ONR-NAVSEA UNDERSEA MEDICINE PROGRAM REVIEW

Quad Charts

2019 ONR Undersea Medicine / NAVSEA Deep Submergence Biomedical Development Program Review
May 14-16, 2019

Monday, May 13

EARLY BIRD SOCIAL – ROOF AT THE DURHAM					5:00 PM	

Tuesday, May 14

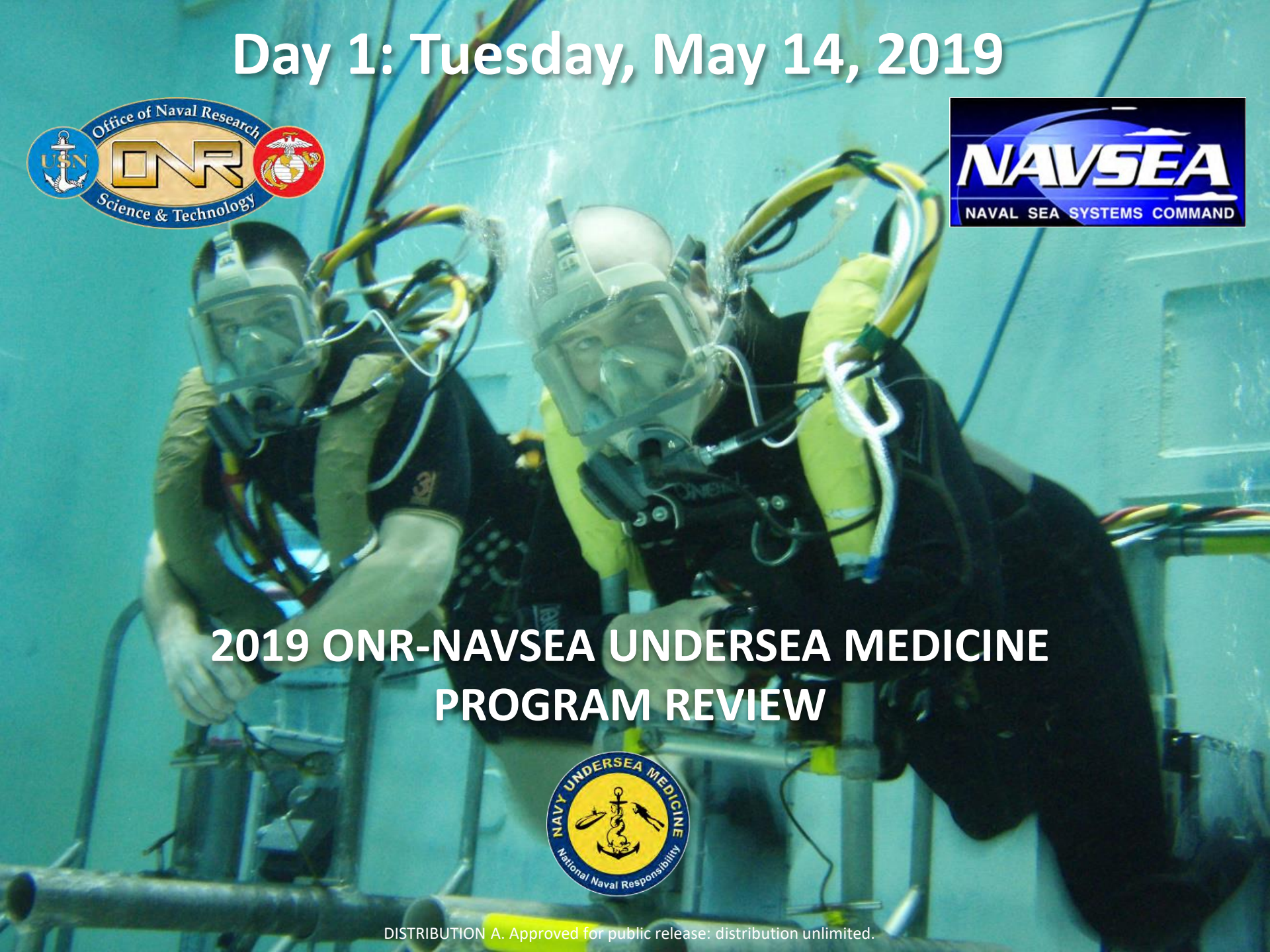
REGISTRATION					7:00 AM	
Chapman	sandra.chapman@navy.mil	Welcome/Umed NNR Program Manager Comments	ONR	INTRODUCTION	8:00 AM	15
Waters T.	edward.t.waters@navy.mil	DSBD Program Manager Comments	DSBD	INTRODUCTION	8:15 AM	15
Webb	ryan.m.webb@navy.mil	SEA00C Program Manager Comments	SEA00C	INTRODUCTION	8:30 AM	15
Waters D.	Deborah.k.waters@navy.mil	PMS391 Program Manager Comments	PMS391	INTRODUCTION	8:45 AM	15
Woodson	peter.woodson@socom.mil	NSW Force Medical Officer Comments	NSW	INTRODUCTION	9:00 AM	15
BREAK					9:15 AM	15

PI	Email	Title	Org.	Session	Time	Time (min)
Mcknight	jcm20@st-andrews.ac.uk	Neurobiological and Physiological Measurements From Free-Swimming Marine Mammals	ONR	GILS	9:30 AM	15
Mason	mason@chemistry.harvard.edu	Porous Metal-Organic Liquids as a New Platform for Investigating Gas-Liquid Interactions	ONR	GILS	9:45 AM	15
Ilardo	melissailardo@gmail.com	Functional Genomics Approaches To Breath-Hold Diving	ONR	GILS	10:00 AM	15
Nocera/Villagran	dnocera@fas.harvard.edu/dino@utep.edu	Studies Toward Closed-Loop Underwater Breathing Applications (SCUBA)	ONR	GILS	10:15 AM	20
QUESTIONS					10:35 AM	10
BREAK					10:45 AM	15
Boron	wfb2@case.edu	Gas Channels/ Molecular Mechanisms and Pathways for Gas Transport Across Biological Membranes	ONR	HYPERBARIC PHYSIOLOGY	11:00 AM	15
Hall	aaron.a.hall6.civ@mail.mil	Assessment of Doxycycline as an Adjunctive Therapy to Prevent Decompression Sickness in Swine	NAVSEA	DECOMPRESSION SICKNESS (DCS)	11:15 AM	15
Moon	richard.moon@duke.edu	Altitude Decompression Tables	NAVSEA	DECOMPRESSION SICKNESS (DCS)	11:30 AM	15
QUESTIONS					11:45 AM	15
LUNCH					12:00 PM	60
Murphy	francis.g.murphy1@navy.mil	Modernization of Navy Thalmann Algorithm Dive Planner	NAVSEA	DECOMPRESSION SICKNESS (DCS)	1:00 PM	15
Doolette	david.doolette@navy.mil	Navy Dive Computer & Dive Planner Algorithm for Constant 1.3 atm PO_2-in-Helium Diving to 300 fsw	NAVSEA	DECOMPRESSION SICKNESS (DCS)	1:15 PM	15
Andrew	brian.t.andrew@navy.mil	Manned Validation of VVAL 79 Air Decompression Schedules for Short Bottom Times in the 130-140 fsw Range	NAVSEA	DECOMPRESSION SICKNESS (DCS)	1:30 PM	15
Gerth	wayne.a.gerth@navy.mil	21st Century Surface Supplied Heliox Decompression Tables	NAVSEA	DECOMPRESSION SICKNESS (DCS)	1:45 PM	15
Mitchell	sj.mitchell@auckland.ac.nz	ONR-G Gas Narcosis in Hyperbaric Environments	ONR	HYPERBARIC PHYSIOLOGY	2:00 PM	15
QUESTIONS					2:15 PM	15
BREAK					2:30 PM	15
Myers	christopher.m.myers1.ctr@navy.mil	Impact of Repeated 6-hour Hyperoxic Exercise Dives at 1.35 ATA on Muscular Performance and Cardiovascular Endurance (RIP-X)	ONR/NAVSEA	DIVER PERFORMANCE & MEDICINE	2:45 PM	15
Syski	andrew.syski@navy.mil	Pulmonary Oxygen Toxicity with an Oxygen Partial Pressure of 1 atm: Possible Mitigation	NAVSEA	OXYGEN TOXICITY	3:00 PM	15
Hall	aaron.a.hall6.civ@mail.mil	Determining DISSUB Survival Rates of 70 Kg Swine Rescued Using SRDRS Standard Operating Procedures	NAVSEA	OXYGEN TOXICITY	3:15 PM	15
Hall	aaron.a.hall6.civ@mail.mil	Evaluation of Tiotropium Bromide Efficacy to Reduce Pulmonary O_2 Toxicity in Divers - FDA Procedure	NAVSEA	OXYGEN TOXICITY	3:30 PM	15
Malmstadt	malmstad@usc.edu	Connecting Lipid Oxidation To Cellular Dysfunction In Hyperbaric Oxygen Toxicity	ONR	OXYGEN TOXICITY	3:45 PM	15
Piantadosi	claude.piantadosi@duke.edu	Oxidative Tissue Damage Mitigation Using Anti-Epileptic Drugs	ONR	OXYGEN TOXICITY	4:00 PM	15

