Research Report

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Toward a Unified Multiscale Computational Model of the Human Body's Immediate Responses to Blast-Related Trauma

Proceedings and Expert Findings from a U.S. Department of Defense International State-of-the-Science Meeting

The topic of the tenth U.S. Department of Defense (DoD) International State-of-the-Science Meeting (SoSM) on Blast Injury Research was "Toward a Unified Multiscale Computational Model of the Human Body's Immediate Responses to Blast-Related Trauma." The meeting was held August 16–17, 2022, at the RAND Corporation office in Arlington, Virginia, and more than 60 scientists, clinicians, and military leaders provided scientific overviews, presentations, and posters describing new and emerging science in the field. Before the meeting, a conference planning committee consulted on the literature review and research questions and served as a peer review panel for submitted abstracts. Five leading scientists and clinicians in related fields were invited to serve on an expert panel, lead working groups, and develop overall recommendations.

State-of-the-Science Meeting Summary

The proceedings and findings from the meeting were intended to help address the objectives of the SoSM, which were to

1. assess the state of the science of unified multiscale modeling of the human body's responses to blast exposure
2. identify major barriers and knowledge gaps impeding progress in the field, along with opportunities for investment in future research
3. identify additional opportunities for collaborative action (both government and public-private) that could accelerate progress
4. provide recommendations to advance preclinical and clinical research, determine key policy gaps, and identify areas to advance production development.

This document represents the complete proceedings of the tenth SoSM. Supporting appendixes provide a list of previous SoSMs (Appendix A); the agenda of the tenth SoSM (Appendix B); and biographies for the keynote speaker and expert panelists (Appendix C). These proceedings will be of particular interest to scientists, clinicians, military personnel, and policymakers working in areas related to military medicine and health, blast injuries, and, of course, burn injury.

The tenth SoSM was the latest meeting in a series established in 2009 under the authority of the DoD Executive Agent for Blast Injury Research. The meeting and these conference proceedings were sponsored by the U.S. Army Medical Research and Development Command and the DoD Blast Injury Research Coordinating Office. The series aims to identify knowledge gaps in blast injury research; ensure that DoD medical research programs address existing gaps; foster collaboration between scientists, clinicians, and engineers in blast injury–related fields; promote information sharing on the latest research; and identify immediate short- and long-term actions to prevent, mitigate, and treat blast injuries. See Appendix A for a list of previous SoSMs and their themes.

Abbreviations

AI	artificial intelligence
BHI	breath-holding index
BOOM	Blast Ordnance and Occupational Exposure Measure
CAVEMAN	Computational Anthropomorphic Virtual Experiment Man
DHS	U.S. Department of Homeland Security
DoD	U.S. Department of Defense
FEM	finite element model
HExCAT	Homeland Explosives Consequence and Threat
ICP	intracranial pressure
i-PREDICT	Incapacitation Prediction for Readiness in Expeditionary Domains: An Integrated Computational Tool
NIH	National Institutes of Health
NSF	National Science Foundation
PPE	personal protective equipment
SoSM	State-of-the-Science Meeting
TBI	traumatic brain injury

Working Group Questions and Answers

Working groups developed responses to four questions, or topics of discussion, designed in advance of the SoSM to address the four meeting objectives. Because the fourth working group question was focused on recommendations, the working group's response to that question is folded into the section titled "Expert Panel Recommendations."

What Is the State of the Science of Unified Multiscale Modeling of the Human Body's Responses to Blast Exposure?

In each of the working groups, the first response to this question was a question in and of itself: Does the research community need one unified multiscale model of the human body, or does it suffice to have low-fidelity models that are representative of the population with multiscale component models available to researchers as needed? The consensus across each of the working groups was that the state of the science for the indefinite future lies in utilizing multiscale component models on an as-needed basis, particularly given the existence of many high-fidelity component models (for components such as the head, lung, and ear). Although many of these models exist, there is a dire lack of interoperability between said models, posing a significant barrier to progress. Furthermore, although multiscale modeling is emerging, it remains rudimentary at best, one of the reasons being that multiscale finite element models (FEMs) are associated with a prohibitively high computational cost.

Another discussion point was the fact that the primary consideration of human body modeling lies in the body's mechanical response to a blast event. The scientific understanding of the body's mechanical response (also known in various disciplines as *biodynamics*, *kinematics*, and/or *external body loading*) is far more advanced and sophisticated than the understanding of the body's pathological response (also known as *tissue biomechanics* or *internal body loading*) to a blast event. Although the current default method for simulating responses at multiple scales is hierarchical modeling, particularly at the component level, subject-matter experts consider even hierarchical modeling to be relatively unsophisticated. For example, the precise formulation of interface conditions between the scales remain a matter of approximations and guesswork. Concurrent modeling schemes that incorporate multiple scales into the same model are nonexistent.

What Are the Major Barriers and Knowledge Gaps Impeding Progress in the Field?

There are various barriers and knowledge gaps impeding progress in the computational modeling of the human body's immediate response(s) to blast exposure:

- There is a lack of diversity in human models because most models represent the average human male. Anatomical variability has a tremendous effect on injury risk and designing personal protective equipment (PPE), among other things, which means that developing models that are increasingly representative of the population is critical to predicting response and subsequent injury. Models beyond the average human male subject are being developed, and this is a space that is rapidly improving for models of the brain, in particular; however, it remains a critical gap.
- The initial conditions (including the stress state), as well as boundary conditions, are often idealized or unknown. For example, tissues are typically studied in the relaxed state even though, in reality, they are in a stressed state before impact. Active muscle creates active loading within the body, which creates an initial level of stress and strain; however, either we do not know this loading or, in cases in which it is known, it is difficult to represent computationally. The idealization of initial and boundary conditions affects researchers' ability to accurately translate results to real-world applications.
- Although the high-fidelity macroscale models of brain biomechanics have been well established, microscale mechanobiology models of injury-sensitive structures (e.g., neurons, glia, axons, synapses, blood barriers) are lacking. Such models are needed to identify potential targets for both acute and chronic neurotherapeutics. It also remains unclear how to specify microscale model initial and boundary conditions from macroscale simulation results.
- There remains a tremendous focus on the impact of the overpressure wave, despite the fact that other forms of energy that cause injury exist.
- As mentioned previously, there is a lack of interoperability between existing high-fidelity component models. These models are not *unifiable*, meaning that it is not possible for researchers to unify individual models as needed to create a multiscale model of the human body or a portion of the human body. There are many reasons that interoperability of models is impeded, including the use of different solver platforms, different licensing rights, and varying classification levels.
- Similarly, the verification, validation, and certification of models must be more rigor-

A significant barrier to progress is a lack of sufficient knowledge integration and data sharing between various communities.

ously established. The limitations of models and subsequent applicability to real-world scenarios must be made transparent to all potential users so that models can become fully interoperable.

- Although animal models have been used to study brain injury neuropathology and cognitive responses for years, they have not necessarily provided a pathway for the translation of successful preclinical results to efficacious treatment for humans. A complementary use of humanized *in vitro* brain-on-chip platforms should be accelerated. It should be easier to develop corresponding mathematical models of such devices than to develop such models of the *in vivo* human brain.
- There is a distinct need to bridge the gap between animal and human models. There is a high dependency on animal models because of an inability to conduct a variety of needed experiments on humans combined with the lack of a correlation between cadavers and living humans. Cadaver models do not take into consideration critical components, such as blood flow, the inflation and deflation of the lungs, and the like, making live animal models that much more important.
- A fundamental gap exists between modelers and clinical researchers because the scientific community is failing to use model-driven experimental design, resulting in a lack of a connection between simulation results and warfighter performance. Because of a lack of collaboration between necessary parties, it remains difficult to correlate actual physical injury into the computational space—a gap that consistently came up throughout the SoSM. There is a need to correlate the probability of effect (derived from computational and experimental work) with clinical endpoints. Barriers to successfully accomplishing this include a lack of quantitative biomarkers to define these clinical endpoints and poor data collection. Improvements must be made to environmental and physiologic sensors to better facilitate data collection and collect model-appropriate measures in real time, allowing the scientific community to first create models and theories before collecting the requisite data to verify the model.
- A significant barrier to progress is a lack of sufficient knowledge integration and data sharing between various communities. More specifically, there is the perception that the military communities must do a better job of supporting the research and scientific communities. The military has access to meaningful datasets at both the individual and population levels, yet gaining access to these samples and data is challenging. Creating access to these data, whether through interfaces, de-identification processes, or other means, would allow the scientific community to develop more-realistic models that would then yield more-applicable, more-relevant results. Such data sharing would also more readily allow for the reuse of models; users within specific communities could simply utilize tools that already exist, making slight modifications to what has already been created as opposed to reinventing models from scratch.
- Although the focus of this SoSM was on the *immediate* effects of a blast on the human body, it is worth noting that there is a lack of knowledge on the temporal effects of blast exposure—particularly, those that arise from repetitive loading (e.g., deterioration, adaptability). It remains unknown how repeated blasts affect tissue over time. Given how many

service members are exposed to repetitive blasts in a nondeployed setting, determining the effects of repetitive exposure is critical. Similarly, correlations between mechanical insult and the biophysical series of cascading events are unknown. For this reason, current predictive capability is limited to acute or primary mechanical response (injury).

