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PRINCIPAL INVESTIGATOR: Dr. Joseph Long

CONTRACTING ORGANIZATION: The Geneva Foundation

Tacoma, WA 98402

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14. ABSTRACT Enter a brief (approximately 200 words) unclassified summary of the most significant findings during the research period. With widespread use of improvised explosive devices and increased survivability due to advances in body armor, blast-induced TBI (bTBI) has emerged as a key military medical issue. In particular, the tremendous recent incidence of mild TBI in combat casualties has triggered several interrelated concerns, including establishment of means to improve mitigation and increase TBI resilience. These improvements are anticipated to hasten safe return-to-duty and minimize long-term and delayed TBI-related debilitations in returning veterans. This objective requires the utilization of high fidelity animal models to investigate the underlying neurobiological mechanisms of injury as a rational basis for establishing effective countermeasures. The etiology of bTBI is largely undefined, and several mechanisms, likely interactive, have been proposed. Using a well-validated blast model, we plan to focus on blast-induced acceleration of the head as one of the primary components of bTBI and establish the extent to which it contributes to the pathophysiology and functional impairments resulting from BOP exposure.					
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INTRODUCTION

The prevalence of blast-induced TBI (bTBI) has prompted an urgent need to develop improved mitigation strategies and advance medical care targeting casualties with bTBI. Despite considerable effort and a broadened interest in the study of mild TBI of all causes, the basic mechanisms of blast induced brain injury are for the most part still undefined. Based largely upon computational modeling, several candidate mechanisms of non-impact blast TBI have been identified and include head acceleration. Animal models are now clearly required to verify and validate these models, to identify the underlying neurobiological events resulting in injury, and to establish effective countermeasures. Examination of each of these proposed mechanisms requires shock wave exposure conditions and specimen targets that are appropriate for the question being asked. We believe that the rat can be employed in a laboratory simulation of blast in a manner that directly addresses the role of acceleration as a critical component of bTBI.

We hypothesize that explosion flow conditions can cause head acceleration sufficient to injure the brain, and that these inertial forces combine with other injury mechanisms to yield blast TBI. Using a highly characterized shock tube simulation of blast, rats will be exposed to BOP with varied peak amplitudes and impulse in association with systematically varied acceleration of head and torso. Comparison of resultant intracranial pressure responses, along with neuropathological, neurochemical, and neurobehavioral consequences of blast exposures under these conditions will provide a basis for determination and quantitation of the relative contribution of these components of blast to bTBI.

BODY

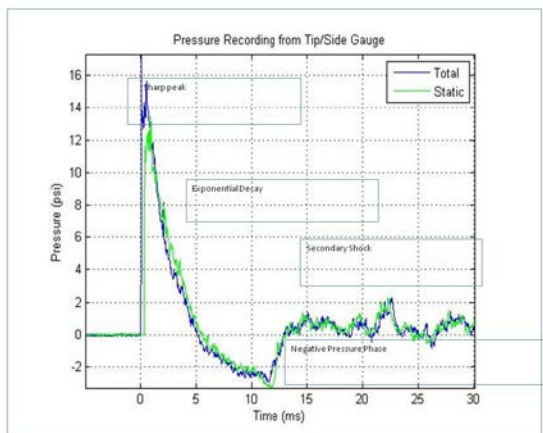
The primary innovation of this project is the development and utilization of a high fidelity simulation of blast flow conditions that are possible through close consultation with blast physics experts who will be actively involved in this project. We will strive to replicate all key features of blast flow wave conditions, including the negative phase and secondary shock. Tight control of these components (notably acceleration and displacement) in combination with functional outcome measures will greatly enhance our understanding of the relation of the former to the latter. As the use of shock tubes has greatly expanded in recent years for biomedical research and TBI research in particular, it is critical that these experimental devices be used in a manner that most effectively simulates explosive blast conditions, recognizing that creating an injury does not constitute validation of an injury model. An explosive shockwave is unlike any other conventional mode of loading and will impart both an abrupt transient crushing action (i.e. static pressure) which envelops the head as well as some aerodynamic drag (i.e. dynamic pressure creating blast wind). The use of animal models to investigate blast-induced neurotrauma requires appreciation of the relative biomechanics and scaling; it is essential to replicate the proper incident blast conditions to assess brain injury mechanisms. Controversies and confusion concerning the contributions of blast-induced head acceleration to blast-induced TBI have in great part resulted from laboratory studies in which blast was inappropriately simulated, and head acceleration was likely in many cases an experimental artefact uniquely associated with those particular exposure conditions. In particular, positioning experimental subjects at or near the mouth of the shock tube exposes them to endjet conditions; practically all flow energy is converted to a collimated jet at the shock tube exit, yielding extreme dynamic pressure and negligible static pressure as end wave rarefaction abruptly reduces static pressure and greatly accelerates flow. In addition, cylindrical shock tubes characteristically produce shock waves with flat tops and greater duration positive phases, which will yield unscaled drag forces greatly exceeding those occurring with an explosion in the free field (Fig 1). Discerning the loading conditions and role of acceleration in blast-