	QUESTIONS				4:15 PM	15
	ADJOURN				4:30 PM	
	MEET & GREET – TOBACCO ROAD SPORT CAFÉ				5:30 PM	
Wednesday, May 15						
	REGISTRATION				7:30 AM	
Chapman	sandra.chapman@navy.mil	Welcome/Umed NNR Program Manager Comments	ONR	INTRODUCTION	7:55 AM	5
PI	**Email**	**Title**	**Org.**	**Session**	**Time**	**Time (min)**
Howle	laurens.howle@duke.edu	Evaluation of and Advances in O_2 Toxicity Models	NAVSEA	OXYGEN TOXICITY	8:00 AM	15
Dean	jdean@health.usf.edu	Cellular Mechanisms of CNS O2 Toxicity During CO_2 Retention and Ketone Metabolic Therapy	ONR	OXYGEN TOXICITY	8:15 AM	15
Ciarlone	geoffrey.e.ciarlone.mil@mail.mil	Assessment of Ketone Ester for the Induction of Ketosis and Delay of CNS O_2 Toxicity in Swine	NAVSEA	OXYGEN TOXICITY	8:30 AM	15
Derrick	bruce.derrick@duke.edu	Ketogenic Diet for Reduction of CNS O_2 Toxicity Symptoms in Working Divers	NAVSEA	OXYGEN TOXICITY	8:45 AM	15
Chon	kchon@engr.uconn.edu	Feasibility of Electrodermal Activity for Detecting Seizures Elicited By CNS O_2 Toxicity Underwater	ONR	DIVER PERFORMANCE & MEDICINE	9:00 AM	15
D'Agostino	ddagosti@health.usf.edu	Optimizing Ketone Metabolic Therapy	ONR	DIVER PERFORMANCE & MEDICINE	9:15 AM	15
	QUESTIONS				9:30 AM	15
	BREAK				9:45 AM	15
Kernagis	dkernagis@ihmc.us	Ketones For High Intensity Mission Operations	ONR	DIVER PERFORMANCE & MEDICINE	10:00 AM	15
Johnson	blairjoh@buffalo.edu	Role of O_2 Breathing on Carotid Body Sensitivity	ONR	OXYGEN TOXICITY	10:15 AM	15
Kelly	karen.r.kelly8.civ@mail.mil	Evaluation of Thermoregulatory Differences Between Insulated Clothing Options During Cold-Water Diving	ONR	DIVER PERFORMANCE & MEDICINE	10:30 AM	15
Campbell	james.e.campbell3.ctr@navy.mil	Measurement of Regional Heat Exchange Using Direct Calorimetry in Cold Water	NAVSEA	DIVER PERFORMANCE & MEDICINE	10:45 AM	15
Maguire	brian.j.maguire12.ctr@mail.mil	Epidemiological Analyses of US Navy Diver Separation Health Assessments	NAVSEA	DIVER PERFORMANCE & MEDICINE	11:00 AM	15
Hostler	dhostler@buffalo.edu	Optimizing Performance During Topside Operations and Diving at Altitude	NAVSEA	DIVER PERFORMANCE & MEDICINE	11:15 AM	15
	QUESTIONS				11:30 AM	15
	LUNCH				11:45 AM	60
Freiberger	john.freiberger@duke.edu	Does Heart Rate Variability Predict Performance Impairment in Divers?	NAVSEA	DIVER PERFORMANCE & MEDICINE	12:45 PM	15
Beaudoin	monique.beaudoin@jhuapl.edu	Applied Systems Engineering to Improve Operational Guidance and Human Safety for Immersion in Warm Water Environments	NAVSEA	DIVER PERFORMANCE & MEDICINE	1:00 PM	15
Reimers	sreimers@pccii.com	Flexible Recompression Chamber	NAVSEA	DIVER PERFORMANCE & MEDICINE	1:15 PM	15
Lance	rachel.lance@duke.edu	Development of a Pulse Oximeter to Independently Monitor Oxygen Levels in Rebreather Divers	NAVSEA	DIVER PERFORMANCE & MEDICINE	1:30 PM	15
	QUESTIONS				1:45 PM	15
	BREAK				2:00 PM	15
McMurtrie	paul.mcmurtrie@navy.mil	Diver Augmented Vision System (DAVD)	ONR/NAVSEA	DIVER PERFORMANCE & MEDICINE	2:15 PM	15
Cunningham	blair.cunningham@codaoctopus.com	CODA Octopus 3D Sonar & DAVD GEN1 Development	ONR/NAVSEA	DIVER PERFORMANCE & MEDICINE	2:30 PM	15
Kvasic	igor.kvasic@fer.hr	Adriatic-Advanced Diver-Robot Interaction Capabilities	ONR	DIVER PERFORMANCE & MEDICINE	2:45 PM	15
Moon	richard.moon@duke.edu	Sildenafil for Prevention of Immersion Pulmonary Edema (SIPE)	NAVSEA	DIVER PERFORMANCE & MEDICINE	3:00 PM	15
Lance	rachel.lance@duke.edu	S.T.E.M.	ONR	MISCELLANEOUS	3:15 PM	15
Broderick	tbroderick@ihmc.us	Biotechnology to Improve Cold-Water Operator Performance	ONR	DIVER PERFORMANCE & MEDICINE	3:30 PM	15

	QUESTIONS				3:45 PM	15
	ADJOURN				4:00 PM	
	COCKTAIL HOUR – CAMERON ATHLETIC CENTER, DUKE UNIVERSITY				6:00 PM	60
	GALA BANQUET – CAMERON ATHLETIC CENTER, DUKE UNIVERSITY				7:00 PM	
Thursday, May 16						
	REGISTRATION				8:30 AM	
Waters T.	edward.t.waters@navy.mil	DSBD Program Manager Comments	NAVSEA	INTRODUCTION	8:55 AM	5
PI	**Email**	**Title**	**Org.**	**Session**	**Time**	**Time (min)**
Reinhart	paul.n.reinhart.ctr@mail.mil	Effects of Disabled Submarine (DISSUB) Stressors on Submariner Cognition	NAVSEA	SUBMARINE RESCUE	9:00 AM	15
Rangamani	padmini.rangamani@eng.ucsd.edu	YIP Non-Equilibrium Thermodynamics of Biological Membranes	ONR	HYPERBARIC PHYSIOLOGY	9:15 AM	15
Casper	brandon.m.casper4.civ@mail.mil	Development of an Interactive Software Application to Provide Recommendations for Human Exposure to Underwater Noise	NAVSEA	HYPERBARIC PHYSIOLOGY	9:30 AM	15
Casper	brandon.m.casper4.civ@mail.mil	Development of a Methodology for Characterization of Acoustic Technologies of Naval UUV Existing and Future Assets	NAVSEA	HYPERBARIC PHYSIOLOGY	9:45 AM	15
Eckmann	eckmann@uphs.upenn.edu	Mitochondrial Stress and Cellular Protection in Undersea Medicine	ONR	HYPERBARIC PHYSIOLOGY	10:00 AM	15
	QUESTIONS				10:15 AM	15
	BREAK				10:30 AM	15
Glandon	glandonh@uncw.edu	Lipid Composition and Nitrogen Solubility of the Spinal Cord and Brain	ONR	HYPERBARIC PHYSIOLOGY	10:45 AM	15
Johnson	blairjoh@buffalo.edu	Autonomic Activity and Water Immersion	ONR	DIVER PERFORMANCE & MEDICINE	11:00 AM	15
Whybourn	lesley.a.whybourn.fm@mail.mil	Medical Response Strategies to Optimize Survival of DISSUB Escapees	NAVSEA	SUBMARINE RESCUE	11:15 AM	15
Schlader	zjschlad@buffalo.edu	Hyperthermia and Hypohydration in Disabled PRM	NAVSEA	SUBMARINE RESCUE	11:30 AM	15
	QUESTIONS				11:45 AM	15
	LUNCH				12:00 PM	60
Sobakin	sobakin@wisc.edu	Improving Safety of Submarine Escape and Rescue from Shallow Depth	NAVSEA	SUBMARINE RESCUE	1:00 PM	15
Keegan	jkeegan@mide.com	Joints for Lightweight Atmospheric Diving Suits	ONR	NEXT GENERATION ATMOSPHERIC DIVING SYSTEM (ADS)	1:15 PM	15
Sorensen	sorensek@spawar.navy.mil	Contaminated Water Research	ONR	MISCELLANEOUS	1:30 PM	15
Howle	laurens.howle@duke.edu	Transfer of Duke University Dive Trial Data to US Navy	NAVSEA	DECOMPRESSION SICKNESS (DCS)	1:45 PM	15
Thom	sthom@smail.umaryland.edu	Micro-particles, Platelet-Neutrophil Aggregation and Decompression Sickness	ONR	DECOMPRESSION SICKNESS (DCS)	2:00 PM	15
Hibbs	stephen@quasarusa.com	Development of Diver Biometric Device (DBD) SBIR Phase II N151-078	ONR	DIVER PERFORMANCE & MEDICINE	2:15 PM	15
	QUESTIONS & CLOSING COMMENTS				2:30 PM	15
	ADJOURN				2:45 PM	
	HYPERBARIC CHAMBER TOUR, DUKE UNIVERSITY				4:00 PM	

Day 1: Tuesday, May 14, 2019



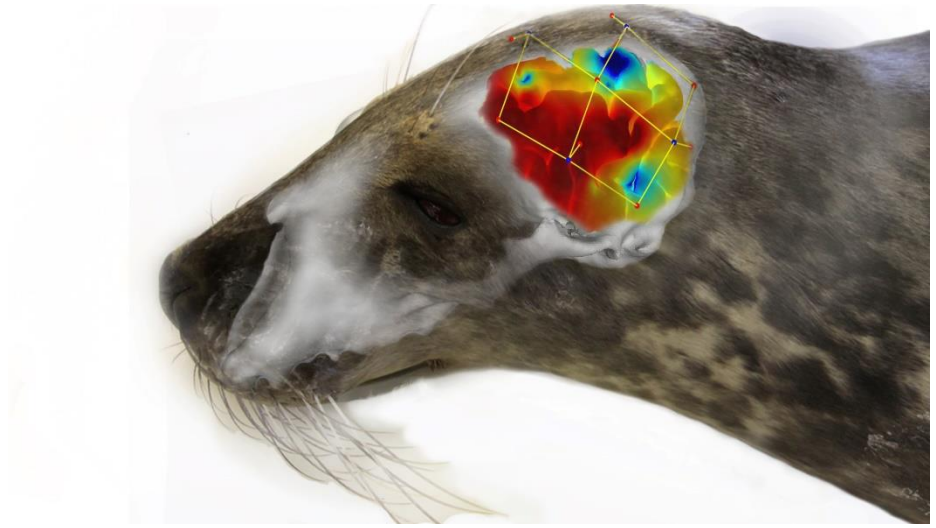
2019 ONR-NAVSEA UNDERSEA MEDICINE PROGRAM REVIEW

Neurobiological and Physiological Measurements from Free Swimming Marine Mammals

Fahlman, A., McKnight, C., Tyack, P., Shorter, K.A., Bogdan, P., Whelan, H.

