Center for Energetic Concepts Development

The Southern Maryland Initiative

for

TRAUMATIC BRAIN INJURY STUDIES

A Response to the Warfighter's Needs

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DEPARTMENT OF MECHANICAL ENGINEERING
A. JAMES CLARK SCHOOL OF ENGINEERING

FOREWORD

Blast-associated brain trauma is the signature injury of the Iraq and Afghanistan wars, with several thousand of the troops dead or severely brain-damaged and possibly tens of thousands of others suffering from long-term neuropsychological problems associated with mild traumatic brain injury (TBI). The most common cause of these catastrophic injuries has been exposure to blasts associated with improvised explosive devices.

CECD/ETC has teamed with NSWCIH and established an interdisciplinary research group to develop bio-medically valid computational models of blast-induced, non-penetrating traumatic brain injury (TBI).

This consortium, from the medical and engineering fields, will conduct research integrating animal-based experimental and computational studies, with advanced magnetic resonance imaging (MRI) serving as the bridge between each approach. In assessing injury, specific emphasis will be placed on the understanding of the transmission of forces to neuron axonal fibers tracts with regard to frequency content as well as maximal peak levels and the impact of these interactions on TBI-sensitive functional outcomes (e.g., memory and olfaction).

This group has a unique combination of expertise in explosive energetics, mechanical sciences, imaging sciences, and the neuroscience of brain injury. Over a four-year period, it is planned to pursue a fully-integrated end-to-end approach, including lab-scale experimentation, clinically-related outcome analyses, and computational modeling.

The group's strategy is to pursue collaborative research, connect with others working in this field, and to broadly disseminate knowledge gained. In this spirit, the team hosted the First Symposium on Traumatic Brain Injury at the University of Maryland in College Park on December 4, 2009. The briefs of the papers presented at this Symposium are included in this document.

The long term objective for a traumatic brain injury project is to develop a blast mitigation scheme for a soldiers head/helmet to prevent/reduce short-term and long-term brain injuries from exposures to non-contact blast overpressures. The proposed research is expected to impact military populations by significantly advancing the knowledge base necessary for the prevention, diagnosis, and ultimately the treatment of TBI.

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EXECUTIVE SUMMARY

An interdisciplinary research effort is proposed to develop bio-medically valid computational models of blast-induced, non-penetrating traumatic brain injury (TBI). The principals of the research team consists of scientists and engineers from CECD/UMCP, NSWCIH, UMSOM, WRAIR, and ETC. Other researchers joining the team for specific projects are from Washington University in St. Louis and the University of Florida, Gainesville.

This consortium from the medical and engineering fields will conduct research integrating animal-based experimental and computational studies, with advanced magnetic resonance imaging (MRI) serving as the bridge between each approach. Head-to-head comparisons will be made between the results of two different experimental paradigms in the following scenarios: 1) blast-tube loading versus explosive detonation-based loadings and 2) explosive detonation-based loadings with and without overpressure. Experimental results are expected to help refine and validate computational mechanics-based models; test the hypothesis that there is no difference between the effects of these experimental paradigms on the outcomes, despite the differences in the nature of the applied physical loading; and facilitate research synthesis to better understand injury mechanisms. This research will address critical TBI knowledge gaps to understand the physical basis and pathophysiology of TBI. The research will also develop computational models that will benefit from accurate assessment of various brain tissue properties and will enable future design and testing of protective systems, including blast sensors and their placement.

This group has a unique combination of expertise in explosive energetics, mechanical sciences, imaging sciences and the neuroscience of brain injury, with over 1000 publications to their credit. Over a four-year period, it is planned to pursue a fully-integrated end-to-end approach, including lab-scale experimentation, clinically-related outcome analyses, and computational modeling with the following research aims:

- Make head-to-head comparisons between blast-tube experiments and explosive detonation-based experiments in terms of characteristics such as frequency content of loading and maximal peak pressures.
- Directly compare clinically-relevant neurologic, anatomic, and metabolic outcome measures obtained at equivalent blast-overpressures using blast-tube and explosion experiments to determine if the biological impacts are equivalent.
- Develop validated computational models for predicting non-impact, TBI and use simulations to explore blast responses at different physical system scales
- Utilize the information obtained from MR imaging and spectroscopy together with histochemistry and behavioral outcome measures to help elucidate the primary mechanism(s) responsible for TBI caused by one or more forces associated with blast exposure.

The group's strategy is to pursue collaborative research in the following:

- computational modeling and simulations,
- experimental studies, and
- MR-based imaging and other clinically-related studies.

The proposed research will result in a detailed knowledge of the physical basis of blast-related TBI in the context of small animal models, as well as a validated computational model for predicting injury. This is an important step that will enable an effective transition to human studies and the development of a computational model for humans that can be used to design, build, and test personal protective systems. Existing models are severely limited by approaching the brain as homogeneous material, without fine structure. The work proposed here will eventually lead to accurate models of the human brain that will incorporate structural variations, mechanical and viscoelastic properties. Comparison between results obtained from magnetic resonance-based measurements and those from behavioral tests could likely lead to a non-invasive, objective means for diagnosing or ruling out TBI.

The proposed research is expected to impact military populations by significantly advancing the knowledge base necessary for the prevention, diagnosis, and ultimately the treatment of TBI thereby improving the physical and psychological health of our warfighters exposed to blasts.

ADVANCED NEURO-IMAGING, MODELING, SIMULATION AND EXPERIMENTAL VALIDATION OF BLAST RELATED TRAUMATIC BRAIN INJURY

1. The Team

An interdisciplinary team consisting of participants from the Center for Energetic Concepts Development (CECD) at the University of Maryland, College Park (UMCP); The Naval Surface Warfare Center at Indian Head (NSWCIH); the Center for Shock, Trauma, and Anesthesiology Research (STAR) at the University of Maryland School of Medicine (UMSOM) Baltimore, MD; Walter Reed Army Institute of Research (WRAIR); and The Energetics Technology Center (ETC) has been formed to conduct various studies relating to traumatic brain injuries.

This team has a unique combination of expertise in explosion physics, computational and experimental mechanical sciences, imaging, and neurosciences. NSWCIH in conjunction with CECD/ETC will assume the lead role in management and coordination of the project. Annual meetings, mini-symposia, and workshops will be conducted by the team to review the progress, exchange data and ideas, and disseminate research findings.

2. Problem Identification

Blast-associated brain trauma is the signature injury of the Iraq and Afghanistan wars, with several thousand of the troops dead or severely brain damaged and possibly tens of thousands of others suffering from long-term neuropsychological problems associated with mild traumatic brain injury (TBI). The most common cause of these catastrophic injuries has been exposure to blasts associated with improvised explosive devices.

While the biomechanics and biochemical basis of civilian brain injury caused by automobile and other accidents have been relatively well studied, very little is known about the physical loads that act directly on the brain or indirectly through protective equipment (helmets and body armor) and blood flow forced up into the cranial vault due to a blast load acting on the thorax and abdomen, during explosions or the chain of events that result in these loads causing the death or dysfunction of neurons in the brain and subsequent neurologic and psychological impairment. Research issues that need to be addressed include the following:

1. construction of appropriate system models that take into account the biological aspects of the animal models at different scales and the physical aspects of different blast loading scenarios,
2. determination of brain tissue material response to high strain rate loading and incorporation of this data into reduced-order models,
3. use of computational physics studies to verify findings from scaled experiments as well as for characterization of blast simulators,
4. use of imaging techniques to understand damage mechanisms and translate findings from animals to humans by defining characteristic pathoanatomical TBI signatures, and finally
5. redesign of protective equipment to mitigate primary blast related injury.

To address the above-mentioned issues, an interdisciplinary group has been formed, with the goal of understanding the primary mechanisms through which blast exposures damage the brain and the secondary mechanisms that result in long-term neuropsychological sequelae.

Specific project goals include the following:

1. Define the physical basis of blast induced traumatic brain injury, construct appropriate experimental platforms with attention to different types of loading encountered in the combat arena, and conduct experiments to study animals at different scales (starting with rats and progressing to larger animals such as pigs) and generate response data including high strain response data.
2. Carry out computational physics studies to understand blast responses of animals (starting with rats), and develop and validate appropriate reduced-order models for predicting and understanding blast response in concert with experimental and clinical findings.
3. Catalog possible damage mechanisms and characterize blast induced TBI signatures in animals and explore translation of these findings to humans.
4. Develop blast injury mitigation strategies by using fluid-structure interactions and structural concepts to redesign protective equipment.

3 Research Tasks

3.1 Computational Modeling and Simulations

Related efforts will build on the decades of the collective expertise of CECD, UMCP, and ETC in the areas of nonlinear system analyses, fluid-structure interactions, and mechanical sciences and the unique computational expertise of the Indian Head Division of the NSWC in studying the responses of fluid-structure systems subjected to shock loading generated by explosives. Appropriate reduced-order models that take into account the physical features of the blast loading (see Figure 1 for the conceptual illustration of the energy pathways to be considered), the three-dimensional geometrical system features, the nonlinear viscoelastic properties of the brain tissue material, the material properties of the skull, the properties of the cerebral spinal fluid, and other important aspects will be developed to understand the blast response of the considered physical systems ranging from rats to pigs to humans. In the efforts of NSWC, the Eulerian-Lagrangian code DYSMAS will be extensively used to obtain three-dimensional blast response information of the different physical systems. Stress-strain data generated in the experimental component of the proposed effort will also be taken into account in the model development. Comparisons will be made with experimental findings to validate and refine the reduced-order models. Data such as that illustrated in Figure 2 will be generated to understand the pressure distribution inside the brain and understand and explore different injury causing mechanisms including counter-coup and other mechanisms. Strategies based on fluid-structure interactions and structural tailoring will be used to develop protective equipment for blast injury mitigation.

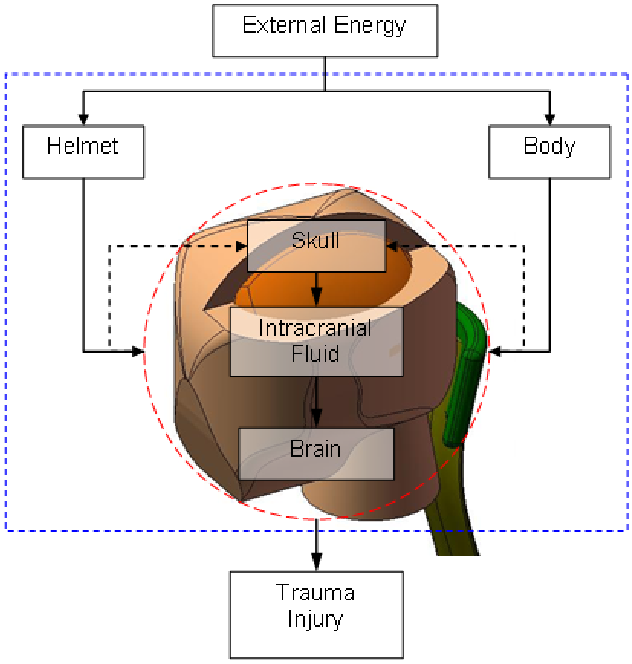

Figure 1: Illustration of direct and indirect energy pathways to the skull-brain system

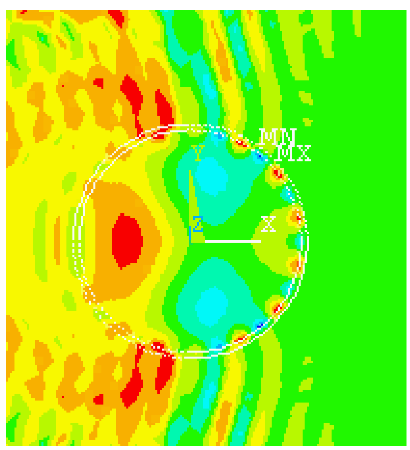

Figure 2: Instantaneous pressure distribution inside the brain due to a blast loading obtained through simulations at CECD

3.2 Experimental Studies

Building on the decades of the experience of UMCP in studying the blast response of structural and mechanical systems, the bio-medical scientific approach of UMSOM, and the biomechanics expertise of WUSTL in carrying out MRI measurements of pressure and shear waves in brain tissue matter, experiments will be initiated with Sprague-Dawley rats (see Figure 3 for illustration of an arrangement relevant for studying the blast response to sublethal, small scale explosions) and phantom gel models. The WUSTL experiments will be used to generate stress-strain data in the presence of high-strain rates and displacement response data in the presence of impact and blast type excitations. As an illustrative example of data to be obtained, in Figure 4, simulation results for shear waves in isotropic and anisotropic viscoelastic materials are shown along with experimental results for shear waves in isotropic gels and mouse brain matter. This stress-strain data will be used to estimate anisotropic, viscoelastic properties of brain tissue and tissue surrogates, and these properties will be used in the model development.