induced TBI requires careful monitoring and validation of the fidelity of the experimental model; as noted, creation of an injury does not constitute validation of an injury model.

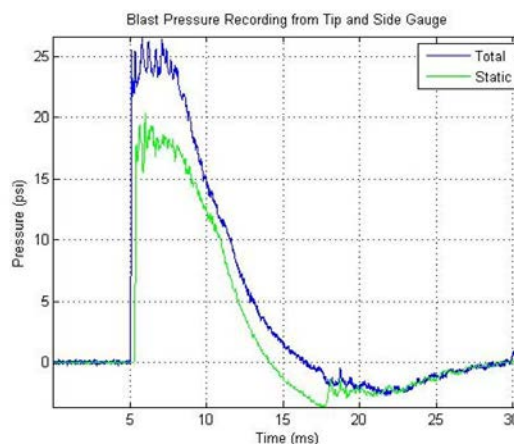
We anticipate these experiments using an advanced blast simulator (ABS), will yield a higher fidelity, ecologically valid simulation of blast and will provide critical insights into the etiology of bTBI that will

Fig. 1. Pressure recordings from the (A) ABS, (B) cylindrical shock tube, 2.5 ft within the mouth of the tube, and (C) cylindrical tube, at the mouth of the tube. Note the high fidelity Friedlander waveform in A, the much greater differences between total and static pressures in B & C, the flat top and long positive phase duration in B, and the greatly exaggerated dynamic pressure impulse in C.

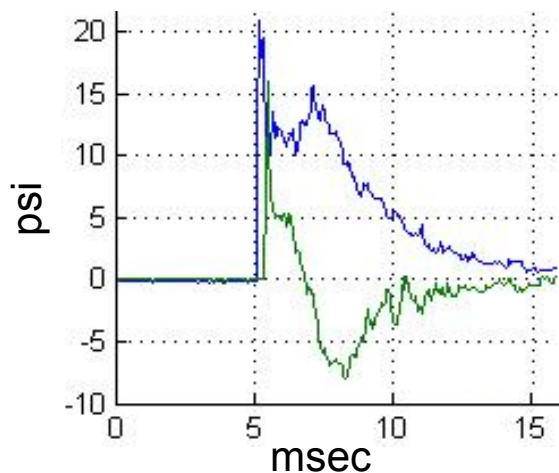
A. ABS test section



B. Inside cylindrical tube



C. Immediately outside cylindrical tube



serve to guide the rational development of mitigation measures and further elucidate pathophysiological mechanisms that can be therapeutically targeted.

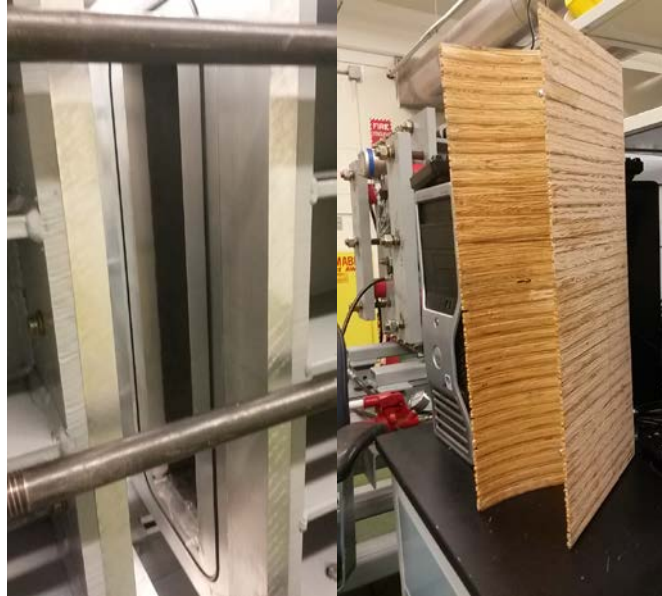
The project is being approached in 3 stages. In the first, along with other inanimate objects an adult-size and weight surrogate rat is used to record acceleration and displacement and establish the shock tube parameters required to optimally and independently manipulate pressure conditions (i.e. peak pressure and impulse) and acceleration and displacement. In the second stage, under these well-defined exposure conditions, anesthetized rats