Background: Marine mammals are exposed to extreme hypoxemia during repeated routine foraging dives. Marine mammals may rely on the dramatic cardiovascular adjustments they make during diving to protect the brain from hypoxic insult. Near-infrared spectroscopy (NIRS) provides a non-invasive technique to investigate hemodynamic and oxygenation changes in the brain of freely diving marine mammals.

Naval & Scientific Benefits: The proposed work will define physiological and behavioral changes caused by stress and will provide tools to quantify health, welfare and stress in marine mammals. The technology developed could be used to monitor physiological and cognitive capacity of human divers, providing enhanced safety and diving capacity.



Objectives: To develop a animal-borne NIRS system that can measure blood oxygen, blood volume and cytochrome-c in freely diving marine mammals by:

1) Characterizing the optical properties of marine mammals tissues (spectrophotometry, Monte Carlo modelling and fMRI).

2) Integrate NIRS with existing animal-borne sensing systems

3) Test and validate NIRS on captive marine mammals

4) Deploy the integrated NIRS system on free-ranging marine mammals.

FY18 Accomplishments, Discoveries, & Inventions

- Measure optical properties of skin and blubber, in-vivo, in seals, porpoise and dolphins.
- Integrate NIRS with pressure, triaxial accelerometry and swim speed sensors, creating an animal-borne package.
- Initial pilot testing on captive marine mammals

FY19 Goals

- Characterize hemodynamic and oxygenation patterns in diving cetaceans
- Characterize the influence of systematic cardiac changes on cerebral hemodynamic homeostasis.
- Validate cerebral measurements by NIRS with fMRI.

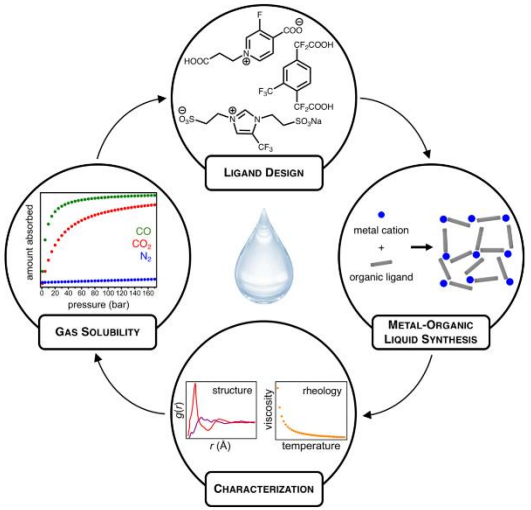
Principal Investigator Contact Email: afahlman@whoi.edu

Porous Metal-Organic Liquids as a New Platform for Investigating Gas-Liquid Interactions

Jarad A. Mason

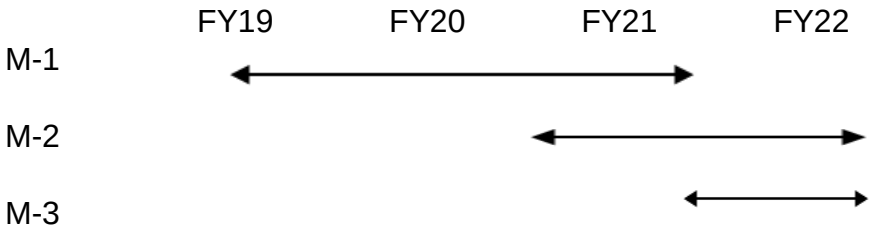
Background: Porosity and fluidity are two extremely useful properties of matter that are rarely encountered together in conventional materials. Guided by coordination chemistry and thermodynamics, this research proposes the design, synthesis, and characterization of a new class of liquids that feature intrinsic porosity.

Naval & Scientific Benefits: Porous liquids will push the boundaries of the properties that can be achieved in porous materials and in liquids, affording new opportunities for the transport, storage, separation, and conversion of small molecules. This research will contribute to new applications of particular importance to ONR, including high-density gas storage and toxic gas removal from confined environments.



Objectives: The objectives of this project are to: 1) synthesize metal-organic liquids with well-defined, transient micropores; 2) characterize the structure and properties of porous metal-organic liquids; and 3) investigate gas absorption and transport properties of porous metal-organic liquids.

Milestone Tracker



FY18 Accomplishments, Discoveries, & Inventions

- Project commenced March 11, 2019.

FY19 Goals

- Synthesize at least 10 organic bridging ligands.
- Demonstrate an extended coordination solid that undergoes a solid-liquid phase transition below 200 ℃.
- Establish initial relationships between the metal-ligand bond strength, dimensionality, and composition of coordination solids with their enthalpies and entropies of fusion.

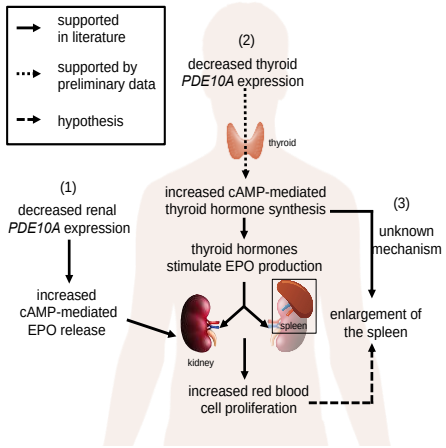
Principal Investigator Contact Email:
mason@chemistry.harvard.edu

A functional genomics investigation of hypoxia tolerance adaptation in Bajau Sea Nomads

Melissa Ilardo

Background: It was recently discovered that the Bajau, a group of traditional divers in Indonesia, are physiologically adapted to hypoxia tolerance through enlarged spleens.

Naval & Scientific Benefits: These experiments will enable us to determine the precise mechanisms that are causing changes in spleen morphology observed in the Sea Nomad divers of Indonesia, and the extent to which these changes increase hypoxia tolerance. The results of these experiments will provide important information for the development pharmacological approaches to increasing hypoxia tolerance. These approaches could provide pharmacological protection during naval training and combat scenarios in which divers are exposed to repeated bouts of apnea.



Objectives: Our aims are to understand the genetic and molecular basis of the large-spleen phenotype through pharmacological and genomic investigations in mice combined with physiological and genetic investigations in additional diving populations.

FY18 Accomplishments, Discoveries, & Inventions

- Discovered first known novel adaptation to diving
- Demonstrated increase in spleen size with pharmacological inhibition of PDE10A in mice

FY19 Goals

- Develop a conditional PDE10A knockout mouse model
- Collect physiological measurements and DNA samples from divers in Malaysia, Korea, and the Philippines
- Perform whole genome sequencing on collected DNA and analyze signatures of adaptation

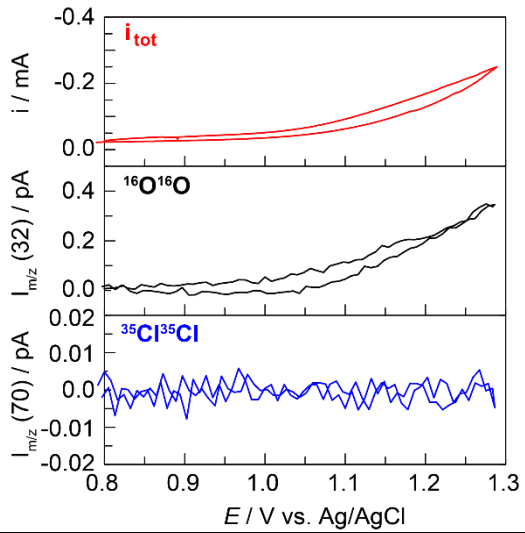
Principal Investigator Contact Email:
melissailardo@gmail.com

Oxygen Generation from Seawater

Daniel G. Nocera
Harvard University

Background: The sea provides a challenging environment to performing naval operations. The ocean contains large concentrations of corrosive salts and miscellaneous organic materials, presents environmentally inhospitable light, temperature and pressure conditions and is power limited. At the same time, the sea is a resource by offering a supply of oxygen.

Naval & Scientific Benefits: Real-time oxygen generation allows for greater flexibility is naval operations. The most basic issue of obtaining oxygen from seawater in appreciable amounts however have not yet been solved. This program targets these scientific issues to enable oxygen generation from seawater.



A cobalt phosphate catalyst generates oxygen from seawater without making harmful chlorine and bromine byproducts, as shown by the differential electrochemical mass spectrograms. This type of selectivity is needed for on demand oxygen generation from seawater.

Objectives: Oxygen may be produced from seawater, in principle, by water electrolysis but for underwater diving applications many basic science challenges must be addressed. Primary among these challenges is the selective production of oxygen without producing harmful products to the human such as chlorine.

Milestone Tracker

FY17 FY18 FY19 FY20

M-1 ⟷ Survey catalysts for selective oxygen generation from seawater

M-2 ⟷ Generalize seawater splitting strategies with new catalyst discovery

FY18 Accomplishments, Discoveries, & Inventions

- Established the feasibility for the generation of oxygen from seawater with negligible chlorine production.
- Developed differential electrochemical mass spectrometry (DEMS) as an accurate measurement technique to monitor toxic byproducts from seawater oxidation (e.g., chlorine and bromine).