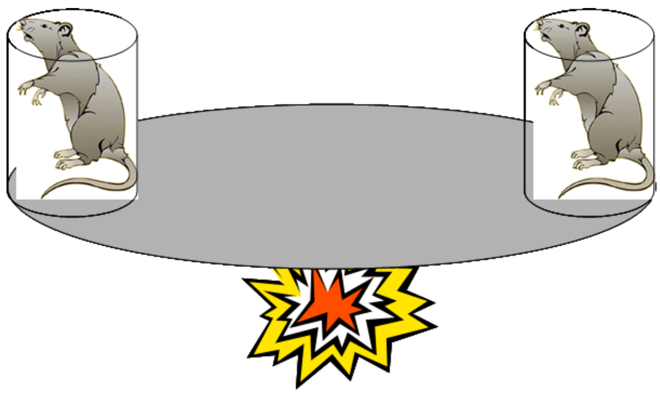

Figure 3: Illustration of experiments to be conducted with Sprague-Dawley rats in the Dynamic Effects Laboratory of UMCP in collaboration with UMSOM

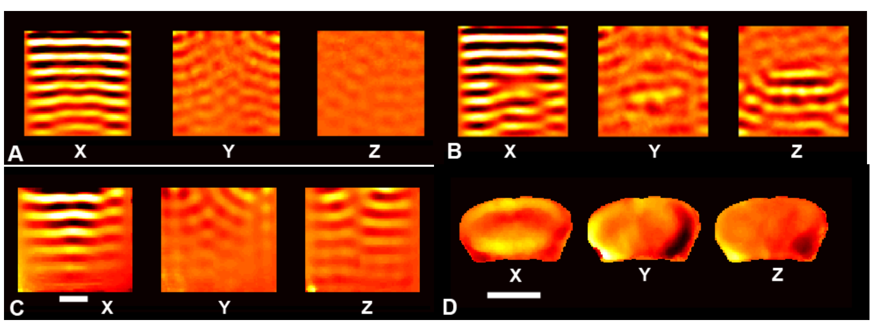

Figure 4: WUSTL shear waves simulations and experiments: (A) simulation, isotropic material μ=1000 Pa, (B) simulation, isotropic material μ=1000 Pa with anisotropic cylinder ("fiber tract") transverse modulus μ_T=800 Pa; parallel modulus μ_P=2000 Pa, (C) experiment, isotropic gel μ≈1400 Pa; (D) experiment: mouse brain. White scale bars in C and D are 5 mm. Such simulations and experiments are expected to help understand the wave interactions inside the brain during a blast loading.

Through the UMCP and UMSOM efforts, the experiments are expected to evolve from rats to larger animals (pigs) over the course of the five-year effort, and the experimental findings will be used to develop and validate clinically relevant reduced-order models for blast TBI. In concert with the clinical and imaging studies, the experimental studies will be used to establish quantitative relationships between the blast loadings and the corresponding neuropathological responses.

3.3 Imaging, Histology, and Neurologic Outcome Studies

A bio-medical research approach will be pursued by UMSOM, UMCP, and UFL to carry out the following: (i) provide accurate information for modeling the rat brain and other anatomy, which will include information on the orientation of the fibers and the location and connectivity of different brain regions from the spinal cord to the cortex through the use of advanced imaging techniques, including diffusion spectral imaging (DSI) and histology and (ii) elucidate both the early and delayed neuroanatomical, physiological, and neurochemical events that occur in the brains of animals exposed to explosive blasts and to isolated blast overpressure at levels that result in mild to moderate TBI without mortality. These data will be used to inform and refine the computational models. As these studies focus on the direct effect of blasts on the brain, rather than indirect affects through other organs (e.g., lungs), the rats will wear body armor during the blast experiments. Magnetic resonance measurements will be made the day before these exposures, within 2-6 hr immediately afterwards, and at 1, 7, and 30 days. Many types of MR-based measurements, including diffusion spectral imaging, arterial spin labeling, and proton and phosphorus spectroscopy, will be performed to provide structural and functional information essential for validating the computational models and to provide physiological and neurochemical information necessary for detailed comparison of the effects of the different blast paradigms and for elucidation of mechanisms responsible for neurologic impairment. Neurobehavioral outcome measures will be used to test the effects of blasts on righting reflex, balance, spatial learning and memory, smell, and oculometrics. Special emphasis will be placed on early tests of olfaction because it is the team’s hypothesis that they are sensitive indicators of even relatively mild forms of TBI that could be easily and rapidly tested in the field, and therefore possibly used as a criterion for return to duty after blast exposure. Histochemical measurements will also be extended throughout the forebrain, cerebellum, and brainstem and compared with the imaging studies. Based on early results obtained from the exposure of rats to blast-tube overpressure and of pigs to explosions, widespread the team anticipates diffuse axonal injury, as detected with silver staining methods. The team will also probe for even minor neuronal death throughout the brain, particularly at the late period of 30 days after exposure, when delayed apoptosis may occur in response to impaired trophic input due to axonal damage. Cresyl violet, NeuN, and Fluorojade C staining techniques will be used to assess neuronal death and degeneration. Temporal and spatial relationships will be established between blast type and intensity, MR measures of neuroanatomic and metabolic alterations, and histologic metrics of axonal and cell injury and mitochondrial dysfunction. This information will be compared to the computational models established by the team to construct a much needed multi-level representation of how specific forces generated by blasts cause physical and neurochemical alterations to the brain that are manifested by neuropsychological abnormalities.

3.4 Analysis, Correlation, and Mitigation

The whole team will analyze the findings obtained through the modeling and simulations, experiments, and clinical and imaging studies to redesign protective equipment such as that shown in Figure 5 as well as to come up with mitigation strategies for blast induced TBI.

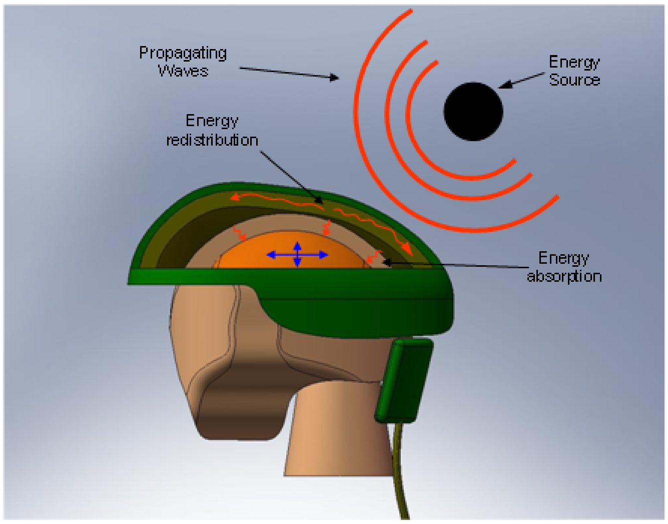

Figure 5: Helmet and other protective equipment redesign based on system analyses and fluid-structure interactions

4. Documentation and Information Dissemination

ETC will organize annual meetings, mini-symposia, and workshops to review the progress, exchange data and ideas, and disseminate research findings. A 'warehouse' of TBI-related information will be maintained for the team and other researchers.

3. Potential Impact on DoD Capabilities

The proposed effort is expected to lead to a better understanding on blast-induced TBI and protective measures one could take to mitigate TBI. Specifically, it is expected to provide an enhancement of the current understanding of the physical basis of blast-related TBI in the context of small animal models, as well as a validated computational model for predicting injury; and formation of basis for non-invasive objective means for diagnosing or ruling out TBI.

The long term objective for a traumatic brain injury (TBI) project is to develop a blast mitigation scheme for a soldiers head/helmet to prevent/reduce short term and long term brain injuries from exposures to non-contact blast overpressures. The proposed research is expected to impact military populations by significantly advancing the knowledge base necessary for the prevention, diagnosis, and ultimately the treatment of TBI.

BACKGROUND

DoD-Related

DoD Directive 6025.21E of 5 July 2006 designated the Secretary of the Army as the DoD executive Agent (DoD EA) for Medical Research for Prevention, Mitigation, and Treatment of Blast Injuries. It also established the Armed Services Bio-medical Research, Evaluation and Management (ASBREM) Committee to coordinate the efforts within DoD. Public Law 110-28 appropriated $150M for research on TBI in 2007. USAMRMC issued BAA 06-1 requesting, among other things, research on the Physics of Blast as it Relates to Brain Injury to include sensors, models and evaluation of field data. The BAA closed in August 2007 with $7.5M budgeted for Physics of Blast. At least some awards are still pending. The DDR&E thrust is the Army's Ft Detrick program (Jim Short). Other research is being funded by DARPA and ONR.

Michael Leggieri, Deputy Coordinator for the DoD Blast Injury Research Program at USAMRMC, Ft Detrick stated in an e-mail to CECD that "One goal of the Blast Injury Research Program is to seek opportunities to team the modelers with the bio-medical researchers who can provide the fundamental injury data necessary to develop and validate the models. We have achieved some success in this area, albeit limited. For example, we recently facilitated the teaming of a computational modeler from the Lawrence Livermore National Laboratory with bio-medical researchers from the University of Nebraska on a project to model brain injury. We are also tracking the progress of two major collaborative brain injury and modeling research projects involving MIT, Harvard, Yale, Purdue, the Walter Reed Army Medical Center, and the Walter Reed Army Institute of Research." "In spite of decades of research on brain injury by the automotive industry and others, we still do not understand the fundamental, tissue-level mechanisms of how a brain is injured by external, mechanical forces like blast or blunt impact. We don't know what structures in the brain actually break, what biomechanical or physiological mechanisms cause them to break, or how the external forces relate to these internal injury mechanisms. We need to understand these fundamentals before we can expect any computational modeling tools to be of immediate value. This is a lesson that we learned during nearly two decades of large animal injury research that led to the development of the MRMC's biomechanical model of blast lung injury. This model has stood the test of time because it is based on the tissue-level mechanisms of blast lung injury, and it was validated with data from more than 2,000 large animal tests."

Sandia National Laboratory and University of New Mexico Health Sciences Center produced a CTH analysis with a CT scan-based brain model in 2007.

James Stuhmiller, with L-3 released a preprint on the state of blast injury modeling in April 2008. Based upon the biomechanically-based INJURY software, he concludes that the strongest blast waves for which there is a high probability of survival have a peak pressure of about 300 psig and duration of a few milliseconds. This limits the range of interest much the same as the DOT does for motorcycle helmet requirements.

Meanwhile, PEO Soldier, PM Soldier Survivability is fielding two helmet mounted sensor systems to collect data. The model worn by the 101st Airborne Division attaches to the back of the Advanced Combat Helmet (ACH) while an internally mounted model will be fielded with the 4th Infantry Division. SIMBEX developed a Head Impact Telemetry (HIT) system which is being used by VT, Oklahoma and NC university football teams. Researchers at the University of Illinois at Urbana-Champaign are developing a more advanced suite with "smart nanotechnology sensors " to monitor wearer's physical condition as well.

General

According to a report by the National Academies, damage to the brain after trauma (for example, a blow or jolt to the head, a penetrating head injury, or exposure to an external energy source) is referred to as traumatic brain injury (TBI). TBI may be open (penetrating) or closed and is categorized as mild, moderate, or severe, depending on the clinical presentation. A brain injury that results from something passing through the skull, such as a bullet discharged from a gun or fragments from a missile, would be referred to as a penetrating or open head injury. A brain injury that results from something hitting the head or from the head hitting something forcefully, such as the dashboard of a car, is referred to as a non-penetrating or closed-head injury. According to the Centers for Disease Control and Prevention, the Mild Traumatic Brain Injury Committee of the Head Injury Interdisciplinary Special Interest Group of the American Congress of Rehabilitation Medicine, and the World Health Organization Collaborating Task Force on Mild Traumatic Brain Injury, mild traumatic brain injury (TBI) is traumatically induced physiological disruption of brain function, as manifested by a least one of the following: i) any period of loss of consciousness; ii) any loss of memory for events immediately before or after the accident; iii) any alteration in mental state at the time of the accident (e.g., feeling of being dazed, disoriented, or confused); and iv) focal neurological deficit(s) that may or may not be transient, but where the severity of the injury does not exceed the following: a) posttraumatic amnesia (PTA) not greater than 24 hours; b) after 30 minutes, an initial Glasgow Coma Scale (GCS) of 13-15; and c) loss of consciousness of approximately 30 minutes or less. Methods other than GCS and instruments have been used to determine injury severity, such as the Abbreviated Injury Scale (AIS) and the International Classification of Diseases (ICD). Clinical measures—such as loss of consciousness (LOC), duration of posttraumatic amnesia (PTA), and computed tomography of brain lesions—have also been used to assess TBI severity.