What Opportunities Exist for Investment in Future Research, as Well as Collaborative Action (Both Government and Public-Private), That Could Accelerate Progress?

There are ample opportunities for investment in future research and collaborative action, all of which could accelerate progress in the field. The working groups outlined the following opportunities for future research:

- Future research should emphasize the development of composite, multiscale, multiphysics models, as well as reduced versions that can be used in rapid field responses.
- The modeling and research communities need further support not only for the development of models but also for maintenance.
- In an effort to make simulation results more realistic and relevant to warfighter scenarios, there is a need to create engineered tissues for model parameterization, testing, and validation. This would allow the community to move away from using cadavers and animals and instead use engineered tissues as more-representative surrogates.
- There is a need to integrate mechanistic and data-driven models, allowing for the creation of a digital twin. This effort could first be piloted with a pig before a digital twin for a human is developed.
- Future research should focus on the development of a robust capability to collect, clean, and prepare data for use in mechanistic models. This effort should allow the modeling community to more efficiently identify appropriate data sources while simultaneously ensuring that all data are ethically sourced.
- A long-term commitment of resources (e.g., funding, personnel, and infrastructure) is necessary to create sustainable solutions, and interdisciplinary collaboration must be encouraged and, when possible, required.

Opportunities for collaborative action include the following:

- An artificial intelligence (AI)–based system should be developed that accesses both DoD and civilian databases to better facilitate data sharing across all sectors. Such a system could also be used for classification arbitration and for determination of privileges to access private information using privacy-preserving algorithms.
- There should exist a central DoD organization that coordinates and sponsors all blast-related activities across the services to marshal resources and coordinate disparate, yet concurrent, efforts. This joint organization would also be responsible for issuing a road map for progress, including tangible, measurable milestones. Additionally, this organization would be responsible for hosting an annual meeting for all stakeholders in blast research, providing a space for thoughtful, focused collaboration.

Expert Panel Recommendations

Following the SoSM, there was a closed session with the expert panel to develop final recommendations for future research and suggestions for policy priorities. Working from the literature review, the SoSM presentations, and the working group findings, the expert panel developed final conference findings with proposed directions for future research. We took notes during the closed session, held on August 18, 2022, at the RAND office in Arlington, Virginia, and subsequently synthesized them in Table 1. Although many of the responses to the working group questions listed above make for compelling recommendations in and of themselves, the expert panel specifically highlighted the recommendations below as being

TABLE 1

Expert Panel Recommendations by Domain

Domain	Expert Panel Recommendation
Research funding	• Research funding should be focused on topics of utmost importance (e.g., investigating correlations between insult, pathology, and treatment). Small Business Innovation Research and Small Business Technology Transfer vehicles could be explored in this regard, encouraging universities to move into this space. • Grand Challenge calls,[a] focused on a larger community of researchers, should be issued to address fundamental gaps in research as outlined above (e.g., the development of human and animal model digital twins). • Funding calls should consider mandating joint collaboration between disciplines (such as mathematicians, clinicians, engineers, statisticians, neuroscientists, and ethicists) because of the multidisciplinary nature of the research space.
Computational modeling	• The nature of this field of study implies that there will likely always be a dependence on animal models. Therefore, future research should focus on bridging the gap between animal and human models. • There should be an emphasis on improving the interoperability of existing high-fidelity component models and on the development of physiological connections between multiscale models. • There should be a focused effort on model-based quantification of the effects of repeated blast dose reaction and response. Additionally, models should consider the behavior of diseased and damaged tissue at multiple scales, given the operational environment of the warfighter.
Data collection and sharing	• An AI-based system should be developed to facilitate data sharing between DoD and civilian databases alike. • The modeling community should be more fully integrated with existing training protocols and existing lines and mandates to collect data for operational exposures.
Road map	• The lack of a true road map is critical and addressable by the Blast Injury Research Coordinating Office at this time. Additionally, if a central DoD organization were to be created (as suggested previously), this organization could prioritize addressing this critical gap.
Ethics and diversity	• Future work should elevate the importance of increased diversity in human models, developing and working with models beyond the average human male. • Credible practices of modeling and simulation should be incorporated throughout the process, particularly with respect to uncertainty quantification, verification and validation, and probabilistic modeling to address variability. • Ethical AI considerations, ethical data collection mindfulness, and specific rules and regulations related to these topics (among others) should be developed and strictly followed by researchers. • Appropriate levels of risk should be communicated between various communities of practice.

[a] Grand Challenges are a family of initiatives fostering innovation to solve key national, or global, problems. Grand Challenge calls are calls for research proposals with ambitious, yet achievable, goals in science, technology, and innovation that address one (or more) of these Grand Challenges specifically.

of critical importance moving forward. However, it should be noted that the recommendations below do not take away from the importance of many of the previously mentioned recommendations related to research and other domains.

Literature Review Summary

In the early 2000s, during the first several years of Operation Enduring Freedom and Operation Iraqi Freedom, improvised explosive devices accounted for a growing proportion of U.S. combat casualties and blast-related injuries. As incidence rates quickly rose, further research into the prevention, diagnosis, and treatment of blast-related injury was needed to identify those in need of care, how to determine their level of impairment, and the efficacy of various treatments and rehabilitation methods (Tanielian and Jaycox, 2008). Advancements in boundary conditions, material properties, the computational modeling of shock tubes that replicate blast waves, the use of animal models and cadavers for data, and validation have all contributed to enhance research about the human body's responses to blast exposure.

Developing comprehensive blast-related injury mechanisms remains an active area of research and exploration. Computational modeling has investigated some of the human body's responses to blast-induced injuries in various body parts, from the cellular level to the tissue system level. Such modeling grants researchers the ability to assess the vulnerability of organs exposed to blast and correlations with clinically measurable injury levels. However, despite significant progress, there are several important factors that remain difficult to measure directly in real time, including the fluid mechanics of the human body (especially the brain), electrochemical and electromechanical components, and the brain's mechanobiology (e.g., intracranial pressure [ICP], deformations, stretch, shear stress and strain, and maximum principal strain). Additionally, as critical as highly-focused computational models of one body part or tissue system are to deepening scientists' understanding, it is infrequent that service members incur injury to only one body part, making validated polytrauma-predictive models essential to fully understanding the body's response to blast.

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Although computational research methodologies have advanced, additional research to validate the accuracy of models and address challenges in modeling the human body from the cellular level to the whole-body level is still needed. Specifically, a multidisciplinary, multiscale computational model that integrates body systems has not been developed, and researchers also have not combined a system of models across multiple scales to achieve the same goal. This literature review we conducted, in advance of the SoSM and only summarized here, describes information about what computational modeling reveals about the human body's responses to blast trauma (Sousa et al., 2021). Specifically, this review aimed to (1) provide the state of the science of multiscale computational modeling of the human body's responses to blast-related trauma, including both descriptions of models used or developed and research findings, and (2) identify future opportunities to strengthen the current research on understanding the human body's responses to blast-related trauma, particularly across multiple scales.

Methods

Using research questions, practical considerations, and input from our expert advisers, we developed a literature review approach that included (1) exploratory search strategies to retrieve articles, (2) initial search terms to search for articles, and (3) inclusion and exclusion criteria to identify potentially relevant articles.

We initially explored the literature on the computational modeling of the human body's responses to blast to identify key studies and develop a focus for a more comprehensive search. We then searched peer-reviewed literature using terms related to blasts (e.g., *explosion*), body parts (e.g., *cortex* or *brain*), and computational modeling (e.g., *FEMs*) to explore multiscale computational modeling that described the human body's responses to blast-related trauma. We searched the following databases: PubMed, Web of Science, the Cumulative Index to Nursing and Allied Health Literature, PsycINFO, the Institute of Electrical and Electronics Engineers, and the Defense Technical Information Center. Because the topic was specific to the human body's responses, we excluded nonhuman studies. It is important to note that this effort was not designed to be a systematic review but rather to assess the state of the science and highlight key themes across the body of literature. Therefore, it is possible that individual articles were missed in the search, despite all efforts made to include relevant literature.

Summary of Findings of the Human Body's Responses

The literature review sought to provide answers to the following basic question: What does computational modeling tell us about the human body's responses to blast injury? The following summary of results begins to answer that question, breaking down findings using the region of the body modeled.