are used to simultaneously record intracranial pressure (ICP), intravascular pressure, and acceleration/displacement of the head and trunk. Acutely collected brain and blood samples are used to investigate the neurobiological underpinnings of the brain injuries resulting from these blast conditions. In the third stage, rats subjected to each of these exposure conditions undergo neurobehavioral and histopathological assessments to comprehensively characterize the resultant injuries and functional impairments.

Task 1. Using rat surrogates in a 24 in diameter advanced blast simulator (ABS), determine the exposure parameters required to optimally and independently manipulate pressure conditions (i.e. peak pressure and impulse) and acceleration and displacement. Establish 12 exposure conditions (including controls) that will be used to systematically pair BOP peak pressure/impulse (3 intensities) and acceleration/displacement (3 intensities).

During this reporting period, a number of characterization and range-finding experiments were conducted with the ABS to define the optimal means to create and monitor varied flow conditions and to explore unrestrained displacement and acceleration of test specimens under these varied flow conditions. After trials with varied membrane materials, we selected acetate sandwiched between sheets of nylon mesh (Fenceguard) as the optimal frangible material to separate driver and test sections. In addition to varying membrane thicknesses to generate waveforms of different peak positive pressures, time pressure tracings using compressed air and helium were compared and a shaped form (Fig 2) inserted into the driver (to reduce driver length) were evaluated as means to generate shortened waveforms.

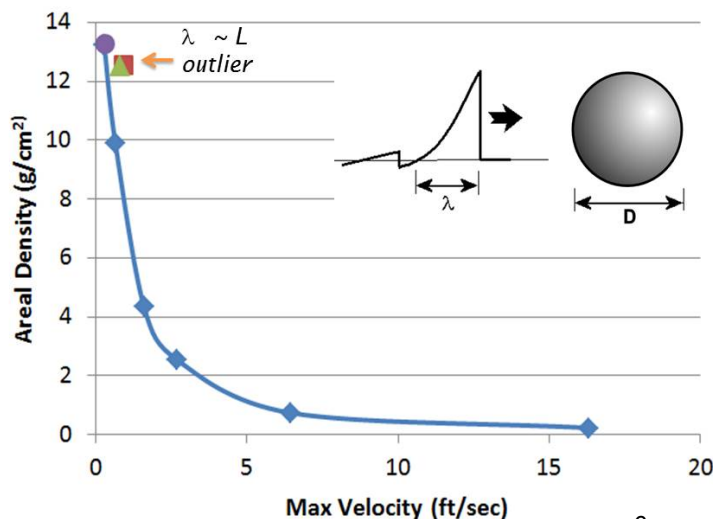
Fig 2. ABS driver (left) and form used to reduce wave duration (right).



As a first step toward understanding the head motion of soldiers exposed to a typical IED blast (<10msec positive phase duration), high speed video recording was utilized to record the motion imparted by the passage of an air shockwave in the ABS to various inanimate spherical objects of different areal densities and to an articulated body, represented by a 1 ft tall wooden artist manikin of a human form. Test objects were carefully suspended in the test section of the ABS by a thread which immediately detached upon arrival of the shock front. Spheres ranged in size from 0.75" diameter steel ball-bearings to a 10" Synbone headform ballasted by water to

imparted by the passage of an air shockwave in the ABS to various inanimate spherical objects of different areal densities and to an articulated body, represented by a 1 ft tall wooden artist manikin of a human form. Test objects were carefully suspended in the test section of the ABS by a thread which immediately detached upon arrival of the shock front. Spheres ranged in size from 0.75" diameter steel ball-bearings to a 10" Synbone headform ballasted by water to

Fig 3. Velocity of spheres as a function of aerial density



approximate the global shape and mass of a human head. Blast exposures were standardized to a 13 psi by 5 msec waveform.

