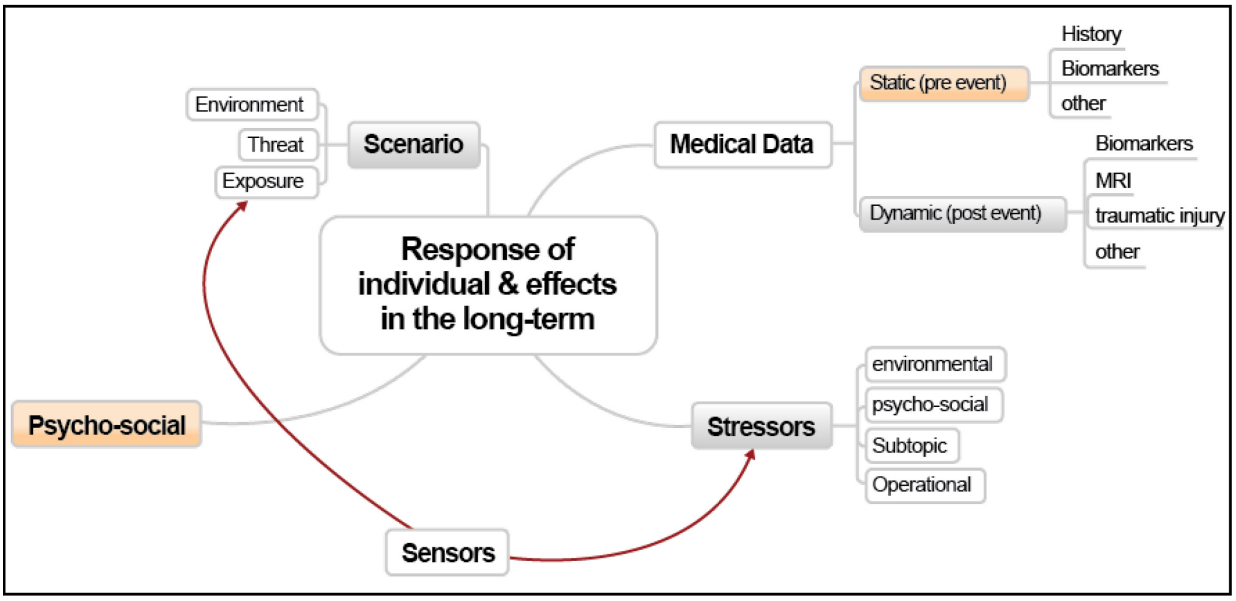

Figure 1-1: Data Elements Required to Understand the Response to Blast Injury [4].

1.2 PREVIOUS NATO ACTIVITY

The Human Factors and Medicine (HFM) Research Symposium (SYM) on Blast Injury (RTO-MP-HFM-207) held in October 2011 revealed a need for continuing NATO-wide research cooperation on the "environmental toxicology" of military personnel in blast exposure environments [5]. Blast injury is a significant source of casualties in current NATO operations and the spectrum of blast injuries and their consequences is broad. To address the research issues posed by the wide spectrum of battle injuries, a scientific interdisciplinary approach will be required. While HFM-207 provided an initial assessment of the current state of relevant interdisciplinary science, it was appreciated that the hard problem of understanding and mitigating blast injury will require a specific NATO technical activity devoted to the "environmental toxicology of blast exposures." Some of the scientific issues include a need for bio-medically valid computational models of primary blast injury that incorporate biomechanical and physiological responses, the establishment of common animal models of blast exposure and the resulting injuries, and an understanding of non-penetrating blast injuries to the brain which are manifest in a host of symptoms whose aetiology is at best vague. In effect HFM-207 (SYM) served as a HFM Exploratory Team in identifying a significant opportunity for a new RTG Technical Activity Proposal (TAP).

The first recommendation from the HFM-207 (SYM) Report identified a future need for a recurring technical exchange venue on blast injury and its mitigation to address advances in medicine and personal protection and their synergy. The second recommendation highlighted the need to explore the concept of "the Toxicology of Blast Injury" and to focus of the following areas:

- Relevancy and commonality of animal models.
- Common dose-response and route of exposure methods.
- Computational Models (blast, physiology, biochemical, toxicological, etc.).
- Dose regimens to human medical endpoints (surgical trauma to mTBI spectrum).
- Methods for translational research leading to medical products and/or physical protection products.

There was an additional recommendation to develop a specific NATO activity devoted to the toxicology of blast exposure, a proposal titled "Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods and Standards." This was approved and resulted in the establishment of a NATO HFM-234 (RTG).

1.2.1 Panel Objectives

To achieve the objectives of the RTG, a kick-off meeting of the Technical Team was held on July 1-2, 2013 in Neuilly-sur-Seine, France at the Collaboration Support Office (CSO) of the Science and Technology Organization (STO). The purpose of the kick-off meeting was to present the guidelines for the upcoming three years of work, review the TAP and Terms of Reference, and establish a Program of Work (PoW).

The RTG will establish a framework for a new interdisciplinary research area – the environmental toxicology of blast. In addition the RTG will:

- Build an evidence-based outline for NATO standards for blast injury analysis.
- Examine opportunities for improvements in the standards of medical care for blast injury.
- Explore advancing the state-of-practice in computational modelling of blast injury in relevant operational environments.
- Explore standardized animal models and toxicology research protocols that could be adopted by Research and Technology (R&T) programs across NATO.

1.3 THE TOXICOLOGY APPROACH

The discussions at HFM-207 (SYM) revealed the importance of a systematic approach to understanding blast injuries and it was proposed to follow the example of the well-established approach used to solve the classical toxicology problem. Therefore in order to determine the aetiology of blast injury there is a requirement to understand the dose, mechanism of delivery of the dosage, and dose-response endpoints.

1.4 FRAMEWORK FOR BLAST TOXICOLOGY

The Technical Team identified a Toxicology Framework during the first meeting in Neuilly-sur-Seine, France, July 2013 that is detailed in Table 1-2.

Table 1-2: Toxicology Framework for Blast Injury.

Blast Injury Toxicology Framework	
Toxicology methods relevant to understanding blast exposure effects and Toxicology methods and metrics	End product – Dictionary of Blast injury Research Terms: • Factors influencing threshold – dose levels, functional, morphological, anatomical, biological (cellular, tissue, organ, and biochemical). • Blast effect on human from outside (whole body to cellular) – failure due to stress, strain, pressure, force, etc.
Define the exposure	Define the threat (environmental circumstances for blast): • How we are going to define – free field. • Understand existence. • Awareness of different consequences of wave complexities.
	Understanding of Exposure (starting point-incident) – define the environment: • What component of blast exposure (primary, secondary, etc.). • Which parts of the body. • Any concomitant injuries (e.g., hemorrhage) or any physiological stress. • Dosimetry pattern. • Dose – exposure to what. • Route of exposure. • Injury/impairment Threshold – biological, physiological or psychological: • Thresholds and components of threshold as appropriate (mechanical, biological, biochemical, physiological, male/female, etc.).
	Blast exposure monitoring methods and metrics.
	Loading mechanism (what is environment doing to body) and how the body reacts.
Response	Injury Threshold (scale): • Dose driven curve. • Biological, mechanical, physiological or psychological. • Performance. • No injury. • Define threshold at cellular, tissue or organ level.
	When – acute to chronic.
	Physical/physiological or combination (target organs, tissues, cellular).
	Psychological and behavioural.
	Systemic – neuroendocrine, immune, epigenetic (changes because of environment), genetic, etc.

Blast Injury Toxicology Framework	
Determine Outcome	Consequence/outcome (for example performance, return to duty, preventative, treatable, short/ long term consequences, etc.).
	Matrices (i.e., list of components (physical/physiological) with weight for each component).
	Criteria for above parameters in regard to operational parameters (when they become serious enough to cause injury) – provide information to risk assessors (operational).
	Where they can be used (PPE, operational or modelling purposes).
Identify community	Vehicle designers, mechanical, medical, material, test and evaluation, as applicable.
Advancing the state of practice in computational modelling of blast injury	Leverage work already done by US DoD Computational Modelling Expert Panel.

1.5 IDENTIFICATION OF KNOWLEDGE / RESEARCH GAPS

Technical Team members identified gaps within the framework in the following four areas:

1) Measuring the blast exposure.
2) Characterizing the blast in operational environment.
3) Epidemiological studies.
4) Response to blast exposure.

A summary of discussions related to specific gaps within the framework are detailed in Table 1-3.

Table 1-3: Summary of Discussions Related to Knowledge Gaps for Blast Injury Research.

Identification of Gaps – Blast Injury Toxicology Framework	
How to measure blast exposure	Define method for measuring blast (i.e., static, dynamic, or total pressure).
	What is being measured – mechanical or biological (for example how to use information from free/pressure field measurements to design PPEs).

	Standardized description of laboratory blast conditions (possible topic for workshop?):
	• Blast/Shock tube:
	  • Material.
	  • Generating blast environment – using gases to generate blast wave (which gas).
	  • Multiple doses.
	  • Dose response curves.
	• Simulation or replication of field blast conditions for laboratory experiments.

Identification of Gaps – Blast Injury Toxicology Framework	
How to measure blast exposure (cont'd)	• Validation of laboratory blast condition. • Creating injury (animal) relevant to military conditions/field. • Sensors (i.e., types and placements). • Data acquisition. • Transfer function (linking different data collected using different methods). • Biological measurements? Translate engineering information into biological (effect!!). • No standard practice for measuring blast exposure (way to measure blast exposure (open free field) – model by taking the outcome into consideration (e.g., New Mexico data – cause of injury leading to identical outcome).
Characterize the blast in operational environment	Techniques/procedures.
	Sensors (could be used to generalize injuries, treat acute injuries).
	Simulation (i.e., recreation of blast conditions).
	Types of blast-primary, secondary, tertiary, etc. (Standard protocol?): • Explosives. • Environment (urban, country side, traditional).
	What does exposure means? (e.g., in mTBI what is the real cause of the problem?)
	Standardized reporting of blast injuries (i.e., use of major events (military/civilian) to characterize).
	Differentiation between mild and sever injuries.
Epidemiological studies	No epidemiological studies linking biological outcome to blast exposure (e.g., prospective longitudinal studies) Workshop: • Guidelines for Conducting Epidemiological Studies of Blast Injury. • Exposure/biological response. • Systemic (i.e., neuroendocrine, immune, epigenetic (changes because of environment), genetic changes for minor and major injury outcomes, etc.).
Response	Injury mechanism (what is the cause; i.e., how blast interacts with human body and causes injuries).
	Current injury scales are not adequate for mild to moderate injuries (e.g., needed for PPE).
	Current ICD codes not adequate for blast injuries.
	Ideal animal or animal model.
	Selection and assurance of relevant biological models.
	Identify which functions in animals translate to human.
	Need for correlation and validation between animal models and psychological functions (e.g., models to validate psychological behavior studies).
	Translation or correlation of animal to human, between animal species (physiological/ biological aspects).

Identification of Gaps – Blast Injury Toxicology Framework	
Response (cont'd)	Linking animal injury/functional research outcome to human injury/function (subjective and objective).
	Basic blast physics for animal and human models (how blast gets into brain).
	Need for a matrix identifying differences and similarities between animal, within animal species, and humans.
	Lack of understanding individual variation in response to similar blast exposure (including compared to pre-existing conditions) – physical, behavioral, biological, etc.
	Understanding material properties (biological, biomechanical, etc.) of human tissues under blast conditions.

A PoW was developed to enable the Technical Team to address these knowledge gaps and define the aims and objective of HFM-234 (RTG).

Minutes from the Meeting in Neuilly-sur-Seine, France, can be found in Annex A.

Chapter 2 − AIMS

2.1 OBJECTIVES

The objective of the HFM-234 (RTG) was to consider the current knowledge gaps for blast injury research in the context of a toxicological approach to investigating blast effects on people.

The Technical Team identified four Work Packages with the aim of harmonising global blast injury research. These Work Packages will provide guidelines for blast injury research. The four Work Packages are as follows:

- Work Package 1 – Dictionary of Blast Injury Terms.
- Work Package 2 – Guidelines for Conducting Epidemiological Studies of Blast Injury.
- Work Package 3 – Guidelines for Reproducing Blast Exposures in the Laboratory.
- Work Package 4 – Guidelines for Using Animal Models in Blast Injury Research.

The Technical Team identified that blast terminology is frequently confused, misrepresented and often incorrect, with different members of the blast injury research community using different terms for the same thing, therefore it was decided that an important first step was to create a Dictionary of Blast Injury Terms.

Chapter 3 − DICTIONARY OF BLAST INJURY TERMS

3.1 AIMS AND OBJECTIVES

It has been noted that the terminology used in blast literature has expanded over the last few years and terminology can be used either incorrectly or individual specialities use different wording for the same term. The aim of the Dictionary of Blast Injury Terms is to consolidate frequently used terms in both engineering and medical blast literature so that specialities can communicate and results be easily translated across the specialties.

3.2 METHODS

The Technical Team established a Working Group that initially created a data base of key blast injury research terms and developed a dictionary structure with contributions from all Technical Team members over the course of the HFM-234 (RTG) three-year term. The Working Group identified biomedical and engineering definitions for each term, and recommended the definition that was most relevant to blast injury research. Additional terms were identified and definitions were added throughout the proceedings of the HFM-234 (RTG) workshops using several sources such as text books and peer reviewed literature. The authoritative sources were used for defining each element in the dictionary as cited, and where appropriate both medical and engineering definitions have been incorporated.

3.3 OUTCOMES

The Dictionary of Blast Injury Terms is found in Annex C.

Chapter 4 − GUIDELINES FOR CONDUCTING EPIDEMIOLOGICAL STUDIES OF BLAST INJURY

4.1 AIMS AND OBJECTIVES

Blast injury results from a complex interaction of the exposure event and the resulting biological response. The long-term effects of blast injury are currently unknown and this creates a challenge for those tasked with developing protection systems as well as therapeutics. Epidemiological studies are critical for obtaining the necessary data to understand the mechanisms of injury caused by blasts, and the resulting response of an individual to a blast event.

The aim of this section is to provide blast injury researchers and clinicians with a basic set of recommendations for blast injury epidemiological study design and data collection guidelines that need to be considered and described when conducting prospective longitudinal studies of blast trauma.

4.2 METHODS

A Technical Team workshop was held in the USA, December 2013 to develop Guidelines for Conducting Epidemiological Studies of Blast Injury. A series of presentations by each participating nation provided information on their country's current guidelines for epidemiological studies (for details – see Annex B) and the Technical Team discussed the draft for Guidelines for Conducting Epidemiological Studies of Blast Injury developed by the host nation (USA). The Technical Team considered the limited data and evidence-based guidelines regarding complex multisystem injuries associated with blast exposure and determined that a well-designed blast injury epidemiologic study at a minimum should include an exposure assessment, an exposed population, and an unexposed population. Accurate blast exposure information is critical as this information is made part of the study and is used to determine health outcomes. The Technical Team emphasized the importance of current and future threat environments and identified the types of data needed to conduct the epidemiological studies under the four broad themes:

1) Defining parameters of interest to track initial exposure to blast.
2) Identifying the types of data needed to link biological outcome to blast exposure.
3) Using sensors.
4) Optimizing existing operational databases for blast injury epidemiological studies.

The guidelines discussed the necessary data to understand the mechanisms of injury caused by blasts, the response of an individual to a blast event, as well as, long-term effects of blast exposure. The guideline requirements for conducting a blast injury epidemiologic study parallel those found in the Institute of Medicine studies [1] and other well documented epidemiological protocols.

The draft guidelines were then circulated to all Technical Team members for changes and comments. During subsequent HFM-234 (RTG) meetings, the guidelines were discussed and further direction by the Technical Team resulted in the final version of the Guidelines for Conducting Epidemiological Studies of Blast Injury.

4.3 OUTCOMES

A suggested epidemiologic study design (prospective longitudinal) for conducting blast injury studies and a detailed discussion on epidemiologic framework elements are provided in the guidelines.

Minutes from the Meeting held in December 2013 can be found in Annex B.

Guidelines for Conducting Epidemiological Studies of Blast Injury can be found in Annex D.

Chapter 5 − GUIDELINES FOR REPRODUCING BLAST EXPOSURES IN THE LABORATORY

5.1 AIMS AND OBJECTIVES

A review of the blast literature has demonstrated considerable variability and reporting of methodologies used to create blast exposure. This makes comparison of results and conclusions between studies problematic. Therefore the aim of this section is to provide blast injury research laboratories with a fundamental set of characteristics that need to be collected and described when generating blast pressure waves. The objectives are:

- To raise awareness with regards to the complexities and pitfalls of blast research.
- To standardize and promote good practices.
- To help the community to generate valid and comparable results.
- To increase the quality of publications in this field of research.

5.2 METHODS

A Technical Team workshop was held in Canada, May 2014, and through a series of lectures from experts in the field and group discussion Draft Guidelines were outlined by the host team (Canada). A small team undertook building the Draft Guidelines using the outline as a guiding template. The Guidelines examined methods to reproduce blast exposures using shock/blast tubes, enhanced shock tubes, and field testing. The Guidelines also discussed what is required to report blast research (i.e., research rationale; blast characteristics; target exposure characteristics; and target response). Within the methods and reporting, specific requirements were considered and guidance provided that, if followed, will help overcome the variability that currently exists in the blast injury literature.

The Draft Report/Guidelines were then circulated to all Technical Team members for changes and comment. During subsequent Technical Team meetings, the Guidelines were discussed and further direction given by the Technical Team that resulted in the final version.

5.3 OUTCOMES

The premise of the Guidelines document is based on the toxicological fundamental that to understand the response to an exposure, the exposure itself must be well characterized and understood. To ensure this, the advantages and disadvantages of methods to create, measure, model, and visualize blast are discussed in the Guidelines. Equally important and considered in detail is the reporting of blast research starting with the basics; research rationale which includes aim, hypothesis, relation to real world operational conditions, and rationale for the exposure level chosen. Several blast characteristics (e.g., simulation methods, ambient conditions, conditions at target) are examined as well as target exposure characteristics (e.g., target type, position, mounting). Also emphasized is reporting of the response of the target to the blast through measurements of motion, surface pressures, strains, internal pressures and physiological parameters, if animal models are used. The analysis, when brought together, resulted in a comprehensive set of Guidelines on reproducing blast exposures in the laboratory.

The Guidelines are an outcome of an attempt to understand how blast exposures can be created and what information is required to allow for the comparisons of research between different laboratories. This is vital to

advance science in blast injury and will provide the best evidence possible to inform those responsible for protection and care of military members.

Minutes for the Meeting held in May 2014 can be found in Annex E. The work from this meeting and the considerable expertise in the Technical Team, and available to its members, resulted in the "Guidelines for Reproducing Blast Exposures in the Laboratory" which can be found in Annex F.

Chapter 6 − COMPUTATIONAL MODELLING FOR BLAST INJURY

6.1 AIMS AND OBJECTIVES

The staggering numbers for blast-induced injuries in recent conflicts and the possibility of long lasting consequences has generated an urgent need to develop mitigation strategies. It is believed that the computational modeling could provide a framework to understand injury mechanisms, guide experimental testing, interpret data and facilitate the development of both protective and treatment strategies. Insights into treatment strategies might also apply to sports related concussive brain injuries which loom as another possible major health problem. A computational model of blast-induced lung injury was previously developed by the US DoD and it has proved to be valuable asset in assessing the risk of being in close proximity to the firing of large cannons and it is used in generating safety criteria for their operation and design.

The aim of this section is to assemble and provide an overview of the on-going computational efforts by the participating nations. The specific objectives are:

- Synthesize proceedings of the DoD Blast Induced Computational Modeling Expert Panel.
- Develop a document capturing blast research infrastructure, cross-NATO research opportunities including past, on-going, and future studies by participating members.
- Reassess HFM-234 (RTG) progress and plan.
- Review blast injury dictionary of terms.

6.2 METHODS

A Technical Team workshop was held in Estonia, October 2014, to summarize and share the on-going computational experience and/or efforts by the participating nations. The Technical Team members of participating nations presented their past, present, and/or future computational modeling efforts. In addition, the TT team assessed the progress of the on-going efforts to include:

- Dictionary of blast injury terms.
- Guidelines for Conducting Epidemiological Studies of Blast Injury.
- Guidelines for reproducing blast exposures in the laboratory.

The first presentation summarized the “DoD Blast Induced Computational Modeling Expert Panel Proceedings”. This panel was chartered in 2010 and their objective was to “Assess state-of-the-science in computational modeling of non-impact, blast-induced mTBI.” They compiled a list of desired attributes of validated computation models for non-impact, blast-induced mTBI, and considered the paradigms of the continuum of modeling and developed recommendations for each, including: in vitro testing and modeling; animal testing and modeling; human surrogates/material modeling; and human simulation/mathematical modeling.

The next seven presentations focused on the different participating nations, including Canada, Estonia, France, Germany, Norway, Sweden, and United Kingdom.

Canada reported on the numerical modelling work being conducted at Defence Research and Development Canada (DRDC) focused on understanding blast loading transmission to different targets. They concluded by discussing the limitations of this work.

Estonia does not have any ongoing blast-related research or computational modeling efforts. They are in the process of conducting a questionnaire on the occupational risk factors experienced by all active duty military officers in the Estonian military, the most common of which are respiratory, musculoskeletal, and hearing loss.

The French presentation focused on the effect of IEDs on dismounted service members. Four different organizations have teams working on various projects with the preliminary findings presented, including: hemoptysis (pulmonary bleeding); risk of disruption of the intestinal wall which can be fatal by septicemia risk (peritonitis); permanent hearing loss (tympanic membrane rupture and possible dislocation of the ossicular chain); risk for eye injury if retina is affected; and projection of the highly contaminated ground fragments (*Acinetobacter baumanii*, etc.).

Germany focused on the multinational epidemiological database (NATO trauma registry) which was established in 2014. Limitations of this registry include: only visible injuries are captured in the registry, and inability to link medical and operational data.

Norway uses instrumented pig models for their mTBI experiments. They compared this experimental data to numerical models and concluded that modelling IED blast related injuries for mounted service members is very challenging, simulations can be used to predict injuries resulting from various types of loading, and more research must be done to create viable numerical models.

Sweden reported their study findings on primary blast resulting in inflammation and cell death in the brain. Rotational acceleration of the brain causes axonal injuries, cell death, gene expression change, and intracellular edema. There is a 60-year old blast tube in Stockholm that they use for their rat experiments.

In addition, the Technical Team members reviewed the HFM-234 progress to date in relation to the PoW. The Technical Team emphasized the importance of continuing to work towards finalizing the Guidelines for conducting epidemiological studies of blast injury and Guidelines for reproducing blast exposures in the laboratory.

6.3 OUTCOMES

Minutes for the Meeting held in October 2014 can be found in Annex G.

Chapter 7 − GUIDELINES FOR USING ANIMAL MODELS IN BLAST INJURY RESEARCH

7.1 AIMS AND OBJECTIVES

Animal experiments are one method to examine and evaluate blast injury mechanisms. Such experiments allow studies that control for specific factors under investigation. Good experimental design and use of appropriate animal models is essential for the translation of results to clinical practice.

The aim of the guidelines is to provide information that should be considered when planning, executing and reporting animal experiments for blast trauma.

7.2 METHODS

A Technical Team workshop was held in Sweden, May 2015, and through a series of lectures from experts in the field of animal models. This was followed by a group discussion of the draft Guidelines for Using Animal Models in Blast Injury Research as outlined by the host team (Sweden). The Guidelines examined rational for the use of multiple animals models, how to frame blast injury as a difficult toxicological problem, good experimental design, model validation, how to address variability in findings, and factors that allow for comparison across labs and translation of findings.

The draft guidelines were produced following the workshop and circulated to all Technical Team members for corrections and comments. During subsequent Technical Team meetings, the Guidelines were discussed and further direction given by the Technical Team that resulted in the final version.

7.3 OUTCOMES

The premise of the guideline document is based on that it is unlikely that any single animal model will address all of the effects of blast exposure seen in human casualties. Each animal model will have strengths, weaknesses, and limitations. Results and conclusions of studies using animal models must therefore be discussed in light of the strengths, weaknesses, and limitations, with clear recommendations as to which elements of the conclusions are valid for the human condition, together with the boundaries and limitations of the interpretation. Multiple models will therefore be required, allowing triangulation of results to ensure appropriate translation of results.

These guidelines will include factors to be considered when planning, executing, and reporting animal experiments for blast injury but will not include specific recommendations for experimental setups. Emphasis will be placed on why experiments must be validated to produce the pathology or pathophysiology that they are supposed to replicate. In addition, measures that facilitate translation should be a fundamental part of each experiment. Physical properties of the exposure, physiological changes, and pathology should be recorded and reported allowing replication of experiments by other laboratories. Rigorously controlling the exposure parameters may also reduce variability and the need for large numbers of animals. Some consequences of blast-induced injuries may be difficult to study in animal models. In conclusion, appropriately designed animal experiments will enhance the state of the science.

Minutes for the Meeting held in May 2015 can be found in Annex H. The work from this meeting and the considerable expertise in the Technical Team, and available to its members, resulted in the “Guidelines for Using Animal Models in Blast Injury Research” which can be found in Annex J.

Chapter 8 − CONCLUSIONS AND RECOMMENDATIONS

8.1 CONCLUSIONS

HFM-234 (RTG) achieved its stated objectives as listed in the Technical Activity Description. This success was due to a multidisciplinary approach and team work within the participating nations. The Technical Team initiated their efforts by identifying a Toxicology Framework to understand the dose, mechanism of delivery of the dosage, and dose-response endpoints of blast exposure, and then identified gaps within the Framework. Based on the Framework and specific gaps, the Technical Team developed a Program of Work with the aim of providing guidelines for blast injury research for each of four Work Packages. The four Work Packages are as follows:

8.1.1 Dictionary of Blast Injury Terms

Dictionary of Blast Injury Terms is a consolidation of frequently used terms and definitions in both engineering and biomedical research literature. This dictionary provides a common vocabulary that will help to eliminate confusion, improve information sharing, and facilitate collaboration across diverse research communities and disciplines.

8.1.2 Guidelines for Conducting Epidemiological Studies of Blast Injury

Guidelines for Conducting Epidemiological Studies of Blast Injury provides blast injury researchers and clinicians with a basic set of recommendations for blast injury epidemiological study design and data collection guidelines that need to be considered and described when conducting prospective longitudinal studies of blast trauma. These guidelines emphasize current and future threat environments and identify four broad themes of types of data needed to conduct epidemiological studies:

a) Defining parameters of interest to track initial exposure to blast.

b) Identifying the types of data needed to link biological outcome to blast exposure.

c) Using sensors.

d) Optimizing existing operational databases for blast injury epidemiological studies.

8.1.3 Guidelines for Reproducing Blast Exposures in the Laboratory

Guidelines for Reproducing Blast Exposures in the Laboratory provides blast injury research laboratories with a fundamental set of characteristics that need to be collected and described when generating blast pressure waves, resulting in studies that allow for the comparison of research between different laboratories.

8.1.4 Guidelines for Using Animal Models in Blast Injury Research

Guidelines for Using Animal Models in Blast Injury Research provide guidelines that need to be considered when planning, executing, and reporting animal experiments for blast trauma. Some consequences of blast-induced injuries may be difficult to study in animal models, however appropriately designed animal experiments will enhance the state-of-the-science and result in the best evidence possible to inform those responsible for the protection and care of military members.

HFM-234 (RTG) was an outstanding success as the four work packages this Technical Team set out to develop have been completed and are appended to this Report.

Finally, HFM-234 (RTG) initiated dissemination of four Work Packages to the medical and health sciences community via its sponsor, the NATO Human Factors and Medicine Panel.

8.2 RECOMMENDATIONS

HFM-234 (RTG) developed guidelines that can be used to provide experimental data necessary to develop and validate computational models of blast exposure that will elucidate the tissue-level mechanisms of injury necessary to guide the development and testing of effective protection systems.

1) The Dictionary of Blast Injury Terms provides a common vocabulary of terminology to improve information sharing and facilitate collaboration across diverse research communities and disciplines.
2) By standardizing data collection and analysis of epidemiological studies of blast injury, the Guidelines for Conducting Epidemiological Studies of Blast Injury will enable international partners to share data, compare outcomes, and collaborate on future multinational studies.
3) Consistent use of the Guidelines for Reproducing Blast Exposures in the Laboratory will allow for reliable comparisons to be made between studies with different laboratory settings, methods of blast wave generation, and types of blast injury.
4) Without being overly prescriptive, the Guidelines for Using Animal Models in Blast Injury Research aim to ensure that experiments can be validated and replicate the human condition to enable the translation of the results.

The Technical Team recommends initiating a new, multidisciplinary HFM technical activity on computational modeling of blast effects on humans. The new activity should leverage previous, ongoing, and planned blast injury biomedical research and computational modeling efforts among the participating nations and lead to a framework for translating scientific information into the capability to model human lethality, injury, and impairment across the spectrum of blast-related threats. This framework will pull together existing scientific data and computational models to identify the gaps in understanding injury mechanisms from both mounted and dismounted personnel. In parallel to the development of the framework for blast injury mechanisms, should be the development of the framework for creating and evaluating effective blast injury protection systems. Creating these frameworks to comprehensively understand blast injury mechanisms and what is required to prevent injury, lethality, and impairment has the potential to reduce the time required to develop and field effective blast injury protection systems.

Chapter 9 − REFERENCES

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[3] DoD Directive (DoDD) 6025.21E *Medical Research for Prevention, Mitigation, and Treatment of Blast Injuries.* July 5, 2006. http://www.dtic.mil/whs/directives/corres/pdf/602521p.pdf.

[4] NATO Science and Technology Organization (NATO). (2013). *Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods and Standards (HFM-234).* Blast Injury Data Collection Guidelines.

[5] *A Survey of Blast Injury across the Full Landscape of Military Science*, RTO-MP-HFM-207, https://www.sto.nato.int/publications/STO%20Meeting%20Proceedings/Forms/Meeting%20Proceedings%20Document%20Set/docsethomepage.aspx?ID=36909, Accessed 17 May 2017.

Annex A − MINUTES FROM KICK-OFF MEETING JUNE 2013

Kick-Off Meeting Summary and Program of Work

Neuilly-sur-Seine, France
July 1-2, 2013

A.1 BACKGROUND

Blast Injury is one of the most important sources of casualties in current NATO operations. The term "blast injury" creates considerable confusion in military medicine. Simply stated, "blast injury" includes the entire spectrum of injuries that can result from exposure to an explosion. It is generally accepted that the taxonomy of injuries can be assigned to five categories: primary, secondary, tertiary, quaternary, and quinary. These are based on the mechanism of injury. Primary blast injuries result from the high pressures created by the blast itself. The high pressures, known as blast overpressure, can cause internal injuries. Primary injuries result from the effects of the shock wave, which travels through the tissues depositing energy particularly where there is a gas-liquid interface. Secondary blast injuries result when strong blast winds behind the pressure front propel fragments and debris against the body and cause blunt and penetrating injuries. The strong winds and pressure gradients also can accelerate the body and cause the same types of blunt force injuries that would occur in a car crash or a fall. These are known as tertiary blast injuries. Quaternary blast injuries are the result of other explosive products, such as heat, light, and toxic gases that can cause burns, blindness, and inhalation injuries. Finally, quinary blast injuries refer to the clinical consequences of "post-detonation environmental contaminants", including bacteria, radiation (dirty bombs), and tissue reactions to fuel and metals:

Consequently, the prevention, treatment and rehabilitation and the continuum of care for the injured from acute treatment to return to duty are of particular interest to NATO members. Several related HFM RTG activities including HFM-175, HFM-193, HFM-198, and HFM-207 have been organized to advance the state-of-the-knowledge. The most recent HFM-207 (SYM) focused on the key aspects of multi-disciplinary science and medicine with three basic goals:

1) Increase the understanding of blast injury in military operations.
2) Explore and describe the range of blast injuries seen in current NATO operations.
3) Delineate some of the medical treatment strategies currently being employed by NATO medical personnel.

The Technical Evaluation Report identified several significant and new contributions from the symposium that included:

- Emergence of an understanding that blast injury will require a disciplined research approach termed "the toxicology of blast".
- Significance of the need for physics-based modeling of primary blast injury for the current blast scenarios.
- Establishment of animal models of injury for the development of the medical sciences base for injury treatments.
- Scientific understanding of non-penetrating blast injuries to the brain.
- Use of existing scientific information to address technical challenges posed by blast injury.

The discussions at HFM-207 (SYM) revealed the importance of a systematic approach to understanding blast injuries much like the well-established approach used to solve the classical toxicology problem where the etiology of the injury requires an understanding of the dose, mechanism of delivery of the dosage, and dose-response endpoints. Also recognized was the pressing need for a multidisciplinary approach to addressing non-penetrating blast injuries to the brain that result in a host of symptoms with vague etiology. In addition, the Technical Evaluation Report emphasized the continued multinational exchanges of scientific and technical advances to respond to blast threat and blast injuries. The first recommendation identified a future need for a recurring technical exchange venue on blast injury and its mitigation to address advances in medicine and personal protection and their synergy. The second recommendation highlighted the need for the development of a Technical Activity Proposal to explore the concept of "the Toxicology of Blast Injury" and suggested to focus the activity on several difficult problems including:

a) Relevancy and commonality of animal models.

b) Common dose-response methods; route of exposure methods.

c) Computational Models (blast, physiology, biochemical, toxicological, etc.).

d) Dose regimens to human medical endpoints (surgical trauma to mTBI spectrum).

e) Methods for translational research leading to medical products and/or physical protection products.

To address the above recommendation and to develop a specific NATO activity devoted to the toxicology of blast exposure, a Technical Activity Proposal titled "Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods and Standards was approved in the fall of 2012 (Appendix A1) which resulted in the establishment of a new NATO Science and Technology Organisation (STO), Human Factors and Medicine (HFM) Panel, Research Task Group (RTG) with the following objectives:

- Build an evidence-based outline for NATO standards for blast injury analysis.
- Examine opportunities for improvements in the standards of medical care for blast injury.
- Explore advancing the state-of-practice in computational modeling of blast injury in relevant operational environments.
- Explore standardized animal models and toxicology research protocols that could be adopted by R&T programs across NATO.

To achieve the objectives of the RTG, a kick-off meeting of the Technical Team was held on July 1-2, 2013 in Neuilly-sur-Seine, France at the Science and Technology Organization (STO) Collaboration Support Office (CSO). The purpose of the meeting was to present the guidelines for the upcoming three years of work, review the Technical Activity Proposal (TAP) and Terms of Reference (TOR), and establish a Program of Work.

This document summarizes the deliberations of the HFM-234 (RTG) Technical Team kick-off meeting and the Program of Work that followed the revised agenda as shown in Appendix A2. Twelve Technical Team members participated in the meeting, representing nine NATO nations.

A.2 WELCOME AND GUIDANCE FOR THE HFM-234 (RTG)

Mr. Mike Leggieri, Chair HFM-234 (RTG), welcomed all the Technical Team (TT) members (Appendix A3) and thanked the NATO, STO-CSO for hosting the meeting. He asked Technical Team members to introduce themselves. After introductions were completed, LtCol Ron Verkerk welcomed everyone and presented the guidance for the HFM-234 (RTG) on the "Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods and Standards".

LtCol Verkerk started his presentation by providing information on the NATO S&T community, North Atlantic Council, Non-NATO S&T partners, mission of positioning S&T investment as a strategic enabler of the knowledge and technology of the defence of NATO nations and partners. He discussed STO's business model, STO Panels and Groups, collaborative environment, and then focused on the HFM Panel mission to optimize the health, safety, well-being, and performance of the human in operational environment. He subsequently highlighted the HFM Panel management, requirements, Technical Activity Proposal, and specific activities to do during the planning phase and the working phase, and recommendations for Program format, reports, publications, and STO website resources available to RTG.

A.3 TECHNICAL ACTIVITY PROPOSAL REVIEW AND REVISION

Mr. Leggieri presented the background information on HFM-207 (SYM) including objectives, lessons learned, and the Technical Evaluation Report leading to the establishment of the HFM-234 (RTG). He discussed the recommendation and the submission of the TAP to establish a framework for a new multidisciplinary research area on the environmental toxicology of blast. Discussion pursued that included authority of NATO standard, implementation across NATO nations, general guidelines, validation of models such as human, animal, mechanical, physiological, cell based, in-vitro, and standards for measurements. In addition, he discussed the composition of the TT members, participating nations, HFM-234 (RTG) TAP objectives, topics and anticipated deliverables of the RTG in the form of technical reports and specific recommendations. He presented the list of participating member nations and noted Dr. John Frazier Glenn is the HFM-234 (RTG) Panel Mentor.

A.4 DEVELOPMENT OF TOXICOLOGY FRAMEWORK AND IDENTIFICATION OF GAPS

Dr. Gupta started his presentation by highlighting the topics for review, specific requirements of the Program of Work, and the need for review and revision of the TAP topics. Following discussion, the TT members decided to first develop an integrated Toxicology Framework to address the objectives as outlined in the Technical Activity Description and Terms of Reference. The following table summarizes the dialogue, in-depth discussion, and deliberations of the TT members for developing the toxicological framework.

Table A-1: Blast Injury Toxicology Framework.

Toxicology methods relevant to understanding blast exposure effects and Toxicology methods and metrics	End product – Dictionary of commonly used terms with definitions: • Factors influencing threshold- dose levels, functional, morphological, anatomical, biological (cellular, tissue, organ, biochemical). • Blast effect on human from outside (whole body-cellular) failure due to stress, strain, pressure, force, etc.
Define the exposure	Define the threat (environmental circumstances for blast): • How we are going to define – free field. • Understand existence. • Awareness of different consequences of wave complexities. Understanding of Exposure (starting point-incident) – define the environment: • What component of blast exposure (Primary, secondary, etc.).

Define the exposure (cont'd)	• Which parts of the body. • Any concomitant injuries (e.g., hemorrhage) or any physiological stress. • Dosimetry pattern. • Dose-exposure to what. • Route of exposure. • Injury/impairment Threshold – biological, physiological or psychological. • Thresholds and components of threshold as appropriate (mechanical, biological, biochemical, physiological, male/female).
	Blast exposure monitoring methods and metrics.
	Loading mechanism (what is environment doing to body) and how the body reacts.
Response	Injury Threshold (scale) – dose driven curve; biological, mechanical, physiological or psychological, Performance, no injury, define threshold at cellular, tissue or organ level.
	When – acute to chronic.
	Physical/physiological or combination (Target organs, tissues, cellular).
	Psychological and behavioral.
	Systemic – neuroendocrine, immune, epigenetic (changes because of environment), genetic.
Determine Outcome	Consequence/outcome for example performance, return to duty, preventative, treatable, short/ long term consequences.
	Matrices i.e., list of components (physical/physiological) with weight for each component.
	Criteria for above parameters in regard to operational parameters (when they become serious enough to cause injury) – Provide information to risk assessors (operational).
	Where they can be used (PPE, operational or modeling purposes).
Identify community	Vehicle designers, mechanical, medical, material, test and evaluation as applicable.
Advancing the state of practice in Computational Modeling of blast injury	Leverage work already done by US DoD blast-induced Brain Injury Computational Modeling Expert Panel.

After the initial Toxicology Framework was completed, the TT members proceeded to identify the gaps associated with the framework in broad categories of measuring the blast exposure, characterizing the blast in operational environment, epidemiological studies linking biological outcome to blast exposure, response, and determining outcome. The overall discussion started with defining the exposure and then led to identification of gaps under four broad categories:

1) How to measure blast exposure.

2) Characterize the blast in operational environment.
3) Epidemiological studies.
4) Response with relevant specific topics to be addressed by the RTG during the next three years.

A synopsis of the discussion and gaps that were agreed upon are summarized in the table below.

Table A-2: Identification of Gaps – Blast Injury Toxicology Framework.

How to measure blast exposure	• Define method for measuring blast (static, dynamic, total pressure).
	• What is being measured – mechanical or biological − (for example how to use information from free/pressure field measurements to design PPEs.
	• Standardized description of laboratory blast conditions (possible topic for workshop?):
	  • Blast/Shock tube:
	  • Material.
	  • Generating blast environment – using gases to generate blast wave (which gas).
	  • Multiple doses.
	  • Dose response curves.
	  • Simulation or replication of field blast conditions for laboratory experiments.
	  • Validation of laboratory blast condition.
	  • Creating injury (animal) relevant to military conditions/field.
	  • Sensors-types and placements.
	  • Data acquisition.
	  • Transfer function (linking different data collected using different methods).
	  • Biological measurements? Translate engineering information into biological (effect!!).
	  • No standard practice for measuring blast exposure (way to measure blast exposure (open free field)-model by taking the outcome into consideration.
	  • Example-New Mexico data-injury-cause of injury then leading to identical outcome.

Characterize the blast in operational environment	• Techniques/procedures.
	• Sensors (could be used to generalize injuries, treat acute injuries).
	• Simulation-recreation of blast conditions.
	• Types of blast-primary, secondary, tertiary… (Standard protocol?):
	  • Explosives.
	  • Environment (urban, country side, traditional).
	• What does exposure means? – mTBI-real cause of problem.
	• Standardized reporting of blast injuries {Use of major events (military/civilian) to characterize}.
	• Differentiation between mild and sever injuries.

Epidemiological studies	• No epidemiological studies linking biological outcome to blast exposure (prospective longitudinal studies) – Workshop:
	  • Guidelines.
	  • Exposure/biological response.
	  • Systemic – neuroendocrine, immune, epigenetic (changes because of environment), genetic changes for minor and major injury outcomes.

Response	• Injury mechanism (what is the cause i.e., how blast interacts with human body and causes injuries). • Current injury scales are not adequate for mild to moderate injuries (e.g., needed for PPE). • Current ICD codes not adequate for blast injuries. • Ideal animal or animal model. • Selection and assurance of relevant biological models. • Identify which functions in animals to human. • Need for correlation and validation between animal models and psychological functions (e.g., models to validate psychological behavior studies). • Translation or correlation of animal to human, between animal species – (physiological/biological aspects), Linking animal injury/functional research outcome to human injury/function (subjective and objective). • Basic blast physics for animal and human model (how blast gets into brain). • Need for a matrix identifying differences and similarities between animal, within animal species, and humans. • Lack of understanding individual variation in response to similar blast exposure (including compared to pre-existing conditions) -physical, behavioral, biological. • Understanding material properties (biological, biomechanical, etc.) of human tissues under blast conditions.

A.5 PROGRAM OF WORK

The discussion and deliberations during the development of the toxicology framework and identification of associated gaps was used as the basis for the overall development of the proposed Program of Work (PoW) as reflected in table titled “HFM-234 (RTG) Program of Work”. The TT members volunteered to conduct and/or host various activities/workshops/meetings with the understanding that they needed to go back and coordinate with their respective organizations to confirm conducting and/or hosting the various activities as listed in the proposed PoW. The TT members agreed that all workshops will be of two to three days in duration with the majority of the time devoted to the specific purpose and objectives of the workshop as identified in the PoW. The last half day of each workshop will be reserved for the TT member’s discussion and deliberations. The half day TT member meeting will be used to assess the progress, status of various activities, course correction and planning for the future or upcoming activities. Generally, each workshop will examine the current status of the blast injury toxicology science and technology with specific focus as reflected in the PoW. Participating scientists, clinicians, operators, and regulators will be drawn from the international, military, academic, and industrial communities with special emphasis on individuals with recent hands on experience. The participants will be asked to present their scientific, technical, clinical, and/or regulatory efforts and participate in working groups as appropriate. These working groups will be asked to address a specific set of questions and identify scientific gaps, and the suggested/recommended guidelines specific to the objectives and focus of the workshop.

Table A-3: HFM-234 (RTG): Program of Work.

Activity/Workshop	Month/Year	Purpose	Host/Location	Point of Contact
Meeting #1	1-2 Jul 2013	HFM-234 (RTG) Kick-off	STO/CSO (Neuilly-sur-Seine)	
Dictionary of Terms	Aug 2013	Develop a dictionary of commonly used terms with definitions (Virtual-Core WG to develop an initial list and distribute to TT members)	Canada (Virtual)	Dr. Cernak
Meeting #2	10-12 Dec 2013	Develop recommendations for collecting data necessary for conducting epidemiological studies	United States (Frederick Ft. Detrick, MD)	Mr. Leggieri
Meeting #3	20-22 May 2014	Develop guidelines to reproduce blast exposure conditions in the laboratory	Canada (Medicine Hat, Alberta)	Mr. Bjarnason
Meeting #4	7-9 Oct 2014	Technical Task Group to synthesize workshops, computational modeling, and review dictionary	Estonia (Tallinn)	Mr. Orru
Meeting #5	12-14 May 2015	Develop recommendations for standardized animal models and a roadmap for dose dependent curves	Sweden (Stockholm)	Dr. Risling
Meeting #6	19-21 Jan 2016	Review draft report	England (Porton Down)	Drs. Kirkman/ Watts

A.5.1 Program of Work, Schedule, and Milestones

1st Meeting 2013: Kick-off (1-2 July 2013 – Neuilly-sur-Seine, FRANCE):

1) Presentations on:
   - Guidance for the HFM-234 (RTG).
   - Technical Activity Proposal and Terms of Reference.
   - Blast: Wounds and Protection.
   - Blast Physiology.
2) Introduction of participating members' background and experience.
3) Discussion on scope of the effort and relevant activities.
4) Development of the Blast Injury Toxicology Framework.
5) Identification of Gaps related to the Blast Injury Toxicology Framework.
6) Determination of the Program of Work (PoW).

Virtual Coordination: Blast Injury Dictionary of Terms (August 2013 − CANADA):

1) Establish a core group of members.
2) Develop a dictionary of commonly used terms with definitions.
3) Provide the dictionary of terms to all TT members.

2nd Meeting 2013: Blast Injury Epidemiological Study Data Collection Guidelines (10-12 December 2013 − Frederick, UNITED STATES):

1) Presentations will be solicited for:
   - Each countries' current guidelines for epidemiological studies.
   - Available data bases.
   - Prospective longitudinal studies linking biological outcome to blast exposure.
2) Identify what is being collected.
3) What type of data to collect?
4) Use of sensors for short, mid, and long term studies (time scale – months, years after exposure).
5) Temporal profile of outcome measures.
6) Define parameters of interest to track personnel after initial exposure to blast event.
7) What to do with existing databases.
8) Identify gaps.
9) Develop recommendations for collecting data necessary for conducting epidemiological studies.

3rd Meeting 2014: Laboratory Blast Exposure Conditions (20-22 May 2014 – Medicine Hat, CANADA):

1) Primary focus is to develop guidelines to reproduce blast exposure conditions in the laboratory.
2) Survey of existing experimental equipment/methods/procedures.
3) Recognize real life blast exposures and be able to recreate relevant aspects in laboratory conditions.
4) Define exposure conditions.
5) Shock/blast tube (NATO guidelines).

4th Meeting 2014: Computational Modeling and Dictionary (7-9 October, 2014 – Tallinn, ESTONIA):

1) Reassess HFM-234 (RTG) progress and plan.
2) Synthesize proceedings of the DoD Blast Induced Computational Modeling Expert Panel.
3) Develop a document capturing blast research infrastructure, cross-NATO research opportunities including past, on-going, and future studies by participating members.
4) Review blast injury dictionary of terms.

5th Meeting 2015: Blast Injury Animal Models and Roadmap for Dose Dependent Curves (12-14 May 2015 – Stockholm, SWEDEN):

1) Identify injuries of concern.
2) Structural damages (mechanical injury criteria).
3) Functional deficits (functional damage criteria).
4) Symptoms and temporal profile of symptoms.
5) Use of relevant parameters for blast exposure.
6) Animal species (test/model).
7) Dose-response relationship.
8) Develop recommendations for standardized animal models and a roadmap for dose dependent curves.

6th Meeting 2015: Review Draft Report (19-21 January, 2016 – Porton Down, ENGLAND):

Review final draft report of the activities of the HFM-234 (RTG).

Following finalization of the Program of Work, the TT members discussed and agreed to establish a mutually agreeable framework for workshops and form a working group for each workshop to plan, conduct, prepare a report, etc. It was emphasized that all TT members work hard to identify the personnel with right expertise and experience to participate in the workshops. The TT members agreed to plan for a half day meeting for the Task Group deliberations/discussion/hot wash, etc. after each workshop. The TT members also discussed maximizing the use of technology to facilitate and streamline the working group interactions by exploring the use of telephone conferences and DCO like capabilities. In addition, TT members emphasized open communication and identified the following activities that could take place between workshops:

1) Planning for future workshops (number of participants, detailed structure, presentation, focused Qs, key issues).
2) Synthesizing workshop findings/recommendations.
3) Preparing report.
4) Distributing interim reports.
5) Formulating specific questions to be addressed for each workshop.
6) Selecting participants for workshops (invited).
7) Translating scientific exposure conditions, parameters, etc. during workshops (as applicable).

The following actions/tasking were made:

1) Dr. Raj Gupta will serve as the secretary for the HFM-234 (RTG).
2) Dr. Ibolja Cernak (Lead), Dr. Emrys Kirkman, and Mr. Mat Philippens will serve as the core working group for developing the dictionary of commonly used terms with definitions relevant to blast injuries.
3) Request assistance from STO office to address Dr. Cernak's affiliation (host country).
4) Mr. Leggieri to discuss with LtCol Verkerk and provide additional information to TT members on:
    a) SharePoint site.

b) Support for workshop.
c) Number of participants in workshops.
d) Distribution of workshop reports.
e) Use of civilian WebEx type capabilities for RTG meetings.

A.6 LIST OF NATIONS

Canada
Estonia
France
Germany
Netherlands
Norway
Sweden
United Kingdom
United States

A.7 NATIONAL AND STO RESOURCES NEEDED

National resources needed: Manpower, travel funds, national data, technical and administrative support for organizing and conducting workshops and writing reports.

Document translation and funding for invited participants to the workshops.

Hardware and Software: Microsoft Office and use of STO SharePoint site.

A.8 TECHNICAL TEAM LEADER AND TEAM MEMBERS (NO RANKS)

Mr. Mike Leggieri (USA), Chair
Dr. Dan Bieler (DEU)
Mr. Stephen Bjarnason (CAN)
Dr. Ibolja Cernak (CAN)
Dr. Raj Gupta (USA)
Dr. Emrys Kirkman (GBR)
Dr. Hans Orru (EST)
Mr. Mat Philippens (NLD)
Dr. Marten Risling (SWE)
Dr. Jean-Claude Sarron (FRA)
Mr. Stian Skriudalen (NOR)
Mr. Jan Arild Teland (NOR)
Dr. Sarah Watts (GBR)
Dr. Arnulf Willms (DEU)

A.9 APPENDICES

A1 − Technical Activity Proposal.

A2 − HFM-234 Kick-off Meeting Revised Agenda.

A3 − HFM-234 Technical Team Members.

Appendix A1: TECHNICAL ACTIVITY PROPOSAL (TAP)

UNCLASSIFIED / UNLIMITED

Technical Activity Proposal (TAP)

Activity reference number	HFM-234	**Activity Title** Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods and Standards	**Approval** TBA
Type and serial number	RTG		**Start** January 2013
Location(s) and Dates		1st Mtg, Paris (FRA) at RTA TBD	**End** January 2016
Coordination with other bodies		COMEDS	
NATO Classification of activity		UU	**Non NATO Invited** Yes
Publication Data		TR	UU
Keywords		Blast modeling, Blast Injury, Toxicology, Occupational Health, Physics-modeling, medical	

I. Background and Justification (Relevance to NATO):

The HFM Research Symposium on Blast Injury (HFM-207) revealed a need for continuing NATO-wide research cooperation on the "environmental toxicology" of military personnel in blast exposure environments. Blast Injury is a significant source of casualties in current NATO operations and the spectrum of blast injuries and their consequences is broad. To address the research issues posed by the wide spectrum of battle injuries, a scientific interdisciplinary approach will be required. While HFM-207 provided an initial assessment of current state of relevant interdisciplinary science, it was appreciated that the hard problem of understanding and mitigating blast injury will require a specific NATO technical activity devoted to the "environmental toxicology of blast exposures". Some of the scientific issues include a need for biomedically valid computational models of primary blast injury that incorporate biomechanical and physiological responses, the establishment of common animal models of blast exposure and the resulting injuries, and an understanding of non-penetrating blast injuries to the brain which are manifest in a host of symptoms whose etiology is at best vague. In effect HFM-207 served as a HFM Exploratory Team in identifying a significant opportunity for a new RTO Technical Activity.

II. Objective(s):

The RTG will establish a framework for a new interdisciplinary research area – the environmental toxicology of blast. In addition the RTG will:
- build an evidence-based outline for NATO standards for blast injury analysis;
- examine opportunities for improvements in the standards of medical care for blast injury;
- explore advancing the state-of-practice in computational modeling of blast injury in relevant operational environments; and,
- explore standardized animal models and toxicology research protocols that could be adopted by R&T programs across NATO.

III. Topic To Be Covered:

The RTG will cover the following topics in the delivered report:
- toxicology methods relevant to understanding blast exposure effects;
- physics-based modeling of animals and man in blast environments;
- physiological modeling of animals and man in blast environments;
- standardized toxicology protocols for blast exposure research;
- medical surveillance data required to monitor acute and chronic effects of blast exposure;
- medical screening methods and metrics;
- blast exposure monitoring methods and metrics;
- toxicology methods and metrics; and,
- survey of blast research infrastructure and identification of cross-NATO research opportunities.

IV. Deliverable (e.g. S/W Engage Model, Database,...) and/or end product (e.g. Final Report):

Technical Report, other deliverable(s) : none

V. Technical Team Leader And Lead Nation:

Chair : Mr Michael LEGGIERI United States

Lead Nation: United States

Technical Activity Proposal (TAP)

VI. Nations Willing/Invited to Participate:

NATO Nations and Bodies : Canada, France, Germany, United Kingdom, United States

PfP Nations : all PfP invited

MD Nations : all MD invited

ICI Nations : none

Global Partners : Australia, Japan, New Zealand, Republic of Korea

Contact / Other Nations : Singapore

VII. National And/Or NATO Resources Needed (Physical and non-physical Assets):

Members to the RTG will be funded bt their nations

VIII. RTA Resources Needed:

RTA meeting room for kick-off meeting.
Funding for 2 consultants

Additional Information

Panel Mentor:
Dr John Frazier GLENN, United States
Limited Participation Techical Team:
No

Comments:
Technical report with specific recommendations on how to advance the state-of-knowledge on blast injury in military personnel.

Related to the HFM-RSY 207.

Approved at the 29 HFM-PBM
To be approved by the FALL 2012 STB.

UNCLASSIFIED / UNLIMITED

Terms Of Reference (TOR)

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

I. Origin

A. Background

The HFM Research Symposium on Blast Injury (HFM-207) revealed a need for continuing NATO-wide research cooperation on the environmental toxicology of military personnel in blast exposure environments. Blast Injury is a significant source of casualties in current NATO operations and the spectrum of blast injuries and their consequences is broad. To address the research issues posed by the wide spectrum of battle injuries, a scientific interdisciplinary approach will be required. While HFM-207 provided an initial assessment of current state of relevant interdisciplinary science, it was appreciated that the hard problem of understanding and mitigating blast injury will require a specific NATO technical activity devoted to the environmental toxicology of blast exposures. Some of the scientific issues include a need for biomedically valid computational models of primary blast injury that incorporate biomechanical and physiological responses, the establishment of common animal models of blast exposure and the resulting injuries, and an understanding of non-penetrating blast injuries to the brain which are manifest in a host of symptoms whose etiology is at best vague. In effect HFM-207 served as a HFM Exploratory Team in identifying a significant opportunity for a new RTO Technical Activity.

B. Justification (Relevance for NATO)

The proposed technical activity has significant implications for advancing approaches to the design of protection systems (e.g., vehicle design, protective vests, helmets) through the interdisciplinary coupling of medical research with physics and engineering sciences. The core contribution of this multidisciplinary cooperation effort will be protocols for setting the metrics and methods for the environmental toxicology of blast environments which can lead to new NATO standards both for mitigating blast effects and, if mitigation fails, for improvement in medical care of injuries.

II. Objectives

The RTG will establish a framework for a new interdisciplinary research area the environmental toxicology of blast. In addition the RTG will:
- build an evidence-based outline for NATO standards for blast injury analysis;
- examine opportunities for improvements in the standards of medical care for blast injury;
- explore advancing the state-of-practice in computational modeling of blast injury in relevant operational environments; and,
- explore standardized animal models and toxicology research protocols that could be adopted by R&T programs across NATO.

III. Resources

A. Membership

Chair : Mr Michael LEGGIERI United States

Lead Nation: United States

Nations Willing/Invited to Participate: Canada, France, Germany, United Kingdom, United States

B. National And/Or NATO Resources Needed :

Members to the RTG will be funded bt their nations

C. RTA resources needed

RTA meeting room for kick-off meeting.
Funding for 2 consultants

IV. Security Classification Level

The security level will be Unclassified/Unlimited

V. Participation By Partner Nations

All NATO, PfP, MD nations, Global Partners (Australia, Japan, New-Zealand and Republic of Korea) and singapore are invited.

PfP Nations : all PfP invited

MD Nations : all MD invited

ICI Nations : none

Global Partners : Australia, Japan, New Zealand, Republic of Korea

Contact / Other Nations : Singapore

VI. Liaison

This activity is relevant to COMEDS

Appendix A2: HFM-234 KICK-OFF MEETING REVISED AGENDA

Monday July 1, 2013		
0900	Welcome and Individual Introductions	Mr. Leggieri
	Introductions (Individual)	Team Members (TM)
	STO – Administrative aspects, Guidelines, and Rules	LtCol Verkerk, HFM Panel Executive
	Break	
	STO – Administrative aspects, Guidelines, and Rules (cont.)	LtCol Verkerk
	Technical Activity Proposal (TAP Review)	Mr. Leggieri / TM
1200	Lunch	
1300	Terms of Reference (Review and Revise)	Dr. Gupta / TM
	Development of HFM 234 Toxicology Framework	TM
	Break	
	Development of HFM 234 Toxicology Framework (cont.)	TM
1900	Dinner	TM

Tuesday July 2, 2013		
0900	Presentation – Blast, Wounds and Protection	Dr. Sarron
	Presentation – Blast Physiology	Dr. Cernak
	Development of HFM 234 Toxicology Framework and Program of Work	TM
	Break	
	Development of HFM 234 Toxicology Framework and Program of Work (cont.)	TM
1200	Lunch	
1300	Development of Program of Work (cont.)	TM
	Final Guidance	LtCol Verkerk
	Next Steps	Mr. Leggieri / TM
1500	Adjourn	

Appendix A3: HFM-234 TECHNICAL TEAM MEMBERS

Dr. Dan BIELER
Central Hospital of the German Federal Armed Forces
Email: dr.dan.bieler@t-online.de
Tel #: 49 173 306 0905

Mr. Stephen BJARNASON
DRDC Suffield
Email: stephen.bjarnason@drdc-rddc.gc.ca
Tel#: 1 403 544 4990

Dr. Ibolja CERNAK
University of Alberta
Email: Cernak@ualberta.ca
Tel #: 1 780 492 8854

Dr. Raj GUPTA (Secretary)
US Army Medical Research and Materiel Command
Email: raj.k.gupta.ngo@mail.mil
Tel #: 1 301 619 9838

Dr. Emrys KIRKMAN
Dstl, Injury Assessment and Management Team
Email: ekirkman@dstl.gov.uk
Tel #: 44 774 713 6964

Mr. Mike LEGGIERI (Chair)
US Army Medical Research and Materiel Command
Email: michael.j.leggieri.civ@mail.mil
Tel #: 1 301 619 7376

Dr. Hans ORRU
Department of Public Health
University of Tartu
Email: hans.orru@ut.ee
Tel #: 372 737 4203

Mr. Mat PHILIPPENS
TNO – Netherlands Organisation for Applied Scientific Research
Email: mat.philippens@tno.nl
Tel #: 31 88 866 13 01

Dr. Marten RISLING
Karolinska Institutet
Email: marten.risling@ki.se
Tel #: 46 8 52487844

Dr. Jean-Claude SARRON
Direction Centrale du Service de Santé des Armées
Email: jean-claude.sarron@intradef.gouv.fr
Tel #: 33 6 87 11 79 44

Mr. Stian SKRIDUDALEN
Norwegian Defence Research Establishment
Email: stian.skriudalen@ffi.no
Tel #: 47 63 80 75 49

Mr. Jan Arild TELAND*
Norwegian Defence Research Establishment
Email: jan.teland@ffi.no
Tel #: 47 63 80 76 19

Dr. Sarah WATTS
Dstl, Biomedical Sciences Department
Email: sawatts1@dstl.gov.uk
Tel #: 44 776 616 0678

Dr. Arnulf WILLMS*
Central Hospital of the German Federal Armed Forces
Email: arnulfwillms@gmx.de
Tel #: 49 177 840 5376

* Not present at this meeting.

Annex B − MINUTES FROM PANEL MEETING DECEMBER 2013

Blast Injury Epidemiological Study Data Collection Guidelines

December 10-12, 2013
Fort Detrick, MD, United States

B.1 BACKGROUND

Blast Injury is one of the most significant sources of casualties in current North Atlantic Treaty Organization (NATO) operations. The term "blast injury" creates considerable confusion in military medicine. Simply stated, "blast injury" includes the entire spectrum of injuries that can result from exposure to an explosion. It is generally accepted that the taxonomy of injuries can be assigned to five categories based on the mechanism of injury: primary, secondary, tertiary, quaternary, and quinary (see Figure B-1). Primary blast injuries result from the high pressures created by the blast itself. The high pressures, known as blast overpressure, can cause internal injuries. Primary injuries result from the effects of the shock wave which travels through the tissues, depositing energy, particularly where there is a gas-liquid interface. Secondary blast injuries occur when the strong blast winds behind the pressure front propel fragments and debris against the body, leading to blunt and penetrating ballistic injuries. Tertiary blast injuries are caused by the strong winds and pressure gradients that can accelerate the body, resulting in blunt force and penetrating injuries similar to those observed in a car crash or a fall. Quaternary blast injuries include burns and inhalation injuries caused by heat, and chemical substances. Finally, quinary blast injuries refer to the clinical consequences of "post-detonation environmental contaminants", including bacteria, radiation (dirty bombs), and tissue reactions to fuel and metals.

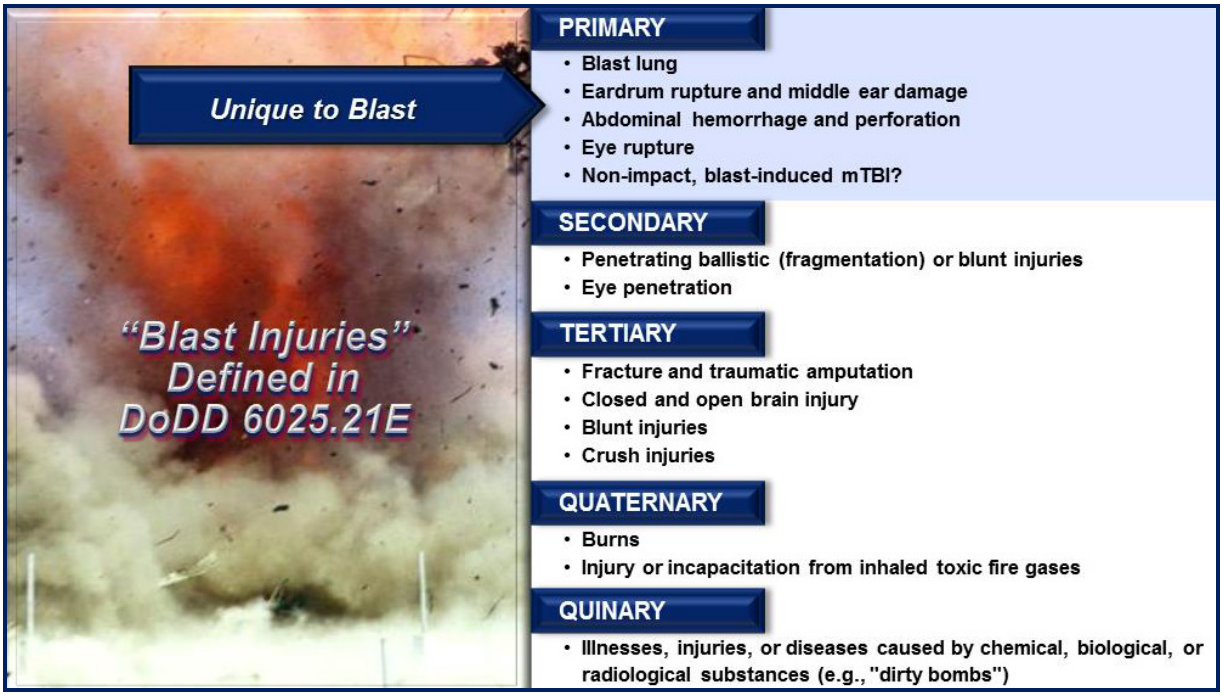

Figure B-1: Taxonomy of Injuries from Explosive Devices per DoDD 6025.21E.

The discussions at the Health Factors and Medicine (HFM)-207 Symposium (SYM) revealed the importance of a systematic approach to understanding blast injuries much like the well-established approach used to solve the classical toxicology problem where the etiology of the injury requires an understanding of the dose, mechanism of delivery of the dosage, and dose-response endpoints. Further recognized was the pressing need for a multidisciplinary approach to addressing non-penetrating blast injuries to the brain that result in a host of symptoms with vague etiology. In addition, the Technical Evaluation Report (HFM-207 (SYM) on "A survey of blast injuries across the full landscape of military science") emphasized the continued multinational exchanges of scientific and technical advances to respond to blast threat and blast injuries.

The first recommendation identified a future need for a recurring technical exchange venue on blast injury and its mitigation to address advances in medicine and personal protection and their synergy. The second recommendation highlighted the need for the development of a Technical Activity Proposal (TAP) to explore the concept of "the Toxicology of Blast Injury" and suggested to focus the activity on several difficult problems including:

1) Relevancy and commonality of animal models.
2) Common methods in dose-response studies; route of exposure methodologies.
3) Computational models (blast, physiology, biochemical, toxicological, etc.).
4) Dose regimens to human medical endpoints (surgical trauma to mTBI spectrum).
5) Methods for translational research leading to medical products and/or physical protection products.

To address the above recommendation and to develop a specific NATO activity devoted to the toxicology of blast exposure, a TAP titled "Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods and Standards" was approved in the fall of 2012, that resulted in the establishment of a new NATO Science and Technology (S&T) Organization HFM Panel RTG with the following objectives:

1) Build an evidence-based outline for NATO standards for blast injury analysis.
2) Examine opportunities for improvements in the standards of medical care for blast injury.
3) Explore advancing the state-of-practice in computational modeling of blast injury in relevant operational environments.
4) Explore standardized animal models and toxicology research protocols that could be adopted by R&T programs across NATO.

To achieve the objectives of the RTG, a kick-off meeting of the Technical Team (TT) was held on July 1-2, 2013 in Neuilly-sur-Seine, France at the Science and Technology Organization (STO) Collaboration Support Office (CSO). The purpose of the meeting was to present the guidelines for the upcoming three years of work, review the TAP and Terms of Reference, and establish a Program of Work (PoW). Twelve TT members participated in the meeting, representing nine NATO nations. A list of all TT members and participating NATO nations is presented in Appendix B1. Details of the meeting summary and the PoW titled "HFM-234 (RTG) Program of Work" can be found on the HFM-234 RTG's SharePoint site.

The present document summarizes the deliberations of the second HFM-234 (RTG) TT meeting that focused on developing Blast Injury Epidemiological Study Data Collection Guidelines. The agenda is presented in Appendix B1. Ten TT members participated in the meeting, representing seven NATO nations. Meeting agenda items included:

1) Receiving an update on the Blast Injury Dictionary of Terms.

2) Reviewing each country's current guidelines for epidemiological studies.
3) Reviewing the temporal profile of outcome measures.
4) Receiving a high level overview of sensors.
5) Conducting group discussions focused on defining parameters of interest to track initial exposure, linking biological outcome to blast exposure, describing the use of pressure sensors, and determining how to optimize existing databases for blast injury epidemiological studies.
6) Developing an outline of recommendations for collecting data necessary for conducting blast injury epidemiological studies.

B.2 WELCOME AND OPENING REMARKS

Mr. Mike Leggieri, Chair HFM-234 (RTG), welcomed all the participants to the second TT meeting and thanked them for their continued support. He was very pleased to see so many people at the meeting, which he felt showed everyone's commitment to the HFM-234 (RTG) goals and objectives.

Mr. Leggieri indicated that Dr. Ibolja Cernak was formally appointment to the TT as a US representative on 4 June 2013. Mr. Leggieri and attending TT members congratulated Dr. Cernak on her official appointment to the TT as a US representative.

Dr. Lucie Martineau was introduced by Mr. Leggieri as an alternate member of the TT. Mr. Leggieri indicated that we will include alternate representatives depending on the focus and topics being discussed at the meeting. He emphasized the importance and participation of relevant subject matter experts during the course of HFM-234 (RTG) activities. Mr Leggieri observed that all of the members have been formally appointed and asked the TT members to introduce themselves. After the introductions were completed, Mr. Leggieri noted that although we could not meet on the first day of the meeting due to inclement weather, we would strive to achieve our objectives in the next two days (see Appendix B1 for final revised agenda).

B.3 STATUS UPDATE – BLAST INJURY DICTIONARY OF TERMS

Dr. Ibolja Cernak (Lead, HFM-234 Working Group) presented an update on the development of a common "dictionary" of blast injury terms. She summarized the current status of the dictionary and commented that the dictionary of terms (also referred to as "elements") should help professionals (e.g., engineers, physicists, biomedical researchers, and clinicians) with different backgrounds and expertise to understand each other with regard to the blast injury terminology. She presented the structure for the dictionary, which included the following four components:

1) Definition of an element using engineering terms.
2) Definition of an element using medical terms.
3) Comparison of the two terms (identical; slightly different; entirely different).
4) Identifying the term preferable for blast research (engineering vs. medical: interchangeable; engineering and not medical; medical and not engineering).

Dr. Cernak led TT members through the working draft of the dictionary, which included approximately 40 elements. TT members emphasized the need to rely on authoritative sources when developing definitions for

elements in the dictionary. They felt that a critical review of peer-reviewed articles (i.e., double peer-review) would be optimal. Another suggestion was to cite formal directives that contain definitions (e.g., Department of Defense (DoD) Directive 6025.21E [Medical Research for Prevention, Mitigation, and Treatment of Blast Injuries], which contains a definition for blast injury). An example of the level of detail to include in the dictionary was provided. For the element "biomarkers," it should include not only molecules and biochemical parameters measured in body fluids but also various types of imaging (e.g., Magnetic Resonance Imaging [MRI]).

Dr. Cernak offered to send the current draft of the blast injury dictionary to TT members by December 15, 2013. She requested that TT members provide input based on their area(s) of expertise no later than March 1, 2014. She asked TT members to notate what they feel is currently acceptable, what they would add, what they would delete, etc. She recommended adding the items that should be defined in experiments related to any new entries in the data dictionary. The core Working Group (WG) plans to compile the input received and post a revised draft of the dictionary on the SharePoint site. TT members will have an opportunity to review the revised draft and offer comments and opinions for further improvements. Finally the latest revised draft of the WG will present the latest draft of the dictionary at the next HFM-234 meeting in May 2014.