Brain trauma. Computational modeling has been used to explain the effects of blast waves on the brain. As noted in the literature, an understanding of the pattern of injury and changes in the stress of the brain can be used to estimate the severity of injury or the likelihood of injury in different brain regions (Chafi, Karami, and Ziejewski, 2010; Pan et al., 2013). Computational modeling findings have also increased knowledge of the increases and decreases associated with blast exposure on ICP, shear stresses, shear strains, and relative displacements in brain tissues (Tan et al., 2021; Zhang, Makwana, and Sharma, 2013). Furthermore, computational modeling results provide an understanding of the role of skull thickness, skull shape and size, vascular networks, and myelination (Garimella, Kraft, and Przekwas, 2018; Ho and Kleiven, 2007; Zhang et al., 2002).

Skeletal trauma. Injuries from underbody blasts often cause injury to multiple areas of the body and can be fatal (Lei et al., 2018; Weaver et al., 2021). Computational modeling results described effects of posture in a vehicle on injury (Tse et al., 2020). Notably, modeling of whole skeletal structures is limited. This might be the case because much of the research conducted is focused on the blast wave's effect on soft fluid or air-filled organs. Additional research to fully understand the mechanism of injury that accounts for a variety of field conditions could be valuable to future design of vehicles and protective equipment.

Ocular trauma. Computational studies provide various results related to ocular injury after blast exposure. Primary blast injuries can induce ruptured globes, hyphemas, serous retinitis, conjunctival hemorrhage, and orbital fracture. More common are secondary blast injuries that typically lead to eye or orbital damage. Findings from studies show how blast waves can cause stresses and strains that can be severe enough to cause loss of vision (Bhardwaj et al., 2014; Karimi et al., 2016; Liu et al., 2015; Notghi et al., 2017; Rossi et al., 2012; Weaver, Stitzel, and Stitzel, 2017).

Auditory trauma. Research conducted with human data is limited. We found one article investigating auditory injury after a blast or explosion using a human cadaver (Leckness, Nakmali, and Gan, 2018). Nonetheless, this finding demonstrates the feasibility of using computational modeling to (1) explore the biomechanical response of the human ear to blast overpressure and (2) subsequently evaluate hearing protection devices. Combining this model of the human ear with other systems could successfully lead to a unified model of the human body's responses to blast trauma.

Thoracic injuries. Although the literature describes findings regarding lung injury (Van der Voort et al., 2016) and rib injury (El-Jawahri et al., 2009; Kang et al., 2015; Poplin et al., 2017) after blast exposure, to our knowledge, there is a lack of a unified computational model of the complete thoracic area, including the heart and related injuries, specifically in a military setting.

Abdominal trauma. We found no computational or experimental research in humans of the abdominal response to blast-related trauma.

Skin trauma because of burns. Although burns are particularly common in cases in which the victim is close to the blast site (Shuker, 2010), computational modeling of burns in humans is almost nonexistent. Using multiscale computational models to understand the mechanisms and progression of injury and the subsequent use of protective equipment and treatment could be quite valuable.

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Future Directions

Although meaningful progress has been made in the computational modeling of the human body's responses to blast exposure, several important issues need to be addressed.

Work Toward Developing a Unified Multiscale Model or Combining Models to More Fully Investigate the Human Body's Responses to Blast Exposure

Research on multiscale modeling of the human body's responses to blast exposure remains nascent. To date, computational models have largely explored individual human body parts, likely because of the challenges associated with modeling complex biological systems. A significant obstacle to developing a unified multiscale computational model of the human body—from the cellular level to the tissue level to the whole-body level—is the need to integrate many different techniques, as described in the computational modeling section of this report. Another challenge to the development of a multiscale model, or combining models, is the need to understand different levels of spatial and temporal detail to fully grasp the effects of blast trauma on the human body. Consider the example of understanding the effects of blast exposure on the chest. Modeling the effects of the blast wave requires a complete understanding of the mechanisms involved as the wave propagates through the body armor, skin, ribs, and then lungs. In this example, a unified model would require multiple computational methods to describe the functioning of the body, which is made up of different solid and fluid types, as well as different scales. Difficulty occurs in determining what scales are involved in this incident, how each scale should be modeled (in terms of elements, properties, and biomechanics), and how different scales should be integrated. Nonetheless, interest in the ability of computational modeling to provide mechanistic insights into the consequences of the human body being exposed to blast waves is increasing. The field should continue its efforts to assess the feasibility of integrating information about the blast wave's path through the human body to help determine the effects of blast exposure. The development of a unified multiscale model of the human body's responses to blast trauma, or the combination of multiple computational models in a systems manner, could improve the understanding of both the short- and long-term effects of a blast on the human physiology.

Establish Clinical Injury Thresholds

To our knowledge, although there are studies that describe multiple aspects of the human body's responses to blast, there are few well-established clinical injury criteria with respect to mechanical responses of the human body to blast shock waves, with the exceptions of lung and chest injuries. This is likely because of several factors, including significant variability in exposures; limited quantification of expected strain and strain rate values; the large variation in published mechanical properties of tissue; and differences in the measurement of tissue, blood, shear stress, and ICP (Singh, Cronin, and Haladuick, 2014). Accordingly, models are unable to relate any kinematical or biomechanical parameters to any injury threshold. Correlating measured response to clinically detectable injury could help improve understanding of the effects of blast injury preclinically and clinically, particularly in the case of multiple subclinical blast exposures (Tan et al., 2021).

Simulate a Wider Variety of Blast Exposures

Many of the discussed reports model events with only a single blast condition, such as distance from blast or charge size, which limits the ability to assess the underlying biomechanics of blast injury, particularly in military-related environments. As multiscale modeling research advances, integrating aspects of the blast environment—such as explosive types (e.g., C-4, trinitrotoluene, dynamite), charge sizes, charge distances, and field conditions (e.g., open spaces or closed spaces)—should be investigated. In order for researchers to fully understand the potential for injury and the underlying mechanisms, computational models need to provide an understanding of the human body's responses under a wider variety of blast exposures.

Collect More-Relevant Blast-Related Military Data for the Purpose of Validating Computational Models

There are limited blast-related data collected in military settings, making it difficult to validate computational blast models and thereby limiting these models' utility. The use of nonmilitary data might not fully correlate with military injury because of the unique features of military-related blast exposure, such as varying explosive types, protective equipment used, and field conditions (e.g., being subject to a blast inside a military vehicle versus in a warehouse or in an open field). Additionally, many of the findings are reported on blast exposures with charge sizes that might not be typically experienced in a military setting (Yokohama et al., 2015). Thus, to validate computational models, there is a need to collect blast-related military data to account for varying conditions specific to military settings.

Evaluate Responses with Multiple Representative Bodies

To fully understand the human body's responses to blast trauma, models need to account for anatomical variation. In the military, weight differences might be minimal. However, other size and gender differences between individuals could affect the results of the models. For example, women have a higher average skull thickness than men (Garimella, Kraft, and Przekwas, 2018). Additionally, height, muscular, and endocrinological differences might correlate to different effects of blast exposure. Developing multiple representative human body models could improve understanding of the effects of blast for the variety of service members exposed to them.

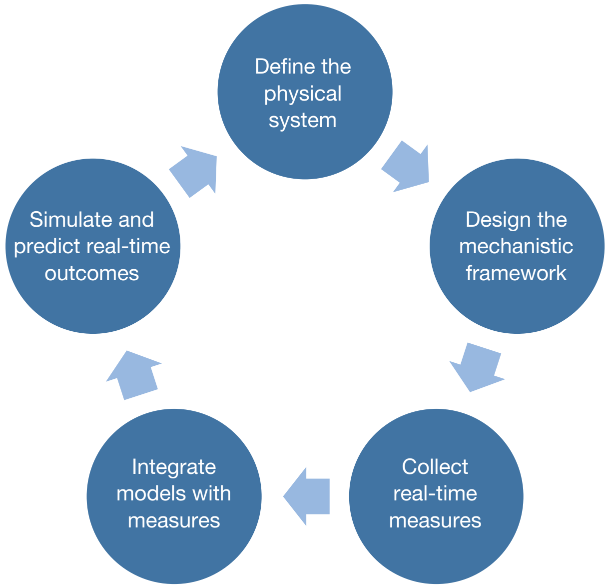
Keynote and Invited Speaker Presentation Summaries

This section provides summaries of the keynote and invited speakers' presentations. The summaries were compiled from notes taken by our team during the SoSM.

Keynote: Grace C. Y. Peng, Ph.D.

A *digital twin* is a mechanistic model of physical systems that is integrated with real-time, longitudinal measures to accurately monitor and predict the function of medical devices and their interaction with physiology as the systems age and evolve (Interagency Modeling and Analysis Group, undated). A digital twin could facilitate real-time prevention, diagnosis, and treatment (Figure 1). For the purposes of modeling the human response to blast injury, Peng challenged the audience to define a physical system and the mechanistic framework of that system. These

FIGURE 1
Digital Twins Conceptualized



SOURCE: Adapted from Peng, 2022.

replicable models could be used for surgery, blast injury protection, or other mechanistic models.