Another type of traumatic brain injury that is beginning to attract attention is blast-induced traumatic brain injury (TBI). While TBI commonly occurs in civilians due to impacts caused by road accidents and sport activities, military personnel confront a much higher risk of TBI due to exposure to IEDs. Notably, TBI is primarily caused by impacts and has been studied from that viewpoint. In contrast, the central finding of recent investigations of TBI is that exposure to a blast wave can cause severe brain damage even in the absence of head motion caused by impact.

Theories for Brain Concussion

There exist two commonly accepted theories to explain brain concussion. According to shear-strain theory (e.g. Holbourn, 1943), the brain damage is mainly due to the high shear strains in the brain tissue caused by rotational acceleration and relative motion between the brain and the skull. On the other hand, according to cavitation theory (e.g. Gross, 1958), the brain tissue damage is caused by the sudden collapse of small bubbles that appear on the opposite location of the impact (see Figure 6). These bubbles are generated as a consequence of the negative pressure developed due to the translational acceleration of the brain. This mechanism, combined with the deformation and posterior restitution of the skull results in cavitations that extend to all of the brain mass.

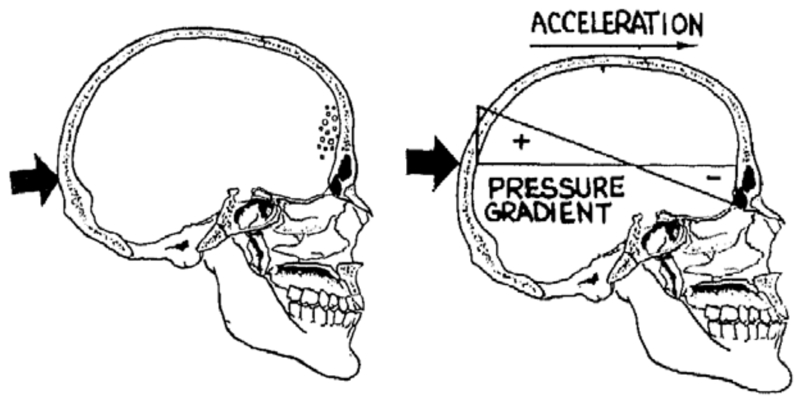

Figure 6: Cavitation at the opposite side of the impact due to an intense low pressure in the intracranial fluid (from Gross, 1958)

Theories addressing TBI are only beginning to emerge in the literature. For instance, Moss, King and Blackman (Moss et. al., 2008) recently suggested that skull flexure from blast waves present a new mechanism for brain injury. They concluded from numerical simulations that non-lethal blasts could produce sufficient flexure of the skull leading to significant brain damage even in the absence of impact. This hypothesis is also supported by independent shock tube experiments, where restrained animals were subjected to blast-like conditions (Cernak *et al.*, 2001).

The simulations showed that a blast produces a supersonic pressure wave that attenuates and slows as it expands. It transits the skull in about 0.3 ms at a speed of 450 m/s and an overpressure of 1 bar. This moving pressure wave generates flexural ripples in the skull. As a result, the skull flexes inwards at certain locations causing increased pressure on the cerebrospinal fluid and brain tissue whilst outward flexing of the skull at other locations causes negative pressure and induces cavitation. The key point is that the skull flexure (not the bulk acceleration) produced most of the mechanical load on the brain tissue in the simulation. Furthermore, simulations with a perfectly rigid skull indicated a five fold reduction in peak brain pressure and order of magnitude reduction in pressure gradients and shear strain thereby confirming the dominant role of skull flexure in TBI.

From the viewpoint of protection research and better design of helmets, additional simulations showed that the current ballistic standard clearance of 1.3 cm between the helmet and the head is sufficient to admit the pressure wave into the clearance and leads to skull flexure and brain injury. Interestingly, the above feature is also independently reported by a David Mott's group at the Naval Research Laboratory (Defense Tech Briefs, 2008). From experiments that placed sensors on helmeted mannequins, they reported that a blast wave produced very high pressures in the countercoup location. In fact, the helmet acted as a focusing mechanism to produce these high pressures at the countercoup location.

Clinical Findings and Experimental Studies

Clinical findings suggest that most injuries in absence of skull fracture occur in the frontotemporal basal area, possibly, as a consequence of frictional forces between the skull and brain tissue in that area.

In vivo experiments with animals have been carried out in order to elucidate the development of pressure gradients on the brain tissue by Krave *et al*. (2005). These results show the development of high transient negative pressures depending on the intensity of the impact. Studies on human cadavers subjected to frontal impact have also been carried out to measure the intracranial pressures [Nahum *et al*., 1977 and Trosseille *et al*., 1992].

Recently, measurements of accelerations and deformations of human brain have been carried out. Bayly *et al*. (2002) measured the linear and angular accelerations that a soccer player's head experiences due to an impact. Bayly *et al*. (2004, 2006) estimated the strain fields in a gel experimental model as well as euthanized and anesthetized rats. The methodology employed is based on non-invasively techniques that rely on magnetic resonance images. Bayly *et al*. (2005) investigated the brain deformation in humans during mild, but rapid, deceleration of the head. The study provides quantitative images of acceleration-induced strain fields in the human brain, which can be useful in validating numerical models of brain trauma. The results provide evidence for the basic mechanism based on brain rotation constrained by basal and frontal tethering.

Additional information on the clinical studies can be found in the recent workshop report authored by Benzinger *et al*. (2008).

Models

Due to the geometric and constitutive complexities of the problem, early models of brain concussion consisted of simple spheres or oval shells filled with some fluid whose mechanical properties were close to that of the brain (Ruan *et al*., 1991). One of the problems that all models of brain concussion face is the lack of accurate data about the brain mechanical properties. Some authors have found that the dynamic bulk modulus of the human brain is approximately that of water. This may be due to the high water content of the brain. Therefore, employing water as the fluid model of the brain tissue seems a reasonable approach (Huang *et al*., 2000).

The absence of accurate experimental methods to measure brain strain and stress during sudden accelerations of the head, as during an impact, has promoted the use of numerical tools to improve the understanding of the subjacent physics of the phenomenon. In particular, finite element models have been used recently to perform biomechanical analysis and provide data that otherwise cannot be measured experimentally. This approach allows one to consider more complex and realistic geometries of the human head. Conditions where the head was directly impacted have been investigated (e.g., Ruan *et al*., 1991; Voo *et al*., 1996; Kumaresan and Radhakrishnan,1996) as well conditions were no impact is present and the head is suddenly accelerated (e.g., Huang *et al*., 2000). Ruan *et al*. (1991) investigated the influence the effects of the membranes and the mechanical properties of the skull, brain, and membrane on the dynamic response of the brain during a side impact by using several two-dimensional finite elements models. Kumaresan *et al*. (1996) investigated the influence of the partitioning membranes of the brain, and the neck in head injury by using three-dimensional finite element analysis. Huang *et al*. (2000) concluded that, in absence of impact, when the head rotates forward and backward, a negative pressure develops in the countercoup region. However, the pressure is not low enough to form bubbles and the posterior cavitations. On the other hand, their results raise the shear strain theory as the more suitable theory to describe the concussion phenomenon in absence of direct impact. Recent finite element efforts include those of Zhang *et al*. (2001a) and Takhounts *et al*. (2003). In the first one, a finite element model of the head has been developed to study direct and indirect impacts. This model includes facial bone details and the damage properties of materials, which enables simulation of bone fracture.

Hong *et al*. (2007) have studied the mechanism of brain contusion by separating the problem into rigid body and brain deformation dynamics. The authors concluded that for low-speed impacts, the mechanisms of brain injury are governed by the rigid-body displacement within the skull. Conversely, at higher impact speeds it is the deformation of the brain, which plays a primary role.

King *et al*. (2003) investigated the relative importance of angular and translational accelerations in the development of brain injury. They employed a helmeted model that was subjected to different head collisions. It was established that although the translational acceleration was reduced by the use of he helmet, the angular acceleration was not. Since helmets have been shown to be a factor in reducing brain injuries, their results may suggest that it is actually the translational acceleration of the brain that may be the main cause of brain damage.

A tabulation of the different models and their features is given in Table 1.

Table 1: Models and their features

Authors	Model Description	Material Properties	Comments
Houlbourn and Phill, 1943	Shear strain injury theory		Shear strain is recognized as the main cause of brain injury.
Gross, 1958	Cavitation injury theroy		Brain injury mainly caused by the implosion of bubbles
Hardy and Marcal, 1973	3-D finite element model of the head without the brain	Skull: linear elastic and isotropic	Analysis of frontal and side pressure load
Shugar, 1975	3-D finite element model of the head filled with a fluid; the skull is three-layered	Linear elastic. Brain: fluid-like, almost incompressible Subarachnoid space: Highly compressible elements	Model analyzed in the presence of frontal and occipital impacts and different boundary conditions.
Hosey and Liu,1981	3-D homeomorphic model of the brain and skull. Includes: three-layered skull, scalp, falx, dura, SCF, spinal cord and cervical column	Brain made up of incompressible matter with high Poisson's ratio	The model was analyzed to sagital impact. The pressure gradient distribution obtained was linear along the impact axis, with zero over the anterior part of the foramen magnum.
Ruan *et al.*, 1991	2-D FE model. Three variants: 1. Axisymetric (spheric shell), 2. Plain strain bilaterally symmetric without interior membranes, 3. Plane strain but with inclusion of falx and tentorium; Skull single-layered.	Brain and CSF modeled as inviscid, incompressible fluid. Linear elastic properties for the other components	Impulsive load on the side of the head. The interior membranes affect both the resonance frequencies and the pressure distribution inside the head. Different constraints were used at the base of the head.
Ruan *et al.*, 1994	3-D FE model which iIncludes the following: three-layered skull, brain, foramen magnum and facial bones. The neck and	Homogeneous, isotropic and linearly elastic. Brain highly compressible.	Impulsive force applied to the free head. Validation against experimental results. Parametric study of the influence of the Skull stiffness and brain bulk modulus.

	interior membranes are not included.		
DiMasi *et al*., 1995	3-D, anatomically simple FE model to model impact against a windshield. Skull modeled as a spheroid shell. Includes dura matter.	Brain: Viscoelastic Dura matter: Linear elastic	Three kinematic conditions analyzed: rotation, translation and rotation+translation.
Kumaresan and Radhakrishnan, 1996	3-D FE model. Includes the following: skull, brain, partitioning membranes, CSF, spinal cord, vertebrae and intervertebral disc		Occipital, frontal and parietal impact conditions analyzed. Coup-counter-coup mechanism only seen under frontal and occipital impacts. Partitioning membranes affect the intracranial pressure distribution. Inclusion of the spinal cord decreased the intracranial pressure.
Willinger *et al*., 1999	3-D FE model. Actual geometry of the head form MRI slices. Includes: skull, falx, tentorium, subarchanoid subspace, cerebral hemisphere and brain stem. The neck was not included.	Two different simulations: 1. All elements linear, elastic, homogeneous and isotropic. 2. The brain modeled with a viscoelastic constitutive model (Boltzman)	Validation against two sets of experimental data. Free boundary conditions applied. The viscoelastic assumption provides improvements over the linear elastic model. Need for using different impact conditions to validate the model is pointed to.
Huang *et al*., 2000	3-D FE model which includes the following: the three-layered skull, dura matter, falx and tentorium, foramen magnum and facial bones.	Homogeneous, isotropic and linear viscoelasitc. A damping factor included for all the structure.	Validation against experimental data, with a moderate underprediction of the pressures. Indirect impact simulation by inducing only rotation to the head. The negative counter-coup pressure was not enough to produce cavitation.
Zhang *et al*., 2005	3-D FE model of the skull and neck. No details of the interior of the head were reproduced. No model of the brain.	Linear elastic, perfectly plastic, homogeneous and isotropic.	Validation against experimental data on near vertex drop impact. Reasonable agreement found. Potential neck injury was analyzed.

