Department of Defense (DoD) Brain Injury Computational Modeling Expert Panel

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DoD Blast Injury Research Program Background

Program History

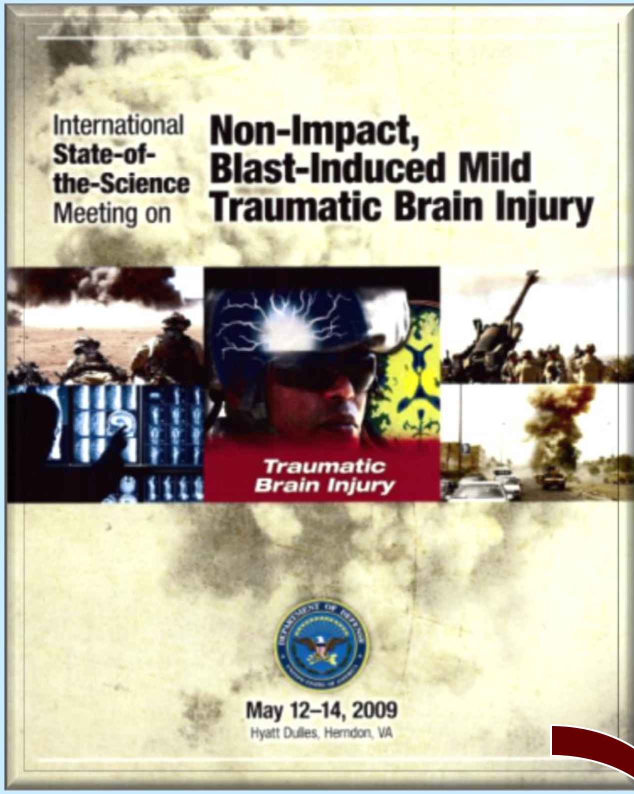
- Established by SECDEF in Jul 06 in response to Congressional mandate (Section 256, FY06 NDAA)
- Objective to coordinate medical research focused on the prevention, mitigation and treatment of blast injuries
- Governing regulation is DoD Directive (DoDD) 6025.21E—Medical Research for Prevention, Mitigation, and Treatment of Blast Injuries, 5 Jul 06
- SECARMY (Executive Agent) delegated to ASA(ALT) then to Cdr, MEDCOM
- Program Coordinating Office (PCO) established at USAMRMC in Jun 07

Key PCO Functions

- Identify blast injury knowledge gaps and prioritize research to fill gaps
- Oversee the JTAPIC Program to enhance Warfighter survivability
- Recommend blast injury prevention standards, including protection equipment performance standards for DoD
- Leverage expertise from industry, academia, and federal agencies to solve difficult blast injury problems
- Serve as "one-stop-shopping" for blast injury research information: **(https://blastinjuryresearch.amedd.army.mil)**

DoD Medical Research Program for the Prevention, Mitigation and Treatment of Blast Injuries

1st International State-of-the-Science Meeting
Non-Impact, Blast-Induced mTBI
(May 12-14, 2009, Chantilly, VA)



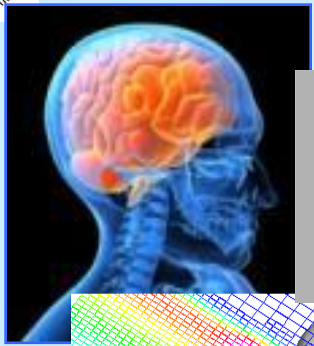
Established DoD Brain Injury Computational Modeling Expert Panel

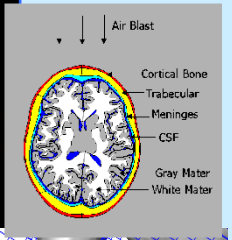
- Assessed what we know and don't know about the existence and mechanisms of this injury
- Attendees from DoD, VA, DOT, academia, and industry (Canada, Japan, the Netherlands, Sweden & USA)
- Key Findings:
  - ✓ Evidence from clinical and animal studies that this injury can occur, **but with many caveats**
  - ✓ Insufficient evidence to support one injury mechanism
  - ✓ Insufficient data to support changes to Warfighter protection systems
- Identified knowledge gaps and recommended improvements in research project coordination and data sharing