Despite the promise of and excitement over these models, Peng presented many challenges. Researchers need to ask themselves the following questions:

- What needs to be predicted?
- What can be modeled and simulated?
- What measures need to be captured?
- Does the technology exist?
- What ethical issues around privacy and consent need to be addressed?

Furthermore, when building these models, researchers need to balance near-term questions with those that have not yet been considered.

Invited Speaker Presentations

Predicting Blast-Induced Traumatic Brain Injury Through High Fidelity Finite Element Head Models and Cellular-Based Injury Criteria

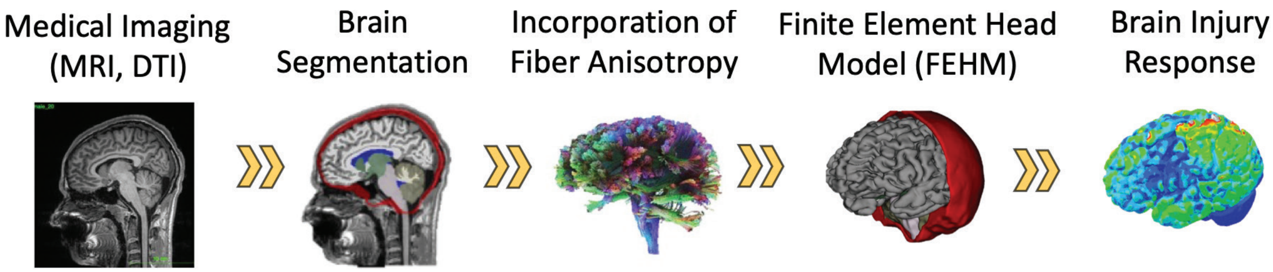
Rika Wright Carlsen, Ph.D., Associate Professor of Mechanical and Biomedical Engineering at Robert Morris University, presented results from the Physics-Based Neutralization of Threats to Human Tissues and Organs (PANTHER) program. By studying underwater blast injury initiation, detection, and prevention at the cellular level, Carlsen's research team sought to look at ICP at every location in the brain and correlate it with cavitation (Figure 2). Cavitation injury risk depends on whether the cavitation bubbles nucleate and the extent of cellular injury resulting from cavitation bubble growth and collapse. With the ultimate goal of identifying the location and extent of brain damage, the team aimed to connect cellular-level with tissue-level findings.

DoD Working Group on Computational Modeling of Human Lethality, Injury, and Impairment from Blast-Related Threats

Anthony Santago II, Ph.D., Principal Scientist at MITRE Corporation, gave an overview of an interagency approach to leverage modeling and simulation of blast injury in all threat environments. In the past 30 years, predictive performance of models and simulations has been improved by increased computational power, improved model fidelity, and detailed experimental results for model development and validation. The desired modeling capability is shown in Figure 3. A pilot computational modeling registry was developed to document metadata for existing computational models of human body effects from blast-related threats. Registries such as these can identify capability gaps and facilitate coordination of blast injury research efforts supporting model development. However, work remains to overcome simulation interoperability, integrate framework software components, and identify inconsistencies regarding guidelines and best practices across research communities. Furthermore, many of these questions will need to be developed before determining how to correlate mechanical and physiologic injury into the computational space.

FIGURE 2

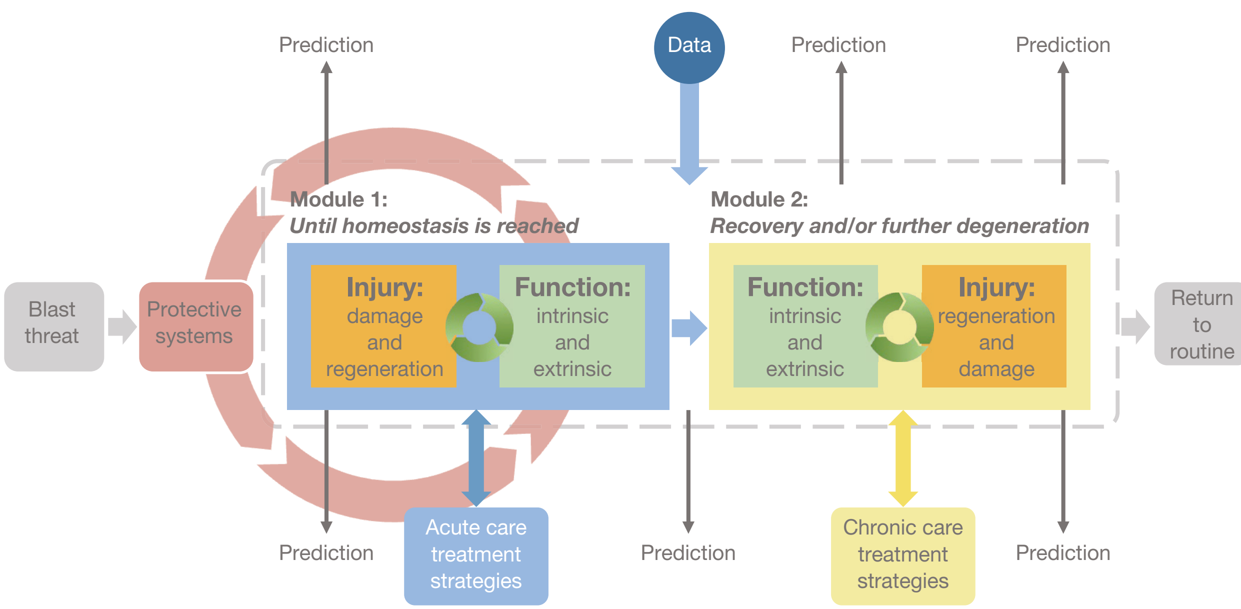
Semiautomated Finite Element Head Model Generation Workflow



SOURCE: Reproduced from Carlsen, 2022. Used with permission.
NOTE: DTI = diffusion tensor imaging.

FIGURE 3

Desired Modeling Capability



SOURCE: Adapted from Santago, 2022.

A National Science Foundation Overview on the Computational Modeling of the Human Body

Siddiq Qidwai, Ph.D., from the Civil, Mechanical and Manufacturing Innovation Division at the National Science Foundation (NSF), provided a high-level overview of the NSF's work on computational modeling of the human body, explaining that the NSF's mission is focused more on expanding the fundamental knowledge base than on conducting applied research. Moreover, the NSF is the home of proof-of-concept research, while the National Institutes of Health (NIH) supports proof of practice. Solicitations are driven from the top down in response to national needs and challenges from White House and DoD directives, NIH 10 Big Ideas, and the NSF Director's vision. Current awards that are relevant to blast injury cross over several different NSF programs. Qidwai highlighted several programs to guide applicants on the best targets for their research. For example, smaller efforts should be directed toward core programs, while larger efforts should be directed toward solicitations and collaborative teams. New research can address how limited data accessibility and data sharing have inhibited the traumatic brain injury (TBI) field from moving from challenges to solutions.

Leveraging Modeling and Experiments to Establish Human Injury Thresholds to Blast and Ballistic Events

Michael Kleinberger, Ph.D., from the Soldier Protection Sciences Branch of the Army Research Laboratory, described how skull biovariability complicates measuring the extent of brain injury after skull fracture. Consistent blast exposure and sensor placement makes modeling preferable to field data and allows researchers to model down to the yarn level of protective equipment. Buried blasts are an added threat to soldiers, particularly in the extremities, where armor is limited. FEMs elucidated how soil interactions can result in armor failure.

i-PREDICT Human Body Model Development and Validation

Daniel Nicolella, Ph.D., from the Office of Naval Research, shared recent developments in building a probabilistic, hierarchically validated model, or a human digital twin of a warfighter. A validated model can be used as a human surrogate for a variety of threats, allow for robust analysis of injury risk, guide readiness planning, and be the foundation of criteria for designing protective equipment and materiel. The probabilistic finite element injury analysis permits a researcher to compute response for an entire population of interest and to integrate findings between tissues, thereby calculating an overall score for a specific threat. Incapacitation Prediction for Readiness in Expeditionary Domains: An Integrated Computational Tool (i-PREDICT) can currently model cardiac, adipose, cartilage, stomach, and splenic tissues. An example of its validation of thoracic impact is in Figure 4. i-PREDICT can be combined with models of armor systems, vehicles, or other threats but does not yet capture the full range of anatomic variability in warfighters.