B.4 CURRENT GUIDELINES AND TYPES OF DATA BEING COLLECTED

B.4.1 Canada – Presented by Mr. Stephen Bjarnason and Dr. Lucie Martineau

Mr. Bjarnason started the Canadian presentation by noting that they are not aware of any official guidelines for epidemiological studies in Canada. When developing recommendations and guidelines, the Canadian Forces (CF) Health Services Group's Directorate of Mental Health has emphasized the need to characterize pre-injury status, standardize the definition of concussion, and develop a better diagnostic test for concussion. The withdrawal of Canadian troops from the current conflict in Afghanistan limits the opportunities to collect blast injury data. A time-intensive post-deployment screening program scheduled to begin in the spring of 2014 will involve auditing all screened cases of concussion in personnel deployed in Afghanistan, with the goal of linking diagnosis to outcomes. Additionally, a Force Health Protection questionnaire has been developed that links mental health issues to personality traits.

Dr. Martineau continued the presentation by noting that the Department of National Defence (DND) and Defence Research and Development Canada (DRDC) had funded a variety of projects and initiatives aimed at increasing soldier survivability. However, it is difficult to establish priorities for developing and implementing protection systems without a thorough understanding of the chain of events that led to a soldier being injured. The Casualty Protective Equipment Analysis (CASPEAN) S&T project was thus developed to determine how the relationship between the threats encountered by CF warfighters, the environment, and the performance of in-service vehicle and personnel protection systems affects the number of casualties and/or injury patterns in ground combat operations. The CASPEAN database is a structured database that validates, consolidates, and links multiple aspects of attacks on CF warfighters. A wide variety of data are collected in the database's 700 fields (e.g., nature of the threat, types of explosives, vehicle damage, physical injuries). The CASPEAN database is classified as secret and contains personal information protected under the *Privacy Act*; hence, the data collected are not shared or linked to other databases and access to the data is strictly controlled. However, the results of injury analyses can be shared with other countries as long that there is no risk of identifying a particular individual. The collection of the operational data, its integration in the CASPEAN database, and its rigorous scientific analysis by DRDC Subject Matter Experts is referred to as CAsualty and Protective System Analysis Capability (CAPSAC). An approach is currently being developed to establish CAPSAC as a Canadian Army capability to support future operations.

Dr. Martineau highlighted some of the limitations of the CASPEAN database. For example, five percent of the database events lack contextual information (e.g., confirmed nature of the threat, mounted or dismounted, etc.). Another data subset lacks information that would allow a better understanding of the mechanism of injury. Additionally, soldiers do not report what they consider minor injuries, including loss of consciousness. There were also evidences of partial records in the Joint Theatre Trauma Registry (JTTR), the latter being the sole source of information for WIA as DRDC cannot currently access the medical records. For example, a JTTR record may have been made for a penetrating injury to the wrist but a concomitant life-changing injury to the nerve may not have been recorded. In addition, the CASPEAN database provides only a snapshot of injuries upon a soldier's admission at the Role 3 Multinational Medical Unit at Kandahar Airfield, and there is currently no link to outcome. An approach is being developed to complete specific injury data records in the CASPEAN database to enhance our ability to identify gaps in personnel protection requirements against life-changing injuries (e.g., helmet damage is observed but no CASPEAN record of loss of consciousness). Despite these limitations, the operational injury analyses carried out have led to equipment acquisition and modifications, enhanced CF personnel survivability, and allowed DRDC to better focus its S&T efforts. Dr. Martineau noted that any identified gaps in operational data collection will be highlighted in a whitepaper to ensure that they are addressed in future CF personnel deployments and lessons learned.

B.4.2 France – Presented by Dr. Jean-Claude Sarron

Dr. Sarron commented that they use the G3 form ("Injury with Firearms or Explosives") to collect a variety of data related to injuries induced by explosions (e.g., circumstances of the accident, type of threat, localization of the injury). He noted that they have only been able to obtain a small snapshot of the big picture using this form, and have many gaps to fill. He welcomed input from TT members on ways to improve the form. Dr. Gupta offered to place the form on the SharePoint site for TT members to access. Dr. Sarron also reviewed the NATO Standardization Agreement 2231 form ("Patient Management System Common Core Information"), which defines the types of data that should be collected.

B.4.3 Germany – Presented by Dr. Dan Bieler

Dr. Bieler started his presentation by noting that they have no guidelines in Germany on how to conduct blast injury epidemiological studies. Their trauma registry includes data from 573 hospitals and more than 122,000 patients (all civilians), and has become increasingly international. The registry includes approximately 100 parameters (preclinical through clinical) up to the point when a patient is discharged from the hospital. The registry is retrospective and 95 percent of the cases are blunt trauma. Dr. Bieler stated that they have developed definitions for the parameters they want to collect, but they do not currently have a military trauma registry in Germany. One of their main obstacles has been the inability to link data that is being collected to the Expert Group for the Technical Analysis of Incidents (ETAV). They can identify injuries in an individual who was involved in a blast-related event, but they cannot relate these injuries to specific details of the blast exposure such as the power of the blast wave that hit the individual. Dr. Bieler noted that they also lack a sufficient system for data exchange for all the information that is collected.

Dr. Bieler stated that they plan to include documentation from first aid to rehabilitation (return to duty) in their registry. They will also include on scene documentation, so they will have prospective data. In addition, they will collect follow-up data, which will be obtained from the military doctors that soldiers go to in their post-military life. Dr. Bieler noted that they plan to evaluate all injured and ill soldiers during a mission, to obtain the data necessary to compare wounds from explosions with those resulting from non-blast related accidents. To aid in collecting data, they are developing a digital-based data acquisition using a DigiPen. While the digital collection method will help to facilitate subsequent data analysis, one drawback is the inability to use free text.

Dr. Bieler reviewed the different types of forms that they will use to collect data, including the Forward Medevac form, Basis form, Trauma Room form, Surveillance form, ICU form, and End of Treatment form. He highlighted the information that will be collected on the Forward Medevac form, including patient data, technical data, anamnesis, first medical findings, medical actions, preclinical course, first diagnosis, and hand over. The inclusion on this form of documentation collected by physicians will represent an advance over the past in which this information was collected separately and then combined at a later time point. Information such as the role of the receiving facility and the triage category will be entered on the Basis form. Sensor-related information will be collected on the Trauma Room form. Information related to the ongoing treatment of the patient will be collected on the Surveillance form. They will collect a variety of physiological parameters on the ICU form, and the End of Treatment form will be used when patients are ready for discharge. Dr. Bieler stated that they also want to capture follow-up data on patients 180 days post-discharge. He noted that they have asked the German Trauma Registry to establish a web-based collection of these forms, which may take up to one year.

Dr. Bieler reviewed their recent efforts aimed at validating the NATO Trauma Registry in San Antonio. They analyzed data from the past seven years from 97 individuals who suffered either blast or gunshot wounds. Data were included from the JTTR, NATO Trauma Registry, and civilian German Trauma Registry. The goal was to compare these data with the paper-based documentation of their hospital. They found that data was not filled in properly for more than 80 percent of the individuals, which severely restricts the ability to perform epidemiological studies. Dr. Bieler noted that this is why they are developing the aforementioned forms for documentation that include all the parameters they want to know to conduct quality epidemiological studies.

B.4.4 Netherlands – Presented by Mr. Mat Philippens

Mr. Philippens commented that he is not aware of any formal guidelines in the Netherlands for conducting blast injury epidemiological studies. They primarily use the Military Acute Concussion Evaluation (MACE) to collect these types of data.

B.4.5 Sweden – Presented by Dr. Marten Risling

Dr. Risling began by noting that they are getting a new medical journal system in their defence department. Currently, the more serious injuries are referred to the German hospitals. There is one contracted hospital in Sweden that takes care of the more seriously injured soldiers. This has been the University Hospital in Uppsala but starting next year it will be the Karolinska Institute in Stockholm. Dr. Risling noted that they use the MACE system for mTBI. There are suggestions to create a trauma registry, which will be collaboration between the Swedish Defence Materiel Administration, FMV and the Karolinska Institute. The idea is to create a link between the type of trauma observed and the type of body protection worn. Dr. Risling noted that sometimes they treat it as a murder case and send the police out to Afghanistan to evaluate what has happened. In such cases, the bodies are returned to Sweden for forensic analysis.

Dr. Risling highlighted some of the recent research studies that are being conducted. Some research focuses on determining better ways of collecting data and what types of data to collect. Dr. Risling noted that they have just begun a study on the current troops in Afghanistan in which they are determining stress tolerance, evaluating biomarkers, performing neuropsychology tests (both before and after rotation), and collecting data on sleep behavior through black box (activity) sensors. They hope next year to begin a Swedish Breacher study that would evaluate the training of Special Forces and the national police Special Forces, and would include biomarkers, neuropsychology and black box sensors. Dr. Risling noted that they have been involved in some evaluation of the Vietnam head injury study, including the questionnaire-based follow-up of mTBI cases with Defence Veterans Brain Injury Center. They anticipate that the results from the Vietnam study will help them

analyze Swedish troops. Dr. Risling noted that they have also completed some research focused on evaluating long-term health in artillery officers. There is also collaboration with civilian TBI databases where they are focusing on biomarkers as predictors of outcome. They are also evaluating input from the experimental research on blast-related injuries and data from body armor protection.

Dr. Risling commented that diffuse brain injury, including axonal injury, is linked more to acceleration injury than pure blast exposure. Meanwhile, changes in brain stem systems appear to be more pronounced in blast injury compared to acceleration. Dr. Risling emphasized the importance of determining signature changes related to each mechanism. He stated that they are trying to bridge the gap between experimental and clinical research. To that regard, they will look at biomarkers as well as diffusion MRI techniques; the current focus for evaluating diffuse brain injuries due to acceleration. They are also collaborating with others to perform modeling aimed at analyzing the typical forces during acceleration or different types of injuries in the rat. They have the experiment set up to validate the predictions from the modeling, although Dr. Risling acknowledged that it will be difficult to scale up to larger heads.

Mr. Leggieri emphasized that determining the types of data to collect in non-combat blast exposures will help us understand blast injury. One TT member acknowledged that the Breacher-related studies represent a good opportunity to define the loads to which individuals are exposed. The type of explosive used and the exposure conditions can be traced in the training environment, which allows a researcher to reconstruct the scenario in a laboratory setting and obtain the correct input to the human system. These types of settings can be used to determine what happens in the field, and can serve as a reference to validate our physical and medical models. One TT member noted that there are likely to be many confounding factors. He felt it was good that there are numerous ongoing studies, as this increases the chances that we will be able to detect the important factors.

B.4.6 United Kingdom – Presented by Dr. Sarah Watts

Dr. Watts provided an overview of some of the ongoing human epidemiological studies in the UK. She noted that the largest study is a retrospective analysis of casualty data but there are some prospective studies focused on the casualties in Afghanistan. Dr. Watts also reviewed some animal studies that they are conducting. Focusing first on casualty analysis, Dr. Watts noted that the UK database contains information on those killed or seriously injured in Iraq and Afghanistan. They are also integrating data from previous conflicts (e.g., Northern Ireland) into the database. Dr. Watts reviewed the UK's JTTR, which incorporates medical data from point of injury right through to the individual's return to the UK, includes data on the actual event/threat, mechanism of injury, actual injuries sustained by casualties, and protective gear worn (including information on whether the protection was defeated). In addition to incorporating data from other conflicts, they are also pursuing wound mapping. Notably, the UK has created its own wound mapping software (Interactive Mapping Analysis Platform [1]).

Dr. Watts noted that the medical data in the UK JTTR is composed of data from several other databases in the medical community. Their major trauma audit for clinical effectiveness (MACE) database contains all of the early data from casualties when they arrive at Role 3. Another database is associated with the Medical Emergency Response Team (MERT), which is a consultant-led helicopter platform that picks up casualties where they have been injured. A medical database, Opudar, contains data from any casualty that arrives at emergency departments in Role 3. Dr. Watts highlighted a publication showing the kind of data that can be extracted from wound mapping, which showed a reduction in serious injuries in individuals who wore eye protection versus those who did not (even if the eye protection is defeated). Besides being used to evaluate protection systems, the JTTR is also used to evaluate medical systems. She reviewed the results of a data analysis comparing the MERT system with other casualty retrieval systems. The MERT system is quite

resource- and labor-intensive. The analysis revealed that for casualties with severe injuries, the consultant-led platform did not offer a survival advantage to the other retrieval platforms. However, the consultant-led platform did offer a survival advantage for those with moderately severe injuries.

Dr. Watts commented that the JTTR database can be used to determine actual (versus perceived) threats, which allows the research community to focus their efforts to offer the best solutions to those on the ground. While the Defence Science and Technology Laboratory (DSTL) is the custodian of the whole UK JTTR database, the medical aspects of the database are held by other authorities such as the Defence Analytical Services Agency (DASA). The UK JTTR database has been shared with other nations, as well as with NATO. Access to raw data is limited to DSTL personnel, but other nations can pose questions for DSTL to investigate. Data sharing is at the Secret clearance level.

Dr. Watts highlighted three prospective studies that are underway focused on casualties in Afghanistan. One study is exploring the effects of trauma on coagulopathy. They established that when casualties arrive at the field hospital the failure in clotting is due to the clot breaking down (fibrolysis), which is consistent with the civilian literature. They are also examining the effects of blast on platelets. Another study is focused on examining the presence and association of pituitary dysfunction after moderate to severe TBI compared to non-blast casualties. They found blast-injured individuals to have a higher incidence of pituitary dysfunction that was associated with skull fractures and lower cognitive function. A follow-on study will explore chronic inflammation associated with blast injury. Dr. Watts highlighted a third study, which was focused on understanding the mechanisms of heterotopic ossification and the differences between military and civilian populations. The study is currently going through ethical approvals, which should be granted soon.

Dr. Watts subsequently reviewed some of their ongoing and completed blast animal studies, which focus on studying mechanisms of blast brain injury in rats and pigs (in collaboration with imaging researchers at Imperial College), biomarkers of brain injury in rats, and resuscitation from a military perspective. They are also studying the influence of blast on the epithelium. Dr. Watts noted that compressed air was used to deliver the blast in these experiments. Mr. Leggieri commented that a tangible product from this group could be the development of guidelines for the various devices that deliver blast waves. One TT member noted that researchers often only measure side on pressure in these types of experiments. He suggested adding a few additional sensors to measure dynamic and stagnation pressures so that more comparisons can be made across studies.

Mr. Leggieri questioned the extent to which the UK could share the data fields in the UK JTTR database. Dr. Watts replied that they should be able to openly share the information in the data fields. Dr. Martineau offered to send a presentation showing the different fields of screens in their database, and Dr. Watts offered to do the same for the UK JTTR database. Dr. Watts noted at the end of her presentation that they are not currently doing anything with sensors in the UK.

B.4.7 United States – Presented by Dr. Raj Gupta

Dr. Gupta reported that he consulted with the Armed Forces Health Surveillance Center (AFHSC) and the Office of the Assistant Secretary of Defense for Health Affairs, which both confirmed that the DoD currently has no official guidelines for conducting blast injury epidemiological studies. Most of the studies conducted in the US are being sponsored by the DoD or are being conducted internally. Each study is unique, containing a specific objective or purpose and a distinct hypothesis (as described in the written proposal). A key element of each proposal is the consent form, which clarifies a number of parameters such as the type of data that will be collected, the populations from which data will be collected, and the databases that will be used in the study. The types of data collected vary from study to study. For example, some studies will involve a combination of real-time data collection and extraction of data from an existing database.

Dr. Gupta highlighted a prospective study that has been funded by the DoD's Congressionally Directed Medical Research Programs (CDMRP) in which the researchers are trying to determine the incidence of injuries (e.g., from blast exposure) in soldiers. He focused on the personnel demographics and related information that has been gathered on study participants. He showed a form they are using to collect a variety of data, including whether an individual was exposed to blast prior to deployment or had any past behavioral or emotional disorders. One TT member noted that there are no questions about concussions or etiology on the form. Another TT member commented that the form would not capture those who were affected by blast during training. Dr. Gupta noted that the form may be missing these questions because proposal review panels typically include very few scientists with blast expertise; most of the reviewers are epidemiologists who are just starting to study the impact of blast-related injuries. Mr. Leggieri noted that this issue underscores the immense value of the TT. For example, the TT could produce recommendations for the types of data that should be included in an epidemiological study of blast injury, which could be used as guidance for developing Program Announcements.

TT members discussed the need to combine self-reported data with other measures, since soldiers sometimes do not report that they have had concussions in the past for fear of being taken out of active duty. While sensor technologies can help in this area, it was noted that there are ways to cheat with sensors as well. One TT member commented that this problem also exists with automotive accidents. He elaborated on a program that involves focusing on trying to capture all of the details on specific accidents to obtain an estimate of the quality of the data in the larger population. Dr. Gupta offered to place the CDMRP study's data collection form on the TT's SharePoint site and noted that it should only be used for purposes related to this group.

Dr. Gupta reviewed the types of data collected on the casualty fields that are used as part of the JTAPIC initiative. Data fields were shown in the top row of the table. The next row included a definition of the data field. The following row included the type of information (e.g., personally identifiable information or personal health information). The last (bottom) row included data on the organization(s) that provided the information into the database. Dr. Gupta noted that the National Ground Intelligence Center (NGIC) provides a unique number for each person, which is how that individual's data are tracked. This number is different than the social security number. It was noted that the "Position" data field is one of the more challenging ones, since you need to determine where people were sitting at the time of an event. Dr. Gupta commented that the US is using the 2005 Abbreviated Injury Scale (AIS) coding system to enter injuries into the database. Germany, Canada and the UK are also using this system. Dr. Gupta offered to post the JTAPIC slides on the group's SharePoint site pending official approval to do so.

Dr. Gupta subsequently highlighted the types of demographic information collected by the DoD Trauma Registry. One TT member noted that the scroll down menu includes the mechanism of injury and the cause of injury, but another line asks for the initial mechanism of injury ("choose the mechanism of injury that started the sequence of events leading to injury"). It would be difficult for those entering data to distinguish between the initial mechanism of injury and the cause of injury. Dr. Gupta reviewed the sequence of events that occurs as a casualty proceeds through the system. For example, data are gathered from the individual in the combat zone, additional data are recorded as the casualty moves through each role of care, and data are also interpreted by the attending physician and medical personnel. One TT member noted that there can be different interpretations regarding the cause of injury. Dr. Gupta noted that definitions are available to help guide those who are entering codes. While a number of individuals enter data related to each casualty, they are all trained in the same coding system.

One TT member emphasized the need for an attending physician to be able to get into the database, and based on a patient's identification, immediately derive specific details related to the blast exposure to aid in medical management and diagnosis. Dr. Gupta commented that attending physicians would have access to all of that

information. He noted that the current DoD medical system is linked to the VA system, and there is a separate icon that allows the attending physician to access the VA system for those who have left the DoD system. He stated that injuries are coded using the current International Statistical Classification of Diseases (ICD), ICD-9 and ICD-10 codes, which are very specific. One TT member questioned whether the database would capture information related to a potential breach in an underbody blast event. Mr. Leggieri replied that the database would not include that level of information, but it would be captured in a JTAPIC analysis of the event.

B.4.8 Norway – Presented by Dr. Raj Gupta

Dr. Gupta presented a summary for Norway on behalf of Mr. Stian Skriudalen and Mr. Jan Arild Teland who were unable to attend the meeting. Based upon Mr. Skriudalen's email message, Dr. Gupta noted that Norway has no past studies linking biological outcome to blast exposure and have no existing guidelines for conducting blast injury epidemiological studies. They are currently discussing how to collect information from prospective studies and are developing databases in close coordination with the United States.

B.5 RECENT BLAST INJURY STUDY − CANADIAN SOLDIERS − Presented by Dr. Ibolja Cernak

Dr. Cernak provided an overview of a longitudinal, prospective study with an overall goal to determine how to measure and define resilience in the military. Dr. Cernak noted that resilience is likely affected by a combination of social, mental, and biological factors. It is important to be able to measure resilience in our military members because those with low resilience are susceptible to developing injuries and/or chronic conditions. In addition, as resilience declines, operational readiness declines.

The study demographic data revealed that 35 percent of the study participants were previously exposed to blast, however, after additional questioning, the proportion of participants with previous blast exposure rose to approximately 50 percent. Study subjects are also being asked to complete a variety of computer-based tests that measure response times, impulse control, attention switching, spatial working memory, and emotional recognition. The emotional recognition test has turned out to be the most sensitive for blast-related emotional problems.

The preliminary data analysis indicated that 75 percent of the blast-exposed participants were well adjusted based on self-reported measures. However, the blast-exposed group had issues with more complex executive functions such as making decisions and solving problems. The blast-exposed individuals performed well on impulse control tests for the first few cycles, but cognitive fatigue eventually set in and their performance level dropped. The preliminary results show an association between nerve growth factor and inflammatory markers in the saliva in association with these declines in cognitive function. Dr Cernak anticipates that by entering all of the physiological, cognitive, psychosocial, and environmental information from this study into a database, the system will in time have a predictive capability and aid in identifying cohorts.

Mr. Leggieri asked whether a positive response to the "were you exposed to blast" question would elicit further inquiry. Dr. Cernak replied that they would have the soldier complete an additional questionnaire, which asked details about the source of the blast, the environment, the symptomology, the subjective field, etc., and whether it was from a rocket-propelled grenade or a soldier firing a shoulder-fired weapon. Mr. Leggieri commented that this is a major gap in many studies of blast exposure, which focus on whether the soldiers were located near Improvised Explosive Devices (IEDs) and overlook these other possibilities.

B.6 HOW BLAST WAVES AMBUSH THE BRAIN − TEMPORAL PROFILE OF OUTCOME MEASURES − Presented by Dr. Ibolja Cernak

Dr. Cernak provided an overview of the potential outcomes to blast exposure. Due to the nature of blast exposure, the entire body is affected and the response involves multiple organ systems that influence each other. Blast outcomes can have different temporal profiles, ranging from non-recoverable injury to complete recovery. Dr. Cernak noted that the "late injury" profile is particularly challenging, since there is no initial diagnosis and the first contact with the soldier is in the VA environment. She commented that the state of the soldier's resilience at the time of injury can predict the development of symptoms at later time points.

Dr. Cernak reviewed the psychological and psychiatric outcomes associated with blast exposure. The major symptoms include anxiety, depression, addiction, and worsening of existing psychiatric disorders. It is often only when the symptoms persist over an extended period that most psychological and psychiatric disorders are identified. Dr. Cernak highlighted an experimental study focused on the acute and long-term behavioral responses to blast in mice. Beginning three days after blast exposure and continuing to 30 days, the mice become disinterested in their environment. These symptoms of major depression in the mice parallel the symptoms observed in soldiers exposed to blast. One of the long-term consequences of blast exposure is Posttraumatic Stress Disorder (PTSD). Dr. Cernak highlighted a 2011 study by Hunter et al. [2] that showed a breakdown in communication between brain structures involved with executive function and emotional control in individuals with PTSD.

Dr. Cernak reviewed the nervous system outcomes to blast exposure. She noted that TBI caused by exposure to blast waves (blast TBI) is distinct from TBI caused by non-blast-related injuries (e.g., closed head injury due to blunt trauma or injury related to acceleration/deceleration). She highlighted a 2012 study by Theeler *et al*. [3]) showing that those exposed to blast had a significantly higher number of days with headaches compared to those not exposed to blast. Dr. Cernak then highlighted a number of secondary studies related to the neurological and behavioral outcomes to blast exposure. She reviewed some recent blast-related imaging studies, including one focused on Diffusion Tensor Imaging (DTI) and another using Positron Emission Tomography (PET) imaging. She reviewed the results of one of her recent experimental studies, which showed that blast exposure causes acute and chronic memory problems as well as acute and chronic motor problems in mice. The motor deficits were not attenuated with the addition of Kevlar suits on the mice. Dr. Cernak highlighted some of her other recent studies in which they found blast injury to lead to a compromised blood-brain barrier, diffuse inflammation in the brain, and changes at the ultrastructural level in the hippocampus. She noted that blast-induced inflammation can be found throughout the brain, but is mostly observed in deep brain structures, including the cerebellum and mesencephalon (midbrain) as well as the sensory organs.

Dr. Cernak noted that it has been recently recognized that hormonal problems that influence wound healing as well as significant and essential neuroendocrine functions could be caused by blast exposure. She highlighted results of one of her studies involving 31 patients with TBI that focused on characterizing thyroid, gonadal and adrenal function following neurotrauma. They found that patients with both direct and indirect TBI demonstrated endocrine alterations after trauma, which could relate to the severity of the amount of brain damage.

Dr. Cernak subsequently noted that we do not typically examine the effects of blast injury on the heart, which is an issue because there is significant injury-dependent heart pathology. For example, mild blast exposure is associated with significant venous congestion and severe blast can lead to ventricular wall infarcts. Dr. Cernak noted that there is a huge body of clinical and experimental data on blast-related lung injuries, which can include alveolar ruptures, small perforations of the alveolar wall, swollen interalveolar septae, pulmonary fat embolisms, etc. Blast exposure also causes liver injury, although the liver effects are manifest mainly through functional

(versus morphological) changes. Liver damage can lead to a susceptibility to vasoconstriction of blood vessels and coagulopathy.

Dr. Cernak reviewed the results of a recently conducted study involving *in vivo* imaging of inflammation in mice after mild intensity blast using the IVIS® bioluminescent camera. In animals with no protection, there was an initial increase in activated macrophages in many areas of the body, including the brain. By three days post-blast (equivalent to several months in a human), there were substantially fewer activated macrophages in these animals. However, the macrophages increased again by seven days post-blast and persisted at these elevated levels through the end of the study at 30 days. Dr. Cernak noted that a chronically inflamed gastrointestinal tract would have adverse effects on the brain. Although the animals with full body protection had an initial increase in inflammation in the head (at one day post-blast), they had very low levels of inflammation in the head at the longer-term time points. Histological analysis of brains from unprotected animals revealed that blast injury led to pathology in the deep brain structures (e.g., cerebellum, brain stem, and sensory pathways). This can be compared to an impact or acceleration/deceleration type of injury in which most of the damage is observed at the cortical level. Animals with head protection but not torso protection still had pathology in the deep brain structures following blast injury, while the brains of animals with torso and head protection were in good shape. Based on this work, we need to protect both the soldier's head and torso.

Discussion followed with comments about real world relation of the *in vivo* classic toxicological mouse study, increased survival or increased quality of life, survival of more soldiers but with an increased number of chronic issues, translating the results of an animal study to what is observed in humans etc. Dr. Cernak emphasized the lack of evidence of the long-term consequences of blast injury, linking observations in various body organ systems to TBI, and acknowledged the challenges associated with engineering scaling and especially with biological scaling. She felt that we will never be able to obtain one model that satisfies all of the scalings and reproduces the human response to blast. Multiple models will be needed, with each model serving to help answer one or more specific questions.

B.7 HIGH LEVEL OVERVIEW OF SENSORS − Presented by Mr. Mat Philippens

Mr. Philippens began by commenting that the US appears to be the only country using sensors on a large scale. He noted that they have vehicle-related sensors in Holland, but for ballistic purposes only. He stated that they do not have the infrastructure in Holland to gather, process, and analyze the data that would be generated from a large scale application of sensors. He asked others to comment on whether they have any large-scale sensor efforts in their countries. One TT member noted that Australia is working with the US, and that the UK and Canada are observers for that effort.

Mr. Philippens recapped his discussions with Allen-Vanguard and DTS, which make helmet-mounted sensor systems. He noted that one of the fundamental problems with the helmet-mounted sensor system is determining how to relate the readings from the pressure sensors to the individual injuries in the head. To determine the locations of the pressure sensors in relation to the blast, you need a three-dimensional system on the helmet from which you can reconstruct the blast. Regarding acceleration, the loose coupling between the helmet and head (necessary for ballistic protection) prevents one from obtaining the details needed to translate the data obtained with what is happening inside the head. We are particularly interested in identifying the low-level injuries, which under these conditions has been a challenge. Allen-Vanguard has provided data on how the helmet motion corresponds with what the head does, but Mr. Philippens has not yet identified a solution to this problem. He commented that we need to be careful in how we use these data, especially on the individual level.

Mr. Leggieri provided an overview of the on-going sensor efforts in the US. He mentioned that the US has had helmet sensors for many years and at present is investigating the second generation of sensors. These sensors are mounted inside the crown of the helmet, and include both blast pressure sensors and accelerometers. Unfortunately, we have not been able to obtain good pressure data with these helmet sensors. Therefore, these helmet sensors are only used for acceleration data. Coupled with the helmet sensors, we also have blast gauges that were developed by the Defense Advanced Research Projects Agency (DARPA) and focus on measuring pressure. The blast gauges are also being fielded whereby the soldier wears three individual sensors in different areas of the uniform. Mr. Leggieri also noted that we are also starting to look at the training base. A major effort is underway to field both the helmet sensor and the blast gauge and assess them in several different training environments. The initial goal is to focus on usability, i.e., whether the sensors and gauges interfere with training in any way. The researchers will also assess other types of head sensors, including technologies where the sensor is directly coupled to the head.

Mr. Leggieri commented that our job in the medical research community is to see if we can make any sense of the data generated by these sensors, e.g., correlating the data with the observed injuries. Mr. Philippens questioned how the data collection is organized. Mr. Leggieri stated that the Program Executive Office (PEO) Soldier has developed very good processes for collecting and managing the data. He feels that we are reaching the point now where we can connect the dots between a sensor and an individual who was in a particular event and who sustained specific injuries. This creates the challenge of getting the sensors onto the soldiers and producing meaningful information with the data. Mr. Leggieri noted that the first generation sensors were implemented so quickly in the field that there was not enough time to develop the processes needed to collect the data generated by the sensors. One TT member questioned whether health data is also being collected on these soldiers. Mr. Leggieri noted that specific studies will be conducted in the training environment and collection of health-related data may be a component of some of those studies.

Dr. Cernak provided an overview of a wireless communication sensor system that has been developed by the Georgia Institute of Technology and the US Army's Rapid Equipping Force. The system involves two series of sensors – one in the vehicle and another on the soldier. As the soldier sits down on a seat in the vehicle, the sensor in the seat collects data. When the soldier stands up and leaves the vehicle, the wireless system takes over and records the environmental information. This sensor system will soon be fielded in training. Mr. Philippens noted that ballistic and blast impacts are high-speed events, which necessitates extremely high sample rates to be able to make sense of the data from a physics standpoint. He commented that they are using miniature electronics and are generating an immense amount of data. He therefore questioned how far along they are with the research. Dr. Gupta noted that they have worked out a lot of the issues over the past five years. One of their main issues now is adequately sustaining the sensors with batteries.

B.8 TYPES OF DATA NEEDED FOR EPIDEMIOLOGICAL BLAST INJURY STUDIES

The discussion on the types of data that are needed to conduct the epidemiological studies focused on the following:

1) Defining parameters of interest to track initial exposure to blast.
2) Identifying the types of data needed to link biological outcome to blast exposure.
3) Using sensors.
4) Optimizing existing operational databases for blast injury epidemiological studies.

The summary of discussion on each of these topics is presented in the following sub-sections.

B.8.1 Define Parameters of Interest to Track Initial Exposure

TT members identified three broad categories:

1) Characterizing the **threat** itself, including the threat environment;
2) Capturing information related to the **individual** affected by the threat; and
3) Capturing **measurements** related to the threat.

The discussion included emphasis on current and future threat environments. The key parameters of interest identified are summarized in the table below followed by a detailed discussion.

Table B-1: Parameters of Interest to Track Initial Exposure to Blast.

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

Category	Parameter
Measurements (cont'd)	Describe the configuration of the suite of multiple sensors used (e.g., location and orientation of sensors with respect to a body coordinate system: aligned along 360 degrees).
	Determine relationship of pressure sensor to exposure source (distance is directly related to amplitude).
	Characterize the side on (static) and face on pressures (amplitude and duration) of the blast.

B.8.1.1 Characterizing the Threat

The discussion centered on the importance of characterizing the nature of the threat. For example, IEDs can now contain components other than explosives (e.g., biological materials, radioactive substances, nails) that can significantly alter the injury pattern. Additional threat characterizing parameters identified included details such as the blast altitude. For example, blast exposure at 7,000 ft in Kabul would be different than blast exposure at sea level.

The importance of measuring the distance from the source as well as body orientation was emphasized. It was noted that one of the current flaws of the US DoD guidelines is that they recommend evaluating an individual who was located up to 50 meters from a blast, but they do not account for the size of the blast. In the Netherlands, they consider an IED an explosive that is less than 50 kg, which is small enough to be hidden. An equation can calculate the pressure generated (in kPa) when you know the size of an explosive and the distance from the threat. In addition, the size and distance of any objects or walls in the environment would be very helpful in evaluating complex waves.

From an engineering perspective, the deployment and training environments could appear to be identical. However, the mental and psychological stress levels are quite different between these two environments. Individuals can be exposed to the same blast loads in these two environments, but the body will respond quite differently in the training scenario.

B.8.1.2 Identifying Information Related to the Blast-Exposed Individual

The key demographics of an individual exposed to the blast should include information such as the individual's identification number, sex, age, weight, medical history, personality traits, immunizations, smoking or non-smoking, the Service(s) in which they have served and whether they were artillery or infantry. In addition, it was determined that an individual's body posture; mounted or dismounted; type, form and fit of personal protective equipment including visor may assist in determining the extent of blast exposure.

TT members recommended assessing for the presence of blunt impact and acceleration/deceleration, including linear and angular acceleration/deceleration of the entire body or body part, and contact pressure. It was noted that there are two injury mechanisms associated with blunt impact. One is local stress involving a local deformation of the skull, where a fracture can lead to the pressure wave passing into your brain. The same blunt impact can also cause an acceleration/deceleration, which would be observed if one is wearing a helmet and gets hit with a baseball bat. An ejection seat is only associated with acceleration/deceleration as an injury mechanism. So to quantify the blunt impact as a loading mechanism leading to injury, one ideally would measure the contact pressure. In addition to the acceleration/deceleration data, it was noted that this would provide information on risks for skull fracture and brain injury.

TT members felt that all types of injuries and medical conditions should be identified, including their effects on the body. It was noted that functional impairments can exist that cannot be observed with various imaging methodologies, versus clinical, morphological impairments that are easily detected. One TT member questioned whether to specify "clinically significant" effects, since a fragment of shrapnel can be lodged in an individual's arm (as a consequence of the injury) that causes no problems whatsoever. Another TT member questioned whether we should say "clinically relevant," meaning something that advances an individual along the pathological continuum past a point of no return. It was noted that there is a great amount of variability among individuals, e.g., some are more biologically resilient than others based on their training. Hence, the clinical relevance of a response for one individual would be different than the response for another person. One issue with the "clinically significant" clause is that what is significant to one person exposed to a blast may not be significant to another who is exposed to the same blast. It was noted that we can obtain blood samples from blast-exposed individuals, but we are not yet at the point where we can link changes in the blood to changes in function. It was also noted that we may need to consider both the acute and chronic effects of a blast injury. One TT member commented that there are markers of an exposure and markers of an effect, and we need to be able to tell what we are measuring means functionally to the individual. Overall, we want to capture all of the changes that affect the quality of life and functioning of an individual.

B.8.1.3 Capturing Measurements Related to the Threat

TT members spent some time discussing sensors, which are useful for measuring pressure or acceleration related to blast exposure. It was felt that the configuration of the sensors with respect to the body and with respect to the explosive load is important information to know. Sensors are one-dimensional, i.e., they can only measure from one direction. Therefore, the orientation of the sensor to the shock front is important. The body itself affects the flow around a sensor. It is therefore easier to obtain accurate measurements from sensors that are not near the body and come in contact with undisturbed shock waves. TT members recommended defining a suite of multiple sensors aligned along 360 degrees, which means that the sensors would be oriented with respect to a "body coordinate system" (X, Y, Z axis system). It was felt that this would provide researchers with a unique definition of where everything is with respect to the anatomical structures. TT members also recommended determining the specifications and capabilities of any sensors used, including information on the type of sensor, brand of sensor, sample rate, etc.

TT members recommended determining the relationship of a pressure sensor to the exposure source. They emphasized the need to characterize the "side on" and "face on" pressures (both amplitude and duration) of the blast. It was noted that the shape and impulse of the pressure from a blast is a measure of the energy that can be transported. The first blast wave from an explosion is the only thing that can be measured in a defined way. If the wave is reflected, the origin of the blast really needs to be determined. It was noted that accurate measurements are not needed for high explosives that are lethal. For blasts in the 60 – 120 kPa range, small increases in amplitude can mean the difference between no injury and injury. It was noted that the amplitude of a blast wave is crucial to determine its effect on the body. Furthermore, the distance from the blast is directly related to amplitude of the wave. Overall, the ability to accurately measure the intensity of blast waves in the 60 – 120 kPa range is needed to obtain quality correlations with the injury.

B.8.2 How to Link Biological Outcome to Blast Exposure

The second segment of the TT discussions focused on determining the type of data needed to understand the response of an individual to a blast event and its long-term effects. The key categories of data identified by TT members, and whether or not these categories represent data that are intrinsically dynamic or static (or both), are summarized in the table below followed by the details of the TT discussion.

Table B-2: Data Needed to Link Biological Outcome to Blast Exposure.

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

It was noted that the overall goal is to determine the response of an individual to a blast event as well as determine what influences that response. We want to build a predictive system that includes signal analysis and pattern recognition. Data must be captured on both the threat and the surrounding environment. Information about the environment is required as we define it to be linked to an outcome if and when it is clinically relevant.

TT members emphasized the need to link medical data with the exposure/event. Medical data would include information related to the active response of the individual to the event, and would include data gathered under the buddy system, medic, various levels of hospitals, medevac, etc. It could also include MACE information, and data derived from blood samples. If there is no injury, then we might not get contact with the patient until much later in a Veterans Affairs hospital. One suggestion was to examine trauma registries with regard to incident data instead of focusing strictly on the medical data. However, incident data is often classified. To get to the answer, those data will need to be included. Overall, we want to be able to link threat, medical, and operational data.

Besides collecting information on an individual's medical and other histories (static), TT members noted that we want to see how individuals respond in the moment in which an event occurs (dynamic). They identified three main categories of dynamic stressors: psychosocial, environmental, and operational. An example of a psychosocial stressor would be a stressful interpersonal relationship in the field. Environmental stressors would include high altitude or extreme hot or cold ambient temperatures. Operational stressors would include fatigue, dehydration, leadership issues, etc. It was noted that while psychosocial stressors would be dynamic, psychosocial data would be static (e.g., the marital status of an individual). It was also noted that resilience would encompass both the psychological and social types of resilience.

TT members discussed biomarkers and noted that we need data on both dynamic and static biomarkers. For example, researchers using functional MRI (fMRI) do not have access to pre-existing data, which makes it impossible to compare pre- and post-injury scenarios. A suggestion was made to add "biomarkers" to the medical history category, since it will be important to know certain biomarkers as part of an individual's medical history.

Another suggestion was to record the personality traits of an individual involved in a blast. It was noted that we need to eliminate the possibility of the subjectivity related to whether or not to record this type of data. Another suggestion was to record the training and job history of the individual. It was noted that capturing information on a person's trade provides an idea of how they think, which may help to explain the biological outcomes of a blast injury. It was also noted that a person's current employment may not be related to their training. Hence, we would like to obtain data on both the training and job history of the individual. These data would allow linkage to various subspecialties of employment. It was noted that we can expand this bullet in the future by adding various subspecialties.

Another suggestion was to identify the mechanism of injury. For example, we would like to know whether an individual's penetrating injury is due to fragmentation or is of ballistic origin. Or an explosion may not lead to any visible injuries, but a person could have other clinical injuries. Hence, it would be important to determine the cause of those injuries. An example was raised where a vehicle steps over an IED; the vehicle flips over but there is no hull breach. The threat was the IED but the mechanism of an observed brain injury would be blunt impact, not overpressure. This illustrates that in the absence of the proper contextual information, the wrong mechanism of injury might be attributed.

Based on the first two segments of the discussions related to identifying the types of data needed for epidemiological blast injury studies, Dr. Bieler led TT members in the development of a chart showing the linkages among the various categories of data that need to be collected in association with a blast event (Figure B-2). Notably, this scenario also applies to non-combat environments (e.g., training).

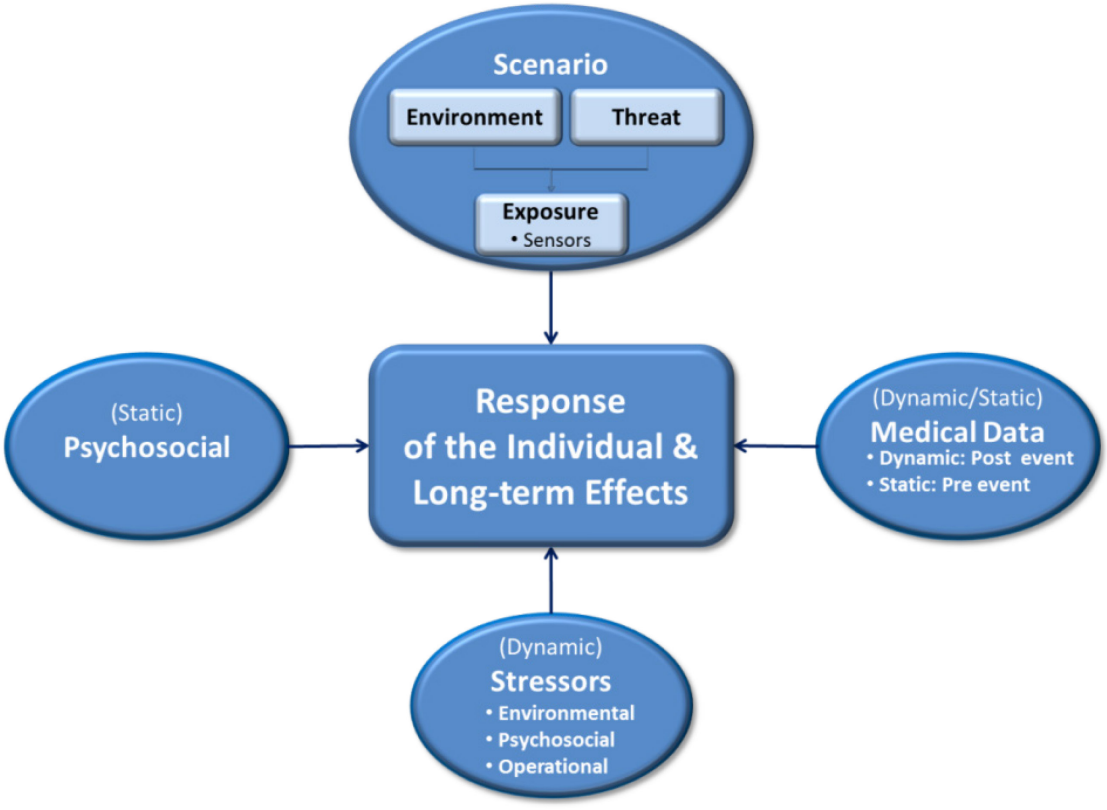

Figure B-2: Types of Data Required to Understand the Response to Blast Injury.

After the meeting, Mr. Bjarnason used Mindjet software to create another view of the relationships among the various categories of data that need to be collected in association with a blast event (Figure B-3).

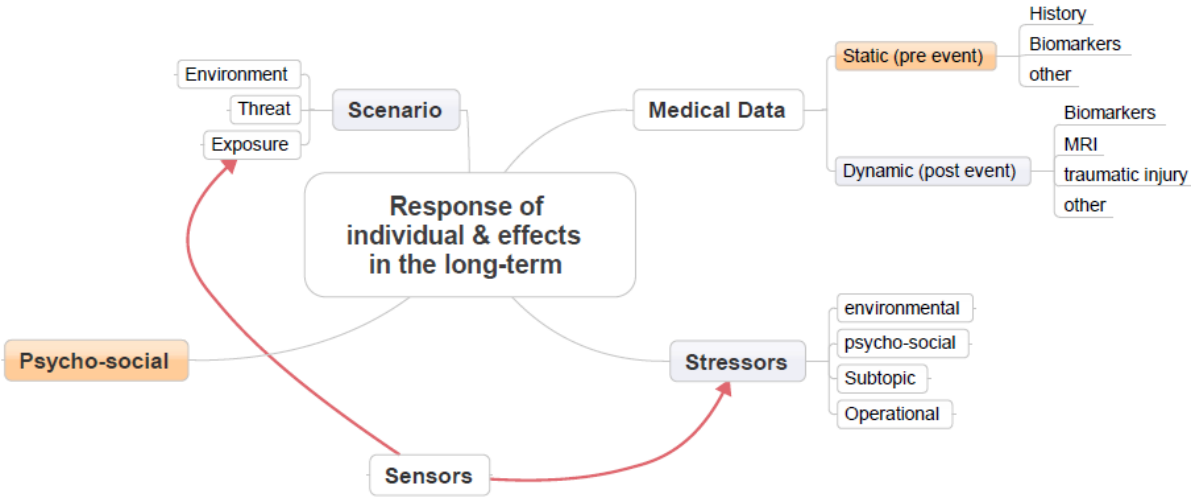

Figure B-3: Types of Data Required to Understand the Response to Blast Injury (Mindjet Version).

B.8.3 Use of Sensors

The third segment of the TT discussions related to identifying types of data needed for epidemiological blast injury studies focused on the use of sensors. The key parameters identified by TT members are summarized in the table below followed by the details of the TT discussion.

Table B-3: Parameters of Interest Related to the Use of Sensors in Blast Studies.

1) Sensors are needed to understand the real exposure.
2) Types of data needed from sensors: • Physiological status of individual. • Exposure level to stressors. • Exposure level to threat.
3) Sensors are crucial to being able to understand the response of an individual to a blast event.
4) Sensors are not limited to the effects of blast exposure, but encompass thermal and other environmental stressors.

One TT member noted that sensors help us obtain data in three key categories relevant to a blast event, including the scenario (threat and environment), the stressors (e.g., temperature and altitude) and the dynamic medical data (e.g., dynamic biological responses such as changes in heart rate and blood pressure). It was noted that the medical record is now annotated to record whether a soldier in the US who was involved in an event was wearing helmet sensors or blast gauges. TT members emphasized that besides being able to link data in the registries with measurements that are being collected with sensors, we need to determine what the sensors are measuring and what these measurements mean to the individual.

It was noted that we need to identify:

1) The important components of the scenario; and
2) The individual's response to that event.

The third step involves measuring 1) and 2) using various types of sensors (e.g., pressure and acceleration sensors). It would be advantageous to be able to also measure some of the environmental characteristics with the sensors. We would also like to know an individual's physiological dynamic response at the time of the event (e.g., measuring breathing using a physiological status monitor). It was noted that using threat and incident data from a blast event, one can effectively recreate the scenario using a manikin.

One TT member commented that one of the main issues with blast as well as other types of exposures is not being able to determine the actual source of the exposure. To understand the response of an individual to a blast event, we need to understand the real exposure. Another TT member commented that many of the exposure monitors (e.g., helmet sensors or blast gauges) use technologies that have existed for some time (e.g., accelerometers, pressure gauges). However, TT members' main concern here is the data that are obtained from the sensors rather than the sensors themselves.

One TT member noted that it depends on how well we understand an individual's immediate response to an event. For example, we need sensors that can be implanted subcutaneously and can biologically measure some of the key biomarkers of interest and show how the person's system is responding (e.g., through coagulation). Overall, it was emphasized that improvement of sensors at all levels, including the threat and the biological response, is crucial.

Besides sensors for blast exposure, we also need other types of sensors (e.g., thermal, psychological/state of mind). It was noted that there have been efforts in the US for decades to field physiological status monitors that would provide a combat medic or a leader some indication of the physiological status of an individual soldier. One TT member noted that they are measuring the various components of resilience in an attempt to use biological and epidemiological data to guide individuals toward a particular service or trade to which they would be most suited and allow tailored training for each soldier.

B.8.4 Optimizing Existing Databases for Blast Injury Epidemiological Studies

The final segment of the TT discussions related to identifying types of data needed for epidemiological blast injury studies focused on determining potential ways to optimize databases for these types of studies. The key ideas generated by TT members are summarized in the table below, followed by the details of the TT discussion.

Table B-4: Recommendations for Optimizing Existing Databases for Blast Injury Epidemiological Studies.

1)	Accurately reflect blast injuries in existing coding systems and databases: • Include data from sensors. • Include code for *cause of injury or the threat (Need mechanism of injury).* • Include detailed wound mapping (e.g., entry and exit data, trajectory).
2)	Share the lessons learned in designing the databases.
3)	Establish a NATO-level process for analyzing and sharing blast injury data that includes medical, intelligence, and operational information. Examples include JTAPIC (US), CAPSAC (Canada), and Casualty Analysis (UK).

4)	Maintain all existing databases and data analysis processes, and continue to invest in them.
5)	Expand existing databases to include information about injuries from occupational exposures to blast, including physical and mental health impairments.

Dr. Gupta began the discussion by commenting that the countries use different databases, which are subject to governmental requirements. He noted that the goals are to compare the similarities and differences in the databases used by the various countries in an effort to develop epidemiological guidelines, and to determine what to do with the existing databases. He felt that it would be beneficial if we could share information from each database while conducting epidemiological studies. One TT member noted that we need to examine the *structures* of the databases. Another TT member commented that we should determine how to optimize existing databases for capturing blast injury epidemiological data. A suggestion was made to define three or four parameters commonly observed with blast injury, and have each nation include these parameters in their existing databases. It was noted that we currently have no biomarkers that automatically confirm blast injury, which makes it difficult to include such parameters. A recommendation was made to capture information in the databases on whether or not sensors were worn at the time of injury, which would aid future analyses. Overall, TT members emphasized the importance of maintaining continued investments in all of the databases, regardless of whether a country is at war or not.

TT members spent some time discussing the need for sharing information across countries and obstacles related to the sharing of databases. Dr. Martineau commented that operational injury patterns are now being shared among nations as one of the activities of The Technical Cooperation Program (TTCP), Technical Panel 5 Personnel Vulnerability and Survivability (Mounted and Dismounted), which involves Australia, Canada, New Zealand, United Kingdom, and the US. However, it took two years to develop the framework that allowed the sharing of the operational injury patterns and lessons learned. TT members highlighted a few reasons for sharing data. One TT member mentioned the need for boosting the "n" number (sample size). Another TT member felt that to achieve pattern recognition of types of injuries based on types of weaponry used by certain terrorist groups; a critical mass of information is needed that is difficult to obtain without combining data from multiple countries. Instead of simply sharing data among countries, Mr. Leggieri questioned whether it may be more important to share *analyses* of the data. He noted that before the JTAPIC program started, the DoD considered developing a large database that would include data from the operational and medical communities. However, they found that merging these databases does not work. A suggestion was made to model a NATO-level process, modeled after JTAPIC and other related efforts, for analyzing and sharing blast injury data that includes medical, intelligence, and operational information.

It was noted that the manner in which injuries are coded in the current system of ICD codes does not capture all of the blast-related injuries. While it would be optimal to accurately reflect blast injuries in the ICD coding system, it was felt that a more feasible goal might be to try to accurately reflect blast injury in the existing databases. One TT member noted that none of the coding systems identify the cause of injury, which is important information to know. Thus, besides continuing to use the current codes for capturing the anatomical classification of injuries, a new code could be added that identifies that the injury was caused by blast. There was some concern that providing a specific code for the cause of injury will lead to incorrect speculations on the mechanism of injury. It was noted that in the US there is a separate code for mechanism of injury, and this information is coded based on the best judgment of the attending physician. Basically, a forensic analysis is conducted in which numerous sources of data (e.g., medical, operational) are used to draw a conclusion about what happened.

Dr. Martineau commented that they have developed a virtual capability in the CASPEAN database that traces the trajectory or path of a fragment through the body, which will help ensure that no injury-related data are overlooked. For example, a blast-related thoracic injury normally receives just one code. Meanwhile, the virtual injury path generated by injury-related information in the database would provide an indication of the full extent of the damage to the body, without affecting the calculation of the ISS (Injury Severity Score) or NISS (New Injury Severity Score). One TT member noted that blast injury is often associated with a multi-organ response, and medics treating affected individuals often focus only on their specialty areas. Therefore, the virtual capability would help to ensure that nothing important is overlooked in the clinic. TT members felt that multiple coding systems could be used when performing the wound mapping associated with the creation of this virtual injury path.

B.9 RECOMMENDATIONS FOR BLAST INJURY EPIDEMIOLOGICAL STUDY DATA COLLECTION GUIDELINES

The final discussion session of the meeting focused on identifying what TT members would like in an optimal blast injury epidemiological study (i.e., the essential questions that would allow biological response to be linked to a defined threat). TT members also briefly discussed issues related to data management during this session.

B.9.1 Development of Recommendations for Blast Injury Epidemiological Study Data Collection Guidelines

It was noted that existing trauma registries do not contain data that provides definitive information about an event, which necessitates the design and execution of a prospective study. The study must examine to some extent the progress and development of a potential disease or pathological factor or the response to blast. A retrospective study (e.g., observational or phenomenological) involving data analysis based on medical history documentation *can* be used to identify certain components of importance *if* a full set of well-defined data exists for a focused hypothesis. However, researchers still need to conduct a prospective study to validate in real time what was observed in the retrospective study.

While prospective studies are optimal, we may not have the luxury to conduct these types of studies in the future due to military drawdowns. However, the military departments are expected to continue to test artillery in a training environment. Therefore, it was felt that researchers should use the training environment to prospectively address challenging blast research questions to guide the finalization of the protocols**.** Any lessons learned from epidemiological studies conducted in a training environment can be operationalized. However, there are differences between the training and deployed environments that need to be considered. For example, moderate to severe injuries and hemorrhage are rare in the training environment. In addition, individuals have a different mindset in deployment versus training, which may affect how they react to physiological stressors.

One type of injury that can occur in both the training and deployed environment and has been a major issue for the military is repeated low intensity blast exposures that do not immediately cause problems but can cause concussions or mild traumatic brain injury (mTBI). It was noted that the vague symptomology associated with this type of injury and the unclear relationship between exposure and outcome was the driving force for the development of this Technical Team. The biological response to this injury can be addressed and validated in a prospective manner in an epidemiological study in a basic training (standardized) environment (e.g., Breacher studies). However, a deployed environment would need to be used if operational stressors have been found to aggravate and worsen the primary blast-induced problems.

Overall, TT members felt that researchers need to conduct prospective longitudinal studies with well-defined populations and the inclusion of a control group to elucidate the response of an individual to a blast event. In general an epidemiological study is based upon a detailed study proposal or protocol, in which the study elements are defined. The proposal or the protocol is a compilation of the most important information necessary for the implementation, application and evaluation of the study. They recommended that the epidemiological studies include, at a minimum, the framework elements outlined in the following table.

Table B-5: Framework for Blast Injury Epidemiological Study Data Collection Guidelines.

Framework Elements	Notes
Well-defined research question	Most epidemiological researchers focus on infectious diseases or occupational studies. Some epidemiological researchers have conducted trauma or injury studies, but not from the blast injury perspective.
Focused hypothesis	This needs to be defined prior to beginning the study. Example hypothesis: People who have weaker biological resilience develop faster blast-induced neurological deficits.
Military relevance	
Well-defined, detailed protocol including study design	Prospective longitudinal studies can be very expensive and resource intensive. With a well-defined protocol, researchers can measure something with the same information value using less expensive technologies and methodologies. Having a solid understanding of what you are measuring can help save money.
Target population and sampling methods	To test some hypotheses, it can be difficult to obtain an adequate control group in an operational environment.
Identify biases and limitations	This includes any types of biases, either intentional or unintentional.
Define all variables and study size	Example: Dependent variables such as measurement and survey methods; Independent variables such as risk factors, etc.
Document survey instruments and operational procedures	
Data collection, management and documentation	For details see *Data Management for Epidemiological Studies* section below.
Analysis phase	We need to use scientific knowledge to establish linkage between injury and threat/exposure, and statistics or tools to detect correlations and relationships between the different elements.
Biological sample bank (tissue, body fluids, biomarkers)	This requirement is specifically recommended for blast injury studies due to the need to collect such samples in these studies.
Quality assurance	
Ethics	National and NATO rules/regulations governing human use, consent forms, protection of privacy, etc.

The guidelines define the framework within which epidemiological studies can be used to its fullest extent. In the US, the elements of the framework listed above are usually defined and explained in the proposal or the protocol before a review process can be initiated. It was noted that the framework elements are similar to those found in Institute of Medicine studies.

B.9.2 Data Management for Epidemiological Studies

Most epidemiological studies involve multiple individuals gathering data at multiple sites. Therefore, data management is an important issue. The integrity of the data must be maintained. It was felt that it should be the Principal Investigator's (PI's) responsibility to ensure the data is collected and prepared appropriately for the database (e.g., de-identification of personal information).

For studies that involve a single PI and single institution, the following actions typically occur:

- Assignment of a bar code to the individual – identifies person from beginning to end of study [The consent form is the only hard copy that links the individual to his/her bar code, and that is in the PI's safe.].
- Demographic data is together with the consent forms, so the PI is the only person preparing and analyzing these data.
- All self-reported and other data are bar coded; data entry occurs through the bar code.
- Data entries are completely scrubbed (de-identified, etc.) so people never see any identifiable information.

The TT recommended using the data management process outlined above for training studies, but not for NATO studies involving numerous nations. The protocol best suited to a particular study should be identified in each case.

B.10 NEXT MEETING – LABORATORY BLAST EXPOSURE CONDITIONS

Mr. Bjarnason discussed plans for the next HFM-234 meeting, which is tentatively scheduled for May 20-22, 2014, at the DRDC Suffield Research Centre, in Medicine Hat, Alberta, Canada. TT members discussed the meeting goal, which they recommended revising to "develop laboratory guidelines for producing militarily relevant blast exposure conditions." Mr. Bjarnason noted that the first day of the meeting will focus on background information related to blast, including numerous presentations by experts. TT members emphasized the need to cover the pros and cons between the different types of shock tubes during this session. Considering the individuals who will be invited to speak, TT members anticipate lively discussions. They felt it would be good to hear what will likely be conflicting information and compare the results from the different experiments. The need for continuous feedback between the field and the laboratory was noted.

The second day will feature a tour of the shock/blast tube facilities at DRDC Suffield Research Centre, and the initiation of guidelines development discussions. On the third day, TT members will conclude the guidelines development discussions and work on producing the first draft document of the guidelines. TT members seemed pleased with the proposed agenda. They considered the possibility of holding the HFM-234 meeting after the HUM TP-12 meeting, which is scheduled for the first week of May 2014. A final decision on the meeting date will be made in the near future.

B.11 ACTION ITEMS / TASKING

The following actions/tasking were made at the conclusion of the meeting:

1) Dr. Cernak will send the current draft of the blast injury Dictionary of Terms to TT members by December 15, 2013. TT members should provide Dr. Cernak with their input no later than March 1, 2014 (sooner if possible) − Working Group to review and present a revised draft of the Dictionary of Terms at the next HFM-234 meeting in May 2014.
2) Dr. Gupta will post the meeting presentations, France's G3 form, and the data collection form from the highlighted CDMRP study on the group's SharePoint site.
3) Dr. Gupta will post the JTAPIC data collection slides and the DoD trauma registry Excel spreadsheet on the group's SharePoint site pending official approvals to do so.
4) Dr. Gupta will confirm Dr. Martineau's official appointment as an alternate member with Ms. Danielle Pelat.
5) Dr. Gupta will distribute the first draft of the meeting report/summary to TT members by January 31, 2014. TT members should provide Dr. Gupta with input no later than April 1, 2014.
6) Mr Stephen and Dr Gupta to explore funding resources available for HFM-234 workshops with LtCol Verkerk / Ms. Danielle Pelat.
7) Dr. Gupta to coordinate with Dr. Sarron for posting of Frances's G3 form ("Injury with Firearms or Explosives") and the NATO Standardization Agreement 2231 form ("Patient Management System Common Core Information") on the HFM-234 SharePoint site.

B.12 LIST OF ATTENDING NATIONS

Canada, France, Germany, Netherlands, Sweden, United Kingdom and the United States.

B.13 APPENDICES

B1 − HFM-234 Technical Team Members.

B2 − HFM-234 December 2014 Meeting Final Revised Agenda.

B.14 REFERENCES

[1] Breeze, J., Allanson-Bailey, L.C., Hunt, N.C., Delaney, R., Hepper, A.E. and Lewis, E.A., 2015. Using computerised surface wound mapping to compare the potential medical effectiveness of Enhanced Protection Under Body Armour Combat Shirt collar designs, J R Army Med Corps. Mar;161(1):22-6.

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[3] Theeler, B.J., Flynn, F.G., Erickson, J.C., 2012. Chronic daily headache in U.S. soldiers after concussion. Headache 52, 732-738.

Appendix B1: HFM-234 TECHNICAL TEAM MEMBERS (AS OF 12 DECEMBER 2014)

Name	Nation	Email
Mr. Michael Leggieri (Chair)	United States	michael.j.leggieri.civ@mail.mil
Maj Dr. Dan Bieler	Germany	dr.dan.bieler@t-online.de
Mr. Stephen Bjarnason	Canada	stephen.bjarnason@drdc-rddc.gc.ca
Dr. Ibolja Cernak	United States	cernak@ualberta.ca
Dr. Raj Gupta	United States	raj.k.gupta.civ@mail.mil
Dr. Emrys Kirkman	United Kingdom	ekirkman@dstl.gov.uk
Dr. Lucie Martineau*	Canada	lucie.martineau@drdc-rddc.gc.ca
Dr. Hans Orru	Estonia	hans.orru@ut.ee
Mr. Mat Philippens	Netherlands	mat.philippens@tno.nl
Mr. Simon Ouellet	Canada	simon.ouellet@drdc-rddc.gc.ca
Dr. Marten Risling	Sweden	marten.risling@ki.se
MC Jean-Claude Sarron	France	jean-claude.sarron@intradef.gouv.fr
Mr. Stian Skriudalen	Norway	stian.skriudalen@ffi.no
Mr. Jan Arild Teland	Norway	jan.teland@ffi.no
Dr. Sarah Watts	United Kingdom	sawatts1@dstl.gov.uk
Maj Dr. Arnulf Willms	Germany	arnulfwillms@gmx.de

*Alternate Member.

Appendix B2: HFM-234 DECEMBER 2014 MEETING FINAL REVISED AGENDA

Tuesday 10 December, 2013		
0830	Snow Emergency – Ft Detrick Closed	
1900	Dinner	TM

Wednesday 11 December, 2013		
0830	Welcome	Mr. Leggieri
	Individual Introductions	Technical Team Members (TM)
	Administrative announcements	Ms. Mohney/Gupta
0835	Status Update: Blast Injury Dictionary of Terms	Dr. Cernak
	Presentations by TM Members or representatives*	
0915	Canada − Current guidelines and types of data being collected	Mr. Bjarnason/ Dr. Martineau
0947	France − Current guidelines and types of data being collected	Dr. Sarron
1000	Break	
1015	Germany − Current guidelines and types of data being collected	Dr. Bieler
1030	Netherlands −Current guidelines and types of data being collected	Mr. Philippens
1032	Sweden − Current guidelines and types of data being collected	Dr. Risling
1050	United Kingdom − Current guidelines and types of data being collected	Dr. Watts
1130	United States − Current guidelines and types of data being collected	Dr. Gupta
1215	Norway − Current guidelines and types of data being collected	Dr. Gupta
1220	Lunch	
1310	Recent Blast Injury Study-Canadian Soldiers	Dr. Cernak
1355	How blast wave ambush the brain (Temporal profile of Outcome Measures)	Dr. Cernak
*All presentations limited to 45 Min.		

Wednesday 11 December, 2013 (cont.)		
1520	Break	
	Presentations by TM Members or representatives* (cont.)	
1545	High Level overview of Sensors	Mr. Philippens
1605	Discussion Items 1: Define parameters of interest to track initial exposure	TM
*All presentations limited to 45 Min.		

Annex C − DICTIONARY OF BLAST INJURY RESEARCH TERMS

C.1 INTRODUCTION

The discussions at the NATO Health Factors and Medicine (HFM) Symposium (SYM) HFM-207 revealed the importance of a systematic approach to understanding blast injuries, much like the well-established approach used to solve the classical toxicology problem where the etiology of the injury requires an understanding of the dose, mechanism of delivery of the dosage, and dose-response endpoints. Also recognized was the pressing need for a multidisciplinary approach to addressing non-penetrating blast injuries to the brain that result in a host of symptoms with vague etiology. In addition, the Technical Evaluation Report from HFM-207 (SYM), "A Survey of Blast Injuries across the Full Landscape of Military Science" [279] emphasized the continued multinational exchanges of scientific and technical advances needed to respond to blast threat and blast injuries. The first recommendation identified a future need for a recurring technical exchange venue on blast injury and its mitigation to address advances in medicine and personal protection and their synergy. The second recommendation highlighted the need to explore the concept of "the Toxicology of Blast Injury" and suggested to focus on several difficult problems including:

1) Relevancy and commonality of animal models.
2) Common dose-response methods.
3) Route of exposure methods.
4) Computational Models (blast, physiology, biochemical, toxicological, etc.).
5) Dose regimens to mimic/replicate human medical endpoints (spectrum of surgical trauma to mild traumatic brain injury).
6) Methods for translational research leading to medical products and/or physical protection products.

To address the above recommendation and to develop a specific NATO activity devoted to the toxicology of blast exposure, a proposal titled "Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods and Standards" was approved which resulted in the establishment of a NATO HFM Research Task Group (RTG) HFM-234 with the following deliverables:

- Guidelines for Conducting Epidemiological Studies of Blast Injury.
- Guidelines for Reproducing Blast Exposures in the Laboratory.
- Guidelines for Using Animal Models in Blast Injury Research.
- Dictionary of Blast Injury Terms.
- Final report on HFM-234 (RTG) activities.

These guidelines are intended to provide blast injury researchers and clinicians with a basic set of recommendations for blast injury epidemiological study design and data collection that need to be considered and described when conducting prospective longitudinal studies of blast injury. It is not the intention of these guidelines to prescribe how to design and conduct prospective longitudinal studies of blast injury but to provide an awareness of what needs to be taken into account, observed, recorded, and collected. Following these guidelines and reporting blast injury epidemiological studies in a consistent manner allows for reliable comparisons to be made between studies regardless of the study environment. Clearly stated, the objectives of this document are:

1) To raise awareness with regards to the complexities and pitfalls of blast injury research.
2) To standardize and promote good research practices.
3) To help the community to generate valid and comparable results.
4) To increase the quality of publications in this field of research.

It is the intention of the HFM-234 (RTG) that these guidelines be used in concert with the companion comprehensive "Dictionary of Blast Injury Research Terms" developed by the NATO HFM-234 (RTG). These guidelines and the Dictionary can be used in conjunction to guide research methods and reporting in the field of experimental blast injury research.

C.2 BACKGROUND

The complexity of blast injuries presents enormous challenges to the biomedical and engineering research communities who are responsible for developing effective strategies to protect service members from injury, and to treat and rehabilitate those who are injured. Lessons learned in recent conflicts highlight the critical importance of communication and collaboration across these diverse communities and disciplines to address complex blast injury challenges. However, long-standing communication barriers have impeded the cross-community collaboration necessary for the timely development and fielding of innovative blast injury prevention, mitigation, and treatment solutions.

A significant barrier to effective communication is the lack of a common vocabulary of blast injury research terms. Often, a single blast injury research term may have more than one meaning. For example, the term "blast injury" is often used to describe those injuries resulting from exposure to blast overpressure, or the primary blast injury mechanism. However, the same term may also be used to describe the range of injuries resulting from exposures to the entire spectrum of blast injury mechanisms, primary through quinary. The use, misuse, or misinterpretation of blast injury research terms causes confusion and stifles effective collaboration.

Recognizing the need for a common vocabulary of blast injury research terms to improve communication and facilitate cross-community collaboration, the NATO HFM-234 (RTG) Technical Team developed this comprehensive Dictionary of Blast Injury Research Terms. This dictionary provides a common vocabulary that will help to eliminate confusion, improve information sharing, and facilitate collaboration across diverse research communities and disciplines.

C.2.1 Methodology

The HFM-234 (RTG) Technical Team established a Working Group that initially created a data base of key blast injury research terms and developed a dictionary structure with contributions by all Technical Team members over the course of the three-year term of the HFM-234 (RTG). The Working Group identified biomedical and engineering definitions for each term, and recommended the definition that was most relevant to blast injury research. Additional terms were identified and definitions were added throughout the proceedings of the HFM-234 (RTG) workshops using several sources such as text books and peer reviewed literature. The source of each definition has been cited, and where appropriate, both medical and engineering definitions have been included.

C.3 DICTIONARY TERMS

C.3.1 Acoustic Barotrauma

- Barotrauma refers to injury sustained from failure to equalize the pressure of an air-containing space with that of the surrounding environment. The most common examples of barotrauma are caused by noise, blast, during air travel, or scuba diving [136], [232], [233].
- Acoustic barotrauma may include the following:
    1) Tympanic membrane rupture (most common);
    2) Hemotympanum (i.e., presence of blood in the tympanic cavity of the middle ear) often without perforation of the eardrum;
    3) Ossicle fracture or dislocation;
    4) Perilymph fistula or forceful distribution of squamous epithelium around air filled spaces with potential to form cholesteatoma [15], [100], [133], [259];
    5) Damage to Corti organ [164]; and/or
    6) Obstruction of the Eustachian tube [147].
- Symptoms of acoustic barotrauma include "clogging" of the ear, ear pain, hearing loss, dizziness, ringing of the ear (tinnitus), and hemorrhage from the ear [228].
- Dizziness (or vertigo) may also occur during diving from a phenomenon known as alternobaric vertigo. It is caused by the difference in pressure between the two middle ear spaces, which stimulates the vestibular (balance) end organs asymmetrically, thus resulting in vertigo [163], [182].

C.3.2 Airburst

An explosion of a bomb or projectile above the surface as distinguished from an explosion on contact with the surface or after penetration [279].

C.3.3 Air Pressure

- The pressure at the point of interest in the air.
- Related term(s): Pressure.

C.3.4 Ambient Pressure

- The pressure in an undisturbed environment at the point-of-interest.
- The static pressure in undisturbed (stable) environment at the point-of-interest. Related term(s): Atmospheric Pressure.

C.3.5 Animal Holders for Blast Injury Research

- The specimen holders are designed to secure the animal safely and firmly in a desired position at an assigned location within the blast field. The choice of the animal holder is a crucial component in shock/blast tube

experiments. Namely, if the animal is fixed on a solid platform, the waves reflected from the solid platform will amplify the primary shock wave and increase the complexity and severity of blast injuries. Thus, if the research aim is to analyze the primary blast-induced injuries, it is recommended that a mesh-type animal holder which causes a minimum reflection be used [35], [36], [42].

- It is also essential that the animal holder *per se* remains steady during the passage of the pressure wave, and does not move in relation to the shock tube or to the animal; otherwise, acceleration of the holder and/or the animal may introduce tertiary blast effects. On the other hand, movement of an animal holder made of a sturdy material (metal or Plexiglas) might bruise the animal [165].

- Moreover, a bulky animal holder when placed inside the shock tube could obstruct the central flow of the shock wave and contribute to nonhomogeneous field conditions as described above. Unfortunately, the majority of shock tube systems currently in use, use large and complicated animal holders comprised of metal frames and attached (usually Plexiglas) containers to restrain the animal. Placed inside the shock tube, the combination of metal frame / container obstruct an overwhelming proportion of the area open to free flow; consequently, the animal is exposed to unsteady shockwave conditions [197], [206].

- Often, the experimental set-up incorporates multiple mistakes with respect to the size and type of the animal holder, as well as, positioning the animal both in relation to the animal holder and the shock wave. For example, an experimental set-up that [101]:

    1) Uses an animal holder that is too large for the shock tube and placed near the shock tube's exit.
    2) Places the animal inside the animal holder so that only its neck and head are outside of the Plexiglas container with neck tightly surrounded by the container's edge.
    3) Positions the holder so that the incident pressure is perpendicular to the animal's neck, exposes the research target to:
        a) Unstable flow with probable turbulence caused by > 30% of blockage and enhanced dynamic pressure due to its close proximity to the shock tube's exit;
        b) Increases the probability of a compression on the animal's neck caused by the movement of the animal or the container during the shock wave propagation; and
        c) Creates a scenario for maximum reflection pressure and forceful head movement with a high probability of a head impact with the container's rim [165].