As summarized in fig 3, the aerial density (i.e. total mass/surface area) presented to the oncoming shockwave) is considered as the dominant factor affecting blast-drag studies, and its inverse is known as the acceleration coefficient (fig 4). The blast-induced velocities of spheres with a wide range of mass and size were tracked as a function of these coefficients. In all cases, blast-induced motion was imparted almost immediately (<1 msec) and terminal velocities were

reached long before the end of the positive phase of the shock wave (fig 5), confirming that displacement was dominated by the diffraction phase and had no relation to the quasi-steady drag forces (i.e. dynamic pressure impulse and blast wind) as has been popularly accepted.

The manikin provided a means to assess effects of neighboring body segments, joint stiffness, and boundary conditions on head motions. Displacements reflecting connectivity/articulation of the segments are shown in fig 6,; these images highlight the need to account for angular accelerations as part of blast induced motion. Similar articulations were seen with recordings of suspended rat cadavers (fig 7).

Task 2. Using the systematic pairings of exposure conditions defined in task 1, record head and trunk acceleration and intravascular and ICP responses under each BOP exposure condition. Collect blood and brain tissue 24 h after exposures to establish neurochemical and biomarker correlates.

Although animal work was not initiated during this reporting period, an animal use protocol was prepared to begin animal experiments as soon as surrogate recordings are completed. Both

Fig 4. Velocity of spheres as a function of acceleration coefficient

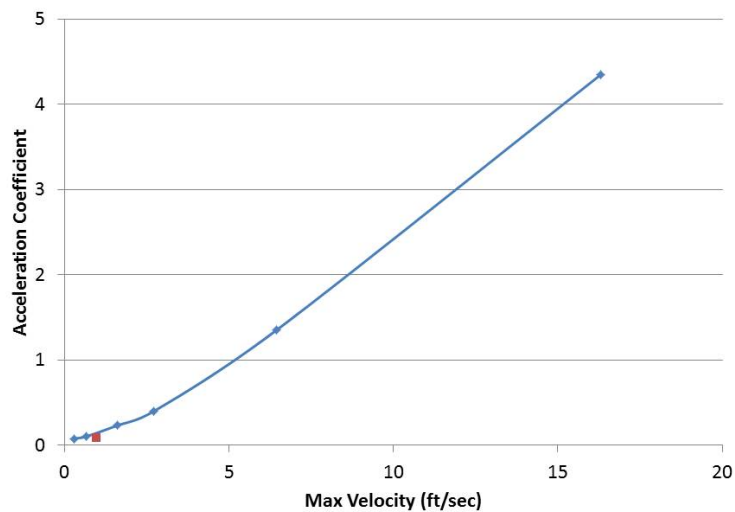
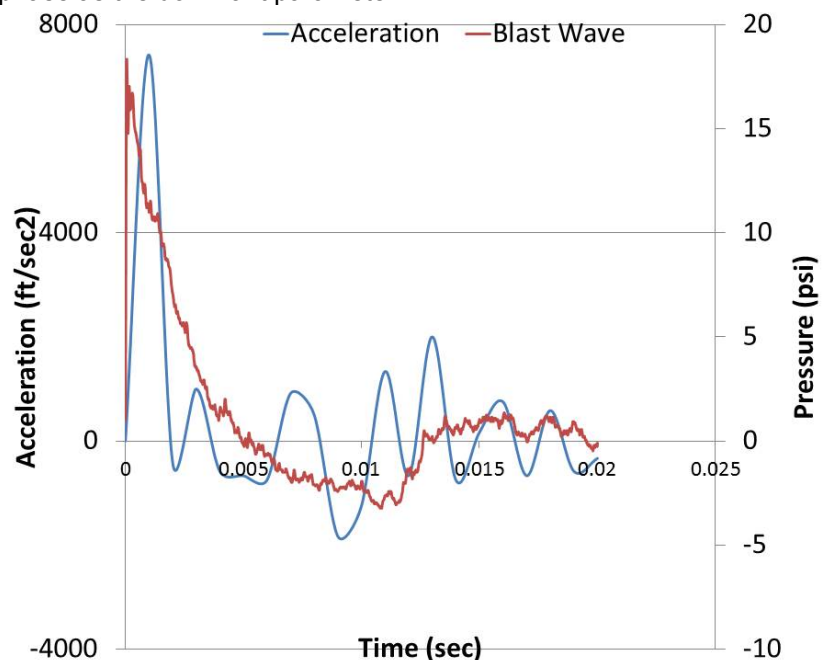
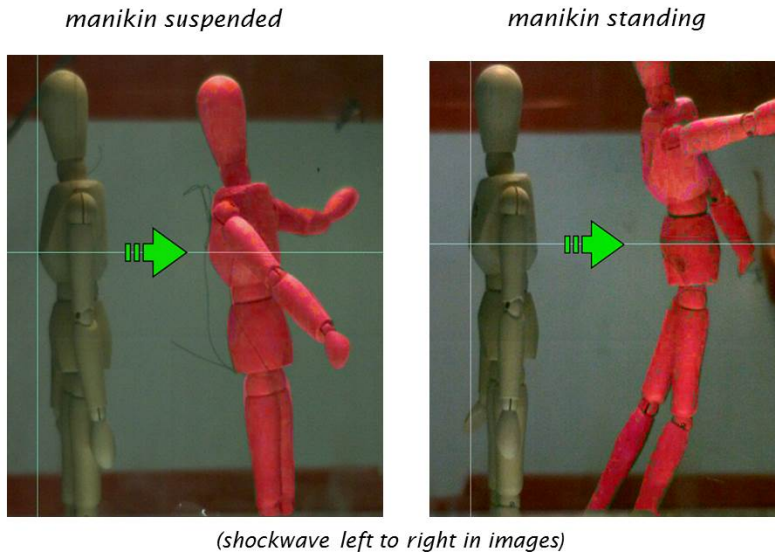