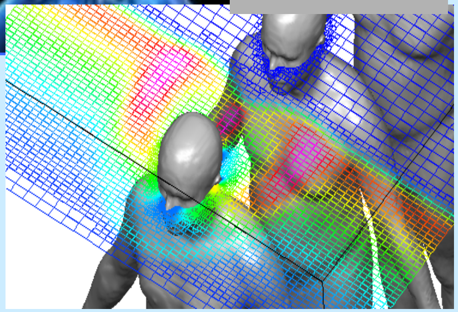
DoD Medical Research Program for the Prevention, Mitigation and Treatment of Blast Injuries

DoD Brain Injury Computational Modeling Expert Panel

- **Objective:** To assess the state-of-the-science in computational modeling of non-impact, blast induced mTBI and to integrate DoD research efforts to accelerate the transition of preventive and treatment strategies
- **Institutions represented:** DoD, other government agencies, academia, industry, and international researchers & clinicians
- **Deliverables (starting March 2011):**
  - ✓ Develop TBI community bench marking (model specifications, sharing, comparative analyses, and validation)
  - ✓ Laboratory Benchmarks to Support Model Validation (In-vitro, animals, and surrogate)
  - ✓ Validation strategy (In-vitro to in-vivo and scaling from animal to human)



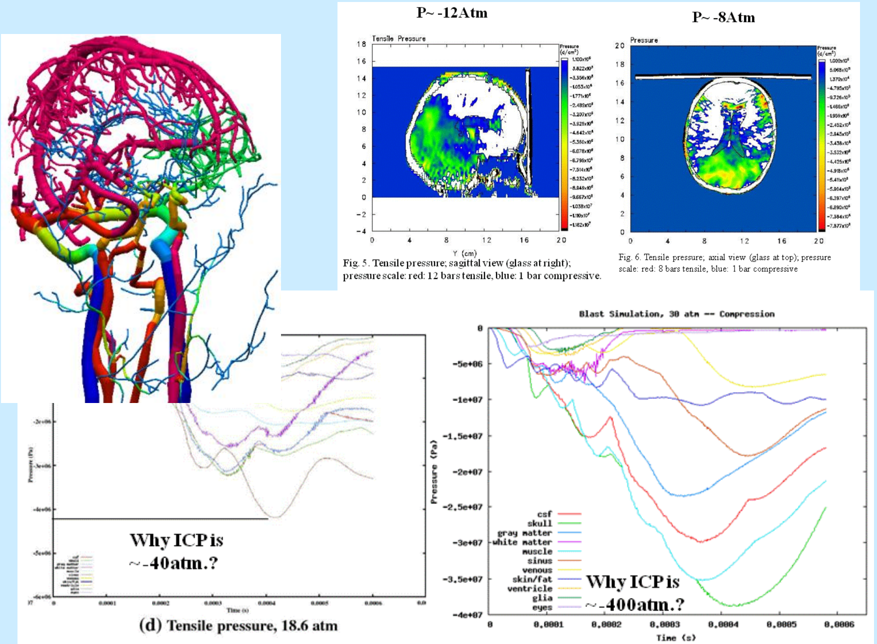




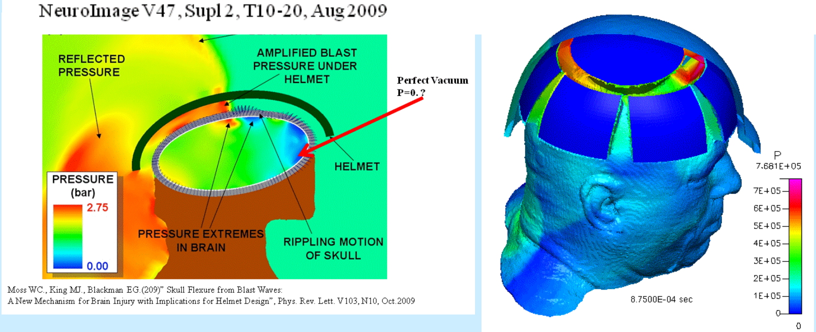
Focus on injury mechanism and "translating" mathematical models to support prevention and treatment strategies