Zong *et al.*, 2006	3-D FE model which includes the three-layerd skull, CSF, brain and neck (spinal cord, cervical bone and disc)	Linear elastic material	Validation against two sets of experimental data. Reasonably good agreement obtained. A new methodology for injury assessment is introduced based on structural intensity measure (SI). Three cases analyzed, frontal, rear, and side impacts. Similar distributions of SI found on all. High values of SI on the spinal cord were observed.
Zou *et al.*, 2007	Theoretical model. Experimental data were used to separate the brain motion into deformation and rigid components.	Isotropic, linear elastic.	Almost pure rigid body motion for low impact speeds. Deformation motion for high impact speeds
Pinnoji and Mahajan, 2007	3-D FE model of a helmeted head, which includes skin, skull, CSF, brain, tentorium, falx and facial bones. Helmet consists of a hard shell and foam.	All materials are linear elastic. Brain: Visco-elastic Foam: Elasto-plastic	The helmet was found to absorb most of the kinetic energy through the foam. Coup pressure is reduced by the helmet. Counter-coup pressure not affected.

Technologies

Pellman *et al*. (2006) investigated the performance of new NFL helmets under impacts. Two kind of impactors were used, pendulum and linear pneumatic. It was shown that newer design improves the absorption of impact energy during normal conditions in a football match. However, better designs are still needed to overcome what is called the elite impact condition, normally at speeds above 11.2 m/s. Sensors have been implemented as shown in Figure 7 to measure real time impacts during college football matches. The collected data may help understand when concussions occur. Accelerometers have been used as sensors in these studies.

Recommended Studies

Further studies need to be conducted to address gaps and questions, which include the following:

- Standard criteria used for establishing an injury (e.g., head injury criterion used in crash tests) consider only the motion of the center of mass of the head. Injury criteria are formulated as empirical relationships that depend on the acceleration of the head. While there is a lot of discussion about the relative importance of linear acceleration versus angular acceleration in causing a brain injury, the approach suffers from the fundamental shortcoming that the relative motion of the brain with respect to the skull is not taken into account. Furthermore, despite the brain being a highly deformable entity, brain deformations are not taken into account in the models.

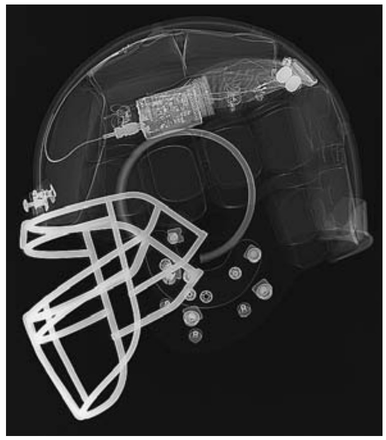

Figure 7: Accelerometers used inside a football helmet to measure hit accelerations during college football matches (from www.spectrum.ieee.org/October 2007)

- According to the National Academies (2008) report, consideration should be given to developing models that would be relevant to human traumatic brain injury that encompass a more comprehensive experimental design.
- According to the St. Louis Workshop report by Benzinger *et al*. (2008), the fundamental biophysics of blast effects on human brain tissue as well as whether and how blast can induce symptoms of traumatic brain injury remain significant gaps in our knowledge.
- Also, according to the St. Louis Workshop report by Benzinger *et al*. (2008), the main challenge is to find or create the appropriate model that exists at the intersection of the biological requirements for the animal model and the physical behavior of the blast simulator. The question of creating the proper stresses and strains at the micro level is very challenging. There are important and uncharacterized differences between human beings and animal model systems. For example, the thickness, deformability, and openings of the rat skull are very different from the human skull. Furthermore, much of the compiled data on material properties of bones, muscles, nerves, etc. is at lower strain rates than those experienced in the blast.
- While finite element models point to coup pressure and shear strain as failure criteria and also show that the use of helmets reduces the pressure and shear stress on the skull elements, they offer little insight into the actual mechanism of energy transfer to the brain as a result of impacts on the skull.

A system approach could be useful in formulating the problem (see Figure 8). This approach can help focus on the response of the brain and seek to formulate injury criteria on that basis as opposed to input parameters.

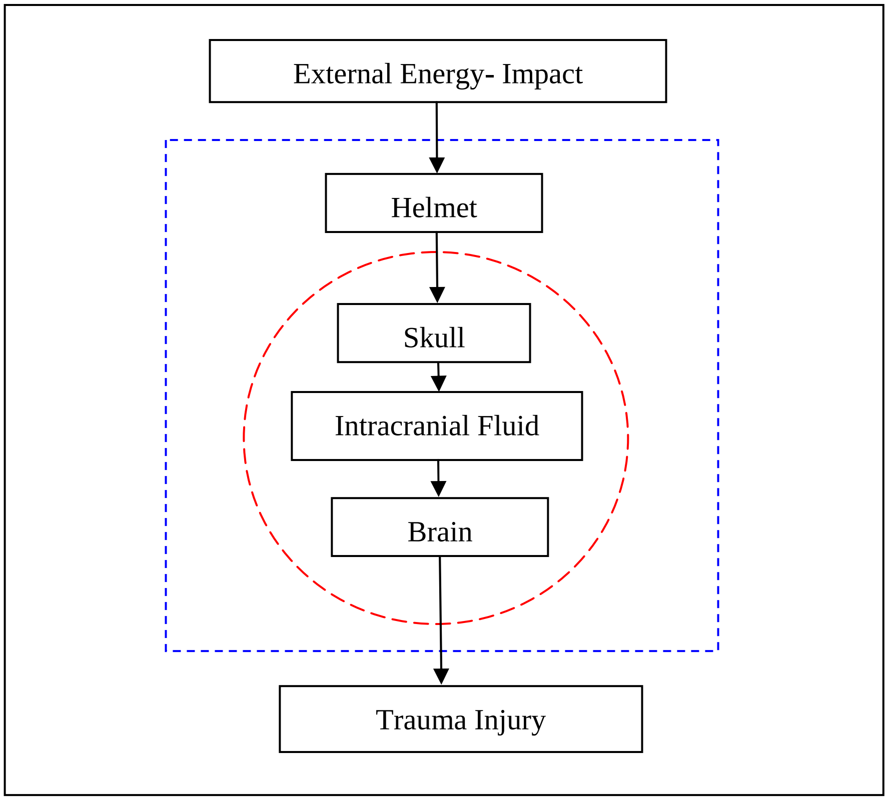

Figure 8: System of interest

Recent experimental work based on MRI methods (the work of Bayly and collaborators) has made in vivo strain measurements on the brain. Their results point to the importance of developing injury criteria that are based on brain deformation. A potential path from here could be taken as follows. One can treat the input as an energy distribution over the entire skull and determine the response in terms of the strain energy of the brain and the associated deformations. Helmets could be designed as energy absorbing and redistributing mechanisms in the energy path to the brain (see Figure 9).

Perhaps a helmet with a harness should be considered to reduce the translational acceleration levels experienced by the brain (see Figures 10 and 11).

The recent work on blast wave induced skull flexure as a mechanism of brain injury (Moss *et al.*, 2008, Mott *et al.*, 2008) presents a new set of insights and challenges in developing theoretical models to understand TBI as well as to design helmets with enhanced protective capabilities. It is clear that helmets need to have enhanced capabilities of absorbing and dissipating energy even as they function to reduce resultant motion of the head. Drawing inspiration from the function of the cerebral spinal fluid in protecting the brain tissue from minor bursts of energy received by the skull due to impacts and other mechanisms, the presence of a layer of fluid of appropriate viscosity (such as a gel) inside the helmet could potentially enhance the efficacy of the helmet in preventing energy transfer to the surface of the skull.

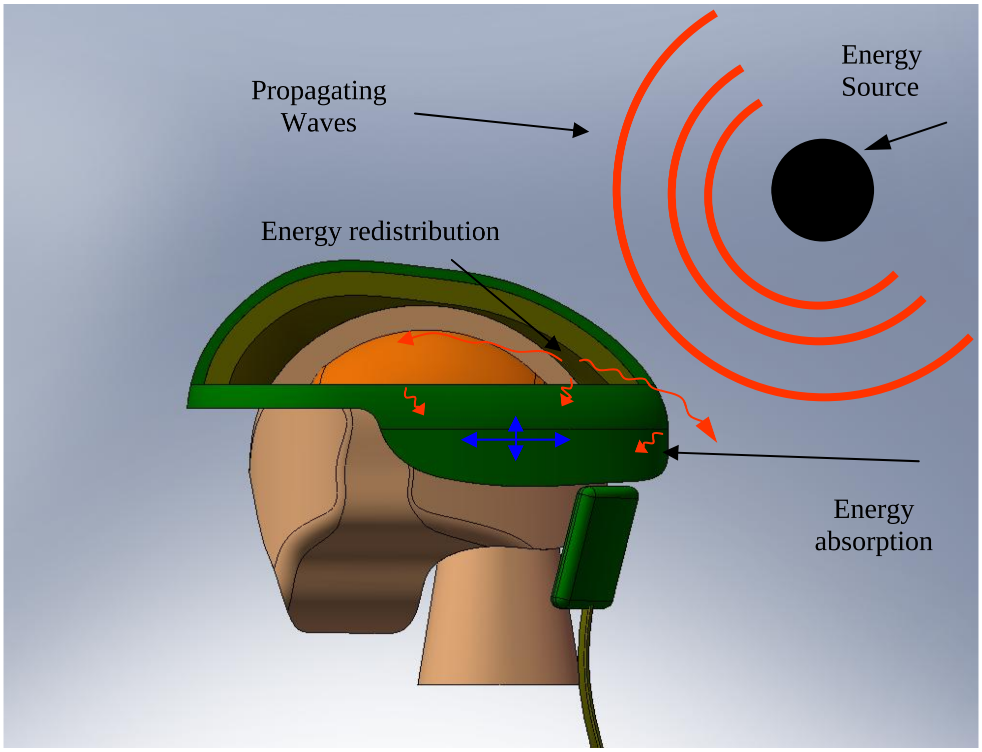

Figure 9: Helmet as an energy absorber as well as an energy redistributor

Figure 10: Helmet with a harness

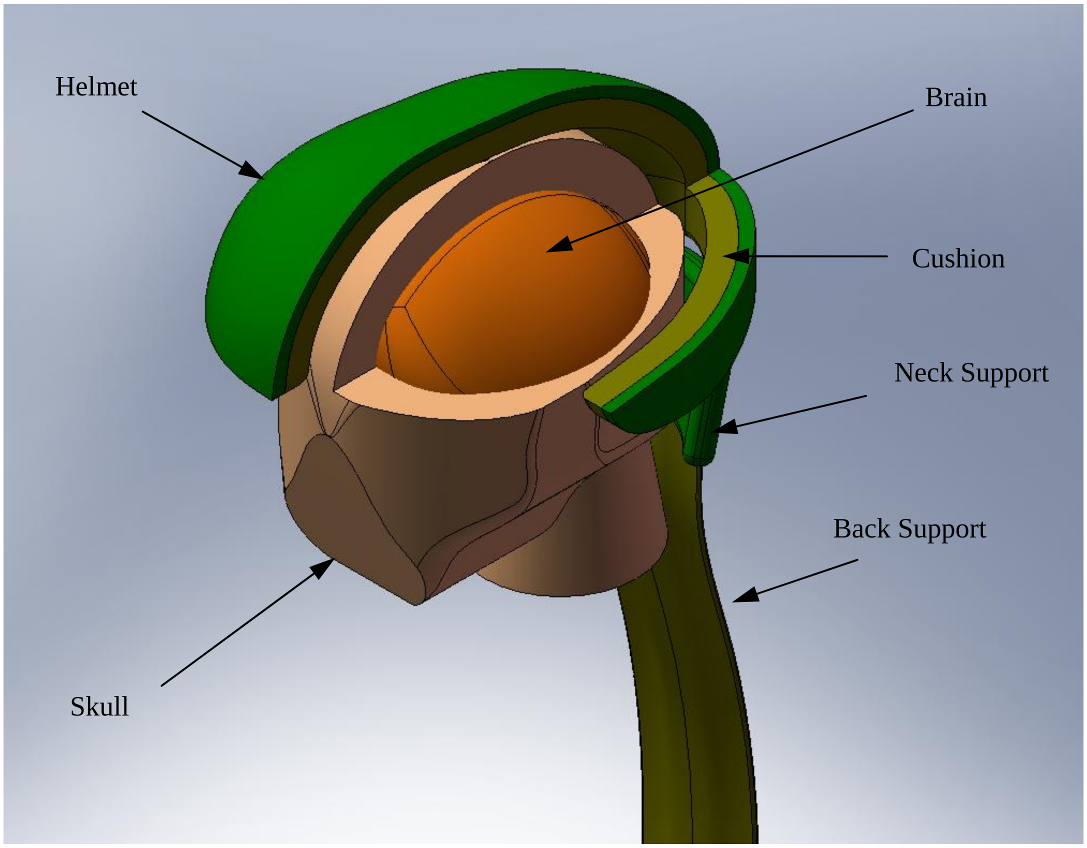

Figure 11: Helmet with a harness

According to the St. Louis Workshop report by Benzinger *et al*. (2008), current helmets have been designed to reduce penetrating injury to the brain, but have not been optimized for reduction of primary blast-related injury.