Fig 5. Acceleration vs blast pressure time scales. Acceleration is concluded before the end of the positive phase, pointing to diffraction phase as the dominant parameter



types of experiments require the blast simulator.

Fig 6. Articulation differences with BOP exposure of suspended and standing manikins



Task 3. Using the systematic pairings of exposure conditions defined in task 1, record accelerations and identify the ensuing neurobehavioral disruptions and histopathological consequences resulting from each of the 12 exposure conditions.

This work was not scheduled to begin during this reporting period.

KEY RESEARCH ACCOMPLISHMENTS

Experimental means to reproducibly generate shock waveforms of varied amplitudes and durations in the ABS were carefully evaluated.

Systematic high speed videography of inanimate spherical objects, articulating manikins, and rat cadavers were successfully employed to assess blast-induced motion and establish scaling for model assessments of rat TBI. These results reveal that displacement is dominated by the diffraction phase rather than by the dynamic pressure impulse or blast wind.

Fig 7. Composite showing backward head rotation of a surrogate rat during BOP exposure.



Fig 8. Composite showing displacement and articulation of unrestrained rat cadaver during BOP exposure. The image on the right was recorded 40 msec after the image on the left.



REPORTABLE OUTCOMES

Insights gained on this project during this reporting period were valuable and were shared in an invited plenary lecture delivered by Mr. David Ritzel at the Military Aspects of Blast and Shock conference held in Oxford, UK from 7-12 September 2014 as well in a poster presentation by Mr.

Stephen VanAlbert at the International State-of-the-Science Meeting on the Biomedical Basis for Mild Traumatic Brain Injury (mTBI) Environmental Threshold Values held in Arlington VA from 4-6 November 2014. Also, based in large part upon the work supported by this award, funding was sought through a research proposals submitted to the BAA CDMRP and DMRP, which included:

CONCLUSION

Despite widespread recognition of the urgent need to develop improved mitigation strategies and advance medical care targeting casualties with blast-induced traumatic brain injury (bTBI), the basic mechanisms of blast induced brain injury are for the most part still undefined and progress toward this critical objective has been hampered by the widespread use of experimental simulations of blast that fail to account for blast flow conditions and the biomechanical loading conditions yielding bTBI among injured Warfighters. Examination of mechanisms and identification of countermeasures require shock wave exposure conditions and specimen targets that are appropriate for the question being asked. By incorporating blast physics expertise into biomedical research, in this project we are attempting to replicate all key features of blast flow wave conditions and address the contribution of blast induced acceleration and displacement to brain injuries and disrupted functional outcome. Experiments conducted during this reporting period reveal that loading is dominated by the shock diffraction phase and that previous simplistic assumptions concerning contributions of dynamic pressure impulse (i.e. blast wind) will require reconsideration.