First Meeting

- March 24-25, 2010, in Frederick, MD
  - Neurotrauma / Neurological deficits
  - Axonal Injury
  - Brain tissue damage/injury criteria thresholds
  - Physical effects of blast induced TBI
  - Dynamic skull flexure
  - High rate brain injury biomechanics
  - Multi-scale modeling
- Developed a working definition of validated computational model
- Components of blast injury relevant to non-impact blast induced mTBI
  - Pathways into brain – thru skull, thru soft tissue, skull acceleration, distortion of skull, surge
  - Internal damage - axons, microtubules, pressure and cavitation
  - Outcomes – loss of memory & consciousness
- Computational modeling challenges (~18)



Moore DF., Jérusalem A., Nyein M., Noels L., Jaffee MS., Radovitzky RA. (2009)" Computational Biology - Modeling of Primary Blast Effects on the Central Nervous System." NeuroImage V47, Supl 2, T10-20, Aug 2009



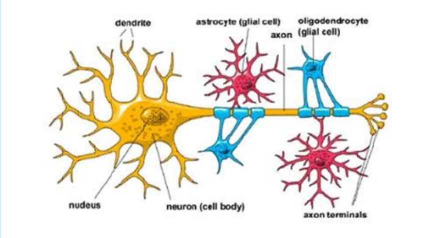
Moss WC., King MJ., Blackman EG.(209)" Skull Flexure from Blast Waves: A New Mechanism for Brain Injury with Implications for Helmet Design", Phys. Rev. Lett. V103, N10, Oct 2009

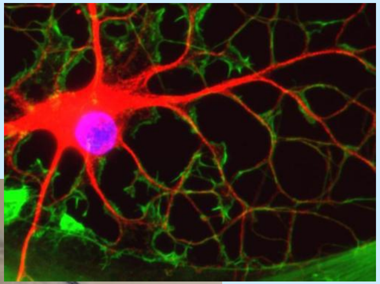
Computational Modeling Challenges

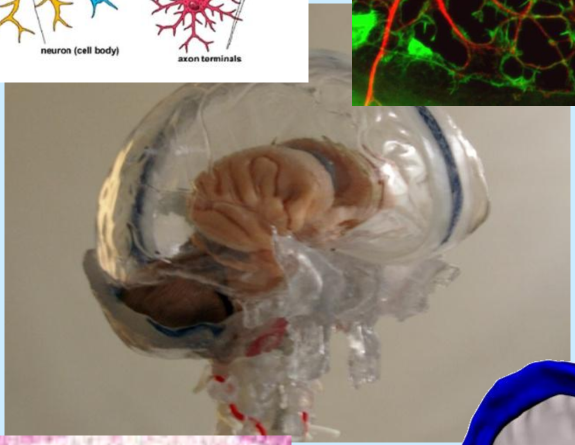
- Developing validated constitutive models for material properties of skull, cerebrospinal fluid (CSF), and brain tissue, particularly for large strain rates and for perfused tissue
- Developing mechanical dose-response models of brain tissue dysfunction
- Developing an objective method to measure blast exposure
- Modeling impact between brain and cranium, and determining how to properly account for the presence of large cerebral blood vessels, bridging veins, and brain perfusion
- Developing benchmark loading paradigm to facilitate model comparison and validation
- Developing adequate models of tissue response/mechanical injury (material failure)
- Modeling soft tissue
- Exploring the issue of cavitation
- Developing criteria for animal models that reproduce injury (determining endpoints)
- Establishing linkages to neurobiology
- Establishing solid models across multiple geometric scales
- Simulating long-time transient brain biomechanics during secondary injury development (e.g., edema, hematoma, and herniation)
- Understanding how mechanical energy translates into a concussion
- Understanding thresholds for injury (e.g., determine whether closed head injury thresholds for TBI in civilians can be applied to mTBI)
- Coupling whole body and the brain