Uncovering Chemo-Mechanical Mechanisms of Traumatic Axonal Injury

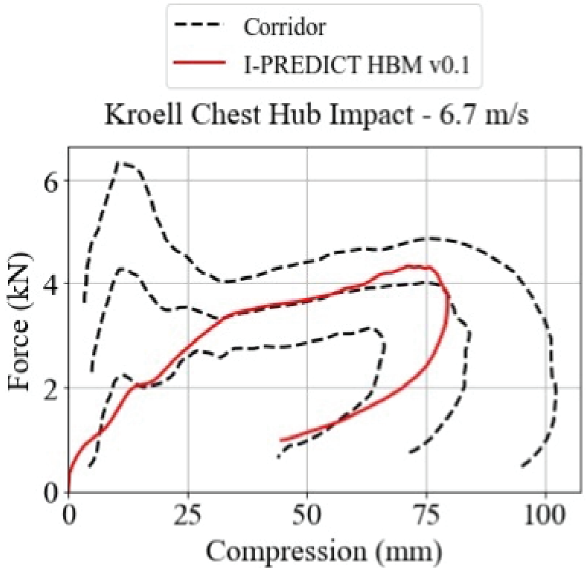
Vivek Shenoy, Ph.D., from the Center for Engineering Mechanobiology and School of Engineering and Applied Science at the University of Pennsylvania, described how blast injuries exhibit hallmarks of diffuse axonal injuries. His team found that microtubule rupture in stretched axons differed depending on the blast loading rate and microtubule length; fast loading and longer microtubules resulted in more injury. As shown in Figure 5, the actin/spectrin cortex and myelin sheath of microtubules act as a shock absorber. This response mechanism, however, is interrupted by repetitive injuries and renders the neurons less capable of response to future insults. Notably, Shenoy's team found that females are at a greater risk of axonal injury, possibly because female axons have a smaller cross-sectional area of microtubules.

Air Force Research Labs Computational Human Body Modeling Efforts

Timothy DeWitt, from the Air Force Research Laboratory, 711th Human Performance Wing/RHBFD, shared how difficult and expensive it is to model human response to ejection and crash from aircraft. Existing models from the automotive industry lack a vertical environment and represent only the 50th percentile for women and the 90th percentile for men. The Computational Anthropomorphic Virtual Experiment Man (CAVEMAN) used a combination of joint angles that could be adjusted in one-degree increments for each simulation (Figure 6). The piecewise scaling approach permitted the body to be broken into segments and the torso to be adjusted from sitting to standing height. Using this approach allows a multiscale model to be developed to incorporate active musculature, incorporate stress, and validate human subject data from the Wright-Patterson Air Force Base vertical accelerator.

FIGURE 4

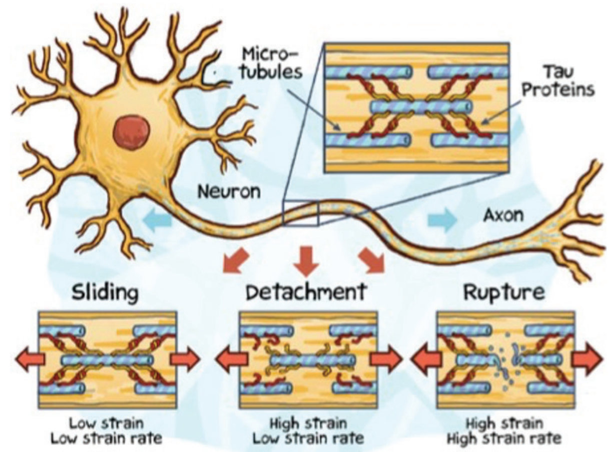
Kroell Chest Hub Impact –6.7 m/s



SOURCE: i-PREDICT program team. Used with permission.
NOTE: HBM = health belief model; kN = kilonewton.

FIGURE 5

Dynamics of Tau Linker Breaking and Reformation



SOURCE: Reprinted from Henry van den Bedem and Ellen Kuhl, "Tau-ism: The Yin and Yang of Microtubule Sliding, Detachment, and Rupture," *Biophysical Journal*, Vol. 109, No. 11, Copyright 2015, p. 2216, with permission from Elsevier.

Homeland Explosives Consequence and Threat (HExCAT) Tool: Probabilistic Analysis of Impact and Response to Explosions

Alexander Dolan, from the Chemical Security Analysis Center at the U.S. Department of Homeland Security (DHS) Science and Technology Directorate, introduced a probabilistic web-based tool built to estimate the public health impact and medical response of explosive-based attacks on civilian targets. This fast-running tool requires minimal user input and can model a wide array of explosions and structures. Its medical mitigation model uses a stock-and-flow framework and an injury severity score to estimate the number of victims saved or benefited by medical response and the volume of resources consumed. The model is currently for classified use on a desktop computer only. Future iterations might be informed by more-validated historic blast data and become "For Official Use Only."

Human Body Modeling: Safety Analysis Decision Making

Joseph Pellettiere, Ph.D., Chief Scientific and Technical Advisor for Crash Dynamics at the Federal Aviation Administration (FAA), explained how the FAA has different vertical impact, pulse, and human subject requirements for crash testing. It has limited access to proprietary data on facets of civilian travel that are less frequently modeled, such as impact with an armrest or the ability to unlatch a seatbelt. Each time the data are modified, the model needs to be validated again. Additionally, once model limitations are identified, the FAA needs to identify alternative means of compliance for those items.

FIGURE 6

Tensed Musculature CAVEMAN Human Body Model Simulating Airmen Injury

SOURCE: Reproduced from DeWitt, 2022. Used with permission.

Scientific Presentation Summaries

This section provides summaries of the scientific presentations. The summaries were compiled from notes taken by our team during the SoSM.

Session One

Evaluation of Explosive Ordnance Disposal Helmet Performance Against Blast Injury

Jean-Philippe Dionne, Ph.D., from MedEng (a brand of the Safariland Group), shared advances in constructing and evaluating protective helmets. Currently, there are standard test methodologies for fragmentation, impact, and heat, but there is no quantitative standard for blast overpressure. Toyota has introduced the higher-fidelity Total Human Model for Safety—which is a combination of Hybrid III mannequins and head forms with numerical simulations—to assess injury reduction and impact frequency. However, the model lacks the fine mesh and computing power necessary for blast injuries. In the future, Dionne's research team hopes to improve mannequins used for bomb suit testing; develop less-expensive, more-advanced blast surrogates; and adjust numerical models to accommodate PPE and resource-intensive computing environments.

3D Biomechanical Model of Human Ear for Predicting Auditory Blast Injury

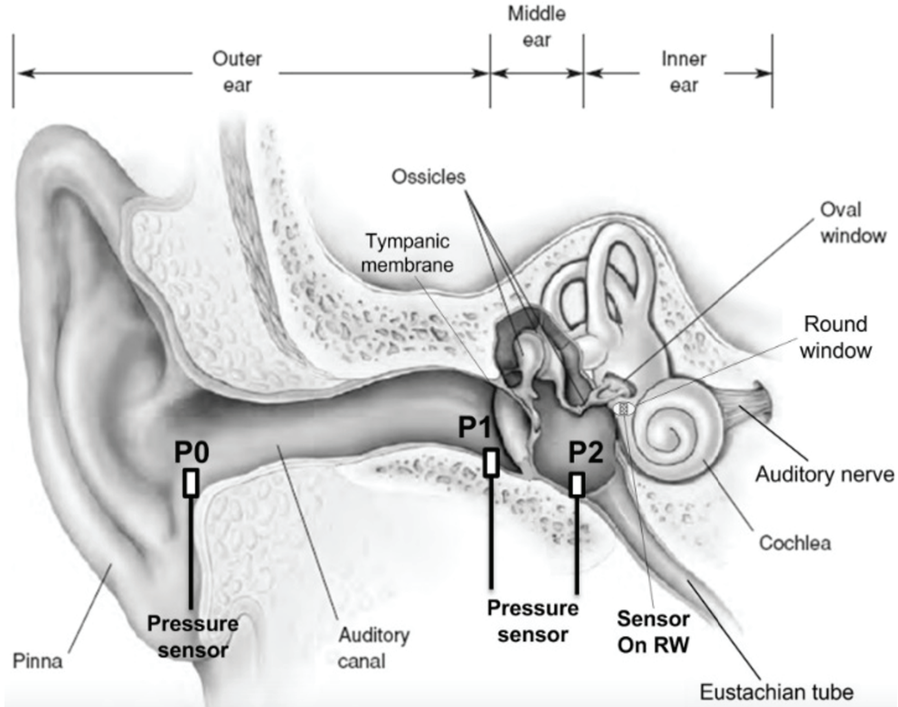
Rong Gan, Ph.D., from the School of Aerospace and Mechanical Engineering at the University of Oklahoma, demonstrated how her team built a comprehensive model of the human ear for predicting auditory blast injury. Earlier computational modeling of the auditory system focused on the peripheral auditory system. Both the peripheral and central auditory systems are susceptible to blast overpressure, leading to tympanic membrane (TM) rupture, ossicular chain disruption, and inner ear damage. Figure 7 displays the placement of pressure sensors to measure TM and stapes footplate motion during blast exposure. Gan's team then developed a three-dimensional FEM to measure blast wave transmission at 24 evenly spaced points. This FEM can accurately determine blast-induced damage in the inner and middle ear and be further refined to determine hearing loss or auditory injury after repetitive exposure to blasts.