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APPENDIX

First Symposium on Traumatic Brain Injury

Friday, December 4, 2009   10am-1pm

Inn and Conference Center, University of Maryland Campus

3501 University Blvd E

Adelphi, MD 20783

Technical Presentations: Room 1312 (new wing; on your right as you exit the parking garage)

Lunch: President's Room

AGENDA

10:00am-10:05am	Dr. D.K. Anand	Welcome
10:05am-10:10am	Mr. Robert Kaczmarek	Opening Remarks
10:10am-10:25am	Dr. Gary Fiskum	"Targets of Neuroprotection for Blast-Induced Traumatic Brain Injury"
10:25am-10:40am	Dr. Rao Gullapalli	"Advanced MR Imaging Markers for the Assessment of TBI"
10:40am-10:55am	Dr. Mike Deeds	"Unpowered MEMS Sensor Suite for Excessive Load/TBI Detection"
10:55am-11:10am	Dr. Tom McGrath	"Development of a Computational Model for Blast-Loading of the Brain including Tissue-Level Damage"
11:10am-11:25am	Dr. Bill Fourney	"Using Explosives to Investigate Brain Injury Mechanisms"
11:25am-11:40am	Dr. Bala Balachandran	"Blast Wave Interactions with Soft Tissue Matter"
11:40am-12:00pm	Questions	
12:00pm-1:00pm	Lunch	

TRAUMATIC BRAIN INJURY: A Public Health Problem

- 1.5 million sustain TBI each year in the United States
  - 250,000 hospitalized
  - 80-90,000/year with long-term disability
  - 50,000 deaths/year
  - No proven neuroprotective interventions
- Estimated 5.3 million men, women and children living with a TBI-related disability
- Leading cause of long-term disability among children in the U.S.
- Increases likelihood of Alzheimer's disease
- Total direct and indirect costs of > $50 billion

TRAUMATIC BRAIN INJURY A Major Warfighter Health Problem

- Mild brain injury-
  - Official DoD numbers – 123,000 since 2000
    http://www.health.mil/Pages/Page.aspx?ID=49
  - 15% of soldiers surveyed 3 months after returning from deployment described either loss of consciousness or temporary amnesia after a blast
    Hoge, et al. NEJM; 358(5):453-63, Jan 2008.
- Moderate to severe brain injury-
  - Official DoD numbers – 29,807 since 2000
    http://www.health.mil/Pages/Page.aspx?ID=49
  - 90% closed-head injuries, 10% penetrating brain injury
    http://www.health.mil/Pages/Page.aspx?ID=49
    Armonda et al Neurosurgery 59:1215-1225, 2006, Neal et al unpublished, personal communication Jim Eckland

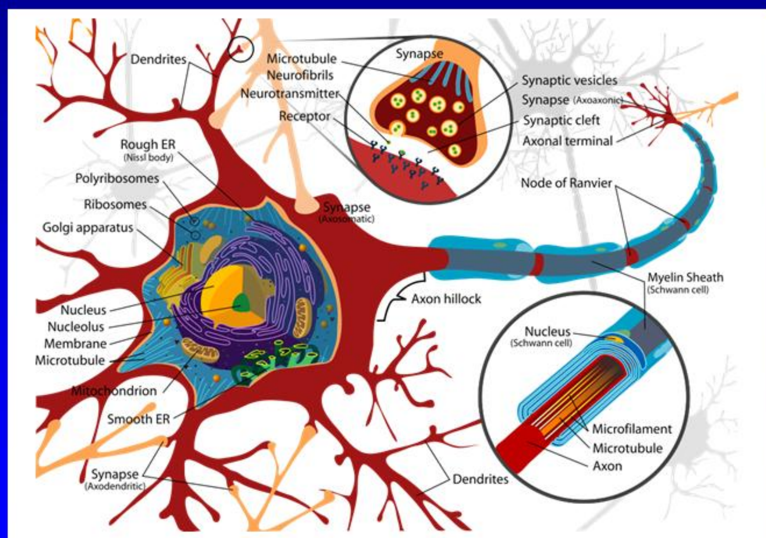
OUR STRATEGY FOR IMPROVING OUTCOMES

- *Improve non-invasive diagnostic tools (e.g., MRI, serum biomarkers), particularly for mild TBI*
- *Obtain ground truth data on incidence and levels of exposure to blasts and compare to incidence of mTBI*
- *Improve design of vehicles, helmets, body armor to reduce primary injury*
- *Develop improved animal models of warfighter TBI, including polytrauma, blasts, acceleration*
- *Computationally model blast TBI and validate with animal models*
- *Improve understanding of physiologic and molecular mechanisms responsible for warfighter TBI through preclinical and clinical research*
- *Translate results obtained in the lab to clinical implementation through trials with TBI patients at the R Adams Cowley Shock Trauma Center and subsequently in the warfighting theatre.*

HYPOTHESES

- *The extent and characteristics of TBI induced by traditional models, shock tube, blast tube, open-field blast, and blast-induced hyper-acceleration are qualitatively and quantitatively different.*
- *Mild TBI induced in blast paradigms is associated with subtle changes in brain energy metabolism (e.g., reduced aerobic metabolism) and in neuronal structure (e.g., diffuse axonal injury).*
- *Computational models of blast TBI can be validated with animal models using combined outcome measures using MRI, histology, and behavioral tests.*
- *Neuroprotection for warfighter-related TBI can be attained through the use of drugs that target multiple mechanisms (i.e., combination therapy).*