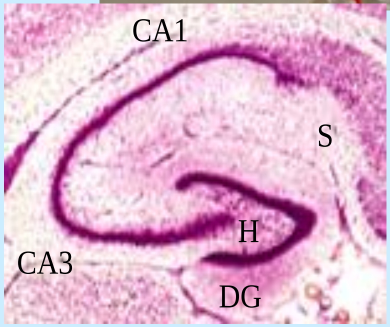
Second Meeting

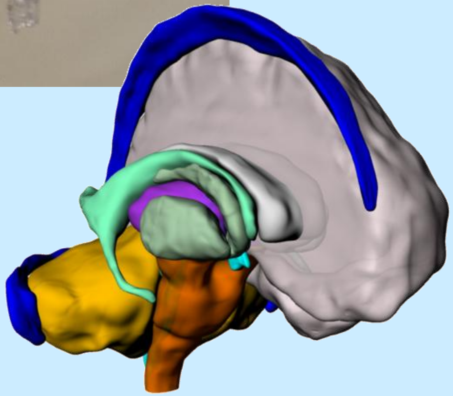
- August 12-13, 2010, in St. Pete Beach, Florida (ATACCC)
  - In-vitro brain mechanism
  - High rate tissue properties
  - Cell level experiments
  - Regional brain-strain properties
  - Brain tissue mechanical characteristics
  - Functional and structural injury thresholds
  - Neuronal chloride regulation in response to blast
- Recommendations
  - Develop bench-mark loading paradigms
  - Models of tissue response/mechanical injury
  - Explore cavitation
  - Models of brain tissue - subcellular & 3D
  - Data repository of scaled imaging models
- Identified soft tissue modeling as an area requiring further discussion