C.3.6 Animal Size-Scaling for Blast Injury Experiments

When modeling human injuries using experimental animals, real-life scenarios should be used as guidance. Currently, the most frequent blast environments are generated by Improvised Explosive Devices (IEDs) and typical munitions such as the rocket propelled grenades, among others, where the positive durations at the pressure levels for human injury range from 1 to 10 milliseconds. A typical, low-intensity blast wave travels at a little more than 1 foot per millisecond, whereas one millisecond is approximately the time that it takes for the shock wave to engulf an erect human. Accordingly, the range of adequate exposure durations should be defined as the time necessary to engulf the target up to 10 times of that duration [165], [206]. The cube-root mass scaling law established by Bowen and colleagues to predict blast-induced lung injuries [23] would translate a 70 kilogram human exposure of 13 milliseconds duration to a 1 millisecond exposure of a 30 gram mouse. For example, in a blast-head scenario, for a given blast, when calculating the net loading scales for cross-sectional area of the skull, even if other parameters would be identical, a specimen 20-fold the size would experience 20-fold less acceleration for the same blast [165], [206]. Hence, if the experiments plan to use mice

as research targets, the total positive duration of the exposure should not exceed 1 millisecond for both the overpressure and the dynamic pressure. On the contrary, if the mouse as a research target is loaded for a duration of 10 milliseconds (which is often a case in many current shock tube experiments), it would translate into a human equivalent of 100 milliseconds exposure, which is 10-times longer than the maximum duration of a reasonable IED blast event giving an effective yield of explosion that has 1,000 times more energy than it is expected in in real-life scenarios [165].

C.3.7 Atmospheric Pressure

- Preferred term: AMBIENT PRESSURE.
- Related term(s): Pressure, Standard atmospheric pressure.

C.3.8 Apnoea or Apnea

Cessation of breathing.

C.3.9 Arena

Site of an open-field experimental set-up.

C.3.10 Arrival Time

The temporal spacing between the generation of a pressure disturbance (for example by an explosive detonation) and its propagation to the point of interest.

C.3.11 Auditory Blast Injury

- Blast injury that involves auditory organs including the external, middle and internal ears [89].
- The distinction between impulse noise and blast is arbitrary but the following criteria are useful in defining blast [97]:
  - Peak overpressures from a blast are often of tens of kilopascals, while in impulsive noise they are usually less than 2 kilopascals.
  - Blast waves involve the movement of considerable volumes of combustion products and air.
  - Impulsive noise often contains low-frequency mechanical clatter.
- Thirty three percent of injuries are associated with ossicular injury, which does not occur in the absence of tympanic disruption. Cholesteatoma from embedded squamous debris is a long-term complication occurring in up to 12% of blast-perforated ears, dictating long-term follow up [100], [133], [134], [212], [259]. Associated ossicular injury is a feature of more severe blast injury in as many as a third of reported cases [78], [155]. Sensorineural hearing loss associated with a high-pitched tinnitus frequently occurs immediately following a blast [130], [227]. Hearing loss may resolve in hours or may become permanent in greater than 50% of patients, as has been reported in some series [82], [161].
- Immediately after blast exposure, the auditory blast injury manifests with high-frequency sensorineural hearing loss (78%), mixed hearing loss (19%), and low-tone conductive hearing loss [163]. While conductive hearing loss had improved by one year, the cochlear hearing loss, in most cases, did not. Only 7% of the patients with tinnitus reported improvement after one year [89], [96].

- Although not a priority for treatment, auditory injury should be addressed within 24 hours and auditory canal(s) cleaned of all debris. Perforation in the antero-inferior part of the pars tensa of the eardrum is the most common manifestation of tympanic injury. Fifty to 80% of ruptured tympanic membranes will heal spontaneously without further treatment [125], [174], [238], [239]. Nevertheless, antibiotic therapy has been shown to facilitate the healing of the tympanic membrane without scars and adhesions, and reduce the incidence of persistent perforation of the tympanic membrane. Early cleaning of margins, reposition of lacerated fragments of the tympanic membrane, and removal of haemorrhagic exudate have also been recommended to prevent posttraumatic complications in the middle ear, Myringoplasty should be performed if spontaneous healing of tympanic membrane did not occur after 6 months [72], [238].
- The first medical writer to mention the effect of blast trauma to the ear was the French military surgeon Ambroise Paré (1510 – 1590):

  "*Isn't it a great thunderous noise, large bells or artillery, and thus one often sees gunners losing their hearing whilst drawing the machinery because of the great agitation of the ear inside the ear which breaks the aforementioned membrane and moves to the bones known as ossicles out of their natural position: so that the air is implanted or absorbed within the sinuses of the mastoid cavity (called by some the "tambourin") and the patient has a continuous noise and air within the ear.*" [162], [181], [213]

C.3.12 Autonomic Nervous System (ANS)

- The ANS is a division of the peripheral nervous system that influences the function of visceral organs, effectors in the skin, and the cardiovascular system. The effectors controlled by the ANS are not under overt voluntary direction and include all neurally-regulated tissues and organs, other than the striated muscles of the limbs, trunk, head and neck [154].
- The autonomic nervous system has two branches: the sympathetic nervous system and the parasympathetic nervous system. The ANS supplies each type of target organs via separate pathways, which consist of sets of pre- and postganglionic neurons with distinct patterns of reflex activity [252].
- Acute and chronic activation of ANS by blast exposure have been shown in experimental studies [34], [45], [117], [173].

C.3.13 Barotrauma

- Barotrauma refers to injury sustained from failure to equalize the pressure of an air-containing space with that of the surrounding environment. The most common examples of barotrauma are caused by noise, blast, during air travel or scuba diving [136].
- Barotrauma typically occurs when the organism is exposed to a significant change in ambient pressure, such as when a scuba diver, a free-diver or an airplane passenger ascends or descends, or during uncontrolled decompression of a pressurized vessel, but can also be caused by a shock-wave [3], [76], [116].
- Trauma caused either by overpressurization or by underpressurization relative to atmospheric pressure [116].
- The numerous possible clinical manifestations of barotrauma include: pneumothorax, pulmonary interstitial emphysema (pie), subcutaneous emphysema, pneumoperitoneum, pneumomediastinum or pneumopericardium, air embolization, tension lung cysts, and hyperinflated left lower lobe [116].

C.3.14 Baker-Strehlow-Tang Blast Curves

The Baker–Strehlow–Tang blast curves are constructed as scaled blast wave properties versus scaled distance and are presented as families of curves with the flame Mach number as the parameter. The flame Mach number is the apparent flame speed divided by the ambient sound velocity. The blast properties and the distance are in non-dimensional coordinates [188]. According to Sach's scaling, the following non-dimensional parameters are used in Baker-Strehlow–Tang blast curves [14], [193], [241]:

$$\overline{P^+} = \frac{p^+_{\max} - p_0}{p_0} \qquad \overline{P^-} = \frac{|p^-_{\max} - p_0|}{p_0}$$

$$\overline{I^+} = \frac{i^+ a_0}{E_t^{1/3} p_0^{2/3}} \qquad \overline{I^-} = \frac{i^- a_0}{E_t^{1/3} p_0^{2/3}}$$

$$\overline{t^+} = \frac{t^+ a_0}{(E_t/p_0)^{1/3}} \qquad \overline{t^-} = \frac{t^- a_0}{(E_t/p_0)^{1/3}}$$

$$\overline{t_a} = \frac{t_a a_0}{(E_t/p_0)^{1/3}} \qquad \overline{U} = \frac{u_{\max}}{a_0}$$

$$\overline{R} = \frac{R}{(E_t/p_0)^{1/3}}$$

where $\mathbf{p_0}$ is atmospheric pressure; $\mathbf{a_0}$ is the sound velocity at ambient conditions; $\mathbf{p^+_{max}}$ is the maximum of positive peak absolute pressure; $\mathbf{p^-_{max}}$ is the maximum of negative peak absolute pressure; **R** is the stand-off distance; E_t is the total energy release from the explosion source; $\mathbf{i^+}$ is positive specific impulse; $\mathbf{i^-}$ is negative specific impulse; $\mathbf{t^+}$ is time duration of positive phase; $\mathbf{t^-}$ is time duration of negative phase; $\mathbf{t_a}$ is the arrival time of wave front; and $\mathbf{u_{max}}$ is the maximum of flow velocity.

C.3.15 Bezold-Jarisch Reflex

- The Bezold-Jarisch reflex is an eponym for a triad of responses (apnea, bradycardia, and hypotension) following intravenous injection of veratrum alkaloids in experimental animals [11]. The observation was first reported in 1867 by von Bezold and Hirt, and confirmed in 1938 – 1940 by Jarisch [145]. The triad depends on intact vagus nerves and is mediated through cranial nervous medullary centers controlling respiration, heart rate, and vasomotor tone. The respiratory effects are mediated through pulmonary vagal afferents and the bradycardia and vasodepression through cardiac vagal afferents [28].

- Pressure receptors in the wall and trabeculae of the left ventricle respond to decreased intracardial volume by activating high-pressure C-fiber afferent nerves to nucleus tractus solitarri. This in turn triggers paradoxical bradycardia and decreased contractility, resulting in additional and relatively sudden arterial hypotension. Originally, this phenomenon was described by von Bezold as a bradycardia reaction to acetic acid veratril in the cardiac pacemaker region. At the same time, Jarisch identified the reaction as chemoreceptor reflex via the vagus nerve, relayed in the nucleus tractus solitarii [118].

- It has been assumed that a sudden increase in the left ventricle due to the blast-induced shock wave passage across the body triggers the Bezold-Jarisch reflex causing sudden bradycardia and even cardiac arrest after blast exposure [42], [45], [49].

C.3.16 Blast

- Blast is the process by which the energy of an explosive event propagates into its surrounding environment, then loads and damages materials, structures, and systems.
- A brief and rapid movement of air, vapour, or fluid away from a center of outward pressure, as in an explosion or in the combustion of rocket fuel; the pressure accompanying this movement. This term is commonly used for "explosion", but the two terms may be distinguished. [279]
- Blast is one of the products of the explosion; it can be defined as a region of highly compressed gas that rapidly expands to occupy a volume several times greater than that of the original explosive, the solid residues from the explosive, or its casing [41]. The blast wave, a sphere of compressed and rapidly expanding gases, travels faster than sound from the source (thus center) of the explosion, displaces an equal volume of surrounding air at high velocity, and subsequently compresses it [211]. This is the **overpressure phase** of the blast wave, which is followed by a short period of negative pressure, so called **underpressure phase** [176].
- Related term(s): Blast wave, Primary Blast Injury.

C.3.17 Blast Bioeffects

The wave of air pressure produced by the detonation of high-explosive bombs or shells or by other explosions; it causes pulmonary damage and hemorrhage (lung blast, blast chest), laceration of other thoracic and abdominal viscera, ruptured eardrums, and effects in the central nervous system [74].

C.3.18 Blast Deaths, Primary Blast-Induced

The immediate cause of death following primary blast injury, in the absence of obvious external injuries, has been the subject of much debate in the literature and a number of theories have been advocated [111], [153], [265], [272]. Beside deaths due to the total disruption of the body very close to a charge [50], [73], [123], [137] and secondary changes such as the development of Adult Respiratory Distress Syndrome (ARDS) and unrecognized gastrointestinal perforation and related peritonitis [221], [231], [255], the chief causes of death can be classified as respiratory and circulatory (cardiovascular).

C.3.18.1 Cardiovascular Causes

It has been well documented that exposure to blast wave overpressure gives rise to profound changes in the circulatory system. Generally it has been thought that death is secondary to obstruction of the pulmonary capillary bed [248]. Nevertheless, intimal tear and/or sub-intimal hemorrhage and related myocardial infarct [124], a greatly dilated right ventricle, and a pericardial tamponade in the absence of penetrating trauma have also been found post-mortem after blast [177].

Air emboli develop as a consequence of the shock wave passing through the body and organs containing media of different densities and constituent states, that is, gas – air; fluid – blood; and solid – parenchyma [36], [60]. Using an ultrasonic Doppler blood-flow detector, Nevison, Mason, and colleagues have demonstrated air emboli passing through the carotid artery in dogs subjected to blast in a shock tube [146], [167]. Interestingly, the dynamics of the air emboli release as recorded by the embolus detector showed a cyclic pattern, initially occurring over the first 10 seconds and again about two minutes and 12 minutes after the blast. It is noteworthy that the air emboli-release occurred parallel with a dramatic decrease in blood-flow velocity and tissue

convulsion likely due to hypoxia/anoxia. Similar experimental findings have been described by others [54], [60], [129] and supported by clinical studies [92], [248], [249]. It is expected that the rate of the air emboli-release is dependent on the intensity of the blast, and the subsequent changes in blood flow and oxygenation level are also graded. Indeed, a massive compressed-air embolism of the aorta and multiple air spaces in the interstitium, compressing the collecting tubules in the kidneys, [92] and venous air embolism in the lungs [248], have been reported in victims of severe blast injury. Air embolism in blast lung injury is the result of air entering the circulation through the damaged alveoli. Air is most commonly found in the coronary arteries, the left side of the heart, and in brain vessels, especially the basilar vessels and in the choroid plexuses.

C.3.18.2 Respiratory Causes

In severe pulmonary blast injury there is massive pulmonary contusion and hemorrhage into the bronchial tree. Bleeding is frequently observed through the mouth and nose [30], [67]. In animals without obstruction of the airways with blood and froth, early pulmonary pathology is not usually sufficient to account for death [129]. The development of pulmonary edema supervening on a physiological shunt through non-aerated contused lung may disturb the pulmonary gas exchange sufficiently to be incompatible with life. Clemedson [57], [59], [63] and Benzinger [20] suggested that respiratory symptoms are not the cause of death but are the consequence of the circulatory failure.

C.3.19 Blast Event

A scenario in which a rapid release of energy (for example from an explosive detonation, or pressure release) results in the generation of a blast wave.

C.3.20 Blast-Induced Neurotrauma (BINT)

- A unique, complex clinical syndrome comprised of acute and chronic neurological deficits that are caused by interwoven mechanisms of systemic, local, and cerebral responses to blast exposure [38], [45], [46], [49].
- Potential mechanisms by which blasts cause brain injury include [36], [42]:
    1) Direct interaction with the head through direct passage of the blast wave through the skull and/or causing acceleration and/or rotation of the head; and
    2) Transfer of kinetic energy from the blast wave through large blood vessels in the abdomen and chest to the central nervous system [34], [229]; namely, as the front of the blast overpressure interacts with the body surface and compresses the abdomen and chest, it transfers its kinetic energy to the body's fluid phase.

  The resulting hydraulic interaction initiates oscillating waves that traverse the body at about the speed of sound in water and deliver the kinetic energy of the blast wave to the brain. Once delivered, that kinetic energy causes both morphological and functional damage to distinct brain structures [43]. The two potential ways of interaction do not exclude each other [18]. Experimental data suggest both the importance of the blast's direct interaction with the head [214], [215], and the role of shockwave-induced vascular load [141] in the pathogenesis of BINT.
- Whereas mild BINT, in general, is induced by primary blast, moderate to severe brain injuries because of blast are part of a pol-trauma and caused by simultaneously acting primary, secondary, tertiary, and sometimes even quaternary effects of the blast [37], [42].

- Clinical data have suggested acute or chronic impairment of the central nervous system in a relatively large number of patients with blast injuries [43], [45]. Based on previous experimental investigations [45], the authors suggested the cerebral response to blast exposure are caused by biochemical and metabolic disturbances in the brain, developed as remote effects of the blast wave and modifying the primary local and general responses to injury.
- Emerging clinical imaging findings suggest that regional brain hypometabolism and abnormalities of brain white matter structural integrity and macromolecular organization may constitute a neurobiological substrate for chronic post-concussive syndrome in Iraq combat Veterans with repetitive blast-induced mild traumatic brain injury [184], [186].
- Recent experimental studies showed a temporal pattern of changes in the serum levels of protein biomarkers after a single exposure of experimental animals (mice, rats, pigs) to low-intensity blast; the results implicated oxidative stress, vascular changes, inflammation, altered cell adhesion, neuronal, and glial damage/ loss in the pathobiology of BINT. The observed temporal profiles of markers illustrated the dynamic nature of numerous molecular mechanisms related to the systemic and cerebral response to blast [5], [6], [103], [244].
- Related terms: Blast-induced Concussion; Blast Traumatic Brain Injury.

C.3.21 Blast Injury

The biomechanical and pathophysiological changes, and the clinical syndrome resulting from exposure of the living body to detonation of an explosive material [257]. Blast injuries result from explosions that have the capability to cause multisystem, life-threatening injuries in single or multiple victims simultaneously through multiple mechanisms [7], [36], [42], [74], [76], [187], [231], [250], [256], [257], [260] illustrated in Figure C-1 [42]*)* below:

1) **Primary blast injury**: caused by primary blast effects, thus solely by the direct effect of blast overpressure on tissue [41], [105], [120], [176], [187], [266].
2) **Secondary blast injur**y caused by the fragments of debris propelled by the explosion [15], [152], [245], [258], [265].
3) **Tertiary blast injury** caused by high-energy explosions; occurs when people fly through the air and strike other objects; or are hit by flying objects [153], [194], [199].
4) **Quaternary blast injuries** encompass all other injuries caused by explosion (such as thermal injury) [190], [208], [270].
5) **Quinary blast injuries** resulting from specific additives such as bacteria, radiation (“dirty bombs”) and fertilizer [131].

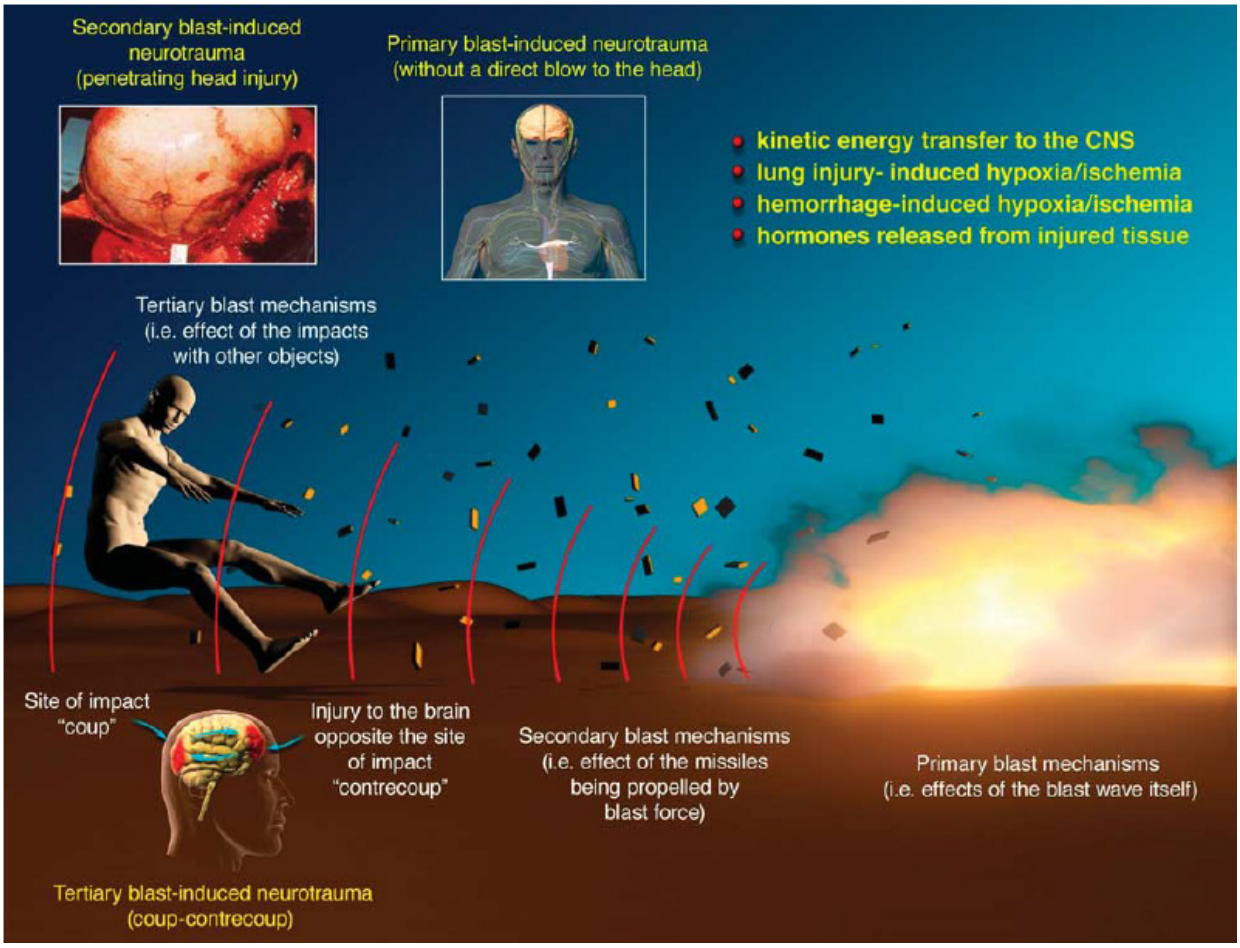


Figure C-1: Complex Injurious Environment Resulting from Blast. Primary blast effects are caused by the blast wave itself (excludes penetrating and blunt force injury); secondary blast effects are caused by particles propelled by the blast (penetrating or blunt force injury); tertiary blast effects are caused by acceleration and deceleration of the body and its impact with other objects (penetrating or blunt force [including "coup-contrecoup"] injury). [42]

The relative frequency of each type of injury is difficult to predict and depends on the quantity and type of explosive, the construction of the explosive device, the proximity of the casualty to the source of the explosion and the environment within which the charge detonates.

C.3.22 Blast Injury – Diagnosis

If the operational environment suggests a possibility of blast exposure, the examination schedule of an injured service member should include the following [43]:

1) **History and questionnaire** on subjective symptoms including the presence of deafness, tinnitus, earache, chest pain, reflex/dry cough, hemoptysis, dyspnea/tachypnea, nausea, vertigo, and retrograde amnesia.
2) **Physical examination** especially focusing on specific clinical signs that may suggest blast injury including blood secretion in the external ear/nose, cyanosis, eardrum hyperemia/rupture, chest

auscultation (few localized-to-widespread rales and rhonchi), abdomen-rigid with direct and rebound tenderness. Neurological examination testing reflex activities and response times could also be very useful, since blast exposure has been seen to cause reflex hypoactivity and increase in response times in various cognitive tests.

3) **Clinical examination**: patients with positive subjective symptoms and positive findings of blast injury by physical examination should be subjected to radiography/computed tomography, ultrasonography, and/or Magnetic Resonance Imaging (MRI) as well as audiometry and vestibular testing. Patients with moderate-to-severe blast injuries and BINT can show pathological changes in the lungs such as various degrees of infiltration, pneumomediastinum, pneumothorax, hemothorax, and pulmonary interstitial emphysema, whereas in the abdomen, gastric dilation and dilated loops of bowel might be seen. Sensorial or sensorineural hearing loss with a dip in hearing at 6,000 Hz has been suggested as an audiometric finding typical for BINT [43]. Vestibular testing confirmed a greater incidence of vestibular and oculomotor dysfunction in personnel with BINT [113]; 50% of BINT subjects with symptomatic (vestibular-like dizziness) had abnormal nystagmus or oculomotor findings revealed by videonystagmography [222]. Similarly, rotational chair testing in this group revealed evidence of both peripheral (33%) and central (17%) vestibular pathology [222].

4) **Routine laboratory analyses** including arterial and venous blood gases immediately after blast exposure, and serum biomarkers of inflammation. Namely, impaired acid-base state (decreased pH values in arterial and/or venous blood, decreased oxygen saturation) has been considered a positive finding for possible blast injury [43], [129].

C.3.23 Blast-Induced Strain Rate

Blast loads typically produce very high strain rates in the range of 10^2 - 10^4 s^{-1}. This high straining (loading) rate would alter the dynamic mechanical properties of target structures and, accordingly, the expected damage mechanisms for various structural elements both of the surrounding or a biological system (humans, animals). The figure below shows the approximate ranges of the expected strain rates for different loading conditions illustrating that while the ordinary static strain rate is located in the range: 10^{-6}-$10^{-}5$ s^{-1}, blast pressures normally yield loads associated with strain rates in the range: 10^2-10^4 s^{-1} [169].

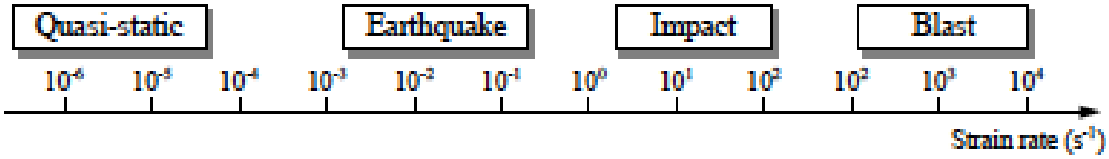


Figure C-2: Strain Rates Associated with Different Types of Loading [169].

C.3.24 Blast Loading

The loading (or force) on an object caused by the air blast from an explosion striking and flowing around the object. It is a combination of overpressure (or diffraction) and dynamic pressure (or drag) loading.

C.3.25 Blast Lung Injury (BLI)

- Generic term for pulmonary injury attributed to pressure disturbances in the media (air, water, etc.) caused by the blast kinetic energy transfer into the thorax.

- The diagnosis of BLI syndrome is based on the triad of respiratory distress, hypoxia, and the characteristic "butterfly" or "batwing" pulmonary infiltrates.
- The characteristic "batwings" or "butterfly" pattern of lung infiltrates on chest x-ray is usually present on admission and may worsen over the first few hours, especially if large-volume fluid replacement is given because of associated injuries. The central location of the infiltrates may serve to differentiate BLI from blunt injuries, which typically causes pleural-based contusion [12].
- Respiratory symptoms include tachypnea, dyspnea, cyanosis, and hemoptysis. In some patients, neurologic signs resulting from hypoxia or cerebral air emboli may be the only presenting findings. These include coma, deteriorating level of consciousness, convulsions, and focal neurologic deficits such as gaze deviation. Physical examination of the lungs may reveal decreased breath sounds and crepitations [12].
- The blast-induced contusions of the lungs show contamination of the alveoli with blood usually without parenchymal laceration [8], [27], [30], [61], [62], [67], [105], [115], [150], [230], [248].
- The contusion may range from scattered petechiae to confluent hemorrhages involving the whole lung. The contusions may be bilateral, but they are frequently confined to the lung facing the blast and they may continue to spread over the ensuing hours and days [12], [217], [236]. A physiological shunt may be established and the lung compliance will decrease, resulting in stiffer lungs and hypoxia [129], [189]. The injury may progress to Acute Respiratory Distress Syndrome (ARDS) [143] often within 24 – 48 hours with the worst of the respiratory distress and hypoxemia being seen within the first 72 hours [32], [188], [217]. Blast lung is therefore a condition that evolves (and can worsen) over a period of hours following blast exposure, i.e., a casualty who may not appear 'too bad' initially, may become critically ill later [112], [266].
- BLI is more common after closed-space explosions (e.g., bus) as compared with open-space explosions (e.g., open market) [138], [240]. Leibovici *et al.* [138] described a significantly increased prevalence of primary blast injuries in general and BLI in particular after closed-space explosions. In a study of severely injured victims of terrorist bomb attacks in Israel between 1995 and 2004, a significant difference in the prevalence of BLI have been found depending on the environment: 72% versus 24% after closed- and open-space explosions, respectively [12].

C.3.26 Blast Lung − Clinical Classification

There are many clinical classifications in the literature based on functional and morphological impairments caused by blast. Pizov and colleagues [189] have combined multiple parameters including the partial pressure of oxygen (PaO_2)/fraction of inspired oxygen (FiO_2) ratio showing the functional level oxygenation as well as the extent of lung damage, assessed based on chest radiograph and presence of bronchial pleural fistula and calculated using the modified Murray score for estimation of lung injury [1].

	Severe BLI	Moderate BLI	Mild BLI
PaO_2/FIO_2	< 60	60 to 200	> 200
Chest radiograph	Massive bilateral lung infiltrates	Bilateral or unilateral lung infiltrates	Localized lung infiltrates
Bronchial pleural fistula	Yes	Yes/No	No

Figure C-3: Blast Lung Injury Severity Score [189].

C.3.27 Blast Lung − Clinical Prognosis

In general, individuals with mild and moderate Blast Lung Injury (BLI) recover from their injuries. Those with severe BLI either die in the first 24 hours, or if they survive this acute post-injury period, often develop Adult Respiratory Distress Syndrome (ARDS). Given appropriate intensive care treatment, the prognosis for those with post-blast ARDS is good with complete recovery of lung function within 1 year [112], [240].

C.3.28 Blast Lung − Experimental Classification

The majority of scoring systems used in experiments to measure the severity of lung damage is based on pathological changes observable with the naked eye or microscopically. The Walter Reed blast overpressure scoring system for blast lung injuries is among the most frequently used methodology [149].

Walter Reed blast overpressure scoring methodology for gross pathological changes

Score	Description
Level 1 (Trace)	Superficial petechial hemorrhages (1–4) involving less than 10% of the lung parenchymal surface
Level 2 (Slight)	Superficial petechial hemorrhages involving greater than 10% of the lung surface to ecchymotic hemorrhages involving less than 10% of the lung surface
Level 3 (Moderate)	Superficial parenchymal ecchymotic hemorrhage extending to subpleural area involving 11–30% of the lung parenchyma
Level 4 (Severe)	Diffuse ecchymotic hemorrhage extending into lung parenchyma involving 31–60% of lung parenchyma

Figure C-4: Walter Reed Blast Overpressure Scoring System for Blast Lung Injuries [149].

C.3.29 Blast Injury − Fluid Resuscitation

- In general, fluid resuscitation occurs during the early/acute clinical management, and includes:
  1) Administration of hypertonic saline, which increases serum osmolality without compromising intravascular volume; as such, it is recommended to address brain swelling [140]. Excessive crystalloid administration, permissive hypotension, hypoxia, and hypercapnia due to their potentially harmful effects should be avoided [209].
  2) Intravenous (IV) boluses of 23% NaCl to address acute increase in Intracerebral Cranial Pressure (ICP) followed by continuous IV infusions of 2% and 3% NaCl solutions to maintain ICP control [192].

3) Early correction of traumatic coagulopathy with combinations of blood, blood products (fresh-frozen plasma, platelets), cryoprecipitate, or prothrombin complex concentrate [56], [209].

- Conventional wisdom suggested "judicious" fluid resuscitation and allowing the patient to remain hypotensive (e.g., with mean arterial blood pressure no greater than 60 mmHg). However, this approach has consequences and the significant challenge facing the clinician is the maintenance of adequate tissue oxygenation without overloading the cardiovascular system or exacerbating pulmonary edema. Hybrid resuscitation (initially adopting a hypotensive target but revising this to a normotensive target after the first hour) may offset the severe consequences of poor tissue oxygen delivery and improve survival [95].

C.3.30 Blast Lung

C.3.30.1 Signs [12]

- Cyanosis.
- Tachypnoea.
- Reduced breath sounds.
- Coarse crepitations.
- Rhonchi.
- Dull to percussion.
- Features of pneumo/haemo-pneumothorax.
- Haemoptysis.
- Subcutaneous emphysema.
- Retrosternal crunch (pneumomedistinum).
- Retinal artery air emboli.

C.3.30.2 Symptoms

- Dyspnoea.
- Cough (dry – frothy sputum).
- Haemoptysis.
- Chest pain/discomfort.

C.3.30.3 Blast Lung, X-Ray Findings

- Pneumothorax.
- Haemothorax.
- Pneumomediastinum.
- Subcutaneous Emphysema.
- Interstitial Emphysema.
- Mediastinal Emphysema.

- Pneumoperitineum – secondary to visceral perforation.
- Rib Fractures.

C.3.30.4 Respiratory Management

The classic teachings in management of blast lung injury are to avoid positive pressure ventilation, if possible, minimize positive end-expiratory pressure ventilation, and use judicious fluid resuscitation strategies. In one series with a low mortality rate of 3%, mechanical ventilation was required in 76% of patients, and several patients needed positive end-expiratory pressure > 10 cm H_2O to allow sufficient oxygenation [12]. Pressure-limited, volume-controlled ventilation with permissive hypercapnia has been advocated in patients sustaining blast lung to minimize mean airway pressure and the chance of air embolism, as well as, to reduce the risk of further pulmonary trauma [204], [237]. High-frequency ventilation and nitric oxide inhalation have also been successfully used [12]. Other sophisticated methods, such as, airway pressure release ventilation, jet ventilation, oscillatory ventilation, and independent lung ventilation, may be useful [148]. When all else fails, the physician may resort to salvage methods like extracorporeal membrane oxygenation [19], [81].

C.3.30.5 Blast Lung and Tympanic Membrane (Ear Drum) Rupture Relationship

The presence or absence of tympanic membrane rupture cannot be used as a surrogate marker since it is neither a sensitive nor specific indicator of blast lung [108], [205]. However, although it has been challenged [185], in the operational environment, it remains a prudent practice, to admit patients with a ruptured eardrum for a period of observation, whilst other more significant injuries are excluded [82].

C.3.31 Blast Overpressure Test Module (BOTM)

- In 1985, the U.S. Army Medical Research and Development Command (now known as the U.S. Army Medical Research and Materiel Command (USAMRMC)) initiated a project to characterize the blast pressure load distribution on the body of a sheep. The purpose was to devise a methodology for collecting data needed to predict injury using a mathematical model. The project involved the design, development, and field testing of a "Blast Overpressure Test Module" [142]. The Blast Overpressure Test Module was an aluminum cylinder, measuring 12 inches (305 mm) in diameter, and 30 inches (762 mm) in length. Four pressure transducers were mounted at equal distances around the circumference of the cylinder. The device was designed to be mounted either horizontally, to represent a standing sheep, or vertically, to represent a standing man.
- A similar device is described by Axelsson and Yelverton in a paper which was published in the Journal of Trauma in 1996 [13].

C.3.32 Blast Scaling Laws

- Blast explosion scaling. Formulas, which permit the calculation of the properties (e.g., overpressure, dynamic pressure, time of arrival, duration, etc.) of a blast wave at any distance from an explosion of specified energy from the known variation with distance of these properties for a reference explosion of known energy (e.g., of 1 kiloton).
- The cube-root mass scaling law established by Bowen and colleagues to predict blast-induced lung injuries [23] would translate a 70 kilogram human exposure of 13 milliseconds duration to a 1 millisecond exposure of a 30 g mouse. Taking a blast-head scenario as an example, for a given blast, when calculating the net loading scales for cross-sectional area of the skull, even if other parameters would be identical, a specimen

20-fold the size would experience 20-fold less acceleration for the same blast. The bottom line is if the shock tube experiments plan to use mice as research targets, the total positive duration of the exposure should not exceed 1 millisecond for both the overpressure and the dynamic pressure. On the contrary, if the mouse as a research target is loaded for a duration of 10 milliseconds (which is often a case in many current shock tube experiments), it would translate into a human equivalent of 100 milliseconds exposure, which is 10-times longer than the maximum duration of a reasonable IED blast event giving an effective yield of explosion that has 1,000 times more energy than it is expected in in real-life scenarios [165].

C.3.33 Blast Tube

- An apparatus, which generates blast waves under controlled conditions using explosive materials [171], [207].
- A blast tube typically consists of a cylindrical tube, and contains a driver section to generate the blast waves, and a test (driven) section(s) to propagate the waves and place a test subject. The driver section produces blast waves through the sudden release of high-pressure gas generated by high explosives or detonable gaseous mixtures, leading to bursting of a diaphragm. Blast tubes can also have a square or rectangular cross-section, although non-cylindrical tubes are less common. Blast tubes can be distinguished from shock tubes in that they use high explosive and are designed to simulate blast waves as opposed step-like shock waves.

C.3.34 Blast Signature

The full characterization of the shockwave including the following parameters [36], [165], [169]:

1) The **static pressure (also known as side-on pressure or overpressure)** represents the above-ambient pressure generated by compression or heating of the gas. The units are force per unit area or energy per unit volume.

2) The **dynamic pressure (also known as differential pressure or gust)** is generated by the motion of gas and it depends on the gas density (ρ) and gas velocity (U):

$$P_D = \tfrac{1}{2} \rho \times U^2$$

The units are force per unit area or energy per unit volume.

3) The **stagnation pressure (also known as total pressure, total head pressure, or pitot pressure)** is the sum of the static and dynamic pressures, expressed as force per unit experienced by an object in a steady flow environment.

4) The **overpressure impulse** in blast physics is a parameter that indicates the total energy in a blast wave. It is defined as the area under the pressure (expressed as force per area) versus time function.

5) The **positive impulse** is the integral of the pressure-time trace during the positive phase.

6) The **positive magnitude** is the difference between peak positive pressure and ambient pressure.

7) The **positive duration** indicates the time between the moments at which the pressure began to rise above ambient pressure (t0) and when the pressure goes below ambient pressure.

8) The **negative magnitude** is the difference between ambient and peak negative pressure.

C.3.35 Blast Wave

- A pressure disturbance that propagates through a material faster than the speed of sound within that material, such that the leading edge of the disturbance is a shock front. For example, an air blast wave produced by an explosive detonation.
- Wave created by the rapid expansion of hot gases in the atmosphere, which results from an explosion. The blast wave is initially a shock wave, which subsequently decays into a sound wave. [279]
- Related term(s): Pressure Wave.

C.3.36 Blast Wind

- The dynamic component of the blast wave that propels solid matter such as glass fragments and rocks hitting surrounding objects [257].
- Generated by mass displacement of air by expanding gases; it may accelerate to hurricane proportions and is responsible for disintegration, evisceration, and traumatic amputation of body parts.

C.3.37 Blast Wave Diffraction

The passage around and envelopment of a structure by the blast wave. [279]

C.3.38 Blast Wave Scaling Laws

- Blast wave scaling laws provide parametric correlations between a particular explosion and a standard charge of the same substance [169].
- In general, all blast parameters are primarily dependent on the amount of energy released by a detonation in the form of a blast wave and the distance from the explosion. A universal normalized description of the blast effects can be given by scaling distance relative to $(E/P_0)^{1/3}$ and scaling pressure relative to P_0, where E is the energy release (kilo joules) and P_0 the ambient pressure (typically 100 kilonewtons per meters^2). For convenience, however, routinely the basic explosive input or charge weight W is expressed as an equivalent mass of TNT. Results are then given as a function of the dimensional distance parameter (scaled distance):

  $$Z = R/W^{1/3}$$

  where R is the actual effective distance from the explosion. W (charge weight) is generally expressed in kilograms.

C.3.39 Blood Gas Changes Due to Primary Blast Injury of the Thorax

Coincident with the cardiopulmonary changes, there are early and prolonged falls in arterial oxygen tension, following thoracic blast (consistent with the development of pulmonary oedema [53]. The partial arterial pressure of carbon dioxide (P_aCO_2) may fall if pulmonary oedema is mild. Nevertheless, it might rise with more severe pulmonary oedema after severe blast injury since pulmonary transfer of carbon dioxide is affected less by oedema than the transfer of oxygen. These changes are associated with increases in lung weight and lung dry/wet weight ratios, both of which are consistent with the development of pulmonary oedema [128], [129].

C.3.40 Booster

- A high-explosive element sufficiently sensitive so as to be actuated by small explosive elements in a fuze (fuse) or primer and powerful enough to cause detonation of the main explosive filling. [279]
- Related term(s): Charge.

C.3.41 Bowen Curves

- A set of three empirical based curves commonly presented in the open literature that represent probit equation based estimates of the probability of survival for a human in relation to the peak incident pressure and positive phase duration of a free-field blast over-pressure loading.
- The different curves address the cases of a person near a reflecting surface, perpendicular to the blast, or parallel to it. The original papers contain other representations of these predictions, their derivation, as well as assumptions and caveats [23], [201].

C.3.42 Bowen Survivability Curves − Humans

- A survival probability curve for humans exposed to a blast wave based on experimental data from studies involving a wide variety of animal species that were exposed to blast overpressures near a reflecting surface. The derived relationship is expressed in terms of peak pressure and duration [23].
- The derived relationship is expressed in terms of a scaled peak reflected overpressure, $\mathbf{p_r}$, and scaled duration, **T**. The scaled peak reflected overpressure is adjusted for a species tolerance to blast overpressures ($\mathbf{P_{sw}}$) and the ambient air pressure, $\mathbf{p_{atm}}$. The scaled duration is adjusted for body mass, **m**, and the ambient air pressure. The curves are therefore meant to be adapted for variations in altitude ($\mathbf{p_{atm}}$), blast tolerance ($\mathbf{P_{sw}}$), and body mass (adult, child). The primary curve is based upon 50% mortality and probit analysis is used to establish the other survivability curves.
- The relationship determined by Bowen to describe the mortality data is given by (1):

$$p_r \left(\frac{61.5}{P_{sw}}\right)\left(\frac{14.7}{p_{atm}}\right) = 61.5(1 + 6.76T^{-1.064})e^{0.1788(5-Z)} \quad (1)$$

where the pressures $\mathbf{p_r}$ and $\mathbf{p_{atm}}$ are in psi, and the scaled duration **T** is in milliseconds. The scaled duration is given by (2):

$$T = t_{dur}\left(\frac{70}{m}\right)^{\frac{1}{3}}\left(\frac{14.7}{p_{atm}}\right)^{\frac{1}{2}} \quad (2)$$

where the mass **m** is in kilograms and $\mathbf{t_{dur}}$ is the positive phase duration of the overpressure at the reflecting surface. Bowen estimated human blast tolerance as $\mathbf{P_{sw}}$ = 61:5, so if the relationships in Equation 1 and 2 are simplified for a 70 kilogram person and a blast near sea level (i.e., $\mathbf{p_{atm}}$ = 14**:**7 psi), then **T** = $\mathbf{t_{dur}}$ and the expression for $\mathbf{p_r}$ becomes (3):

$$p_r = 61.5(1 + 6.76t_{dur}^{-1.064})e^{0.1788(5-Z)} \quad (3)$$

C.3.43 Bowen Curve – Body Orientation Effects

- Survivability is influenced by several factors, including a person's body position relative to the blast wave and the presence or absence of a reflecting surface. To predict mortality rate in conditions where a reflecting surface exists, Bowen postulated the conditions needed for equivalent biological damage to relate the free-field (incident) pressures experienced for a particular body orientation to the measured peak reflected pressures in the experiments [23], [201].
- The lethality curves for the peak reflected pressure and duration of positive phase are expressed by:

$$P_{reflected} = P^{*}(1 + aT^{-b})$$

- Where **P** is the maximum of the reflected pressure at the wall and not the incident pressure. **a, b** and **P*** are determined by statistical analysis. **A** = 6.76 and **b** = 1.064 are constants and **P*** changes with the level of lethality risk. For instance for 50% lethality risk **P*** = 423 kPa.
- For free field it is assumed that the survival percentage is equivalent for a situation where the total pressure in free field equals the reflected pressure for the near wall situation. The total pressure is equivalent to the incident (side on or static) pressure plus the dynamic pressure. The reflected pressure is not convenient to use and is converted to the incident pressure, which would lead to the reflected pressure, thus the survival curves in Figure C-5 are converted to the peak pressure of the incident (side on) pressure of the incoming shockwave for a man located close to a flat surface. Only the incident pressure is relevant for a free field situation with prone body, longitudinal axis aligned with shock wave propagation. The survival curves are presented in the figures below.

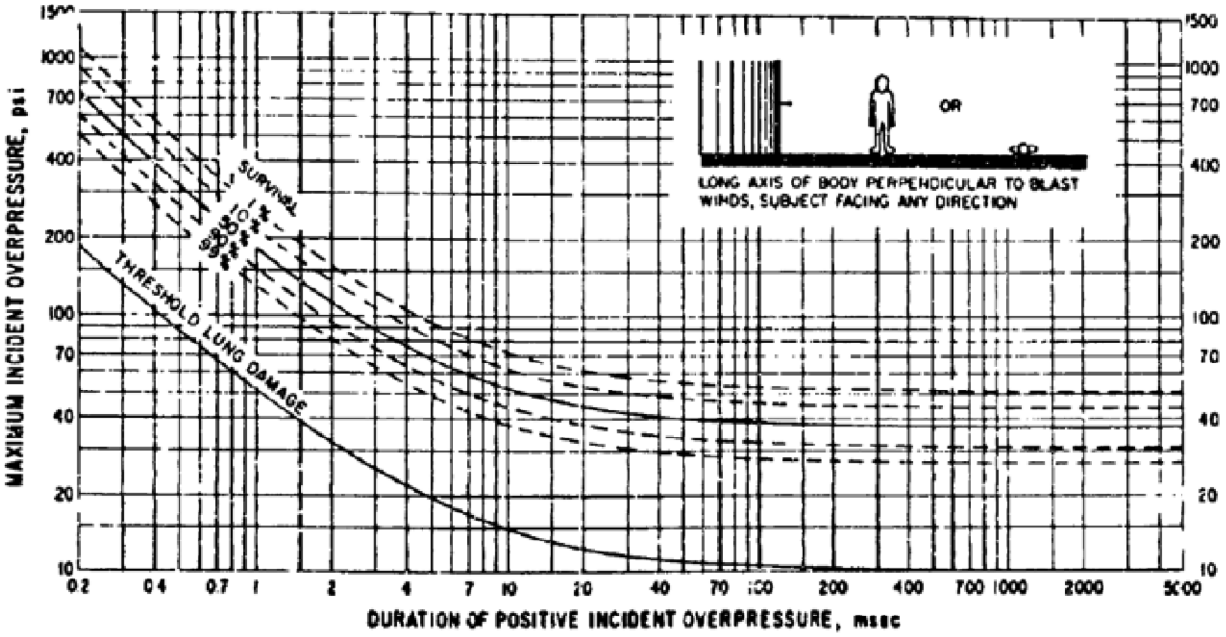


Figure C-5: Bowen Survival Curves for Peak Incident Pressure (Side On) of and Positive Phase Duration of an Incoming Shockwave for a 70 Kilogram Man Located in Free Field with Longitudinal Body Axis Perpendicular to the Direction of Propagation of Shock Blast Wave [23].

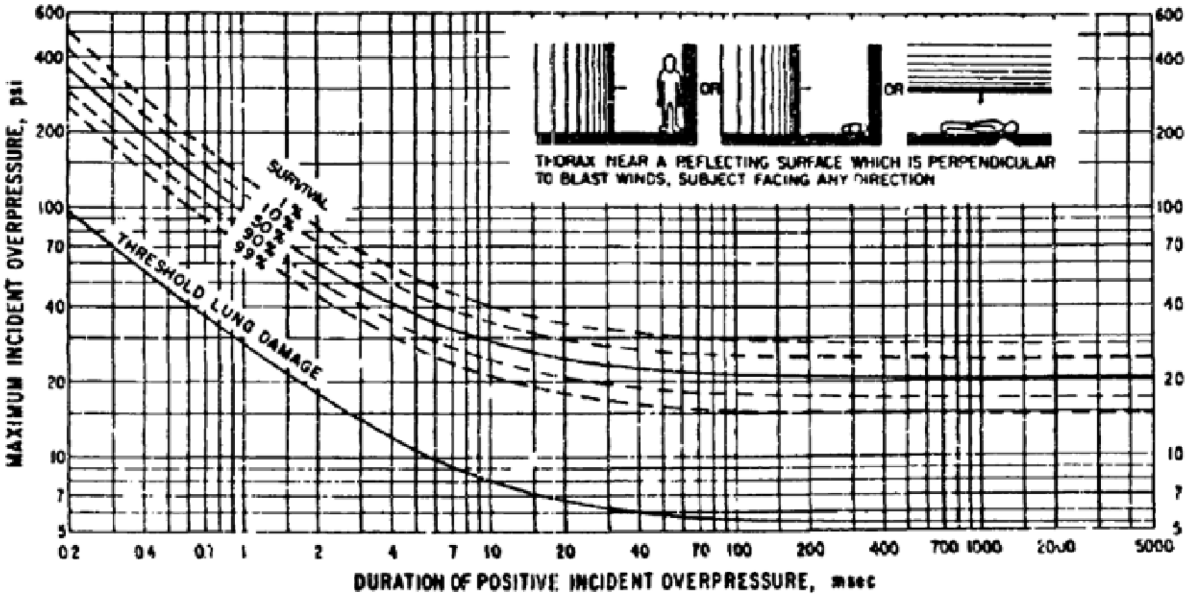


Figure C-6: Bowen Survival Curves for Peak Incident Pressure (Side On) of and Positive Phase Duration of an Incoming Shockwave for a 70 Kilogram Man Located Against the Reflecting Surface [23].

C.3.44 Bowen Survivability Curves – Animals

Tentative estimates of the sharp-rising overpressures as a function of duration, which represent a lethal hazard for eight larger mammals and five smaller species in 1, 50, 90, and 99 percent of the time were presented. The predictions were based on interspecies correlations and extrapolations encompassing blast-tolerance data for 12 mammalian species including burro, monkey, sheep, swine, goat, dog, cat, sheep, rat, hamster, rabbit, mouse, and guinea pig [71], [200].

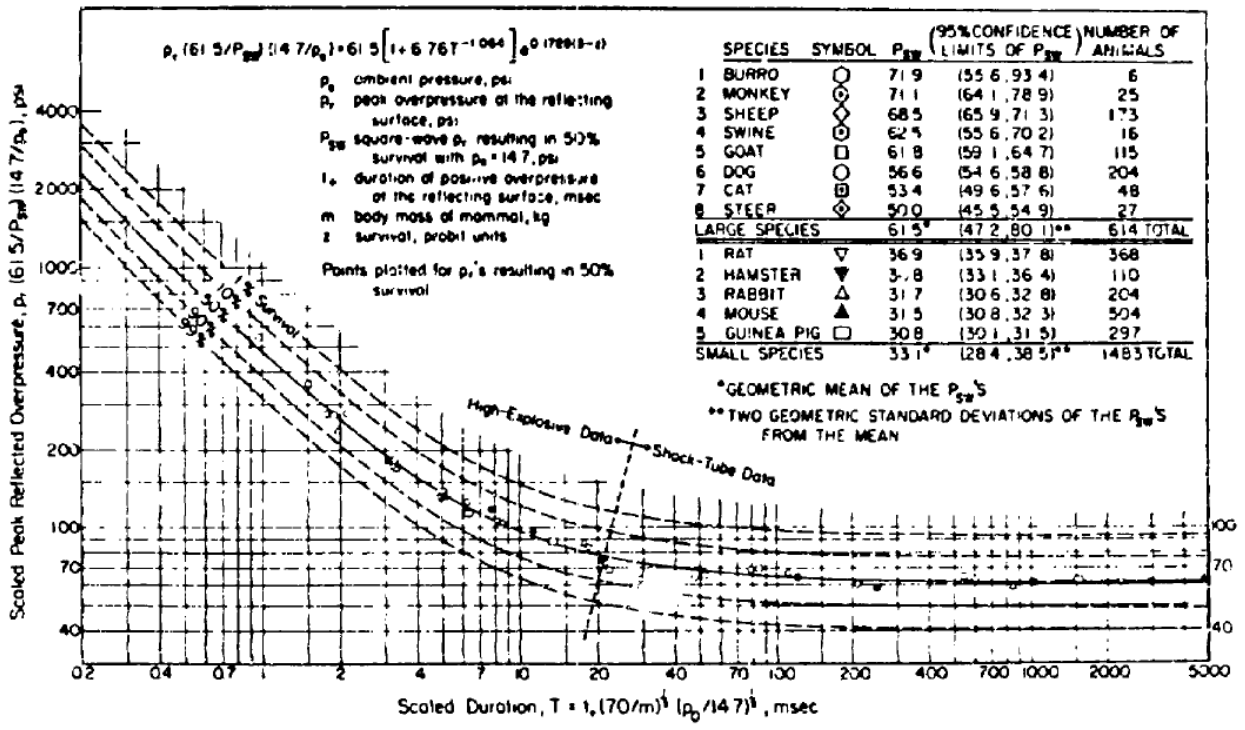


Figure C-7: Survival Rate Measured 24 Hours After an Exposure to a Sharp-Rising Blast Wave, Derived from Analysis of Data for 12 Mammalian Species [25].

C.3.45 Bradycardia

Heart rate below normal resting levels.

C.3.46 Brode's Equation for Peak Overpressure Prediction

- In 1955, Brode developed an estimation of peak overpressure due to spherical blast ($\mathbf{P_{so}}$) based on scaled distance $\mathbf{Z = R/W^{1/3}}$, where **Z** = scaled distance, **R** = actual effective distance from the explosion, and **W** = charge weight [26], [169]:

$$P_{so} = \frac{6.7}{Z^3} + 1 \text{ bar } (P_{so} > 10 \text{ bar})$$

$$P_{so} = \frac{0.975}{Z} + \frac{1.455}{Z^2} + \frac{5.85}{Z^3} - 0.019 \text{ bar}$$

$$(0.1 \text{ bar} < P_{so} < 10 \text{ bar})$$

- Related terms: Newmark and Hansen Equation.

C.3.47 Cardiovascular and Cardiorespiratory Responses to Primary Blast Injury

A number of experimental studies and clinical reports indicated that primary blast injury to the thorax produces bradycardia, prolonged hypotension and apnoea followed by rapid shallow breathing [198]. Initially, it was thought that the bradycardia was a preterminal event, possibly associated with cessation of coronary blood flow [211]. However, more recent studies have demonstrated that bradycardia is a consistent finding following thoracic blast, even in surviving animals [258], and is due to an autonomic reflex. Note that these cardiovascular and cardiorespiratory changes have been characterized principally in experimental studies of "pure" primary thoracic blast injury, without the secondary, tertiary and other blast effects. Thus, there is a possibility that in presence of a more pronounced peripheral injury (such as musculo-skeletal injuries), the pattern and extent of the cardiovascular and cardiorespiratory response mechanisms may be substantially altered when there is concurrent systemic.

C.3.47.1 Time-Course

A detailed study of the immediate response to primary blast injury to the thorax has shown that the cardiovascular and respiratory responses are not instantaneous; the bradycardia had a latency of onset of approximately 4 seconds, while blood pressure began to fall approximately 2 seconds after blast (37). This latency is consistent with the response being reflex in nature rather than being the consequence of direct effects (e.g., on the heart or CNS). The initial bradycardia was seen to resolve quickly after blast although some degree of bradycardia persisted for up to 1 hour after thoracic blast, while hypotension persisted for several hours. Recent studies have shown that the response also includes a reduction in vascular resistance, at least in skeletal muscles.

C.3.47.2 Mediation of the Hypotensive Response

The etiology of the hypotension seen after primary blast injury is complex. The fall in blood pressure appears to be due to a fall in peripheral resistance and cardiac output, the latter because of myocardial impairment, which can last many hours after blast injury [58]. Although the Autonomic Nervous System (ANS) plays some part in the hypotension, it is not solely responsible for this physiological process. Accordingly, the hypotension is only reduced but not abolished in animal studies where the vagus nerve has been cut before blast exposure [45], [117], [173]. Recent findings have suggested that primary blast injury causes a rapid release of the potent vasodilator nitric oxide (NO) from the pulmonary circulation [275], [276]. It is thought that such a brisk overproduction of NO could lead to a systemic response that includes vasodilatation [129].

C.3.47.3 Mediation of Bradycardic and Respiratory Responses

The bradycardia and apnoea seen after blast are both mediated by a vagal reflex [45], [117], [173], [211], the most likely candidate being the pulmonary afferent C-fibre reflex (previously known as the pulmonary J-receptor reflex) [42], [49], [178], [274]. The afferent pathway (pathway from detecting receptor to brain) is carried in the vagus nerve. The efferent pathway mediating the bradycardia (from the brain to the heart) is also carried in the vagus nerve. In animal studies, both the bradycardia and apnoea can be abolished if the vagus nerve is cut before blast exposure, establishing that the response is a reflex involving the vagus nerve. The bradycardia can also be blocked with drugs (such as atropine) that block the effects of the efferent vagus on the heart.

C.3.47.4 Response to Blast-Induced Hemorrhage

Immediately after hemorrhage, blood pressure is initially maintained by the action of the baroreceptor reflex, which increases systemic vascular resistance and heart rate to compensate for a fall in cardiac output and

decreased cardiac stroke volume. Later, blood pressure falls precipitously as a second reflex reduces vascular resistance and heart rate (this is thought to be a mechanism to protect the heart). This response is modified by the responses to concomitant thoracic blast injury and musculo-skeletal tissue injuries. Blood pressure falls more rapidly when hemorrhage occurs after blast injury. This is thought to be due to and interaction between the autonomic responses to hemorrhage and blast injury [128]. This is in contrast to the effects of musculo-skeletal injury on the response to blast injury, where blood pressure is maintained until a greater volume of blood loss. The "three way" interaction between hemorrhage, blast and musculo-skeletal injury is of great clinical importance because blast exposure can induce primary, secondary, and tertiary blast injuries in parallel, thus causing a complex "blast plus" polytrauma including blast lung, hemorrhage, and musculo-skeletal injuries, respectively [219].

C.3.48 Cavitation

When the tensile stress in a liquid medium such as water exceeds the tensile strength of the medium, localized pockets of void or gas can be generated, appearing as a cloud of small bubbles. The liquid can be put under tension quasi-statically, where the liquid remains in thermodynamic equilibrium, or dynamically. When cavitation bubbles collapse, they can create localized spots of potentially damaging high pressure and temperature. Dynamic tension can result from the depressurization associated with the reflection of an underwater blast with a free surface [190]. It has been speculated that cavitation is one of the possible mechanisms for blast injury [99].

C.3.49 Charge

- A given quantity of explosive, either in bulk or contained in a bomb, a projectile, a mine or similar device, or used as a propellant. [279]
- Related term(s): Booster.

C.3.50 Choice of Experimental Models for Blast Injury Research

- The purpose of experimental models of injuries is to replicate certain pathological components or phases of clinical trauma in experimental animals, aiming to address pathology and/or treatment. The goal of research specifies the design and choice of the experimental model [36], [203]. The extremely complex nature of blast injuries requires full understanding of blast physics, and a model reproducing multiple aspects of blast injuries should be defined with particular scientific fidelity to conditions observed in theater. Otherwise, a model will lack military and clinical relevance and the obtained results might be dangerously misleading.
- There are several decision-making steps in the process of choosing a model for blast research shown on the figure below. Most importantly, the researcher should identify which of the blast effects should be reproduced. If the choice is primary blast, the experimenter should ensure the animals are restrained so that there will be no blast-induced acceleration of the body/head during the exposure (thus, tertiary blast effects). Namely, in a situation where the body/head is allowed to move, the injury mechanisms would involve both primary and tertiary blast effects; this would make the interpretation of the results difficult. Next, a decision should be made about the biological complexity of the research study. This factor will dictate the choice of the biological surrogate used to reproduce blast-induced pathologies seen in humans (e.g., cell culture, tissue, small or large experimental animals, and nonhuman primates); positioning of the biological surrogates; means of generating a shock wave (open field, shock or blast tubes); and length of the experiment, among others. Thus, based on the research question and the scale of complexity, a choice is made between non-biological and biological models [37], [41].

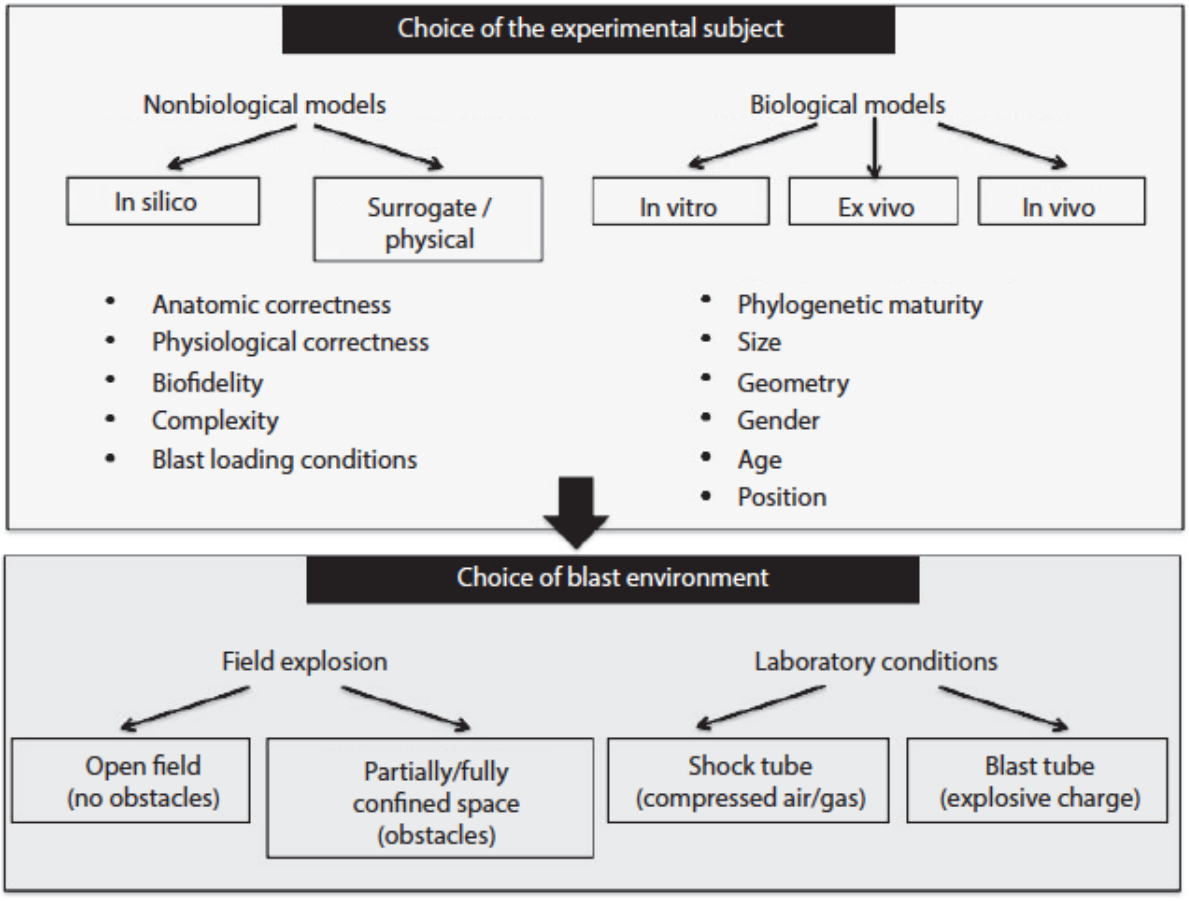


Figure C-8: Factors Influencing the Choice of Blast Injury Models. (Created by Ibolja Cernak for the Committee on Gulf War and Health: Long-Term Effects of Blast Exposures Institute of Medicine, U.S. National Academies, Copyright 2014).

C.3.51 Clearing

The phenomena of the actual reflected pressure on an object being below the theoretical reflected pressure on an infinite object due to edge effects such as diffraction.

C.3.52 Complex Blast

A blast that does not conform to a free-medium blast.

C.3.53 Complex Wave

- Wave that has reflected against one or several obstacles and therefore does no longer have the standard Friedlander waveform.
- When a blast occurs in a closed space, the shock wave will reflect off the various surfaces in the environment, resulting in a complex pressure time-history [180].

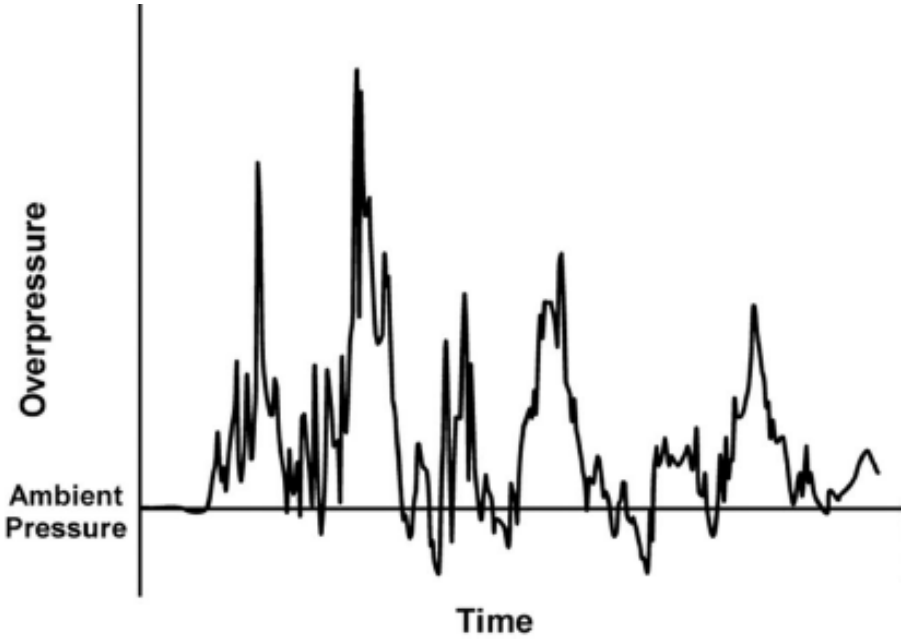


Figure C-9: Complex Blast Wave in a Closed Space [180].

C.3.54 Composite Explosive

Composite explosives are mixtures that might contain fuels and oxidizers, and other self-explosive ingredients. Most rock-blasting explosives fall into this category, with Ammonium Nitrate-Fuel Oil (ANFO) being the classic example. Some composite explosives also contain ingredients such as water or ballast materials that do not add energy to the reaction but modify the mixture's flow properties or consistency. Without exception, composite explosives must contain some mixture of carbon, oxygen, and nitrogen [183].

C.3.55 Conditions

All parameters relevant to response of the object exposed to blast including information on blast, environment, and an object exposed to blast. For the blast-related parameters see the above specification of blast (Entry: Blast Signature). The information about environment could include humidity, temperature, terrain, and obstacles, among others. The object related parameters could include geometry, position, orientation, and its preceding and concurrent states.

C.3.56 Confined Explosions

When an explosion occurs inside a building or vehicle, the presence of the walls and ceiling significantly increases the number of blast wave–structure interactions. Multiple reflections take place, and many waves coalesce to produce enhancements in corners and other local constrictions. The reflections can enormously amplify the peak pressures associated with the initial shock front. In addition, and depending upon the degree of confinement, the effects of the high temperatures and accumulation of gaseous products produced by the chemical process involved in the explosion will exert additional pressures and increase the load duration within the structure. The biggest difference between internal and external explosions, however, is the presence of the quasi-static gas pressure. Condensed explosives are approximately a thousand times denser than air.

The detonation of an explosive in a building will introduce a quantity of hot gas into the building, as well as the shock waves [90], [172].

C.3.57 Contusion

A medical term describing injury to tissues with skin discoloration and without breakage of skin; also called bruise. Blood from the broken vessels accumulates in surrounding tissues producing pain, swelling, and tenderness, whereas the discoloration is the result of blood seepage under the skin.

Related term(s): bruise.

C.3.58 Coup-Contre-Coup Injury

Coup and contre-coup injuries are associated with cerebral contusions, a type of traumatic brain injury in which the brain is bruised: a coup injury occurs under the site of impact with an object, and a contre-coup injury occurs on the side opposite the area that was hit. Coup and contre-coup injuries are considered focal and diffuse brain injury (https://en.wikipedia.org/wiki/Focal_and_diffuse_brain_injury), those that occur in a particular spot in the brain, as opposed to diffuse injuries, which occur over a more widespread area [19], [175].

C.3.59 Cube Root Law

- A scaling law applicable to many blast phenomena. It relates the time and distance at which a given blast effect is observed to the cube root of the energy yield of the explosion [24].
- Many States use rules based upon the explosives, their quantity, and the distance from the explosive to where people are at risk. These rules are known as Quantity-Distance (Q-D) criteria, and are based on the approach derived from the Hopkinson-Cranz Scaling Law, which is further amended by a range of coefficients. It is the basis of much of the work on the estimation of appropriate quantity and separation distances [251].
- Related terms: Scaling Law; Hopkinson-Cranz Scaling Law; Sachs' Scaling Law.

C.3.60 Detonator

A device containing a sensitive explosive intended to produce a detonation wave. [279]

C.3.61 Detonation Pressure

Provides an indicator of an explosives ability to do work and determines whether it is a high or low brisance explosive. It can be approximated as [251]:

$$P_{det} = 2.5 \cdot V_d \cdot (D/0.0000001)$$

where, $\mathbf{P_{det}}$ = Detonation Pressure (GPa); $\mathbf{V_d}$ = Velocity of Detonation of Explosive (m/s); $\mathbf{D}$ = Density (g/cm^3).

C.3.62 Dismounted Operations

A tactical movement of troops and equipment primarily by foot, with limited support by combat and tactical vehicles. [280]

C.3.63 Dismounted Complex Blast Injury

- Explosion-induced battle injuries with distinct injury patterns sustained by troops engaged in dismounted operations. Injuries typically include traumatic amputation of the lower extremities, severe injuries to the upper extremities, and pelvic, abdominal, or urogenital injuries [9].
- The pattern of this polytrauma (often dubbed "Blast +") dependent on the distance to the explosion, and frequently incorporates consequences of primary, secondary, and tertiary blast effects; consequently, it represents combination of overpressure-induced injuries, penetrating injuries, and burning wounds [91].
- Initial resuscitation and multidisciplinary surgical management appear to be the keys to survival. Definitive treatment follows general principals of open wound management and includes decontamination through aggressive and frequent debridement, hemorrhage control, viable tissue preservation, and appropriate timing of wound closure. These devastating injuries are associated with paradoxically favorable survival rates, but associated injuries and higher amputation levels lead to more difficult reconstructive challenges [9].

C.3.64 Drag Loading

The force on an object or structure due to transient winds accompanying the passage of a blast wave. It is the product of the dynamic pressure and the drag coefficient, which is dependent upon the shape or geometry of the object or structure. [279]

C.3.65 Drag Pressure

Product of the dynamic pressure and the drag coefficient, which is dependent upon the shape (or geometry) of the structure or object [166].

C.3.66 Dynamic Pressure

- Pressure resulting from some medium in motion, such as the air following the shock front of a blast wave. [279]
- The pressure which results from the mass flow (e.g. wind) inside and behind the shock front of a blast wave. It is equal to the product of half the density of the medium through which the blast wave passes and the square of the particle (or wind) velocity behind the shock front as it impinges on the object or structure [166].
- As the blast wave propagates through the atmosphere, the air behind the shock front is moving outward at lower velocity. The velocity of the air particles, and hence the wind pressure, depends on the peak overpressure of the blast wave. This later velocity of the air is associated with the dynamic pressure, $\mathbf{q}(\mathbf{t})$. The maximum value, $\mathbf{q_s}$, is given by [169], where $\mathbf{p_{so}}$ is the peak overpressure and $\mathbf{p_o}$ is the ambient pressure:

$$q_s = 5p_{so}^2 / 2(p_{so} + 7p_o)$$

- Related term(s): Drag Loading.

C.3.67 Electromagnetic Pulse

A sharp pulse of radio-frequency (long wavelength) electromagnetic radiation produced when an explosion occurs in an unsymmetrical environment, especially at or near the earth's surface or at high altitudes.

C.3.68 Environmental Exposure Sensor

A tool or technique that measures or quantifies the contact of humans with chemical, physical, or biologic stressors over space or time.

C.3.69 Equivalent Weight of TNT

See: TNT Equivalency.

C.3.70 Event

- Exposure to blast.
- Related term: Blast Event.