MICRONEUROANATOMY

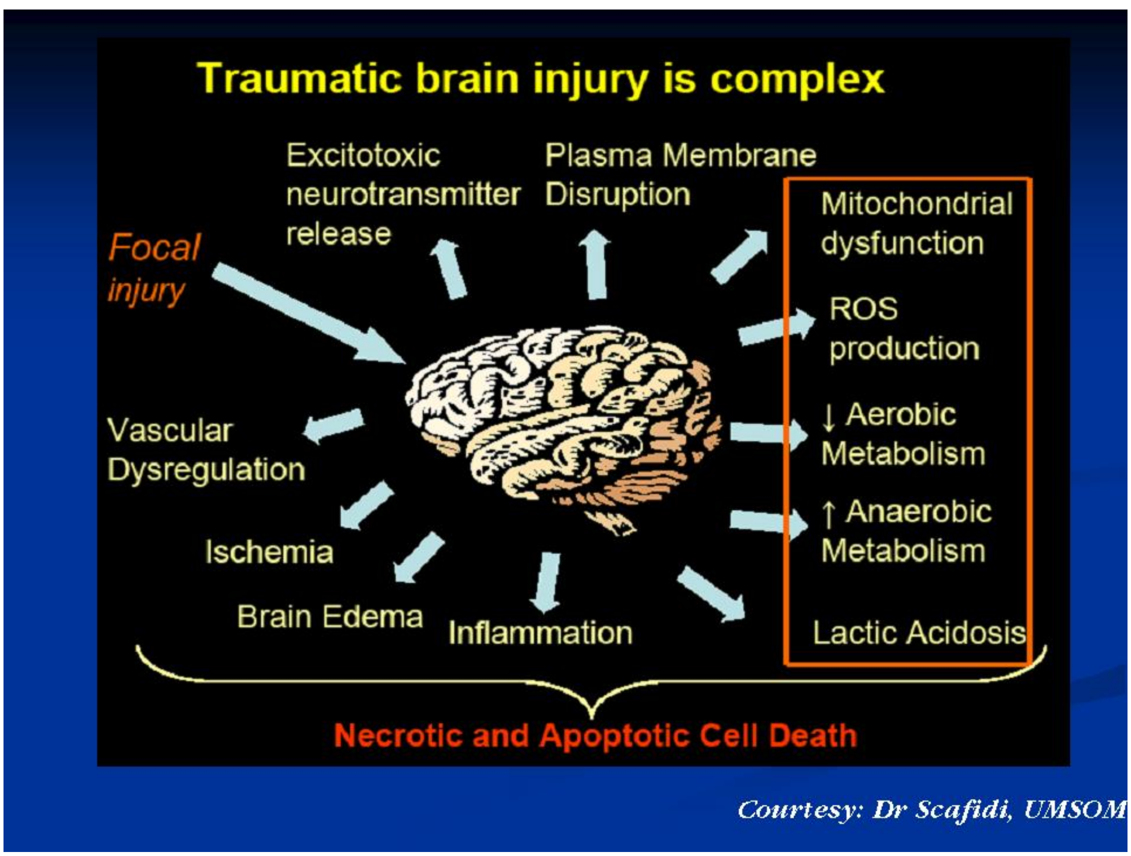


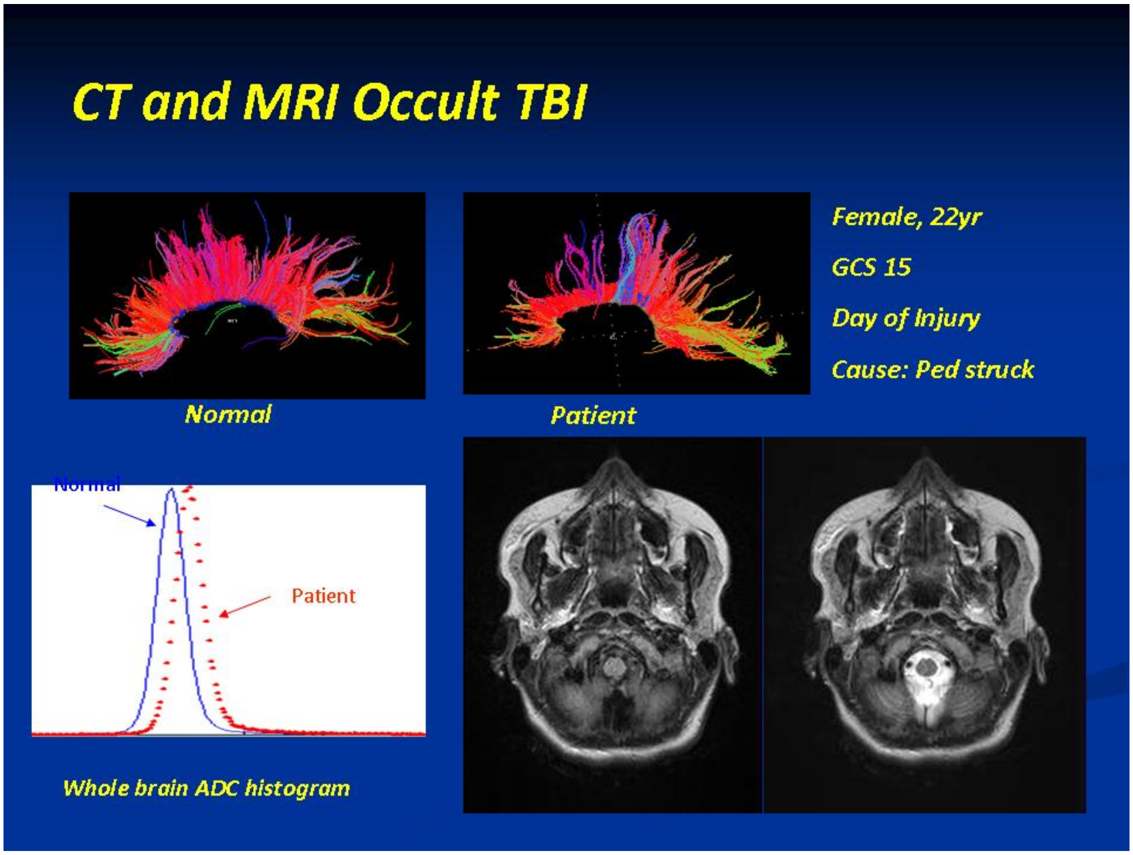
EXAMPLES OF NEUROPROTECTIVE INTERVENTIONS UNDER INVESTIGATION

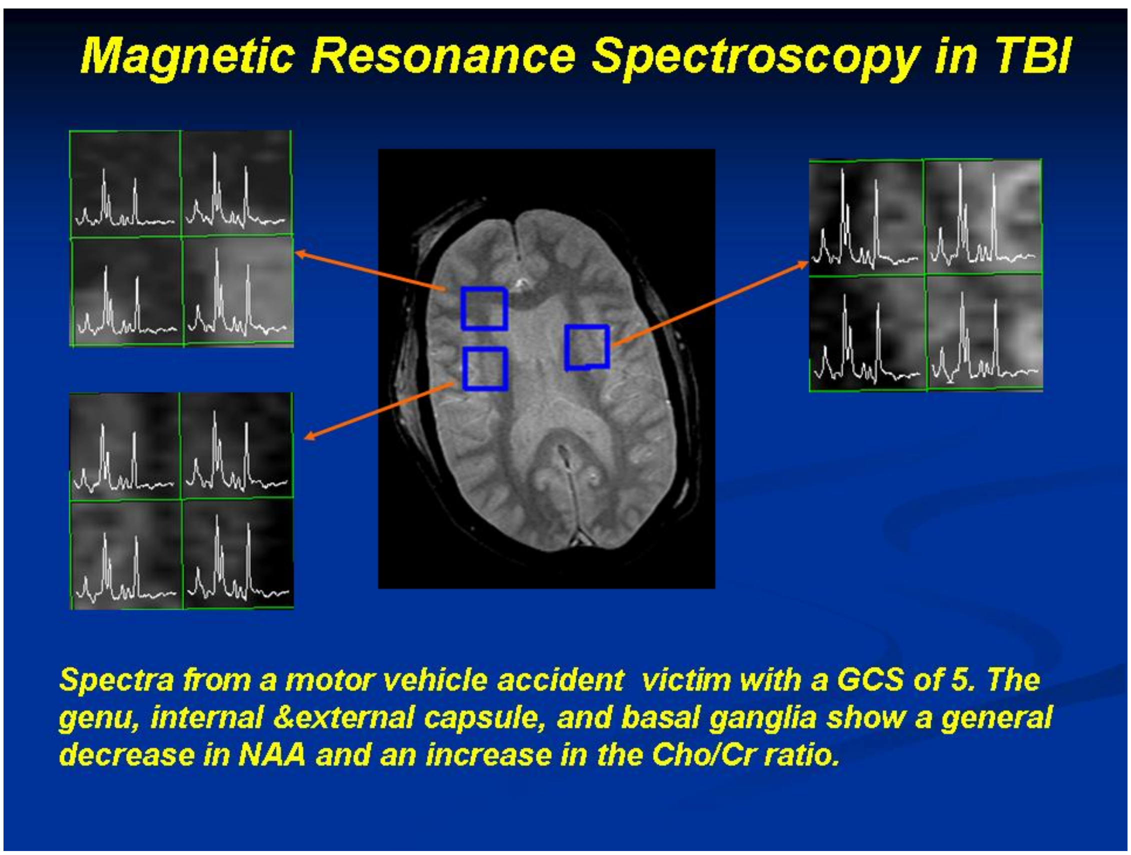
- ***Decompressive craniectomy*** *(de-inhibits blood flow caused by brain swelling)*
- ***Hypothermia*** *(generally reduces biochemical mechanisms of injury)*
- ***Progesterone*** *(stimulates expression of cell death gene products and stimulates "inhibitory" neurotransmission)*
- ***Hyperbaric oxygen*** *(promotes aerobic energy metabolism)*
- ***Glybenclamide*** *(inhibits brain swelling)*
- ***Antioxidants*** *(inhibit oxidative stress)*
- ***Acetyl-L-carnitine*** *(promotes aerobic energy metabolism and inhibits inflammation)*
- ***Sulforaphane*** *(stimulates expression of endogenous protective genes including those for antioxidants and anti-inflammatory proteins)*

CONCLUSIONS

- ***Warfighter TBI, particularly blast TBI, is a major health problem and a highly complex medical scientific problem.***
- ***A multidisciplinary approach to solving this problem is necessary, requiring the skills of energetics engineers, MRI physicists, neuroanatomists, biochemists, and trauma physicians.***
- ***The consortium of scientists at UMCP and UMSOM represents a multidisciplinary team uniquely qualified to improve the understanding of blast TBI, developing the tools to protect against injury, and testing safe medical interventions in the lab and with TBI patients.***




CT and MRI Occult TBI
Female, 22yr
GCS 15
Day of Injury
Cause: Ped struck
Normal
Patient
Normal
Patient
Whole brain ADC histogram


Magnetic Resonance Spectroscopy in TBI
Spectra from a motor vehicle accident victim with a GCS of 5. The genu, internal &external capsule, and basal ganglia show a general decrease in NAA and an increase in the Cho/Cr ratio.

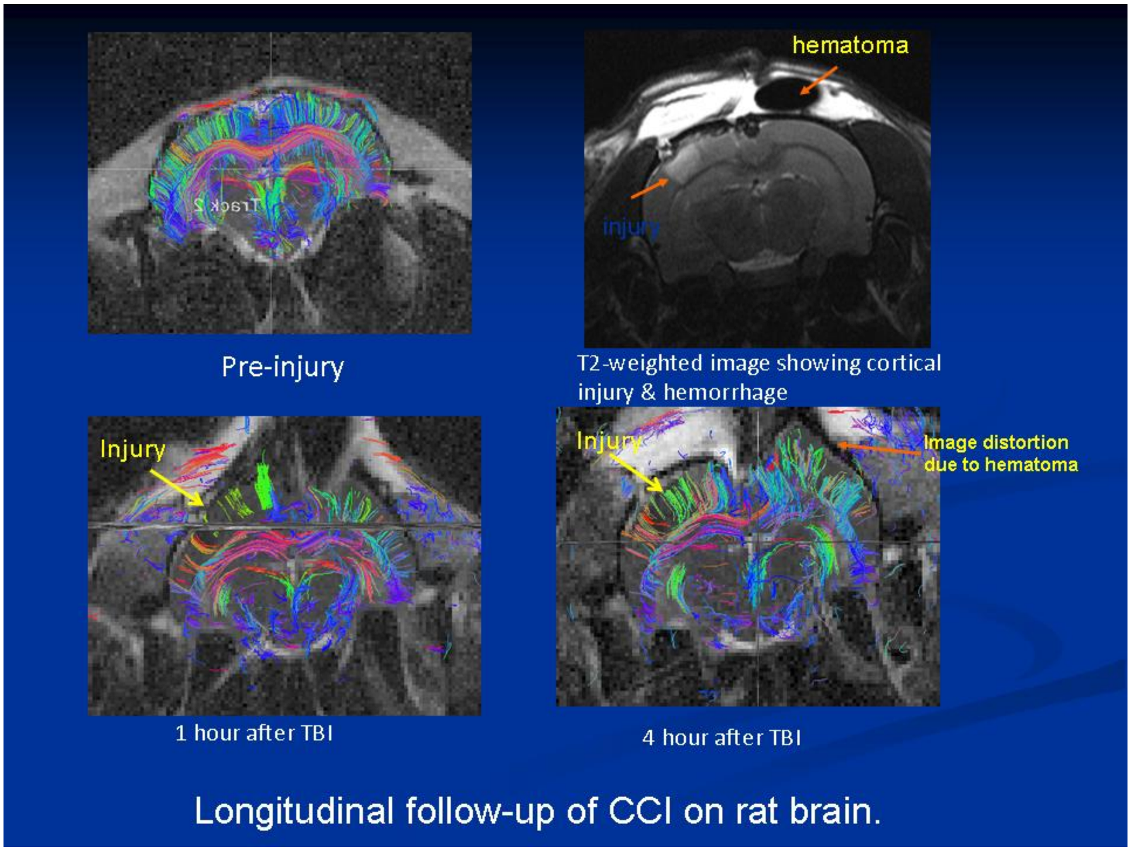
Core for Translational Research in Imaging @ Maryland

Controlled Cortical Impact Model of TBI

Pre-Injury

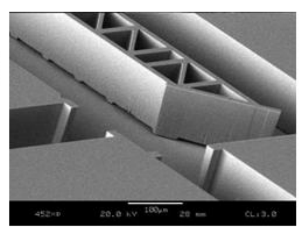
Post-Injury

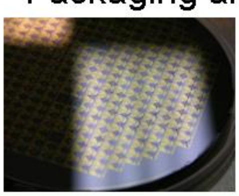
Proton Density | T1-weighted | ADC image | Fractional Anisotropy Image | Fractional Anisotropy Image

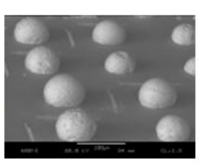


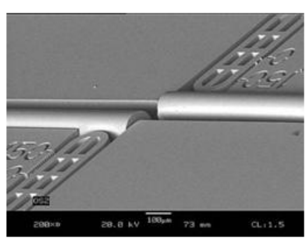
Microsystem Technology at Indian Head

- DoD leader in advancing MEMS for military applications
  - 13 patents and 24 pending patents over the last 10 years
- Successful in transitioning R&D efforts to acquisition programs
- Design, modeling, and layout of micromachined devices
  - Silicon and metal based
  - ***Sensors***, actuators, locks, and packaging structures
- Packaging and integration









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TBI Dosimeter Concept

Helmet mounted sensor suite that indicates excessive load exposure

- Acceleration load
- Blast pressures

Unpowered MEMS Sensor Suite
Attributes

- Sensors are self-contained in a disposable sensor suite
- Excessive load events recorded without an electrical power source
  - Always ready to record
  - Eliminates need for battery
  - Indefinite life (unloaded)
- Excessive load data is stored on the sensors for later retrieval
  - “Alarm” triggered at predetermined levels
  - Eliminates energy & time consuming data analysis
  - Does not record false events due to electrical glitches
- Excessive load event reported when passed through scanner

Sensor suites act as a “go/no go” indication of excessive loading condition

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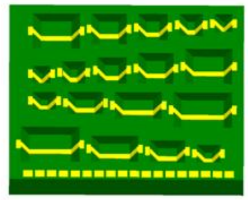
Unpowered Pressure Sensors

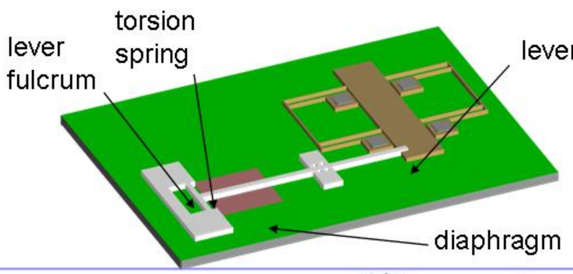
Description: ***unpowered*** sensor that can be queried to report if predetermined pressure threshold(s) has been exceeded

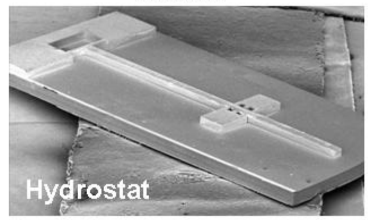
Threshold sensor operation

- Pressure wave experienced
- Diaphragms deflect
- If threshold exceeded, diaphragm breaks
  - Switch opens
  - Shock event recorded
- If threshold not exceed, sensor returns to ready state



Array of pressure sensors





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TBI Dosimeter

Project Impact

- Unpowered sensor suite does not fail to record excessive loading event; nor does it record reams of unnecessary data
- Inexpensive nature and small size of MEMS permits the application of sensor suites in a tape-like manner
- Dosimeter allows for real time evaluation of exposed soldier, allowing for responsive course of action
- TBI dosimeter could protect soldiers from suffering successive brain injuries during vulnerable period after initial exposure
- Dosimeter could be used to activate active constraint system for soldier protection

Real-time diagnosis of potential mTBI exposure

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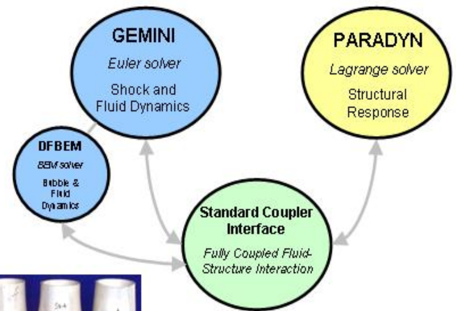
M&S with DYSMAS

DYSMAS (Dynamic System Mechanics Advanced Simulation): *A fully-coupled hydrocode for studying explosively-driven fluid-structure interaction problems*

- $33M investment in code development to date (+$17M over next 5 years)
- Parallel fluid and structural solvers
- Developed in a joint project agreement with Germany and maintained by Indian Head Division NSWC
- Incorporates advanced material models and algorithms for: explosive detonation, shock propagation, fluid-structure interaction
- Distributed to 100+ users nationwide
- **Comprehensive verification and validation database**
  - **Lab-scale to full-scale**

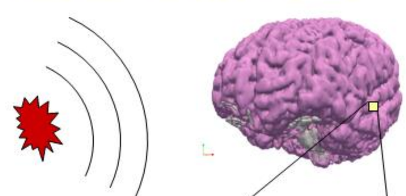


M&S Research Strategy

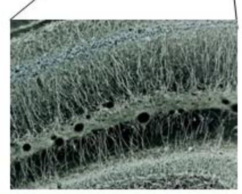
A multi-scale strategy will investigate the effects of blast-loading on the macro- and micro-scales.