REFERENCES

None

SUPPORTING DATA

None

APPENDICES

- Poster – “Blast-Induced Motion and Scaling for Model Assessments of Blast TBI”
- Abstracts (2) – “Blast-Induced Motion and Scaling For Model Assessments Of Blast TBI”

Blast-Induced Motion and Scaling for Model Assessments of Blast TBI

Stephen Van Albert^{1,2}, Steven Parks³, Joseph Long¹, David Ritzel⁴

¹Blast-Induced Neurotrauma Branch, Center for Military Psychiatry and Neuroscience, Walter Reed Army Institute of Research, Silver Spring, MD;
²As Contracted Through The Geneva Foundation, Tacoma, WA; ³OKA, Inc., Fredericksburg, VA; ⁴Dyn-Fx, Inc., Amherstburg, Ontario, Canada



Background

The use of animal models, especially small mammals, to investigate any mechanically induced neurotrauma in humans requires understanding the relative biomechanics and scaling. It has been speculated that blast-induced global motions may be responsible for inflicting brain trauma, although in fact there is little information available regarding the motion imparted by short duration blast waves characteristic of Improvised Explosive Devices (IEDs). An explosive shockwave is entirely unlike any conventional mode of loading and will impart both an abrupt transient crushing action (static pressure) which envelops the head as well as some aerodynamic drag (dynamic pressure). It is essential to replicate the proper incident blast conditions, and invalid simulations in the current literature have lead to misleading ideas regarding blast-induced acceleration. In the current study blast-induced acceleration of generic shapes, articulated bodies, as well as a rodent model are measured in order to resolve scaling criterion. Experiments were conducted using the Advanced Blast Simulator at WRAIR generating high-fidelity blast-waves.

Introduction

The motion induced to objects by passage of an air shockwave has been studied considerably although for different contexts than the current interest in the head motion of soldiers exposed to typical IED blast. In the case of generic shapes such as spheres, work has been limited to 'step-function' shock profiles. Studies involving blast displacements have been limited to nuclear-scale threats having very long duration (>100ms) from which it was concluded the *dynamic pressure impulse* (DPI), or 'blast wind', controlled the induced motion.

Step shock-wave drag on 'small' spherical particles:
Jourdan et al., Sun et al., Igra et al.,

Step shock-wave diffraction on 'large' spheres:
Tanno et al., Glaizer et al., Skewes et al., Falcoitz et al., Schwer

Blast-wave drag on 'small' particles ($\lambda \gg L$)
Lovell foundation, Lee et al

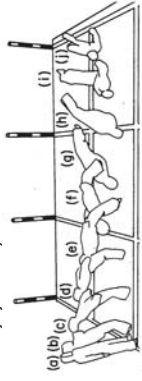
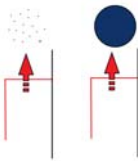


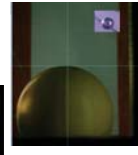
Figure 1. Domain 'Blast-Induced Translational Effects' (BITE) 1998, Nov 1998.

Aim of Study

The objective of the current work was to resolve the scaling rules for animal studies relevant to interpreting the blast-induced motion of the human head subjected to short-duration (<10ms) blast. In its simplest form, the problem was reduced to two studies: factors governing motions of an articulated body, and the blast-induced motion of generic shapes beginning with spheres.

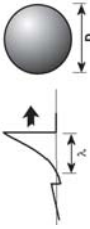
I: Blast-wave induced motion of articulated body

- Effects on head motion due to body articulation, joint freedom, mass distribution, boundary conditions (eg ground bearing)



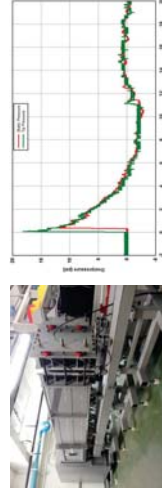
II: Blast-wave acceleration of spheres

- scaling rules for imparted velocity ($\lambda \gg L$)
- roles of diffraction vs drag phases
- wavelength scaling effect: strong free-field gradients during shock diffraction ($\lambda \sim L$)



Materials and Methods

The Advanced Blast Simulator (ABS) at WRAIR was used to generate repeatable high-fidelity blast-wave profiles: the ABS has a 2ft-sq cross-section capable of testing objects presenting 1sq-ft obstruction for blast-drag studies. Test objects were carefully suspended in the Test Section by means of a thread which became detached with the arrival of the shock front; subsequent motion was precisely tracked by high-speed video (HSV).