C.3.71 Experimental Criteria for Blast Injury Models

- The purpose of the experimental models of blast injuries is to replicate certain pathological components or phases of clinical trauma in experimental animals aiming to address pathology and/or treatment. Accordingly, the design and choice of the specific model should match the goal of research [33]. Regardless of the research questions the study aims to address, the criteria every clinically and militarily relevant blast injury model should fulfill are the following:
    1) The injurious component of the blast should be clearly identified and reproduced in controlled, reproducible, and quantifiable manner;
    2) The inflicted injury should be reproducible, quantifiable, and mimic components of human blast injuries;
    3) The injury outcome established based on morphological, physiological, biochemical, and/or behavioral parameters should be related to the chosen injurious component of the blast; and
    4) The mechanical properties (intensity, complexity of blast signature, and/or its duration) of the injurious factor should predict the outcome severity.
- Guided by their research question, the researchers should clearly define which blast effects they need to reproduce. If the study focuses only on primary blast injuries, the researchers should pay special attention to prevent any secondary or tertiary blast effects potentially interacting with the animal's body. For example, if the body would be allowed to move during the blast exposure, the injury mechanisms would involve both primary and tertiary blast effects; this would make the interpretation of the results quite complicated.
- The biological complexity of the research question is one of the most essential factors guiding the choice of research environment, methods of generating a shock wave, research subjects and their positioning, and length of the experiment. For instance, the analysis of behavioral and cognitive changes, thus higher brain functions, will require an experimental set-up that closely mimics the details of real-life blast scenarios soldiers are frequently exposed to. Moreover, accumulating evidence shows the importance of a

well-defined experimental setting including the animal's body position toward incoming shock wave, among others, for the outcome of the experiments, thus for the final conclusion the study [4], [40], [52].

C.3.72 Explosive

- A compound or mixture of compounds which, when initiated by heat, impact, friction, or shock, undergoes a rapid decomposition, releasing tremendous amounts of energy in the form of heat and gas.
- A substance or mixture of substances, which, under external influences, is capable of rapidly releasing energy in the form of gases and heat. [279]

C.3.73 Explosion

- A sudden and violent increase in volume inducing increased pressure and accompanied by noise and release of energy. It can be generated by chemical change, nuclear reaction, or escape of gases or vapors under pressure.
- Examples:
    1) Decomposition of an explosive through self-propagating, exothermic reaction; or
    2) Instantaneous release of gas from high-pressure chamber.
- Briefly, an explosion starts with a detonation, during which a transformation of a liquid or solid explosive material into gas releases a large amount of energy. Blast is one of the products of the explosion.

C.3.74 Exposure

An event when an object resides in an environment, which is being changed by the full spectrum or any components of blast. Quantifying the exposure would include number and frequency of events, duration, and intensity.

C.3.75 Extremely Light Casings

A case that surrounds an explosive charge and has a mass of 3% or less of the charge mass. Although this ratio appears small, the effects on air-blast may be significant [166].

C.3.76 Far Field Blast

A region surrounding the explosion where the blast properties depend solely on the energy released during the detonation.

C.3.77 Flow Mach Number

The ratio of the flow velocity to the local sound speed. Because this is a ratio, the number is unitless. Although unitless, this should be expressed as a vector, i.e., the direction should be specified [166].

C.3.78 Fluid

- A substance that flows, i.e., a liquid or a gas.

- A collective term embracing liquids or gases. A "perfect fluid" offers no resistance to change of shape, i.e., it has zero viscosity [264].

C.3.79 Fluid Mechanics

- Physical science dealing with the action of fluids at rest or in motion, and with engineering applications and devices using fluids [264].
- The branch of applied mechanics concerned with the statics and dynamics of fluids – both liquids and gases. The analysis of the behavior of fluids is based on the fundamental laws of mechanics, which relate continuity of mass and energy with force and momentum together with the familiar solid mechanics properties.

C.3.80 Fragmentation

- A process of disintegration of the casing during the detonation of explosive material.
- Because the detonation pressure is much higher than the material strength, the initial shock travels through the case thickness and starts accelerating the case material. The high pressure in the detonation products compresses the case material as is starts to expand and keeps the case material in compression during the expansion until the case reaches nearly twice its original diameter. At a radius of about twice the original case radius, the pressure in the detonation products has dropped by more than an order of magnitude. The acceleration of the case has also been reduced by more than an order of magnitude; consequently, the case begins to form tensile cracks near the outer surface. It has been calculated that the fraction of energy used to overcome the material strength is less than 1% of the kinetic energy of the case material [166].

C.3.81 Free Air Overpressure

The un-reflected pressure, in excess of the ambient atmospheric pressure, created in the air by the blast wave from an explosion. [279]

C.3.82 Free-Field Exposure

Said of an explosion or blast wave generated in an environment free of any reflecting surfaces such as the ground, walls, or nearby objects.

C.3.83 Frequency-Dependence of Primary Blast Injuries

Recent results suggest a frequency dependence of the primary blast effects. High-frequency (0.5 – 1.5 kHz) low-amplitude stress waves have been observed to target mostly organs that contain abrupt density changes from one medium to another (e.g., the air–blood interface in the lungs or the blood–parenchyma interface in the brain). On the other hand, low-frequency (< 0.5 kHz), high-amplitude shear waves show a tendency to disrupt a tissue by generating local motions that overcome natural tissue elasticity (e.g., at the contact of gray and white brain matter) [36], [66], [102].

C.3.84 Friedländer Wave Form

An idealized shape of a blast wave generated by a free-field detonation of an explosive [93].

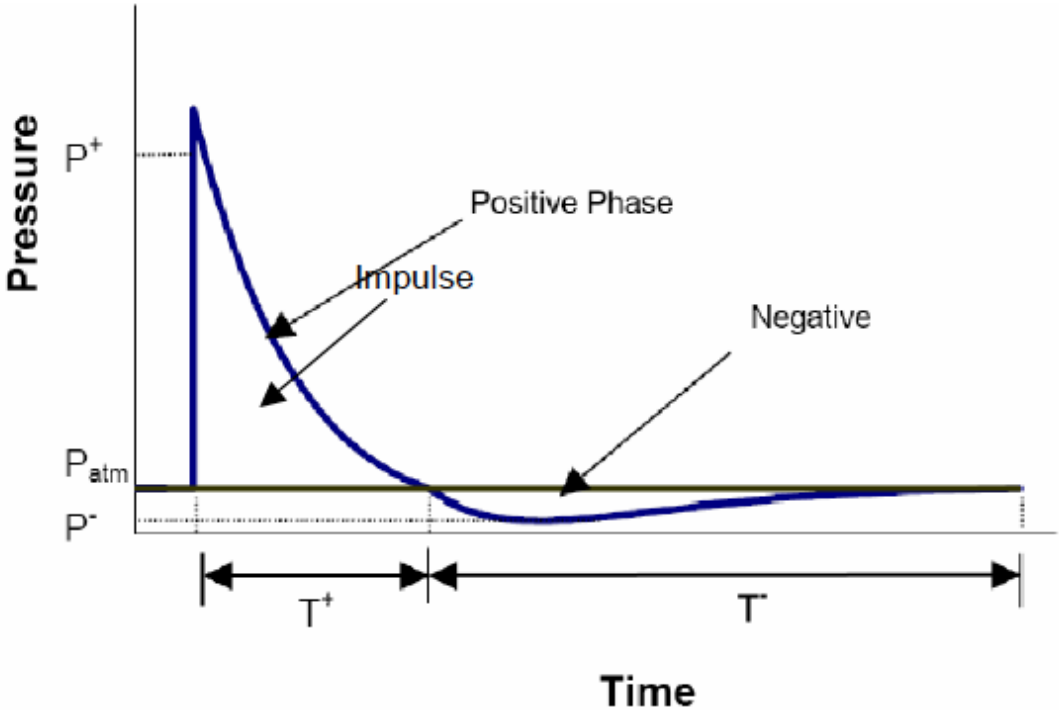


Figure C-10: Ideal Blast Wave (adapted from Ref. [278]).

C.3.85 Fuel-Air Explosion

- Explosion generated by igniting a cloud of fuel mixed with the ambient surrounding air.
- Explosive fuel-air clouds are typically produced by dispersing a liquid or gaseous fuel in the ambient air atmosphere [166].

C.3.86 Gurney Relations

- The Gurney Equations are a range of formulae used in explosives engineering to predict how fast an explosive will accelerate a surrounding layer of metal or other material when the explosive detonates. This determines how fast fragments are released on detonation of an item of ammunition. This initial fragment velocity can then be used with other ballistic equations to predict either danger areas or fragment penetration [251].
- Gurney relations analyze the fragment velocities in terms of explosive and case properties, and define the mean velocity of the case fragments, known as Gurney velocity. The basic premise is that the fragment mean velocity is a function of the charge to case mass ratio:

$$V_0 = \sqrt{2ER},$$

where **E** is referred to as the Gurney energy and is dependent on the properties of the specific explosive being used, and **R** is a geometric factor.

- For cylindrical charges, the equation is:

$$R = \frac{C}{M + \frac{C}{2}},$$

where **C** is the explosive mass per unit length and **M** is the mass of the case over the same unit length.

- For spherical charges, the equation is:

$$R = \frac{C}{M + \frac{3C}{5}},$$

where **C** is the explosive mass and **M** is the case mass.

- Since **E** has units of energy and √**E** has units of velocity, Gurney derived the equation from the initial one as:

$$V_0 = V_1\sqrt{R},$$

where $\mathbf{V_1}$ is a velocity characteristic of the explosive.

- For TNT, Gurney suggested 8,000 feet/second is an adequate value for $\mathbf{V_1}$ [166].
- The Gurney Constant √**2E** is usually very close to 1/3 of the Detonation Velocity of the explosive [251].

C.3.87 Haemorrhage or Hemorrhage

Loss of blood from the cardiovascular system.

C.3.88 Height of Burst

- The vertical distance from the earth's surface or target to the point of burst. [279]
- Related term(s): optimum height of burst; safe burst height.

C.3.89 Hopkinson-Cranz (or Sachs') Scaling Law

- Provides a basis for Quantity-Distance (Q-D) criteria and calculation of safe distance from the explosives:

$$(R_1/R_2) = (W_1/W_2)^{1/3}$$

$$R = Z.W^{1/3}$$

where, **R** = Range (**meters**); **Z** = Constant of Proportionality (dependent on acceptable blast overpressure); and **W** = Explosive Weight (kilograms) [251].

- Related terms: Cube Root Scaling Law; Scaling Law; Sachs' Law.

C.3.90 Impact Pressure

The difference between pitot pressure and static pressure. [279]

C.3.91 Implosion

One of the main physical mechanisms of blast-body interactions. It occurs when the shockwave compresses a gas bubble in a liquid medium, raising the pressure in the bubble much higher than the shock pressure; as the pressure wave passes, the bubbles can re-expand explosively and damage surrounding tissue [20], [37].

C.3.92 Improvised Explosive Device (IED)

A device placed or fabricated in an improvised manner incorporating destructive, lethal, noxious, pyrotechnic or incendiary chemicals and designed to destroy, incapacitate, harass, or distract. [279]

C.3.93 Incident Pressure (Side-On Pressure)

Used here to describe the blast overpressure that may be recorded in free space, such that its recording does not perturb the blast field. This pressure is normally approximated in explosive trials by the use of streamlined pressure gauges [166].

C.3.94 Inertia

One of the basic physical mechanisms of blast-body interactions. Inertial effects occur at the interface of the different densities; the lighter object will be accelerated more than the heavier one, creating a large stress at the boundary [36], [216].

C.3.95 Inertial Effects

Inertial effects occur at the interface of the different densities: the lighter object will be accelerated more than the heavier one, so there will be a large stress at the boundary [36], [216].

C.3.96 Injury Mechanism

The term injury mechanism is often confused and may be described in the following ways:

- Mechanism as an injurious factor, it is caused by a physical load (e.g., blast, or road traffic accident).
- Mechanism as a consequence of the interaction between the injurious factor and the biological system (exceeding the strain tolerance of tissue/cells resulting in contusion or bone fracture for example).
- Mechanism as a biological process (e.g., cytokine release, or vascular leak).

C.3.97 Injury Model

A representation of injury circumstances, physics, biomechanics, physiological responses, and pathological mechanisms comparable to clinically relevant conditions. That representation may be physical (e.g., a wooden mock-up), virtual (computer-based) or biological (animal).

C.3.98 Intermediate-Field Blast

A region around the explosion in which the transverse waves subside and a truly one-dimensional blast wave emerges [166].

C.3.99 Internal Explosions

Likely produce complex pressure loading profiles as a result of the resulting two loading phases. The first results from the blast overpressure reflection, and due to the confinement provided by the structure, re-reflection will occur. Depending on the degree of confinement of the structure, the confined effects of the resulting pressures may cause different degrees of damage to the body and structure [169]. The probability of severe blast injuries and blast poly-trauma in individuals exposed to internal explosions is much higher than those exposed in free-field conditions.

C.3.100 Intestinal Blast Injuries

C.3.100.1 Characteristics

The injury mechanism includes reflection of the shock wave as it travels across density borders into gas filled areas of the gut (similar to blast lung injury) causing contusion. In addition, displacement and shearing effects can cause tearing of mesenteric and peritoneal attachments with bleeding, and devascularizing injury. The characteristic injury seen is a multifocal intramural hematoma beginning in the submucosa, extending with increasing severity to large transmural confluent hematoma, and may involve the mesentery and vascular supply. Serosal injury should always be considered indicative of transmural injury.

C.3.100.2 Prognosis and Treatment

Cripps [69], [70] identified those lesions at greater risk of perforation in experimental studies in pigs, suggesting that serosal lesions greater than 15 millimeters in the small intestine and greater than 20 millimeters in the large bowel are at higher risk of perforation and should be resected. Delayed perforation up to 14 days post injury can occur and most likely is related to progressive ischemia and necrosis with transmural injury or adjacent mesenteric injury. In the case of immersion blast or in enclosed spaces, primary blast injury to the gut may occur even more frequently than pulmonary injury and at less intense exposure to dynamic overpressures.

C.3.101 Bezold-Jarisch Reflex

See Bezold-Jarisch Reflex.

C.3.102 Kingery and Bulmash Equations

Equations to estimate blast over-pressure at range for determining free-field pressures and loads on structures. These equations are widely accepted as engineering predictions for determining free-field pressures and loads on structures and form the basis of the US Conventional Weapons Effects Programme (ConWEP) software. Their report contains a compilation of data from explosive tests using charge weights from less than 1 kilogram to over 400,000 kilograms [251].

C.3.103 Light Casings

Cases surrounding the explosives that have a mass between about 3% of the charge mass to about the same as the charge mass. As the case mass ratio increases from 0.03 toward a ratio of 1, the velocity of the fragments is reduced and the fraction of the detonation energy transferred to kinetic energy of the fragments increases. At just over 3% of the charge mass, the case fragment kinetic energy is about 12%. When the case mass ratio approaches 1, the kinetic energy fraction approaches 0.5 and the fragment velocities decrease to 7 or 8,000 feet/second [166].

C.3.104 Loading

The force on an object or structure or element of a structure. The loading due to blast is equal to the net pressure in excess of the ambient value multiplied by the area of the loaded object.

C.3.105 Long-Duration Blast

- A term used in reference to lung blast injuries and denotes a blast wave where the positive phase duration is longer than 10 milliseconds, although the dividing value differentiating the short-duration from long-duration blasts is not strictly defined [17].
- "Long"-duration blast injuries are more diffuse pulmonary injuries, caused by gross lung compression owing to a larger momentum transfer to the thorax during blast exposure [65]. These blasts are typically produced by large charge high explosives of more than 100 kilograms TNT (e.g., vehicle-borne IEDS and bombs dropped by aircraft), thermobaric explosives, and nuclear bombs, in addition to testing using long air-driven shock tubes [179].

C.3.106 Lovelace Curves

- Preferred term: Bowen Curves.
- Related term(s): Bowen Curves.

C.3.107 Mach Front

Preferred term: Mach stem.

C.3.108 Mach Reflection

When the reflected shock is able to catch the incident shock, a single combined shock is formed. This phenomenon is called Mach reflection and the merged shock is called the Mach stem. The point at which the incident, reflected and Mach shocks intersect is called the triple point [166].

C.3.109 Mach Stem

The shock front formed by the fusion of the incident and reflected shock fronts from an explosion. The term is generally used with reference to a blast wave, propagated in the air, reflected at the surface of the earth. In the ideal case, the Mach stem is perpendicular to the reflecting surface and slightly convex (forward). [279]

C.3.110 Mach Region

The region on the surface at which the Mach stem has formed as the result of a particular explosion in the air.

C.3.111 Mechanism

C.3.111.1 General

The fundamental processes involved in or responsible for an action, reaction, or other natural phenomenon (http://www.merriam-webster.com/dictionary/mechanism).

C.3.111.2 Biology

In biology, "mechanism" has three distinct meanings, which can be distinguished and defined as follows [170]:

- **Mechanicism**: The philosophical thesis that conceives living organisms as machines that can be completely explained in terms of the structure and interactions of their component parts. Mechanicism has been one of the most influential schools of biological thought since the late seventeenth century. Most recently, the emerging field of synthetic biology, with its aim to apply engineering principles in order to design and manufacture living cells from scratch, constitutes the newest expression of the mechanistic research program in biology [170].
- **Machine Mechanism:** The internal workings of a machine-like structure. Machine mechanisms, biological and technological, are often analyzed in isolation as a whole or disintegrated into smaller machine mechanisms [170].
- **Causal Mechanism:** A step-by-step explanation of the mode of operation of a causal process that gives rise to a phenomenon of interest. This approach acquired scientific validity in biology in the twentieth century, and enables the identification of causal relations [170].

C.3.112 Mills Equation for Peak Overpressure Prediction

In 1987, Mills [156] provided an equation for calculating the maximum of peak overpressure, $\mathbf{P_{so}}$, in which **W** (charge weight) is expressed as the equivalent charge weight in kilograms of TNT, and **Z** is the scaled distance [83], [169]:

$$P_{so} = \frac{1772}{Z^3} - \frac{114}{Z^2} + \frac{108}{Z}$$

C.3.113 Moderate-to-Heavy Casings

Casings surrounding the explosive charges that have a case-to-charge mass ratios ranging from 1 to 5 or more. At these mass ratios the case becomes a dominant factor in early blast wave formation. The expansion velocity of the case is reduced to levels of 3,000 feet/second and the fragment kinetic energy may exceed half of the detonation energy of the explosive. The average fragment size increases as the case mass ratio increases. For some 2,000 pound class penetrating warheads the larger fragment masses may exceed a kilogram [166].

C.3.114 Modified Pathology Scoring System for Blast Injuries

- Cernak *et al.* [43], [47] modified the Yelverton Pathology Scoring System for Blast Injuries (see entry: Yelverton Pathology Scoring System) [267], which has been developed to quantify the anatomical/ morphological changes caused by blast in experimental animals, to distinguish clinical outcome in victims with blast injury.
- The modified version included Yelverton's Injury Score (PSS/IS) without further calculation of the Severity Injury Index (SII). The PSS/IS was defined for non-auditory blast injury as:

$$IS = (E + G + ST)\,(SD)$$

  or for auditory blast injury:

$$IS = (E + G)\,(SD)$$

  where **E** = extent of injury in terms of component parts to an organ or system; **G** = injury grade including surface area of the lesion or the percentage of the organ traumatized or the number of fractures; **ST** = severity type elements measuring the type of the worst-case lesion to an organ or system; **SD** = severity depth elements estimating the depth or degree of disruption of the worst-case lesion.
- The in vivo estimation of the **E**, **G**, **ST**, and **SD** elements in patients was performed using the findings of bronchoscopy, CT, and ultrasonography. Cardiac functional impairments were estimated on the basis of electrocardiographic (ECG), radiographic, and CT findings. Furthermore, functional impairments were assessed based on blood analysis of glucose; electrolytes (Na, K, Cl, Ca); enzymes: creatine phosphokinase (CK, EC 2.7.3.2.), total lactic-acid dehydrogenase (LDH, EC 1.1.1.27), aminoalaninetransferase (ALT, EC 2.6.1.2.), aminoaspartatetransferase (AST, EC 2.6.1.1.), and angiotensinconverting enzyme (ACE, EC 3.4.15.1.); cytokines: interleukin-1 (IL-1), tumor necrosis factor-α (TNFα); amino acids: total, branched-chain, aromatic, essential, nonessential; and eicosanoids: thromboxane A_2 (TxA_2), prostaglandin I_2 (prostacyclin / PGI_2), and peptidoleukotrienes C4, D4, E4 (pLTs).
- In comparison with the anatomically based injury scoring systems such as the Red Cross Wound Classification (RCWC) and the Injury Severity Score (ISS), the modified Pathology Scoring System combining both pathological and functional parameters providing a more accurate injury outcome prediction.

C.3.115 Molecular Explosive

Are substances that contain all that is needed for reaction within each well-defined molecule? Trinitrotoluene (TNT) and Nitro-Glycerine (NG) are examples of molecular explosives.

C.3.116 Model

- Graphical, mathematical, physical, biological, or verbal representation, or simplified version of a concept, phenomenon, relationship, structure, or system(s).
- The objectives of a model include:
  1) To facilitate understanding by eliminating unnecessary components:
  2) To aid in decision making by simulating 'what if' scenarios: and
  3) To explain, control, and predict events on the basis of past observations.

Since most objects and phenomenon are very complicated (have numerous parts) and much too complex (parts have dense interconnections) to be comprehended in their entirety, a model contains only those features that are of primary importance to the model maker's purpose.

- Definition from the online Business Dictionary (http://www.businessdictionary.com/definition/model.html#ixzz3xmBulPnhComputational).

C.3.117 Mott's Distribution

Defines the fragment size distribution as the complement of an exponential distribution function for the square root of fragment weights. Thus:

$$G(\sqrt{W_f}) = 1 - F(\sqrt{W_f}) = \exp(-\sqrt{W_f}/M_A),$$

where $\mathbf{W_f}$ is the fragment weight (in pounds) and **MA** is the fragment weight probability distribution parameter (√pounds), which is a function of the explosive type and steel casing geometry. $\mathbf{M_A}$ is defined as:

$$M_A = Bt_c^{5/6} d_i^{1/3} \left(\frac{1 + t_c}{d_i}\right)$$

and is the expected value of the distribution parameter. **B** is a constant depending on the explosive properties and the casing type, with units of $pound^{1/2}/ft^{7/3}$. The parameters $\mathbf{d_i}$ and $\mathbf{t_c}$ are the average case inside diameter and the case thickness. As the expected value:

$$M_A = E(\sqrt{W_f})$$

The average value of the fragment weight (= $\mathbf{E(W_f)}$) is twice the square of $\mathbf{M_A}$. Thus, $E(W_{f.}) = 2M_A^2$ [166].

C.3.118 Mounted Operations

A tactical movement of troops and equipment by combat and tactical vehicles. [280]

C.3.119 Mounted Blast Injuries

- Injury caused by an explosion acquired by an individual as a passenger inside an armored or not-armored vehicle.
- The injury pattern results when the overpressure of the blast wave is transferred into the vehicle, and could raise a more likely spine fracture due to the acceleration of the vehicle by the explosion [80], [235].

C.3.120 Near-Field Blast

- The near field is defined as the region between the original charge surface and the position of the air shock wave when it has separated from the fireball surface.
- Near field overpressure waves travel supersonically through the atmosphere and are not significantly affected by differing meteorological conditions as they expand radially from the explosion's source. As the

wave energy dissipates to levels less than a few pounds per square inch, the wave's propagation pattern changes to more closely resemble a standard acoustic wave.

- The near-field region can also be defined as the region within 15 – 20 times radii (for an equivalent spherical blast source) of the face of the explosive with which the blast loading is affected by local phenomena such as the expansion of the detonation products and after-burn [169].

C.3.121 Newmark-Hansen Equation for Peak Overpressure Prediction

In 1961, Newmark and Hansen (1961) developed an equation to calculate the maximum blast overpressure, $\mathbf{P_{so}}$, in bars, for a high explosive charge detonates at the ground surface [83], [168], [169]:

$$P_{so} = 6784\frac{W}{R^3} + 93\left(\frac{W}{R^3}\right)^{\frac{1}{2}}$$

where, **R** = the actual effective distance from the explosion; **W** = charge weight generally expressed in kilograms.

C.3.122 Non-Auditory Blast Injury

Injuries caused by blast exposures and blast effects that involve all organs and organ systems (e.g., lungs, abdominal organs, and brain, among others) but not the auditory system [13], [79], [86], [218], [268], [269].

C.3.123 Overpressure

- The pressure above ambient pressure.
- The pressure resulting from the blast wave of an explosion.
- Note: It is referred to as positive when it exceeds atmospheric pressure and negative during the passage of the wave when resulting pressures are less than atmospheric pressure. [279]

C.3.124 Oxygen Delivery (DO_2) and Consumption (VO_2)

- The **delivery of oxygen to tissues** (DO_2) calculated as the product of oxygen content of arterial blood (CaO_2) and blood flow (cardiac output for whole body oxygen delivery).
- The **consumption of oxygen by tissues** (VO_2) can be measured directly by calorimetry or indirectly as the difference between arterial and venous oxygen content multiplied by tissue blood flow (arterial and mixed venous oxygen content multiplied by cardiac output for whole body oxygen consumption).
- The point at which VO_2 becomes dependent on DO_2 is called the "**critical oxygen delivery**" (DO_{2Crit}) and represents the point at which organs in the body start to suffer physiological damage because of an inadequate DO_2. This often happens in severe blast injuries with polytrauma and massive hemorrhage [143].

C.3.125 Parallel Orientation in Relation to Blast Wave Propagation

- A position, where the long axis of the body is parallel to the blast wave propagation.

- For this position, Bowen postulated that equivalent biological damage would occur if the incident pressure was equal to the reflected pressure [23].

C.3.126 Peak Overpressure

- The maximum value of overpressure at a given location, which is generally experienced at the instant the shock (or blast) wave reaches that location. [279]
- At the arrival time t_A, following the explosion, pressure at that position suddenly increases to a peak value of overpressure, P_{so}, over the ambient pressure, P_o. The pressure then decays to ambient level at time t_d, then decays further to an under pressure P_{so-} (creating a partial vacuum) before eventually returning to ambient conditions at time $t_d + t_{d-}$. The quantity P_{so} is usually referred to as the peak side-on overpressure, incident peak overpressure or merely peak overpressure [169], [246].
- A recent study [234], which computed blast pressures for different weights of surface blast or TNT and varying stand-off distances for a multi-storeyed framed building while adopting wave scaling laws given by U.S. Army technical manual [281] showed that:
  - The peak static pressure P_{so} increases as the weight of blast increases. For example, the peak static pressure increases by 66.6% if the blast weight increases from 100 to 200 kilograms. If the value of blast weight increases from 100 to 300 kilograms then the value of peak static pressure increases by 122% at a stand-off distance of 20 meters. It shows the dependency of blast pressures on weight of TNT or blast.
  - The peak static pressure P_{so} decreases as the stand-off distance increases. For example, the peak static pressure decreases by 45% to 50% if the stand-off distance changes from 20 to 30 meters. On further increasing the stand-off distance, i.e. from 20 to 40 meters, the value of pressure decreases by approximately 65% to 70%. It shows the dependency of blast pressures on stand-off distance of explosion from the building.
  - The peak reflected overpressure P_r increases as the charge weight of blast increases. For example, the peak reflected overpressure increases by 77.27% if the blast weight increases from 100 to 200 kilograms. If the value of blast weight increases from 100 to 300 kilograms then the value of peak reflected pressure increases by 150% at a stand-off distance of 20 meters. It shows the dependency of blast pressures on weight of TNT or blast.
  - The peak reflected overpressure P_r decreases as the stand-off distance increases. For example, the peak reflected overpressure decreases by 50%, if standoff distance changes from 20 to 30 meters. On further increasing the stand-off distance i.e. from 20 to 40 meters, the value of pressure decreases by approximately 75%. It shows the dependency of blast pressures on stand-off distance of explosion from the building.

C.3.127 Perpendicular Orientation in Relation to the Blast Wave

- A standing position with the long axis of the body perpendicular to the blast wave propagation.
- This body orientation also corresponds to a prone position where the blast wave approaches from the person's side.
- For this body position, Bowen postulated that the incident pressure plus dynamic pressure must equal the measured reflected pressure for equivalent biological damage to occur [25].

C.3.128 Petechia (Petechiae)

A petechial (plural petechiae) is a small (1 – 2 milimeter) red or purple spot on the skin or in tissue caused by a minor bleed from broken capillary blood vessels.

C.3.129 Phantom

- A dummy of the human or animal body or any of their parts made from non-biological materials that approximate the physical properties for the purpose of calibrating or determining exposure conditions to radiation, over- and under-pressure, or other physical conditions.
- An inanimate physical representation of a target, often used to facilitate predictions of exposure in living targets during explosive trials.

C.3.130 Plastic Explosive

Explosive that is malleable at normal temperatures. [279]

C.3.131 Positive Overpressure Impulse

In general, the positive overpressure impulse is the decisive parameter for the damage caused by air blast is. It should be determined by integration of the positive over-pressure phase, (i.e. defined by the total area below the pressure-time curve) [251]:

$$I_s = \int P_s \,.\, t.\, dt$$

where, $I_s i$ = Scaled Impulse (kilogram.meter/second); $\mathbf{I_s}$ = Side-On Impulse (kilogram.meter/second); P_0 = Ambient Pressure (kilopascal); M = Mass of Individual (kilogram).

C.3.132 Positive Phase Duration

- The time between when the pressure first increases above ambient and when it returns to ambient.
- For an idealized free-air blast wave, that corresponds to the time between the start of the initial shock front to the cross-over between the region of positive pressure and negative pressure [166].

C.3.133 Precursor

C.3.133.1 Physics

An air pressure wave, which moves ahead of the main blast wave for some distance as a result of a nuclear (or atomic) explosion of appropriate yield and low burst height over a heat-absorbing (or dusty) surface. The pressure at the precursor front increases more gradually than in a true (or ideal) shock wave, so that the behavior in the precursor region is said to be non-ideal.

C.3.133.2 Medical

A molecule that precedes and/or initiates biological processes as a consequence of a blast exposure.

C.3.134 Pressure

- The force per unit area exerted by a gas having non-zero energy [166].
- The force caused by the molecular or atomic linear motion of the gas.
- Pressure may also be expressed in terms of energy per unit volume.
- Common units are: dynes per square centimeter, ergs/cubic centimeter, Pascals (Newtons per square meter), Joules per cubic meter, pounds force per square inch (psi), Torr, bars or atmospheres (not the same).

C.3.135 Pressure Front

Preferred term: shock front. [279]

C.3.136 Primary Blast Injury

Blast overpressure injury resulting in direct tissue damage from the shock wave coupling into the body [41], [105], [120], [176], [187], [266].

C.3.137 Primary Blast Injury Levels

The United Nations International Ammunition Technical Guideline [251] recommends estimation of primary blast injury levels based on:

- The Kingary-Bulmash equation (see the entry: Kingary-Bulmash equation).
- Comparison of the blast over-pressure to injury threshold levels derived from Bowen curves (34.5 kilopascal for onset of hearing damage, 207 kilopascal for lung damage and 690 kilopascal for fatality) [23].
- The Explosives Storage and Transport committee (ESTC) Outdoor Blast Model, which is based on a review of available literature on primary and tertiary blast effects:

$$P_{fatality} = (e^{(-5.785 \,.\, (R \,/\, M1/3) + 19.047)}/100)$$

where, $\mathbf{P_{fatality}}$ = Probability of Fatality; **e** = Exponential; **R** = Range (meters) M1/3 = Cube Root of Explosive Mass (kilograms).

This model is only valid within the limits of the scaled distance 'S' ($S = R/M^{1/3}$) where 2.5 meter.kilogram$^{1/3}$ < S < 5.3 meter.kilogram$^{1/3}$. For S > 5.3 meter.kilogram$^{1/3}$ the fatality probability is zero whilst for S < 2.5 meter.kilogram$^{1/3}$ 100% fatalities should be expected.

C.3.138 Primary (Biological) Injury Mechanisms

Primary injury to the organ/tissue is caused by the damage of its integrity by external force, which could induce:

1) A direct contusion of the organ/tissue.
2) Organ/contusion caused by a movement against rough interior surfaces of skeleton/skull and/or other supporting elements.

3) Shearing and stretching of the organs/tissue compartments due to the energy propagation causing motion in relation to the skeleton and each other.

4) Vascular response to the injurious force including leakage of the walls of blood vessels or rupture of blood vessels [33], [122], [139].

C.3.139 Prospective Study

- A prospective study scrutinizes for outcomes, such as the development of a disease, during the study period and relates this to other factors such as suspected risk or protection factor(s). The study usually involves taking a cohort of subjects and observing them over a long period. The outcome of interest should be common; otherwise, the number of outcomes observed will be too small to be statistically meaningful (indistinguishable from those that may have arisen by chance). All efforts should be made to avoid sources of bias such as the loss of individuals to follow up during the study. Prospective studies usually have fewer potential sources of bias and confounding than retrospective studies.

- In prospective cohort studies the investigators conceive and design the study, recruit subjects, and collect baseline exposure data on all subjects, before any of the subjects have developed any of the outcomes of interest. The subjects are then followed into the future in order to record the development of any of the outcomes of interest. The follow up can be conducted by mail questionnaires, by phone interviews, via the Internet, or in person with interviews, physical examinations, and laboratory or imaging tests. Combinations of these methods can also be used (http://sphweb.bumc.bu.edu/otlt/MPH-Modules/EP/EP713_CohortStudies/EP713_CohortStudies2.html).

- A prospective, longitudinal epidemiologic study is often the best non-experimental means to confirm and quantify associations between exposure factors and health outcomes, although rigorous planning, coordination, and cost factors must be considered (see The North Atlantic Treaty Organization (NATO) Human Factors and Medicine (HFM) HFM-234 Research Task Group (RTG) "Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods, and Standards" − Guidelines for Conducting Epidemiological Studies of Blast Injury).

C.3.140 Pulmonary Barotrauma

See BLAST LUNG.

C.3.141 Quasi-Static Gas Pressure

- As the blast waves from explosions within suppressive structures reflect and re-reflect, and as the energy available from the explosive source is added to the air within the structure, long-term pressures can build up within the structure. These pressures are termed "quasi-static pressures'' because they can last long enough to apply essentially static internal gas pressure loads to the structure.

- During confined-space explosion, depending on the relative magnitudes of the mass of the explosive and the volume of the building/vehicle, the gas pressure may be the dominant loading mechanism on the building/vehicle elements. Because normal buildings/vehicles (as opposed to containment buildings) have doors, windows, heating ducts, etc., which allow the gas to vent into adjacent rooms or the outside world, the gas pressure does not persist. The decay of the pressure, however, takes place in a time-scale much longer than the duration of the individual shock reflections, and the overall duration is typically much longer than the structural response time of elements loaded in the building/vehicle. For this reason it is referred to as quasi-static gas pressure [10], [144].

C.3.142 Quaternary Blast Injury

Clinical consequences of the explosive products including heat (radiant and convective), toxic byproducts of chemical reactions initiated by detonation, toxidromes from fuel, metals, among others. [282] These may include causing burns and inhalation injury [190], [208], [270]. Burn injuries can be experienced in isolation or as part of multiple injuries caused by blast. The pattern of burn injury is variable and is dependent on the weapon used. A casualty close enough to conventional munitions to receive burns in an open environment is likely to have suffered severe or fatal secondary (fragment) and primary blast injuries. The incidence of burns in survived infantry soldiers is therefore low; however this incidence is higher when the injuries occur in vehicles, ships and aircraft [94], [121]. Inhalational injury can be subdivided into:

1) Direct thermal injury above the larynx;
2) Injury below the larynx; and
3) Local pulmonary and systemic effects of inhaled toxins [271].

C.3.143 Quinary Blast Injury

Clinical consequences of "post detonation environmental contaminants" including bacteria (deliberate and commensal, with or without sepsis), radiation (dirty bombs), tissue reactions to fuel, metals, etc. [131], [282].

C.3.144 Reflected Pressure

- The pressure caused by the reflection of a shock wave from a surface or interface (change in medium). This pressure is maximum when the incident shock velocity is perpendicular to a non-responding surface, but is not a monotonic function of the incident angle [166].
- If the medium struck (e.g., the ground or a structure) is denser than the medium in which the shock wave is traveling (e.g., air), the reflected pressure is positive (compression). If the reverse is true (e.g., when a shock wave in the ground or water strikes the air surface) the reflected pressure is negative (rarefaction or tension).
- If the blast wave encounters an obstacle perpendicular to the direction of propagation, reflection increases the overpressure to a maximum reflected pressure $\mathbf{P}_r$ as:

$$P_r = 2P_{so}\left\{\frac{7P_o + 4P_{so}}{7P_o + P_{so}}\right\}$$

  where, $\mathbf{P_{so}}$ is the peak overpressure, and $\mathbf{P_o}$ is the ambient pressure [169].
- The table below shows some representative numerical values of peak reflected overpressure, $\mathbf{P_r}$ (in megapascal), with different **W** (charge weight) – **R** (the actual effective distance from the explosion) combinations [169], [246].

Table C-1: Representative Numerical Values of Peak Reflected Overpressure (Pr, in MegaPascal) with Combinations of Different Charge Weights (W) and Actual Effective Distances from the Explosion (R).

W / *R*	100 kg TNT	500 kg TNT	1000 kg TNT	2000 kg TNT
1m	165.8	354.5	464.5	602.9
2.5m	34.2	89.4	130.8	188.4
5m	6.65	24.8	39.5	60.19
10m	0.85	4.25	8.15	14.7
15m	0.27	1.25	2.53	5.01
20m	0.14	0.54	1.06	2.13
25m	0.09	0.29	0.55	1.08
30m	0.06	0.19	0.33	0.63

C.3.145 Reflection Factor

The ratio of the total (reflected) pressure to the incident pressure when a shock (or blast) wave traveling in one medium strikes another.

C.3.146 Retrospective Study

- This is a study when the disease/exposure has already occurred before the onset of data collection [84].
- A retrospective study (e.g., observational or phenomenological), involving data analysis based on medical history documentation, can be used to identify certain components of importance if a full set of well-defined data exists for a focused hypothesis. However, researchers often still need to conduct a prospective study to control for variability in the study population, data collection protocols, and data elements of interest to which registry data may not be focused (see The North Atlantic Treaty Organization (NATO) Human Factors and Medicine (HFM) HFM-234 Research Task Group (RTG) "Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods, and Standards" − Guidelines for Conducting Epidemiological Studies of Blast Injury).

C.3.147 Rise Time

For a blast wave it is the time measured by a sensor from the initial rise in pressure to the maximum positive pressure recorded (usually microseconds or milliseconds) [254].

C.3.148 Sachs' Scaling Law

In the case of blast waves from explosions produced at altitude, where ambient conditions can be very different from those at sea level, the most commonly used scaling law is that developed by Sachs in 1944. The application of the Sachs scaling law leads to the formulation of altitude scaling factors [251]:

Scaled Distance at Altitude 'z'

$$S_{dz} = (P_0/P_z)^{1/3}$$

Scaled Pressure at Altitude 'z'

$$S_{pz} = (P_z/P_0)$$

Scaled Impulse at Altitude 'z'

$$S_{iz} = (P_z/P_0)^{2/3} \cdot (T_0/T_z)^{1/2}$$

Scaled Impulse at Altitude 'z'

$$S_t = (P_0/P_z)^{1/3} \cdot (T_0/T_z)^{1/2}$$

where, $\mathbf{S_{dz}}$ = Scaled Distance at Altitude **'z'** (meters); $\mathbf{P_0}$ = Ambient Pressure (kilopascals) (101.33 kPa) $\mathbf{P_z}$ = Pressure at Altitude **'z'** (kilopascals); $\mathbf{S_{pz}}$ = Scaled Pressure at Altitude **'z'** (kilopascals); $\mathbf{S_{iz}}$ = Scaled Impulse at Altitude **'z'** (skilogram.meter/second); $\mathbf{T_0}$ = Ambient Temperature (Kelvin) (288.160 K); $\mathbf{T_z}$ = Temperature at Altitude **'z'** (Kelvin); $\mathbf{S_t}$ = Scaled Times at Altitude **'z'** (seconds).

C.3.149 Scaling

- Representing something in proportional dimensions [283].
- Scaling is concerned with the effects or consequences of a change in size [223].
- The numerous biological scaling methods include several basic principles such as elementary geometry, similarities in mammalian morphology, and similarities in physiology [21], [98], [223].

C.3.149.1 Isometric Scaling

Bodies that are geometrically similar, or isometric, are characterized by equality of linear proportions, i.e. a change in any one characteristic linear dimension is accompanied by a change in all other linear dimensions in exactly the same proportion. The essentials of isometric geometry can be summarized as follows:

- Surface $\propto$ (Length)^2;
- Volume $\propto$ (Length)^3; and
- Surface $\propto$ (Volume)$^{2/3}$, this line simply stating that as the volume of a body is increased, its surface does not increase in the same proportion, but only in proportion to the two-thirds power of the volume [223].

C.3.149.2 Non-Isometric or Allometric Scaling

From the Greek "alloios" meaning "different"; a great variety of observations that relate biological variables to body size conform to the allometric equation:

$$y = b\, x^{a}$$

or:

$$\log y = a \cdot \log x + \log b$$

where the exponent **a** represents the slope of the straight line obtained in the logarithmic plot [223].

C.3.150 Scaled Impulse

Is often used to predict the effects of blast on humans [251]:

$$I_{si} = I_s / P_0^{1/2} \cdot m^{1/3}$$

where, $\mathbf{I_{si}}$ = Scaled Impulse (kilograms per meters per second); $\mathbf{I_s}$ = Side-On Impulse (kilograms per meters per second); $\mathbf{P_0}$ = Ambient Pressure (kilopascals); **M** = Mass of Individual (kilograms).

C.3.151 Scaling Law

- A mathematical relationship which permits the effects of an explosion of given energy yield to be determined as a function of distance from the explosion (or from ground zero) provided the corresponding effect is known as a function of distance for a reference explosion, e.g., of 1-kiloton energy yield. [279]
- Related terms: Cube Root Scaling Law; Hopkinson-Cranz Scaling Law; Sachs' Scaling Law.

C.3.152 Schlieren Photography

- A visual process used to photograph the flow of fluids of varying density.
- The historical visualization method of the shockwave progression was based on the Schlieren effect (from German; singular "Schliere", meaning "streak") identifying optical inhomogeneities in transparent material, which otherwise are not visible to the human eye. This principle, first described by Robert Hooke in 1665 [114], is based on the fact that the optical inhomogeneities are localized differences in optical path length causing light deviation; this light deviation, in turn, produces localized brightening, darkening, or even color changes in an image, depending on which way the light ray deviates [202]. The typical conventional Schlieren system includes a single light source, lenses, knife-edge and image plane. The small light source with finite width is collimated by the first lens and passes through the test section. The passing light is then focused by the second lens and projected on the image plane. At the focal point, the knife-edge is introduced to cut off part of light source image [16]. In circumstances when flow is established in the test section, any light beam, which passes through a region in which there is a density gradient normal to the light direction, will be deflected under an angle. The resulting image is nearly independent of the position along the optical axis of the density gradients; accordingly, the final light intensity depends on the sum of the density gradients caused by the light beam passing through a flow field. Accumulating experimental evidence has established that the conventional Schlieren system lacks a focusing property normal to optical path in the test section. The modernized version of the classical Schlieren concept, the Laser-Schlieren (LS), provides a much-improved temporal and/or spatial resolution of the shock front propagation. The LS is a narrow laser beam deflection technique [127] offering good resolution and sensitivity for fast processes.

C.3.153 Secondary Blast Injury

Injury caused by secondary blast effects (e.g., fragments originating from the exploding device (preformed or natural / unformed) casing fragments, and other projectiles deliberately introduced into the device to enhance the fragment threat); and fragments generated during the explosion from the environment (debris, vehicular metal, etc.) ([15], [152], [245], [258], [265], [282]).

C.3.154 Secondary Blast Injury Levels

The United Nations International Ammunition Technical Guideline [251] lists the calculations provided by Gilbert, Lees and Scilly for defining probability values for building occupants suffering fatal, serious, or light injuries. These are shown in the table below.

Table C-2: Probability Values for Building-Occupants to Suffer Fatal, Serious, or Light Injuries.

Damage Category	Damage Definition	Probability (Fatality)	Probability (Fatality or Serious Injury)	Probability (Fatality, Serious Injury or Light Injury)
		P(K)	P (K + I)	P (K + SI + LI)
A_a	Houses totally demolished.	0.96	1.0	1.0
A_b	Houses almost completely demolished.	0.57	0.66	0.82
A	Houses demolished.	0.62	0.71	0.84
B	Houses so badly damaged they are beyond repair and require demolition.	0.096	0.15	0.38
C_b	Houses rendered uninhabitable but can be repaired with extensive work.	0.009	0.043	0.13
C_a	Houses rendered uninhabitable but can be repaired reasonably quickly.	0	0.002	0.006
D	Houses requiring repairs to remedy serious inconvenience but remain habitable.	0	0	0

C.3.155 Secondary (Biological) Injury Mechanisms

These include complex biochemical and physiological processes, which are initiated by the primary insult and manifest over a period of hours, days, and months to years [33], [122]. These events of this secondary injury process can be usefully divided temporally into multiple contiguous phases: immediate, acute, intermediate, and chronic stages.

C.3.156 Shock Mach Number

The ratio of the shock velocity to the ambient speed of sound. Because this is a ratio, the number is unitless. Although unitless, this should be expressed as a vector, i.e., the direction should be specified [166].

C.3.157 Side-On Pressure

The term incident pressure is used here to describe the blast overpressure that may be recorded in free space, such that its recording does not perturbed the blast field. This is normally approximated to in explosive trials by the use of streamlined pressure gauges.

Related term(s): incident pressure.

C.3.158 Specific Impulse

Total impulse per unit area [14].

C.3.159 Shock Front

The sharp boundary between the pressure disturbance created by an explosion (in air, water, or earth) and the ambient atmosphere, water, or earth, respectively. It constitutes the front of the shock (or blast) wave [166].

C.3.160 Shock Tube

- It is an instrument that allows simulation of a shock wave using compressed air or gas as compared to a blast tube where a blast wave is generated using an explosive.
- The shock tube has at least two basic components (see the figure below): a driver section where the compressed gas pressure builds, and a driven section where the shock wave forms and propagates. The two sections are separated by a barrier, i.e. membrane, which ruptures when the pressure in the driver reaches the critical level. This allows the gas to be released from the driver section into the driven section [171], [207].

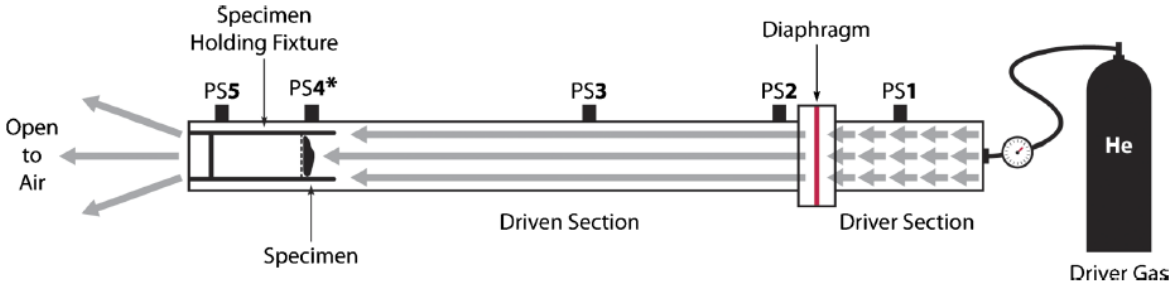


Figure C-11: Diagram of the Shock Tube System Generally Used to Induce Blast in Laboratory Conditions [132]. The shockwave is generated using a compressed gas such as by helium or air, breaking through a diaphragm to the driven section that can be open to ambient air (as on this figure) or closed with a muffler. The subject-holding fixture is positioned inside the driven section near the open end of the tube (left). The intensity of the generated shockwave is recorded with sensors PS1 – PS5.

C.3.161 Shock Wave

- A region of abrupt change of pressure and density moving as a wave front at or above the speed of sound [166].
- A large-amplitude wave formed by the sudden compression of the medium through which the wave moves. Shock waves can be caused by explosions or by objects moving through a fluid at a speed greater than the speed of sound.
- A continuously propagated pressure pulse (or wave) in the surrounding medium, which may be air, water, or earth, initiated by the expansion of the hot gases produced in an explosion. A shock wave in air is generally referred to as a blast wave, because it resembles and is accompanied by strong, but transient, winds. The duration of a shock (or blast) wave is distinguished by two phases. First there is the positive (compression) phase during which the pressure rises very sharply to a value that is higher than ambient and

then decreases rapidly to the ambient pressure. The positive phase for the dynamic pressure is somewhat longer than for overpressure, due to the momentum of the moving air behind the shock front. The duration of the positive phase increases and the maximum (peak) pressure decreases with increasing distance from an explosion of given energy yield. In the second phase, the negative (suction, rarefaction, or tension) phase, the pressure falls below ambient and then returns to the ambient value. The duration of the negative phase may be several times the duration of the positive phase. Deviations from the ambient pressure during the negative phase are never large and they decrease with increasing distance from the explosion.

C.3.162 Short-Duration Blast

- A term used in reference to lung blast injuries and denotes a blast wave where the positive phase duration is equal or less than 30 milliseconds, although the dividing value differentiating the short-duration from long-duration blasts is not strictly defined [17].
- "Short"-duration blast injuries are generally localized pulmonary injuries, presumably based on the spalling of the alveolar surfaces owing to the mismatch of local impedance of the tissues [65]. These blasts typically occur from low momentum blast exposures produced by the detonation of high explosives of less than 100 kilograms (such as IEDs, mines, rockets, or artillery rounds) or testing using short helium-driven shock tubes [179].

C.3.163 Shunt, Physiological

The blood that traverses that enters the arterial system without going through the ventilated areas of the lung. The effect of the addition of this poorly oxygenated blood is to depress the arterial oxygen tension (PaO_2). An important feature of a shunt is that the hypoxemia is difficult to abolish by giving the patient 100% oxygen to breathe. This is because the shunted blood bypasses the ventilated alveoli and is not exposed to the elevated oxygen levels in the alveoli so that is continues to depress the arterial oxygen tension. The additional oxygen added via the well ventilated areas of the lung has relatively little effect because most of the oxygen is carried bound to hemoglobin, which is these well ventilated areas of the lung is already fully saturated. The small amount of extra oxygen dissolved in the plasma of the well ventilated areas of the lung is quickly sequestered by the relatively unsaturated hemoglobin originating from the poorly ventilated areas of the lung once the blood from both well and poorly ventilated areas of the lung mix when the blood enters the left side of the heart [104].

C.3.164 Skull Flexure

- A proposed mechanism of blast-induced brain injury whereby the blast wave acts directly on the head causing the skull to flex, creating potentially damaging loads in the brain [160].
- A dynamic deformation of the skull creating localized regions of high and low pressure [22].

C.3.165 Spallation

Disruption that occurs at the boundary between two media of different densities; it occurs when a compression wave in the denser medium is reflected at the interface [20], [37].

C.3.166 Specimen Positioning for Blast Injury Research

- Proper positioning of the specimen and its orientation in relation to the incident shock wave in the shock tubes play a key role in scientifically appropriate blast injury models [36], [40]. It has been established that

the biomechanical and biological responses of an animal exposed to the shockwave significantly depends on its location inside the tube [242] as well as on its orientation in relation to the propagating incident shock wave [40], [253].

- The majority of the currently existing literature supports the need of placing the specimen inside the shock tube [242], [253]. It has been shown that when the animal is positioned inside the shock tube, it is subjected to a load that is due to the close-to-pure blast wave, which is comparable to the shock wave generated in free-field conditions. In contrast, when the animal is positioned at or near the shock tube's exit, there is a sharp decay in pressure after the initial shock front, which is caused by the expansion wave from the exit of the shock tube eliminating the exponentially decaying blast wave [242]. This phenomenon leads to significant decrease of the positive blast impulse and conversion of most of the blast energy from supersonic blast wave to subsonic jet wind [109], which has significantly different effects from those generated by a blast wave. Because of the jet wind, the restrained animal is exposed to more severe compression of the head and neck, whereas the thoracic cavity is exposed to higher pressure of longer positive-phase duration.

- Svetlov and colleagues [243], [244] demonstrated the importance of an animals positioning in relation to the shock tube (inside versus outside) by exposing rats to blast loading 50 millimeters outside the shock tube. Their results suggested that the subsonic jet wind represented the bulk of the blast impulse, and the injuries were caused by the combination of blast wave and subsonic jet wind, as opposed to a pure blast wave injury. These findings have been comparable to those described in experiments with surrogate physical models (dummy heads) placed at the exit of the shock tube [77].

C.3.167 Specimen Size for Blast Injury Research

- In shock tube/blast tube experiments, special attention should be paid to the tube cross-section/specimen size ratio to avoid a blockage of the shockwave flow. The acceptable ratio depends on the research question, i.e., blast conditions the researcher aims to replicate [36].

- The specimen in a shock tube constricts the area open for flow in the tube, which can significantly modify the flow field around the specimen as compared to a free/open-field encounter with the same shock wave [88]. The reflected shock modifies the flow directly upstream from the target decelerating the flow, increasing its stagnation temperature and decreasing its stagnation pressure. These effects of the reflected shock are more pronounced in a shock tube than in the free/open field because the reflected shock is prevented from free expansion by the shock tube walls [88]. To calculate the acceptable level of blockage, the following equation calculating the blast-induced drag could be useful [88], [165]:

$$Q_b = Q_0 [\exp (2.64 \text{ X } R^{1.038})]$$

where $\mathbf{Q_b}$ is the dynamic pressure in a partially obstructed shock tube, $\mathbf{Q_0}$ is the dynamic pressure in a shock tube without obstruction, i.e., without specimen, **R** is the blockage ratio calculated as the cross-sectional area the specimen divided by the cross-sectional area of the shock tube test section. The equation clearly shows that compared to the empty shock tube (thus, free/open-field conditions), 10% of blockage increases the dynamic pressure by 27%, 20% of blockage leads to dynamic pressure increase by 64%, whereas 30% of obstruction increases the dynamic pressure by 113%. The problem of shock tube blockage by specimen is not only in increasing the dynamic pressure; as previously outlined, the blockage also generates turbulence and unstable flow conditions, which makes any scientifically sound conclusion about causal relationships between blast conditions and resulting injuries almost impossible.

C.3.168 Stagnation Pressure

- The total pressure **(**sometimes called "pitot" pressure) is the stagnation pressure for compressible flow where the flow is brought to rest adiabatically. It closely represents the pressure that the specimen experiences when facing the shock wave. Consequently, the pitot pressure sensors often have a pencil shape pointing directly towards the center of the flow [55].

- In shock tube experiments, to measure the total pressure for each test condition, the tests need to be conducted with a pressure probe inserted in place of the specimen. For example, in their recent paper, Sawyer *et al*. [220] reported measuring total pressures experienced by the test animal, which has been located at 4280 millimeters from the diaphragm inside their shock tube (Advanced Blast Simulator/ABS) using a Pitot probe (Endevco 8530B pressure transducer) orientated such that it measured the total pressures at the test location.

- Related term(s): total pressure, pilot pressure.

C.3.169 Static Pressure

Defined as the gas pressure, above ambient, which is caused by compression or heating of the gas. The units are force per unit area or energy per unit volume. It results in a crushing force on an object [165].

Related term(s): overpressure, side-on pressure, gauge pressure.

C.3.170 Strain

C.3.170.1 Engineering

Quantity that describes the relative deformation or change in shape and size of a material.

- Strain is the response of a system to an applied stress. When a material is loaded with a force, it produces a stress, which then causes a material to deform. Engineering strain is defined as the amount of deformation in the direction of the applied force divided by the initial length of the material. This results in a unitless number, although it is often left in the unsimplified form, such as inches per inch or meters per meter. For example, the strain in a bar that is being stretched in tension is the amount of elongation or change in length divided by its original length. As in the case of stress, the strain distribution may or may not be uniform in a complex structural element, depending on the nature of the loading condition (https://www.nde-ed.org/EducationResources/CommunityCollege/Materials/Mechanical/StressStrain.htm).

- If the stress is small, the material may only strain a small amount and the material will return to its original size after the stress is released. This is called elastic deformation, because like elastic it returns to its unstressed state. Elastic deformation only occurs in a material when stresses are lower than a critical stress called the yield strength. If a material is loaded beyond it elastic limit, the material will remain in a deformed condition after the load is removed. This is called plastic deformation.

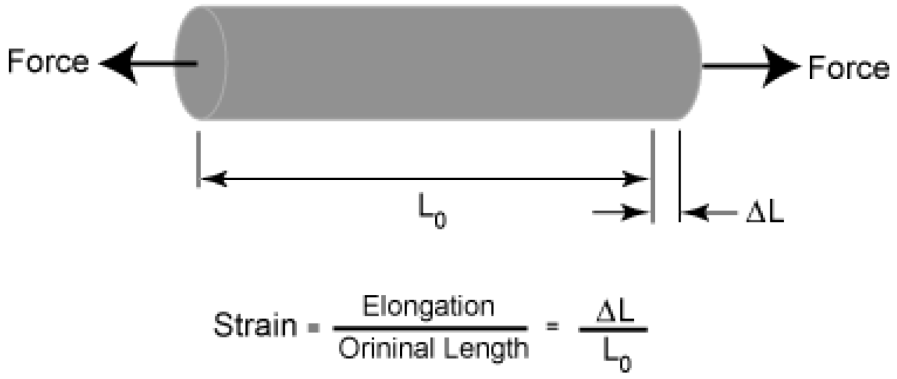


Figure C-12: Schematic Representation of Principles Defining Strain as They Relate to Relative Deformation or Change in Shape and Size of a Material.

C.3.170.2 Medical

- A strain is a stretching or tearing of muscle or tendon. A tendon is a fibrous cord of tissue that connects muscles to bones. Strains often occur in the lower back and in the hamstring muscle in the back of the thigh. Initial treatment for both sprains and strains includes rest, ice, compression and elevation. Mild sprains and strains can be successfully treated at home. Severe sprains and strains sometimes require surgery to repair torn ligaments, muscles or tendons (http://www.mayoclinic.org/diseases-conditions/sprains-and-strains/basics/definition/con-20020958).
- A population of homogeneous organisms possessing a set of defined characteristics. In bacteriology, the set of descendants that retains the characteristics of the ancestor; members of a strain that subsequently differ from the original isolate are regarded as belonging either to a sub-strain or to a new strain.
- Specific host cell(s) designed or selected to optimize production of recombinant products.

C.3.171 Stress

C.3.171.1 Engineering

The term stress(s) is used to express the loading in terms of force applied to a certain cross-sectional area of an object. From the perspective of loading, stress is the applied force or system of forces that tends to deform a body. From the perspective of what is happening within a material, stress is the internal distribution of forces within a body that balance and react to the loads applied to it. The stress distribution may or may not be uniform, depending on the nature of the loading condition. For example, a bar loaded in pure tension will essentially have a uniform tensile stress distribution, whereas a bar loaded in bending will have a stress distribution that changes with distance perpendicular to the normal axis.

(https://www.nde-ed.org/EducationResources/CommunityCollege/Materials/Mechanical/StressStrain.htm).

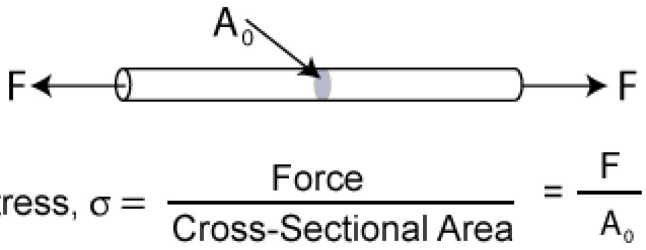


Figure C-13: Schematic Representation of Principles Defining Strain as They Relate to Force Applied to a Certain Cross-Sectional Area of an Object.

Some common measurements of stress are:

- Psi = lbs/in^2 (pounds per square inch).
- ksi or kpsi = kilopounds/in^2 (one thousand or 10^3 pounds per square inch).
- Pa = N/m^2 (Pascals or Newtons per square meter).
- kPa = Kilopascals (one thousand or 10^3 Newtons per square meter).
- GPa = Gigapascals (one million or 10^6 Newtons per square meter).

C.3.171.2 Medical

In a medical or biological context, **stress** is a physical, mental, or emotional factor that causes bodily or mental tension. Stress factors can be external (from the environment, psychological, or social situations) or internal (illness, or from a medical procedure). Stress can initiate the "fight or flight" response, a complex reaction of neurologic and endocrinologic systems [224], [225], [226]:

- Catecholamine hormones, such as adrenaline or noradrenaline, facilitate immediate physical reactions associated with a preparation for violent muscular action. These include the following:
  1) Acceleration of heart and lung action, paling or flushing, or alternating between both;
  2) Inhibition of stomach and upper-intestinal action to the point where digestion slows down or stops;
  3) The general effect on the sphincters of the body;
  4) Constriction of blood vessels in many parts of the body;
  5) Liberation of nutrients (particularly fat and **glucose**) for muscular action;
  6) Dilation of blood vessels for muscles;
  7) Inhibition of the lacrimal gland (responsible for tear production) and salivation;
  8) Dilation of pupil (mydriasis);
  9) Relaxation of bladder;
  10) Inhibition of erection;
  11) Auditory exclusion (loss of hearing);
  12) Tunnel vision (loss of peripheral vision);
  13) Disinhibition of spinal reflexes; and
  14) Shaking [29], [261], [262], [263].

- Stress can cause or influence the course of many medical conditions including psychological conditions such as **depression** and **anxiety** [31]. Medical problems can include poor healing [87], **irritable bowel syndrome** [158], [191], **high blood pressure** [85], [110], [210], poorly controlled **diabetes** [107], and many other conditions.
- Stress management is recognized as an effective treatment modality to include pharmacologic and non-pharmacologic components [126], [196].

C.3.172 Surrogate

A substitute or replacement.

C.3.173 Systemic Response to Blast

- Multiple physiological, biochemical, and molecular processes stimulated by blast exposure including but not limited to the activation of autonomic nervous system; sudden pressure increase in vital organs such as lungs and liver; and activation of neuroendocrine-immune system. These processes are often interacting and/or inter-dependent and significantly influence the progress and outcome of blast injury [34], [43], [45], [47].
- Even when the multi-organ responses are mild, systemic changes significantly extend the original organ damage and influence their severity and functional outcome. Air emboli, activation of the autonomic nervous system, vascular mechanisms, and systemic inflammation are among the most important deleterious systemic alterations that could modify the initial injuries due to blast [36].

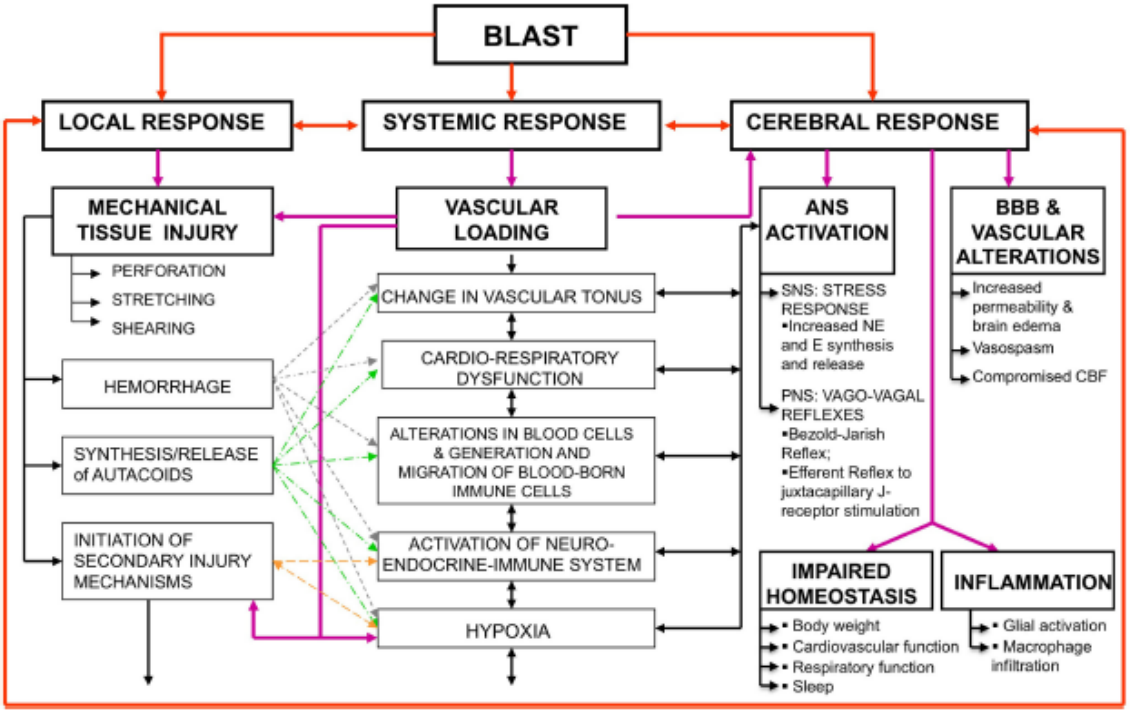


Figure C-14: Simultaneous Activation of Systemic, Local, and Cerebral Responses to Blast Exposure and Interactive Mechanisms Causing or Contributing to the Pathobiology of BINT [34].

- Simultaneous activation of systemic, local, and cerebral responses to blast exposure and interactive mechanisms causing or contributing to the pathobiology of blast-induced neurotrauma. ANS, Autonomic Nervous System; BBB, Bloodbrain Barrier; CBF, Cerebral Blood flow; E, Epinephrine; NE, Norepinephrine; SNS, Sympathetic Nervous System; PNS, Parasympathetic Nervous system. [34]

C.3.174 Tertiary Blast Injury

Displacement of the body or part of body by the blast overpressure causing acceleration/deceleration to the body or its parts, which may subsequently strike hard objects causing typical blunt injury (translational injury), avulsion (separation) of limbs, stripping of soft tissues, skin speckling with explosive product residue and building structural collapse with crush and blunt injuries, and crush syndrome development [199].

C.3.175 Thermobaric Bomb

- An enhanced blast weapon that creates a blast wave that is generally lower pressure but has a longer duration and over a greater area than a conventional explosive. There is an initial dispersal of a vapour cloud then there is detonation of the vapour cloud and the generation of a blast wave and significant thermal output [75], [157].
- An explosive or detonable mixture of chemicals, which include active metal particulates such as aluminum, magnesium, titanium, boron, zirconium, or mixtures or alloys of these metals, among others. The metal particles may be coated with Viton or Teflon, both of which release fluorine upon heating, at a temperature lower than the metal particles ignition temperature. The fluorine can react with the oxide coatings of the metal particulates before the oxide melts thus reducing the effective ignition temperature. The particulates may be spheroids or flakes with sizes ranging from nanometers to millimeters. A sub-set of the thermobaric mixtures is Solid Fuel Air Explosives (SFAE). In SFAE, the metal particulates surround a central high explosive charge, which disperses and initiates the burn of the particulates [166].

C.3.176 Thoracic Barotrauma

- Produces the following unique cardiovascular response: a decrease in heart rate, stroke volume, and cardiac index; the normal reflex increase in systemic vascular resistance does not occur, so blood pressure falls; and if this response is not fatal, recovery usually occurs within 15 minutes to 3 hours.
- It was hypothesized [44], [45], [49], [274] that blast overpressure may cause sudden hyperinflation of the lungs [63] and subsequent mechanical irritation of juxtacapillary J-receptors located in the alveolar interstitium and innervated by vagal fibers [178]. The stimulation of the J-receptors causes a vago-vagal reflex leading to apnea followed by rapid breathing, bradycardia, and hypotension, which are frequently observed immediate symptoms after blast exposure. Additionally, chemoreceptors located primarily in the left ventricle can be stimulated by hypoxia/ischemia caused by pulmonary vagal reflex, and subsequently trigger a cardiovascular decompressor Bezold-Jarisch reflex, which involves marked increase in vagal (parasympathetic) efferent discharge to the heart [273]. This causes reduction of heart rate (bradycardia) and dilatation of the peripheral blood vessels with resulting lowering of the blood pressure, which could further contribute to cerebral hypoxemia [34], [39], [44], [45], [129].
- Related term(s): Barotrauma, Lung Barotrauma.

C.3.177 Thoracic Surge

A blast wave that impacts the thorax causes a rapid transient pressure wave (a hydrodynamic pulse) to be transmitted to the brain by way of major blood vessels [42], [45], [48], [68], [172], [229].

C.3.178 Threshold

C.3.178.1 General

The magnitude or intensity that must be exceeded for a certain reaction, phenomenon, result, or condition to occur or be manifested.

C.3.178.2 Medicine

- The point at which a stimulus is of sufficient intensity to begin to produce an effect (psychology or physiology).
- The point that must be exceeded to begin producing a given effect or result or to elicit a response.

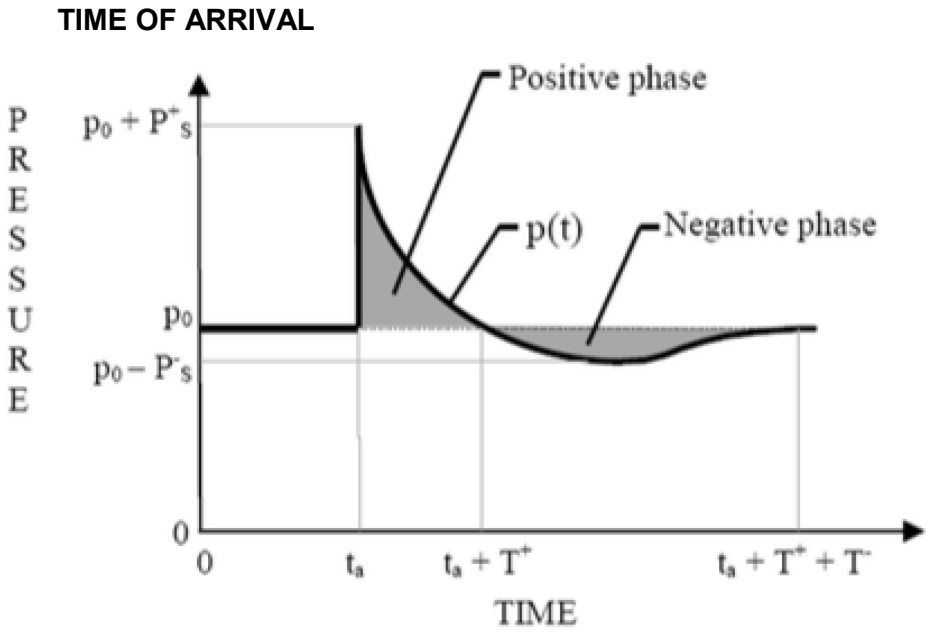


Figure C-15: The Friedländer Wave Describing an Ideal Blast from a Spherical Source in an Open Environment (t0 is the time at which the pressure began to rise above ambient pressure). Positive magnitude is the difference between peak pressure and ambient pressure. Positive duration is the time between t0 and when the pressure goes below ambient pressure. Positive impulse is the integral of the pressure-time trace during the positive phase. Negative magnitude is the difference between ambient and peak negative pressure). [169].

where the initial pressure is the ambient pressure $\mathbf{p_0}$ before the shock wave front reaches the given point. At time $\mathbf{t} = \mathbf{t_a}$, the pressure rises discontinuously to the peak value ($\mathbf{p_0} + \mathbf{P_s^+}$), where $\mathbf{P_s^+}$ is the peak overpressure and decays to the ambient pressure in a time **T**, which is referred as positive phase. Then the pressure drops to a

partial vacuum of value ($\mathbf{p_0 - P^-}$) and returns to the ambient in a time $\mathbf{T^-}$ referred as negative phase [51]. The pressure profile curve **p(t)** can be approximately described by the modified Friedlander equation as:

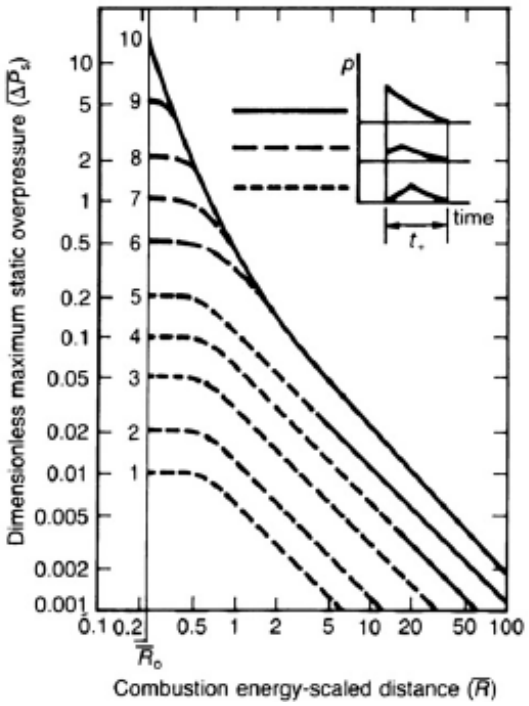
$$p(t) = p_0 + P_s^+ (1 - t/T^+) e^{-bt/T+}$$

where, time t is measured from time of arrival t_a.