- Macro-scale studies will investigate the response of the entire head/body to blast loading
  - Model validation
  - Biophysical injury indicator identification
  - Protective technology development and assessment
- Micro-scale studies refining tissue-level detail will investigate effects on and around fine structures
  - Guided by findings from whole-brain response model and medical knowledge
  - Example: *Effect of shock interaction with networks of axonal fibers*

Fully-coupled modeling of the response of the brain to blast-loading



Response translation to tissue-level model



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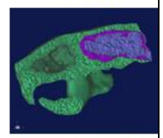
M&S Research Strategy: Macro-scale Model Development and Validation

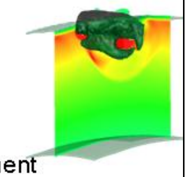
Computational models of small animals will be developed; simulations will be performed and validated with experimental results.

- DYSMAS will allow for fully-coupled 3D simulations capturing the initiating explosive event, interaction of the blast with the head, transmission of loads through anatomical structures, and time-resolved stress-strain state of the brain
- **First step: Finite Element Model Generation of Animal**
  - Geometry defined from medical imaging: segmented MRI data will delineate materials for the model (skull, CSF, gray & white matter, etc.)
  - Material properties will be guided by existing literature and improved by material property investigations led by UMCP
- **Second step: Simulation**
  - Perform computational simulations of well-characterized and controlled laboratory tests performed by UMCP and UMSOM
  - Analyze the biophysical response of the brain; identify regions of extreme positive and negative pressures, stress concentrations, cavitation, etc.
- **Third step: Validation**
  - Compare computational predictions with experimental outcome measures
  - Identify biophysical indicators linked to observed injury or functional impairment

FEM of Rat Head



Airblast Simulation



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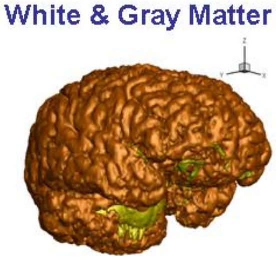
Extension to Humans

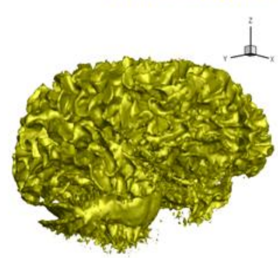
Nobody cares about rats.

- Small animal models are necessary for model validation because controlled tests can be performed
- M&S allows for the study of blast-injury of humans, including TBI
- MRI image resolution is more favorable for human studies than rats
- The study of scaling effects is key
  - Material properties
  - Do the biophysical indicators of injury observed in small animals apply to humans?
- Correlation of injury indicators will require comparison with available injury data with some knowledge of loading environment

White & Gray Matter



White Matter



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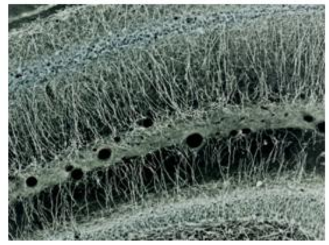
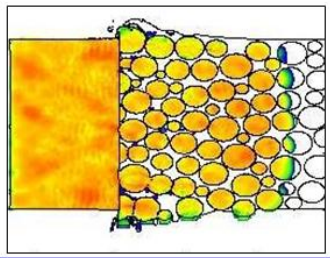
Micro-scale Modeling of Tissue Damage

Micro-scale models will capture tissue-level structures to investigate damage mechanisms at fine-scales.

- Continuum mechanics modeling at micro-scales is an emerging research technique
- The energetics community heavily uses this as a tool for investigating initiation and sensitivity of high-explosives
- We intend to apply this technique to investigate the phenomenology of bTBI
- Methodology:
  - Build tissue-level model of brain matter
  - Use knowledge gained in macro-scale simulations to apply appropriate loadings
  - Analyze results and compare with medical observations to help elucidate the biophysical-physiological link for bTBI

TBI Sensitive Neuron Axonal Fibers





Model of stress-wave propagation through fine-scale structure of explosive

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Protective Technology Development

A validated M&S capability will facilitate and accelerate protective technology development.

- Knowledge of bTBI damage mechanisms will drive the development of advanced protective systems
- M&S will play a major role developing and assessing concepts
- A validated M&S tool is crucial for producing reliable assessments
- Funding M&S development and validation efforts is crucial for:
  - Understanding the biophysical mechanisms of bTBI
  - Developing reliable tools for protective technology development

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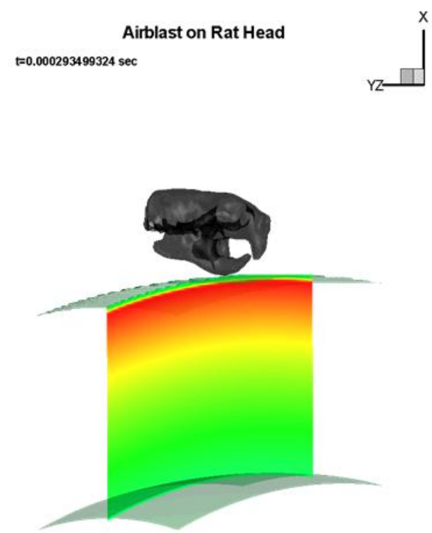
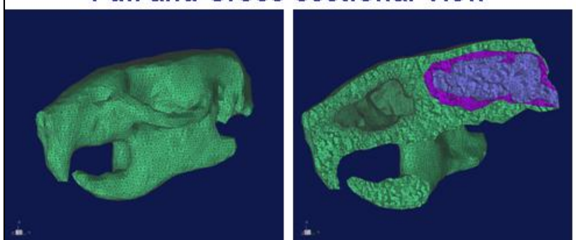
Example DYSMAS Calculation: Blast-Loading on a Rat

- Fully-coupled 3D DYSMAS simulation of explosively-generated shock impacting rat head
- Head model consists of skull, CSF and brain
  - Future models will contain more detail



Finite Element Model of Rat Head: Full and Cross-sectional View



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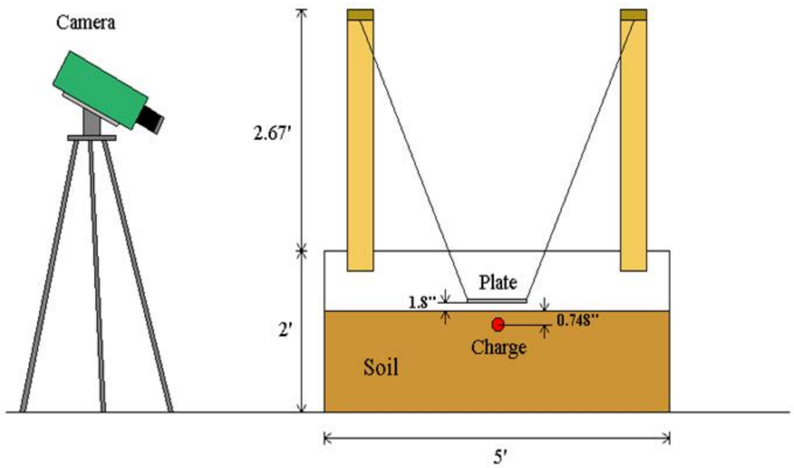
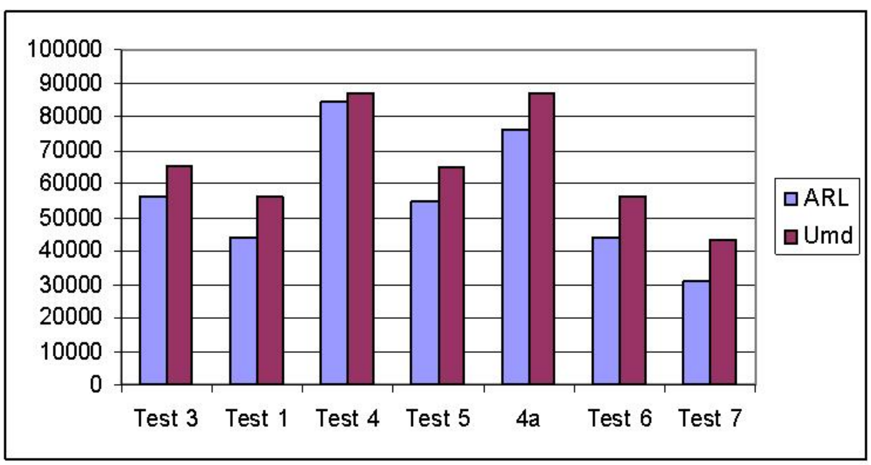
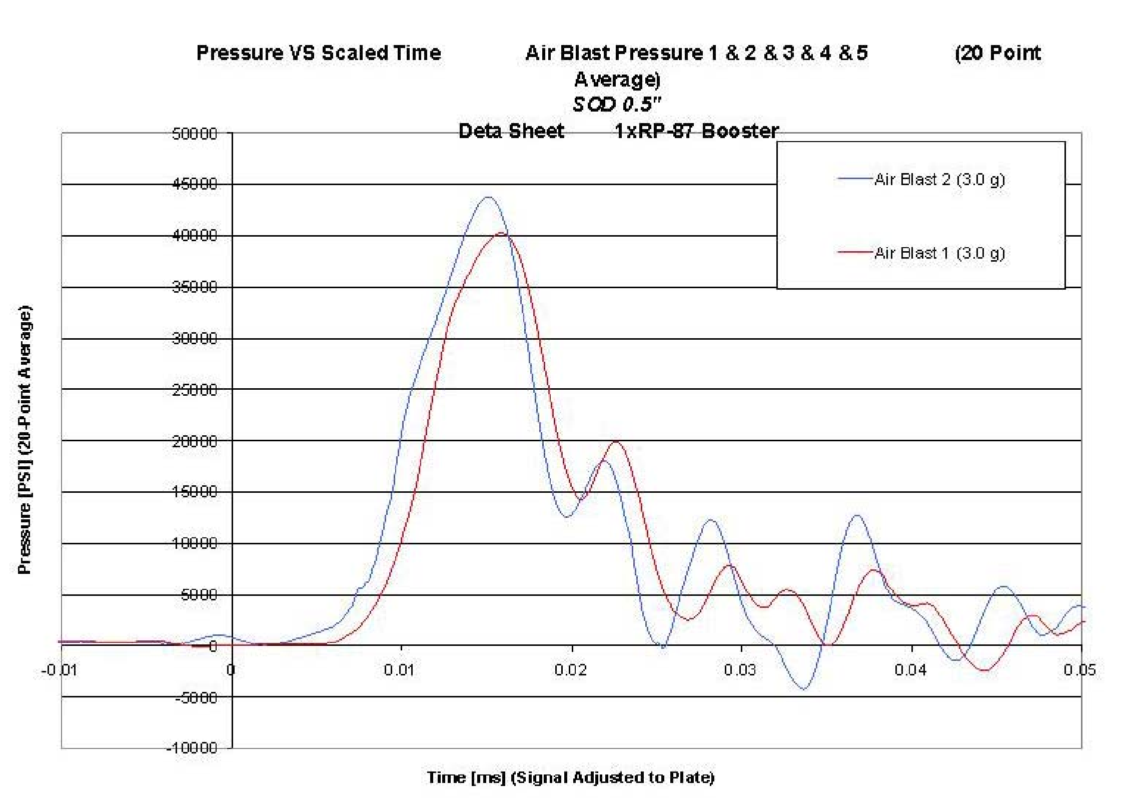
Impulse Testing



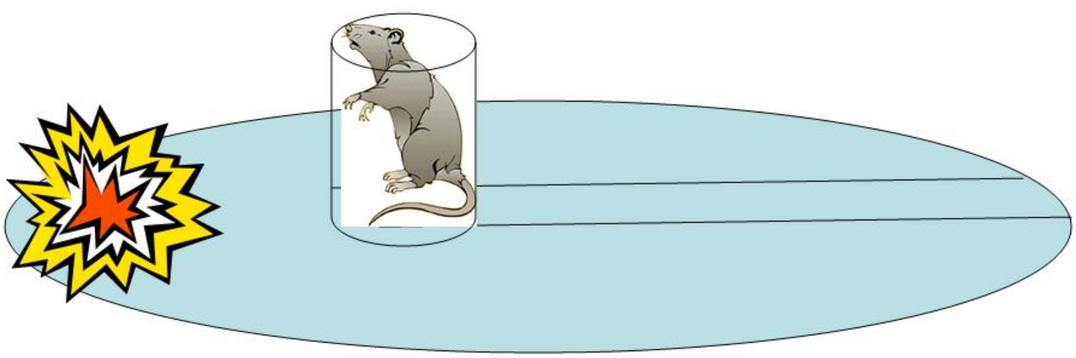
Note: Drawing not to scale.