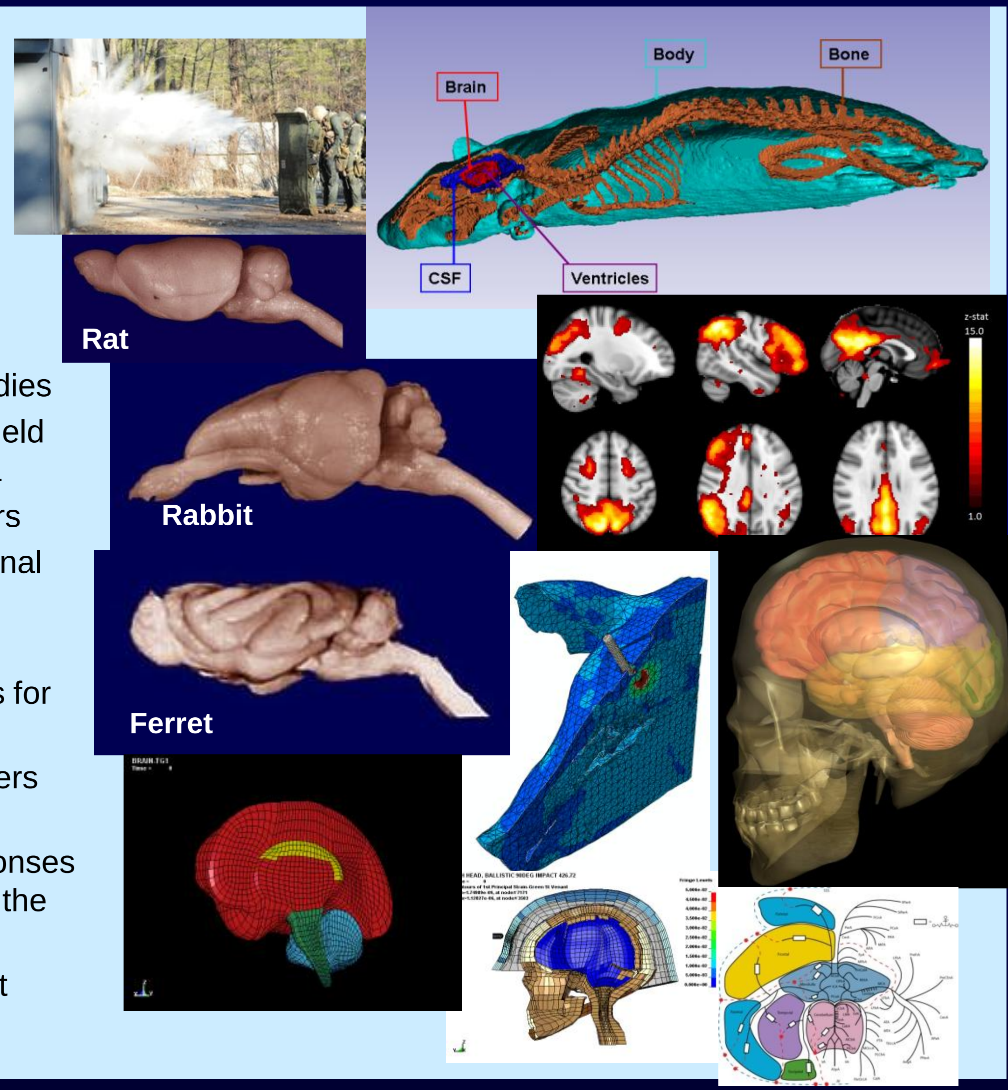






Third Meeting

- December 8-10, 2010 at JHU APL
  - Animal modeling
    - Rodents to nonhuman primates
  - TBI-Simulated Injury Model SIMon)
  - Clinical aspects of blast-induced mTBI
  - Epidemiology of blast injury
- Recommendations included:
  - Integrate clinical/epidemiology/animal studies
  - Mimic the physics of real-life blast in the field
  - Identify the neurobiology underlying blast-induced mTBI functional deficits in Soldiers
  - Develop models based on specific functional problems that are military-relevant
  - Conduct whole animal experiments
  - Define a series of multi-scale experiments for modelers
  - Obtain improved clinical histories of Soldiers exposed to blast
  - Elucidate the immediate biophysical responses to shock wave propagation in the brain at the cellular and sub-cellular levels
  - Sharing of computational models and test data

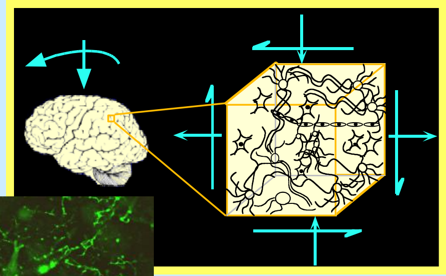


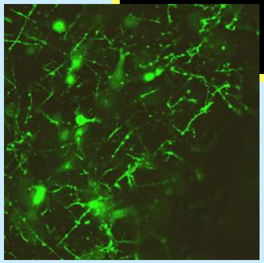
Fourth Meeting

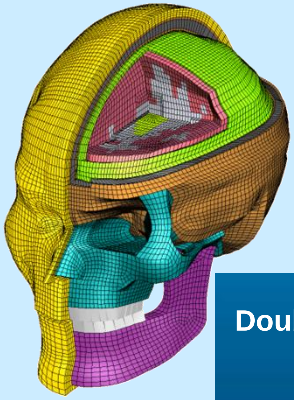
- March 29-31, 2011 at ISN-MIT
  - Soft tissue modeling
  - Brain Biomechanics