FY19 Goals

- Generalize the initial discovery to new catalysts
- Develop a model for self-healing in seawater, necessary for long term catalytic stability for prolonged operation.
- Increase activity of the catalysts and assess system requirements to generate oxygen at breathing rates

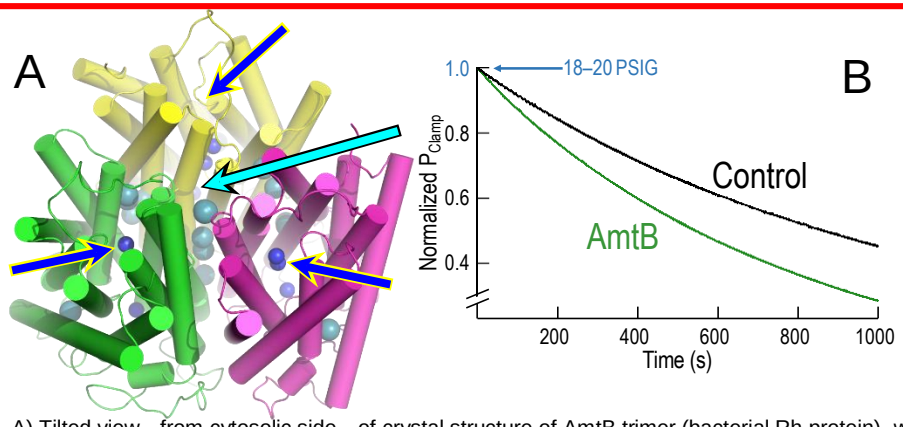
Principal Investigator Contact Email: dnocera@fas.harvard.edu

Characterization of Gas Transport through Biological Membranes

Walter F. Boron et al.

Background: Gases cross biological membranes via membrane [1] lipids and—in a major paradigm shift—[2] gas-channel proteins. Gas permeability depends on the properties of the gas, membrane-lipid composition, impermeant blocking proteins that displace lipids and restrict access to the lipid bilayer, and gas channels. Native gas-channels proteins exhibit gas selectivity, inhibitor sensitivity, and susceptibility to mutations.

Naval & Scientific Benefits: Understanding gas-channel biology will enhance warfighter/patient management. Controlling channels (inhibitors, regulation of expression) could revolutionize our approach to DCI, O_2 toxicity, AMS, burns, shock, and reperfusion injury—and enhance performance. Designer channels could form highly selective gas filters, with applications for divers/DISSUB (e.g., CO_2 removal) and chemical processes.



A) Tilted view—from cytosolic side—of crystal structure of AmtB trimer (bacterial Rh protein), with 4 Xe atoms (cyan) in central pore (arrow), and NH_3 molecules (blue) in 3 monomeric pores (arrows) that conduct NH_3. Presumably moving via central pore are O_2, CO_2 and N_2. B) AmtB's N_2 permeability. Injecting oocyte with N_2 gas makes it float. A computer then applies pressure (P_{Clamp}) to compress bubble and achieve neutral buoyancy, 5 cm beneath surface. P_{Clamp} falls as N_2 leaves bubble and exits cell.

Objectives: Using interdisciplinary approaches (e.g., X-ray crystallography, molecular dynamics (MD), reconstitution of purified channel proteins in giant unilamellar vesicles [GUVS], molecular biology, KO mice, stopped-flow spectroscopy of RBCs, exercise tolerance, electrophysiology), our immediate goal is to understand how individual gases move through membrane lipids and particularly gas-channel proteins—tetrameric aquaporins (AQPs) and trimeric rhesus (Rh) proteins—and influence physiological function and performance.

Longer-term goals are to prepare the field for:

(1) Biomarkers: Are polymorphisms predictive of performance or susceptibility to "dys-gas-ias" (e.g., DCI, O_2 toxicity)?

(2) Interventions: Drugs to block channels/increase expression.

(3) Designer channels. In gas-tight block copolymer membranes, they would be ultra-selective molecular gas filters.

FY18 Accomplishments, Discoveries, & Inventions

- Submitted 7 mss, including: (a) 1st AQP7 crystal structure. Shows 1st internal gating of pores, blockade by exogenous molecule. (b) Discovery of 1st O_2 channels—AQP1, RhAG.
- 1st crystal structure of a gas (Xe) in a channel (AmtB).
- Novel "bubble" assay, enabling discovery of 1st N_2 channels.
- Block copolymer membrane blocks gas transport into GUVs.
- New MD method: establish gas gradients across membrane.

FY19–21 Goals (selected)

- New: Begin "Designer channels," permeable to only 1 gas.
- MD: Simulate blocking proteins (extensive protein crowding).
- New structures of channels with Xe, or with blockers.
- Studies of mutant channels in GUVs to establish mechanism.
- Role of channels in performance (treadmill, brain O_2).

Contact PI: WF Boron, 216-368-3400, wfb2@case.edu

Assessment of Doxycycline as an Adjunctive Therapy to Prevent Decompression Sickness in Swine

Dr. Aaron Hall, LT Angela Senese, LT Nicholas Roney, LT William Johnson, CDR Hugh Dainer

NAVSEA
NAVAL SEA SYSTEMS COMMAND
Supervisor of Salvage & Diving

Background: The lack of an adjunct therapy for preventing/mitigating DCS when recompression therapy is unavailable or delayed is a significant capability gap for diving and submarine operations. Preliminary swine work suggests that doxycycline is efficacious at reducing morbidity and mortality from DCS at high doses. The current study seeks to corroborate and expand on these findings with respect to optimal dosing and operational suitability.

Naval & Scientific Benefits: Severe DCS is a risk inherent to diving operations which cannot be fully mitigated through the use of decompression tables or recompression therapy. Doxycycline, if efficacious as an adjunct therapy, would help further mitigate this risk and is already distributed fleet-wide.

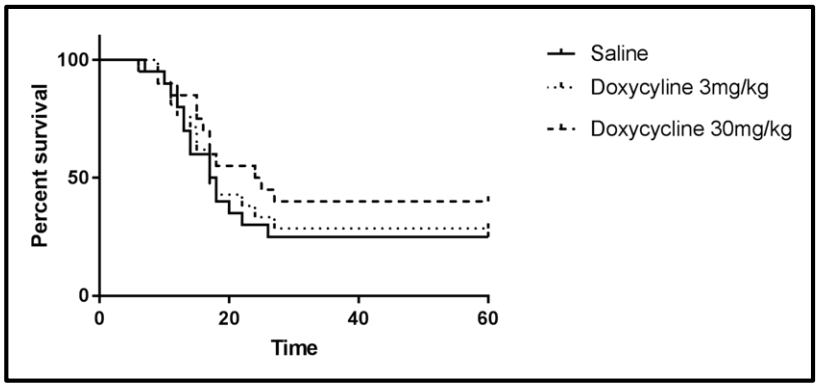


Figure 1. Swine survival rates following a 240fsw bounce dive (31min bottom time) during Phase 1 experiments.

Objectives:

Phase 1: Compare the efficacy of 3 mg/kg doxycycline, 30 mg/kg doxycycline, or saline infusion on DCS survival.

Phase 2: Evaluate the effect of high dose doxycycline on surface interval survival following maximum pressurized rescue module (PRM) decompression from air saturation at 70fsw.

Milestone Tracker

	FY17	FY18	FY19	FY20
M-1		←	→	
M-2			←	→

FY18 Accomplishments, Discoveries, & Inventions

- All Phase 1 animal studies completed

FY19 Goals

- Complete data analysis
- Submit manuscript for peer-review

Principal Investigator Contact Email:
Aaron.a.hall6.civ@mail.mil

Altitude Diving

P.I. Richard E. Moon

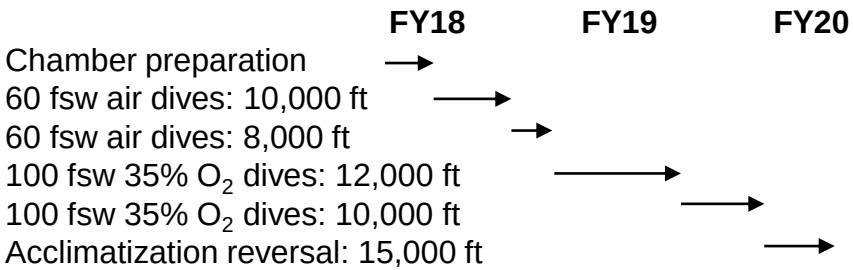
Background: Altitude diving requires considerations that include (a) use of alternate decompression procedures and (b) acclimatization and resolution of altitude illness. Navy decompression guidelines Cross Corrections, which have not been formally tested and in Navy diving apply only to air or He-O_2 dives up to 10,000 ft. De-acclimatization occurs slowly after return to sea level. Whether hyperbaric hyperoxia (e.g. a dive) induces rapid de-acclimatization is unknown.

Naval & Scientific Benefits: These studies will test Cross Corrections for a 60 fsw no-stop air dive at 8,000 and 10,000 ft, and for a 100 fsw enriched O_2 dive (35% O_2, bal N_2) at 10,000 and 12,000 ft. De-acclimatization after a hyperoxic dive will be tested at 15,000 ft after 1.3 ATM PO_2 exposure.

Objectives:

- Test Cross corrections for no-stop air dives to 60 fsw at altitudes of 8,000 and 10,000 ft. and no-stop enriched O_2 (35% O_2) 100 fsw dives at 10,000 and 12,000 ft.
- After acclimatization at 15,000 ft, assess AMS recurrence after a 2 hour exposure to PO_2=1.3 ATM.

Milestone Tracker



FY18 Accomplishments, Discoveries, & Inventions

- Human volunteer no-stop air dives (60 fsw/30 minutes) complete following acclimatization to 8,000 and 10,000 ft.
- No DCS or VGE observed at either altitude.
- Nitrox dives at 12,000 ft started: VGE in 1/4 subjects.
- Mild AMS during 10,000 ft exposures.

FY19 Goals

- Complete 12,000 ft nitrox dives (N=28).
- Start 10,000 ft nitrox dives (N=16).