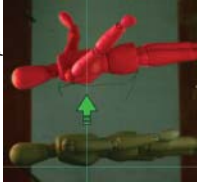


A commercially available 1ft wooden artist manikin of a human form was used for the 'articulated body' study. This manikin was not intended as a similitude model but to investigate phenomenology relevant to understanding effects of neighboring body segments, joint stiffness, and boundary conditions on head motions. For the 'sphere motion' study, a range of smooth spheres of different materials or fills was tested from 0.75" steel ball-bearings to a 10" "Synbone" headform ballasted with water to approximate the global shape and mass of a human head.

Results

For the first phase of testing reported here, the blast exposure was standardized to a nominal 13psi x 5ms waveform. It is important to note that the ABS waveform includes a negative phase in static pressure and flow velocity as develops in actual blast.

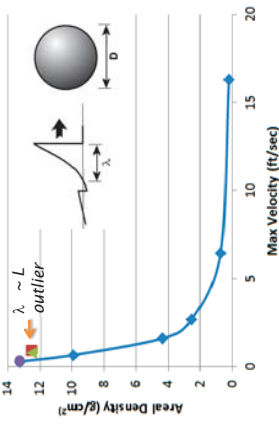
manikin suspended



(shockwave left to right in images)

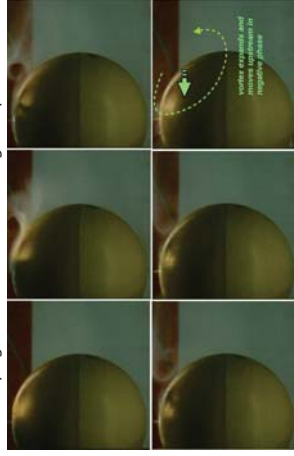
- The connectivity/articulation of the segments of the human body affects the blast-induced acceleration of body segments such as the head or head/neck particularly wrt angular acceleration vs considered in isolation
- Factors such as initial orientation of segments and boundary conditions such as bearing load at the feet are important; bearing load was not scaled in the current simplified phenomenological model
- Apart from matters of scaling, anesthetized animals have negligible neck stiffness vs conscious upright humans and this will exaggerate head motions
- Upcoming studies: effects of joint freedom and blast scaling ($\lambda \sim L$)

The 'areal density', (total mass)/(presented area), is considered a dominant factor for blast-drag studies, and its inverse is also known as the 'acceleration coefficient'. The blast-induced velocity of spheres having a wide range of size and mass was tracked as a function of this coefficient.



In all cases of blast-induced motion of spheres it was clear that a distinct velocity was imparted almost immediately from the shock-diffraction phase which had no relation to quasi-steady 'drag' forces as popularly accepted. For the case of the Synbone headform, unexpectedly high velocity was imparted. This effect seems related to the details of the flow development during the shock-diffraction phase when the blast wavelength is comparable to the characteristic size of the object as in the case of the human/IED problem.

Development and behaviour of vortex field for decaying blast-wave flow with negative phase



Summary and Conclusions

- Preliminary studies have been conducted using the WRAIR ABS to investigate phenomenology and scaling rules relevant to blast-induced head acceleration
- Early results confirm that it is critical to account for the articulation and boundary/initial conditions of a segmented body to assess accelerations of elements such as the head, particularly for angular accelerations
- Studies with generic spheres confirm that 'terminal' velocity is reached long before the end of positive phase, hence the diffraction phase dominates the imparted velocity and total DPI and quasi-steady forces are unlikely relevant
- The use of even a 'dynamic' drag coefficient, a concept from quasi-steady flow, to determine acceleration and motion under blast seems questionable especially when the blast wavelength is comparable to the characteristic length of the target

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BLAST-INDUCED MOTION AND SCALING FOR MODEL ASSESSMENTS OF BLAST TBI

Stephen A. Van Albert¹, David V. Ritzel², Joseph B. Long³

¹*The Geneva Foundation supporting Walter Reed Army Institute of Research, Walter Reed Army Institute of Research, 503 Robert Grant Drive, Silver Spring, MD, 20910-7500, USA;* ²*Dyn-FX Consulting Ltd, 19 Laird Ave North, Amherstburg, ON, N9V 2T5, Canada;* ³*Walter Reed Army Institute of Research, 503 Robert Grant Drive, Silver Spring, MD, 20910-7500, USA*