TEST RESULTS





PROPOSED MODEL OF BLAST TBI USING RATS IN KEVLAR "BODY ARMOR" WITHIN A RESTRAINT THAT RIDES ON RAILS, MODELING BLAST TBI TO A WARFIGHTER ON THE GROUND



Brain Tissue: Experimental Characterization

• Brain tissue is anisotropic and non-homogeneous. White and grey matter, as well as the internal venation system lead to different properties, in different directions throughout the brain.

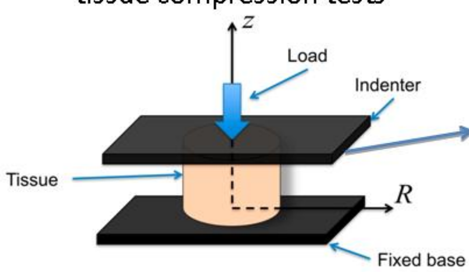
• Experiments with swine and rat brain tissue in tension, compression and shear deformation reveal that brain tissue behaves as a nonlinear visco-elastic material.

• Complete experimental characterization of brain tissue behavior requires tests over a wide range of strain rates. High strain rates are particularly important and relevant to blast loadings. However, brain tissue characterization at high strain rates remains to be addressed.

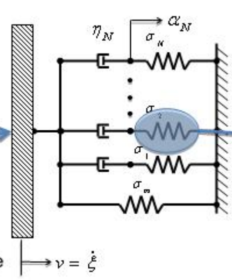
• Reduced-order models can be helpful for studying different material constitutive laws that can later be introduced into FEM models.

Brain Tissue: Experimental Characterization

Experimental set up for brain tissue compression tests



General Maxwell's Model

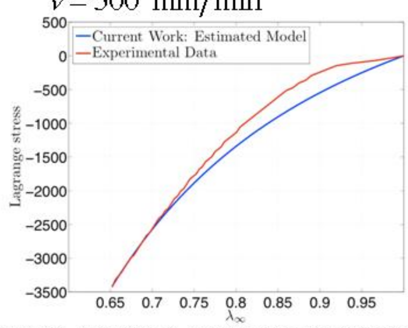


Hyper-elastic constitutive law:
Mooney-Rivlin

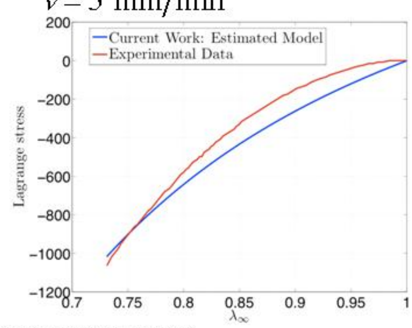
$$\sigma_i = 2\left(\lambda_i^2 - \frac{1}{\lambda_i}\right)\left(c_{1i} + \frac{1}{\lambda_i}c_{2i}\right)$$

Experimental data for compression test with nonlinear visco-elastic model

$v = 500\ \text{mm/min}$



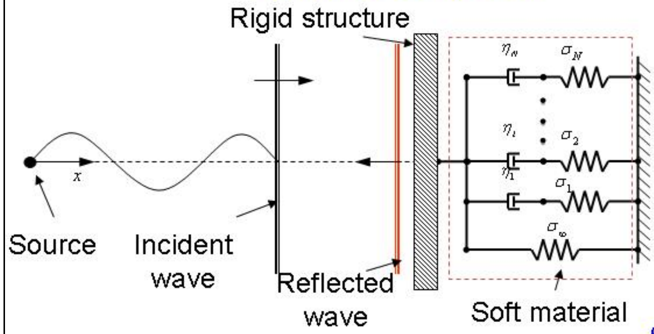
$v = 5\ \text{mm/min}$



Source: Miller K., Chinezi K, 2002. Mechanical properties of brain tissue in tension. *Journal of Biomechanics* **35**, 483-490.

Wave Interactions With Soft Material

Model description



- ξ Plate displacement
- σ_∞ Stress in the parallel nonlinear spring
- σ_i Stress in Maxwell's mode *i*
- f Incident pressure pulse
- g Reflected pressure pulse
- η_i Damping coefficient of Maxwell's mode *i*

Equations of motion

$$\ddot{\xi} = \frac{1}{m}\left(\sigma_\infty(\xi)+\sum_{i=1}^{N}\sigma_i(\lambda_i)+f+g\right)A$$

$$\dot{\lambda}_i = -2\left(\frac{\sigma_i(\lambda_i)A_0}{\eta_i L_0(L_0-\xi)}+\frac{\dot{\xi}}{L_0}\right)$$

$$\frac{\partial g}{\partial t} = -(\dot{\xi}+a)\left[\frac{\rho}{m}\left(\sigma_\infty+\sum_{i=1}^{N}\sigma_i+f+g\right)+\frac{\partial f}{\partial \xi_1}\right]$$

Stress in a nonlinear hyper-elastic rod: Mooney-Rivlin model

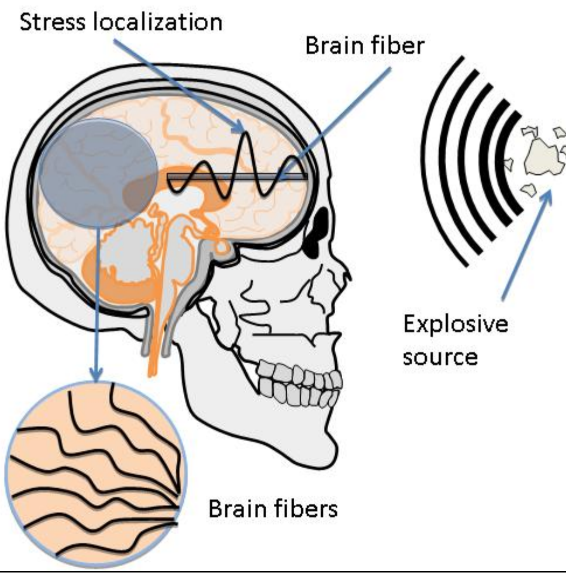
$$\sigma_i = 2\left(\lambda_i^2-\frac{1}{\lambda_i}\right)\left(c_{1i}+\frac{1}{\lambda_i}c_{2i}\right)$$

In previous studies,[1] interactions of blast wave with rigid structures supported by linear visco-elastic material have been considered. *The current work is unique in that it treats soft material as a nonlinear visco-elastic material.*

1. N. Kambouchev. *Analysis of Blast mitigation strategies exploiting Fluid-Structure Interaction.* PhD Thesis, Massachusetts Institute of Technology, 2007

Wave Phenomena Characterization

Studying the propagation of stress waves in a longitudinal brain fiber can help develop a fundamental understanding of the effects of nonlinear brain tissue properties and non-homogeneity in stress localization phenomena.



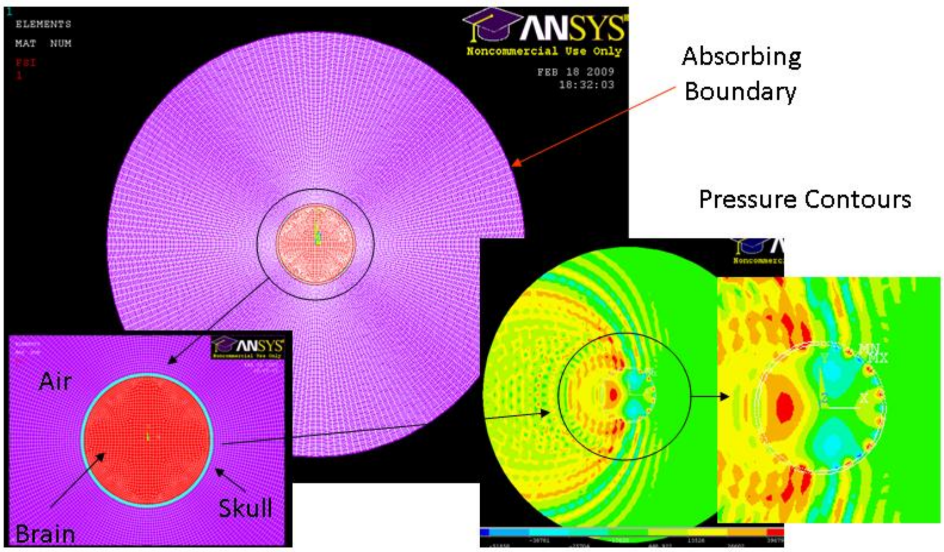
Fundamental questions

- ✓Which frequency contents of the loading lead to undesirable stress localization?
- ✓Which combinations of load amplitude and frequency are potentially harmful?
- ✓How can the knowledge be used to construct protective equipment for particular scenarios?

Blast Wave Interactions with Skull-Brain System

2-D Finite Element model

- Cylindrical shell (skull) filled with a water-like fluid (brain)
- Model accounts for fluid-structure interactions
- Pressure waves in the air generated by a point source



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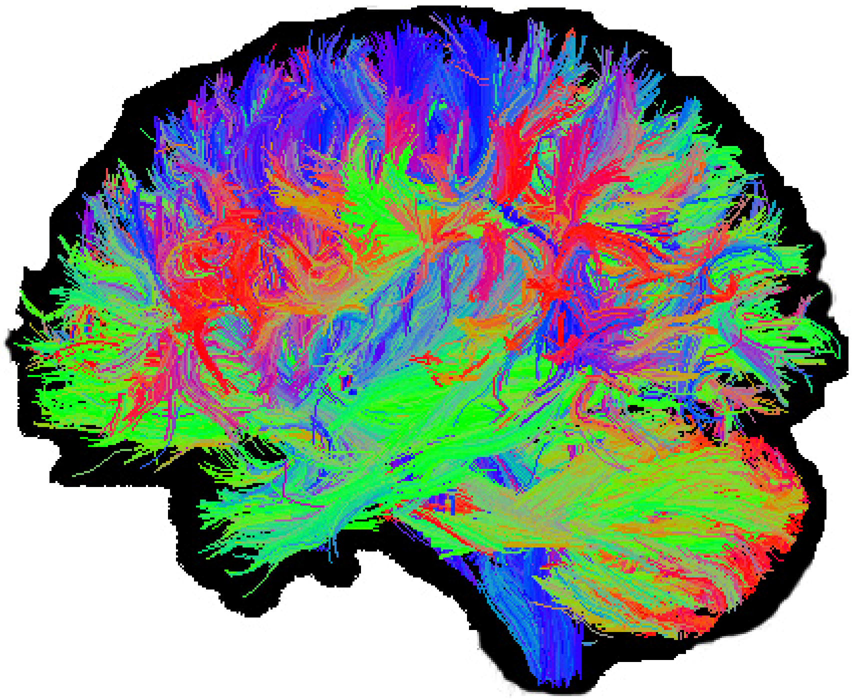
Growing Science & Technology in Southern Maryland

A Catalyst for Science and Technology in Southern Maryland



Our mission for this initiative is to reduce the mortality and improve the quality of life for warfighters that experience traumatic brain injury (TBI).