Principal Investigator:
Richard Moon, MD
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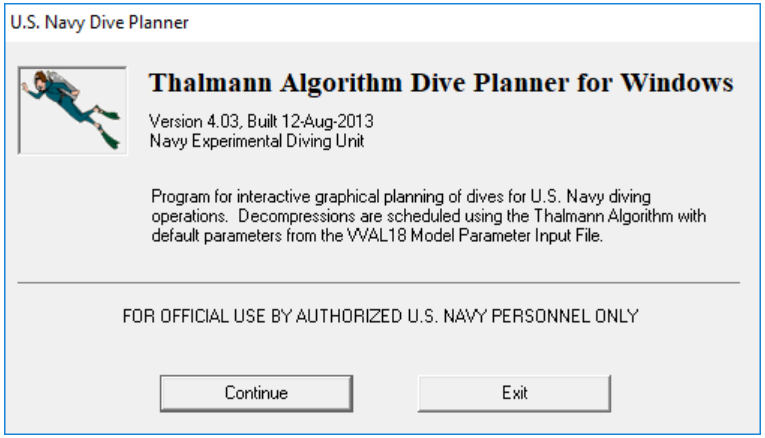
Modernization of the U.S. Navy Thalmann Algorithm Dive Planner

F. Gregory Murphy, Ph.D.

NAVSEA NAVAL SEA SYSTEMS COMMAND
Supervisor of Salvage & Diving

Background: The current U.S. Navy Thalmann Algorithm Dive Planner (NDP) is written in Microsoft Visual Basic 6 (VB6). Extended support ended for it in 2008 leaving it noncompliant with cybersecurity. Due to the language becoming unsupported, maintaining the existing code base has become unduly cumbersome. Updating to a modern object oriented programming language will make maintenance easier and combine the DISSUB Rescue Decompression Planner (DISSUB RDP) and NDP into a single product.

Naval & Scientific Benefits: The cost of maintaining the NDP will be reduced. Further, significant enhancements made to the RDP will now be available in the NDP. The cybersecurity posture of the NDP will also be improved.



Legacy Thalmann Algorithm Dive Planner Splash Screen

Objectives: Recreate the NDP and DISSUB RDP in the C# .Net programming language using an object oriented programming paradigm.

A. Contact current user SMEs to determine any current deficiencies in the NDP GUI.
B. Design overall layout of new code base.
C. Implement new NDP/ DISSUB RDP code base in C# .Net.
D. Generate verification and validation documentation.
E. Complete and submit modernized NDP/RDP documentation to support SECNAVINST 5200.40 VV&A requirements for independent third party review by Sandia National Laboratory.

FY19 Accomplishments

- Feedback received from NEDU and URC NDP/RDP SME's.
- Completed data structure and UI design.
- Hired new contractor Mr. John Ammerman to aid in development.
- Began software development.
- IV&V review scheduled for legacy DISSUB RDP.

FY20 Goals

- Complete software development.
- Complete V&V documentation.
- Complete independent V&V review.

Sponsor: DSBD

Principal Investigator: F. Gregory Murphy, Ph.D.,
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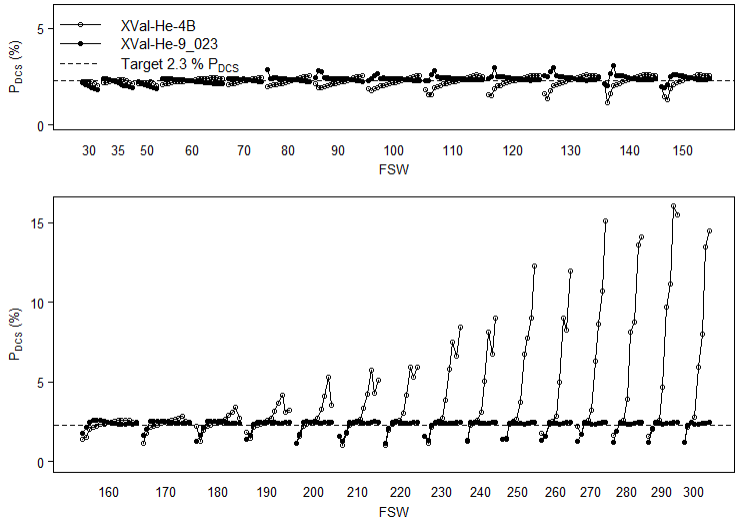
Navy Dive Computer and Navy Dive Planner Algorithm for Constant 1.3 atm PO_2-in-Helium Diving to 300 fsw

David J. Doolette

Background: U.S. Navy 1.3 atm PO_2 He-O_2 Decompression Tables support diving to 300 fsw. These tables are based on the LEM-he8n25 probabilistic decompression model and have near-uniform estimated probability of decompression sickness (P_{DCS})=2.3%. The He III 200-1.3 NDC supports 1.3 atm PO_2 He-O_2 diving to a maximum depth of 200 fsw because it uses the XVal-He-4B-Thalmann Algorithm which was engineered to emulate LEM-he8n25 schedules to 200 fsw, and emulation is poor deeper than 200 fsw. We have identified a method to improve the emulation across a broad depth / time range.

Naval & Scientific Benefits: NDCs provides substantial increase in decompression efficiency for multi-level diving and for repetitive diving compared to using decompression tables.



Objectives: This project developed decompression algorithms for use in the NDC that provide acceptable P_{DCS} schedules for the full 300 fsw range of 1.3 atm PO_2 He-O_2 operations:

- Develop a Thalmann Algorithm parameter set to emulate current 2.3% P_{DCS} LEM-he8n25 decompression schedules
- Develop parameter sets with 4% and 5% target P_{DCS}, and accelerated decompression, that would allow selection of P_{DCS} in accord with mission requirements.

Milestones: Project completed. Fleet customer for higher P_{DCS} parameter set funded limited validation of schedules, conducted under separate tasking.

FY18 Accomplishments, Discoveries, & Inventions

- Augmented probabilistic-to-Thalmann Algorithm method
- Developed "XVal-He_9_023" parameter set: emulates U.S. Navy 1.3 atm PO_2 He-O_2 Decompression Tables to 300 fsw
- Developed "XVal-He_9_040" and Xval-He-9_050" parameter sets: emulate LEM-he8n25 4.0% and 5.0% P_{DCS} schedules to 300 fsw and 4 h BT
- Thalmann algorithm parameter sets for support of constant 1.3 atm PO_2 He-O_2 diving to 300 fsw, NEDU TR 18-05, Dec 2018

Principle Investigator: David J Doolette
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email: david.doolette@navy.mil
Associate Investigators: F Greg Murphy, Wayne A Gerth

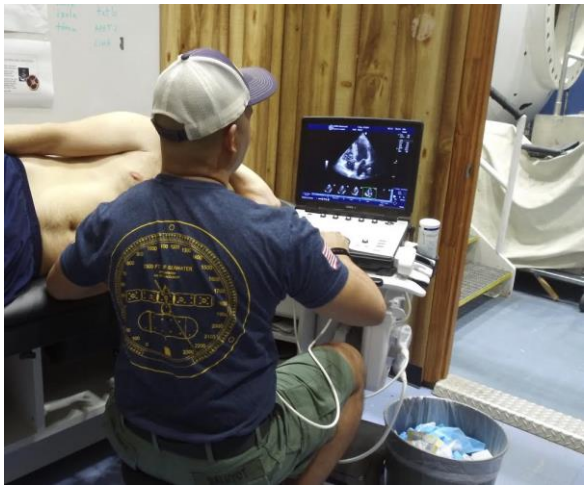
Manned Validation of U.S. Navy Diving Manual, Revision 7 (VVal-79 Thalmann Algorithm) Schedules for Short Bottom Time, Deep Air Decompression Dives

Brian Andrew, LT, MC, USN

NAVSEA
NAVAL SEA SYSTEMS COMMAND
Supervisor of Salvage & Diving

Background: The U.S. Navy Diving Manual Air Decompression Table was promulgated in 2008, and a revised version, calculated with the VVal-79 Thalmann Algorithm, was promulgated in 2016. The Swedish Armed Forces Diving and Naval Medicine Center (DNC) conducted a laboratory dive trial using the 2008 Air Decompression Table. 32 dives to 132 fsw (40 msw) for a 20-minute bottom time resulted in two cases of decompression sickness (DCS), and a median venous gas emboli (VGE) measurement at rest of KM grade III.

Naval & Scientific Benefits: All air decompression dives with less than 15 minutes of stops are expected to be suitable for routine use. The DNC study motivated an examination of U.S. Navy Air Decompression schedule for 132 fsw / 20-minutes.



Venous Gas Emboli measurements using 2-D Echocardiography

Objectives: Provide a relatively precise estimate of the probability of DCS of the VVal-79 Thlamann Algorithm schedule for 132 fsw for a 20-minute bottom time under dive conditions typical of previous U.S. Navy trials

Milestone Tracker

	FY18	FY19	FY20
1) Protocol development	→	→	
2) Conduct manned-diving		→	
3) Analyze and report data			→

FY18/19 Accomplishments

- Protocol approved by NEDU's CO after evaluation by NEDU's TRC, SRC, and IRB
- Diver-subject recruitment complete
- Manned-diving ongoing: 64 of 96 planned dives complete as of 31 Mar 19

FY 19/20 Goals

- Complete manned-diving
- Data analysis and completion of Technical Report

Principal Investigator: David Doolette, Ph.D.,
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Assistant Investigator: LT Brian Andrew, M.D.
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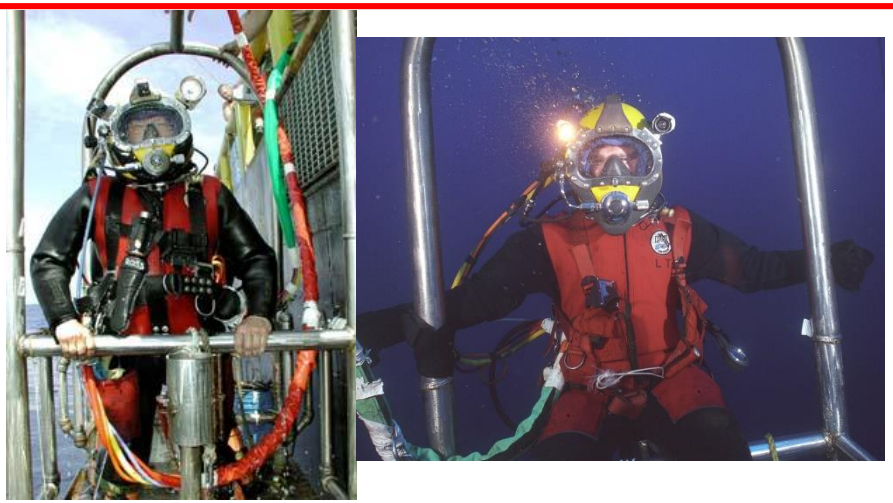
21st Century Surface-Supplied Heliox Decompression Tables

Wayne A. Gerth, Ph.D.