C.3.179 TNO Multi-Energy Method

- One of the most widely used methods for evaluating the blast potential from vapor cloud explosions [106]. The available combustion energy from a potential vapor cloud inside the plant together with an anticipated explosion strength is used to create blast-curves [252].
- Application of the TNO Multi-Energy method requires knowledge of two parameters describing the explosion: a charge size and a charge strength. During the last years, research has led to an improved determination of the charge strength, i.e., the class number or source overpressure, to be chosen to apply the blast charts. A correlation has been derived relating the charge strength to a set of parameters describing the boundary conditions of the flammable cloud and the fuel in the cloud [154]. Similar methods like Baker-Strehlow [14], [188], [193], [241] and CAM [106] also incorporate findings from experiments to make correlations for source strength. Some weaknesses with these methods are:
  1) These methods have limited ability, if any, to predict the actual explosion source strength or dynamics. Source explosion strength has to be estimated based on limited experimental data, predictions using more detailed Computational Fluid Dynamics (CFD) tools, or estimated near-field blast damage.
  2) Some of the methods are calibrated based on experiments at limited scale, and are incapable or inappropriate for scaled-up explosions.
  3) These methods have limited ability to take into consideration directional effects, asymmetric explosions, or effects due to partial confinement.
  4) Blast-wave interaction with structures in near- and far-field, or the effect of protection walls cannot be predicted [106].

The TNO Multi-Energy method is illustrated by Figure C-16 below.



$$\overline{\Delta P_s} = \frac{P_{static} - P_o}{P_o}$$

P_o = ambient pressure

P_{static} = static total blast pressure

$$\overline{R} = R[P_o / E]^{1/3}$$

R = distance from the center of explosion

E = total available combustion energy

Figure C-16: A Scaled Distance is Estimated Based on the Available Combustion Energy of a Gas Cloud Inside a Plant. With this scaled distance, and assumption of explosion strength (curves 1e10 representing 1 kilopascal [gauge] to w1000 kilopascal [gauge] source strength), the pressure as a function of distance (see above plot) and other parameters can be estimated. This method has been used to predict the quantity of fuel involved and the consequences of vapor cloud explosions. From Hansen *et al.* [106]: Illustration of TNO Multi-Energy method [252].

C.3.180 TNT Equivalence

- A measure of the energy released in the detonation of a nuclear (or atomic) weapon, or in the explosion of a given quantity of fissionable material, expressed in terms of the mass of TNT (Trinitrotoluene), which would release the same amount of energy when exploded.
- The TNT equivalence is usually stated in kilotons or megatons. The basis of the TNT equivalence is that the explosion of 1 ton of TNT is assumed to release 109 calories of energy. [279]
- TNT equivalence can be regarded as a conversion factor by which the available heat of combustion can be converted into blast energy. In one sense, TNT equivalency expresses the efficiency of the conversion process of chemical energy (heat of combustion) into mechanical energy (blast) [32].
- The TNT equivalence can be calculated as [251]:

$$\mathbf{M_{TNTe} = (E^d_{exp}/E^d_{TNT}) \, . \, M_{exp}}$$

- where, $\mathbf{M_{TNTe}}$ = TNT Equivalent Mass (kilograms); $\mathbf{E^d_{exp}}$ = Specific Detonation Energy of Explosive (Joules/kilogram); $\mathbf{E^d_{TNT}}$ = Specific Detonation Energy of TNT (Joules/kilogram); $\mathbf{M_{exp}}$ = Mass of Explosive (kilograms).

- To convert the charge mass into and equivalent mass of TNT, the charge mass of explosive is multiplied by the conversion factor based on the specific energy of the charge and the TNT. Specific energy of different explosive types and their conversion factors to that of the TNT are given in the table below [83].

Table C-3: Conversion Factors for Explosives [83].

Explosive	Specific energy	TNT equivalent
	Q_x / kJ/kg	Q_x/Q_{TNT}
Compound B (60 % RDX, 40 % TNT)	5190	1,148
RDX (Ciklonit)	5360	1,185
HMX	5680	1,256
Nitroglycerin (liquid)	6700	1,481
TNT	4520	1,000
Explosive gelatin (91 % nitroglycerin, 7,9 % nitrocellulose, 0,9 % antracid, 0,2 % water)	4520	1,000
60 % Nitroglycerin dynamite	2710	0,600
Semtex	5660	1,250
C4	6057	1,340

C.3.181 TNT-Equivalency Method for Blast Prediction

- Convert the available combustion energy in a vapor cloud into an equivalent charge weight of TNT with the following formula:

$$W_{TNT} = \alpha_e \frac{W_f H_f}{H_{TNT}} = \alpha_m W_f$$

where, $\mathbf{W_f}$ = the weight of fuel involved (kilograms); $\mathbf{W_{TNT}}$ = equivalent weight of TNT or yield (kilograms); $\mathbf{H_f}$ = heat of combustion of the fuel in question (Joules/kilograms); $\mathbf{H_{TNT}}$ = TNT blast energy (Joules/kilograms); $\boldsymbol{\alpha_e}$ = TNT equivalency based on energy (-); $\boldsymbol{\alpha_m}$ = TNT equivalency based on mass (-).

- TNT equivalency is also called equivalency factor, yield factor, efficiency, or efficiency factor. If the equivalent weight of TNT is known, the blast characteristics, in terms of the peak side-on overpressure of the blast wave, can be derived for varying distances from the explosion. This is done using charts containing scaled, graphical representations of experimental data. Various data sets are available that may differ substantially. They are different because they result from substantial differences in experimental setup such as a surface burst of TNT or a free-air burst of TNT. TNT-equivalency methods are the simplest means of modeling vapor cloud explosions [166].

C.3.182 Total Pressure

- Is the stagnation pressure for compressible flow where the flow is brought to rest adiabatically? It closely represents the pressure that the specimen experiences when facing the shock wave.

- To measure the total pressure for each test condition, shock tube tests need to be conducted with a pressure probe inserted in place of the specimen. For example, in their recent paper, Sawyer *et al*. [220] reported measuring total pressures experienced by the test animal, which has been located at 4280 millimeters from the diaphragm inside their shock tube (Advanced Blast Simulator/ABS) using a Pitot probe (Endevco 8530B pressure transducer) orientated such that it measured the total pressures at the test location. The pitot pressure sensors often have a pencil shape pointing directly towards the center of the flow.
- Related term(s): Stagnation Pressure.

C.3.183 Underbelly Blast / Under-Body Blast

- A specific loading condition where an explosive detonates under a vehicle causing a rapid vertical acceleration and results in unique injury patterns [151].
- When an explosive detonates under a vehicle, the two dominant load-transfer mechanisms to the target vehicle result from the expansion of the detonation products and energy transfer from soil ejecta. The gas phase provides the first phase of this impulse. During this phase, any portion of the vehicle located in the expansion zone of the detonation products is exposed to a transient, high-pressure blast. In cases where the floor remains intact, rapid deflection of floor plates in localized regions might serve as a pressure-transfer mechanism; as such, it presents a great danger to occupants. In the case when the floor is ruptured, the secondary fragments and superheated gases could injure the occupants. In the second phase, impact by the soil ejecta acts on the whole vehicle and results in aggressive acceleration of the vehicle. Both these mechanisms transfer large amounts of energy to the axial skeleton, with the lower limbs being particularly affected [195].
- The underbelly/under-body blast leads to mounted blast injuries.

C.3.184 Under-Pressure

The pressure below ambient pressure.

C.3.185 Underwater Blast

- Blast wave generated by an underwater explosion, such as a high-explosive or nuclear charge. Underwater blasts are typically an order of magnitude shorter in duration and higher in peak pressure compared to air blast waves due to the relative incompressibility of water [64]. The increased density, speed of sound, and viscosity of water relative to air mean that underwater blast injuries occur almost exclusively as the direct result of overpressure or primary blast [135]. Underwater blast waveforms are affected by numerous parameters including charge depth, bottom depth, gage depth, bottom reflectivity, and gas bubble fluctuations following detonation [64].
- The increased viscosity virtually eliminates the potential for injury from fragments (referred to as secondary blast injuries) at moderate distances from the charge. Similar to air blast, the gas-containing organs such as the lungs and guts are by far the most affected in an underwater blast exposure. Occasional lesions of the liver occur, but the majority of injuries occur in the lungs and intestinal tracts through fragmenting of epithelium and microvasculature into air spaces. The high prevalence and severity of intestinal damage is unique to underwater blast injuries. In addition, most available cases occur near the surface of the water [2], [8], [119], [159], [247].

- A recent meta-analysis by Lance *et al*. [135] that aimed at deriving injury risk assessments for underwater blast using well-characterized human underwater blast exposures in the open literature, established a human injury dataset based on 34 case reports on underwater blast exposure to 475 personnel, dating as early as 1916. Using severity ratings, computational reconstructions of the blasts, and survival information from a final set of 262 human exposures, injury risk models were developed for both injury severity and risk of fatality as functions of blast impulse and blast peak overpressure. Based on these human data, the authors reported that the 50% risk of fatality from underwater blast occurred at 302±16 kilopascals-millisecond impulse, which translates into a conservative estimation of a 20% risk of pulmonary injury at a kilometer from a 20 kilogram charge. From a clinical point of view, this study suggests the large distances possible for potential pulmonary and gut injuries in water compared with air.

C.3.186 Vago-Vagal Reflex

A reflex where both afferent and efferent pathways are carried in the vagus nerve leading to sudden m activation of the parasympathetic nervous system. After blast exposure, both experimental and clinical data suggest the onset of several vago-vagal reflexes (see Bezold-Jarish/Jarish-Bezold reflex; and C-fiber reflex) that might cause sudden respiratory and cardiac arrests, hypopnea, and bradycardia, among others [34], [39], [44], [45], [128], [129], [173].

C.3.187 Vapor Cloud Explosion (VCE)

Is the result of a release of flammable material in the atmosphere, a subsequent dispersion phase, and, after some delay, an ignition of the vapor cloud [32]. A flame must propagate at a considerable speed to generate blast, especially for 2-D (double-plane configurations) and 3-D (dense-obstacle) environments. The figure below illustrates the relationship between flame speed and overpressure for three different geometries. In order to reach these speeds, either the flame has to accelerate or the cloud has to be ignited intensely, thereby producing direct initiation of a detonation. Flame acceleration is only possible:

1) In the presence of outdoor obstacles, for example, congestion due to pipe racks, weather canopies, tanks, process columns, and multilevel process structures.
2) In a high-momentum release causing turbulence, for example, an explosively dispersed cloud or jet release.
3) In combinations of high-momentum releases and congestion.

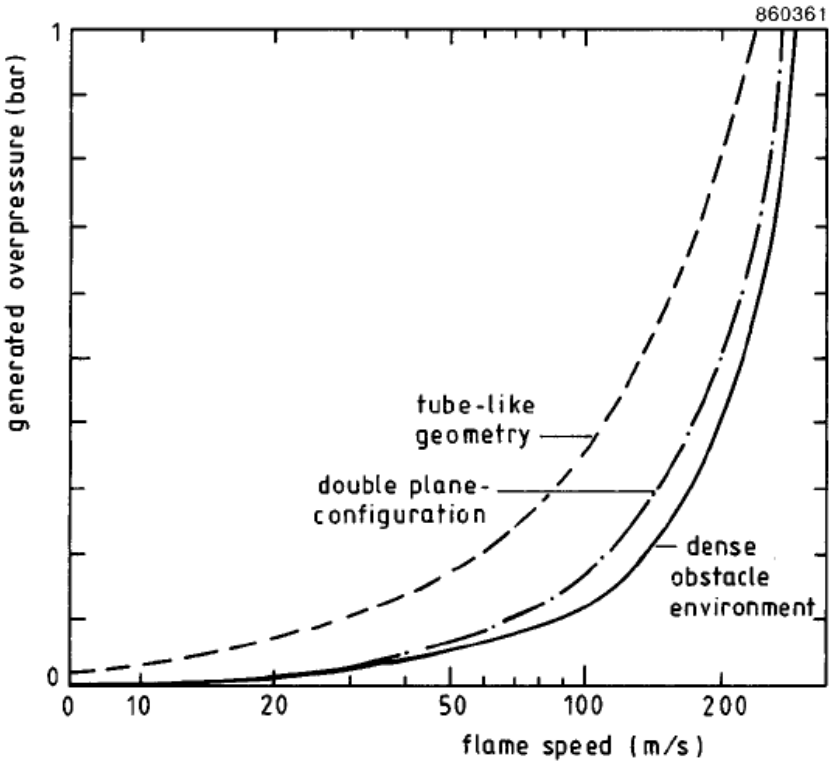


Figure C-17: Overpressure as a Function of Flame Speed for Three Geometries. The relationships are based on calculations by use of a self-similar solution [32].

C.3.188 Vapor Cloud Explosion (VCE) Prediction Methodologies

Are mathematical models and tests aiming to better understand vapor cloud explosions, and provide a more accurate definition of the flame speed applicable to a given combination of congestion, confinement, and fuel reactivity [188]. These tests have demonstrated that the previously published flame speeds are not conservative for all configurations for the case of no confinement (3-D flame expansion). The three most widely used simplified VCE blast load prediction models are the TNT equivalent method [32], the TNO multi-energy method [1], and the Baker–Strehlow–Tang (BST) method [14], [241]. All three methods use non-dimensionalized blast curves to predict the blast load for a given source energy and standoff distance. The methodologies differ only in the number and type of curves used. Because all three of these simplified methods are based on looking up values from numerically derived non-dimensional blast curves that provide pressure, impulse, and duration; the main difference between the methods is the means of selecting which curve to use.

- The **TNT equivalent model** has one pressure and one impulse curve and inherently assumes that all VCEs are detonations that behave like a condensed-phase high explosive. This assumption represents a gross simplification, and this method is no longer widely used.
- The **TNO multi-energy method** provides ten numerically derived curves for both pressure and duration. These curves span a range of severities from mild deflagrations to detonations, with the curves evenly spaced based on their maximum pressures. Each curve is assigned an integer "severity number" with pressures increasing from severity 1 (mild deflagration) to severity 10 (detonation). The applied impulse can be estimated from the pressure and duration data provided by the curves.

- The **Baker–Strehlow–Tang method** uses a continuum of numerically determined pressure and impulse curves that are based on the Mach number of the VCE flame front relative to a stationary point of reference. Duration can be calculated from pressure and impulse.

C.3.189 Yelverton Pathology Scoring System for Blast Injuries

- The Yelverton Pathology Scoring System (PSS) is a comprehensive method for assessing the severity of pathological changes in animals exposed to blast [267]. The PSS is an alphanumeric measure of the injury severity of various lesions caused in animals by the blast wave, including those induced by secondary or tertiary effects, to arrive at a Severity of Injury Index (SII) for each subject. This complex system correlates external lesion, injury grade, severity type, and severity depth or disruption of the injury in 11 organs / organ systems (external; fractures; burns; pharynx/larynx; trachea; lungs; heart; hollow abdominal organs; solid abdominal organs; right ear; and left ear) with the presence/absence of some complications (pneumothorax, hemothorax, hemoperitoneum, coronary air, and cerebral air), as well as with the trauma outcome (survivor, fatality).

- For every organ, the elements of the Injury Score (IS) equations are defined as:

$$IS = (E + G + ST) \times SD$$

  where: **E** = extent of injury to organ or organ system components; **G** = injury grade, which includes the surface area of the lesion or the percentage of the organ traumatized or the number of fractures in the case of the skeletal system; **ST** = severity type elements, classifying the type of the worst-case lesion to an organ or system; and **SD** = severity depth elements, indicating the depth or degree of disruption of the worst-case lesion.

- The individual ISs are then entered into an Excel(R) spreadsheet and divided by their maximum possible score to obtain the injury ratios. The ratios then are added together to get the sum of the ratios, which are added to the morbidity factors for that animal and multiplied by 1 (or 2 if the subject was a lethality) to obtain the SII. Morbidity factors included the presence or absence and the extent of a pneumothorax, hemothorax, hemoperitoneum, coronary air embolism, or cerebral air embolism in a subject.

- Thus, SII is expressed by the following equation:

$$SII = [\text{Sum of Ratios} + \text{Sum of Morbidity Factors}] * \text{Morbidity Multiplier}$$

  The value of Morbidity Multiplier for Survival = 1; and for Fatality = 2.

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Annex D − GUIDELINES FOR CONDUCTING EPIDEMIOLOGICAL STUDIES OF BLAST INJURY

D.1 INTRODUCTION

The discussions at the NATO Health Factors and Medicine (HFM) Symposium (SYM) HFM-207 revealed the importance of a systematic approach to understanding blast injuries, much like the well-established approach used to solve the classical toxicology problem where the etiology of the injury requires an understanding of the dose, mechanism of delivery of the dosage, and dose-response endpoints. Also recognized was the pressing need for a multidisciplinary approach to addressing non-penetrating blast injuries to the brain that result in a host of symptoms with vague etiology. In addition, the Technical Evaluation Report from HFM-207 (SYM), "A Survey of Blast Injuries across the Full Landscape of Military Science" [1] emphasized the continued multinational exchanges of scientific and technical advances needed to respond to blast threat and blast injuries. The first recommendation identified a future need for a recurring technical exchange venue on blast injury and its mitigation to address advances in medicine and personal protection and their synergy. The second recommendation highlighted the need to explore the concept of "the Toxicology of Blast Injury" and suggested to focus on several difficult problems including:

1) Relevancy and commonality of animal models.
2) Common dose-response methods.
3) Route of exposure methods.
4) Computational Models (blast, physiology, biochemical, toxicological, etc.).
5) Dose regimens to mimic/replicate human medical endpoints (spectrum of surgical trauma to mild traumatic brain injury).
6) Methods for translational research leading to medical products and/or physical protection products.

To address the above recommendation and to develop a specific NATO activity devoted to the toxicology of blast exposure, a proposal titled "Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods and Standards" was approved which resulted in the establishment of a NATO HFM Research Task Group (RTG) HFM-234 with the following deliverables:

- Guidelines for Conducting Epidemiological Studies of Blast Injury.
- Guidelines for Reproducing Blast Exposures in the Laboratory.
- Guidelines for Using Animal Models in Blast Injury Research.
- Dictionary of Blast Injury Terms.
- Final report on HFM-234 (RTG) activities.

These guidelines are intended to provide blast injury researchers and clinicians with a basic set of recommendations for blast injury epidemiological study design and data collection that need to be considered and described when conducting prospective longitudinal studies of blast injury. It is not the intention of these guidelines to prescribe how to design and conduct prospective longitudinal studies of blast injury but to provide an awareness of what needs to be taken into account, observed, recorded, and collected. Following these guidelines and reporting blast injury epidemiological studies in a consistent manner allows for reliable

comparisons to be made between studies regardless of the study environment. Clearly stated, the objectives of this document are:

a) To raise awareness with regards to the complexities and pitfalls of blast injury research.

b) To standardize and promote good research practices.

c) To help the community to generate valid and comparable results.

d) To increase the quality of publications in this field of research.

It is the intention of the HFM-234 (RTG) that these guidelines be used in concert with the companion comprehensive "Dictionary of Blast Injury Research Terms" developed by the NATO HFM-234 (RTG). These guidelines and the Dictionary can be used in conjunction to guide research methods and reporting in the field of experimental blast injury research.

D.2 BACKGROUND

Explosions are one of the most significant sources of casualties in recent NATO operations. Consequently, the primary focus of blast injury research is on the prevention, treatment, rehabilitation, and continuum of care for the injured from acute treatment to the return of duty.

For the purpose of this discussion, the term "blast injury" refers to the entire spectrum of injuries that can result from exposure to an explosion. The taxonomy of blast injuries are defined in Table D-1 based on the type of injury: primary, secondary, tertiary, quaternary, and quinary.

**Table D-1: Taxonomy of Injuries from Explosive Devices
Adapted from DoD Directive (DoDD) 6025.21E.**

Taxonomy of Blast Injuries	
Primary	Blast Overpressure (BOP) injury resulting in direct tissue damage from the shock wave coupling into the body.
Secondary	Injury produced by primary fragments originating from the exploding device (preformed and natural (unformed) casing fragments, and other projectiles deliberately introduced into the device to enhance the fragment threat); and secondary fragments, which are projectiles from the environment (debris, vehicular metal, etc.).
Tertiary	Displacement of the body or part of body by the BOP causing acceleration/deceleration to the body or its parts, which may subsequently strike hard objects causing typical blunt injury (translational injury), avulsion (separation) of limbs, stripping of soft tissues, skin speckling with explosive product residue and building structural collapse with crush and blunt injuries, and crush syndrome development.
Quaternary	Other "explosive products" effects − heat (radiant and convective), and toxic, toxidromes from fuel, metals, etc. − causing burn and inhalation injury.
Quinary	Clinical consequences of "post detonation environmental contaminants" including bacteria (deliberate and commensal, with or without sepsis), radiation (dirty bombs), tissue reactions to fuel, metals, etc.

NATO forces regularly sustain attacks from blasts by Improvised Explosive Devices (IED), land mines, and Rocket-Propelled Grenades (RPG). The United States (US) Department of Defense (DoD) reports that the use of IEDs and other explosive devices have led to an injury landscape different from that in previous wars [2]. The complexity of physical trauma resulting from direct or indirect exposure to an explosion has challenged medical practitioners across the spectrum of disciplines from surgery to mental health. Especially challenging are blast injuries to the brain where neither injury pathophysiology nor medical diagnosis are well understood. Moreover, the number of casualties incurred in NATO operations brings urgency to the blast injury research community to use medical information in the design of better protection technologies and the development of new treatment strategies for service members [1].

Blast injuries are often caused by more than one mechanism, do not occur in isolation, and typically elicit a secondary multisystem response. Research efforts often do not separate blast injuries caused by blast waves from those caused by blunt force trauma and other mechanisms. To add more complexity to elucidating blast injury pathophysiology, symptoms are often not immediately recognized or noticeable by a blast-exposed individual, especially when the individual is exposed to the blast waves but do not sustain blunt force trauma [1]. Currently, limited data and evidence-based guidelines exist regarding complex, multisystem injuries associated with blast exposure. Epidemiological studies are critical for obtaining the necessary data to understand the mechanisms of injury caused by explosions, the response of an individual to a blast event as well as long-term effects of blast exposure. Data elements required to evaluate an individual's response to blast exposure are summarized in Figure D-1.

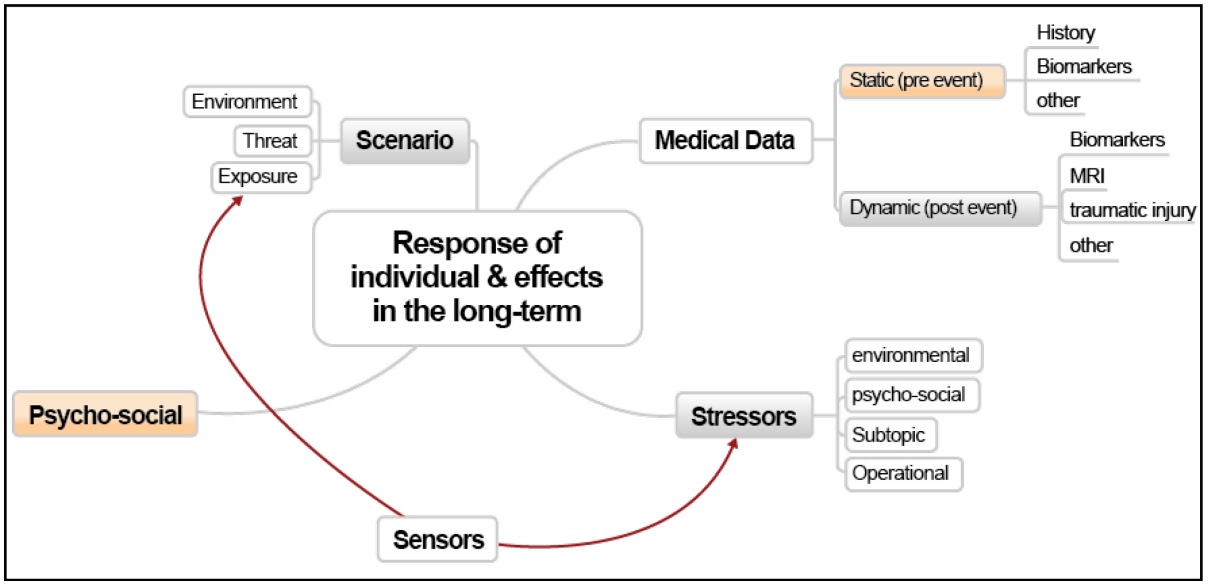

Figure D-1: Data Elements Required to Understand the Response to Blast Injury [3].

D.3 REQUIREMENTS FOR CONDUCTING A BLAST INJURY EPIDEMIOLOGICAL STUDY

A well-designed blast injury epidemiologic study should include an exposure assessment, an exposed population, and an unexposed population. Accurate blast exposure information is critical as this information is made part of the study and is used to determine health outcomes [4]. The framework requirements for conducting a blast injury

epidemiologic study are similar to those found in Institute Of Medicine (IOM) studies [2] and other well documented epidemiological protocols. A suggested epidemiologic study design (prospective longitudinal) for conducting blast injury studies and a detailed discussion on epidemiologic framework elements are provided in the following sections. An overview of epidemiologic framework elements with best practices can be found in Appendix D1.

D.3.1 Prospective Longitudinal Studies for Blast Injury – Study Design

There is currently limited evidence available regarding epidemiological studies on the health effects of blast exposure [3]. In addition, existing blast injury registries do not contain data that provide definitive information about blast events [3]. Consequently, to obtain the necessary data elements for determining the health outcomes associated with blast exposure, researchers should conduct prospective longitudinal studies. Researchers should ensure that their studies examine to some extent the progress and development of a potential disease or pathological factor or the response to blast.

A prospective, longitudinal epidemiologic study is often the best non-experimental means to confirm and quantify associations between exposure factors and health outcomes, although rigorous planning, coordination, and cost factors must be considered. The ultimate goal of conducting blast injury studies is to elucidate the physical, biological, and psycho-social mechanisms that cause blast injuries so that control measures can be implemented to prevent or reduce additional illness. A study needs to examine to some extent the progress and development of a potential disease or pathological factor or the response to blast.

Alternatively, a retrospective study (e.g., observational or phenomenological) involving data analysis based on medical history documentation can be used to identify certain components of importance if a full set of well-defined data exists for a focused hypothesis. However, researchers often still need to conduct a prospective study to control for variability in the study population, data collection protocols, and data elements of interest to which registry data may not be focused. Accurate blast exposure information is critical this information is made part of the study and is used to determine health outcomes [4]. Efforts should be made to make the response to blast exposure as specific as possible.

D.3.1.1 Framework Elements − Recommendations/Advantages

The framework requirements for conducting a blast injury study are similar to those found in IOM studies and other well-documented epidemiological protocols. A list of framework elements required to conduct an epidemiological study and the specific requirements for executing a blast injury study are described in the following section.

Well-Defined Research Question

Research questions should be clear, focused, clinically relevant, and answerable [6]. Example research questions in blast injury research might relate to the role of Personal Protective Equipment (PPE) in primary prevention, or to a treatment method to reduce long-term sequelae. In general, the primary research question(s) should be clearly stated and will usually specify the population to be studied, the intervention to be implemented, and other circumstantial factors, including specific outcomes of interest [6].

Focused Hypothesis

Focused hypotheses have several characteristics, including a clear rationale, an if–then format, and a clear description of the relationship between the variables of interest in the study [5]. A hypothesis should be defined

prior to conducting the study. The hypothesis should explain the specific exposure(s) that may have caused the disease. To test or prove the hypothesis, more analytical techniques, such as statistical testing, should be applied. An example of a simple hypothesis is: *People who have weaker biological resistance develop faster blast-induced neurological deficits*.

Well-Defined Research Plan

Researchers should include clear objectives of the study and specifics on how the study will be conducted, as well as an overview of how the data will be analyzed. The primary criteria to be considered in the choice of an appropriate epidemiological study protocol are the objectives of the study and the validity of the findings. A secondary consideration is the scientific capacity and availability of the population in which the study is to be conducted. Framework elements should be thoroughly described in the description of the design of the study [6]. For example, if the primary objective of the study is to define the relationship between blast exposure and injury with maximum precision, a Randomized Controlled Trial (RCT) provides the most appropriate protocol. In summary, the choice of epidemiological study design will be driven by the study objectives [6]. A well-defined protocol can help researchers save money and maximize resources.

Sampling Methods

Sampling methods will be largely dependent on the target study population. In blast injury studies, existing registries, and trauma wards may serve as excellent sources for identifying sampled individuals in the exposed group. Unfortunately, no general guideline may be given for sampling methods of a control group, this will completely depend on the definition of the population, discussed in more in-depth later. Once a study question has been formulated and study subjects are identified, it is important that these subjects are recruited uniformly and that data about their health and exposure be collected consistently. If a certain class of subjects is excluded from the study, or if information is collected non-uniformly from different subjects, the resulting bias has the potential to invalidate the study [6].

Identifying Biases and Study Limitations

Bias is a systematic error that leads to an incorrect estimate of effect or association. Many factors can bias the results of a study such that they cancel out, reduce, or amplify a real effect. Bias can occur in RCTs but tends to be a much greater problem in observational studies [7]. Researchers need to be aware of the potential for biases and exert extra care to eliminate or lessen the effect. Generally three types of bias are distinguished in epidemiologic studies: confounding, selection bias, and information bias. Confounding is distinguished from selection and information bias in that mathematical modeling can be used to correct the biased estimates of association between exposure and disease. However, for selection bias and information bias there are only limited statistical means to counteract the effects. In blast studies, some potential sources of bias include: selection bias introduced when specific subgroups self-select out of the study or are not included due to difficulties with identification; and information bias when self-reporting of blast exposure details is associated with health outcomes. For example, populations with poor access to care who may not present for wound care (selection bias), or individuals with better mental health outcomes may under-report exposure severity (information bias). A prospective study design can help mitigate some of these biases by allowing for correction of confounding and by limiting information bias by assessing exposure prior to assessing outcomes.

Data Analysis Plan: Defining All Variables and Sample Size Requirements

The data analysis plan for a study drives not only how the study data will be analyzed at the completion of data collection, but also determines what data elements will be collected and the sample size requirements of the

study. Recruitment and retention of adequate sample sizes in both exposed and non-exposed groups is critical in order to detect an association and test a research hypothesis. A study that falls short of sample size requirements may fail to find statistical significance of an effect when one truly exists (Type II statistical error). Researchers should work closely with statisticians and data managers to ensure that all required variables be collected and that sample size requirements can be met.

One critical factor in the successful execution of a data analysis plan is receiving data in a reasonably complete state. Data managers and statisticians should work together with Principal Investigators (PI) to ensure required variables are not only included in study data forms, but also that the data elements are collected in a manner to facilitate complete and usable data. Specific concerns may include the reduction or elimination of open-ended text questions and other highly subjective responses. These types of variables are both difficult to prepare for analysis and provide limited utility. Other recommendations may include utilizing data elements that are directly comparable to data elements used in other studies, when available; this practice results in better reception of corroborating or supporting study results and interpretations.

Documenting Survey Instruments and Operational Procedures

In addition to demographic and other regional effects introduced into a large prospective study, differential instrumentation and operational procedures can add both unnecessary variability and bias. To combat this, survey instruments and operational procedures must be standardized so that study participants are observed and data collected in identical manners regardless of timing, location, and study personnel. Optimally, procedures and instruments should be created and disseminated to study personnel and remain constant throughout the study.

Occasionally, additional data elements may be dictated by progression in blast science and allowable by review boards. Such procedural or instrument revisions should be kept to a minimum and should also be executed as additions rather than changes to existing data elements. Major changes to participant burden can affect instrument completion and study completion rates, and changes to data elements can have a major impact such as decreased statistical power for analyses.

Other Potential Considerations

Besides the framework elements, discussed above, which relate mainly to the epidemiologic design of the study, other major considerations to note in the design and execution of a prospective epidemiologic study of blast injury would include the analysis phase, banking of biological samples and specimens, Quality Assurance (QA), and ethics.

Analysis Phase

Many challenges and roadblocks encountered during the analysis phase of a study can be mitigated by more efficient and effective data management. Though the need for some level of data cleaning is almost always required during the analysis phase, this can be minimized through preventative steps using data management QA techniques that can be done in tandem with the main study operations.

Banking of Biological Specimens

Banking of biological specimens should be encouraged. In a blast injury study, banking of biological specimens (e.g., blood) presents unique challenges due to the physical conditions under which samples may be collected. Proximity to laboratories, specimen identification and records management, and potential international transport

are some of the potential considerations. Although biological sampling adds to the complexity of a study, it may yield highly valuable information (e.g., when researching biomarkers as well as biologic/genetic vulnerability and pathophysiological reactions to blast injury). Such information will be of particular value when considered in the context of epidemiological studies on the same group of service members.

Interdisciplinary Approach

The need for an interdisciplinary approach to blast injury research, covering military logistics, blast physics, neurobiology, trauma medicine, and psychology, should be emphasized as useful and oftentimes much needed for a comprehensive understanding of blast injuries and their human consequences. The need for an interdisciplinary approach should be evaluated throughout the planning phase of a study. Rather than having blast victims studied separately by different groups of scientists, an integrated approach should be sought, if possible.

Quality Assurance

QA activities may be grouped into two functional categories, those involving operational activities, and those involving data analysis activities. Operational activities include documenting deviations from protocol (e.g., exceptions to exclusion criteria), reviewing instrument usage and adherence to scheduling (e.g., if blast injury victims complete survey instruments related to health outcomes prior to collection of self-reported exposure data), and compliance with the study's privacy policies. Data analysis activities involve investigating outliers, as well as data that is potentially duplicative, incomplete, or inconsistent (e.g., discrepant ages or reported health history across data sources).

Ethics

Ethical considerations, including privacy and justification of benefit to individuals, are imperative in any study, but blast injury studies may require additional unique considerations. For example, ethical considerations for blast injury studies include: special or protected populations, or the potential influence induced if study participation or refusal to participate is job-related (e.g., military personnel when the study is conducted within the context of the military health system), review by multiple, and possibly international Institutional Review Boards (IRB), and access to highly sensitive Protected Health Information (PHI).

D.3.1.2 Study Population and Sampling Methods

The choice of the study population, including both the exposed and the control (i.e., unexposed) groups is a key factor in the design of a longitudinal study. The choice of study population affects not only operational aspects such as cost, administration, and field operations, but also generalizability and overall impact of results. Further, the designation of the study population may lend itself to the choice of the control group, but the choice of the control group also has major ramifications on the aforementioned operational and impact aspects.

Target Population

Target populations for a study may range from very broad and general, to very limited and specific (Table D-2). Potential target populations for a blast injury study might include all military ground troops within a defined set of missions (limited and specific) or all individuals (both civilian and military) within a designated region (broad and general). Using a more narrowly targeted study population has many benefits such as ease of identification, enrollment, and contact for follow-up. These benefits can minimize the range of strategies and approvals required, which can result in reduced cost and administrative burden.

Table D-2: Benefits and Costs Associated with Choice of Target Population.

More Restricted, Narrow Population	More General, Less-Restricted Population
• Potentially easier to identify, enroll, and follow the study cohorts (both exposed and control). • Potentially more nuances and limitations to the generalizability of the results. • Potentially smaller sample size requirement.	• Potentially more difficult to identify, enroll and follow the study cohorts. • Potentially fewer nuances and results may be generalizable both to a broad and to stratified sub-groups. • Potentially higher sample size requirements.

Although a very restrictive target population has many benefits, researchers should keep in mind that a narrow target population can limit the generalizability of study results since the effects of the blast exposure cannot necessarily be shown to hold true for other populations. Narrow study populations may limit variability in other outcome-related factors (e.g., psychological health such as baseline resiliency) and a more restricted study population may result in a smaller sample size requirement. Less restrictive, broader study populations often result in interpretations that can be both generalizable to a wide population and also drilled-down to stratified, group-specific effects, but can be more difficult to identify, enroll, and follow due to the numerous operational challenges when spanning geographic, organizational, and cultural barriers. For example, there may be differential self-reports of exposure or outcome, access to or acceptance of medical treatment, or consent to participate in a study, across different cultural groups.

Control Group Selection

Further consideration must be given to the choice of the control group, based on the target population. The control group affects study outcomes and statistical inference by influencing statistical power to detect an effect (and thus sample size requirements) as well as operations.

The basic purpose of a control group is to have a comparison to what is observed in the exposure group. Besides ensuring that a research hypothesis can be tested, the controls also serve to limit variability in that comparison. Ideally, the control group exhibits what the outcomes would likely have been for the blast-exposed group had they not been exposed to a blast injury. In fact, if the control group is extremely similar to the exposure group, the effect is beneficial to statistical power and reduces the sample size requirements for a study. Additional variability between the control and exposed groups will increase total variation in any statistical models and thus reduce the power to detect associations between the exposure and specific health outcomes.

In the case of an exposure such as blast injury, a control group may be more difficult to identify and follow than the exposed group due to the exposed group's reliance on continuing care, which may result in passive data collection through systems such as claims databases. A control group may be less motivated to enroll or contribute to on-going study and may not have such associations, resulting in the need for more active data collection. Identification of a control sample can be difficult, since the control group must be similar to the exposure group in as many ways as possible (e.g., demographics, cultural, socio-economic status, and medical history) other than the exposure status. Careful selection of the control group can alleviate these issues, with selection methods such as sibling or organizationally-matched controls.

Limitations

Although prospective studies are optimal, researchers may be limited in their ability to conduct these types of studies in the future due to cost, operational complications, and adequate sample sizes of exposed groups.

Costs associated with initial identification of study participants, especially with identification of adequate control groups, as well as active data collection increase quickly when multi-national or long-term longitudinal studies are being considered. Additionally, the coordination and approval chains for oversight agencies involved when conducting such studies across multiple organizations can lead to long lags in time to actually execute such a study. Finally, any research involving blast exposure is dependent on appropriate numbers of blast-exposed individuals in the target population.

In the case of blast exposure, sample size limitation is most noticeably impacted by military drawdowns. Nonetheless, military departments continually test artillery in training environments. The training environment can therefore be used to prospectively address challenging blast research questions to guide the finalization of future protocols. Any lessons learned from epidemiological studies conducted in a training environment can be operationalized, and the administrative coordination (e.g., IRB and other approvals) would be simplified by use of such a highly specified target population.

Using a training environment to conduct blast injury epidemiological studies has advantages and disadvantages. From an engineering perspective, the deployment and training environments could appear to be identical. However, the mental and psychological stress levels are quite different between these two environments. Individuals can be exposed to the same blast loads in these two environments, but the body will respond quite differently in the training scenario. In addition, moderate to severe injuries and hemorrhage are rare in the training environment. Consequently, researchers must consider the differences between the training and deployed environments as these differences can have a significant impact on study outcomes.

One type of injury that can occur in both the training and deployed environment which has been a major issue for the military is repeated low-intensity blast exposures that do not immediately cause problems but can cause concussions or mild traumatic brain injury. The biological response to this injury can be addressed and validated in a prospective manner in an epidemiological study in a standardized training environment (e.g., Breacher studies). A deployed environment must be used if operational stressors have been found to aggravate and worsen the primary blast-induced problems.

D.3.2 Blast Injury Data Collection

To determine and understand the etiology associated with blast exposure, researchers should collect both initial exposure data, as well as data related to linking biological health outcomes to blast exposure.

D.3.2.1 Parameters of Interest to Track Initial Exposure to Blasts

Three broad categories have been identified as parameters of interest to track initial exposure to blast:

- Characterizing the threat itself, including the type and size of explosive, the exposure environment, and the distance and orientation of the service member from the threat.
- Capturing information related to the individual affected by the threat as well as the scenario (e.g., air sentry partly exposed, dismounted personnel kneeling down behind wall).
- Capturing exposure measurements related to the threat.

Detailed information regarding the types of data required to track the initial exposure is discussed below and summarized in Figure D-1 for quick reference.

Characterizing the Threat

When characterizing the threat, researchers should collect the following information:

- Type of threat (e.g., type of IED, mine).
- Charge estimate, type of explosive (e.g., pure charge versus mixture of components).
- Road and soil conditions.
- Apparent crater dimensions.
- Detonation method.

The threat must also be characterized in terms of the blast environment (e.g., altitude, open air, explosion within or behind structures, ambient temperature, etc.). Researchers should estimate the distance between the service member and the threat as well as the body orientation. One of the current flaws of the US Directive-Type Memorandum 09-033, "Policy Guidance for Management of Concussion/Mild Traumatic Brain Injury in the Deployed Setting" [8] is that Commanders or their representatives are required to evaluate an individual who was located within 50 meters of a blast, but they do not account for the size of the blast. In the Netherlands, researchers consider an IED an explosive that is less than 50 kilograms, which is small enough to be hidden. An equation can calculate the pressure generated in kiloPascals (kPa) when the size of an explosive and the distance from the threat is known. The size and distance of any objects or walls in the environment would be very helpful in evaluating complex waves.

Capturing Information Related to the Blast-Exposed Individual Affected by the Threat

Researchers must be certain to capture key demographics of a service members exposed to the blast such as the individual's unique identification number, sex, age, weight, marital status, occupation, medical history, personality traits, immunizations, smoking or non-smoking, the military service(s) in which they have served, rank, unit, time in theater, and whether they were artillery or infantry. In addition, researchers should collect data on a service member's body posture; mounted or dismounted; and type, form, and fit of PPE, especially head borne equipment, to assist in determining the extent of blast exposure. Researchers should also assess for the presence of blunt impact and acceleration/deceleration, including linear and angular acceleration/deceleration of the entire body or body part, contact pressure, the nature of operational context, and the event timeline and location. Sample data collection forms can be found in Appendix D4.

Capturing Exposure Measurements Related to the Threat

Sensors could be used in the future for measuring pressure or acceleration related to blast exposure. Detailed information on parameters to track when using sensors can be found in Table D-3. The configuration of the sensors with respect to the body and to the explosive load is important information to capture. Sensors are one-dimensional (i.e., they can only measure from one direction); therefore, the orientation of the sensor to the shock front is important. The body itself affects the flow around a sensor. It is therefore easier to obtain accurate measurements from sensors that are not near the body and come in contact with undisturbed shock waves. Researchers should define a suite of multiple sensors aligned along 360 degrees, which means that the sensors would be oriented with respect to a body coordinate system (X, Y, Z axis system). This information will provide researchers with a unique definition of where everything is located with respect to the anatomical structures. The specifications and capabilities of any sensors used should be documented (e.g., information on the type of sensor, brand of sensor, sample rate).

Table D-3: Parameters of Interest to Track Initial Exposure to Blasts.

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

In addition, researchers should determine the relationship of a pressure sensor to the exposure source. There is an increased emphasis on the need to characterize the side on and face on pressures (both amplitude and duration) of the blast. The shape and impulse of the pressure from a blast is a measure of the energy that can be transported. The first blast wave from an explosion is the only thing that can be measured in a defined way. If the wave is reflected, the origin of the blast really needs to be determined. Accurate measurements are not needed for high explosives that are lethal. For blasts in the 60 – 120 kPa range, small increases in amplitude can mean

the difference between no injury and injury. Knowing the amplitude of a blast wave is crucial to determine its effect on the body. Furthermore, the distance from the blast is directly related to amplitude of the wave. Overall, the ability to accurately measure the intensity of blast waves in the 60 – 120 kPa range is needed to obtain quality correlations with the injury.

D.3.2.2 Parameters Related to the Use of Sensors in Blast Studies

Sensors are useful for obtaining data in three key categories relevant to a blast event, the scenario (threat and environment), the stressors (e.g., temperature and altitude), and the dynamic medical data (e.g., changes in heart rate and blood pressure). It is also important to note that researchers need to determine what the sensors are measuring and what these measurements mean to the individual as this information is critical for accurately interpreting the results. The recommended categories for which researchers should collect data include:

- Physiological status of individual.
- Exposure level to stressors.
- Exposure level to threat.

Table D-4: Importance of Using Sensors in Blast Studies.

1) Sensors are needed to understand the real exposure.
2) Types of data needed from sensors:
   - Physiological status of individual.
   - Exposure level to stressors.
   - Exposure level to threat.
3) Sensors are crucial to being able to understand the response of an individual to a blast event.
4) Sensors are not limited to the effects of blast exposure, but encompass thermal and other environmental stressors as well.

When using sensors, researchers need to identify:

1) The important components of the scenario; and
2) The individual's response to that event.

Another process involves measuring the first two steps using various types of sensors (e.g., pressure and acceleration sensors). Measuring some of the environmental characteristics with the sensors is an option that researchers should consider. Data providing information on an individual's physiological dynamic response at the time of the event (e.g., measuring breathing using a physiological status monitor) would also be useful. Using threat and incident data from a blast event, one can effectively recreate the scenario using a manikin.

D.3.2.3 Data Required to Link Biological Health Outcomes to Blast Exposure

Data linking biological outcomes to blast exposure must be captured in order to determine the response of an individual to a blast event, as well as determine what influences that response. To collect these data, researchers should build a predictive system that includes signal analysis and pattern recognition. Data should be captured on both the threat and the surrounding environment.

When conducting a blast injury epidemiology study, all types of injuries and medical conditions and relevant physiological status (e.g., dehydration, fatigue/exhaustion, fitness level), and their effects on the body (including clinical, paraclinical, and biological) must be identified. An indication of the blast injury data collection timeline must also be provided. Data collected should capture all changes that affect the quality of life and functioning of a blast-exposed individual such as functional impairment. Currently, there are no markers of an exposure and markers of an effect (i.e., chronic versus acute exposure), and thus a researcher needs to be sure that he or she is able to decipher what measurements being captured actually mean functionally to the individual. Examples of data collection forms can be found in Appendix D4. It is important to note that functional impairments can exist that cannot be observed with various imaging methodologies, versus clinical, morphological impairments that are easily detected.

Researchers should record the personality traits of an individual involved in a blast as well as capture information on an individual's occupation. These data can provide an idea of how individuals think and may react to a stressor, which may help to explain the biological health outcomes of a blast injury. Considering that current employment may not be related to past training, researchers should obtain data on both the training and job history of the individual. Sample data collection forms can be found in Appendix D4. This information should allow linkage to various subspecialties of employment. A chart showing linkages among the various categories of data that need to be collected in association with a blast event was previously presented in Figure D-1, while key categories of data required to link biological outcome to blast exposure and whether or not these categories represent data that are intrinsically dynamic or static (or both) are summarized below in Table D-5.

Table D-5: Data Needed to Link Biological Health Outcomes to Blast Exposure.

Category	Type
1) Environment.	Dynamic
2) Threat.	Dynamic
3) Stressors (environmental, operational, psychosocial).	Dynamic
4) Medical data (static and dynamic): • Link medical data with incident data (includes data from trauma registries, medical records, and other sources). • Data collected at event. • Previous concussions (e.g., car accidents, sports).	Static and Dynamic
5) Psychosocial factors.	Static
6) Personality traits of the individual.	Static
7) Training and job history of the individual.	Static
8) Identification of the cause of injury.	N/A

D.3.3 Blast Injury Data Management

Whether a prospective longitudinal study is implemented or a minimum set of data specifications is agreed upon for data sharing between blast injury registries, guidelines for optimizing existing databases can be implemented

to standardize the quality and content of these databases. This section discusses the challenges with sharing data between organizations, describes existing databases, and discusses best practices for ensuring existing databases have maximum benefit for later retrospective or cross-sectional analyses.

D.3.3.1 Challenges with Sharing Data

Ideally, researchers would be able to share information from multiple databases while conducting epidemiological studies. For example, to achieve pattern recognition of types of injuries based on types of weaponry used by certain terrorist groups, a critical mass of information is needed that is difficult to obtain without combining data from multiple countries. However, functional, political, and other logistical issues often preclude such data sharing.

Functional challenges, such as structure and content, are the most concrete barriers to sharing data. When data registries collect different data, either using different case definitions, using non-compatible coding or classification systems, or inconsistent linkage structures, it may be impossible to combine data across sources. For example, if two registries exist and one collects all International Classification of Diseases and Related Health Problems (ICD) diagnostics and Current Procedural Terminology (CPT) codes for all medical encounters following a blast exposure, and the other registry only collects a single, or primary diagnostic code and/or procedure codes from only the first encounter, the data will not be comparable when shared. Further, if a database exists to aggregate all claims or procedures related to blast injury, even with detailed diagnostic and sensor coding, but the data are not linked to the blast-exposed individual for longitudinal time-course and treatment plan tracking, these data may have no utility when shared with a more straight-forward database linking only ICD and CPT codes but at the individual level. DoD considered developing a large database that would include data from the operational and medical communities; however, it was found that merging these databases does not work for such functional reasons.

Data sensitivity is another challenging affecting data sharing. Information such as PHI and personally identifiable information may be necessary for data linkages and claims databases, but poses risks for data sharing. Often when participants sign consents to allow their data to be used for research purposes, they authorize a specific entity to execute the research, and data sharing may not be explicitly allowed by the consent. Further, in the case of blast injury data, information may be collected that, in either isolation or in aggregation, may indicate sensitive information at a national or political level.

An advantage of sharing data is the potential to increase sample size for analysis. However, this assumed advantage is limited by the variability introduced by the collection of non-comparable data elements and by the collection from non-comparable populations. In such cases, there may not be any statistical gain by sharing data. When these elements, content and population, are not comparable, meta-analysis may be more beneficial than data sharing. For a discussion of data sharing versus meta-analyses, see Appendix D2.

D.3.3.2 Existing Databases

Existing databases which function as blast registries were developed to meet government and other regulatory functions specific to that nation or organization. Databases such as the Casualty Protective Equipment Analysis, and the Joint Theatre Trauma Registry, as well as data collected with forms like the Military Acute Concussion Evaluation (MACE), or data collected by existing programs such as the Joint Trauma Analysis and Prevention of Injury in Combat (JTAPIC) may provide additional resources for researches in blast injury to conduct studies. Data in these existing sources range from mental health and personality traits, to exposure and injury or casualty information.

D.3.3.3 Recommendations for Optimizing Existing Databases

Although there may be vast differences, including such key differences as structure, content, and population, between existing databases, this section discusses recommendations for optimizing existing databases to enable any potential data sharing that may be feasible in contributing to epidemiologic study.

Accurately Reflect Blast Injuries

Blast injuries may be documented in a multitude of ways, as discussed in the previous section on blast injury data collection. In order to accurately reflect blast injuries, owners of existing blast injury databases might consider including data from sensors, codes for cause and mechanism of injury in addition to standard diagnostic codes, and detailed wound mapping. In this context, cause is used to identify the initiating event (e.g. explosive incident), while mechanism of injury refers to the specific mechanism of loading to the body that caused the actual injury (e.g. blunt impact). This leads to an internal (biological) injury mechanism (e.g. rupture of blood vessel) causing hemorrhage which leads to the final clinical outcome. In an optimal case, there will be four codes documenting the injury:

1) Initiating event;
2) Mechanism of loading;
3) Internal mechanism; and
4) Clinical outcome.

The manner in which injuries are coded in the current system of ICD codes does not capture all possible blast-related injuries; therefore additional fields are needed to capture the four codes discussed above. Aspects of the clinical outcome can be based on existing coding systems (e.g., Abbreviated Injury Scale (AIS), Glasgow Coma Scale (GCS)). Finally, blast injury is often associated with a multi-organ response, which adds an additional dimension of a clinical outcome score (e.g. Glasgow Outcome Scale (GOS) for brain injury), and a virtual injury path analysis to map the complete wounded area would allow for coding of all affected organs and more accurately reflect the blast injury.

Designate a Data Manager

Epidemiological studies and registries often involve multiple individuals gathering data at multiple sites. Therefore, data management is an important issue. The integrity of the data must be maintained and ensured by a qualified data manager, either the PI or another individual to whom these responsibilities are assigned. The data manager will:

- Ensure adequate database specifications, security, structure, and functionality.
- Prepare the data for the database (including, but not limited to ensuring adaptation of a protocol for de-identification of PHI).
- Assess data quality through periodic review and mitigate all data quality issues.
- Assemble data for review and analysis.

Establish a NATO-Level Process for Data Sharing

Due to complications with data sharing, it may be worthwhile to model a NATO-level process after JTAPIC (http://jtapic.amedd.army.mil/) and other related efforts, for analyzing and sharing blast injury data that includes medical, intelligence, and operational information.

Maintain or Expand Existing Databases

As blast injury research is a relatively new field, all data available on blast exposures has potential analytical benefit. Existing data should be maintained or imported into newer databases, as appropriate. Expanding databases by adding newly available metrics, diagnostic features, and other elements related to blast exposure, should occur as medical advances, technology, and scientific curiosity dictate. Some examples of modern and advanced metrics for inclusion are biomarkers for exposure (if they become known), scales such as the Injury Severity Score or New Injury Severity Score, and indicators of whether sensors were worn. Maintaining existing databases and continuing to invest for either expansion or upgrade of these resources is critical, regardless of whether a country is at war or not.

D.3.3.4 Additional Considerations

Although investigation of many research questions will not be feasible via data sharing using existing data registries, some case-control, cross-sectional, retrospective, and even prospective studies may be feasible based on data sharing of minimum data elements contained in these databases. For this reason, these databases should be optimized for data sharing. As these databases evolve to include more advanced measures of both exposure and outcomes, these legacy databases can be grandfathered in to preserve this existing bank of information.

D.4 DISCUSSION

Blast injury is a significant and complex problem facing military forces. The complexity of the injuries, particularly the multisystem response has made understanding blast injury etiology very challenging. In addition, limited blast injury data poses a significant challenge for researchers. Development of these guidelines represent a significant step forward toward gathering the appropriate data to understand blast injury etiology and also highlights the value of facilitating a forum where multiple countries can share ideas and work together to solve an important health problem. To completely understand the nuances of blast injury etiology, continued multinational exchanges of scientific information will be crucial for improving health outcomes associated with blast injuries.

This document provides researchers with a solid epidemiologic framework and best practices to collect the appropriate data required to determine the response of an individual to blast exposure. These guidelines will benefit from their application and feedback to serve as a living guideline for future work in blast injury research. Although this document provides guidance on conducting blast injury epidemiologic studies to collect and manage blast injury data, there is still a need to have more detailed discussions on the toxicology of blast, particularly toxicological methods, and protocols relevant to understanding blast exposure effects. A concerted effort to bridge the fields of epidemiology and toxicology in a way that can impact and hopefully reduce burdens associated with blast injuries is imperative. Ultimately, to elucidate the biological mechanisms that cause blast injury pathophysiology, researchers need to have a solid toxicology framework as well. This framework needs to include at minimum, methods of understanding the dose, mechanism of the dosage and dose response endpoints of blast exposure (toxicology framework).

Lastly, these guidelines provide the minimum requirements to conduct a blast injury epidemiologic study and do not represent an exhaustive list. Some of the framework elements may differ by country. Thus, researchers admonished to follow guidance and adhere to rules and regulations provided by their respective nations.

D.5 REFERENCES

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Appendix D1: FRAMEWORK FOR BLAST INJURY EPIDEMIOLOGICAL STUDY DATA COLLECTION GUIDELINES

Framework Element	Summary of Best Practices
Well-Defined Research Question	Research questions should be clear, focused, clinically relevant, and answerable. In general, the primary research question should be clearly stated and usually specifies the population to be studied, the intervention to be implemented and other circumstantial factors [5].
Focused Hypothesis	A hypothesis should be defined prior to conducting the study. The hypothesis should explain the specific exposure(s) that may have caused the disease. To test or prove the hypothesis, one has to apply one or more analytical techniques, such as statistical testing [5].
Well-Defined, Detailed Protocol Including Study Design	In general, an epidemiological study is based upon a detailed study protocol. The protocol is a compilation of the most important information necessary for the implementation, application and evaluation of the study [3]. The research plan should address why the study is being done, i.e., what is the objective, and how it will be conducted. Framework elements should be thoroughly described in the description of the design of the study [6].
Target Population and Sampling Methods	A target population must be chosen, within which a sampling strategy will be implemented. The target population has direct effects on generalizability of study results as well as impact on operational aspects.
Identify Biases and Limitations	Data analysis should include the steps taken to control bias, specifically, selection, misclassification, and confounding bias. Additionally, Researchers should account for intentional and unintentional bias.
Define all Variables and Study Size	The numerical size of exposed and non-exposed groups is a critical factor that must be considered in the conduct of epidemiological studies. The sizes of these groups are governed by the frequency of occurrence of the health effect under study. Expert advice should be sought with regard to population size before conducting an epidemiological study.
Document Survey Instruments and Operational Procedures	Survey instruments and all study procedures must be standardized to ensure that data is collected identically, regardless of data collector, location, and time of collection, and study participant.
Data Collection, Management, and Documentation	The approaches for collecting exposure and health effects data should be described in detail. This includes the use of questionnaires and other sources of health data, as well as methods used for collecting exposure data. For additional information, refer to Section D.3.3 Blast Injury Data Management.
Analysis Phase	Researchers must use scientific knowledge to establish linkage between injury and threat/exposure, and statistics or tools to detect correlations and relationships between the different elements. The statistical evaluation procedures should be fully described.
Biological Sample Bank (Tissue, Body Fluids, Biomarkers)	This requirement is specifically recommended for blast injury studies due to the need to collect such samples in these studies and to identify biomarkers.

Framework Element	Summary of Best Practices
Quality Assurance	All of the measures taken to ensure the quality of the data should be described including the technical qualifications of all scientists participating in the study.
Ethics	The study plan should always be submitted to a Human Investigations Committee, or its equivalent, to ensure that any regulatory limitations regarding human studies will be met, especially confidentiality restrictions and informed consent procedures.

Appendix D2: DATA SHARING VERSUS META-ANALYSES

Groups all over the globe are currently doing blast studies, and this information could be leveraged to draw generalizable inferences about blast exposures. Two main methods, data sharing and meta-analysis, are well-suited for such inter-organizational collaboration in the case of both shared priorities and unique data collection systems exist. In the data sharing model, organizations collaborate to collect the same data within their respective purviews, and the organizations later combine the data prior to analysis. For meta-analysis, organizations design their own protocols for data collection, conduct their own analysis, and later an interested researcher combines these analyses to strengthen the findings of both analyses or to highlight differential findings and discuss potential reasons. An overview of the benefits and limitations of both data sharing and meta-analysis is given in Table D-6.

Table D-6: Comparison of Data Sharing and Meta-Aanalyses.

Research Condition	Data Sharing	Meta-analysis
Shared research goals	✓	✓
Data collection via separate instruments and/or databases	✓	✓
More statistically powerful, and therefore potentially higher impact	✓	
Require same target populations, protocol and study content, and inclusion criteria, or detailed documentation regarding both	✓	
Flexible for differing study designs, including similar but different content		✓
Requires major upfront investment, planning, organization, and cooperation	✓	
Flexible for constraints on data ownership and other logistical issues, including		✓

Data sharing, though it may be optimal with regard to research impact, may be more resource-intensive and require significantly more collaboration and infrastructure prior to study as compared to meta-analysis. Data sharing requires that data be collected from similar target populations, with similar inclusion criteria, with the same protocol and instrumentation. This may sometimes take the form of a collaborative agreement wherein member organizations may or may not have individual research goals, but additionally agree to collect some specified data for the data sharing coordinating center. Minimum data specifications are overseen by the coordinating center, and data quality may be reviewed at both the organizational and the coordinating center levels. De-identification of study participants may occur at either level, depending on agreements and approval from both the organization and the coordinating center's IRB. Prior to data collection, organizations which submit data agree to data use requirements and accessibility guidelines—these guidelines may or may not allow the member organizations to conduct analyses on the data collected for the data sharing program, and also specify how an organization would later access the aggregated data from the coordinating center to test a specific research hypothesis. Data access and writing team committees may be creating by the coordinating center to oversee these processes.

Meta-analyses require much less infrastructure, but may not gain the scientific impact of a well-organized study utilizing shared data. Meta-analyses generally occur when a researcher would like to combine the information from two data sources, but the data sources may not be compatible, directly comparable, or available. Instead of

gaining the statistical power of combining multiple datasets (and therefore strategically increasing sample size), meta-analysis combines analytic results to draw information across different conditions. In comparison to the logistical and administrative complexities of data sharing, meta-analyses often do not involve privacy, data ownership, or database infrastructure and content issues. Meta-analyses are a useful way to gain strength from multiple analytic results when sharing data is not feasible.

Appendix D3: DATA INPUT REQUIREMENTS

When inputting data, researchers should ensure that they are accurately and consistently reflecting blast injuries in existing coding systems and databases. Researchers should also create a standard working method that includes the following elements:

- Code for the injury or the threat:
  - Initiating event;
  - Mechanism of loading;
  - Internal mechanism; and
  - Clinical outcome.
- Detailed wound mapping (e.g., entry and exit data, wound, wound track).

For studies that involve a single PI and single institution, the following actions typically occur:

- Assignment of a bar code to an individual identifies a person from beginning to end of study (the consent form is the only hard copy that links the individual to his/her bar code, and that is appropriately safeguarded by the PI).
- Demographic data is stored with the consent forms, so the PI is the only person preparing and analyzing the data.
- All self-reported and other data are bar coded; data entry occurs using the bar code.
- Data entries are completely scrubbed (i.e., de-identified) so people other than the PI never see any identifiable information.

Recommendation: The data management process outlined above should be used for a training study, but not for a NATO study involving more than one nation. The protocol best suited to a particular study should be identified in each case.

Appendix D4: EXAMPLES OF DATA COLLECTION FORMS

Prior Health & Demographics Questionnaire

Visit: ○ Baseline

Demographics

Age: ☐☐

Sex:
- ○ Male
- ○ Female

Marital Status
- ○ Single (never married)
- ○ Married
- ○ Widower
- ○ Divorced

Race:*
- ○ Caucasian
- ○ African-American
- ○ Asian
- ○ Other: _____

Ethnicity:*
- ○ Hispanic
- ○ Non-Hispanic

Pay Grade:*

○ E1	○ E8	○ O1	○ 08
○ E2	○ E9	○ O2	○ 09
○ E3	○ W1	○ O3	○ 10
○ E4	○ W2	○ O4	Other: ____
○ E5	○ W3	○ O5	
○ E6	○ W4	○ O6	
○ E7	○ W5	○ O7	

Education
- ○ Non-High School graduate
  (list highest grade completed) ☐☐
- ○ High School graduate
- ○ Some college but no degree
- ○ College graduate
- ○ Post-graduate degree

Branch of Service:*
- ○ Air Force
- ○ Army
- ○ Navy
- ○ Marine Corps
- ○ Coast Guard
- ○ Civilian Employee

Status prior to deployment:*
- ○ Active Duty
- ○ Selective Reserves
- ○ Civilian Government Employee
- ○ Other: _____

* Disclaimer - Terms used in this data collection form reflect United States Military examples. This form may to be modified to reflect the terminology and examples used by country using the data collection forms.

Prior Health & Demographics Questionnaire

Visit: ○ Baseline

Health

Have you ever been prescribed medications for a behavioral, emotional, or thought disorder?

○ Yes ○ No

If Yes, complete the following:

List medications and condition:

Did you ever receive school help for conditions such as: Attention Deficient Hyperactive Disorder (ADHD) or a learning disability (such as dyslexia)?

○ Yes ○ No

If Yes, complete the following:

Specify condition:

Medical

Have you had any concussions or head injuries prior to your tour?

○ Yes ○ No

If Yes, complete the following:

If yes, how many total? ☐☐

Out of those, did any cause you to …

be in a coma longer than 24 hours? ○ Yes ○ No

have bleeding in your brain? ○ Yes ○ No

have a blood clot in your brain? ○ Yes ○ No

not be able to remember the first week after injury? ○ Yes ○ No

Prior Health & Demographics Questionnaire

Visit: ○ Baseline

Health (continued)

Total Deployments in Past 5 Years:**

○ 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 or more

Most Recent Location of Operation(s)**:

○ Operation Name (e.g., OEF,OIF): _____

Date arrived in Theater: | | | | | | | | | | |
(d d) (m m) (y y y y)

Date departed Theater: | | | | | | | | | | |
(d d) (m m) (y y y y)

Since return from deployment you most recently have*:

○ Maintained/returned to previous status
○ Transitioned to Selected Reserves
○ Transitioned to Individual Ready
○ Retired from Military Service
○ Separated from Military Service
○ Other: _____

Were you medically evaluated during deployment?

○ Yes *If Yes, complete the following:*
○ No

If yes, what date? | | | | | | | | (m m) (y y y y)

Was it for one of the explosions already listed or a separate injury?

○ Explosion
○ Separate Injury

If separate injury, describe:

*Disclaimer - Terms used in this data collection form reflect United States Military examples. This form may to be modified to reflect the terminology and examples used by country using the data collection forms.

** Tour names will need to be modified according to country of use.

Prior Health & Demographics Questionnaire

Visit: ○ Baseline

Health (continued)

Did you have any head injuries or concussions during your deployment that were NOT related to an explosion?

○ Yes
○ No

If Yes, complete the following:

How many: ○ 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 or more

*Answer the following questions about the **worst** of these head injuries or concussions:*

Estimated Date: ☐☐ ☐☐ ☐☐☐☐
(d d m m y y y y)

Describe what happened:

Do you remember the injury itself? ○ Yes No

Estimate of time period not remembered before injury:

- ○ None, I remember all time up until injury
- ○ Less than 1 hour - estimate # minutes not remembered ☐☐
- ○ Between 1 hour and 24 hours - estimate # of hours not remembered ☐☐
- ○ More than 24 hours - estimate # of days not remembered ☐☐

Estimate of time period not remembered after injury:

- ○ None, there is no time after the explsoion I don't remember
- ○ Less than 1 hour - estimate # minutes not remembered ☐☐
- ○ Between 1 hour and 24 hours - estimate # of hours not remembered ☐☐
- ○ More than 24 hours - estimate # of days not remembered ☐☐

Did an observer report your losing consciousness (knocked out):

- ○ No
- ○ Yes, for less than 1 minute
- ○ Yes, for 1-60 minutes - estimate # of minutes unconscious ☐☐
- ○ Yes, for longer than 60 minutes - estimate # of hours unconscious ☐☐

(Continued on next page)

Prior Health & Demographics Questionnaire

Visit: ○ Baseline

Health (continued)

*(continued from previous page for head injuries or concussions during deployment that were **NOT** related to an explosion)*

Were you wearing full body armor? ○ Yes ○ No

Were you wearing a helmet? ○ Yes ○ No

If you had hearing problems, has this been medically evaluated? ○ Yes ○ No

If Yes, complete the following:

Did you have a tympanic membrane rupture? ○ Yes ○ No

Was some other problem identified? ○ Yes ○ No

If Yes, complete the following:

Specify:

If you have had visual problems, was it medically evaluated? ○ Yes ○ No

If Yes, complete the following:

List problem identified:

Example of Blast Experience Screening Questionnaire

Visit: ○ Baseline

During your tour or training,* did you experience (were affected by) an explosion (IED, Rocket Propelled Grenade-RPG), land mine, grenade, etc.)?	○ Yes	*If Yes, complete the following:*
	○ No	How many did you experience: ○ 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 or more

* his question can be modified to reflect the specific names of operations/tours and trainings that are relevant to soldiers in their respective countries (e.g., Operation Iraqi Freedom [OIF]).

The rest of this form has a series of questions on each of these explosive events that you experienced. You will begin on the next page with the one explosive event that was your WORST experience (e.g., due to the severity of your injuries, near miss, etc).

NOTE: If you experienced more than 3 explsoive events, then you will only be asked about the 3 worst.

Example of Blast Experience Screening Questionnaire

Visit: ○ Baseline

Worst Experience

Briefly describe your worst explosion you experienced in a way that will help you to recall it later (please write 3 or less sentences):

NOTE: If you experienced more than one and are not sure which was the WORST, to help you decide consider the immediate physical and/or mental effects.

Estimated Date: | | | | | | | | | | |
(d d) (m m) (y y y y)

Deployment:

○ Tour Name: _____

Explosive Type (select one):

○ RPG Mortar IED
○ Land mine
○ Grenade
○ Other: _____

Where were you at the time of the explosion?

○ Inside a vehicle as driver
○ Inside a vehicle as a front seat passenger
○ Inside a vehicle in back seat
○ Outside a vehicle with cover
○ Outside a vehicle without cover
○ On a vehicle (example: gunner)

How far were you from the explosion?

○ Within 5 feet
○ Between 5-10 feet
○ Between 10-15 feet
○ Over 15 feet
○ I do not know

Example of Blast Experience Screening Questionnaire

Visit: ○ Baseline

Worst Experience (continued)

To your best recollection, what did you experience during or immediately after the explosion? (Select all that apply)

- ○ Dazed
- ○ Confused
- ○ Headache
- ○ Dizziness
- ○ Irritability
- ○ Memory Gap
- ○ Hearing Loss
- ○ No symptoms
- ○ Blinded
- ○ Abdominal Pain
- ○ Shortness of Breath
- ○ Struck by Debris
- ○ Knocked over or down
- ○ Knocked into or against something
- ○ Evacuated for medical reasons
- ○ Other: _____

Not counting normal sleep time, do you **personally remember** the explosion and **all time immediately before and after**?

- ○ Yes, my memory for the experience is continuous (may have fuzzy parts)
- ○ No, I have no memory at all for some period of time (whether brief or long) during, immediately before or immediately after the explosion

If No, answer next three questions:

1. Do you remember the explosion itself?

   - ○ Yes
   - ○ No

2. Estimate of time period not remembered before the explosion:

   - ○ None, I remember all time up until the explosion
   - ○ Less than 1 hour - estimate # minutes not remembered ☐☐
   - ○ Between 1 hour and 24 hours - estimate # of hours not remembered ☐☐
   - ○ More than 24 hours - estimate # of days not remembered ☐☐

3. Estimate of time period not remembered after the explosion:
   - ○ None, there is no time after the explosion I don't remember
   - ○ Less than 1 hour - estimate # minutes not remembered ☐☐
   - ○ Between 1 hour and 24 hours - estimate # of hours not remembered ☐☐
   - ○ More than 24 hours - estimate # of days not remembered ☐☐

Example of Blast Experience Screening Questionnaire

Visit: ○ Baseline

Worst Experience (continued)

Did an observer report your losing consciousness (knocked out):

- ○ No
- ○ Yes, for less than 1 minute
- ○ Yes, for 1-60 minutes - estimate # minutes unconscious ☐☐
- ○ Yes, for longer than 60 minutes - estimate # of hours unconscious ☐☐

Were you wearing full body armor? ○ Yes ○ No

Were you wearing a helmet? ○ Yes ○ No

Were you wearing facial protection? ○ Yes ○ No

Were you wearing hearing protection? ○ Yes ○ No

Did you have hearing problems that were medically evaluated? ○ Yes ○ No

If Yes, complete the following:

Did you have a tympanic membrane rupture? ○ Yes ○ No

Was some other problem identified? ○ Yes ○ No

If Yes, complete the following:

Specify:

Did you have visual problems that were medically evaluated? ○ Yes ○ No

If Yes, complete the following:

List problem identified.