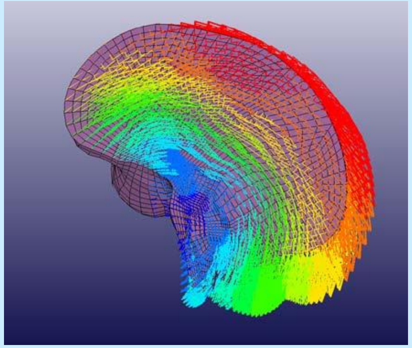
- Recommendations included:
  - Establish benchmark test cases
  - Develop new finite element method solvers (hour glassing, fluid/solid interaction, etc)
  - Determine material properties for various regions of the *in vivo* brain
  - Determine effects of repetitive blast on material properties
  - Identify biologically relevant interfaces (skull/cerebrospinal fluid/soft tissue)
  - Obtain multi-scale data

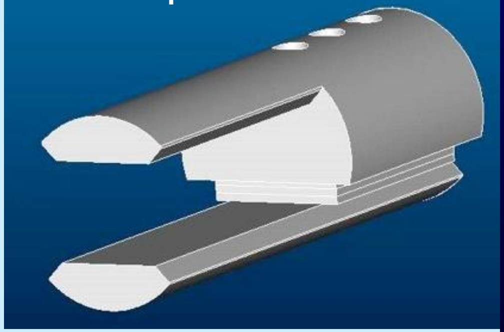
Complex strain Fields



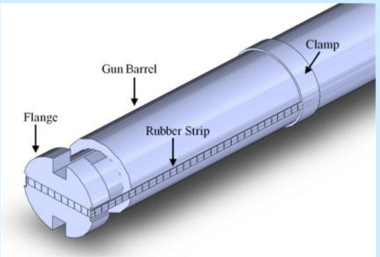








Double-Lap Shear Fixture



Next Steps

- Developing a road map and scientific approach for a validated blast-induced mTBI computational Model including:
  - Specifications (sharing models, comparing model results, comparing of different models, and validation of results)
  - Benchmark
    - In-vitro (brain slices, neuronal cell cultures)
    - Bench mark small animal
    - Phantom (surrogate)
  - Validation strategy
    - In-vitro to in-vivo
    - Scaling from animal to human

Focus on injury mechanism and "translating" mathematical modeling to expedite prevention and treatment strategies