NAVSEA
NAVAL SEA SYSTEMS COMMAND
Supervisor of Salvage & Diving

Background: The current U.S. Navy Surface-Supplied Helium-Oxygen Decompression Table, which is an edited version of an original 1939 issue, has a limited record of success in operational dives to depths of 240 feet sea water (fsw) or shallower. Recent theoretical evaluations indicate that tabulated schedules for dives to deeper depths, depths that are increasingly within the scope of desired U.S. Navy diving operations, will incur unacceptably high risks of decompression sickness (DCS).

Naval & Scientific Benefits: A new model for predicting the occurrence of DCS in many types of undersea operations. An updated Surface-Supplied Helium-Oxygen Decompression Table with schedules verified to have acceptable risks of DCS.



Divers on stages conducting surface supplied dive operations.

Objectives: Replace the Surface-Supplied Helium-Oxygen Decompression Table in the U.S. Navy Diving Manual with a new table of schedules for dives to depths up to 380 fsw (310-380 fsw being exceptional exposure) with verified risks of DCS.

Phase I (JPC-5 funded) Milestones:

- Establish calibration data set
- Develop a model optimization and evaluation framework
- Develop/implement a heliox 3RUT-MB bubble model
- Optimize model parameters
- Model selection
- Table generation
- Protocol for man-trials

Phase II (NAVSEA DSBD funded): Man-trials in the Navy Experimental Diving Unit Ocean Simulation Facility to validate the new table.

FY19 Accomplishments, Discoveries, & Inventions

- JPC-5 funding received Jan 2019
- New software development tools acquired
- New model fitting architecture and methods implemented
- Model calibration data expanded

FY19 Goals

- Complete 3RUT-MB model implementation in new architecture
- Commence model optimization on expanded calibration data

Principal Investigator: Wayne A. Gerth, Ph.D.
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Associate Investigators: F. Gregory Murphy, David J. Doolette

Gas narcosis in hyperbaric environments

THE UNIVERSITY OF AUCKLAND
FACULTY OF MEDICAL AND HEALTH SCIENCES

Professor Simon Mitchell

Background: A Navy diver may experience narcosis induced by gases respired under pressure. Nitrogen is known to cause narcosis, helium produces very little, and the role of others such as oxygen and carbon dioxide is poorly characterized. Cognitive impairment by gas narcosis is operationally dangerous.

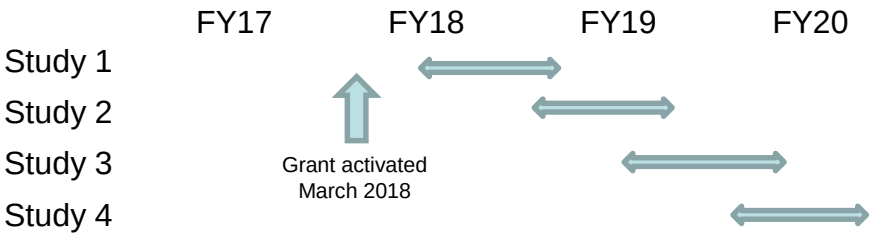
Naval & Scientific Benefits: The study of gas narcosis is hampered by lack of an objective, sensitive means of measuring its effects. Development of a measurement technique based around the electroencephalogram (EEG) may significantly enhance applied research on the problem. Determining the relative narcotic potency of different gases will enhance safety in operational dive planning.

Study 2. Baseline measurement inside the hyperbaric chamber.

Objectives:

- Develop a qEEG algorithm to objectively assess the narcotic effects of gases in hyperbaric environments.
- Determine the relative narcotic effects of nitrogen (study 2), oxygen (study 3) and carbon dioxide (study 4).

Milestone Tracker



FY18 Accomplishments, Discoveries, & Inventions

- Activated grant (March 2018)
- Completed logistic, research compliance, and subject recruitment tasks
- Completed study 1 (nitrous oxide study) with initial appraisal of EEG data
- Commenced study 2 (nitrogen narcosis)
- Presented pupillometry data from study 1 at Tricon meeting

FY19 Goals

- Complete EEG analysis of nitrous oxide study
- Complete study 2 and develop qEEG algorithm
- Commence measurements in study 3 (oxygen narcosis)

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Impact of Repeated 6-hour Hyperoxic Exercise Dives at 1.35 ATA on Muscular Performance and Cardiovascular Endurance

John P. Florian PhD[1,2], Christopher M. Myers PhD[1,2], James E. Campbell[1,2], PhD, & Erin E. Simmons PhD[1]
[1]Navy Experimental Diving Unit, [2]Florida State University

Background: Breathing 100% O_2 during repeated 6-hour dives can elicit both beneficial (↑ cardiovascular stability) and detrimental (↓ exercise performance) effects on surface physiological function as compared to that after similar air dives. This project examines the cause of reductions in performance from exercise diving with 100% O_2 and the recovery time required to maintain performance.

Naval and Scientific Benefits: The current work will provide guidance to enable better dive planning for combat swimmer, or other long duration repeated dive operations. This effort may allow the future development of countermeasures to enhance safety, human performance, and mission completion.

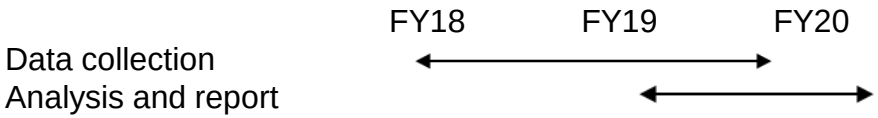
Protocol:

1. Exercising 100% O_2 dives in Test Pool (2018-2019) – (n=16)
2. 6-hr exercise dives
   a. 30-min biking; 30-min rest
   b. HR: 105±5 BPM
3. Surface testing
   a. Pre- & post-dive
   b. 24-hr & 72-hr post-dive

Objectives:

1. To characterize changes in physiological and neuropsychological performance after single and repeated hyperoxic exercise dives and extent of recovery by 72-hrs post-dive
2. Examine the degree to which acute and repeated hyperoxic exercise dives alter biomarkers of oxidative stress, muscle breakdown, and microbiota.

Milestone Tracker



FY18 Accomplishments, Discoveries, & Inventions:

- Completed Groups A and B testing.
- Hurricane Michael recovery.
- Published several journal articles & abstracts.

FY19/20 Goals:

- Complete 100% O_2 exercise dives Groups C – F.
- Continue to publish results in peer reviewed journals and technical reports. Transition information to Fleet.
- Begin execution of future funded research.

Principal Investigator: Dr. John Florian, NEDU, 850-230-3157, john.florian@navy.mil

Associate Investigators: Dr. Chris Myers, Dr. James Campbell, & Dr. Erin Simmons

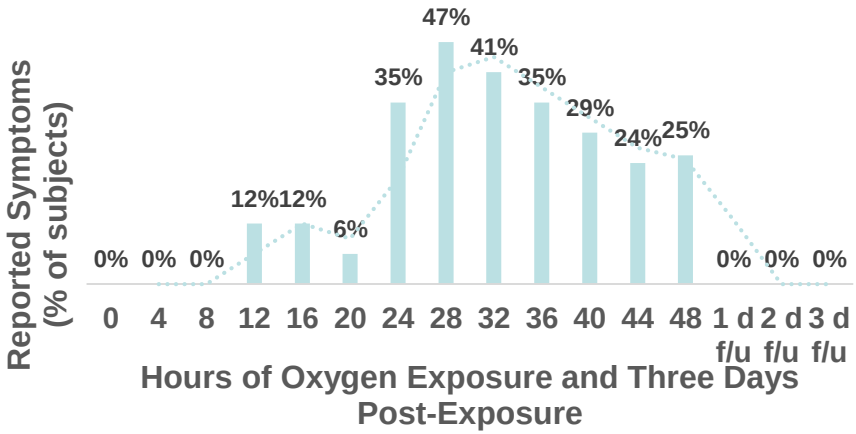
Pulmonary Oxygen Toxicity with Oxygen Partial Pressure 1 ATM: Possible Mitigation

Patrick Hennessey, CDR, MC, USN
Andrew Syski, LT, MC, USN

NAVSEA
NAVAL SEA SYSTEMS COMMAND
Supervisor of Salvage & Diving

Background: A Disabled Submarine (DISSUB) could lose its atmospheric control and become pressurized. An internal pressure of 5 atmospheres absolute (ATA) of air would expose survivors to a toxic level of 1 atmosphere of O2.Time to rescue of at least 72 hours could lead to serious symptoms/pathology and make accelerated decompression or recompression treatment difficult. There is thus an impetus to further understand the mechanisms of pulmonary oxygen toxicity and develop potential mitigations.

Naval & Scientific Benefits: Knowledge gained from the study of pulmonary oxygen toxicity can be applied to submarine rescue planning.



Symptoms of 18 subjects while breathing 100% O2

Objectives: Clearly define the development of pulmonary oxygen toxicity at a PO2 of 1atm and test if normoxic intervals could delay or prevent development of pulmonary oxygen toxicity.

Milestone Tracker

	FY17	FY18	FY19
1) Protocol development	→		
2) Conduct manned-diving		→	
3) Analyze and report data			→

FY18 Accomplishments

- 18 48-hour continuous O2 Exposures completed; protocol terminated early due to minimal lung function decrements in control group.
- Only mild symptoms observed. No significant change in lung spirometry (FVC, FEV1, FEF25-75, and DLCO).
- One subject terminated at 40 hours due to forced vital capacity (FVC) criteria; the remainder saw average decrement of only 1% in FVC over 48 hours.