○ Yes *If Yes, complete the following:*

Example of Blast Experience Screening Questionnaire

Visit: ○ Baseline

Worst Experience (continued)

Did you experience any physical pain during or immediately following this explosion?	○ No	If yes, please make a selection on the number scale below that best represents the level of your pain **at that time.** 1 ○ NO PAIN 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10 ○ WORST PAIN POSSIBLE

Example of Blast Experience Screening Questionnaire

Visit: ○ Baseline

Second Worst Experience

Beginning on this page, you will be asked about your **second worst** explosion you experienced. (If you experienced only one explosion, then **STOP** here, you are finished with this form.)

Briefly describe your **second worst** explosion you experienced in a way that will help you to recall it later (please write 3 or less sentences):

Estimated Date: | | | | | | | | |
(d d) (m m) (y y y y)

Deployment:

○ Tour Name: _____

Type of explosion (select one):

○ RPG Mortar IED
○ Land mine
○ Grenade
○ Other: _____

Where were you at the time of the explosion?

○ Inside a vehicle as driver
○ Inside a vehicle as a front seat passenger
○ Inside a vehicle in back seat
○ Outside a vehicle with cover
○ Outside a vehicle without cover
○ On a vehicle (example: gunner)

How far were you from the explosion?

○ Within 5 feet
○ Between 5-10 feet
○ Between 10-15 feet
○ Over 15 feet
○ I do not know

Example of Blast Experience Screening Questionnaire

Visit: ○ Baseline

Second Worst Experience (continued)

To your best recollection, what did you experience during or right after the explosion? (Select all that apply)

- ○ Dazed
- ○ Confused
- ○ Headache
- ○ Dizziness
- ○ Irritability
- ○ Memory Gap
- ○ Hearing Loss
- ○ No symptoms
- ○ Blinded
- ○ Abdominal Pain
- ○ Shortness of Breath
- ○ Struck by Debris
- ○ Knocked over or down
- ○ Knocked into or against something
- ○ Evacuated for medical reasons
- ○ Other: _____

Not counting normal sleep time, do you **personally remember** the explosion and **all time immediately before and after**?

- ○ Yes, my memory for the experience is continuous (may have fuzzy parts)
- ○ No, I have no memory at all for some period of time (whether brief or long) during, immediately before or immediately after the explosion

If No, answer next three questions:

1. Do you remember the explosion itself?

   - ○ Yes
   - ○ No

2. Estimate of time period not remembered before blast:

   - ○ None, I remember all time up until the explosion
   - ○ Less than 1 hour - estimate # minutes not remembered ☐☐
   - ○ Between 1 hour and 24 hours - estimate # of hours not remembered ☐☐
   - ○ More than 24 hours - estimate # of days not remembered ☐☐

3. Estimate of time period not remembered after the explosion:
   - ○ None, there is no time after the explosion I don't remember
   - ○ Less than 1 hour - estimate # minutes not remembered ☐☐
   - ○ Between 1 hour and 24 hours - estimate # of hours not remembered ☐☐
   - ○ More than 24 hours - estimate # of days not remembered ☐☐

Example of Blast Experience Screening Questionnaire

Visit: ○ Baseline

Second Worst Experience (continued)

Did an observer report your losing consciousness (knocked out):

- ○ No
- ○ Yes, for less than 1 minute
- ○ Yes, for 1-60 minutes - estimate # minutes unconscious ☐☐
- ○ Yes, for longer than 60 minutes - estimate # of hours unconscious ☐☐

Were you wearing full body armor? ○ Yes ○ No

Were you wearing a helmet? ○ Yes ○ No

Were you wearing facial protection? ○ Yes ○ No

Did you have hearing problems that were medically evaluated?

○ Yes *If Yes, complete the following:*

○ No

Did you have a tympanic membrane rupture? ○ Yes ○ No

Was some other problem identified? ○ Yes ○ No

If Yes, complete the following:

Specify:

Did you have visual problems that were medically evaluated?

○ Yes *If Yes, complete the following:*

○ No

List problem identified.

Did you experience any physical pain during or immediately following this explosion?

○ Yes *If Yes, complete the following:*

○ No

If yes, please make a selection on the number scale below that best represents the level of your pain **at that time.**

1	2	3	4	5	6	7	8	9	10
○	○	○	○	○	○	○	○	○	○
NO PAIN									WORST PAIN POSSIBLE

Example of Blast Experience Screening Questionnaire

Visit: ○ Baseline

Third Worst Experience

Beginning on this page, you will be asked about your **third worst** explosion you experienced. (If you experienced only two explosions, then **STOP** here, you are finished with this form.)

Briefly describe your **third worst** explosion you experienced in a way that will help you to recall it later (please write 3 or less sentences):

Estimated Date: ☐☐ (d d) ☐☐ (m m) ☐☐☐☐ (y y y y)

Deployment:

○ Tour Name: _____

Type of explosion (select one):

○ RPG Mortar IED
○ Land mine
○ Grenade
○ Other: _____

Where were you at the time of the explosion?

○ Inside a vehicle as driver
○ Inside a vehicle as a front seat passenger
○ Inside a vehicle in back seat
○ Outside a vehicle with cover
○ Outside a vehicle without cover
○ On a vehicle (example: gunner)

How far were you from the explosion when it detonated?

○ Within 5 feet
○ Between 5-10 feet
○ Between 10-15 feet
○ Over 15 feet
○ I do not know

Example of Blast Experience Screening Questionnaire

Visit: ○ Baseline

Third Worst Experience (continued)

To your best recollection, what did you experience during or right after the explosion? (Select all that apply)

- ○ Dazed
- ○ Confused
- ○ Headache
- ○ Dizziness
- ○ Irritability
- ○ Memory Gap
- ○ Hearing Loss
- ○ No symptoms
- ○ Blinded
- ○ Abdominal Pain
- ○ Shortness of Breath
- ○ Struck by Debris
- ○ Knocked over or down
- ○ Knocked into or against something
- ○ Evacuated for medical reasons
- ○ Other: _____

Not counting normal sleep time, do you **personally remember** the explosion and **all time immediately before and after**?

- ○ Yes, my memory for the experience is continuous (may have fuzzy parts)
- ○ No, I have no memory at all for some period of time (whether brief or long) during, immediately before or immediately after the explosion

If No, answer next three questions:

1. Do you remember the explosion itself?

   - ○ Yes
   - ○ No

2. Estimate of time period not remembered before the explosion:

   - ○ None, I remember all time up until the explosion
   - ○ Less than 1 hour - estimate # minutes not remembered ☐☐
   - ○ Between 1 hour and 24 hours - estimate # of hours not remembered ☐☐
   - ○ More than 24 hours - estimate # of days not remembered ☐☐

3. Estimate of time period not remembered after the explosion:
   - ○ None, there is no time after the explosion I don't remember
   - ○ Less than 1 hour - estimate # minutes not remembered ☐☐
   - ○ Between 1 hour and 24 hours - estimate # of hours not remembered ☐☐
   - ○ More than 24 hours - estimate # of days not remembered ☐☐

Example of Blast Experience Screening Questionnaire

Visit: ○ Baseline

Third Worst Experience (continued)

Did an observer report your losing consciousness (knocked out):

- ○ No
- ○ Yes, for less than 1 minute
- ○ Yes, for 1-60 minutes - estimate # minutes unconscious ☐☐
- ○ Yes, for longer than 60 minutes - estimate # of hours unconscious ☐☐

Were you wearing full body armor? ○ Yes ○ No

Were you wearing a helmet? ○ Yes ○ No

Were you wearing facial protection? ○ Yes ○ No

Did you have hearing problems that were medically evaluated? ○ Yes ○ No

If Yes, complete the following:

Did you have a tympanic membrane rupture? ○ Yes ○ No

Was some other problem identified? ○ Yes ○ No

If Yes, complete the following:

Specify:

Did you have visual problems that were medically evaluated? ○ Yes ○ No

If Yes, complete the following:

List problem identified.

Did you experience any physical pain during or immediately following this explosion? ○ Yes ○ No

If Yes, complete the following:

If yes, please make a selection on the number scale below that best represents the level of your pain **at that time.**

1	2	3	4	5	6	7	8	9	10
○	○	○	○	○	○	○	○	○	○
NO PAIN									WORST PAIN POSSIBLE

Blast Experience Interview

Visit: ○ Phase 2

Interviewer: _____

Introduction

Refer to the Blast Experience Screening Questionnaire (BESQ) to fill in the blanks in question 1 in the "Description of Event and Experience" section (below), and be prepared to refer to the BESQ for question 1b. Then, instruct the subject:
You filled out a questionnaire [earlier / during your last visit] that indicated you were exposed to at least one explosion while deployed. I would like to spend the next 15 to 30 minutes asking some additional questions about this event.

Description of Event and Experience

1. You indicated on _____
[date of BESQ worst experience]
that you experienced an explosion during tour.
You described it like this:

_____
_____
_____
_____
_____
[subject's written description from BESQ]

You also indicated that it was your [only/worst] explosion you experienced. Is that correct?

○ Yes *If Yes, skip to Question 2 (next page*

○ No *If No, ask the following:*

1a. This interview will be only about your worst explosion you experienced. So I need to understand which that is. I will read back the descriptions that you gave on the screening form.

Read back the dates and written descriptions of all explosion experiences (worst, second and third worst) from the BESQ. Then ask:

If you are not sure which was the WORST, to help you

decide consider the immediate physical and/or mental effects. Please tell me which experience was your worst?

- ○ Worst on BESQ
- ○ Second Worst on BESQ
- ○ Third Worst on BESQ
- ○ Other (not described on BESQ)

Blast Experience Interview

Visit: ○ Phase 2

Description of Event and Experience (continued)

2. On the screening form, we asked you to describe this event and what you experienced in three sentences or less.
   Today, I would like you to tell me in as much detail as possible what happened to you and what you felt.
   (Make sure to get a clear narrative about events leading up to the explosion, information about the explosion, and information about what happened after the explosion including what he/she experienced physically and emotionally).

Blast Experience Interview

Visit: ○ Phase 2

Recollection of Event

1. Do you have personal memory of the explosion itself?

○ Yes
○ No

If Yes, complete the following:

1a. Do you recall feeling a "blast wave" moving through your body?

○ Yes
○ No
○ Don't Know

2. Is there a period of time just BEFORE the explosion for which you think you observed or experienced things but for which you have no memory at all?

○ Yes
○ No

If Yes, complete the following:

2a. What is the last thing that you personally remember occurring just BEFORE the explosion?

2b. How long was the period of time between [the thing in 2a response] and the explosion?

☐ ☐ ☐ ○ Seconds
○ Minutes
○ Hours

If subject responds in units other than those listed, record here:

_____

and convert later.

If subject is unable to provide a measurable response to 2b then instruct him/her: I understand that this is time that you do not remember, but please give me your best guess. *Then repeat question 2b.*

If subject is STILL unable to provide a response then instruct him/her: Please try and make your guess by what other people may have later told you, or on events that you think passed during that time. *Then repeat question 2b.*

Blast Experience Interview

Visit: ○ Phase 2

Recollection of Event (continued)

3. Is there a period of time just AFTER the explosion for which you think you observed or experienced things but for which you have no memory at all?

○ Yes *If Yes, complete the following:*
○ No

3a. What is the first thing that you personally remember occurring just AFTER the explosion?

3b. How long was the period of time between the explosion and [the thing in 3a response]?

☐ ☐ ☐ ○ Seconds ○ Minutes ○ Hours

If subject responds in units other than those listed, record here: _____ *and convert later.*

If subject is unable to provide a measurable response to 2b then instruct him/her: I understand that this is time that you do not remember, but please give me your best guess. *Then repeat question 3b.*

If subject is STILL unable to provide a response then instruct him/her: Please try and make your guess by what other people may have later told you, or on events that you think passed during that time. *Then repeat question 3b.*

4. *Interviewer: Review the prior answers. Are the responses* ***Yes*** *(#1),* ***No*** *(#2), and* ***No*** *(#3)?*

○ Yes *If Yes, complete the following:*
○ No

4a. It sounds like there are no holes or gaps in your memory from that day, is that correct? ○ Yes ○ No

If no:
Inform subject: "I need to understand how this fits with the earlier questions," then re-administer questions 1-3. If responses are still ***Yes*** *(#1),* ***No*** *(#2), and* ***No*** *(#3), then contact a clinical research staff member to help intervene.*

Blast Experience Interview

Visit: ○ Phase 2

Injury Mechanism

Advise the subject:
Some of the next questions may seem repetitive, but please bear with me, as we are trying to learn as much as possible about what you have experienced. If there are any questions where you are not sure of the answer, please try to give me your best guess.
(If subject states he/she has already told you the answer to any of the following questions, then read back the statement you think applies and ask if you got right, then insert/amend as he/she indicates.)

1. What were you doing at the time of the explosion?

2. Were there others with you at the time of the explosion? ○ Yes ○ No
3. Were you wearing a helmet at the time of the explosion? ○ Yes ○ No
4. Were you wearing full body armor at the time of the explosion? ○ Yes ○ No
5. Were you wearing ear protection at the time of the explosion? ○ Yes ○ No
6. Were you wearing facial protection at the time of explosion? ○ Yes ○ No

7. Were you positioned inside or on a vehicle at the time of the explosion?
   ○ Yes ○ No
   If Yes, complete the following:
   - 6a. What kind of vehicle was involved?
   - 6b. Describe your position (in relation to the vehicle).

8. Did you have any other cover at the time of the explosion (other than or in addition to a vehicle)?
   ○ Yes ○ No ○ Don't Know
   If Yes, complete the following:
   - 7a. Describe the cover
   - 7b. Describe your position (in relation to the cover).

9. About how close were you to the explosion? ☐☐☐ ft
   ○ Don't Know
   If subject responds in units other than feet record here:
   _____ *and convert to feet later.*

Blast Experience Interview

Visit: ○ Phase 2

Injury Mechanism (continued)

10. What direction from you was the explosion?
- ○ Left
- ○ Right
- ○ Above
- ○ Front
- ○ Behind
- ○ Below
- ○ Don't Know

11. Were you thrown or knocked to the ground?
- ○ Yes
- ○ No
- ○ Don't Know

If Yes, complete the following:

10a. Estimate how far you were thrown: ☐☐☐ ft

If subject responds in units other than feet record here: _____ *and convert to feet later.*

12. Were you thrown against or knocked into something else?
- ○ Yes
- ○ No
- ○ Don't Know

If Yes, complete the following:

11a. Describe the vehicle, structure, etc:

13. To your knowledge, was your head struck or did your head hit something?
- ○ Head was struck
- ○ Head hit something
- ○ No
- ○ Don't Know

If Yes, complete the following:

Based on the answer to 10, ask either:

12a. [What struck your head?] *or*
[What did your head hit?]

12b. What side of your head was struck or hit?
- ○ Forehead
- ○ Back of the head
- ○ Face or chin Left side Right side Don't Know
- ○ Other: _____

Blast Experience Interview

Visit: ○ Phase 2

Consciousness

1. Did you become unconscious, that is, you could not see, speak, and move for any period of time?

○ Yes ○ No ○ Don't Know

If Yes, complete the following:

2. Were you told this by a witness, or is your report of unconsciousness based upon your experience?

○ Witness ○ Own Experience

If Yes, complete the following:

2a. How did you determine you were unconscious?

○ Events that passed
○ Evidence from a watch, time on a phone, video, etc.
○ Guess
○ Other: _____

3. How long were you unconscious?

☐ ☐ ☐ ○ Seconds ○ Minutes ○ Hours ○ Don't Know

If subject responds in units other than those listed, record here: _____ *and convert later.*

Symptoms

1. Did you feel dazed?

○ Yes ○ No ○ Don't Know

If Yes, complete the following:

1a. How long after the explosion did you start feeling dazed?

☐ ☐ ☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds or immediate onset, code as 0 minutes.

1b. How long did it last?

☐ ☐ ☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds, code as 0 minutes. If continuously experienced through today, note in margin, then code appropriately post-interview.

1c. Do you feel that you were more dazed than what you should expect, considering the danger and surprise of what happened? ○ Yes ○ No

Blast Experience Interview

Visit: ○ Phase 2

Symptoms (continued)

2. Did you feel confused?

○ Yes ○ No ○ Don't Know

If Yes, complete the following:

2a. How long after the explosion did you start feeling confused?

☐ ☐ ☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds or immediate onset, code as 0 minutes.

2b. How long did it last?

☐ ☐ ☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds, code as 0 minutes. If continuously experienced through today, note in margin, then code appropriately post-interview.

2c. Do you feel that you were more confused than what you should expect, considering the danger and surprise of what happened? ○ Yes ○ No

3. Did you see stars?

○ Yes ○ No ○ Don't Know

If Yes, complete the following:

3a. How long after the explosion did you start seeing stars?

☐ ☐ ☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds or immediate onset, code as 0 minutes.

3b. How long did it last?

☐ ☐ ☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds, code as 0 minutes. If continuously experienced through today, note in margin, then code appropriately post-interview.

4. Did you feel dizzy?

○ Yes ○ No ○ Don't Know

If Yes, complete the following:

4a. How long after the explosion did your feeling dizziness start?

☐ ☐ ☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds or immediate onset, code as 0 minutes.

4b. How long did it last?

☐ ☐ ☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds, code as 0 minutes. If continuously experienced through today, note in margin, then code appropriately post-interview.

Blast Experience Interview

Visit: ○ Phase 2

Symptoms (continued)

5. Did you feel irritable?

○ Yes ○ No ○ Don't Know

If Yes, complete the following:

5a. Did you have any irritability before the explosion? ○ Yes ○ No

If no, skip to Question 5c

5b. Did the irritability that you had before the explosion get **worse** after the explosion? ○ Yes ○ No

If no, skip to Question 6

If subject indicated increased irritability after the explosion, include words in [brackets], otherwise leave out.

5c. How long after the explosion did you start feeling [more] irritable?

☐ ☐ ☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds or immediate onset, code as 0 minutes.

5d. How long did the [increased] irritability last?

☐ ☐ ☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds, code as 0 minutes. If continuously experienced through today, note in margin, then code appropriately post-interview.

5e. Do you feel that your irritability was stronger than what you should expect, considering the danger and surprise of what happened? ○ Yes ○ No

6. Did you lose your hearing in one or both ears?

○ Yes ○ No

If Yes, complete the following:

6a. How long after the explosion did your hearing loss start?

☐ ☐ ☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds or immediate onset, code as 0 minutes. Likewise, if less than 30 seconds or immediate onset upon removal of hearing protection, code as 0 minutes.

6b. How long did it last?

☐ ☐ ☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds, code as 0 minutes. If continuously experienced through today, note in margin, then code appropriately post-interview.

Blast Experience Interview

Visit: ○ Phase 2

Symptoms (continued)

7. Did you have ringing in one or both ears?

○ Yes *If Yes, complete the following:*
○ No

7a. How long after the explosion did the ringing start?

☐ ☐ ☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds or immediate onset, code as 0 minutes.

7b. How long did it last?

☐ ☐ ☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds, code as 0 minutes. If continuously experienced through today, note in margin, then code appropriately post-interview.

8. Did you go blind?

○ Yes *If Yes, complete the following:*
○ No

8a. How long after the explosion did you go blind?

☐ ☐ ☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds or immediate onset, code as 0 minutes.

8b. How long did it last?

☐ ☐ ☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds, code as 0 minutes. If continuously experienced through today, note in margin, then code appropriately post-interview.

Blast Experience Interview

Visit: ○ Phase 2

Symptoms (continued)

9. Did your head ache? ○ Yes ○ No

If Yes, complete the following:

9a. Did you have any head ache **before** the explosion?? ○ Yes ○ No

If no, skip to Question 9c

9b. Did the head ache that you had before the explosion get **worse** after the explosion? ○ Yes ○ No

If no, skip to Question 10

If subject indicated increased head ache after the explosion, include words in [brackets], otherwise leave out.

9c. How long after the explosion did your [increased] headache start?

☐ ☐ ☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds or immediate onset, code as 0 minutes.

9d. How long did the [increased] head ache last?

☐ ☐ ☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds, code as 0 minutes. If continuously experienced through today, note in margin, then code appropriately post-interview.

9e. How long after the explosion was the pain at its worst?

☐ ☐ ☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds or immediate onset, code as 0 minutes.

9f. Please rate the pain when it was at its worst on a scale of 0 to 10, where 0 is no pain and 10 is the worst possible pain.

1	2	3	4	5	6	7	8	9	10
○	○	○	○	○	○	○	○	○	○
NO PAIN									WORST PAIN POSSIBLE

Blast Experience Interview

Visit: ○ Phase 2

Symptoms (continued)

10. Did you feel abdominal or stomach pain?

○ Yes — *If Yes, complete the following:*

○ No

10a. Did you have any abdominal or stomach pain **before** the explosion? ○ Yes ○ No

If no, skip to Question 10c

10b. Did the abdominal or stomach pain that you had before the explosion get **worse** after the explosion? ○ Yes ○ No

If no, skip to Question 11

If subject indicated increased abdominal or stomach pain after the explosion, include words in [brackets], otherwise leave out.

10c. How long after the explosion did you feel increased pain?

☐ ☐ ☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds or immediate onset, code as 0 minutes.

10d. How long did the [increased] pain last?

☐ ☐ ☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds, code as 0 minutes. If continuously experienced through today, note in margin, then code appropriately post-interview.

10e. How long after the explosion was the pain at its worst?

☐ ☐ ☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds or immediate onset, code as 0 minutes.

10f. Please rate the pain when it was at its worst on a scale of 0 to 10, where 0 is no pain and 10 is the worst possible pain.

1	2	3	4	5	6	7	8	9	10
○	○	○	○	○	○	○	○	○	○
NO PAIN									WORST PAIN POSSIBLE

Blast Experience Interview

Visit: ○ Phase 2

Symptoms (continued)

11. We have covered head, abdominal, and stomach pain. Did you feel any other physical pain?

○ Yes
○ No
○ Don't Know

If Yes, complete the following:

11a. What part or parts of your body were in pain?

If multiple parts were given in 11a, ask subject:

11b. What part was the most painful?

For the following questions, replace [body part] with the (most) painful part indicated in 11a/11b.

11c. Did you have any [body part] pain **before** the explosion?
○ Yes
○ No
If no, skip to Question 11e

11d. Did the [body part] pain that you had before the explosion get **worse** after the explosion?
○ Yes
○ No
If no, skip to Question 12

If subject indicated increased pain after the explosion, include words in [brackets], otherwise leave out.

11e. How long after the explosion did the [increased] pain start?

☐☐☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds or immediate onset, code as 0 minutes.

11f. How long did the [increased] pain last?

☐☐☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds, code as 0 minutes. If continuously experienced through today, note in margin, then code appropriately post-interview.

11g. How long after the explosion was the [increased] pain at its worst?

☐☐☐ ○ Minutes ○ Hours ○ Days ○ Months

If less than 30 seconds or immediate onset, code as 0 minutes.

11h. Please rate the pain when it was at its worst on a scale of 0 to 10, where 0 is no pain and 10 is the worst possible pain.

1	2	3	4	5	6	7	8	9	10
○	○	○	○	○	○	○	○	○	○
NO PAIN									WORST PAIN POSSIBLE

Blast Experience Interview

Visit: ○ Phase 2

Symptoms (continued)

12. Did you have any other feelings or problems right after the explosion that I did not ask?

○ Yes *If Yes, complete the following:*
○ No

12a. Other symptom:

12a1. How long after the explosion did this symptom start?

☐☐☐ ○ Minutes ○ Hours ○ Days ○ Months *If less than 30 seconds or immediate onset, code as 0 minutes.*

12a2. How long did it last?

☐☐☐ ○ Minutes ○ Hours ○ Days ○ Months *If less than 30 seconds, code as 0 minutes. If continuously experienced through today, note in margin, then code appropriately post-interview.*

12b. Other symptom:

12b1. How long after the explosion did this symptom start?

☐☐☐ ○ Minutes ○ Hours ○ Days ○ Months *If less than 30 seconds or immediate onset, code as 0 minutes.*

12b2. How long did it last?

☐☐☐ ○ Minutes ○ Hours ○ Days ○ Months *If less than 30 seconds, code as 0 minutes. If continuously experienced through today, note in margin, then code appropriately post-interview.*

12c. Other symptom:

12a1. How long after the explosion did this symptom start?

☐☐☐ ○ Minutes ○ Hours ○ Days ○ Months *If less than 30 seconds or immediate onset, code as 0 minutes.*

12a2. How long did it last?

☐☐☐ ○ Minutes ○ Hours ○ Days ○ Months *If less than 30 seconds, code as 0 minutes. If continuously experienced through today, note in margin, then code appropriately post-interview.*

Blast Experience Interview

Visit: ○ Phase 2

Outcome

1. To your knowledge, did you sustain any physical injury(s) from the explosion?

○ Yes
○ No

If Yes, complete the following:

2. Did your injuries include a skull fracture or a brain bleed?
○ Yes
○ No
○ Don't Know

3. What were your injuries?

4. What kind of treatment did you receive for your injuries? (specific medication, treatment of wounds, etc.)

5. Tell me all the places where you received treatment.

6. Were you placed into a medically induced coma as part of your treatment?
○ Yes
○ No
○ Don't Know

If Yes, ask the following

6a. What was the reason?

6b. How many days were you in a medically induced coma? ☐☐☐ days

Blast Experience Interview

Visit: ○ Phase 2

Outcome (continued)

7. re you evaluated by a medic after the explosion?
   - ○ Yes
   - ○ No
   - ○ Don't Know

8. Were you medically evacuated or treated after the explosion at an aid station or other medical center "in country"?
   - ○ Yes
   - ○ No

9. Were you medically evacuated outside of the theater of operation for assessment or treatment due to injuries from the explosion?
   - ○ Yes
   - ○ No

10. Did you miss duty while you were being evaluated or treated?
    - ○ Yes — *If Yes, ask the following:*
      - 10a. How many days were you off duty? ☐☐☐ days
    - ○ No

Events Checklist for Military Personnel

Visit: ○ Baseline

DIRECTIONS: On this page are several events which you may have experienced during combat or training. Please carefully read each statement. Mark "Yes" if you have experienced the event and "No" if you have not experienced the event. **If you have never been deployed to a warzone, skip to *Other Events* below (section B, page 3).**

Combat Experiences:

A1.	Went on a combat patrol, convoy, or other mission that provided risk of death?	○ Yes	○ No
A2.	Experienced incoming small arms fire from enemy troops (or friendly fire)?	○ Yes	○ No
A3.	Experienced incoming artillery, rockets, mortars, or bombs from enemy troops (or friendly fire)?	○ Yes	○ No
A4.	Experienced an improvised explosive device (IED) that was detonated?	○ Yes	○ No
A5.	Witnessed the serious injury or death of enemy troops?	○ Yes	○ No
A6.	Witnessed the serious injury or death of someone from my unit, an ally unit, or other friendly personnel?	○ Yes	○ No
A7.	Witnessed the serious injury or death of a citizen noncombatant?	○ Yes	○ No
A8.	Observed seriously injured or dead bodies?	○ Yes	○ No
A9.	Became a prisoner of war?	○ Yes	○ No
A10.	Experienced any other combat-related events that were life threatening, caused serious injury, or were highly distressing or traumatic (for example, car crash	○ Yes	○ No
A11.	Have you had any combat-related experiences like these that you feel you can't tell about? (note: you don't have to describe the event)	○ Yes	○ No

Events Checklist for Military Personnel

Visit: ○ Baseline

Combat Experiences Continued

A12. **Which of the combat experiences listed on the prior page (A1-A11) was the <u>MOST</u> distressing or traumatic?** Fill in the bubble of the item number of the experience below (e.g., A9 for "prisoner of war").

○ A1 ○ A2 ○ A3 ○ A4 ○ A5 ○ A6 ○ A7 ○ A8 ○ A9 ○ A10 ○ A11

A13. When did this most distressing/ traumatic combat event happen? ☐☐ ☐☐☐☐ mm d d d d *(If necessary, please estimate)*

A14. How old were you? ☐☐ *(If necessary, please estimate)*

A15. Did you experience intense fear, helplessness, or horror when the event occurred? ○ Yes ○ No

A16. In response to the event, did you experience intense fear, helplessness, or horror at some later time, **<u>after</u>** the event occurred? ○ Yes ○ No

A17. Did you experience intense anger when it occurred ○ Yes ○ No

A18. Did you feel that your life was in danger? ○ Yes ○ No

A19. Did you feel that someone else's life was in danger? ○ Yes ○ No

A20. Were you physically injured during the event? ○ Yes ○ No

A21. Was someone else physically injured or killed during the event? ○ Yes ○ No

A22. How distressing or traumatic was the event for you **<u>at that time</u>** (fill in the corresponding bubble)?

1	2	3	4	5	6	7
○	○	○	○	○	○	○
Not at all						Extremely

A23. How distressing or traumatic is the event for you **<u>now</u>** (fill in the corresponding bubble)?

1	2	3	4	5	6	7
○	○	○	○	○	○	○
Not at all						Extremely

Events Checklist for Military Personnel

Visit: ○ Baseline

DIRECTIONS: On this page are several events which you may have experienced **outside of combat**. They may have occurred during deployment, but did not occur as a result of engagement with the enemy, friendly fire, sniper fire or an IED or in training. For each of the following events, indicate that you experienced the event by filling in the bubble next to the description.

Other Experiences (that were not experienced during combat):

B1.	Experienced a natural disaster (such as a hurricane or earthquake)?	○ Yes	○ No
B2.	Been involved in a motor vehicle accident that was life threatening, caused serious injury, or was highly disturbing or distressing?	○ Yes	○ No
B3.	Been involved in any other kind of accidents that were life threatening, caused serious injury, or were highly disturbing or distressing? (examples: a plane crash, nearly drowning, getting shocked, or injured in an industrial accident, or a home fire)	○ Yes	○ No
B4.	Been a victim of a violent crime such as robbery, assault, or someone threatening to seriously injure or kill you?	○ Yes	○ No
B5.	Had a life threatening illness, miscarriage or other health-related event (yourself)?	○ Yes	○ No
B6.	Witnessed a violent crime such as robbery, assault, or someone threatening to seriously injure or kill another person?	○ Yes	○ No
B7.	Had a loved one experience (and survive) a life threatening or permanently disabling accident, assault, or illness?	○ Yes	○ No
B8.	Experienced the sudden and unexpected death of a close friend or loved one?	○ Yes	○ No
B9.	Witnessed the sudden and unexpected death of a stranger?	○ Yes	○ No
B10.	Experienced physical abuse from a spouse, partner or date?	○ Yes	○ No
B11.	Experienced physical abuse from a family member, caretaker, or teacher? (not from a spouse, partner, or date)	○ Yes	○ No
B12.	Witnessed family violence?	○ Yes	○ No
B13.	Experienced unwanted sexual experiences that may or may not have included the threat or use of force?	○ Yes	○ No
B14.	Experienced (or seen) any other events that were life threatening, caused serious injury, or were highly distressing or traumatic? (examples: lost in the wilderness, attacked by an animal)	○ Yes	○ No
B15.	Have you experienced any other distressing or disturbing events that you feel you can't tell about?	○ Yes	○ No
B16.	I have never experienced any of the events listed above.	○ Yes	○ No

If you never experienced any of these events (B1-B15), please SKIP the rest of this questionnaire.

Events Checklist for Military Personnel

Visit: ○ Baseline

Other Experiences (that were not experienced during combat) continued

B17. **Which of the events you listed on the prior page (B1-B15) was the MOST distressing or traumatic thing to have happened in your life outside of combat?** Fill in the bubble of the item number of the event below (e.g., B12 for "witnessed family violence").
○ B1 ○ B2 ○ B3 ○ B4 ○ B5 ○ B6 ○ B7 ○ B8 ○ B9 ○ B10 ○ B11 ○ B12 ○ B13 ○ B15 ○ B15

B18. When did this most distressing/ traumatic event happen? ☐☐ ☐☐☐☐ mm d d d d *(If necessary, please estimate)*

B19. How old were you? ☐☐ *(If necessary, please estimate)*

B20. Did you experience intense fear, helplessness, or horror when the event occurred? ○ Yes ○ No

B21. In response to the event, did you experience intense fear, helplessness, or horror at some later time, **after** the event occurred? ○ Yes ○ No

B22. Did you experience intense anger when it occurred ○ Yes ○ No

B23. Did you feel that your life was in danger? ○ Yes ○ No

B24. Did you feel that someone else's life was in danger? ○ Yes ○ No

B25. Were you physically injured during the event? ○ Yes ○ No

B26. Was someone else physically injured or killed during the event? ○ Yes ○ No

B27. How traumatic was this event for you **at that time** (fill in the corresponding bubble)?

1	2	3	4	5	6	7
○	○	○	○	○	○	○
Not at all						Extremely

B28. How distressing or traumatic is the event for you **now** (fill in the corresponding bubble)?

1	2	3	4	5	6	7
○	○	○	○	○	○	○
Not at all						Extremely

B29. **Of all the traumatic combat and non-combat events** that you have experienced, was the **MOST** traumatic event experienced during combat **or** outside of combat? (select only **ONE**) ○ During Combat ○ Outside of Combat

Annex E − MINUTES FROM PANEL MEETING MAY 2014

Reproducing Blast Exposure Conditions in the Laboratory

DRDC – Suffield Research Centre
Medicine Hat, Alberta, Canada
May 21-23, 2014

E.1 BACKGROUND

Blast Injury is one of the most important sources of casualties in current NATO operations. The term "blast injury" creates considerable confusion in military medicine. Simply stated, "blast injury" includes the entire spectrum of injuries that can result from exposure to an explosion. It is generally accepted that the taxonomy of injuries can be assigned to five categories: primary, secondary, tertiary, quaternary, and quinary. These are based on the mechanism of injury. Primary blast injuries result from the high pressures created by the blast itself. The high pressures, known as blast overpressure, can cause internal injuries. Primary injuries result from the effects of the shock wave, which travels through the tissues depositing energy particularly where there is a gas-liquid interface. Secondary blast injuries result when strong blast winds behind the pressure front propel fragments and debris against the body and cause blunt and penetrating injuries. The strong winds and pressure gradients also can accelerate the body and cause the same types of blunt force injuries that would occur in a car crash or a fall. These are known as tertiary blast injuries. Quaternary blast injuries are the result of other explosive products, such as heat, light, and toxic gases that can cause burns, blindness, and inhalation injuries. Finally, quinary blast injuries refer to the clinical consequences of "post-detonation environmental contaminants", including bacteria, radiation (dirty bombs), and tissue reactions to fuel and metals.

The discussions at HFM-207 (SYM) revealed the importance of a systematic approach to understanding blast injuries much like the well-established approach used to solve the classical toxicology problem where the etiology of the injury requires an understanding of the dose, mechanism of delivery of the dosage, and dose-response endpoints. Also recognized was the pressing need for a multidisciplinary approach to addressing non-penetrating blast injuries to the brain that result in a host of symptoms with vague etiology. In addition, the Technical Evaluation Report emphasized the continued multinational exchanges of scientific and technical advances to respond to blast threat and blast injuries. The first recommendation identified a future need for a recurring technical exchange venue on blast injury and its mitigation to address advances in medicine and personal protection and their synergy. The second recommendation highlighted the need for the development of a Technical Activity Proposal (TAP) to explore the concept of "the Toxicology of Blast Injury" and suggested to focus the activity on several difficult problems including:

- Relevancy and commonality of animal models.
- Common dose-response methods; route of exposure methods.
- Computational Models (blast, physiology, biochemical, toxicological, etc.).
- Dose regimens to human medical endpoints (surgical trauma to mTBI spectrum).
- Methods for translational research leading to medical products and/or physical protection products.

To address the above recommendation and to develop a specific NATO activity devoted to the toxicology of blast exposure, a TAP titled "Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods

and Standards was approved in the fall of 2012, which resulted in the establishment of a new NATO Science and Technology Organization HFM Panel RTG with the following objectives:

- Build an evidence-based outline for NATO standards for blast injury analysis.
- Examine opportunities for improvements in the standards of medical care for blast injury.
- Explore advancing the state-of-practice in computational modeling of blast injury in relevant operational environments.
- Explore standardized animal models and toxicology research protocols that could be adopted by R&T programs across NATO.

This document summarizes the deliberations of the HFM-234 (RTG) Technical Teams (TT) meeting focused on developing guidance on reproducing blast exposure conditions in the laboratory. The agenda for this meeting is shown in Appendix E1. Meeting agenda items included a full day of presentations on how different laboratories create blast exposures followed by considerable discussion. Presenters were from the Technical Team as well as external experts. Discussion on what form guidance should take started after the presentations. The following day a tour and demonstration of DRDC Suffield Research Centre facilities highlighted the efforts at that laboratory to reproduce blast exposures. A sub-group from the Technical Team met to continue discussions on the blast injury dictionary of terms while the rest of the team received an update on the epidemiology of blast guidelines. The balance of the day was used to further develop the guidance document for reproducing blast in the laboratory. The objectives for the next meeting in Tallinn, Estonia (7-9 October 2014) were also discussed. Eleven TT members participated in the meeting, representing seven NATO nations. The list of TT members is attached (Appendix E2).

E.2 WELCOME AND OPENING REMARKS

Mike Leggieri (Chair) opened the meeting welcoming the TT members and invited speakers to the meeting. The goal of the meeting was to come to a consensus on some fundamental concepts of how to reproduce blast exposures that would allow for analysis of the exposure conditions used. There is a necessity for this given the variance in reporting blast exposure information in the literature and the ensuing confusion created in understanding blast injury effects, especially mild Traumatic Brain Injury (mTBI). The desired product from the meeting is some form of guidelines or guidance document that clearly describes what characteristics must be included when reporting the exposure conditions for blasts created in the laboratory. Following the chair's opening remarks, individual introductions of those present in the room were then done.

E.3 CREATING BLAST EXPOSURES IN THE LAB – PRESENTATIONS

Dr. Mårten Risling gave the first presentation describing blast injury research at the Karolinska Institute in Sweden. He described research using:

1) A primary blast tube that uses a charge;
2) A system that creates focal TBI by cortical impact; and
3) A system where TBI is a result of acceleration.

Several different models of injury are used at Dr. Risling's laboratory, *in vivo* and *in vitro*. Additionally, several endpoint methods are used depending on the research question (e.g., imaging, neurobehaviour, gene arrays, biomarkers) as well as finite element modelling.

Mr. Mat Philippens followed with a presentation on blast TBI shockwave simulation at TNO. He stressed the need to be aware of not only the static pressure but also the dynamic pressure and the relationship between the two. Location in a shock tube is sensitive with respect to the positive phase static pressure and for the static to dynamic pressure ratio. On a micro scale the injury is strain related that triggers a physiological response. Pressures are critical and Mr. Philippens questioned what limits are relevant in the compression and/or tensile regime for mild injuries? With respect to laboratory experiments reproducing 'real' effects in an experimental setup requires an accurate setup: free field versus shocktube. The loading must always be well defined (and recorded) during experiments.

Dr. Jim Stuhmiller, an invited speaker from L3 Jaycor, gave a presentation on blast simulation where he discussed the types of simulation, why simulations are important and the absolute requirement to validate the simulation with relevant field data. The use of shock tubes is important and can simulate blasts over limited ranges of target areas and responses but the parameters must be carefully considered and there are trade-offs to be aware of. Dr. Stuhmiller also pointed out that simulations using animal subjects must be scaled to account for the size and response mechanisms. Target loading and the motion of the target must be considered and validated.

Dave Ritzel, an invited speaker from Dyn-FX Consulting Limited gave a talk on blast physics, laboratory simulation, and metrics. He started out describing the mess that blast injury is in due to poor understanding and reporting on blast exposure conditions. A review of basic blast physics was followed by discussion on blast simulation in the laboratory. Mr. Ritzel spoke to the confusion regarding terminology for pressure that needs to be clarified. He pointed out that it is important to note that these are pressure terms defining 'free-field' flow properties, and are not target-loading pressures. Static, dynamic, total and reflected pressure was defined and he pointed out that pressure is not the only physical characteristic that must be understood: the relationship between pressure, density, flow velocity and temperature must be taken into account. Mr. Ritzel described shock tube technology and advanced blast simulators. Ideally, apparatus for simulating blast insult would be standardized as done for other brain-injury testing, but at minimum, simulators should be qualified with respect to ability to replicate credible static and dynamic (or total) overpressure conditions representative of blast-wave profiles.

Dr. Julian Lee, a defence scientist from the Military Engineering Section (MES), DRDC Suffield Research Centre gave a presentation on creating blast exposures at DRDC Suffield Research Centre. From a blast physics perspective, to characterize blast insult on a human brain one needs to start with a timescale analysis using a sphere for modelling. From this analysis the shock transit times are of the same order of magnitude so the wave processes are coupled. Dr. Lee spoke to the measurements required for determining the head response to a blast. As part of the blast there are three measurements: static pressure; reflected pressure; and dynamic pressure. Inside the head, intracranial pressure is required and deformation, or strain, of the head must be considered. He then spoke to the issue of which gauges to use with the Millar gauge being the winner so long as a different signal conditioner than that provided with the gauge is used. Selection of the right gauge is significant in measuring blast exposure in the laboratory. Dr. Lee then spoke about the capability to measure strain using a 3D image correlation system (ARAMIS) using the small shock tube (Advanced Blast Simulator 30; ABS30). Next he discussed the large blast tube (1.8 m x 45 m) at DRDC Suffield Research Centre and the modifications underway that will allow for shorter duration, higher pressure blast waves required to simulate modern threats (e.g. IED blast). Dr. Lee finished his presentation discussing the study using a biosensor system (brain cell aggregate culture) and the underwater explosive pond to investigate primary shock mechanisms on living cells.

Tyson Josey, an engineer from the Military Engineering Section, DRDC Suffield Research Centre gave a presentation where he discussed DRDC shock tubes in detail and numerical modelling. The ABS30 at DRDC Suffield Research Centre was discussed focussing on the wave shaping section and the End Wave Eliminator (EWE). The importance of driver gas selection, specifically the attributes of helium, was pointed out by

Mr. Josey. Additionally the use of bursting diaphragms composed of layered sheets of acetate and the effort spent calibrating the diaphragm packages through extensive trials was noted. Several driver improvements (o-ring; bolting vs hydraulics; driver filling; cellular insert) to the ABS30, a sensitive and semi-automated data acquisition system and the EWE have all contributed to high repeatability between trials. To help understand the wave form generated down the tube and the effect of obstructions and forms, Mr. Josey does numerical modelling using experimental data that allows for the computation of the entire blast flow field. With respect to the effect of obstructions, numerical analysis has allowed for the study of the effect of: the specimen holder used; a fragmentation deflector; shape of head forms; kinematic analysis of head movement; and type of head restraint.

Simon Ouellet, a defence scientist from DRDC Valcartier Research Centre and a member of the RTG team gave a presentation on efforts at Valcartier to develop a blast induced Brain Injury Protection Evaluation Device (BIPED) and considerations that must be given when reproducing blasts. When the device was being developed considerations were given to studying the effects of different blast/shock scenarios. Free field blast trials were used to evaluate the device with high importance placed on loading characterization and repeatability. Mr. Ouellet observed repeatable pressures in the device regardless of gauge location and the intracranial pressure followed the initial forehead overpressure history with even the ground reflection peak visible. A comparison study between the BIPED and post-mortem human heads showed that the two are generally comparable with the exception of resonant frequencies. Mr. Ouellet discussed future work on the BIPED and the need for characterization of different blast scenarios such as breacher studies.

E.4 GUIDELINES DEVELOPMENT DISCUSSION

The guidelines development discussion opened with a reminder from the chair, Mr. Leggieri of the objective of the meeting which was to come up with guidelines that delineate the critical elements that must be addressed by researchers in consideration of their exposure systems. It was decided by the team that a template be created that lists the parameters or characteristics of a blast exposure that need to be documented. The blast injury dictionary and the blast exposure guidelines should both develop in a parallel manner as the dictionary will provide guidance for using the template and the template will populate the dictionary. A draft of the characteristics required was started during this session and is attached to this report as Appendix E3. The necessity for a dictionary of terms that is related to the guidelines template became obvious when discussion about target loading went around the table.

E.5 TOUR OF B19 (SMALL SHOCK TUBE FACILITY) AND RITZEL CENTRE (LARGE TUBE AND UNDEX FACILITY)

The TT was toured through the small shock tube facility at DRDC Suffield Research Centre by Dr. Thomas Sawyer and Mr. Tyson Josey. Dr. Sawyer leads the biomedical portion of the blast injury program and Mr. Josey leads the physics/engineering/modelling efforts in the facility. Dr. Sawyer described the animal and *in vitro* models in use; the advantages and disadvantages of each and why it is important to control for exposure variables. He also described the research questions being pursued on exposure to a primary shock pressure wave and why from a toxicological perspective they are important. Mr. Josey then described the ABS30 system and the advancements that have been made in tailoring a pressure wave to closely represent that of a free field blast. Many of the engineering advances were made in collaboration with Dyn-FX Consulting Ltd. A ‘shot’ was then set up by Mr. Josey for the Technical Team and the pressure wave discussed afterwards. The advancements made with the tube have resulted in a narrow variance from desired target pressures (± 3%) and high repeatability between ‘shots’.

The TT was then taken to the Ritzel Centre on the Experimental Proving Grounds at DRDC Suffield Research Centre which is the location of the large blast tube (1.8 m x 45 m) and the underwater explosion (UNDEX) pond. Dr. Julian Lee described the work being undertaken in the UNDEX pond and the relevance of using underwater explosive trials to understanding blast pressure waves in air. When single pulse shock waves are generated underwater, and they impact a thin membrane bound cylinder of fluid, the shock wave progresses through the cylinder largely unchanged. This methodology will be used to examine whether the single pulse shock wave generated underwater produces changes in brain aggregates (as opposed to the complex pressure wave profile found in sphere work using the ABS30). This approach will also be used to ascertain what aspects of the shock wave are the most damaging; the overpressure or the duration, or whether it is the total amount of energy within the shockwave (the impulse) that is the primary determinant of cellular damage. Dr. Lee, with Gerry Rude (Sr Tech, MES) gave a tour of the large blast tube including the test section, driver section, and control room. Mr. Rude then set up and ran a 'shot' of the tube for the TT and the pressure wave was collected and discussed after the 'shot'. The tube was built for nuclear blast pressure waves, which have a long duration but it is now undergoing a re-fit to provide pressure waves more indicative of standard explosive duration. The tube can then be used for testing the effects of blast pressure waves on a variety of targets.

E.6 UPDATE ON BLAST INJURY EPIDEMIOLOGICAL STUDY DATA COLLECTION GUIDELINES

Dr. Raj Gupta provided the TT with an update on the epidemiological guidelines development. At the time of the meeting at DRDC Suffield Research Centre, Dr. Gupta was waiting for comments from Dr. Hans Orru (TT member, Estonia). The guidelines document from the December meeting at Ft. Detrick has been closed for comments and Dr. Gupta will send this to the TT. Questions arose about how to disseminate the information and Dr. Gupta will contact Ron Verkerk at NATO STO (see item 1) a) in Section E.7).

E.7 NEXT MEETING – COMPUTATIONAL MODELLING AND DICTIONARY

The next meeting of the Technical Team will be in Tallinn, Estonia, on 7-9 October 2014, to discuss computational modeling in the context of blast injury. The Blast Injury Dictionary discussions will also continue. The tentative plan is as follows:

1) Reassess HFM-234 (RTG) progress and plan:

   a) Update on coordination for publication of Blast Injury Epidemiological Study Data Collection Guidelines with Ron Verkerk (STO).

   b) Coordinate with STO to explore teaming among NATO nations for conducting collaborative blast injury studies.

   c) Status of Laboratory Blast Exposure Guidelines.

2) Review of Blast Injury Epidemiological Study Data Collection Guidelines:

   a) Look in multinational data bases to add parameters related to Blast Injury Epidemiological Study Data Collection − Dr. Dan Bieler to present concept and parameters for inclusion in NATO trauma registry.

3) Present proceedings of the DoD Blast Induced Computational Modeling Expert Panel (2 – 3 hrs).

4) Develop a document capturing blast research infrastructure, cross-NATO research opportunities including past, on-going, and future studies by participating members:
   a) Dr. Cernak to prepare draft template (Dr. Kirkman) – Raj Gupta.
5) Review blast injury dictionary of terms.

E.8 UPDATE ON BLAST INJURY DICTIONARY OF TERMS

The group of TT members (Dr. Ibi Cernak (USA); Dr. Emrys Kirkman (GBR); Mat Philippens (NLD)) working on the dictionary reported back to the TT that there were 65 terms in the dictionary that are essential and 70 – 75 references in total. The essential terms need to be brought forward to the exposure guidelines template. It was presented to the TT that each term in the dictionary will start with a generalized description and through the use of examples be narrowed or specificity added.

E.9 GUIDELINES DEVELOPMENT DISCUSSIONS (CONT.)

The discussions on developing the exposure guidelines template continued and work continued on the outline (Appendix E3). It was noted during this session that the exposure guidelines are not intended to dictate how studies are done but are intended to ensure that critical information is collected on how the exposure conditions are created.

E.10 ACTION ITEMS / TASKINGS

The following actions/tasking were made at the conclusion of the meeting:

1) Dr. Gupta will send the meeting notes from the December meeting in Ft Detrick to the TT. He will also contact Ron Verkerk at NATO STO with respect to publication of the guidelines.
2) Dr. Cernak will build a blast injury capabilities/infrastructure data spreadsheet. She will forward this to Dr. Gupta.
3) Stephen Bjarnason will compile the notes from this meeting and send the draft to Dr. Gupta.

E.11 ATTENDING LIST OF NATIONS

Canada
Germany
Netherlands
Norway
Sweden
United Kingdom
United States

E.12 APPENDICES

E1 – HFM-234 May 2014 Meeting Final Revised Agenda.

E2 – HFM-234 Technical Team Members (as of 21 May 2014).

E3 – HFM-234 Draft Guidelines for Required Blast Exposure Characteristics.

Appendix E1: HFM-234 MAY 2014 MEETING
FINAL REVISED AGENDA

Wednesday 21 May, 2014		
0730	Meet at hotels, leave Medicine Hat	
0815	Meet at CFB Suffield, issuance of security passes	
0830	Welcome	Mr. Bjarnason
	Individual Introductions	Technical Team Members (TM)
	Administrative announcements	Mr. Bjarnason
0900	Creating Blast Exposures in the Lab #1	Dr. Risling
0945	Creating Blast Exposures in the Lab #2	Mr. Philippens
1030	Break	
1045	Creating Blast Exposures in the Lab #3	Dr. Stuhmiller
1130	Creating Blast Exposures in the Lab #4	Mr. Ritzel
1215	Lunch – Officer's mess	
1300	Creating Blast Exposures in the Lab #5	Dr. Lee
1345	Creating Blast Exposures in the Lab #6	Mr. Josey
1430	Creating Blast Exposures in the Lab #7	Mr. Ouellet
1515	Break	
1530	Discussion	All
1730	Close out for day	
1740	Return to Medicine Hat	

Thursday 22 May 2014		
0830	Tour of B19 (Small Tube); Large Blast Tube	TM
1200	Lunch – Officer's Mess	
1300	Parallel Sessions:	
	Working group on Dictionary of Terms*	Dr. Cernak, Mr. Philippens, Dr. Kirkman
	Epidemiology of Blast – Update	All others
	Next meeting – Tallinn, Estonia; 7 – 9 October 2014	Dr. Gupta
1500	Break	

Thursday 22 May 2014		
1515	Status Update: Blast Injury Dictionary of Terms	Dr. Cernak
1600	Guidelines development discussions	All
1650	Closing Remarks	Mr. Leggieri
1700	Return to Medicine Hat	
1830	Dinner	

* The working group may join the other group any time they are done.

Appendix E2: HFM-234 TECHNICAL TEAM MEMBERS (AS OF 21 MAY 2014)

Name	Nation	Email
Mr. Michael Leggieri (Chair)	United States	michael.j.leggieri.civ@mail.mil
Maj Dr. Dan Bieler	Germany	dr.dan.bieler@t-online.de
Mr. Stephen Bjarnason	Canada	stephen.bjarnason@drdc-rddc.gc.ca
Dr. Ibolja Cernak	United States	cernak@ualberta.ca
LtCol Dr. Axel Franke	Germany	axel1franke@bundeswehr.org
Dr. Raj Gupta	United States	raj.k.gupta.civ@mail.mil
Dr. Emrys Kirkman	United Kingdom	ekirkman@dstl.gov.uk
Dr. Lucie Martineau	Canada	lucie.martineau@drdc-rddc.gc.ca
Dr. Hans Orru	Estonia	hans.orru@ut.ee
Mr. Simon Ouellet	Canada	simon.ouellet@drdc-rddc.gc.ca
Mr. Mat Philippens	Netherlands	mat.philippens@tno.nl
Dr. Marten Risling	Sweden	marten.risling@ki.se
MC Jean-Claude Sarron	France	jean-claude.sarron@intradef.gouv.fr
Mr. Stian Skriudalen	Norway	stian.skriudalen@ffi.no
Mr. Jan Arild Teland	Norway	jan.teland@ffi.no
Dr. Sarah Watts	United Kingdom	sawatts1@dstl.gov.uk
Maj Dr. Arnulf Willms	Germany	arnulfwillms@gmx.de

Appendix E3: HFM-234 DRAFT GUIDELINES FOR REQUIRED BLAST EXPOSURE CHARACTERISTICS

The following guidelines are intended to provide blast injury research laboratories with a fundamental set of characteristics that need to be collected and described when generating blast pressure waves. It is not the intention to prescribe how to create the blast pressure waves but to provide an awareness of what needs to be taken into account and measured when creating blast exposures. Following these guidelines and reporting the exposure conditions in a consistent manner allows for reliable comparisons to be made between studies being reported regardless of the laboratory.

It is the intention of HFM-234 (RTG) that these guidelines be used in concert with the 'Blast Injury Dictionary' being developed by the group. The Guidelines and the Dictionary will be further refined as both are used to guide research methods and reporting in the field of experimental blast injury research.

EA3.1 RESEARCH RATIONALE

1) Goal of the experiment.

2) Hypothesis to be tested.

3) Describe how experiment answers the hypothesis.

4) Specify if and how experiment relates to real world operational conditions; explain why the exposure level was chosen.

EA3.2 BLAST EXPOSURE CHARACTERISTICS

1) Specify blast simulation method.

2) Specify sensor and data acquisition, make/model, type, sample frequency, filtering, etc.

3) Fully characterize pressure at target location.

4) Highly recommended to do the same at set distances before and after the target location.

5) Specify the reproducibility of the exposure condition, number of shots, and variation of the range of the blast parameters.

6) Include other structures in the shockwave field in the blast characterization.

7) Ambient pressure.

8) Overpressures – underpressure relative to ambient:

   a) $P_{stagnation}(t) = P_{static}(t) + P_{dynamic}(t)$.

   b) $P_{stagnation} == P_{pitot} == P_{total.}$

   't' interval should cover full exposure including reflected shockwaves, specifically for biological experiments.

c) Maximum values for all three pressures.

d) Describe method for peak determination.

e) Specify method for positive/negative phase determination.

f) Duration of positive phase.

g) Duration of negative phase.

9) Provide impulse of positive phase.

EA3.3 TARGET EXPOSURE CHARACTERIZATION

1) Describe the target in more technical detail: e.g. surrogate, animal, pmhs, cellular material, object:
   a) Detailed documentation of biological specimen is required with respect to bio-physiological/chemical preconditioning. Refer to Annex J, Section J.3.
2) Position/orientation of target.
3) Geometry.
4) Mounting of the target, especially for biological specimens.
5) Measurable exposure related responses:
   a) Motion:
      i) Position (t);
      ii) Velocity (t); and
      iii) Acceleration (t).
   b) Surrounding pressure.
   c) Reflected pressure.
   d) Strain.
   e) Internal pressures and strains.
   f) Loads (forces and moments) applied from target to mounting.

Annex F − GUIDELINES FOR REPRODUCING BLAST EXPOSURES IN THE LABORATORY

F.1 INTRODUCTION

Discussions at a NATO Human Factors and Medicine (HFM) Symposium (SYM) HFM-207 revealed the importance of a systematic approach to understanding blast injuries much like the well-established approach used to solve the classical toxicology problem where the etiology of the injury requires an understanding of the dose, mechanism of delivery of the dosage, and dose-response endpoints. Also recognized was the pressing need for a multidisciplinary approach to addressing non-penetrating blast injuries to the brain that result in a host of symptoms with vague etiology. In addition, the Technical Evaluation Report HFM-207, "A Survey of Blast Injuries across the Full Landscape of Military Science" [5], emphasized the continued multinational exchanges of scientific and technical advances to respond to blast threat and blast injuries. The first recommendation identified a future need for a recurring technical exchange venue on blast injury and its mitigation to address advances in medicine and personal protection and their synergy. The second recommendation highlighted the need to explore the concept of "the Toxicology of Blast Injury" and suggested to focus on several difficult problems including:

a) Relevancy and commonality of animal models.

b) Common dose-response methods.

c) Route of exposure methods.

d) Computational Models (blast, physiology, biochemical, toxicological, etc.).

e) Dose regimens to mimic/replicate human medical endpoints (spectrum of surgical trauma to mild traumatic brain injury).

f) Methods for translational research leading to medical products and/or physical protection products.

To address the above recommendation and to develop a specific NATO activity devoted to the toxicology of blast exposure, a proposal titled "Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods and Standards" was approved which resulted in the establishment of a NATO HFM Research Task Group (RTG) HFM-234 with the following deliverables [2]:

- Guidelines for Conducting Epidemiological Studies of Blast Injury.
- Guidelines for Reproducing Blast Exposures in the Laboratory.
- Guidelines for Using Animal Models in s Blast Injury Research.
- Dictionary of Blast Injury Terms.
- Final report on HFM-234 (RTG) activities.

These guidelines are intended to provide blast injury research laboratories with a fundamental set of characteristics that need to be collected and described when generating blast pressure waves. It is not the intention to prescribe how to create the blast pressure waves but to provide an awareness of what needs to be taken into account, measured, and updated when creating blast exposures. Following the guidelines of this document and reporting the exposure conditions in a consistent manner allows for reliable comparisons to be made between studies being reported regardless of the laboratory setting. Laboratory set-ups can range from

shock or blast tubes to free-field experimentation; and research areas may include, but are not limited to: theoretical blast physics, protection, and biomedical injury. Clearly stated, the objectives of this document are:

1) To raise awareness with regards to the complexities and pitfalls of blast injury research.
2) To standardize and promote good practices.
3) To help the community to generate valid and comparable results.
4) To increase the quality of publications in this field of research.

It is the intention of HFM-234 (RTG) that these guidelines be used in concert with the companion comprehensive "Dictionary of Blast Injury Research Terms" developed by the NATO HFM-234 (RTG). These guidelines and the Dictionary can be used in conjunction to guide research methods and reporting in the field of experimental blast injury research.

F.2 BACKGROUND

These guidelines were developed in response to the considerable variability and reporting of methodologies used to create blast exposure. This has resulted in an inability to compare results and conclusions generated by different research institutes engaged in blast injury research. Significant variability exists in the methodologies used by different groups to create the blast pressure wave (e.g., shock tubes; target inside versus outside of tube; advanced blast simulators; field tests). Often there is a lack of information reported in publications that does not allow for a complete understanding of the experimental conditions. A significant portion of blast injury research is focussed on neurotrauma and the mild Traumatic Brain Injury (mTBI) research community is multi-disciplinary in nature with a good portion of the community not necessarily having expertise in blast physics/engineering. Not fully understanding and characterizing the exposure metrics has resulted in a detrimental effect on developing evidence-based solutions for problems such as blast-induced mTBI.

F.3 REPRODUCING BLAST EXPOSURE AND CONDUCTING BLAST EXPERIMENTS

It is imperative that there is an understanding of actual operational blast exposures in order to simulate such exposures in the laboratory especially for reproducing clinically relevant injury patterns.

Generating blast pressure waves can be achieved using different devices and/or methodologies. A common device in many institutions is a shock tube using compressed gas in the driver section and a frangible membrane that upon bursting sends the pressure wave down the tube. Similar but using a different driver is a blast tube that uses an explosive charge to generate the pressure wave. Field testing requires the use of an open area and an explosive charge to generate the pressure wave. Each method of generating pressure waves has advantages and limitations. Tubes suffer from exposure artefacts such as rarefaction from tube end, jet effects, and secondary pressure waves from the driver section being generated that are not observed in a typical field explosion. The advantage to using tubes is that several experimental runs can be made during a day and it is possible to have a high level of reproducibility between runs. Field testing has the advantage that it accurately mimics an open explosion but is limited by: limited runs per day, an increased number of factors influencing variability between runs, and the requirement for a field safety system. These are only examples of advantages and limitations to the exposure systems currently used. Other systems are used for blast injury but these are not being considered here as an exposure to blast requires the generation, at minimum, of a primary shock pressure wave that passes through the test subject. The advantages and limitations must be considered when choosing which system to use for blast injury research.

The consequences of not understanding the limitations and physics/engineering of the different methods has the potential to cause significant errors in interpretation of measured endpoints. In a classical toxicological sense, if the 'dose' is not well characterized then it is difficult to properly understand the 'response' of the target/test system. Not understanding or accounting for the various artefacts created by a shock tube can lead to misinterpretation of the 'true' exposure a test subject receives and thus the response being measured.

This section will provide information on the above referenced systems and the influence of their principal parameters.

F.3.1 Shock/Blast Tubes

A shock tube in its simplest form is an apparatus used to generate a shock wave for testing purposes. Shock tubes allow for scaled experiments, have quick turnaround times, and can improve repeatability over free-field blast experiments. They have a lower operating cost and smaller footprint compared to free-field experiments. Shock tubes can also be used as platforms to generate blast waves without the use of explosives.

A shock tube is essentially a tube with two sections separated by a frangible diaphragm: the driver section and the driven section. The driver section is charged with a high pressure gas and when the diaphragm is ruptured this high pressure gas rushes into the driven section, developing a shock wave (Figure F-1).

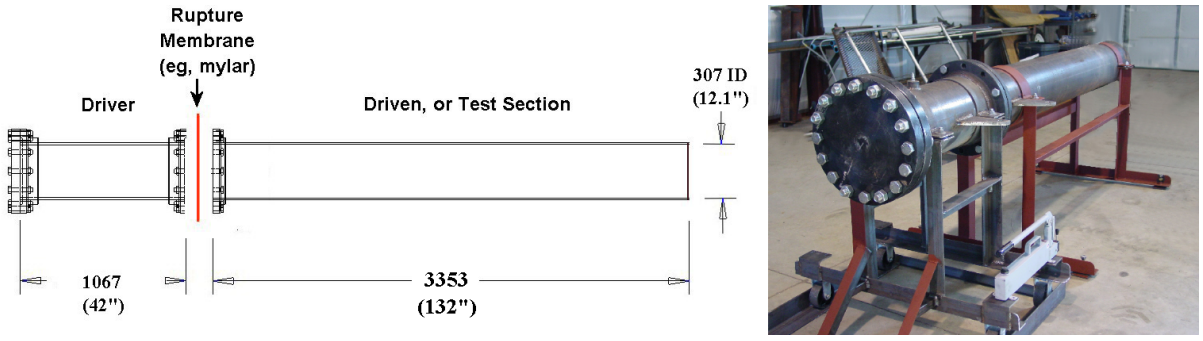


Figure F-1: Schematic of a Gas Driven Shock Tube.

The high pressure gas can be achieved in the driver by flowing compressed gas from a high pressure vessel or in the case of a blast tube by igniting a combustible gas mixture or by detonating explosives. Single or multiple drivers can be used depending on whether single or multiple shock waves are desired.

For the purposes of investigating injury, the target should be placed inside of the driven section, at a location where the flow is fully developed. The range of achievable wave profiles and positive phase durations are dependent on the design of the shock tube. Tubes can be designed to test nuclear type blasts which consist of long durations or small anti-personnel blasts that have short durations (Figure F-2). It is recommended that a particular threat be identified and the shock tube be designed or tailored to the threat of interest.

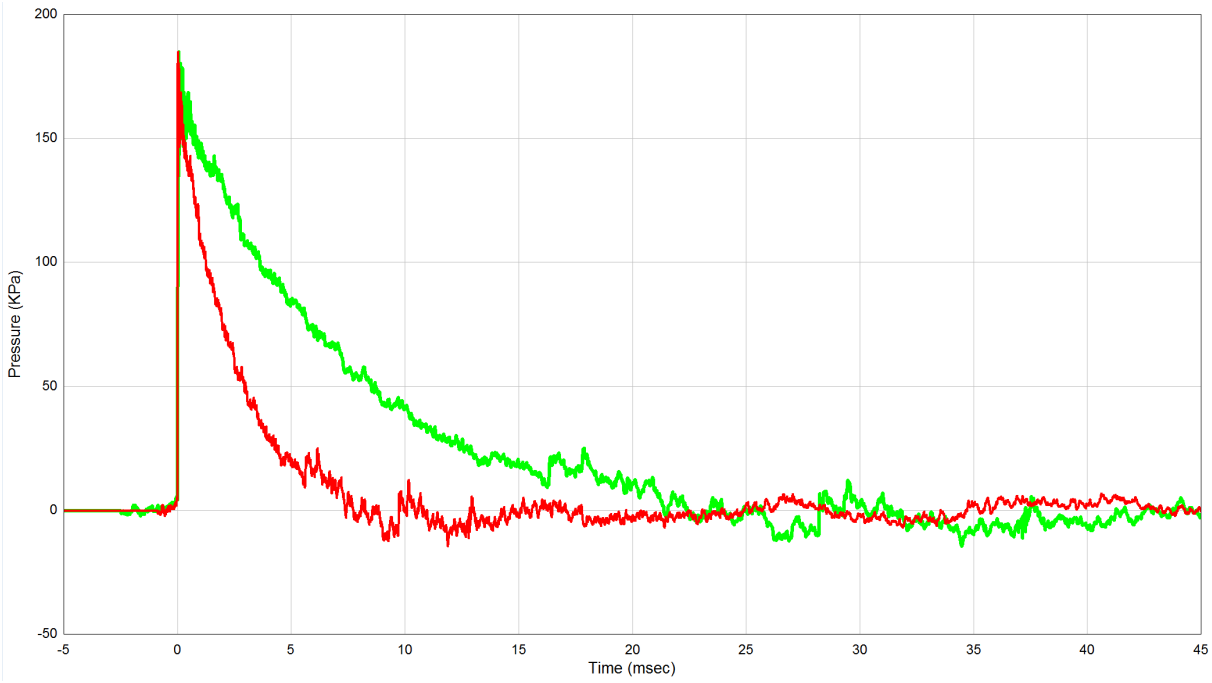
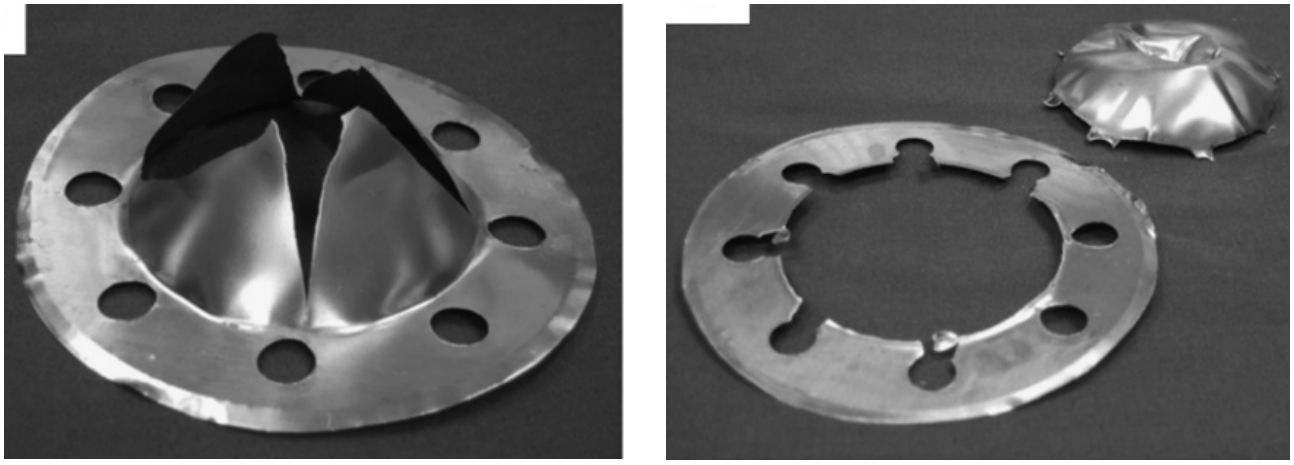


Figure F-2: Different Wave Profile Equating to Very Different Exposure Conditions.

There are a number of potential issues when using shock tubes to investigate mTBI. Below is a sample of some potential issues arising from a lack of control over specific test parameters or simply from a lack of understanding of shock/blast physics.

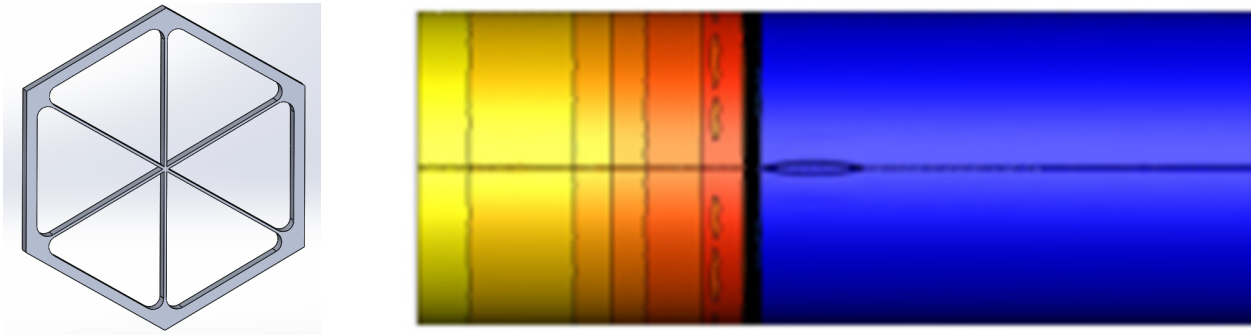
F.3.1.1 Diaphragm

Diaphragms are generally used to separate the high pressure driver section from the driven section. The diaphragm material and structure can influence the exposure experienced by the test subject. Prior to failing, diaphragms generally experience a bulging distortion effect followed by a failure allowing the high pressure gas to flow downstream. The type of failure experienced by the diaphragm can be a petalling type failure or a fragmentation rupture of the diaphragm. In the case of a petalling failure, the orifice created by the petalling diaphragm needs to be sufficiently large such that the flow is not restricted as it escapes the driver. If the orifice is not large enough then a jetting-type behaviour of the driver will result and the downstream shock will develop into an unwanted shock wave profile caused by flow separation. In the case of a fragmentation type failure, the orifice created by the rupture of the diaphragm can also cause a jetting effect if the orifice produced is not large enough. Diaphragm material should be selected to maximize the designed burst orifice (Figure F-3). Single, thick diaphragm materials will generally reduce the size of the orifice and produce larger fragments as compared to a diaphragm package consisting of multiple thin sheets. Fragments need to be controlled in such a way that they do not travel downstream and cause issues as they impact the test subject. The fragments may have high velocities as they travel downstream; even low weight fragments can impart a significant amount of energy. Materials should be selected such that large fragments are reduced. The design of the shock tube should incorporate the behaviour of the diaphragm; this should include the projected orifice size created by the failed diaphragm and a fragmentation mitigation device positioned upstream of the test section (Figure F-4). In general a complete fracture of the diaphragm is desired allowing the full cross sectional area to be used to allow the gas to escape from the driver to the driven section.