Exploration of Lower Extremity Injury in the Under Body Blast Environment Using a Human Body Finite Element Model

Zachary Hostetler, Ph.D., from Virginia Tech–Wake Forest University Center for Injury Biomechanics, described validation results from a combination knee and lower extremity model, derived from the Global Human Body Models Consortium, exposed to underbody blast. After running 33 different validation cases—23 from pendulum experiments and ten from Vertec experimental data—Hostetler's team found agreement in vertical and horizontal loading directions. The next steps will be to develop injury curves specific to injuries resulting from underbody blast and incorporate more-biofidelic foot models.

FIGURE 7

Biomechanical Measurements in the Ear Exposed to Blast



SOURCE: Reproduced from Rong Z. Gan, Kegan Leckness, Don Nakmali, and Xiao D. Ji, "Biomechanical Measurement and Modeling of Human Eardrum Injury in Relation to Blast Wave Direction," Military Medicine, Vol. 183, Supp. 1, March–April 2018, p. 246, by permission of Oxford University Press.

Validation of the CAVEMAN Human Body Model Pelvis Response to Vertical Accelerative Loading and the Effects of Seated Posture on Skeletal Fracture

To improve energy-attenuating seat design, Kevin Lister, Ph.D., from the University of Virginia, measured how differences in warfighter pelvis geometry and seated posture affect injuries in vehicle blast events. The CAVEMAN is 934 individually hex-meshed components combined to model the musculoskeletal system and internal organs, as shown in Figure 8. Initially, Lister's team used CAVEMAN to understand how posture affected the risk of pelvic injury, comparing past cadaveric pelvic tests using a variety of input conditions, from minimal to severe. Similar to other models, the posterior series revealed transverse sacral fractures, suggesting that, if the posterior tilt is changed, the bottom side of the pelvis could be better protected. Because high-fidelity modeling can predict injury risk across a variety of energy levels, the team is able to study differences in gender and geometry, as well as the influence of posture on lumbar spine injuries going forward.

Soft-Armor Vest Effectiveness and Intrathoracic Biomechanics in Rodents Exposed to Primary Blast

Elizabeth McNeil, Ph.D., from the Blast-Induced Neurotrauma Branch at the Walter Reed Army Institute of Research, transitioned the discussion to animal models. Ten percent of blast injuries involve the thorax, and current PPE standards address blast and impact protection. However, the Bowen curves used to measure pulmonary injury were developed in 1968 with 13 animal models and do not relate well to present-day, real-world scenarios. Although current blast test surrogates are more biofidelic, they remain far from human. Cadaveric models, for example, lack blood flow and lung inflation, and the transition from rodents to warfighters requires validations with larger animal models. The rat model proved that the relationship between external pressure and internal

FIGURE 8

Example of CAVEMAN Full-Body Finite Element Model

SOURCE: Reproduced from Lister, 2022. Used with permission.

pressure could be measured in live animals. Findings can inform computational models, surrogates, and injury criteria.

A Biomechanics-Based Computational Framework to Simulate Injury from Clinical Brain Imaging

X. Gary Tan, Ph.D., from the U.S. Naval Research Laboratory, presented some of the challenges of modeling warfighter protection against a variety of threats, including ballistic, blast, blunt trauma, and thermal threats. Linking clinical and biomechanics research requires collection of data that are representative of real-world injuries, as well as simulations that reconstruct the injuries. Using the measures in Table 2, Tan's team used a finite element cranial model to compare kinematic conditions and biomechanical response immediately before and after impact. Tan's team found the model to be sensitive to hemorrhage. It will continue to collect clinical data to validate findings and extend this model to blast injuries and other forms of blunt impact trauma.

Session Two

Effect of Combat and Mission-Related Repetitive Blast and Blunt Force TBI on Cerebral Autonomic Function and Response to Integrative Medicine Therapies

Thomas DeGraba, Ph.D., Chief Innovations Officer at the National Intrepid Center of Excellence at the Walter Reed National Military Medical Center, used real-world blast exposure data to determine how integrative medicine therapies affect recovery and response. In a four-week observational study of service members suffering from TBI after Operation Enduring Freedom and Operation Iraqi Freedom, DeGraba's team assessed the persistence of autonomic disturbance following intensive integrative medicine therapies (e.g., yoga and art therapy) combined with conventional neurological rehabilitation. The average adult would have a breath-holding index (BHI) of 1.4 percent per second; at baseline, 38 percent of non–special forces service members had an abnormal BHI of less than 1.0. Lower BHI is associated with a lower score on other neurological tests and a lower likelihood of fitness for duty. After four weeks, the majority of patients showed an improved BHI score at discharge. Although four weeks is considered an insufficient time for recovery, these improvements in BHI are promising.

Dynamic Response of Histology-Informed White Matter Hybrid Model Using Computational Simulations and 3D Convolutional Neural Networks

John G. Georgiadis, Ph.D., Professor and Chair of Biomedical Engineering at the Illinois Institute of Technology, imparted recent research on bridging the scale gap in central nervous system (CNS) mechanics. Because CNS data can be sparse and noisy, integrating machine learning into multiscale models of white matter can bridge scales and predict CNS response to mechanical loading. Georgiadis's team created a mosaic of representative elementary volumes with orthotropic properties to form two axes and simulate the harmonic response of a two-axon system. Machine learning algorithms were found to be an effective solution of white matter computational micromechanical models without simulation mesh

TABLE 2

Computed Variables Used to Compare with MRI Data

Variable	Symptom
Deformation	• Indentation of skull and brain
Strain related	• First principal strain, effective strain • Effective strain rate • Product of effective strain and effective strain rate
Stress	• Pressure, maximum shear stress, Von-Mises stress
Energy	• Dilatational and distortional strain energy densities

SOURCE: Tan, 2022.

failure while using less computational power than a direct FEM.

NICoE Blast Ordnance and Occupational Exposure Measure (BOOM)

Chandler Rhodes, Ph.D., from the National Intrepid Center of Excellence at the Walter Reed National Military Medical Center, asked how blast exposure can be quantified over a military career. Currently, there is no standard method to collect exposure data across clinical departments or research studies, nor are there validated assessments to do this on a clinical scale. Rhodes's team surveyed subject-matter experts, clinicians, and patients on measures related to blast, exposure, and associated symptoms. Findings informed a research protocol, Evaluation of Self-Reported Lifetime Blast Exposure Measures, that will soon be compared with other self-reported blast measures, such as the Blast Exposure Threshold Survey and the Blast Frequency and Symptom Severity.

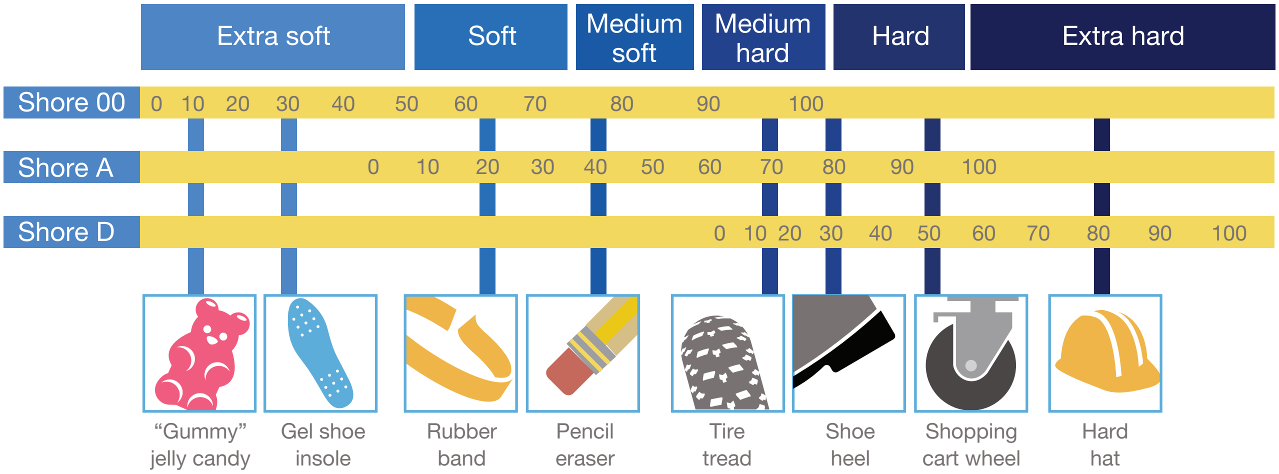
Cerebral Vasculature Influences Blast-Induced Biomechanical Responses of Human Brain Tissue

Jose Rubio, Ph.D., from the DoD Biotechnology High Performance Computing Software Applications Institute Telemedicine and Advanced Technology Research Center at the U.S. Army Medical Research and Development Command, used a mathematical model to simulate the interaction of blasts to the skull and estimate ICP in the brain. Using a high-fidelity computational human head model that can describe the vasculature, Rubio observed differences in the distribution and magnitude of strains. In addition, Rubio detected regional differences in biomechanical responses; the brain stem consistently showed the highest level of response. Rubio hypothesized that the vasculature could act as a siphoning support to the brain.