Principal Investigator: CDR Patrick Hennessey, M.D. Ph.D., patrick.hennessey@navy.mil
Associate Investigator: LT Andrew Syski, M.D.
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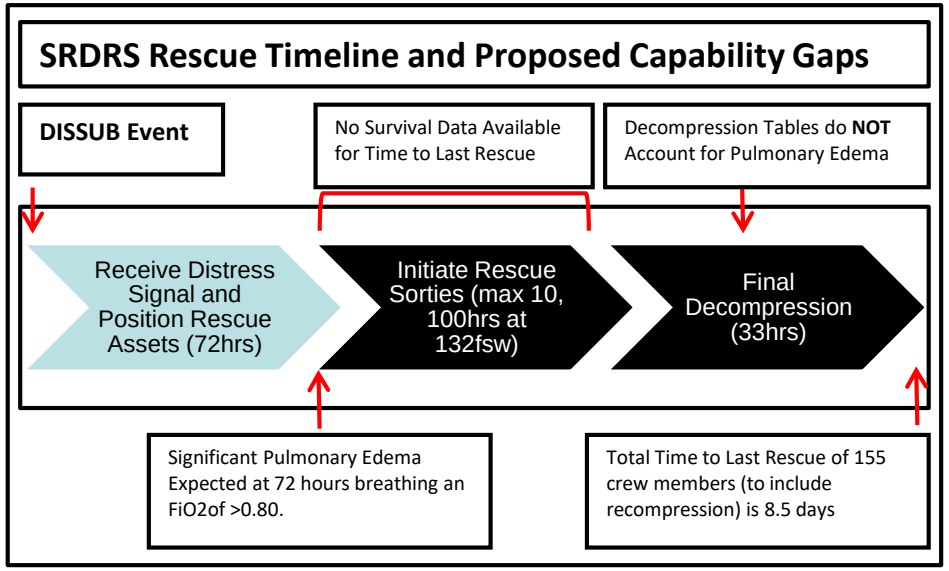
Determining DISSUB survival rates of 70 Kg swine rescued using SRDRS standard operating procedures

Dr. Aaron Hall, LT William Johnson, CAPT (ret) Rich Mahon, CDR Hugh Dainer

Background: Executing a disabled submarine (DISSUB) rescue operation will require mobilization of significant manpower and resources and will require significant time to accomplish. The current rescue system used by the US Navy is capable of rescuing DISSUB casualties from submarines internally pressurized up to 5ATA (132fsw). This study used a human surrogate swine model to provide direct data on the survivability of our current DISSUB rescue plan at the maximum depth of 5ATA.

Naval & Scientific Benefits: Enhancing submariner survivability in a DISSUB is a focus area for DSBD. Directly testing casualty survivor in a simulated DISSUB provides important data to support mission planning, life support systems, and senior survivor guidance.



Objectives:

Determine the survivability of hyperbaric air exposure at 5ATA for the time required to execute a DISSUB rescue mission (172hrs).

If hyperbaric air exposure for 172hrs is survivable, determine incidence and severity of DCS following oxygen accelerated decompression

Milestone Tracker FY18 FY19

M-1 ⟷

M-2 ⟷

FY18 Accomplishments, Discoveries, & Inventions

- Swine study completed
- Data analysis completed
- Discovered that all subjects died prior to minimum time required for DISSUB rescue (72hrs)
- Research findings communicated to stakeholders

FY19 Goals

- Publish findings in a peer-reviewed journal

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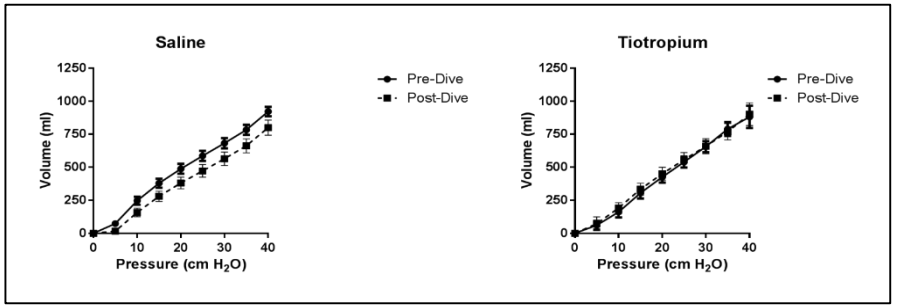
Evaluation of Tiotropium Bromide Efficacy to Reduce Tracheobronchitis and Pulmonary Function Decrements in Divers During Operationally Relevant Hyperbaric Oxygen Exposures

Aaron Hall, PhD, Richard Mahon MD

NAVSEA NAVAL SEA SYSTEMS COMMAND
Supervisor of Salvage & Diving

Background: Tiotropium bromide is a promising therapeutic to prevent pulmonary oxygen toxicity (PO_2T). This study builds on previous swine studies by determining the efficacy of tiotropium bromide prophylaxis to reduce pulmonary function decrements associated with PO_2T associated with operationally relevant dive profiles.

Naval & Scientific Benefits: Special Operations Forces are limited in their diving duration secondary to PO_2T. In closed circuit 100% oxygen rebreather dives at 1.3 ATA O_2, it is predicted that 17% of divers will have mild PO_2T at 4 hours and 33% at 6 hours. This study is designed to satisfy regulatory and administrative requirements to support transition to human trials.



Pulmonary compliance from swine following a 2.5ATA, 5.5hr hyperbaric oxygen exposure. Tiotropium bromide treated animals had reduced compliance decrements after hyperbaric oxygen exposure when compared to saline treated controls.

Objectives:

- Establish a partnership with a clinical research group
- Prepare required documentation to support FDA IND application
- Establish a plan to satisfy required regulatory and fiscal requirements

Milestone Tracker

	FY18	FY19	FY20
Establish Clinical Partner	⟷		
Submit IND to FDA	⟷		

FY18 Accomplishments, Discoveries, & Inventions

- Established a collaboration with Dr. Richard Moon at Duke
- Non-provisional patent application filed protecting domestic and international intellectual property rights

FY19 Goals

- Engagement with Boehringer Ingelheim
- IND application submission
- Draft IRB preparation
- Finalize study design and budget projection

Principal Investigator Contact Email:
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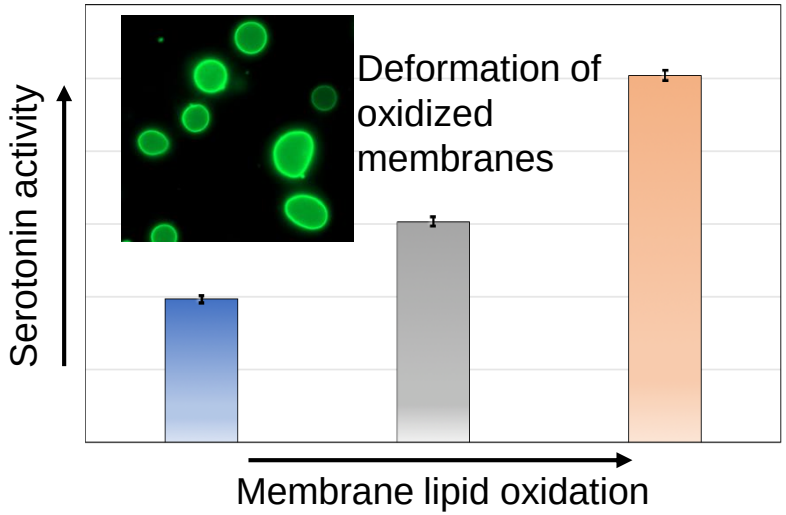
Connecting lipid oxidation to cellular dysfunction in hyperbaric oxygen toxicity

Noah Malmstadt, University of Southern California

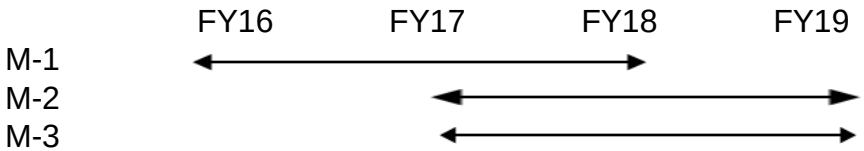
Background: Hyperbaric oxygen toxicity—a condition in which individuals breathing high concentrations of oxygen experience a series of symptoms including pulmonary distress and seizure—has been recognized as a danger to divers for over a century. However, little is known regarding how high oxygen concentrations damage cells on the molecular level.

Naval & Scientific Benefits: Oxygen toxicity is an ongoing risk to Navy divers. Understanding the molecular etiology of oxygen toxicity is key to further improving diving protocols, identifying which divers are at particular risk at high oxygen partial pressures, and predicting potential long-term oxygen toxicity effects among those who show no acute symptoms.



Objectives: There are three objectives or milestones: (1) Quantify changes to lipid composition in cells that have been treated in oxidizing conditions. (2) Determine how lipid bilayer mechanics, permeability, and structure change under conditions consistent with cellular damage by hyperbaric oxygen. (3) Quantify changes to the behavior of key neurotransmitter receptor proteins in lipid bilayers with compositions that match those of the plasma membranes of cells that have been treated with hyperbaric oxygen.

Milestone Tracker



FY18 Accomplishments, Discoveries, & Inventions

- Discovered that lipid oxidation activates serotonin signaling.
- Correlated oxidation in cell membranes with cell death.
- Formed giant plasma membrane vesicles from oxidized cells.
- Correlated mechanical deformation of GPMVs to oxidation.
- Simulated nanoparticle interactions with oxidized membranes.

Future plans

- Perform and interpret lipidomic analysis of oxidized cells.
- Measure permeability and mechanics of oxidized GPMVs.
- Extend serotonin results: additional neurotransmitters.
- Extend serotonin results: additional lipid compositions.