(a) (b)

Figure F-3: Examples of Petalling or Fragmenting Diaphragms Showing (a) Flow-Restricting Orifice and (b) Complete Opening [6].



(a) (b)

Figure F-4: Example of Fragmentation Mitigation Devices – (a) Mesh Insert and (b) Airfoil Deflection Device.

Diaphragms can be ruptured either mechanically through a piston and sting type approach or can be ruptured by a catastrophic failure when the driver pressure exceeds the strength of the diaphragm material. The driver pressure should be monitored and the failure of the diaphragm or diaphragm burst pressure must be predetermined and be used to control the downstream pressure.

A high level of repeatability is required to ensure that multiple tests are conducted at the same blast exposures. One way to enhance repeatability is by obtaining a repeatable diaphragm burst behaviour pattern and driver pressure.

F.3.1.2 Exposure Characteristics

Typical static pressure measurements measured on the side of the shock tube alone (Figure F-5 – red line), do not provide the necessary insights to understand the loading on the subject. For example the incident

pressure[1] inside the tube may closely match the incident pressure at the open end of the tube but the loading experienced by the test subject may be vastly different. The flow field developed in the shock tube can be represented by knowing the density, velocity and pressure of the blast wave. To accurately simulate a blast wave, the flow field must match the free-field conditions. Matching the incident or side-on pressure gauge profile provides only partial insight into the actual flow field. Matching the incident pressure between the shock tube and free-field blast in no way guarantees that the shock tube is producing a flow field equivalent to a free field-blast (Figure F-6). Although it is impractical to directly measure density and flow velocity the dynamic pressure can be obtain through the use of a pitot probe (Figure F-5 – blue line).

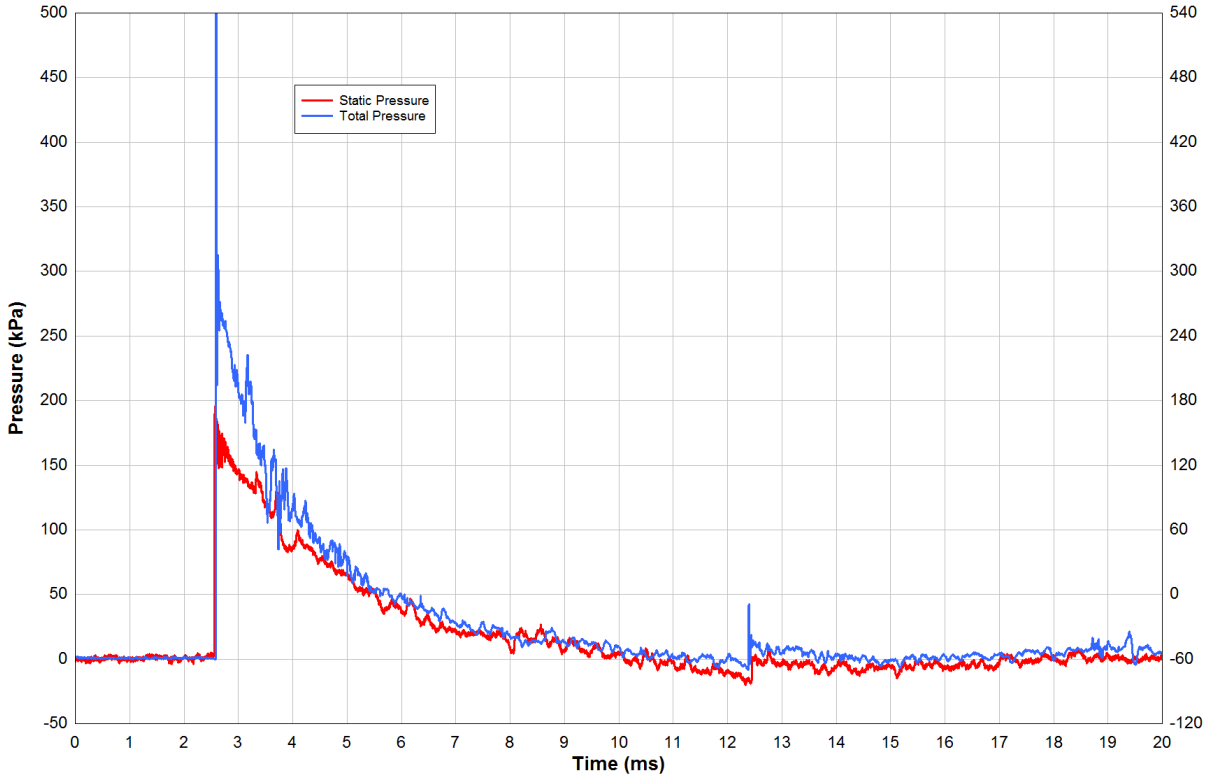


Figure F-5: Characterization of the Exposure Using a Wall-Mounted Incident Pressure Gauge and a Pitot Probe to Measure Total Pressure.

[1] Incident Pressure/Side-on Pressure: The term pressure here is used to describe the blast overpressure that may be recorded in free space, such its recording does not perturb the blast field. This is normally approximated to in explosive trials by the use of streamlined pressure gauges. [1]

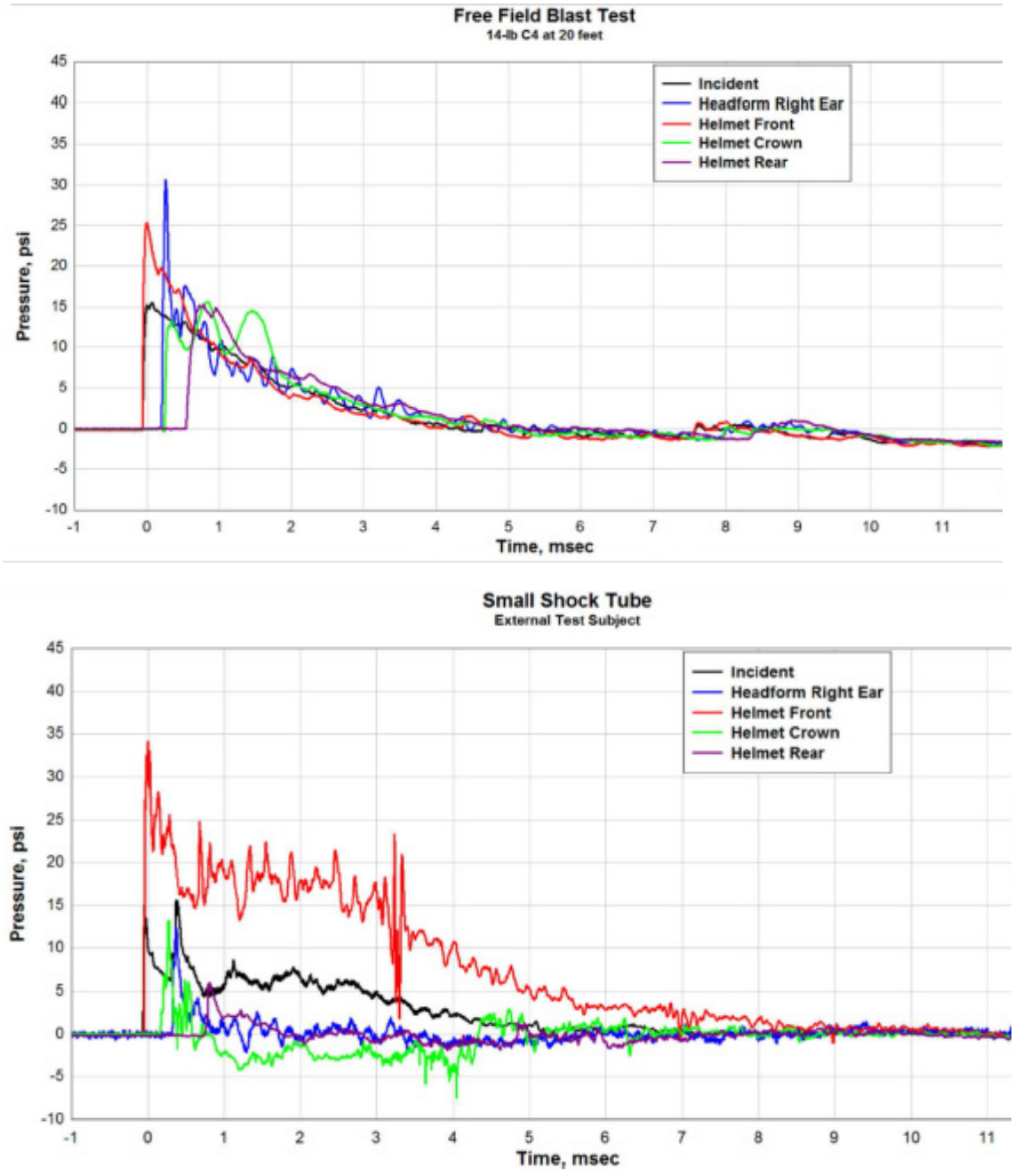


Figure F-6: Examples of Matching Incident Pressure Profile with Very Different Flow Field Characteristics (Different Dynamic Pressure Profile).

The pitot probe captures the density and velocity and measures the total pressure of the flow field. Knowing the total pressure and incident pressure, the dynamic pressure can be obtained. The dynamic pressure cannot be overlooked/ignored and may be a source of significant loading, especially if the test subject is positioned outside the blast tube.

F.3.1.3 Exposure Characteristics Scaling

In the case of mTBI, it is currently unclear what type of scaling law could make a correlation between the exposures of a rodent to that of a human. Some have speculated that scaling should be based on duration, whereas others have proposed that peak pressure be scaled or even both [4]. It is premature to conclude that animals with low body mass should be subjected to short durations and heavier animals should be subjected to longer durations. Until this issue is resolved, testing should be conducted over a range of durations.

F.3.1.4 Tube Diameter versus Target Dimensions

The diameter of the shock tube will limit the size and geometry of the test subject that can be used inside the tube. A rule of thumb is that the test subject be limited to block no more than 10% of the cross sectional area of the tube and Needham et al. [4] suggest 5% or less. Utilizing larger test subjects, will restrict the flow and cause unwanted loading. The end result will not accurately represent the flow field; the blockage may cause large reflections and wave perturbations (Ref. [4], Figure F-7).

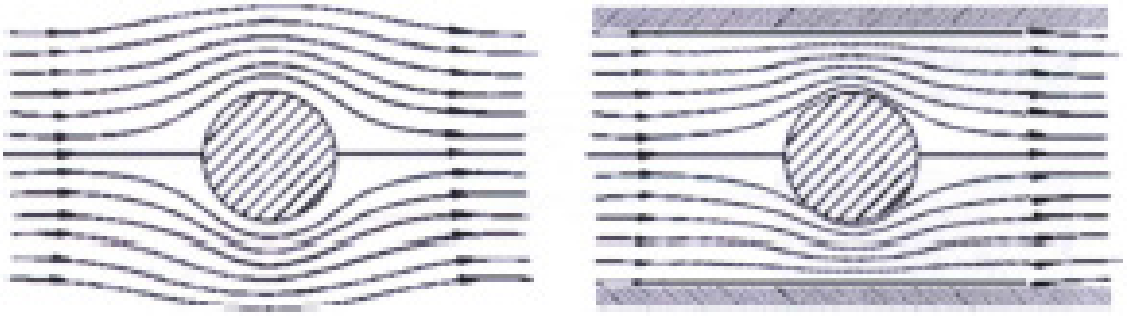


Figure F-7: Simulation Showing How Flow Field can be Perturbed by Blocking a Large Portion of the Tube with the Test Subject (from Dyn-FX Consulting Ltd.).

F.3.1.5 Position of Target

Test subjects should be placed inside the shock tube at all times. Subjects placed outside of the tube are subject to severe dynamic loads and wave perturbations that are not observed in a free-field blast environment. Although certain testing can be performed outside of the shock tube, this scenario is not appropriate for investigating injury, as this type of testing does not represent the flow field of a free-field blast. Similar to a wind tunnel, the test article must be placed inside the flow field and not subject to boundary condition reverberations (Figure F-8).

Inherent problems exist when conducting testing outside of an open ended tube or testing too close to the end of the tube (see Ref. [4] for a detailed discussion.) As the shockwave travels down and meets the open end of the tube, a rarefaction wave occurs, the outflow velocity is increased and a shock travels up the tube. This shock can travel back up the tube and impact the test subject from the opposite direction from the initial shock (Figure F-9).

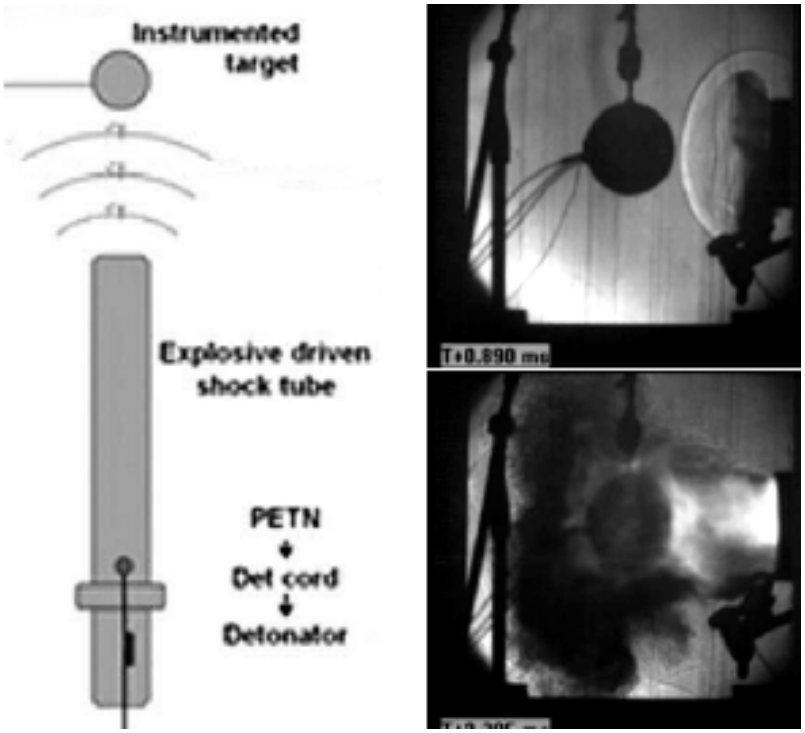


Figure F-8: Specimen Outside the Tube Experiencing a Highly Disturbed Flow Field.

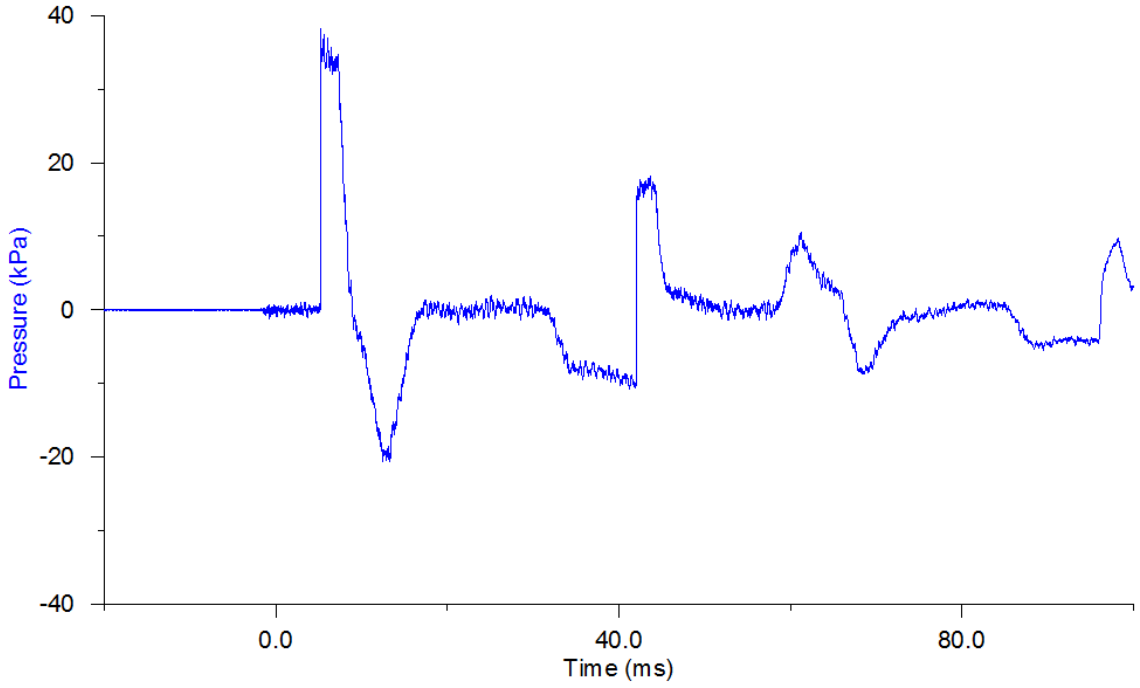


Figure F-9: Pressure Trace Showing Specimen Being "Hit" by Rarefaction Wave.

F.3.1.6 Gas/Combustion Product

When animal testing is used, the driver gas or combustion products (in the case of a combustible driver) should be restricted from reaching the test subject so as not to complicate the insult experienced by the test subject. The contact surface must be determined to ensure it does not reach the test subject.

F.3.1.7 Exposure Monitoring

Measurements should be conducted with side-on pressure gauges along the length of the tube and surrounding the test subject. Gauges can be located throughout the tube, but it is especially important to have gauges located upstream and downstream of the test section and in an area of the tube where the flow is deemed to be fully developed. A pitot probe gauge capable of measuring total pressure should be used to obtain the dynamic pressure. Incident pressure gauges are easily placed along the sidewall of the tube. Pitot probes need to be placed directly in the flow field. The pitot probe shall be made aerodynamic and small enough such that it minimizes flow disruption. All measurements should be compared to numerical and analytical models to ensure the shock tube is producing representative shock waves.

Measurements in the center of the tube should be conducted to characterise the boundary layer effect that may be present. Ideally the pressure experienced in the cross sectional center of the tube should match that experienced at the sidewall. Understanding the size of the boundary layer will aid in determining the relevant position for the test subject.

The raw data from the gauges needs to be filtered or interpreted as, very often, the signal can contain artefacts; the peak signal is the result of an artefact and likely does not represent the actual peak of the pressure trace.

Instrumentation used inside the shock tube should be regularly calibrated and compared to standard tests conducted throughout the lifetime of the tube. This will ensure that any deviations are captured and investigated. They can also be used as a baseline for upgrades and can help identify any drift issues.

The data acquisition system should be sampled at an appropriate rate that captures the peak pressure, and gauges should be used that are capable of reacting fast enough and are appropriate for shock wave measurements.

F.3.1.8 Numerical Modelling

Instrumentation and computational modelling should be used to characterize the blast exposure characteristics.

During the development of the tube, numerical modeling should be conducted to provide ideal operating characteristics that will allow the flow to be fully simulated and visualized. The visualization through a computer model provides insight and data that is not possible through experiments alone.

F.3.1.9 Shock Visualisation

If possible, a clear test section or viewing and lighting ports should be incorporated into the tube. This allows for the visualization of the shock wave and response of the test subject through the use of high speed video.

F.3.2 Enhanced Shock Tube

A shock tube is a general instrument that can be used for a number of applications, however, an enhanced shock tube is better suited for the purpose of investigating blast injury. This type of shock tube resolves a number of issues seen in conventional shock tubes and is tailored to produce Friedlander type blast waves.

A basic shock tube will not accurately reproduce the flow conditions and wave dynamics generated from a free field explosive. In certain circumstances this can be important in reproducing clinically relevant injuries. In these situations, the shock tube waveform needs to be tailored in order to represent a free-field blast wave. This wave tailoring and the ability to reproduce gas dynamics are inherent in an enhanced shock tube such as the Advanced Blast Simulator (ABS) used at Defence Research and Development Canada (DRDC) – Suffield Research Centre. The basic principle of the ABS is that it provides a means of wave tailoring and represents the actual expansion from an idealized explosive. This is generally done through the geometry of the tube.

F.3.2.1 Design

The DRDC ABS has four sections: the driver, expansion section, driven section, and end wave eliminator. The driver section operates similarly to that of the standard shock tube; the geometry of the ABS is made in such a way that the driver gas is allowed to expand appropriately which is then tailored by the transition section (Figure F-10 and Figure F-11). The range of achievable wave profiles is directly related to the length of the tube, the driver geometry and the charged pressure. A single tube may be adapted to test a range of peak overpressure and positive phase durations by modifying the driver pressure and moving the test subject to different locations within the tube. The desired pressure and positive phase range for testing of the tube should be determined in the design phase of the tube.

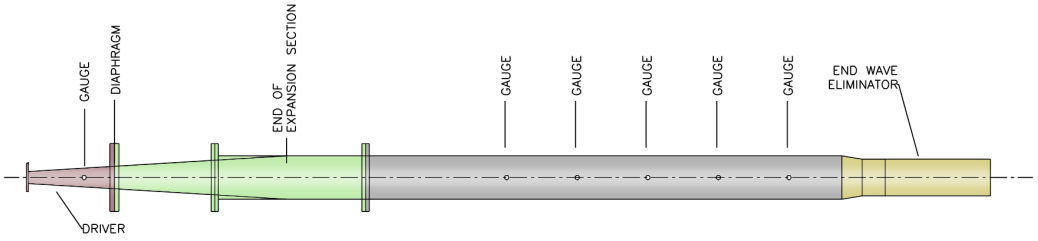


Figure F-10: Schematic and Picture of an Advanced Blast Simulator.

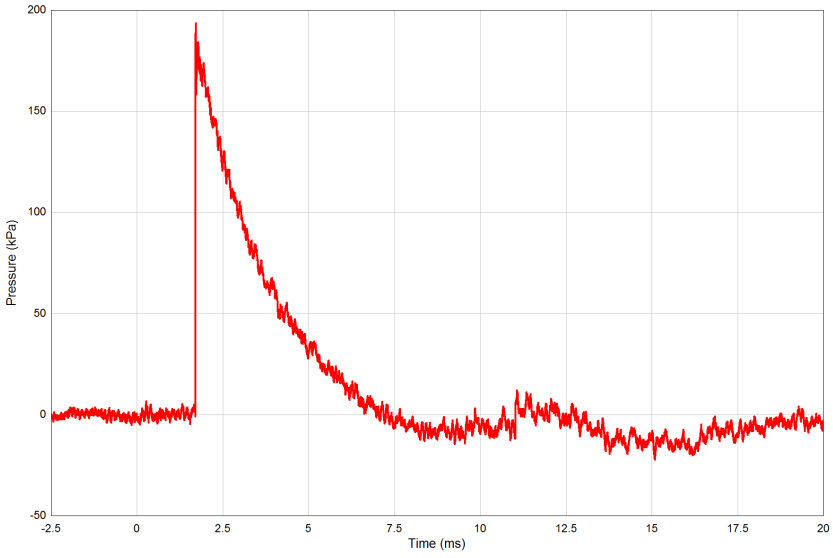


Figure F-11: Example of Achievable Wave Profile with an Advanced Blast Simulator.

F.3.2.2 Driver Section

In general, the driver volume controls duration. It is best to know a range of durations, based upon a particular threat. However, the wave tailoring shape of the driver must be maintained to allow for a properly developed flow field. Multiple drivers can be utilized on the same tube to produce different blast durations. The DRDC ABS has a shaped driver section, of known volume, that allows for wave shaping into the expansion section (see Figure F-10), which further tailors the pressure wave as it gets to the driven section of the tube.

F.3.2.3 Driver Gas

The DRDC ABS can be driven with compressed gas, combustible gases, or explosives. If compressed gas is used, it is recommended that a low molecular weight gas be used, i.e. Helium. The low molecular weight gases produce higher peak pressures, short durations, and a much less prominent negative phase. Other gases can be used, but they will not produce an idealistic shock wave shape; i.e. less representative of an actual blast.

F.3.2.4 End Wave Eliminator

If rarefaction and reflected waves are not wanted, then an enhanced shock tube will require the use of some type of apparatus at the end of the tube to eliminate these types of waves. The DRDC ABS uses a mechanism that allows controlled venting of the blast wave for this purpose (Figure F-12). This device is tuned for each shock wave, as higher shock waves will require a different venting than less powerful waves. The controlled venting allows for the virtual elimination of secondary waves traveling back up the tube and reaching the test section (Figure F-13). Alternatively a very long tube with the test subject located sufficiently far away from the end of the tube may provide similar results. This may prove impractical due to the length requirements.

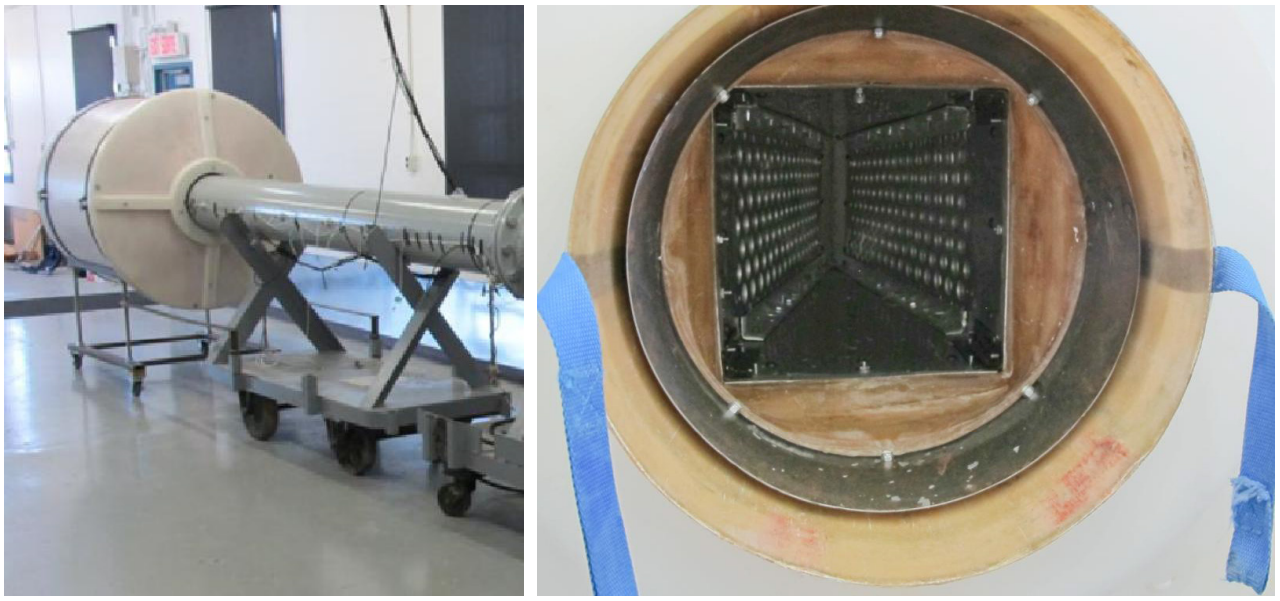


Figure F-12: Example of an End Wave Eliminator.

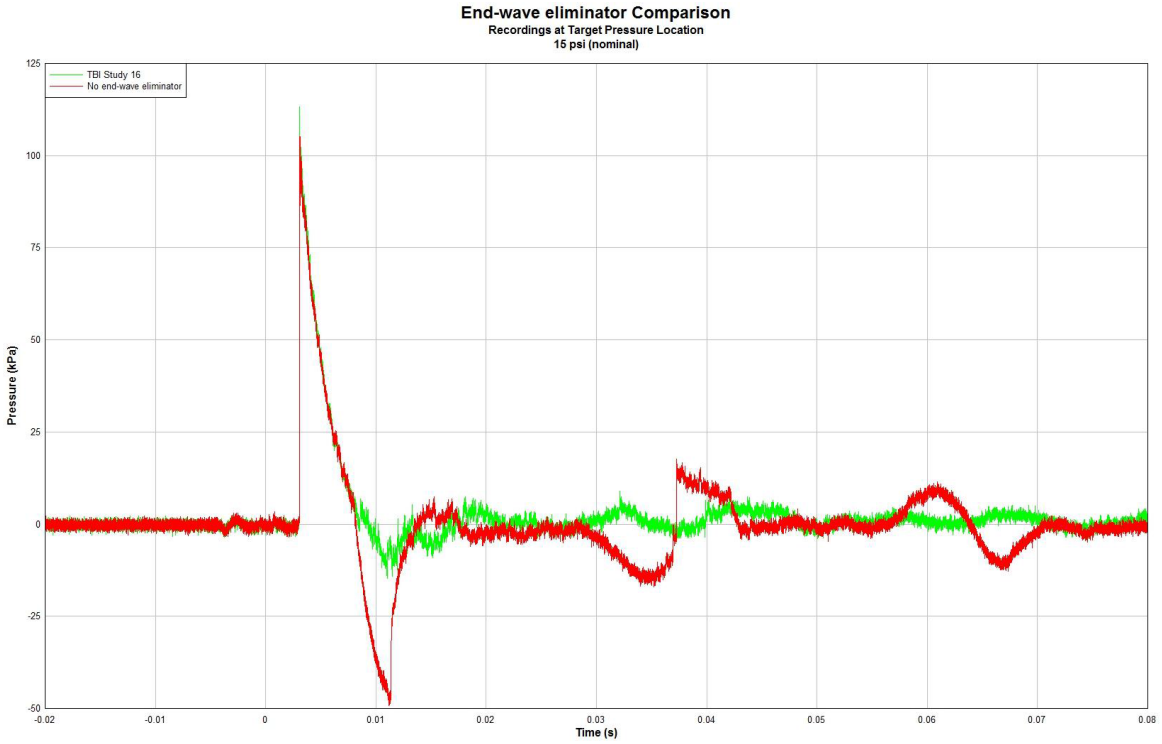


Figure F-13: Example Traces Without (Red) and With (Green) End Wave Eliminator.

F.3.3 Field Testing

Field testing is often seen as the closest representation of an operational blast scenario. However, conducting a full-scale field blast trial with an operationally relevant quantity of explosive does not guarantee, by itself, that target loading conditions are repeatable and suitable. In the current context, field blast tests are no different than laboratory experiments with regards to the level of control that is necessary over the generated loading conditions. The quantity of parameters which can have an effect on the blast 'dose' experienced by a target is probably the highest in this type of testing. Nevertheless, the level of repeatability achievable in field testing can be sufficient when experiments are carefully executed, and when appropriate equipment is used. The following sub-sections attempt to provide a comprehensive list of parameters that should be carefully controlled when conducting full scale, open field blast experiments.

F.3.3.1 The Explosive Charge

The first inherent source of variation in field experiments often comes from the explosive charge itself. The choice of explosive material may be driven by past experience, availability, or knowledge of explosive material characteristics. In all cases, the experimentalist should know what level of repeatability should be expected from the selected energetic material. The following list highlights ways to limit variability due to the explosive charge:

- The first way of reducing the potential for variability in a series of trials is to use explosive from a similar production batch. Variation between batches can exist and is hard to characterize or predict.
- Charge weighing should be performed rigorously.

- Charge preparation is critical to obtain a consistent detonation process and minimize anomalies in the near- and mid-field regime. Moulding/shaping methods for the charge should be reproducible as much as possible. Methods where moulding pressure can be tightly controlled are preferred.
- Some solid explosives will require a confinement material to maintain the required shape. Variations in that confinement, its composition, layering and thickness can induce undesired variations in the blast wave and affect uniformity.
- Charge geometry is crucial as this will affect blast wave uniformity in, or at the limit of, the near-field regime. Blast wave from cylindrical charges in particular will require a finite distance to reach uniformity and may produce a different interaction with the ground when detonated at a low Height of Burst (HoB).
- The suspension or holding method should also be reproducible and interfere with the charge as little as possible. Charges are typically either suspended with thin ropes or netting or simply put on a supporting friable structure. In both cases, the charge supporting structure can disturb the blast flow field nearby as they are destroyed or pulverized.
- Finally, detonator type and placement play a role in the detonation process and can therefore induce variability. Type and placement should not be varied within test series.

F.3.3.2 The Physical Environment

The nature of the physical environment may be categorized as free-field or complex[2]. In both cases, and regardless of the intent of the experiment, it is critical to understand and control the effects that surrounding obstacles, reflecting surfaces, and other experimental set-ups can have on the blast wave flow field. This section provided background information on the physical parameters that should be considered when using field blast trials for blast injury research.

When carrying out open-field trials, a very common test configuration is to have the explosive charge at the center of a circular path on which targets and sensors are deployed. Exposure characteristics are then varied by increasing or decreasing the circle radius and by modifying the nature, size or HoB of the explosive charge.

It is often assumed that in such conditions, targets will be exposed to a relatively unperturbed blast wave propagating outward from the blast source in a unique direction. However, shock reflections may still occur from the different test set-ups dispersed around the blast source. Targets and sensors positioned on a similar or different radius, whether they are side by side or facing each other from both sides of the charge can generate shock reflections which have the potential to influence the individual loading histories in terms of magnitude and direction.

Whether these reflections overlap the main loading phase, or occur later in the loading history, they should be carefully identified, characterized, and preferably, eliminated. While measurements taken from individual pressure transducers or from artificial physical models can be cropped to eliminate secondary loading from reflections, biological models cannot. When looking at pressure, force, or acceleration histories on a target, wave reflections may cause relatively sudden magnitude variation. However, they can also happen undetected when, for example, the direction of propagation is not aligned with the sensor reading direction. High-speed videography can help identify sources of reflections, but in general, the best practice is to understand and plan the test lay-out carefully to avoid them.

[2] Free Field Blasts: Said of an explosion or blast wave generated in an environment free or any reflecting surfaces such as the ground, walls, or nearby objects; Complex Blasts: A blast that does not conform to a Free-Field blast. [1]

When testing in an environment where a single or multiple reflecting surfaces are present (e.g., mimicking an urban-like environment or testing inside a room/chamber), understanding wave reflections throughout the event timeframe, their occurrence and timing, is even more critical since part of these reflections are desired while part of them may not be. When conducting such experiments, it is recommended to run experiments without targets to solely focus on characterizing the complex blast flow field. Advanced validated computational fluid dynamics models can also be very valuable tools to help perform this task.

F.3.3.3 The Blast Flow Regime

Notwithstanding the effect of the physical environment, the distance of the target to the explosive charge can play an important role on the degree of repeatability and uniformity of the loading conditions. Different blast flow regimes are usually defined with regards to the target distance relative to the blast fireball.

The near-field regime is typically defined within the radius or just on the edge of the fireball. Within that range, the medium is multi-phase (mix of air and detonation products) and the shock structure is likely to be very complex (more so if the charge geometry is not spherical). This is generally not the ideal regime to conduct controlled blast testing as the exposure risks vary greatly from test to test and can be more unpredictable. The blast energy is partitioned differently in this regime compared to regimes at higher standoff distances, with the kinetic energy of the detonation product playing an important role. As such, a target placed in that range may experience much stronger dynamic pressure than desired. Also, the instrumentation sensitivity to heat loads becomes an important factor and cannot be overlooked. It is generally recommended to avoid testing in the near-field, or fireball range, when the intention is to maximize repeatability.

The mid-field regime is defined between 1 radius and 10 radii of the fireball. This is the regime within which most full scale target field tests are done because it is practical in terms of space and test site, it is operationally relevant, and the blast dose is likely to be in the range of potential injury thresholds. However, testing just outside the fireball can still cause repeatability and predictability problems.

Blast wave anomalies are fairly common close to the boundary between near-field and mid-field regime. Raleigh-Taylor instabilities can occur at the interface between the detonation product and the surrounding air which can disrupt the uniformity of the blast wave and generate significant difference in the blast dose seen locally by a target. Jetting, a phenomena often caused by porosity or an “air-pocket” in the explosive charge, may create a similar effect where locally, the expanding shock is disturbed. These anomalies eventually disperse and attenuate as stand-off distance increases, and are typically not a problem in the far-field regime.

Shock curvature is also more important close-in and should be taken into consideration when monitoring, for example, the pressure field around a large target. Time of arrival of the blast wave at different locations around the target will change slightly compared to an ideal planar blast wave and, this alone, may influence target response, particularly if the target response is driven by the excitation of specific natural deformation modes, i.e. a dominant resonant frequency.

Also, close to the contact surface (boundary of the fireball), wave reflections may occur between it and the target, leading to more complex loading conditions which may not have a high degree of repeatability.

Another consideration is that targets in the mid-field regime will most probably experience multiple shock loading, as the ground reflection generated by an above-ground detonation, will still be separated from the main incident blast wave at the target location.

Sensors and wiring may still experience heat effects at the beginning of mid-field regime; adequate shielding should be used.

The far-field regime is defined for stand-off distances over 10 radii of the fireball. In this regime, the Mach stem and ground reflections are no longer an issue and the overpressure history is probably the closest to the idealized Friedlander curve. The shock curvature is low and at the scale of biological targets, it may be assumed to be planar (1D shock). This is the ideal regime to maximize repeatability but unfortunately, it is often impractical since peak overpressure levels may be too low for subtle injury studies. In addition, testing tens of meters away from the explosive charge can require big trial sites that are often not readily available.

F.3.3.4 The Charge Height of Burst (HoB)

During field testing, the incident air blast wave generated from an explosive charge detonated above the ground, inevitably interacts with the denser ground medium, to create a reflected blast wave. This up and outward travelling reflected wave will propagate in a compressed heated air medium and, since shock velocity increases with medium density, will have a higher velocity than the initial incident wave. The reflected wave can eventually catch up with the incident wave and create a "superposed" wave structure called the Mach stem.

An implication of this phenomenon is that, for the same weight of explosive, the exposure history at a specific location can vary greatly depending on the charge height of burst.

If the target falls within the Mach stem region, it may see a high single overpressure peak followed by a relatively uninterrupted decay. If the reflected wave is still catching up to the incident wave at its location, the target may see an initial overpressure peak, a partial decay followed by a second overpressure peak and decay. The two loading scenarios are very different and have unknown differential effects.

The directions of propagation of the incident wave, reflected wave, and Mach stem are different. This can have a significant influence on target response, more so on protected targets, where the wave propagation direction can make the difference between a shielded "entry" point and an exposed area.

If the experimentalist is not familiar with the wave propagation directions at the target location, it is recommended to perform preliminary tests with adequate videography in order to characterize these features, and ensure that the target will be oriented properly with regards to the desired exposure conditions.

By extension, target height is critical for the same reason. It should be adjusted to obtain the desired overpressure history with careful consideration of the directionality of the wave propagation.

HoB should not be varied between tests if the objective is to repeat similar blast exposure conditions.

F.3.3.5 Target Orientation

Target orientation with respect to the blast wave propagation direction should be carefully selected to represent the desired scenario. For example, if the scenario to be reproduced is the close detonation of a ground improvised explosive device, orientation should be chosen so that the blast wave strikes the target with a particular angle of incidence.

This orientation dictates the manner in which the blast wave reflects off and diffracts around the target. As such, it defines which part or surface of the target will experience, for example, a highly reflected pressure, which part will be only exposed to a grazing shock, and which part will be exposed to something in between (oblique shock

reflection). In other words, it defines the pressure field history around the target to create loading conditions that are unique to any blast wave–target configuration.

Biological structures, and ideally the physical models made to represent them, are sensitive to loading orientation. First, the global response of a target will vary with its orientation because the size of the exposed area changes the total magnitude of the force applied to the structure. For example, the human head hit from the side presents a larger area than when facing the blast wave. Conversely, the compliance of the neck is also different between an anterior-posterior flexion and for a lateral flexion, which can also change the resulting target global motion. Second, local structural responses also vary with loading orientation. For example, a structure like the human skull, with a complex geometry of varying thicknesses and composed of different bones, will have a range of different compliances. Such a structure might also even have different modal responses depending on the location of the excitation. Finally, pathways for the blast wave to propagate within a structure will change with orientation.

The target support should have all the necessary degree of freedom to allow for a precise control of the orientation. It should have the ability to secure the target in the appropriate position. Orientation should be measured based on a fixed reference point before every test and readjusted, if necessary, between tests. Consideration should be given to the movement of the target, which should be controlled as appropriate, with respect to the experimental question.

F.3.3.6 Target Support

Target support is an important consideration that must be addressed because it will affect the target response to the blast. Since all blast tests require that the target is supported, the manner in which the target is supported will depend upon the research question being addressed. For example, head models using a rigid neck or an overly stiff neck articulation may not capture an important aspect of the target response. Target support structure may vibrate or resonate when struck by a blast wave. These vibrations can be transmitted to the target itself. It is recommended to mount the target in such way that potential external vibration would be damped.

Additionally, the effect of the support structure on the blast flow should be considered, as it may cause artificial perturbations and generate undesired wave reflections. Ideally, the blast wave propagation around the target should be unaffected by the presence of the support frame. Numerical simulation can again be a valuable tool to analyze the effect of the support method and refine the design of the support structure.

F.3.3.7 Monitoring of Exposure

In the study of the effect of blast wave on a target, the magnitude of the target response needs to be correlated to some measure or description of the level of blast exposure.

A qualitative description of the severity of blast exposure is not sufficient to draw quantitative trends across different exposure levels and compare with other scenarios. Quantitative assessment of the blast wave itself, near the location of the target, or on the target, allows for a more straightforward and simple comparison across test scenarios and methods. However, if the targets are not identical, scaling issues must be considered [3].

Near-target monitoring of exposure can be fairly simple to do when running a true free-field blast test (relatively high standoff distance approaching ideal blast wave loading conditions), or a test with a single blast propagation direction. However, in more complex environments, where reflecting surfaces are close enough to affect the exposure conditions, monitoring is not straightforward as the target may experience waves coming from different orientations. It then becomes impossible to obtain a pure static or reflected pressure measurement.

Evaluating the true level of exposure and its directionality in such scenarios need to rely on a combination of experimental measurement and numerical simulations.

F.3.3.7.1 Free-Field Testing

In open free-field testing, the blast wave can be monitored by deploying a line array of static pressure gauges pointing toward the blast source. Ideally, one of the pressure gauges from the array is on the same radius as the target, as close as possible to it while making sure not to create any interference between the two set-ups. Each target should have a reference blast gauge associated to it and located nearby. When possible, it is recommended to use several blast gauges on the radius of interest, around the source, to obtain a direct evaluation of the uniformity of the blast wave and of the possible interference between gauges and target(s). Relying, for example, on a single gauge to measure the blast wave at a particular distance, and assuming that all targets around the source are exposed to the same overpressure levels, can generate significant variations in the blast dose-target response correlation.

For a free-field test, the blast exposure level may be defined using the collected static overpressure histories. Shock velocity derived from 2 successive pressure gauges, along with local air properties, will allow calculation of other quantities of interest such as dynamic and theoretical reflected pressure, through analytical correlations.

Different designs of gauges exist to measure static overpressure, but the general principle is the same. A pressure sensor is mounted with its sensitive element oriented perpendicular to the blast flow, in a profiled structure carefully oriented to avoid flow perturbation. Discs, profiled plates, and pencil gauges are of that type. Orientation of these gauges is critical and must be checked prior to every test. A few degrees of misalignment can induce undesired variabilities in the measurements.

Pitot probes are typically used to derive a dynamic pressure history through the measurement of the Pitot stagnation pressure (Total pressure). However, it is important to note that the correlation:

$$P_{tot} = P_s + P_d$$

where P_{tot} is total pressure, P_s static pressure, and P_d dynamic pressure, applies to steady incompressible flow condition, which is not the case of a blast wave. One must be careful when interpreting the absolute values of dynamic pressure obtain through this method.

F.3.3.7.2 Complex Blast Waves

The concepts of static and dynamic pressures lose their meaning in a scenario where blast reflections and reverberations are present. The presence of reflecting surfaces, such as walls and ground, will result in the generation of a reflected wave with different propagation directions. For example, a static pressure gauge which is carefully oriented with the initial incident blast wave may not be oriented parallel to the blast flow once reflections reach it. Hence, the gauge will not record a purely static pressure throughout the event, but rather reflected pressures from oblique or perpendicular waves.

In such conditions, numerical simulation can be really useful to characterise the blast field around a potential target and evaluate the intensity and propagation direction of the incident and reflected blast waves. Running experiments without the target, but with a suite of pressure gauges around the test site, and with varying orientation, may be very useful to understand the nature of the exposure and validate the numerical model. Once this is done, experiments can be performed with the target/phantom and a reduced amount of gauges. Pressure

measurements are still important to collect during each test, to assess the consistency and repeatability of the experiment.

A more complete way of monitoring the exposure of a target in a complex condition, is by monitoring the loading of the target itself by, for example, using an ensemble of surface mounted pressure sensors on the target. By having gauges all around the target, one should be able to deduce the origin and orientation of the different reflected waves. The downside of this method is that, using multiple gauges on the target may interfere with its natural response.

Because of small nuances, for example, in target positioning which are impossible to control with living targets, the predictions generated by models and phantoms will provide a useful estimate of the exposure experienced by the target but not necessarily the exact exposure. Such difficulties render comparison of results between studies using different targets more problematic, since target loading depends greatly on target geometry. Near target pressure measurements are still important to collect during each test.

F.3.3.8 Monitoring the Target

Animal and physical model experiments often use target-mounted sensors to monitor target response. The monitoring of a physical model target (e.g., phantom) response is mechanical in nature. The response of such targets is related to loading, motion, and deformation. Animal model target monitoring can be physiological and mechanical. Since the NATO HFM-234 (RTG) is also producing a guideline document on animal model experiments, this sub-section will focus on mechanical response monitoring as it is not specific to animal models [3].

Typical sensors for measuring mechanical responses include: accelerometers, external and internal pressure transducers, strain gauges, and force transducers. There are general considerations that apply to all types of sensors in the context of target blast response monitoring.

The potential influence of the sensor on the response of the target should be evaluated. First, the sensor or sensor suite should not restrain or modify the local or global motion of the target. Sensor wires should be routed away from the target in a way that does not hinder target movement. The added mass and inertia from the sensor should be negligible compared with the target native mass and moments of inertia.

In general, size of the sensors should be minimized as much as possible, and be an order of magnitude smaller than the target itself. Stress wave dynamics within the target structure, are likely an important aspect of biological responses. With regards to wave dynamics, sensors are by definition intrusive, because they consist of a foreign object that is not part of the structure being studied or represented. A large sensor will likely affect wave dynamics over a considerable region of the target, which is contradictory to the purpose of the monitoring. By choosing small enough sensors, the effects may be kept local and not change the overall response. Still, the effect of a sensor on its own reading should be evaluated. For example, a cylindrical pressure sensor oriented opposite to the wave propagation direction may not measure the pressure wave adequately since its body is "in the way" of the sensing diaphragm.

The use of small sensors may be limited by other requirements, such as, sensor capacity and overall robustness. Numerical modelling may be used to fully understand the effect of sensor size and placement on the stress wave dynamics within the target, and could help optimize these parameters accordingly.

Sensors mounted (glued, screwed in, etc.) or inserted in the structure of interest may affect its mechanical integrity, induce stress concentration, or change its preferred deformation mode and natural (resonance)

frequencies. Inducing damage to the structure during the mounting or insertion should be avoided, whenever possible, and the less intrusive mounting techniques should be preferred. For physical models, in-situ sensors may be cast during the model fabrication to minimize alteration of the surrounding media post fabrication.

Using sensors with animal models, Post-Mortem Human Subjects (PMHS), or physical models often means mounting sensors on/in deformable surface or structures. Great care must be taken to make sure that there is intimate contact between the sensor and the surface/structure of interest, and that this interface remains unchanged during the loading and unloading. Whether it is an accelerometer, a force transducer, a strain gauge, or a cast pressure transducer, interface separation often renders the signal unreliable. Vibration and slapping of the sensor or on the sensor will often generate erratic signals or unrealistic peaks that must not be confounded with the actual signal. Experiment repetition is key in assessing the quality of the mounting or casting process, as unstable interfaces rarely generate repeatable results.

High speed imagery can be useful to track target motion. Target deformation can be evaluated through the use of Digital Image Correlation techniques for example. The challenge in using these techniques in field testing is that high speed video equipment needs to be protected adequately and positioned at a reasonable distance from the target to avoid damaging it. More importantly, the shock wave, fireball, air flow, and detonation products can all distort or obstruct the field of view during part of the blast test.

F.3.3.9 Instrumentation, Data Acquisition and Processing

To accurately reproduce blast exposure in a laboratory environment implies that the method used to measure the blast exposure is also accurate and adequate. While it is outside the scope of this document to discuss in depth technical requirements for sensors meant to be used in blast tests, it is important to acknowledge a few aspects of the selection of instrumentation, the signal acquisition process and post-processing routines.

When selecting sensors, one needs to validate that sensor capacity is high enough to measure the maximum expected peak values. It is recommended to use a reasonable safety factor on sensor capacity to avoid signal saturation, but also keep it within the same order of magnitude as the expected signal to maintain adequate resolution.

The mounted sensor resonance frequency should exceed the expected frequencies in the responses to be measured. This implies knowledge of the nature of the target response *a priori.* Sensor bandwidth is particularly important when measuring initial peak values generated by the passage of a shock, as the upper bound of the bandwidth (highest frequency) puts the limit on the shortest resolvable signal rise time. If the sensor cannot respond fast enough to capture the initial signal rise, initial peak values will be underestimated. As a general rule, sensor bandwidth should be maximized whenever possible. The presence of sensor-born mechanical or electrical filters should also be verified, as their cut-off frequency should not be in the measurement relevant frequency range.

Sampling frequency should be at least 2 times, or in common practice 5 times, the highest expected frequency in the perturbation being measured (Nyquist theorem). The use of an anti-aliasing filter is recommended since other outside stimuli may superpose on the measured signal and contain even higher frequencies that may be under sampled.

Acquired signals may be filtered in post-processing to remove undesirable noise in the measured signal. The source of the noise should be analysed so that the filtering scheme can be focused as much as possible. Knowledge of the expected signal true bandwidth is again very valuable to avoid filtering out actual relevant

content of the true signal. Different methods exist to validate that the filtering scheme did not remove important content.

F.4 REPORTING RESEARCH WORK

The information that must be addressed and then reported, where relevant, is detailed in this section of the guidelines and has been broken down into four constituent parts: research rationale, blast characteristics, target exposure characteristics, and target response. Each section highlights the information that should be included in a publication reporting experimental test results.

F.4.1 Research Rationale

A clear articulation of the rationale for the research must be provided and must include, but is not limited to, the following items.

F.4.1.1 Aim of the Experiment

The aim of the experiments must be clearly stated in the context of the problem that it is intending to address.

F.4.1.2 Hypothesis to be Tested

The hypothesis that will be tested must be stated, as this may influence the research best practices needed to address the hypothesis.

F.4.1.3 How Experiment Answers the Hypothesis

How the experiment answers/verifies the hypothesis must be clearly stated. Any assumptions made must also be stated. It is important that this is addressed to ensure that the experimental methods used are appropriate with respect to the hypothesis posed.

F.4.1.4 How Experiment Relates to Real World Operational Conditions

The relationship between the experimental conditions and operational conditions must be clearly articulated. This increases the impact of the research by making a direct link for the operational community, such that evidence-based decisions can be made affecting protection, prevention, and treatment. If this link is tenuous, as may be the case in fundamental research where a mechanistic or fundamental question is being addressed, then this must be explained including possible future implications/impact.

Experiments that do not address the relationship between experimental and real world operational conditions and result in research using an unrealistic exposure/response regime can lead to confusion in the community. In this case, if the experiment is to proceed, the limitations must be clearly accounted for.

F.4.1.5 Why the Exposure Level was Chosen

A rationale for the selection of exposure level(s) must be provided. This is important to provide the reader/ reviewer with an understanding of the potential relationship between the exposure and the response. This is especially important if the research is aimed at inflicting an injury, or at evaluating the potential of injury at a given exposure. There may be scaling implications and, if so, they must be explained.

F.4.2 Blast Characteristics

A distinction needs to be made between blast characteristics and exposure/target loading conditions. The blast characteristics define a scenario independently of any target, while the interaction of the blast characteristics with the target determines the exposure conditions. Target exposure conditions are discussed in the next sub-section.

F.4.2.1 Blast Simulation Method

The method of blast simulation must be clearly described. The information to provide includes, but is not limited to:

- Type of method (e.g., shock tube, blast simulator, full-scale field test).
- Type and nature of blast source (e.g., compressed helium, combustible mixture, Composition B explosive).
- Source quantity and physical characteristics (e.g., gas pressure, mixture proportions, weight of explosive, charge dimensions, charge confinement).
- Detailed description of test apparatus (e.g., dimensions, assembly, achievable loading profile, embedded instrumentation, charge holding method).
- Source and target location (e.g., distance from diaphragm, distance from charge, height of burst).

F.4.2.2 Ambient Conditions

This will include, but is not limited to: pressure, temperature, humidity, precipitation, and noise.

F.4.2.3 Data Acquisition and Processing

This includes but is not limited to: acquisition cards and sensors make/models/type; sensor mounting technique, cable type and length, sensor and cable shielding, sampling frequency; analog filters used during conditioning; and digital filter and general post-processing routines.

F.4.2.4 Blast Characteristics at Target Location

Fully characterize the blast at the target location. These characteristics are ideally monitored during a pre-test performed without the actual target, but with the target support structure in place whenever possible. Report static and dynamic pressure history; dynamic pressure history may be estimated from computer simulation or derived from Pitot probe measurements, when appropriate. Peak pressure values and phases duration do not suffice to provide a full understanding of the exposure. Provide the full history over the complete duration of the event. If it is not possible to provide full pressure traces, report the following:

- Peak values.
- Duration of positive and negative phases.
- Impulse of positive and negative phases.
- Method for peak determination.
- Method for positive/negative phase determination.
- Method for impulse determination.

F.4.2.5 Duration of Recording

The time interval reported should cover the full exposure history including negative phases and reflected shockwaves which are especially important for biological experiments. The exposure should be considered over when static and dynamic pressure fluctuations become negligible.

F.4.2.6 Level of Reproducibility and Number of Repeats

Report the overall reproducibility of blast characteristics and the number of repetitions for each tested conditions.

F.4.2.7 Effects of Sample Holders and Other Structures

Report all structures, other than the target itself, that are in the path of the blast wave including the target holder.

F.4.2.8 Exposure Level Along the Propagation Direction

Reporting of the exposure characteristics along the propagation line is very useful to understand the directionality of the different waves composing the exposure at the target location (e.g., rarefaction waves coming from shock tube opening). It can aid in identifying the source of undesirable reflections and helps to globally understand the specifics of the blast simulation method.

If the exposure level is reported at additional locations in front or behind the target location, it should be done in the same manner and with the same amount of details. Given that this information is particularly useful for wave tracking, full pressure histories are preferred over simple peaks and duration reporting.

F.4.3 Target Exposure Characteristics

The target exposure, or loading conditions, is the result of the interaction between the blast characteristics and the target. It is influenced by various factors including target type, geometry, position, orientation, mounting, and protection.

The emphasis is put on the reporting of a set of parameters which fully describe the loading conditions and indirectly inform on the level of reproducibility of the loading.

F.4.3.1 Target Type

Provide a description of the type of target (e.g., physical surrogate, animal model, PMHS, cellular material, other object) selected for the study. Include a rationale for selection of target type. Discuss advantages and disadvantages of the target, and how these were taken into consideration in the experiment.

F.4.3.1.1 Animal Models

Provide a full description of the animal model system including detailed documentation of the model with respect to any bio-physiological/chemical preconditioning (see Ref. [3] regarding the use of animals).

F.4.3.1.2 Physical Model/Surrogates/Phantom

Provide a full description of the physical model, including details on the geometry (external and internal) and its origin (anthropometric survey data, 3D scan, commercially available geometry etc.), model mass and general

dimensions. Provide a description of the different model components, along with information on their construction and the material of which they are made. Detailed information should be provided on any mounted instrumentation (type, make and model) and their mounting method. Any previous validation of the model response to relevant loading conditions should be referenced.

F.4.3.1.3 Post-Mortem Human Subject (PMHS)

Describe the methodology for selecting PMHS specimens. Provide a detailed description of the PMHS inclusion/exclusion criteria, specimen preservation methods and preparation procedures prior to testing. Age, sex, height, and weight should be stated. Describe all instrumentation used in conjunction with the PMHS with respect to their nature and mounting method. Complete details of insertion/mounting technique are particularly important for intrusive instrumentation. Describe the steps taken to ensure that the PMHS specimens do not desiccate or degrade during the testing. The use of pre- and post-testing digital imagery techniques (e.g., X-ray, computerized tomography scans) to verify the PMHS condition post-testing should be included.

F.4.3.1.4 Cellular Material (In Vitro)

Provide a full description of the cell culture (in vitro) system. Discuss the culture conditions, cell type, etc., and the advantages/disadvantages and limitations of the system. Explain how the cells are exposed to the blast pressure wave.

F.4.3.1.5 Other Objects

If targets other than those described above are used, provide information to substantiate the choice of targets for experimentation. For example, information on what the target represents and what it is made of should be provided.

F.4.3.2 Position/Orientation of Target

Provide accurate information with respect to the target positioning and orientation. For example, in a free-field test, distance from the center of the charge, as well as height of the specimen and orientation in the three axes should be provided. In shock tubes, report the distance from the driver to the specimen and orientation. For biological specimens (animal and cellular), a full description of orientation is needed. For more detail on animal / live tissue target position and orientation (see Ref. [3]).

F.4.3.3 Mounting of the Target

Describe and discuss details on the mounting or holding system with respect to any artefacts that may be introduced due to the system. Clarify how these artefacts will be accounted for in the results. For example, the mounting structure should be described with respect to how it is fixed to the tube/ground and how it might influence the blast flow (possible reflections). The reader must be able to figure out all the degrees of freedom of the target and where the target is rigidly fixed. Any accidental interaction of the target with the supporting structure should be identified. For more detail on mounting animal/live tissue targets, see Ref. [3].

F.4.3.4 Protective Equipment

Describe the Protective Equipment (PE) when used with the target. For commercial and military equipment, provide the make, model, size and weight of the PE. When available, the composition (materials) and fabrication

of the PE should be provided. If modifications had to be made to accommodate the experiment or the target, they should be reported. For custom protective system, provide the geometry, weight, composition, and fabrication. A detailed description of how the system was fitted and secured on the target is necessary. A description of the interaction of the PE with the target during the experiment should be included in the analysis, as it may play a critical role in the response of the target and its monitoring.

F.4.4 Target Response

This section emphasizes the importance of monitoring and reporting relevant response related data in a complete manner. For any response monitoring done using a sensor, the relevant sensor technical specifications should be provided; describe sensor location and mounting technique; and provide and explain signal sampling rate and processing scheme.

F.4.4.1 Motion

Motion data is important when studying the response of a target. In the field of head injuries, acceleration and other acceleration derived quantities have been used as injury predictors. It is still unclear how head motion may be correlated to injury in blast-induced mTBI, but it remains the most popular measure of target mechanical response. In the absence of dynamic pressure data, the motion of the target may be indicative of the magnitude of the dynamic impulse it is subjected to.

Report the specimen motion data over the full duration of the experiment. Motion data may include rotational and translational position, velocity, and acceleration. If motion data is not derived directly (e.g., from high speed imagery), report the derivation method (e.g., position derived from acceleration measurement). The reference coordinate system and other reference points (head center of gravity or other) need to be identified.

F.4.4.2 Target Surface Pressures

Surface pressure data add to the interpretation of the target response as surface pressures provide a true measurement of direct loading on the target. If such data is monitored, report the pressure history over the full duration of the experiment. Describe any potential obstruction of the pressure sensor during the experiment (e.g., protective system shielding the sensor) during the analysis. Report any slapping or impact near the transducer. When reporting pressure data, an analysis of the signal peak values should accompany the results. Report any unexpectedly high or low values.

F.4.4.3 Strains

Report strain data collected. Strain data provides a direct local measurement of the effect of the loading on the target structure. They can provide a global understanding of the modes of deformation of the target and help describe how stress is transmitted through that structure. If a strain gauge is used, describe how the gauge is mounted.

F.4.4.4 Internal Pressures

Report internal pressure data which can provide a unique *in situ* measurement of the effect of external loading. The quality of such measurement is highly dependent on the intimacy of the contact between the pressure transducer and the surrounding medium. As such, internal pressure data should be analysed for irregularities and repeatability, as gauges may be displaced and interfaces may separate within the medium without being noticed.

The use of multiple transducers can help understand the dynamics of the pressure field within the structure of interest. When available, data from multiple sensors should be analysed jointly to identify the origin and propagation direction of stress waves. As with the other types of measurement, report the internal pressure history over the full duration of the experiment.

F.4.4.5 Physiological Parameters

If animal models are used as a target, discuss any physiological parameters measured pre- and post-exposure. These may be collected by telemetry devices or through other means. Include a rationale for the parameters collected. See Ref. [3] regarding the use of animals.

F.5 CONCLUSION

Creating blast exposures in a laboratory setting is not a trivial undertaking; it requires expertise, knowledge, and capabilities in blast wave physics, as well as, engineering. Understanding the complexities of generating reproducible blast waves is critical for recreating relevant military exposures in the laboratory. As with other toxicology research, characterising the 'dose' is crucial to understanding the 'response' of a test system. Whether shock/blast tubes are used or free-field blast trials are performed, several irregularities must be recognized, and either controlled or explained as to the effect on the test system, and the resulting limitations to the results generated. These guidelines are intended to ensure the reporting of blast injury research exposures in a systematic fashion so research from different laboratories can be compared.

Given the complexity of blast exposure, understanding the injury effects that may result from the different components of a blast (e.g., pressure, duration) are sometimes needed before the overall effect from a blast exposure can be explained, depending on the research question asked. This is similar to understanding the toxicology of complex mixtures of chemicals where the toxic effects of the individual components is required before an understanding of the effects from the mixture can be understood. Given the response is in a complex biological system, understanding 'mixture' effects is not easy. Combining complex exposures such as blast with complex responders such as humans makes the interpretation even more challenging.

These guidelines are the outcome of an attempt to understand how blast exposures can be created and the information that is required to allow for experimental work from different laboratories/institutions to be compared. Ultimately this will advance the state of the science and result in the best evidence possible to inform those responsible for the protection and care of military members.

F.6 REFERENCES

[1] NATO HFM-234 (RTG) "Dictionary of Blast Injury Research Terms", 2016, Neuilly-sur-Seine, France.

[2] NATO HFM-234 (RTG) "Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods and Standards" Kick-Off Meeting and Program of Work, July 1-2, 2013, Neuilly-sur-Seine, France.

[3] NATO HFM-234 (RTG) "Guidelines for Using Animal Models in Blast Injury Research", 2016, Neuilly-sur-Seine, France.

[4] Needham, C.E., Ritzel, D., Rule, G.T., Wiri, S. and Young, L. (2015) "Blast testing issues and TBI: Experimental models that lead to wrong conclusions", *Frontiers in Neurology*, 6(Article 72):1-10.

[5] NATO Science and Technology Organization. (2011) "A Survey of Blast Injury across the Full Landscape of Military Science", Retrieved from https://www.cso.nato.int/pubs/rdp.asp?RDP=RTO-MP-HFM-2071.

[6] McShane, G.J., Stewart, C., Aronson, M.T., Wadley, H.N.G., Fleck, N.A. and Deshpande, V.S., "Dynamic rupture of polymer–metal bilayer plates", *International Journal of Solids and Structures* 45 (2008) 4407-4426.

Annex G − MINUTES FROM PANEL MEETING OCTOBER 2014

University of Tartu
Tallinn, Estonia
October 7-9, 2014

G.1 BACKGROUND

Blast Injury is one of the most important sources of casualties in current NATO operations. The term "blast injury" creates considerable confusion in military medicine. Simply stated, "blast injury" includes the entire spectrum of injuries that can result from exposure to an explosion. It is generally accepted that the taxonomy of injuries can be assigned to five categories: primary, secondary, tertiary, quaternary, and quinary. These are based on the mechanism of injury. Primary blast injuries result from the high pressures created by the blast itself. The high pressures, known as blast overpressure, can cause internal injuries. Primary injuries result from the effects of the shock wave, which travels through the tissues depositing energy particularly where there is a gas-liquid interface. Secondary blast injuries result when strong blast winds behind the pressure front propel fragments and debris against the body and cause blunt and penetrating injuries. The strong winds and pressure gradients also can accelerate the body and cause the same types of blunt force injuries that would occur in a car crash or a fall. These are known as tertiary blast injuries. Quaternary blast injuries are the result of other explosive products, such as heat, light, and toxic gases that can cause burns, blindness, and inhalation injuries. Finally, quinary blast injuries refer to the clinical consequences of "post-detonation environmental contaminants", including bacteria, radiation (dirty bombs), and tissue reactions to fuel and metals.

The discussions at HFM-207 (SYM) revealed the importance of a systematic approach to understanding blast injuries much like the well-established approach used to solve the classical toxicology problem where the etiology of the injury requires an understanding of the dose, mechanism of delivery of the dosage, and dose-response endpoints. Also recognized was the pressing need for a multidisciplinary approach to addressing non-penetrating blast injuries to the brain that result in a host of symptoms with vague etiology. In addition, the Technical Evaluation Report emphasized the continued multinational exchanges of scientific and technical advances to respond to blast threat and blast injuries. The first recommendation identified a future need for a recurring technical exchange venue on blast injury and its mitigation to address advances in medicine and personal protection and their synergy. The second recommendation highlighted the need for the development of a Technical Activity Proposal (TAP) to explore the concept of "the Toxicology of Blast Injury" and suggested to focus the activity on several difficult problems including:

a) Relevancy and commonality of animal models.

b) Common dose-response methods; route of exposure methods.

c) Computational Models (blast, physiology, biochemical, toxicological, etc.).

d) Dose regimens to human medical endpoints (surgical trauma to mTBI spectrum).

e) Methods for translational research leading to medical products and/or physical protection products.

To address the above recommendation and to develop a specific NATO activity devoted to the toxicology of blast exposure, a TAP titled "Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods and Standards was approved in the fall of 2012, which resulted in the establishment of a new NATO Science and Technology Organization HFM Panel RTG with the following objectives:

- Build an evidence-based outline for NATO standards for blast injury analysis.
- Examine opportunities for improvements in the standards of medical care for blast injury.
- Explore advancing the state-of-practice in computational modeling of blast injury in relevant operational environments.
- Explore standardized animal models and toxicology research protocols that could be adopted by R&T programs across NATO.

This document summarizes the deliberations of the HFM-234 RTG Technical Teams (TT) meeting focused on sharing experience about computational modeling and research done in blast injury in all participating countries in this meeting. The agenda for this meeting is shown in Appendix G1. Meeting agenda items included a full day of presentations of every participating country. Presenters were from the Technical Team mostly. Main discussions were at the end of the presentations. A sub-group from the Technical Team continued on work with blast injury dictionary of terms. All members viewed a draft about epidemiology of blast guidelines and this was sent to each participant to give their comments. The objectives for the next meeting in Stockholm, Sweden (12-14 May 2015), were also discussed. Fifteen TT members participated in the meeting, representing eighth NATO nations. The list of TT members is attached (Appendix G2).

G.2 WELCOME AND OPENING REMARKS

Mr. Mike Leggieri (Chair) and Dr. Hans Orru opened the meeting welcoming all members and introduced the meeting programme. Total 15 members participated. Personal introductions followed by all members. New member from France, Mr. Philippe May, was invited to speak for French army experience about blast injury studies. The goal of the meeting was to share experience about computational modeling in all participating countries, continue work on developing Dictionary of Terms about Blast Injury terminology and discuss on blast epidemiology guidelines draft.

G.3 COMPUTATIONAL MODELING – PRESENTATIONS FROM DAY 1

Dr. Raj Gupta opened the presentations session with “Computational modeling of non-impact, blast-induced mild traumatic brain injury”. This presentation focused on expert panel proceeding about computational modeling. It was pointed out that to better solve TBI caused problems; different communities (engineers, medical doctors, mathematicians, etc.) must work together. Mr. Leggieri said that TBI affects both civilian and military personnel. More than 1.4 million US civilians suffer TBI. From the presentation we know that physiology-based computational/mathematical modeling tools of blast head injury may provide a framework to understand injury mechanisms and guide experimental testing. Computational modeling is considered to be difficult because it involves both biomechanics, physiology, data from engineering and it all must be linked together.

Then the presentation concentrated to finding of the expert panel. It was brought together in 2010 and included clinicians, engineers, mathematicians, modellers, neuroscientists. Objective of this panel was to assess state-of the science in computational modeling of non-impact, blast inducted mTBI. In the first meeting, experts agreed that the research must be field consistent, framework must be well-defined, injury can be predicted and use in vivo and in vitro models. Dr. Gupta the showed graphs about model validation. He said that we can control blast exposures and make simulations. Blast is leading cause of TBI for active duty military personnel in war zones and we do not have a good overview of the injured service people. Dr. Gupta suggested the following:

- Define an objective method to assess blast exposure in the field.
- Collect historical data about blast exposure research.
- Study how blast injury relates to brain injury.
- Develop *in vitro* assays, rapid influx of calcium in neurons, platform form high testing strain testing, study damage to astrocytes, using Kolsky bar.
- Develop short term and chronic term injury models.
- Define relation between exposure characteristics and organ damage.
- Create full body "digital warrior".
- Develop full body model (e.g., surrogate).
- Conduct literature review.
- Validate current models.
- Develop a new "Bowen curve".
- Solve data sharing problems (data from medicine and military).
- Carry out clinical trials for humans.

G.3.1 Followed with Presentations about Computational Modeling in Canada

Mr. Simon Ouellet (Canada) gave a presentation about the use of numerical modeling in blast-induced TBI research performed by DRDC. They are using numerical modeling to understand the interaction between selected blast waves and different types of targets. In particular, DRDC Suffield uses a CFD code (Chinook) coupled to a hydrocode (Ls-Dyna) to model shock tube experiments on simplified targets such a sphere or a simplified mouse head. DRDC Valcartier performs simulations of free-field blast scenarios using Ls-dyna. 2D simulations were performed on complex human head models and 3D simulations were performed on a model of the physical head surrogate that DRDC uses in full scale experiments.

Both labs performed several studies focused on:

- The effects of domain boundary conditions on wave propagation.
- The effects of different material constitutive models.
- The effect of different element formulation.
- The effect of cavitation model.
- The effect of element size.
- The importance and role of different head structure in the transmission of blast loads.

Of particular interest is the method used by DRDC Suffield to more efficiently generate numerical loading conditions that are as close as possible to the ones observed in their shock tube experiments. Modelling of entire tube is impractical because of run time and needed mesh refinement. A "wave reconstruction method" has been developed and allows for the computation of the entire blast flow field at the boundary of the target section based on a single experimental pressure trace. This method decrease calculation time and allow higher model resolution in the target area. The CFD code is interfaced, or coupled, with a hydrocode to study target structural response.

Based on experiences, some suggestions and limitations about numerical modeling were provided:

- Mesh size should be dependent on the wave speed.
- Materials should be tested in laboratory rather than relying on the literature, where the variance is quite large (especially for biological materials).
- Meshing detailed geometry is difficult; fluid-structure coupling should be included.
- Tetrahedron elements are prone to volumetric locking, which results in a "stiffer" response.
- There are many models out there, but little sharing of geometry or meshed models.
- The level of fidelity of complex models should match the level of detail of the geometry.
- There is no point in having a finely detailed model with fine geometry if all materials are the same.
- Blast load conditions should match actual blast waveforms as much as possible.

G.3.2 Followed with Presentations about Computational Modeling in Estonia

Dr. Hans Orru gave his presentation about the ongoing project among Estonian military personnel to determine their occupational-related health risks. Estonian defence forces have been active in many NATO operations and gave their effort to cyber defence. Dr. Orru gave overview of the Estonian military structure and its duties and about studies in Department of Public Health in University of Tartu.