The investigation of blast-induced neurotrauma requires development of an injury model, whether biofidelic/physical, cadaver, computational, animal, or newly proposed ‘hybrids’ of these types. Blast exposure thresholds have already been proposed from some studies, yet all models have deficiencies and some have serious errors regarding their simulation of blast insult and the interpretation of blast response dynamics. The traditional use of animal models, especially small mammals, for such injury assessments in neuroscience may be confounding outcomes and interpretations with respect to humans for several reasons including matters of scaling and the injury biomechanics. In the current study blast-induced acceleration of objects is assessed using generic shapes as well as a rodent model in order to resolve scaling criterion. Experiments were conducted using the Advanced Blast Simulator at WRAIR generating high-fidelity blast-wave conditions. Simplistic methods for predicting blast-induced motion of objects do not give good agreement with the experimental results, and it appears that when loading is dominated by the shock diffraction phase, as with most IED threats, a revised analysis is required which is discussed.

Studies show that if the head is treated as a responding structure, such as a fluid-filled elastic shell rather than a rigid body, maximal internal stress conditions are imparted during the shock diffraction phase prior to onset of quasi-steady drag and detectable global motions. Therefore, apart from scaling tests for proper acceleration of models, the particular structural response dynamics of the skull/brain system appear critical to the injury outcome. Although preliminary, these results suggest animal models are unlikely to yield blast-induced brain stress conditions and consequent injuries directly analogous to that of humans. Despite such limitations animal models for blast TBI nevertheless remain indispensable for understanding relevant neurobiological phenomena and sensitivities to shock-wave exposures.

BLAST-INDUCED MOTION AND SCALING FOR MODEL ASSESSMENTS OF BLAST TBI

David V. Ritzel¹, Stephen A. Van Albert², Thomas W. Sawyer³, Tyson Josey³,
Joseph B. Long⁴

¹*Dyn-FX Consulting Ltd, 19 Laird Ave North, Amherstburg, ON, N9V 2T5, Canada;* ²*The Geneva Foundation supporting Walter Reed Army Institute of Research, Walter Reed Army Institute of Research, 503 Robert Grant Drive, Silver Spring, MD, 20910-7500, USA;* ³*DRDC, Suffield Research Centre, Medicine Hat, AB, T1A 8K6, Canada;* ⁴*Walter Reed Army Institute of Research, 503 Robert Grant Drive, Silver Spring, MD, 20910-7500, USA*

Key Words: Blast scaling, target response, blast simulators, blast injury

The air blast from improvised explosive devices (IEDs) has been speculated to inflict mild traumatic brain injury (mTBI) without overt signs of external wounding to the head. To properly investigate this matter, it is necessary to understand the biomechanics by which stress would be imparted to the brain; several mechanisms have been proposed including global acceleration of the head and skull flexure for example. The traditional use of animal models, especially rodents, for such injury assessments in neuroscience may be confounding outcomes and interpretations with respect to humans for several reasons including matters of scaling and the injury biomechanics. In this study blast-induced acceleration of objects is assessed using generic shapes as well as a rodent model in order to resolve scaling criterion. Experiments were conducted using Advanced Blast Simulators generating high-fidelity blast-wave conditions. Current semi-empirical methods for predicting blast-induced motion of objects do not show good agreement with the experimental results, and it appears that when loading is dominated by the shock diffraction phase, as with most IED threats, a revised analysis is required which is discussed.

Further studies show that if the head is treated as a responding structure, such as a fluid-filled elastic shell rather than a rigid body, maximal internal stress conditions are imparted during the shock diffraction phase prior to onset of quasi-steady drag and detectable global motions. Therefore, apart from scaling tests for proper acceleration of models, the particular structural response dynamics of the skull/brain system appear critical to the injury outcome. Although preliminary, these results suggest animal models are unlikely to yield blast-induced brain stress conditions and consequent injuries directly analogous to that of humans. Despite such limitations animal models for blast TBI nevertheless remain indispensable for understanding relevant neurobiological phenomena and sensitivities to shock-wave exposures.