DoD Blast Injury Research PCO Points of Contact

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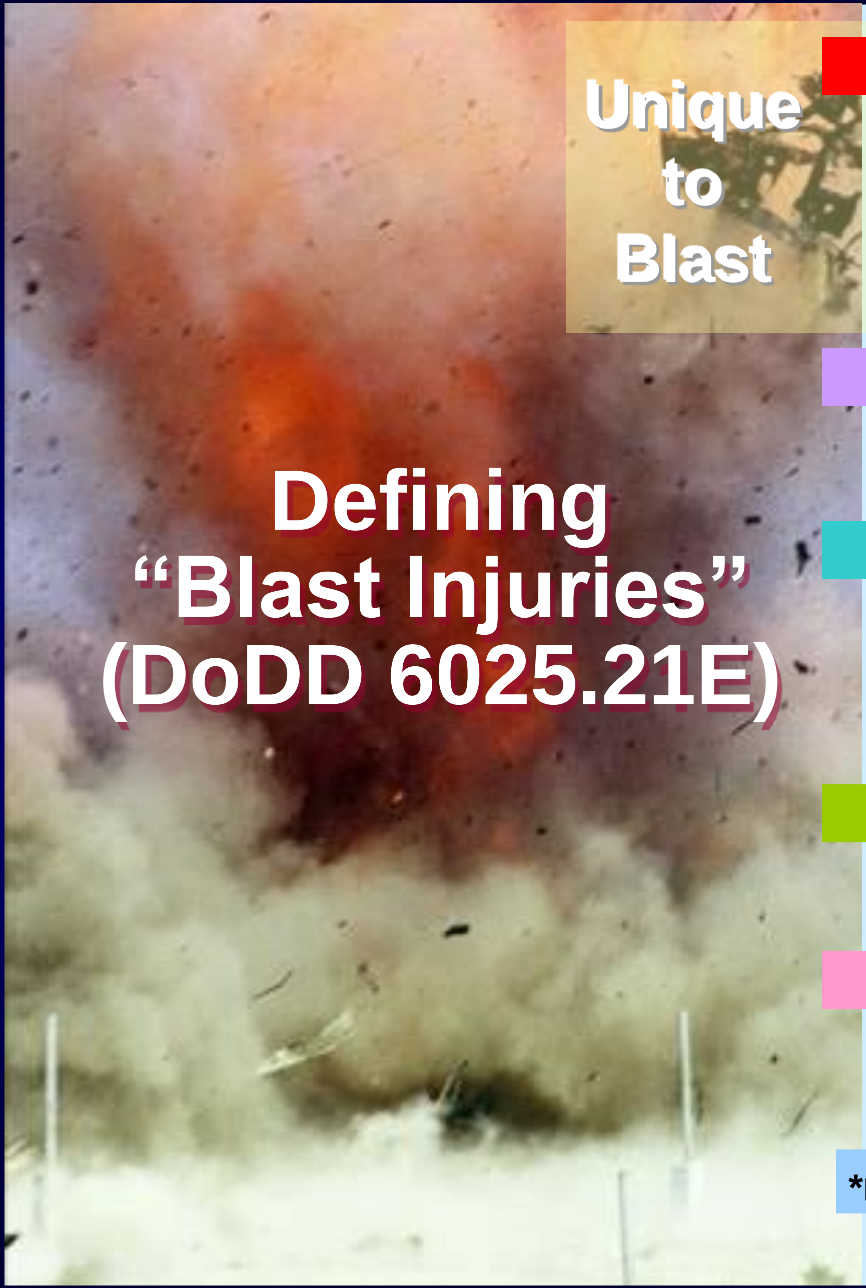
Back up

DoD Medical Research Program for the Prevention, Mitigation and Treatment of Blast Injuries



PRIMARY

- Blast lung
- Eardrum rupture and middle ear damage
- Abdominal hemorrhage and perforation
- Eye rupture
- Non-impact, blast-induced mTBI?

SECONDARY

- Penetrating ballistic (fragmentation) or blunt injuries
- Eye penetration

TERTIARY

- Fracture and traumatic amputation
- Closed and open brain injury
- Blunt injuries
- Crush injuries

QUATERNARY

- Burns
- Injury or incapacitation from inhaled toxic fire gases

QUINARY

- Illnesses, injuries, or diseases caused by chemical, biological, or radiological substances (e.g., "dirty bombs")

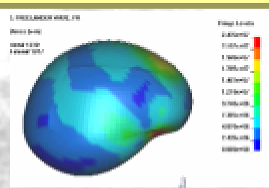
***Psychological trauma (including PTSD)**

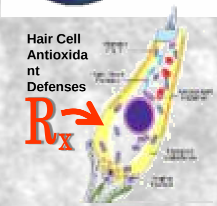
*Added based on latest research suggesting a high risk of developing PTSD following a concussion

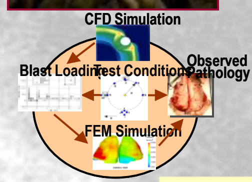
Key Blast Injury Research Topics

Injury Prevention

- Existence and mechanism of non-impact, blast-induced mTBI?
- Drugs to prevent and treat blast-related hearing loss
- Analysis of combat injuries and PPE performance (JTAPIC)
- Multi-effect blast injury models to improve protective equipment
- Resilience enhancement and prevention of PTSD







Acute Treatment

- Diagnostics and neuroprotectant drugs for TBI
- Hemorrhage control & blood products
- Treatment of psychological trauma
- Damage control orthopedics
- Pain management

Reset

- Tissue engineering and prosthetics
- Return-to-duty Standards
- Recovery of function