A Computational Model for Selecting Neck Design Parameters of a Blast Overpressure Bomb Suit Evaluation Surrogate

Nicholas A. Vavalle, Ph.D., from the Applied Physics Laboratory at Johns Hopkins University, sought to pilot test a new silicone human neck surrogate that produces biofidelic head motion. Figure 9 shows the variety of silicone durabilities, geometries, and nodding block materials that Vavalle tested. Dynamic simulations of whiplash in a shock tube evaluated the amount of forward lean of the head and neck with a bomb suit helmet. After 18 different designs were evaluated, a final surrogate model was selected, which used four nodding blocks with three layers of Shore 60A silicone to achieve an appropriate biofidelic head motion, as required.

FIGURE 9
Silicone Durability Comparison



Appendix A. Previous State-of-the-Science Meetings

TABLE A.1
Previous SoSMs

Topic	Date	Location	Source
Non-Impact, Blast-Induced Mild TBI	May 12–14, 2009	Herndon, VA	U.S. Department of Defense, 2009.
Blast Injury Dosimetry	June 8–10, 2010	Chantilly, VA	U.S. Department of Defense, 2010.
Blast-Induced Tinnitus	November 15–17, 2011	Chantilly, VA	U.S. Department of Defense, 2011.
Biomedical Basis for Mild TBI Environmental Sensor Threshold Values	November 4–6, 2014	McLean, VA	U.S. Department of Defense, 2014.
Does Repeated Blast-Related Trauma Contribute to the Development of Chronic Traumatic Encephalopathy?	November 3–5, 2015	McLean, VA	U.S. Department of Defense, 2015.
Minimizing the Impact of Wound Infections Following Blast-Related Injuries	November 29–December 1, 2016	Arlington, VA	U.S. Department of Defense, 2016.
Neurological Effects of Repeated Exposure to Military Occupational Blast: Implications for Prevention and Health	March 12–15, 2018	Arlington, VA	Engel, Hoch, and Simmons, 2019.
Limb Salvage and Recovery After Blast-Related Injury	March 5–8, 2019	Arlington, VA	Piquado, Hoch, and Engel, 2020.
Mitigating the Effects of Blast-Related Burn Injuries from Prolonged Field Care to Rehabilitation and Resilience	March 3–5, 2020	Arlington, VA	Hoch et al., 2020.

Appendix B. Agenda of the Tenth State-of-the-Science Meeting

TABLE B.1
Agenda of the Tenth SoSM

Time	Event	Speaker or Moderator
	Tuesday, August 16, 2022	
7:00 a.m.	Registration opens	
8:00 a.m.	Welcome from the Director, DoD Blast Injury Research Coordinating Office	LTC Jacob Johnson
8:15 a.m.	Brief meeting overview from lead researcher, RAND Corporation	Dr. Samantha McBirney
8:30 a.m.	Keynote address with Q&A	Dr. Grace C. Y. Peng
9:00 a.m.	Literature review briefing	Dr. Éder Sousa
9:20 a.m.	Invited Presentations, Session One 15-min presentations with 15-min Q&A at the end of the session	
9:20 a.m.	Predicting Blast-Induced Traumatic Brain Injury Through High Fidelity Finite Element Head Models and Cellular-Based Injury Criteria	Dr. Rika Wright Carlsen
9:35 a.m.	DoD Working Group on Computational Modeling of Human Lethality, Injury, and Impairment from Blast-Related Threats	Dr. Anthony Santago
9:50 a.m.	A National Science Foundation Overview on the Computational Modeling of the Human Body	Dr. Siddiq Qidwai
10:05 a.m.	Q&A	Moderated by Dr. Charles Engel
10:20 a.m.	A.M. break	
10:45 a.m.	Invited Presentations, Session Two 15-min presentation with 15-min Q&A at the end of the session	
10:45 a.m.	Leveraging Modeling and Experiments to Establish Human Injury Thresholds to Blast and Ballistic Events	Dr. Michael Kleinberger
11:00 a.m.	i-PREDICT Human Body Model Development and Validation	Dr. Daniel Nicolella
11:15 a.m.	Uncovering Chemo-Mechanical Mechanisms of Traumatic Axonal Injury	Dr. Vivek Shenoy
11:30 a.m.	Q&A	Moderated by Dr. Charles Engel
11:45 a.m.	Lunch	
1:00 p.m.	Scientific Presentations, Session One 15-min presentations with 30-min Q&A at the end of the session	
1:00 p.m.	Numerical Simulations of Explosive Ordnance Disposal Helmet Performance Against Blast Injury	Dr. Jean-Philippe Dionne
1:15 p.m.	3D Biomechanical Model of Human Ear for Predicting Auditory Blast Injury	Dr. Rong Gan

Table B.1—Continued

Time	Event	Speaker or Moderator
1:30 p.m.	Lower Extremity Validation of a Human Body Model in High-Rate Axial Loading for Applications in the Underbody Blast Environment	Dr. Zachary Hostetler
1:45 p.m.	Validation of the CAVEMAN Human Body Model Pelvis Response to Vertical Accelerative Loading and the Effects of Seated Posture on Skeletal Fracture	Dr. Kevin Lister
2:00 p.m.	Soft-Armor Vest Effectiveness and Intrathoracic Biomechanics in Rodents Exposed to Primary Blast	Dr. Elizabeth McNeil
2:15 p.m.	A Biomechanics-Based Computational Framework to Simulate Injury from Clinical Brain Imaging	Dr. X. Gary Tan
2:30 p.m.	Q&A	Moderated by Dr. Charles Engel
3:00 p.m.	P.M. break	
3:20 p.m.	Scientific Presentations, Session Two 15-min presentations with 30-min Q&A at the end of the session	
3:20 p.m.	Effect of Combat- and Mission-Related Repetitive Blast and Blunt Force TBI on Cerebral Autonomic Injury and Response to Integrative Medicine Therapies	Dr. Thomas DeGraba
3:35 p.m.	Dynamic Response of Histology-Informed White Matter Hybrid Model Based on Computational Simulations and 3D Convolutional Neural Networks	Dr. John Georgiadis
3:50 p.m.	NICoE BOOM	Dr. Chandler Rhodes
4:05 p.m.	Cerebral Vasculature Influences Blast-Induced Biomechanical Responses of Human Brain Tissue	Dr. Jose Rubio
4:20 p.m.	A Computational Model for Selecting Neck Design Parameters of a Blast Overpressure Bomb Suit Evaluation Surrogate	Dr. Nicholas Vavalle
4:35 p.m.	Q&A	Moderated by Dr. Charles Engel
5:00 p.m.	Closing remarks	Dr. Samantha McBirney
5:10 p.m.	Adjournment	
	Wednesday, August 17, 2022	
7:00 a.m.	Registration opens	
8:00 a.m.	Day Two welcome	Dr. Samantha McBirney
8:10 a.m.	Invited Presentations, Session Three 15-min presentation with 15-min Q&A at the end of the session	
8:10 a.m.	Air Force Research Labs Computational Human Body Modeling Efforts	Timothy DeWitt
8:25 a.m.	DHS S&T HExCAT Tool: Probabilistic Analysis of Impact and Response to Explosions	Alex Dolan

Table B.1—Continued

Time	Event	Speaker or Moderator
8:40 a.m.	Human Body Model Usage for Regulatory Decision Making	Dr. Joseph Pellettiere
8:55 a.m.	Q&A	Moderated by Dr. Charles Engel
9:10 a.m.	A.M. break	
9:30 a.m.	Working group roles and responsibilities	Emily Hoch
9:45 a.m.	Break into working groups	Led by expert panelists
11:30 a.m.	[Working] Lunch break	
12:30 p.m.	Return to working groups	
4:00 p.m.	Outbriefs from working groups	
4:00 p.m.	Question #1	
4:20 p.m.	Question #2	
4:40 p.m.	Question #3	
5:00 p.m.	Question #4	
5:20 p.m.	Closing remarks	Dr. Samantha McBirney

NOTE: Q&A = question and answer.