Dr. Orru introduced the ongoing project among all active duty military officers in Estonian military. Postal questionnaire (ca 2800) will be conducted to find out occupational risk factors. Most common are respiratory and musculoskeletal system diseases. Hearing loss is also a very common problem. There is no blast-related research in Estonia, no computational modeling.

G.3.3 Followed with Presentations about Computational Modeling in France

M. Philippe May from France presented their research about blast threat for the dismounted soldier. Dismounted soldiers are subjected to a ground burst during IED attack. Thoracoabdominal areas are first injured before the neck and the head of the subject are affected. Hemodynamical and respiratory dysfunctions could appear, sometimes with a short loss of consciousness. An amplification of the intrathoracic pressure could also be observed in case of a too restricted or soft ballistic vest. French blast program started in 2013. They started experiments on pigs and gather information about their injuries after contact with explosives. They used animal modeling and data from different sensors (EKG, EEG, etc.). Furthermore, they made a full scale dummy and measured blast pressure. From the experiments they learned that: if exposed to a blast event 500 kPa at distance 3 meters, firstly hemoptysis and risk of the intestinal wall are occurs; also permanent hearing loss.

G.3.4 Followed with Presentations about Computational Modeling in Netherlands

There was no presentation as Mr. Phillipens did not attend the meeting.

G.3.5 Followed with Presentations about Computational Modeling in Norway

Mr. Jan Arild Teland presented about computational modelling done in Norway. Numerical simulation of the shock waves showed that waves propagate into the brain through the skull. They also used pigs in their experiments. They modelled a situation, when head rotates in 90 degrees; rotation increases variation of the pressure. Furthermore, they made skull models in 3D. It showed, that the skull offers little protection to the brain

when exposed to a blast wave. The blast waves propagate directly through the skull and into the brain just as easily as through openings in the skull. Head geometry and orientation relative to the blast wave have some importance to the pressure distribution in the brain. The results are not very sensitive to the material parameters used for the brain and skull. 3D models give better animations and more details. No major difference between full 3D and simplified 2D models.

Difficult to create an accurate numerical model. Good model requires adequate representation of the geometry and correct material models for the involved materials.

Potentially the method of simulation can be used to determine what kind of injury results from various types of loading

Closing the day.

G.4 DAY 2 – PRESENTATIONS ABOUT COMPUTATIONAL MODELING AND DISCUSSION ABOUT DICTIONARY OF TERMS DOCUMENT

Day 2 began with a presentation from Dr. Marten Risling about components in blast TBI. In their studies they observed that primary blast wave causes inflammation and cell death in the brain. Rotational acceleration of the brain causes axonal injuries, cell death, gene expression change and intracellular edema. Also he introduced their animal components. They made their experiments on rats. There is a 60-year old blast tube in Stockholm.

End of presentation raised some topics like:

- When comparing acceleration model and blast model – more is seen in acceleration model.
- Primary blast does not show white matter injuries.
- Appropriate use of instruments for animal studies?

Presentation section ended with the discussion block. It raised some topics, including:

- Do we need to put the summary together about the panel proceedings?
- Need to write publication, find suitable journal to share the information.

Dr. Ibolja Cernak showed the Dictionary of Terms document to the members and then all had a chance to make recommendations about the terms to include into this document.

Members made some suggestions:

- Every term needs additional definition – how it is defined in the medical community as well as and in the engineering community.
- Additional terms were proposed, including but not limited to:

  Ambient pressure, Bowen curve, incident pressure, loading, pulmonary neurotrauma, underbelly blast, underwater blast, model (different types), impulse noise, blast overdose, auditory blast injury, coup countercoup-injury, cavitation, static pressure, deck slap, underbody blast, quasi-static pressure, duration, time of arrival, rise time, scaling, free field, Freelander wave, complex blast wave, dismounted blast, parallel orientation, perpendicular orientation, shock tube, blast tube, prospective study, retrospective study, arena, fuel-air explosion, thermo baric bomb, skull fracture, EMP, thoracic surge, environmental exposure sensor, incident, blast signature, dose, exposure, epidemiology of blast.

Draft of the blast dictionary of terms will be sent to all members with a deadline for their response. All changes must be made using the tracking tool. The final version will be made accessible in the NATO page and will allow a search of the terms.

A parallel session was held with Dr. Raj Gupta who showed a draft of the blast injury epidemiology guidelines. He showed the structure of the document. This draft also synthesized summaries of all meetings. The draft will be sent to all members; a deadline was set for the members to propose changes to the document. Finally this will be published as an official NATO document.

Discussion revealed some general topics:

- What are other confounding factors in the environment that are related to mTBI?
- There is a need to optimize the data collection efforts in future studies Conduct multinational studies.
- Do other countries have a policy for mandatory medical evaluation?
- Every member country must define the safe distance from the blast.
- Examples of the study questionnaires.

Maj. Dr. Dan Bieler then gave his presentation about multinational epidemiological databases (NATO trauma registry). The first example of such a registry is found in the USA (1969); Germany followed with their trauma registry in 1993. The NATO trauma registry was established in 2014. He showed a database and described how the data is added to the registry entered. It was noted that only visible injuries are inserted. There is no data in the registry that allows for the prediction of mTBI. Members made a suggestion to create module “Blast injury” into this registry. They also discussed the problem of linking medical data with assessment of the operational context – (classified data; as well as whether or not the military operational data can be shared?).

Mr. Stephen Bjarnason then introduced a report draft of guidelines on the blast exposure characteristics. Some topic emerged such as:

- Give guideline checklist.
- Target exposure characterization.

Closing the day.

G.5 DAY 3 – DISCUSSION ABOUT BLAST INJURY DICTIONARY OF TERMS AND NEXT MEETING ARRANGEMENTS

Dr. Ibolja Cernak started a discussion about blast research and several topics rose, such as:

- What is the experimental setup to do blast research?
- Rehabilitation issues after blast injuries.
- Surrogate blast models.
- Demographic questionnaire.

Dr. Raj Gupta talked about blast epidemiology. Topics discussed were:

- How to make data available for all members (Server Monkey system)?
- Each member must communicate their nation military to see what type of data can be shared.

- Start using ServerMonkey.
- Who will me maintaining the website?
- Setting some deadlines for completing working documents.

Mr. Leggieri closed this topic. Dr. Gupta will send all members his version of the guidelines draft. Mr. Bjarnason will finish his draft about blast studies in laboratory. Maj. Dr. Bieler will look into the publication of the guidelines being prepared by the HFM-234 TT team in collaboration with Dr. Gupta.

G.6 NEXT MEETING IN STOCKHOLM

Dr. Risling talked about next meeting in Stockholm held in May 12-14. The format will be similar to that of the meeting held in Canada. Mr. Leggieri closed the meeting and thanked everybody for their participation.

G.7 ACTION ITEMS / TASKINGS

The following actions/tasking were made at the conclusion of the meeting:

1) Dr. Gupta will send final guidelines draft.
2) Mr. Bjarnason will finish his draft about blast studies in laboratory.
3) Maj. Dr. Bieler will look into publication issues together with Dr. Gupta.

G.8 ATTENDING LIST OF NATIONS

Canada
Germany
Norway
France
Sweden
United Kingdom
United States
Estonia

G.9 APPENDICES

G1 – HFM-234 October 2014 Meeting Final Revised Agenda.

G2 – HFM-234 Technical Team Members (as of 6 October 2014).

Appendix G1: HFM-234 OCTOBER 2014 MEETING FINAL REVISED AGENDA

Tuesday 7 October, 2014		
0830	Welcome	Mr. Leggieri, Dr. Orru
	Individual Introductions	Technical Team Members (TM)
	Administrative announcements	Dr. Orru
0900	Presentation of summary of DoD Blast Induced Computational Modeling Expert Panel Proceedings	Dr. Gupta
1030	Break	
1100	Presentation of summary of DoD Blast Induced Computational Modeling Expert Panel Proceedings (cont'd)	Dr. Gupta
1130	Computational modelling – Canada	Mr. Oullet
1200	Computational modeling – Estonia	Dr. Orru
1230	Lunch	
1330	Computational modeling – France	MC May
1400	Computational modeling – Germany	Dr. Bieler
1430	Computational modeling – Netherlands	TBD
1500	Break	
1530	Computational modelling – Norway	Mr. Teland
1600	Discussion	TM
1700	Close out for day	
1900	City walk and dinner	

Wednesday 8 October 2014		
0830	Computational modeling – Sweden	Dr. Risling
0900	Computational modeling – United Kingdom	Dr. Sarah Watts
0930	Discussion – Synthesizing the DoD Blast Induced Computational Modeling Expert Panel Proceedings	TM
1030	Break	

Wednesday 8 October 2014		
1100	Parallel Sessions:	
	Working group on Dictionary of Terms	Dr. Cernak, Mr. Philippens, Dr. Kirkman
	Epidemiology of Blast – update	Dr. Gupta, Dr. Orru
	Reproducing Blast Exposure Conditions in Laboratory	Mr. Bjarnason,
1230	Lunch	
1330	Parallel Sessions continuous	TM
1500	Break	
1530	Parallel Sessions (change of working group members*)	TM
	Working group on Dictionary of Terms	Dr. Cernak
	Epidemiology of Blast – update	Dr. Gupta
	Reproducing Blast Exposure Conditions in the Laboratory	Mr. Bjarnason
1700	Close out for day	
1900	Dinner	

* Working group members will be moved to another working group to review the work and give new insights. Working group leaders will stay in their working group.

Thursday 9 October 2014		
	Plenary meeting, status update	
0830	Blast Injury Dictionary of Terms	Dr. Cernak
0850	Epidemiology of Blast	Dr. Gupta
0910	Reproducing Blast Exposure Conditions in Laboratory	Mr. Bjarnason
0930	Multinational Epidemiological data bases: Concept and parameters for inclusion in NATO trauma registry	Dr. Bieler
1030	Break	
1100	Cross-NATO blast research infrastructure/opportunities – Past, Present and Future	TM
1130	Reassessment of HFM-234 RTG progress, plan and review of working plan/tasking	Mr. Leggieri
1230	Next meeting – Stockholm, Estonia; 12 – 14 May 2015	Dr. Risling
1245	Closing remarks	Mr. Leggieri
1300	Lunch and Farewell	

Appendix G2: HFM-234 TECHNICAL TEAM MEMBERS (AS OF 6 OCTOBER 2014)

Name	Nation	Email
Mr. Michael Leggieri (Chair)	United States	michael.j.leggieri.civ@mail.mil
Dr. Raj Gupta	United States	raj.k.gupta.civ@mail.mil
Dr. Ibolja Cernak	United States	cernak@ualberta.ca
Mr. Stephen Bjarnason	Canada	stephen.bjarnason@drdc-rddc.gc.ca
Mr. Simon Ouellet	Canada	simon.ouellet@drdc-rddc.gc.ca
Maj Dr. Dan Bieler	Germany	dr.dan.bieler@t-online.de
LtCol Dr. Axel Franke	Germany	axel1franke@bundeswehr.org
Dr. Hans Orru	Estonia	hans.orru@ut.ee
Mr. Mihkel Pindus	Estonia	mihkel.pindus@ut.ee
Dr. Marten Risling	Sweden	marten.risling@ki.se
MC Jean-Claude Sarron	France	jean-claude.sarron@intradef.gouv.fr
Mr. Philippe May	France	philippe.may@intradef.gouv.fr
Mr. Stian Skriudalen	Norway	stian.skriudalen@ffi.no
Mr. Jan Arild Teland	Norway	jan.teland@ffi.no
Dr. Sarah Watts	United Kingdom	sawatts1@dstl.gov.uk

Annex H − MINUTES FROM PANEL MEETING MAY 2015

HFM-234 – A Workshop with Aim to Develop Recommendations for Standardized Animal Models and a Roadmap for Dose Dependent Curves

Stockholm, Sweden
May 12-14, 2015

H.1 RATIONALE FOR RECOMMENDATIONS FOR STANDARDIZED ANIMAL MODELS

Blast injuries typically involve a number of complex physical interactions, which can be difficult to model in laboratory environment. However, experimental models can provide a way to study isolated mechanisms in a well-controlled situation. The translation between experiments and real-life situation is difficult, though. In addition, it has been found that there are a number of difficulties also in translation between different experiments and that when experiments have been repeated under seemingly similar conditions the outcome of the experiments has been dissimilar. This creates a need to define recommendations for experimental work in blast.

The aims of the workshop were to identify potential problems with different experimental models and to analyze how recommendations for standardization could increase the quality of the experiments. A number of models and methods for analysis of outcome were presented during the meeting. It was concluded that several models indeed are needed to capture all mechanisms and details in blast, but that there is a need to give advice for good planning and monitoring of experiments. Animal work can help us define the importance of the different mechanisms. But there is a knowledge gap about the propagation of the primary blast wave. Is it hitting the brain directly or can it be transmitted to the head from the trunk?

Mechanisms to be considered in modeling of a blast exposure:

- Primary;
- Focal impact;
- Acceleration, Rotational; and
- Heat, gases and EMP emission.

Each of these mechanisms may require a separate model. Models can also be created to analyze combinations of different mechanisms in blast. The duration is usually very short for each of these. Models for civilian trauma are therefore not always relevant.

The meeting included a number of presentations on the use of different models and a final discussion on recommendations for future experimental work and translation of data.

H.2 PRESENTATIONS

H.2.1 Translational Aspects, by Professor Denes Agoston, The Uniformed Services University of the Health Sciences, United States

Timetables for pathological and physiological response to trauma may be dissimilar in humans and experimental animals. Models typically employ species like mice, rats and pigs that all have different timeframes for reactions to trauma compared to humans. There may also be a large variation between different species of experimental animals and even between different strains of the same species.

Research often, only evaluate a single time point and try to come up with a biomarker or to cure TBI. Need to consider that a disease like TBI is not a static condition. Need to understand the temporal changes and we will be able to model the disease better. A number of parameters need to be analysed in more detail in terms of time tables. This includes metabolic changes, vasculature changes (including in the brain), inflammation, cell death and axonal injury.

The energy transfer in liquids and soft tissue needs to be analyzed in more detail with regard to scalability.

We mostly seem to model the severe TBI as the animals die, or the moderate TBI. Difficult to model the mild TBI. A need to sub-classify TBI, based on functional outcome measures. We do not understand the processes which one is first, and leads to the next or the time scale of it.

We don't know how our model time and human time correlate. A rough calculation: Life span of a rat: 13.2 rat days equate to 1 human year. RNA turnover is 2.5x times faster in the rat, protein 10x faster and metabolic rate 6.4x faster.

85% of TBIs are mild, is it possibly to identify, from experimental models, the critical window where the brain is most vulnerable to another insult?

Serum biomarkers can be useful for translation. Take blood, prepare serum and use different proteins related to different pathologies that have gone into the blood stream. It is non-invasive, can take as many samples as you want, clinically translatable. But need to know if these proteins are coming from the brain or elsewhere. Since, they are not always brain specific as in the case of inflammatory markers.

Cerebral glucose metabolic rate drops initially and then recovers following TBI. In rat the maximum depression is 1 d in the rat and by 10 d it recovers. In humans it is 3 d and recovers 30 d later, even at 10 – 15 d depression is still around 50%. This is hugely important; how long do we need to allow for recovery.

Vasculature changes. We measure ICP in the patient. In the rat we measure the water content. Peak in the rat is around 2 – 3 d. In the human it is 10 – 15 d. But these changes depend on the period of the rat life, i.e. weaning, adolescence, aged rats, or those in adulthood.

H.2.2 Multiple Experimental Models, by Professor M. Risling, Karolinska Institutet, Stockholm, Sweden

Three different models that represent different injury mechanisms are available at Karolinska Institutet. These have been developed and validated in Sweden. These models have constructed to provide good control over the physics and can generate threshold values. The work has identified different patterns in the outcome:

- The blast tube here has a very short duration peak pressure compared to the shock tubes in most labs. In the system real explosives are used. Have made some measurements and see quite reproducible blast waves with this model. See changes in the neurotransmitter systems post-exposure to the primary blast wave.
- Rotational injury can stress and shear axons. Have created curves of the acceleration.
- 3rd model, aimed to create focal impact, the speed and shape of the projectile can be changed, the impact of fragments into the skull. The shape of the projectile, how deep it penetrates the brain, etc., can also be changed and measured.

Based on the limited behavior changes, have concluded that the *rotational* and *blast* models are mild. But see some memory impairments in the *penetration* model.

Translation between animal work and clinical studies is difficult. There is a need for tools to decrease the gap between these models and real life. Serological biomarkers and imaging are important tools for translation. A 9.4T system is available at the institute. Ex-vivo MRI can be used for terminal studies. One benefit is the absence of respiratory movements and a possibility for long exposure times. The system can be used for diffusion protocols and tractography to analyze volume changes in the different tracts, such as the corpus callosum.

The Vietnam head injury study provides a possibility to translate from humans to experimental animals. Veterans have had cognitive tests before deployment, which they repeated after deployment. The study has generated long-term outcome data, imaging data and a possibility to match different outcomes with gene analysis. Such data can provide background for directed animal studies and indicate gene variations that might affect the outcome. For example, gene variations for the growth factor BDNF (Brain Derived Neurotrophic Factor) was shown to correlate with outcome. That observation initiated a study on BDNF after penetrating TBI in rodents.

Secondary lesions: Models can be used to look at these changes such as odema or hypoxia.

H.2.3 Validation of Rodent Models, by Dr. Davidsson, Chalmers Technical University, Gothenborg, Sweden

The work with validation of a model for rotational acceleration of the rat head was described. Centre of rotation close to the center of the skull base. Have found animal mortality increased with lower weight, over all body mass i.e. younger animals. Sham or lower graded rotational injuries have no DAI – here there is a time aspect as sampled at many different time points and these vary. Pro-inflammatory cox-2 marker is increased as acceleration levels go up, 2 h post-injury.

Still need to be done: The effect of reducing the duration, will there still be injury. Brain-tissue scaling method. Reproduce the animal test with a computational model, find out the threshold level and apply it to a computer model of a human and then develop crash test dummies. The rat is 10x softer than the human brain. Brain moves relative to the skull. This was modelled by using a inserting a pin into the brain, exposed it to the trauma and then followed the scar it produced. Managed to get the FE (Finite Element) model to reproduce the scarring, hence movement of the brain. Now looking at reproducing strain in the FE model.

Low to high acceleration correlate with increasing DAI. But this also increases in soft vs stiff brain tissue. Brain stem is more vulnerable than the rest of the brain to TBI.

The penetration TBI: Can vary the speed of the projectile, but we not know if this is scalable to the speed of the shrapnel in a detonation. Also what are the volumes and cavities of shrapnel injuries in humans. Primary cavity, which then collapses and a secondary cavity occurs. In this experimental model get a cavity in 65% of the brain. Pressure highest in the contral lateral ventricles, and duration is very small about 0.1 ms. Again have used FE-modelling. With the hope of being able to give some information about injury thresholds.

Final conclusion: If animal models are combined with mathematical models, get better idea of injury mechanisms. Will get tissue criteria (strain) and global criteria (human head). Important to find validation data to develop mathematical models preferably using standardized methods.

H.2.4 Models for Blast Overpressure vs. Survival-Dose Response for Primary Blast Brain Injury Animal Models in a Wide Range of Field-Relevant Shock Pressures, by Professor Namas Chandra, New Jersey Institute of Technology, United States

Lots of ideas from the civilian injury that can be used to evaluate blast-related injury. Charge and radial distance can however be confounders. I.e. if the charge is underground or above, outcome will be different. Or if it is not detonated properly and slowly does.

Relation insult-> injury -> medical outcome: The *injury* can be divided into a number of events, physical injury such as edemas and sub arachnoid injury etc. Then can have cellular and subcellular changes. These occur at different time points.

The cascades that are initiated by the mechanical disruption. The change may not necessarily be an injury, but if it persists then it is a problem. *Insult* – external mechanical force that disrupts the body. In the brain can be the blast or ballistics and so comes the *injury*. The *medical outcome*, the doctor will be looking at this.

Need to link all these. If the injuries do not cause a medical outcome we don't need to worry about it.

What type of blast are we talking about? Need to quantify reasonably well what we are interested in:

- Blast overpressure; and
- Duration of pressure.

Does primary blast cause concussion? TBI? BINT? Does the current design of helmets mitigate the effect? What is the dose response curve? What are the basic mechanisms?

As a first step need field validated animal injury models. Human data is scarce as a pure primary TBI is limited, usually see a combination.

Shockwave or shock profile: large burst of energy, compresses the air. Shock continues to spread until the velocity dies down, lower impulse and longer duration till it dies down. As it moves, it becomes flatter and flatter; this part is called a plain wave.

Higher detonation weights have increased peak pressure and duration.

Strategy for experiments: Found BOP 30 – 450 kpa, duration 3 – 7 msec from the field experiments, based on the strength and type of blast. Use a shock tube to recreate the physics of the blast in the lab that is faithful to the field measurements. Pressure controlled shock tube. Use different driver gas helium, nitrogen they produce different pressure profiles.

When the membrane breaks, it pushes the air. At some point in the middle it will have a Friedlander wave. Need to be aware of sudden expansion, jet winds not the primary wave at some point after this wave. Some shock tubes don't generate a primary blast wave, just jet winds. Need to load the animal close to this Friedlander wave.

Validation of the shock tube: Need a MHz sensor system as close to the animals as possible. No side reflections. Need to make sure the duration is no more than **7 ms** for it to be field relevant.

Musts of animal models:

- Orientation of the animal; and
- Reproducibility of the findings in different labs.

Dose response: Upper threshold based on peak pressure of blast exposure of mild/moderate/severe and lethal. Mild and moderate? Define severe as they start to die? Conclude there are dysfunctions at 123 kpa and below possibly at 100 kpa. Primary blast does cause TBI There are triggering mechanisms, changes in the vasculature, oxidative stress and BBB disruption. Not finding behavior changes.

H.2.5 Usefulness and Present Limitation of Laser-Induced Shock Waves for Research on Blast-Induced Traumatic Brain Injury: Study Using Rat Models, by Dr. Shunichi Sato, Division of Biomedical Information Sciences, National Defence Medical College Research Institute, Japan

Dr. Sato presented work with pulsed laser-induced stress waves employing a Nd:YAG laser. The pulsed light was focused with a plano-convex lens to a spot of 3 mm in diameter on the target, which is a black rubber disk of 0.5 mm in thickness. This device can be used to induce stress waves, single or repeated, that can be used in cell cultures or TBI research. The pulses have peak pressures in the range of 100 MPa and duration of less than 1 μs. In a recent study (PLoS ONE 9(4): e95067. Doi: 10.1371/journal.pone.0095067) this model was used to analyze spreading depression and vasoconstriction after TBI.

H.2.6 Systemic and Immunological Response to Blast, by Drs. Cernak and Kirkman (Presented by Dr. Kirkman) Dstl, Porton Down, United Kingdom

Indirect kinetic energy transfer of the blast wave *via* oscillating pressures in fluid phase (large blood vessels) to the CNS. Or direct interaction with the skull or interaction with the spine. When a blast generated by explosion strikes a living body, part of the shock wave is reflected and another fraction is absorbed becoming a tissue-transmitted shock wave [1], [2]. The transferred kinetic energy causes low-frequency stress waves that accelerate a medium from its resting state, leading to rapid physical movement, displacement, deformation, or rupture of the medium [1], [2]. Thus, a militarily relevant blast injury model should be able to capture and measure these phenomena based on sufficient knowledge of shock wave physics, the characteristics of the injurious environment generated by an explosion, and the clinical manifestations and sequelae of the injuries [3]. The velocity of the wave is thereby reduced so that the main part of the pulse travels with sonic or even subsonic speed and, therefore, it no longer retains the characteristics of a shock wave in the true sense of the word.

The high explosive shock wave in air travels with supersonic speed. Actually, this is a condition to be fulfilled for it to be a real shock wave. Clemedson and Jonsson [6] showed that the velocity of the shock wave impacting on or passing over the surface of the animal varied between 440 and 550 m/sec for the different weights of charge used. When entering the body, the original shock wave is changed through interaction with the inhomogeneous tissue elements causing dispersion, divergence and attenuation. The velocity of the wave is

thereby reduced so that the main part of the pulse travels with sonic or even subsonic speed and, therefore, it no longer retains the characteristics of a shock wave in the true sense of the word. The notation "pressure wave" or "pressure pulse" is used instead. When a shock wave generated by detonating a high-energy explosive strikes a living body, tissues typically respond.

- Either on the impulse of the shock wave − this response is of longer duration.
- On the pressure variations of the shock wave, and this response is in a form of oscillations or pressure deflections of shorter duration [4].
- Different organ and body structures differ in their reaction, for example, in experiments.
- Tissues in the abdomen and costal interspaces (i.e., thoracic organs) react with typical impulse response.
- Whereas the rib and the hind leg responded with a more or less pure maximum pressure type curve [4], [5].

Since the type and extent of the biological response to blast depends on tissue properties, blast injuries are position-dependent – i.e., the pattern, organ distribution, and severity of damage caused by tissue transmitted shock wave depends on the position of the body in relation to the external blast wave [3], [7].

Position-dependence of injury severities:

a) Supine position (facing with torso the incoming shock wave front): the majority of the tissue damage found in respiratory organs, heart, and kidneys.

b) Prone position (facing with back the shock wave front): the majority of the tissue damage found in respiratory organs, liver, and spleen.

The Bezold – Jarisch Reflex:

a) A cardiovascular depressor reflex involving a marked increase in vagal (parasympathetic) efferent discharge to the heart.

b) Elicited by stimulation of chemoreceptors, primarily in the left ventricle.

c) Causing a slowing of the heart beat (bradycardia) and dilatation of the peripheral blood vessels with resulting lowering of the blood pressure.

Juxtacapillary J-Receptors:

a) Located in the alveolar walls and in close contact with the capillaries.

b) Stimulated by hyperinflation of the lungs, accumulation of interstitial fluid in the lung parenchyma (lung edema) and pulmonary capillary engorgement.

c) Impulses travel up the vagus nerve via slowly conducting unmyelinated C-fibers and may induce rapid shallow breathing, and sensation of dyspnoea.

The currently existing body protection modifies but not prevents energy transmission from external shock wave:

a) The large differences in the velocity of the incident shock wave and of the pressure wave in the various thoracic and intrathoracic structures certainly must be of great significance for the relationship between the external pressure field and the resulting distribution patterns of the intrathoracic pressure in an

organism exposed to a shock wave, and consequently, also for the generation of the intrathoracic lesions in blast injury.

b) They may also be one of the reasons, why it has not been possible to demonstrate a pressure wave leaving the body on its rear side.

H.2.7 Models of Complex Blast Injury and Interaction Between Component Systemic Responses, by Dr. Kirkman and Watts, Dstl, Porton Down, United Kingdom

Which components need to be modeled?

a) Shock front:

   i) Blast wave.

   ii) Blast wind, through things and body.

b) Edge of explosive products.

c) Primary: Blast lung – brain injury?

d) Secondary: Penetrating injury, bleeding.

e) Tertiary: Limb avulsions.

f) Rat fall in blood pressure.

g) Effect on respiration center in brain stem.

h) Vagotomi blocks apnea and bradycardia.

i) Bradycardia can be blocked by atropine.

j) Blast modifies the reactions after other injuries.

k) Implications for resuscitation: blast and hypovoleamia: reduced risk of rebleeding. Poor tissue perfusion. Hypoxia. Severe ischemia and chock.

l) Normotensive resuscitation better perfusion.

m) Hypotensive resuscitation acceptable for 1 h and seems to provide a reduced risk for repeated bleeding.

n) Effect on clotting: elevated clotting directly after injury. Persist for at least 1 h. Effect does not persist if there is concomitant shock.

H.2.8 Studies on Pressure Propagation in a Skull Phantom, by Dr. Hassel, FFI, Norway

Dr. Hassel described the work with an *in vitro* model of the human head filled with 37°C water. Cylinder with synaptosomes from rat brain.

Two types of exposures: Pressure measurements after a hit with a hammer/pendulum raised to angle of 45 or 90 degrees or blast experiments with 100 g C4 at a distance of 5 meters.

Outcome measures: LDH release after impact with pendulum, with graded effect. No effect with pendulum set to 45 degrees but LDH release if set to 90 degrees. Ca^{2+} influx?

H.2.9 Biomarkers: Repeated Injury Military Setting and Sports Medicine – Translational Aspects, by Professor Kaj Blennow, Clinical Neurochemistry Lab, Department of Neuroscience and Physiology University of Gothenburg, Sweden

The group has a long experience with studies on Neuropathology of dementia. Found hyperphosphorylated tau and β-amyloid plaques.

Chronic Traumatic Encephalopathy (CTE) was also called a tau pathology, but now have also seen β-plaques. **Military CTE**. Perivascular foci of tau and also in the deep layers of the cortex, distorted axonal retraction and activated microglia where you have tau. Given the similarities with Alzheimer's disease, have a number of biomarkers for CTE.

Total tau – neuronal and axonal degeneration. Phosphorylated or native tau.

Find 300% increase in AD.

Aβ-42 – see a decrease of approx. 50% in AD patients.

Use of biomarkers in TBI, important to:

- Rule out or identify neuronal damage.
- Guide return to duty.
- Study the acute TBI pathobiology.

DAI appears to be a central mechanism of TBI so the tau and β-amyloid biomarkers are top candidates. Marked elevated tau level at even 2 – 3 days post TBI (severe/moderate) correlates to death or poor outcome. A number of studies have been done monitoring the biomarker Neurofilament Light-chain (NFL). See major elevation in many hits vs control 7 – 10 d post-bout in amateur boxers compared to controls. The controls are athletes but swimmers or handball players. CSF markers were sampled over an extended period of time from a boxer after he was knocked out. Although MRI scans showed no change in the brain. The markers sampled were elevated and only normalized after 36 weeks.

The group has performed a controlled study on blast overpressure by sampling biomarkers following firing of heavy weapons. No signs of BBB damage, no NFL, GFAP, S-100β or T-tau change at a number of time points and not even after 100 charges. 42% of military servicemen who had been exposed to a blast had hypopituitarism. How about blood biomarkers which would be easier than CSF. Issue so far has been a sensitive enough technique to detect the small amount of protein that would be present.

Single molecule array, Simoa, is a step-forward. Reactions occur on the surface of a bead and the fluorescence of each bead is measured. Thus it becomes more sensitive than standard assays.

Measured all variants of tau including phosphorylated or not – found Simoa was 1000x more sensitive than ELISA. Started with a disease where they knew there was brain damage and that was cardiac arrest.

Took repeated blood sampling and found an early peak in tau after 12 h, dramatic increase

Ice Hockey players – took blood samples, didn't see the same extreme increase in tau but still appeared to be predictive of severity of injury. NFL levels in TBI GCS less than 8. Seems to elevate from day 0 to day 12.

But normalize after 1 year. Already significant changes are seen at day 1, but best at 10 – 12 days post-TBI. Hence in the military group you have more than 1 week to monitor neuronal damage.

Conclusion: Promising biomarkers for TBI: Serum tau and NFL and for CTE: Aβ-42, t-tau and p-tau.

H.2.10 Animal Models of Blast-Induced TBI, by Dr. Steven Bjarnason DRDC, Suffield Research Centre, Department of National Defence / Government of Canada

Problems with animal model: human relevancy, exposure methodologies are challenging.

Experimental animal models isolate the different mechanical and pressure wave forces produced in an explosion.

- Penetration model. Sweden has a good model.
- Impact-acceleration. Most models use craniotomy and death is not uncommon.
- Primary blast model. Reproducibility of generating the insult.
- Measuring the insult – not all gauges are created equal.
- What are the end points that are critical?

It is a multidisciplinary effort. ICP measurements: use the Millar ICP cather guage, cannot use the signal conditioner that comes with it as it misses things i.e. it misses the peak pressure. Use Vishay which has a large bandwidth condition. Also have a gas driven shock tube. Overpressure, underpressure and a lot of other waves that are not wanted, over time have managed to eliminate some of these. There are gauges spaced all the way along the tube so they can see what is happening throughout the tube. Have also measure both static and dynamic pressures. Have 2 head holding devices: a support and a restraint. But high speed video showed the head was moving a lot. So injuries could not be only due to shock wave. Some results. Glutamine synthetase and AChE differ depending on the head support or restraint.

Dose response 15, 20, 25 and 30 psi.

NFH was sampled at 1 d and 7 d using the head restraint. Found reduction at 7 d in the cortex, which further decreases with the increasing psi.

See decreased in GFAP at 7 d in the cortex (others show it increasing), suggest this decrease is due to the head being restrained.

H.3 DISCUSSION ON RECOMMENDATIONS FOR ANIMAL MODELS

The intended audience for these guidelines are:

- The experimenter in planning stages: to be used almost like a checklist.
- The funding body: to see if the work is well planned.
- Reviewers in journals: if the work is relevant and meaningful.

H.3.1 Aim of the Guidelines

At the highest level trying to advance the science to answer the questions – does being exposed to blast cause injury, how and can we treat it. The many components of an explosion that should not be overlooked and the synergies between these components.

We need eliminate our own bias so that we do not limit the research, i.e. talking about the shock wave and just the shock wave causing an injury.

H.3.2 Rationale for the Use of Multiple Models

A typical blast injury has many aspects such as primary to quaternary and the multiple trauma aspect. These cannot be caught in one model so require many.

Along the line new aspects of the pathology will be detected and will call for new additional directed models to investigate issues.

Hence could include an argument for not selecting the same model.

But need to be able to have cross validation and comparison studies these are critical.

Should encourage collaborations.

H.3.3 Frame as a Difficult Toxicological Problem

In other areas of toxicology these things are just too hard to solve (cube analogy by Steven). But here making some recommendations. Need a multidisciplinary approach. Part of this multidisciplinary approach even if it is on a consultancy basis, should include a clinician to make sure you have some translatability of the research as the ultimate aim is to get to clinical trials.

H.3.4 The Research Group

Need to show that the group has the knowledge, skills, and expertise to address the questions.

H.3.5 Model Validity and Good Experimental Design

Need to show why your model is valid, and a clear articulation and justification for the experiment plan.

- Start with a clearly stated question you wanted to answer.
- What was the rationale for selecting the model you did?
- The model must be a valid model for replicating blast.
- Have recognition that there are limits to your model – so results are not over interpreted.
- Need to ask if these changes you see in the animal model are changes we would see in humans.
- Rationale for using the animal model, the species, weight, gender, age etc. a description of all the things that matter – i.e. 20 kg vs. 60 kg pig is important.
- Expected kinetic, therefore the rationale for choosing specific time-points. Justification of your end points.

- Where are the animals placed in a test field? Rationale for this. In the guide will describe draw backs, or issues with placing an animal in certain areas of the tube.
- Have to give the relevant exposure for the question they are answering, not over or under exposing the animals for the problem they are trying to answer.
- Justification for the use of a certain technique.
- A plan for the statistics, and where possible a power calculation, and estimation of n numbers.

H.3.6 What Do We Mean by a Validated Model?

- Currently either a known input – i.e. biomechanically it replicates the real life situation.
- Or a known outcome i.e. results in the symptomology/pathobiology seen in humans.
- Guidelines for how to report animal experiments for example as stated by PLOS Biology.

H.3.7 Variability

Can never eliminate the variability between labs and experimental models, but can aim to contain it.

- Encourage people to do relevant experiments and to show why their results are valid.
- The value of the finding will be enhanced if findings can be replicated across species – goes back to recommendation to collaborate and use different models.
- Or sharing of tissue, blood, and facilities, to validate your own findings.

H.3.8 If You Have Multiple Blasts

- Still need to prove it is a mild injury: so might include markers for cell death, axonal injury, inflammation and include some general physiology, i.e. don't get the lung injuries that would cause hypoxia in the brain. Might also be looking for outcome measures that would facilitate comparisons across experiments biomarkers might be good for this and for treatment options.
- Where possible, always include parameters to facilitate comparisons across labs, such as cardiac rhythms, biomarkers, general physiology. Describe known physical antagonists, every mediator will have antagonists.
- Can probably state that certain outcome measures are very good for translational purposes such as biomarkers and imagining tools like DTI.

H.4 END OF THIS GUIDELINE DISCUSSION

Should sort out clearance from the beginning of October for next meeting in the United Kingdom.

Final Report: will state clearly this group accomplished what it set out to accomplish, but there are certain tasks that will need to be addressed by a diff group. Agreed the final report should include:

- Meeting summaries and the guidelines as appendices.
- Should also include an executive summary.

- What should and could be done, recommendations, the main points that have to be looked at in the future.
- Exploitation strategy, publications, etc.

H.5 REFERENCES

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Annex I − MINUTES FROM FINAL WORKING MEETING JANUARY 2016

Defence Science and Technology Laboratory, Porton Down, Salisbury, Wiltshire, England 19-21 January 2016

Meeting called by: Michael J. Leggieri	**Date:** 19-21 January 2016
Note taker: Mark Bates Dstl Project Manager	

Attendees:	
Michael Leggieri (ML), Chair	Stephen Bjarnason (SB)
Raj Gupta (RG)	Ibolja Cernak (IC)
Emrys Kirkman (EK)	Dan Bieler (DB)
Sarah Watts (SW)	Marten Risling (MR)
Mat Philippens (MP)	Mark Bates (MGB)

Apologies:	
Hans Orru	Simon Ouellet
Lucie Martineau	Stian Skriudalen
Phillippe May	Axel Franke

Links:

N/A

1	**Minutes from previous meetings** NA	
2	**Actions from previous meetings** NA	
3	**Introduction** The Chair welcomed everyone to the meeting and thanked all contributors for their efforts in supporting the group. All were reminded that this would be the final face-to-face meeting prior to the scheduled completion in July 2016. The main purpose of the meeting would be to review, amend and agree the five group deliverables which are listed below: 1) Guidelines for Conducting Epidemiological Studies of Blast Injury. 2) Guidelines for Reproducing Blast Exposures in the Laboratory. 3) Guidelines for Using Animal Models in Blast Injury Research. 4) Comprehensive Dictionary of Blast Injury Research Terms. 5) Final Report on HFM-234 Activities.	**Actions**

3	**Introduction (cont'd)**	**Actions**
	Action − A request has been made for NATO to confirm the acceptability of the Guideline format RG to follow up and advise on the response.	HFM-234/ 2016-01 **RG**
	RG briefed on the NATO reporting formats and the process for submission.	
	ML Questioned – What level is this sign off?	
	RG Responded – Author or Task group level is required.	
	RG Stated that NATO Form 13-1(E) "Publication Release Form" will require signatures from all contributing nations prior to submission to NATO.	
	Action – Each contributing country is to gain security approval for release, it was agreed that 8 weeks prior to delivery date would be required for clearance signatures, using NATO Form 13-3(E) "Publication release and clearance certificate".	HFM-234/ 2016-02 **ALL**
	ML Questioned – Who should be the "Lead Controller"?	
	All agreed – the Chair and Group should be the primary name but expand to include all contributors.	
	ML Questioned – What should the security classification of the final documents be?	
	All Agreed – where possible the documents should be "suitable for public release".	
	Action – Confirmation to be sought from NATO to confirm this security classification is acceptable.	HFM-234/ 2016-03 **RG**
	Action – The requirement for NATO Form 13-3(E) Para. 4a to be completed is to be confirmed by all members by end of Feb 2016.	HFM-234/ 2016-04 **ALL By 28 Feb 16**
	RG briefed on the Executive summary guidelines for the final report and stated that it should cover the entire HFM-234 deliverables document package to provide a "top level" overview.	
	Question from the floor – Does the HFM-234 group require clearance or permission to publish from NATO in order to publish to a wider audience?	
	Question ML – Has any group member had work published that was carried out on behalf of NATO?	
	Response − No.	
	Action – Formalize the requirement to gain permission to publish from NATO.	HFM-234/ 2016-05 **ML**
	ML stated that he was keen to gain publicity highlighting the group's efforts as it has achieved an important goal in providing documentation to support the understanding of Environmental Toxicology of Blast Exposures: Injury Metrics, Modelling, Methods and Standards.	

4	**Deliverable 1 – Guidelines for Conducting Epidemiological Studies of Blast Injury** RG – Stated that the latest version had been distributed to all group members prior to this meeting for comments which had been included where appropriate. The Guidelines for Conducting Epidemiological Studies of Blast Injury were then reviewed, amended and agreed as final by all members of the meeting.	
5	**Deliverable 2 – Guidelines for Reproducing Blast Exposures in the Laboratory** SB – Introduced the document and highlighted the contributions made by Tyson and Simon. **Action** – Formatting of Deliverable 2 should be carried out using the using the NATO guidance. **Action** – Clarification of engineering terms is to be sought for section Deliverable 2 para 3.3.3 **Action** – Definitions of all "models" are to be added to the dictionary (Deliverable 4) for example "Physical". The Guidelines for Reproducing Blast Exposures in the Laboratory were reviewed, amended and agreed as final by all members of the meeting, subject to inclusion of action points above and final formatting.	HFM-234/ 2016-06 **SB** HFM-234/ 2016-07 **SB/EK** HFM-234/ 2016-08 **IC/EK**
6	**Deliverable 3 − Guidelines for Using Animal Models in Blast Injury Research** Question from the floor – Does this guidance document relate specifically to Air Blast or is it generic? Response – the question was addressed in the process of review and amendment and found to be appropriate for generic use. The Guidelines for Using Animal Models in Blast Injury Research were reviewed, amended and agreed as final by all members of the meeting, subject to inclusion of action points above and final formatting. **Action** – Definitions of all "Mechanisms" are to be added to the dictionary (Deliverable 4) for example "Injury". **Action** – Definition of "Tissue Compartments" is to be added to the dictionary (Deliverable 4). **Action –** Format "Guidelines for Using Animal Models in Blast Injury Research into NATO Template.	HFM-234/ 2016-09 **IC/EK** HFM-234/ 2016-10 **IC/EK** HFM-234/ 2016-11 **SB**

7	**Deliverable 4 − Comprehensive Dictionary of Blast Injury Research Terms** The Comprehensive Dictionary of Blast Injury Research Terms was reviewed, amended and points for clarification identified by members of the group refer to master document "track changes" for current status.	
	Action − Final document to be circulated to all group members for Approval.	HFM-234/ 2016-12 **IC**
	Action – Confirm Axelsson Blast Test Device (BTD).	HFM-234/ 2016-13 **ML/MP**
	Action – Confirm Axelsson Curve formula.	HFM-234/ 2016-14 **MR**
	Action – Confirmation that the terms used within the HFM-234 document set are included in this Dictionary will need to be carried out.	HFM-234/ 2016-15 **EK/SW/EK**
	Action – Write Dictionary introduction and cross refer document with Deliverable 1 to ensure all definitions are captured. Merge Deliverable 2 and 3 definitions into document and deliver to SB for final formatting prior to review.	HFM-234/ 2016-16 **IC** 01/04/16
	Action – Cross refer with Deliverable 2 to ensure all definitions are captured, and supply to IB for integration.	HFM-234/ 2016-17 **SW**
	Action – Cross refer with Deliverable 3 to ensure all definitions are captured, and supply to IB for integration.	HFM-234/ 2016-18 **EK**
	Action – Format "Comprehensive Dictionary of Blast Injury Research Terms" Into NATO Format.	HFM-234/ 2016-19 **SB**
8	**Deliverable 5 − Final Report on HFM-234 Activities**	
	Action – Extract and merge information from Deliverables 1 thru 4 to form the Final report and submit to group for review.	HFM-234/ 2016-20 **EK/SW** 16/04/16
9	**AOB** EK proposed the publication of the outputs from the HFM-234 group in the Journal of the Royal Army Medical Corps, and requested confirmation that it would be acceptable to the group. All group members agreed it was acceptable.	**Actions**

9	ML informed the group that a proposal has been submitted to form a new NATO group covering Computational modelling using a multidisciplinary team, HFM-234 members will be updated accordingly. **Action** – All deliverables are to be finalized by 1 May 2016.	HFM-234/ 2016-21 **ALL** 01/05/16
10	**Date of Next Meeting** N/A HFM-234 is due to complete in July 2016.	

Summary of Actions

Action	Description	Person	Due Date	Complete
HFM-234/ 2016-01	A request has been made for NATO to confirm the acceptability of the Guideline format RG to follow up and advise on the response.	RG		
HFM-234/ 2016-02	Each contributing country is to gain security approval for release, it was agreed that 8 weeks prior to delivery date would be required for clearance signatures, using NATO Form 13-3(E) "Publication release and clearance certificate".	ALL		
HFM-234/ 2016-03	Confirmation to be sought from NATO to confirm "Suitable for public release" security classification is acceptable.	RG		
HFM-234/ 2016-04	The requirement for NATO Form 13-3(E) Para. 4a to be completed is to be confirmed by all members by end of Feb 2016.	All	28/02/16	
HFM-234/ 2016-05	Formalize the requirement to gain permission to publish from NATO.	ML		
HFM-234/ 2016-06	Formatting of Deliverable 2 should be carried out using the using the NATO guidance.	SB		
HFM-234/ 2016-07	Clarification of engineering terms is to be sought for section Deliverable 2 para 3.3.3.	SB/EK		
HFM-234/ 2016-08	Definitions of all "models" are to be added to the dictionary (Deliverable 4) for example "Physical".	IC/EK		
HFM-234/ 2016-09	Definitions of all "Mechanisms" are to be added to the dictionary (Deliverable 4) for example "Injury".	IC/EK		
HFM-234/ 2016-10	Definition of "Tissue Compartments" is to be added to the dictionary (Deliverable 4).	IC/EK		

Summary of Actions				
Action	**Action**	**Action**	**Action**	**Action**
HFM-234/ 2016-11	Format “Guidelines for Using Animal Models in Blast Injury Research into NATO Template.	SW/SB	SW 31/01/16 SB 29/02/16	
HFM-234 /2016-12	Deliverable 4 Final document to be circulated to all group members for Approval.	IC		
HFM-234/ 2016-13	Confirm Axelsson Blast Test Device (BTD).	ML/MP		
HFM-234/ 2016-14	Confirm Axelsson Curve formula.	MR		
HFM-234/ 2016-15	Confirmation that the terms used within the HFM-234 document set are included in this Dictionary will need to be carried out.	EK/SW/EK		
HFM-234/ 2016-16	Write Dictionary introduction and cross refer document with Deliverable 1 to ensure all definitions are captured. Merge Deliverable 2 and 3 definitions into document and deliver to SB for final formatting prior to review.	IC	01/04/16	
HFM-234/ 2016-17	Cross refer with Deliverable 2 to ensure all definitions are captured, and supply to IB for integration.	SW		
HFM-234/ 2016-18	Cross refer with Deliverable 3 to ensure all definitions are captured, and supply to IB for integration.	EK		
HFM-234/ 2016-19	Format “Comprehensive Dictionary of Blast Injury Research Terms” Into NATO Format.	SB		
HFM-234/ 2016-20	Extract and merge information from Deliverables 1 thru 4 to form the Final report and submit to group for review.	EK/SW	16/04/16	
HFM-234/ 2016-21	All deliverables are to be finalized by 1 May 2016.	ALL	01/05/16	

Annex J − GUIDELINES FOR USING ANIMAL MODELS IN BLAST INJURY RESEARCH

J.1 INTRODUCTION

The discussions at the NATO Human Factors and Medicine (HFM) Symposium (SYM) HFM-207 revealed the importance of a systematic approach to understanding blast injuries, much like the well-established approach used to solve the classical toxicology problem where the etiology of the injury requires an understanding of the dose, mechanism of delivery of the dosage, and dose-response endpoints. Also recognized was the pressing need for a multidisciplinary approach to addressing non-penetrating blast injuries to the brain that result in a host of symptoms with vague etiology. In addition, the Technical Evaluation Report from HFM-207 (SYM), "A Survey of Blast Injuries across the Full Landscape of Military Science" [3] emphasized the continued multinational exchanges of scientific and technical advances needed to respond to blast threat and blast injuries. The first recommendation identified a future need for a recurring technical exchange venue on blast injury and its mitigation to address advances in medicine and personal protection and their synergy. The second recommendation highlighted the need to explore the concept of "the Toxicology of Blast Injury" and suggested to focus on several difficult problems including:

1) Relevancy and commonality of animal models.
2) Common dose-response methods.
3) Route of exposure methods.
4) Computational Models (blast, physiology, biochemical, toxicological, etc.).
5) Dose regimens to mimic/replicate human medical endpoints (spectrum of surgical trauma to mild traumatic brain injury).
6) Methods for translational research leading to medical products and/or physical protection products.

To address the above recommendation and to develop a specific NATO activity devoted to the toxicology of blast exposure, a proposal titled "Environmental Toxicology of Blast Exposures: Injury Metrics, Modeling, Methods and Standards" was approved which resulted in the establishment of a NATO HFM Research Task Group (RTG) HFM-234 with the following deliverables:

- Guidelines for Conducting Epidemiological Studies of Blast Injury.
- Guidelines for Reproducing Blast Exposures in the Laboratory.
- Guidelines for Using Animal Models in s Blast Injury Research.
- Dictionary of Blast Injury Terms.
- Final report on HFM-234 (RTG) activities.

These guidelines provide principles that should be considered when planning, executing, and reporting animal experiments for blast injury. It is not the intention of these guidelines to provide specific recommendations for experimental setups but rather to highlight specific principles to be considered when using animal models in blast injury research. Adherence to these principles will ensure that the experimental design will result in replication of human exposures, producing the pathology or pathophysiology seen in human injuries following blast exposure, and incorporation of measures that facilitate translation. Monitoring and reporting the physical properties of the exposure, physiological changes, and pathology will enable replication of experiments by other

laboratories. Clear definitions of essential experimental conditions and adherence to consensus about their utilization will also provide a platform for successful translation of experimental findings into clinical settings. Clearly stated, the objectives of this document are:

a) To raise awareness with regards to the complexities and pitfalls of blast injury research.

b) To standardize and promote good research practices.

c) To help the community to generate valid and comparable results.

d) To increase the quality of publications in this field of research.

It is the intention of the HFM-234 (RTG) that these guidelines be used in concert with the companion comprehensive "Dictionary of Blast Injury Research Terms" developed by the NATO HFM-234 (RTG). These guidelines and the Dictionary can be used in conjunction to guide research methods and reporting in the field of experimental blast injury research.

J.1.1 Overview of Main Challenges that Impact on Blast Injury Modelling in Living Systems

There are many challenges that impact blast injury modelling in living systems. Blast injury is highly complex and is influenced by a number of factors including the physical loading resulting in tissue injury; initial biological response; secondary 'spill-over' of effect from other organ systems; secondary influence of other pathophysiological responses; impact of treatments; sequelae such as long-term inflammation; and poorly understood consequences such as Posttraumatic Stress Disorder (PTSD).

The physical loads are complex and comprise multiple elements with varying time-course from ultra-short (micro to few milliseconds, e.g., shock wave) to short (few to hundreds/thousands of milliseconds, e.g., body acceleration/movement and blast wave). When animals of varying sizes are used as surrogates for human casualties, scaling issues for physical loading and responses become important.

The initial biological response in affected tissue depends on local molecular responses that can vary between species. Additional biological responses may result from secondary 'spill-over' such as inflammation from organs directly injured from the blast to other organs; and other injury modalities such as hypoxia or hypoperfusion.

Blast injury is a very complex phenomenon. In any particular organ, the final injury depends on the initial trauma (caused by the physical loading), which is then modified by both the response to other injury modalities (as above) and by the effects of medical treatment focused on these secondary modalities.

There are large variations in the ability of particular models (species) to express sequelae, such as, long-term inflammation, as well as, poorly understood conditions like PTSD, presenting challenges in assessing consequences in relation to features of interest in human casualties.

Blast induced injury may result in multiple injuries and it may not be possible to recreate all injury types in one model. It is therefore unlikely that any single model will address all of the effects seen in human casualties. Each model will have strengths, weaknesses, and limitations. Results and conclusions of studies using animal models must therefore be discussed in light of the strengths, weaknesses, and limitations, with clear recommendations as to which elements of the conclusions are valid for the human condition, together with the boundaries and limitations of the interpretation. Multiple models will therefore be required, allowing triangulation of results to ensure appropriate translation of results.

J.2 BACKGROUND

Blast injuries are often the result of a complex propagation of forces in different directions. The duration of these forces is usually very short, while its magnitude is very abrupt and it can therefore be difficult to analyze the mechanisms for injury. The importance and thresholds for different biological injury mechanisms is still poorly understood. Injury parameters (e.g., diffuse axonal injury or vascular leakage) at the tissue level are different for different external loading mechanisms (i.e., blast, blunt, and ballistics). Important parameters for the medical outcome, not only depend on the loading and injury mechanisms of the injury, but can be affected by age, tissue properties (e.g., elasticity), gender, and other genetic variables. The shape and size of different tissue compartments can be assumed to represent factors that determine the loading when energy is dissipated during a fraction of a second. Such energy dissipation during the acute phase of injury can initiate secondary biochemical cascades that can lead to chronic injury and a variety of medical outcomes.

Animal experiments are one method to examine and evaluate injury mechanisms in a more controlled manner, allowing variables such as primary or secondary blast injury for example, to be isolated and manipulated as required. In addition, animal experiments may be required to evaluate novel treatment strategies or protection systems. Fundamental to the translation between animal experiments and clinical practice is good experimental design and use of appropriate animal models. However, new candidates for pharmacological treatment after trauma have usually been difficult to translate from animal studies into successful clinical studies. The reason for such failures may be due to mistakes in the experimental design and not considering the translation aspects of the study from the start.

Animal experiments provide possibilities to separate the various loading mechanisms using separate, well-defined models for individual types of energy transfer and loading modes. For example, it is possible to isolate a primary blast loading mechanism or a particular injury (such as lung injury) in an animal model. This is useful in identifying and understanding the effects of specific loading on the pathophysiology of injuries. Animal experiments can control age, gender, and other genetic parameters. Physiology can be monitored, and it is possible to manipulate oxygen saturation for example, to evaluate the effect of hypoxia.

J.3 REQUIREMENTS FOR CONDUCTING ANIMAL EXPERIMENTS FOR BLAST INJURY

This document provides guidance that should be considered when planning, executing, and reporting animal experiments for blast injury. Specific recommendations for experimental setups are not provided. However researchers should be cognizant that the experiments must be validated to produce the pathology or pathophysiology that they are supposed to replicate. In addition, measures that facilitate translation should be a fundamental part of each experiment. Physical properties of the exposure [1], physiological changes, and pathology should be monitored and reported in a way that enables replication of experiments by other scientists, and can provide a platform for translation into clinical settings. Clear definitions of essential experimental conditions and adherence to consensus about their utilization will also provide a platform for successful translation of experimental findings into clinical settings.

J.3.1 Validation of Animal Models

Validation is a critically important aspect of animal models:

- The model should generate the injury or a component of the injury that it is supposed to model. Thus, the model is an accurate representation of the real life injury.

- The injury mechanism should, in most cases, be the same as in human injuries or diseases, but there might be exceptions to this rule.

Validation of animal models is difficult if the pathology of the human injury is not clearly defined. For example, due to the complexity of the blast environment and its interactions with the human body, the similarities and differences between the mechanisms underlying mild traumatic brain injury and PTSD are still under debate, they could still arise from variable pathology. In such complicated pathological conditions, the model could be validated to replicate a specific component of either a cause or process of the impairment. For example, when focusing on pathologies caused by primary blast only, care must be taken to be explicit about the focus to avoid over-interpretation of the findings by those reading the report.

J.3.2 Dose-Response Relationships

Regardless of the research questions to be addressed, the criteria elements every clinically and militarily relevant blast injury model should fulfill are the following:

1) The injurious component of the blast should be clearly identified and reproduced in a controlled, reproducible, and quantifiable manner.
2) The inflicted injury should be reproducible, quantifiable, and mimic components of human blast injury.
3) The injury outcome established based on morphological, physiological, biochemical, and/or behavioral parameters should be related to the chosen injurious component of the blast.
4) The mechanical properties (intensity, complexity of blast signature, and/or its duration) of the injurious factor should predict the outcome severity.

Fulfilling the above-listed criteria, it becomes clear that dose-response curves can be an important part of validation of a new model. Namely, the dose-response curves establishing a relationship, which implies that with the increasing intensity of the blast exposure the biological responses will also be more pronounced and the pathological consequences more severe.

Moreover, dose-response studies are necessary for threshold and saturation values, where the aim is to identify the intensity, type, and number of blast exposures that are tolerated by the human body without any, acute and/or chronic pathological (physical, physiological, and/or psychological) consequences.

The widely-used Bowen curves [2] provide a visualization of a complex dose-response relationship between the intensity of primary blast, represented by both the positive peak pressure and positive pulse duration, and biological response/outcome presented both as thresholds for lung injury and lethality. While the Bowen curves that have been characterized for twelve different species (including humans) provide an excellent framework for experiments analyzing the relationship between primary blast exposure(s) and tissue/organ damage, their usefulness is limited for chronic biological or psychological outcomes. Moreover, besides primary blast, the Bowen curves do not include other blast effects (secondary, tertiary, quaternary, etc.). Thus, new dose-response curves are needed, based on appropriate scaling laws that would establish the relationship between individual blast components and biological/psychological outcome measures, while taking into account the size, composition, and geometry of the exposed body and/or organ.

J.3.2.1 Rationale for the Use of Multiple Models

An explosion results in a range of injury patterns that can be very complex, from minor injury to multiple injuries, i.e., polytrauma. This cannot be represented by one model so several different models may be required.

With changes in threat, Personal Protective Equipment (PPE), etc., new injury patterns may emerge that will require additional directed models to address these changes.

J.3.2.2 The Research Group

The complexity of blast injuries requires a multi-disciplinary, and possibly multi-national, collaboration between blast physicists, biomedical researchers, clinicians, and computational modelers, for example. The research group must have the appropriate capability, knowledge, skills, and expertise to address the proposed research questions.

J.3.2.3 Experimental Design

Good experimental design is key for any research, and animal research is no different, hence there needs to be a clear articulation and justification of the experimental design, methodology, and research plan. This should include a statistical plan and power calculation for example, so that an estimation of sample size is identified. Below is a list of considerations (it is not intended to be exhaustive).

J.3.2.3.1 Aim of the Experiment

The aim of the experiment(s) must be clearly stated in the context of the problem that it is intending to address.

J.3.2.3.2 Hypothesis to Be Tested

The hypothesis that will be tested must be stated as this may influence the research best practices needed to address the hypothesis.

J.3.2.3.3 How the Experiment(s) Answers the Hypothesis

How the experiment(s) supports/verifies the hypothesis must be clearly stated. Any assumptions made must also be specified. It is important that this is addressed to ensure that the experimental methods used are appropriate with respect to the hypothesis posed.

J.3.2.3.4 How the Experiment(s) Relates to Real World Operational Conditions

The relationship between the experimental and operational conditions must be clearly articulated. This increases the impact of the research by making a direct link for the operational community such that evidence-based decisions can be made affecting protection, prevention, and treatment. If this link is tenuous, as may be the case in fundamental research where a mechanistic or fundamental question is being addressed, then this must be explained, including possible future implications/impact.

Experiments that do not address the relationship between experimental and real world operational conditions and result in research using an unrealistic exposure/response regime can lead to confusion in the community. In this case, if the experiment is to proceed, the limitations must be clearly accounted for.

J.3.2.3.5 Choice of Experimental Model

There are several key steps in the process of choosing a model for blast research. Most importantly, the researcher should identify which of the blast effects should be reproduced. If the choice is primary blast effects, the experimenter should ensure the animals are protected from blunt and/or penetrating injuries caused

by particles generated during exposure to blast, i.e., thus preventing secondary blast-effects induced pathologies. Similarly, if the research question focuses on pathological changes caused by primary blast, any acceleration/ deceleration of the body or body parts needs to be prevented by the animal's restrain. Namely, in a situation where the body/or body part is allowed to move, the injury mechanisms would involve both primary and tertiary blast effects, this would make the interpretation of the results difficult.

The type of the blast effect that is the focus of the research study, guides the choice of the experimental environment. Experimental studies on primary blast-induced biological responses are performed either in a free-field or laboratory conditions. The free-field exposure studies use animals exposed to a blast wave that is generated by detonation of an explosive. Although such an experimental setting is more comparable with operational conditions, the physical characteristics (such as homogeneity of the blast wave) are less controllable, so a broader range of biologic responses should be expected.

Experiments performed in laboratory conditions use either shock tubes (which use compressed air or gas to generate a shock wave) or blast tubes (which use explosive charges). Both of these tubes generate the blast wave energy that travels in a linear direction from the source to the subject. Although shock/blast tubes are convenient means of generating shock waves, they lack the ability to generate the acoustic, thermal, optical, and electromagnetic components found in actual blast environments.

For a more in depth discussion of blast exposure methodologies in the laboratory see NATO HFM-234 "Guidelines for Reproducing Blast Exposures in the Laboratory", 2016, Neuilly-sur-Seine, France [1].

J.3.2.3.6 Exposure Conditions

Exposure conditions include both exposure level and positioning of the animal target.

A rationale for the selection of exposure level(s) must be provided. This is important to provide the reader/ reviewer with an understanding of the potential relationship between the exposure and the response. This is especially important if the research is aimed at inflicting an injury or at evaluating the potential of injury at a given exposure. There may be scaling implications and, if so, they must be explained.

a) Position of animal:

   Special consideration should be given to positioning of the animal in the shock/blast tubes, and its orientation in relation to the incident shock wave. There is an ongoing debate about whether the specimen should be positioned inside or outside shock/blast tubes. Namely, the biomechanical response of the animal significantly depends on the placement location in the tube, as well as, on the orientation of the specimen as compared with the propagating incident shock wave. The majority of the currently existing literature supports placing the specimen inside the shock/blast tube. Experimental studies have shown that when the animal is positioned inside the shock tube, it is subjected to a load that is due to the pure blast wave comparable to the shock wave generated in free-field conditions (near-optimal, so-called Friedlander-type shock wave). When the animal was positioned at the exit, there was a sharp decay in pressure after the initial shock front, which was caused by the expansion wave from the exit of the shock tube, eliminating the exponentially decaying blast wave. This phenomenon led to a significant decrease in the positive blast impulse and conversion of most of the blast energy from supersonic blast wave to subsonic jet wind, which has effects that are significantly different from those generated by a blast wave. Namely, because of the jet wind, the restrained animal experiences more severe compression of the head and neck and the thoracic cavity is exposed to higher pressure of longer positive-phase duration. Moreover, the subsonic jet wind represents the bulk of the blast impulse, and the injuries are

caused by the combination of blast wave and subsonic jet wind, as opposed to a pure blast wave injury. There is also a possibility that the environment inside a shock/blast tube induces artificially enhanced injuries because of reflected shock waves and rarefaction waves; thus, exposure of animals to shock waves in a shock/blast tube might cause severe, rare, and complex blast injuries, which are not comparable to injuries acquired in real-life, free-field blast conditions.

b) Orientation to blast way front:

Prone position with head and body oriented along the direction of shock wave propagation (perpendicular to the shock front) is the most commonly used orientation in current rodent model studies with shock tubes. However, although this position is natural for quadrupeds, it does not reproduce the most frequent human scenario when the soldiers are in an upright position and facing with torso toward the front of an incoming shock wave. It has been shown, that both the pattern and severity of organ damage caused by blast, depends on the orientation of the body toward the shock wave front. The lung seems to be the most vulnerable organ to the effects of blast across injury severity and in both prone and supine body positions. Similarly, blast severity appears to be positively correlated with lesion frequency and severity in both prone and supine positions. A supine position is also associated with more severe findings in the heart, such as dilation of ventricles and atria, on the right more than the left. In contrast to lung injuries, a prone position causes more severe liver pathology, such as congestion, mottling, and white discoloration adjacent to apparently hemorrhagic sites, compared with supine positioning. In the prone, but not the supine position, there was some association between blast severity and liver infarct rate. The prone position is linked to more damage in the kidneys and spleen. Similarly, cognitive and behavioral responses to blast exposure in animals, is also dependent on the orientation of the animal.

c) Animal Holder:

The choice of the animal holder is another important component in shock/blast tube experiments. Namely, if the animal is fixed on a solid platform, the waves reflecting from it will amplify the primary shock wave and increase the complexity and severity of resulting blast injuries. Furthermore, a bulky animal holder when placed inside the tube could obstruct the central flow of the shock wave propagating along the driven section.

J.3.2.3.7 Species Selection

Next, a decision should be made about the biological complexity of the research study. This factor will dictate the choice of the biological surrogate used to reproduce blast-induced pathologies seen in humans (e.g., cell culture, tissue, small or large experimental animals, nonhuman primates); positioning of the biological surrogates; means of generating a shock wave (free- field, shock/blast tubes); and length of the experiment, among others. Thus, based on the research question and the scale of complexity, a choice is made between non-biological and biological models. The end-points must be translatable to the clinical question being addressed.

Non-biological models such as in silico and surrogate physical models provide an experimental platform for analyzing interactions between blast loading and different types of materials; the obtained information then is extrapolated to biological materials at different levels of scaling. The biofidelic computer (i.e., in silico) models provide spatially and temporally resolved descriptions of stress, strain, and acceleration that blast waves generate; as such, they are helpful tools in characterizing the physics of the blast-induced mechanical changes of the target organ/system. The physical surrogate models use a human surrogate torso or head, which are made from synthetic materials (such as glass/epoxy/polyurethane) with biofidelic properties and incorporate multiple displacement and pressure sensors molded into the organs systems material to record the biomechanical parameters such as linear/angular acceleration, velocity, displacement, force, torque, and pressure.

The non-biological models can be valuable in identifying blast-induced biomechanical alterations and suggest potential consequences in biological systems. Nevertheless, they are unable to give explanations for functional and physiological changes in a living system caused by blast exposure. Hence the need for biological (in vitro, ex vivo, and in vivo) models, which use biological systems of differing complexity. The in vitro models use cell cultures and can be helpful in characterizing the cell-response mechanisms to blast loading in a highly controlled experimental environment. The ex vivo models use an organ or a segment of a specific tissue, such as brain or spinal cord, taken outside the organism into an artificial environment, which is more controlled than is possible with in vivo experiments. As for all blast injury models, applying operationally relevant loading histories is critical for both the in vitro and ex vivo models. Namely, mechanisms of the energy transfer to the tissue and the resultant biological response can be reliably analyzed only when blast-loading conditions are realistic and would happen at the cellular or tissue level of an individual who had been exposed to and survived in operational conditions.

The success of a research study using biological models, especially at the whole-animal level, depends on rigorous selection of animal species used as experimental models. Following the definition of the research question, several factors are essential in deciding which animal species will be used in the study:

1) Similar physiological responses to blast;
2) Similar anatomical properties as compared to humans; and
3) Research feasibility and limitations.

Rodents are the most frequently used experimental animals in trauma research. The relatively small size and low cost of rodents permit repetitive measurements of morphological, biochemical, cellular, and behavioral parameters that require relatively large numbers of animals; this, because of ethical, technical, and/or financial limitations, is less achievable in phylogenetically higher species.

Nevertheless, the anatomical and physiological differences between humans and rodents, especially in the circulatory and nervous systems, limit the utilization of small experimental animals in blast injury research. Thus, when the research study focuses on the response mechanisms of those organs and organ systems, the physiological and anatomical similarities play an important role in choosing the animal species.

It is important to discuss the limitations of the model and the implications for research translation to clinical applications so that results are not misinterpreted.

J.3.2.3.8 Data Collection

Animal model target monitoring can be physiological and mechanical. See NATO HFM-234 “Guidelines for Reproducing Blast Exposures in the Laboratory”, 2016, Neuilly-sur-Seine, France regarding reproducing blast exposures in the laboratory that addressed mechanical monitoring, this sub-section will focus on physiological response monitoring.

Due to the diversity of experiments needed it is not possible to provide a comprehensive list of parameters to be measured and the exact data collected will depend on the actual research question. The choice of data collected and omitted will need to be described and justified (see Appendix J1). Below is a suggested list not all inclusive of parameters that should be considered and/or measured:

- The parameters being recorded must be described.
- The method of data collection must be described. For example frequency of response of transducers is also relevant here and the frequency of sampling must be appropriate to the parameter being assessed.

- Time-courses for the same processes are different in different species and so choice of sampling timing should be justified.
- Post-experimental analyses must be described.

J.3.2.3.9 Experimental Variability

Variability between laboratories is inevitable and cannot be fully eliminated; however, efforts should be made to limit the impact. Some of the reasons for the variability may be derived from inappropriate measuring, monitoring, and reporting of crucial parameters in the experiment. Also unknown genetic differences between different animal populations may be of fundamental importance for the outcome of the experiment. For example, Sprague Dawley rats from different breeders may exhibit large variations in physiological response to injury. Reducing or explaining the variability can be achieved by measuring as many critical parameters as possible, and controlling the animal species across laboratories. The value of the findings will be enhanced if findings can be replicated across species. Sharing of tissue, blood, and facilities, can be used as a tool to validate findings.

J.4 CONCLUSION

Animal experiments can sometimes generate valuable data from small populations. Carefully designed animal experiments may reduce variability in the outcome, for example, genetic variation may be limited by using animals such as, inbred rodents. The age, gender, and size of the animals can also be controlled. However, such methodological decisions may also reduce the applicability of the study. Rigorously controlling the exposure parameters may also reduce variability and the need for large numbers of animals. Some consequences of blast-induced injuries may be difficult to study in animal models. However appropriately designed animal experiments will enhance the state of the science.

J.5 REFERENCES

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Appendix J1: CHECKLIST FOR EXPERIMENTAL DESIGN

1) Start with a clearly stated question you wanted to answer.

2) What was the rationale for selecting the model you did?

3) The model must be a valid model for the question.

4) What parameters will be measured (both biomechanical and biological) and how are they related to real-life conditions or other published work?

5) Can you vary the parameters accurately within field-relevant range, so you can examine the range of observed injuries?

6) Have recognition that there are limits to your model – so results are not over interpreted.

7) Need to ask if these changes you see in the animal model, are changes we would see in humans.

8) Rationale for using the animal model, the species, weight, gender, age, etc., a description of all the things that matter – i.e. 20 versus 60 kilogram pig is important as well as how firmly they are fixed.

9) Expected kinetic, therefore the rationale for choosing specific time-points. Justification of your end points. This may be species specific?

10) Where are the animals placed in a test field? Show clearly in a diagram with respect to loading source. Rationale for this. In the guide will describe draw backs, or issues with placing an animal in certain areas of the tube.

11) Have to give the relevant exposure for the question they are answering, not over or under exposing the animals for the problem they are trying to answer.

12) Can you relate observed pathophysiological changes as a function of external loading and different time points?

13) Justification for the use of a certain technique – for example use of explosives instead of compressed gas for primary blast experiments.

14) Justify the specific placement and binding of the animal in the experimental model through direct pressure, acceleration, and strain measurements on the animal or animal surrogates.

15) A plan for the statistics, and where possible a power calculation, and estimation of *n* numbers.

16) Can rodents be used or would gyrencephalic species, such as ferrets or pigs be needed?

17) Will the skull thickness, head shape and orientation of the animals affect the result when translated to an erect human with face forward to blast?

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14. Abstract

Explosions are one of the most significant sources of casualties in recent NATO operations. The complexity of physical trauma resulting from direct or indirect exposure to an explosion has challenged medical practitioners across the spectrum of disciplines from surgery to mental health. Epidemiological studies are critical to understanding the mechanisms of injury caused by explosions, the response of an individual to a blast event, as well as, the long-term effects of blast exposure. The NATO Health Factors and Medicine (HFM) Research Task Group (RTG) HFM-234 titled "Environmental Toxicology of Blast Exposures: Injury Metrics, Modelling, Methods and Standards" developed a dictionary of blast injury terms, and guidelines for conducting epidemiological studies, reproducing blast exposures in the laboratory, and using animal models in blast injury research. It is the intention of the HFM-234 (RTG) that these guidelines be used in concert with the companion dictionary to guide research methods and reporting in the field of experimental blast injury research.

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