Appendix C. Expert Panelists and Keynote Speaker Biographies

An expert panel of five subject-matter experts, representing policymakers, clinicians, and scientists, helped lead and focus discussions during the plenary sessions. The expert panel members also chaired working group sessions, during which participants discussed the meeting questions. Dr. Grace C. Y. Peng, one of the expert panelists, also served as the keynote speaker for the tenth SoSM.

Rong Z. Gan, Ph.D. Dr. Rong Gan is the George Lynn Cross Research Professor, Charles E. Foster Chair, and Presidential Research Professor in Biomedical and Mechanical Engineering at the University of Oklahoma. She is a fellow of the American Institute for Medical and Biological Engineering. Since joining the University of Oklahoma in 1999, Dr. Gan has developed a research program in biomechanics for protection and restoration of hearing funded by DoD, NIH, the NSF, the Whitaker Foundation, and the state of Oklahoma. Her research has resulted in numerous publications and led to breakthroughs in (1) experimental measurements of sound transmission in humans and animals and biomechanical tests of ear tissues, (2) 3D reconstruction and computational modeling of the ear for prediction of hearing damage induced by blast overpressure and hearing protection mechanisms, and (3) development of implantable hearing devices and therapeutics for hearing restoration. Two patents have been granted in totally implantable hearing devices and 3D computational modeling of the human ear, and two more patents are currently pending. Dr. Gan holds a B.S. in mechanical engineering, M.S. degrees in biomechanics and applied mathematics, and a Ph.D. in biomedical engineering.

Grace C. Y. Peng, Ph.D. Dr. Grace C. Y. Peng is the Director of Mathematical Modeling, Simulation and Analysis at the National Institute of Biomedical Imaging and Bioengineering (NIBIB) at NIH. In this capacity, she has programmatic oversight of extramural activities in these areas. Dr. Peng received her B.S. in electrical engineering from the University of Illinois at Urbana and her M.S. and Ph.D. in biomedical engineering from Northwestern University. She performed postdoctoral and faculty research in the neurology department at Johns Hopkins University. In 2000, she became the Clare Boothe Luce professor of biomedical engineering at the Catholic University of America. Since 2002, Dr. Peng has been a program director in NIBIB, overseeing various programs promoting the development of mathematical and statistical modeling and analysis methods; medical simulation tools; and next-generation engineering systems for rehabilitation, robotics, neuroengineering, and surgical systems. In 2003, Dr. Peng led the creation of the Interagency Modeling and Analysis Group, which consists of program officers from multiple federal agencies of the U.S. government and has supported funding initiatives targeted to multiscale modeling of biomedical, biological, and behavioral systems. Dr. Peng also has served in leadership roles in the NIH Stimulating Peripheral Activity to Relieve Conditions (2014–2016) program, the Brain Research Through Advancing Innovative Neurotechnologies Initiative (since 2014), and the Bridge2AI Program (since 2020).

An expert panel of five subject-matter experts, representing policymakers, clinicians, and scientists, helped lead and focus discussions during the plenary sessions.

Andrzej Przekwas, Ph.D. Dr. Andrzej Przekwas, chief technology officer at CFD Research Corporation (CFDRC), obtained his Ph.D. from the Wrocław University of Science and Technology and his postdoctoral fellowship at the Imperial College of Science, Technology, and Medicine in London.

Dr. Przekwas leads CFDRC's Computational Medicine and Biology (CMB) Division, which works on the development of multiscale computational tools for modeling human physiology, cell-tissue biology, pharmacology, and injury biomechanics. His CMB team conducts research in two main areas: (1) military medicine, focusing on mechanobiology of TBI, neuropharmacology, medical countermeasures for chemical and biological warfare agents, injury biomechanics, physiological performance, and protection, and (2) civilian medicine, focusing on multiscale computational pharmacology, translational pharmacology, biomarker kinetics, microfluidics-based multi-organ-on-chip devices, formulation effects on bioequivalence of generic drugs, neuropharmacology, respiratory diseases, and others. He has been the principal investigator on several projects with the Defense Advanced Research Projects Agency, DoD, NIH, the Centers for Disease Control and Prevention, and the Food and Drug Administration. Dr. Przekwas has published three book chapters and more than 290 papers and currently serves on the Technical Advisory Committee for the U.S. Department of Commerce Bureau of Industry and Security.

Siddiq M. Qidwai, Ph.D. Dr. Siddiq Qidwai is the program director of the Mechanics of Materials and Structures program and the Foundational Research in Robotics program of the Division of Civil, Mechanical and Manufacturing Innovation at the NSF. Before joining the NSF in 2016, he was the acting section head in the Materials Science and Technology Division of the U.S. Naval Research Laboratory. Several years before that, Qidwai received his Ph.D. in aerospace engineering from Texas A&M University. Qidwai has authored or coauthored several publications and is a fellow of the American Society of Mechanical Engineers. He also serves on editorial and advisory boards at the NSF.

Adam M. Willis, M.D., Ph.D., Lt Col, U.S. Air Force, Medical Corps, Flight Surgeon. Lt Col Adam M. Willis, currently serves as a medical director for joint integrated clinical medicine in the Office of the Chief Scientist, 59th Medical Wing, Lackland Air Force Base, Texas. Lieutenant Colonel Willis previously served as a staff neurointensivist and neurologist at Brooke Army Medical Center and continues as the Director of Scholarly Activity within the Department of Neurology. He was commissioned in 1999 and then attended the Air Force Institute of Technology/Civilian Institution Program at the University of Illinois at Urbana-Champaign. His education includes a B.S. in physics, an M.S. and a Ph.D. in theoretical and applied mechanics, a clinical residency in neurology, and fellowship training for neurocritical care with board certification (active) in both neurology and neurocritical care. Lieutenant Colonel Willis is an adjunct assistant professor in the Mechanical Engineering Department at Michigan State University and has research interests in how mechanical exposures alter cellular physiology and predicting the mechanical response of intracranial tissue under blast and blunt exposures.

Acknowledgments

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- Kyleanne Hunter, Ph.D., senior political scientist, RAND Corporation
- Beth Lewandowski, Ph.D., THREAD project scientist, National Aeuronautics and Space Administration Glenn Research Center
- Thuvan Piehler, Ph.D., deputy project manager, injury prevention, U.S. Army Medical Research and Development Command
- LTC Julie Rizzo, M.D., Fellow, American College of Surgeons, burn and trauma surgeon, U.S. Army Institute of Surgical Research Burn Center
- Anthony Santago, Ph.D., principal biomedical engineer, MITRE Corporation.

These individuals helped us identify and rank candidates for the expert panel, advised on invited speaker topics, nominated invited speakers, peer-reviewed submissions for the SoSM abstract, provided input to SoSM working group discussion questions, helped refine the SoSM agenda, and moderated the SoSM question-and-answer panels. We derived inspiration, support, and collaboration from the expert panel of the SoSM. Each expert panelist chaired a daylong SoSM participant working group. Key parts of this document (findings, conclusions, and recommendations) were written in close consultation with these respected scholars:

- Rong Z. Gan, Ph.D., George Lynn Cross Research Professor, Charles E. Foster Chair, and Presidential Research Professor in Biomedical and Mechanical Engineering at the University of Oklahoma
- Grace C. Y. Peng, Ph.D., Director of Mathematical Modeling, Simulation and Analysis at the National Institute of Biomedical Imaging and Bioengineering at the National Institutes of Health
- Andrzej Przekwas, Ph.D., chief technical officer at CFD Research Corporation
- Siddiq M. Qidwai, Ph.D., program director of the Mechanics of Materials and Structures program and the Foundational Research in Robotics program of the Division of Civil, Mechanical and Manufacturing Innovation at the National Science Foundation
- Adam M. Willis, M.D., Ph.D., Lt Col, U.S. Air Force, Medical Corps, Flight Surgeon, medical director for joint integrated clinical medicine, Office of the Chief Scientist, 59th Medical Wing, Lackland Air Force Base, Texas.

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About These Conference Proceedings

This document represents the complete proceedings of the tenth U.S. Department of Defense (DoD) International State-of-the-Science Meeting (SoSM) on Blast Injury Research, held August 16–17, 2022, at the Arlington, Virginia, office of the RAND Corporation. The topic of the tenth SoSM was "Toward a Unified Multiscale Computational Model of the Human Body's Immediate Responses to Blast-Related Trauma." The SoSM aims to identify knowledge gaps in blast-injury research; ensure that DoD medical research programs address existing gaps; foster collaboration; promote information-sharing on the latest research; and identify short-term, intermediate, and long-term actions to prevent, mitigate, and treat blast injuries. Participants and presenters consisted of scientists, clinicians, and policymakers from DoD, including from the departments of the Army, Navy, and Air Force; the Marine Corps; the National Institutes of Health; and the U.S. Department of Veterans Affairs; as well as representatives from academia and industry and scholars from several different countries. This research should be of interest to senior military and medical leaders.

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