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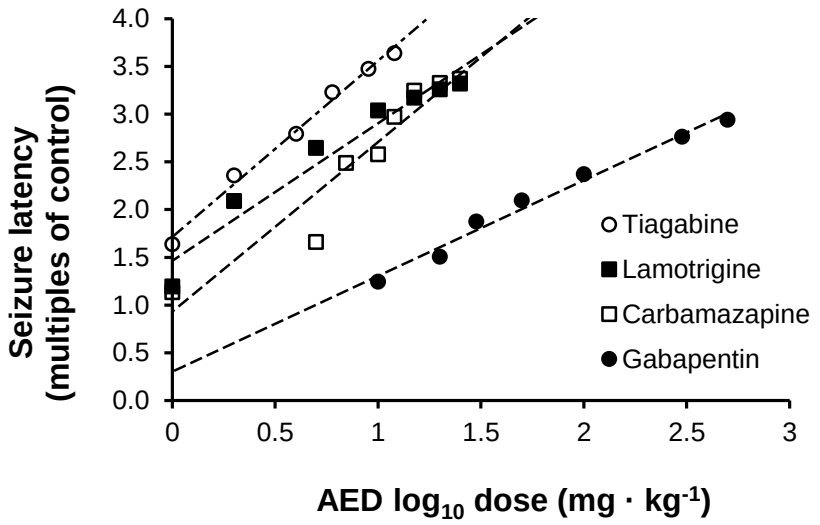
Oxidative tissue damage after HBO_2 exposure using selected FDA-approved anti-epileptic drugs (AEDs)

C.A. Piantadosi, MD
Professor of Medicine and Pathology
Duke University Medical Center

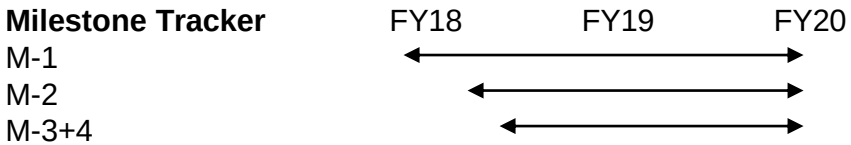
Background: Hyperbaric oxygen (HBO2) elicits acute CNS toxicity that limits safe exposures ~1.6 ATA. Convulsions in diving is a neurological emergency that we cannot now prevent. We have determined that certain FDA-approved antiepileptic drugs (AEDs) alone and in combinations prevent HBO2 seizures in unrestrained mice exposed to 100% O2 at 5 ATA. Although seizures are blocked for various periods of time, we do not yet know whether AEDs mitigate or promote biochemical oxidant damage to neurons or glia during maximal tolerable exposures.

Naval & Scientific Benefits: The potential benefits the Navy/Marine Corps and the scientific community is safer extension of HBO2 exposure times for military divers, crew escape in a DISSUB and patients receiving HBO2 therapy.



Objectives: Aim 1: Measure oxidative tissue damage by 5ATA HBO_2 in mouse forebrain and hindbrain under conditions of A) Control, B) HBO_2, C) AED combinations alone, and D) HBO_2 plus AED combinations. Aim 2: Measure basic NT levels in mouse brain under A) Control, B) HBO_2, C) AED combinations alone, and D) HBO_2 plus AED combinations. Aim 3: Measure inflammatory activity in mouse brain, lung, and plasma and compare the four conditions above. Aim 4: Measure cell death at days 1 and 7 in the brain and compare it with changes in memory and coordination.

Milestone Tracker



FY18 Accomplishments, Discoveries, & Inventions

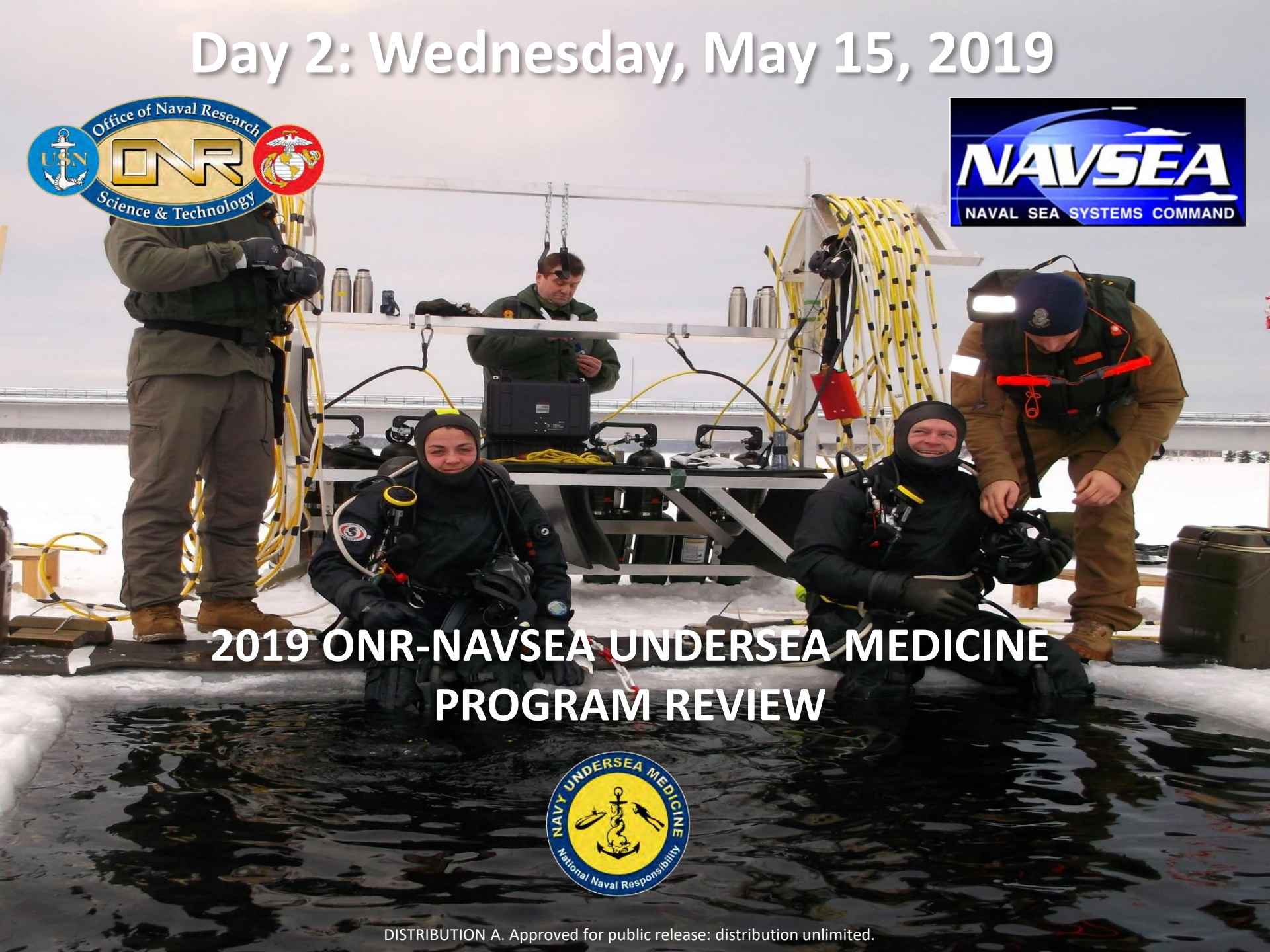
- 1- Certain AED combinations (TGB+CMZ and GBP+LTG) had synergism vs. HBO2.
- 2- Tiagabine (GABAergic) is the single best agent and will be used in combination with LTG and CMZ (Na channel agonists) to test for oxidant damage
- 3- Spatial learning and memory tests in Barnes maze shows deficits after one exposure to 5 ATA for 90 min

FY19 Goals

- Complete biochemical analyses of GSH/GSSG, OHdG, protein carbonyls and MDA in brain tissue
- Complete NT measurements in brain tissue, compare all with NP testing in Barnes maze
- Begin lung tissue measurements

PI Contact Email: piant001@mc.duke.edu

Day 2: Wednesday, May 15, 2019



2019 ONR-NAVSEA UNDERSEA MEDICINE PROGRAM REVIEW

Advances in and Evaluation of Oxygen Toxicity Models

Laurens E. Howle, Ph.D. P.E.

Duke
MECHANICAL ENGINEERING & MATERIALS SCIENCE

NAVSEA
NAVAL SEA SYSTEMS COMMAND
Supervisor of Salvage & Diving

Background: This project has two specific aims. Specific Aim 1: Develop optimize, and evaluate models to predict the risk of central nervous system (CNS) oxygen toxicity. Specific aim 2: Develop decompression sickness (DCS) models including counter perfusion/diffusion to allow for gas switching.

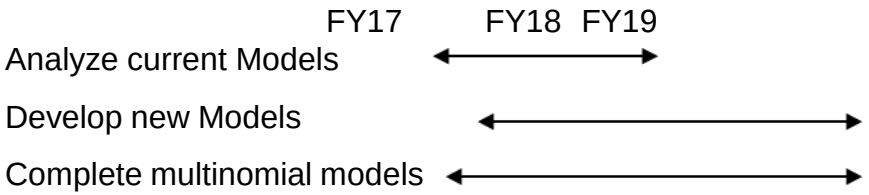
Naval & Scientific Benefits: The Navy has stated needs for improvements in models to predict CNS oxygen toxicity and probabilistic DCS theory, models, and methods. Additionally, there are Navy needs for improved understanding of counter diffusion in isobaric and non-isobaric exposures.

Model	LL	PCNS
Harabin 93 Exp	-152.6	134.3
Howle 18C	-190.6	135.0
Howle 18D	-190.6	135.0
Howle 18E	-190.6	135.0
Howle 19H	-190.6	135.0
Harabin 95 Exp	-218.9	115.6
Howle 18A	-224.5	121.5
Harabin Auto	-266.3	115.0
Howle 18F	-325.7	35.1
Howle 18B	NA	NA
Howle 19I	NA	NA

Model optimization results for Harabin subset 2 of CNS oxygen toxicity data. For this subset, 275 exposures resulted in 135 dive-ending oxygen toxicity events.

Objectives: The objective of this project is to develop, optimize, and evaluate models to predict the risk of CNS oxygen toxicity. Recent USN studies have collected additional data on CNS oxygen toxicity. These new data will enable new efforts at creating and refining CNS oxygen toxicity models.

Milestone Tracker



FY18 Accomplishments, Discoveries, & Inventions

- Corrected and transferred OxTox data to USN.
- Re-optimized and evaluated previous OxTox Models.
- Developed, optimized, and evaluated eight new OxTox models.

FY19 Goals

- Continue development and evaluation of CNS OxTox Models
- Publish trinomial marginal DCS and tetranomial marginal DCS studies.

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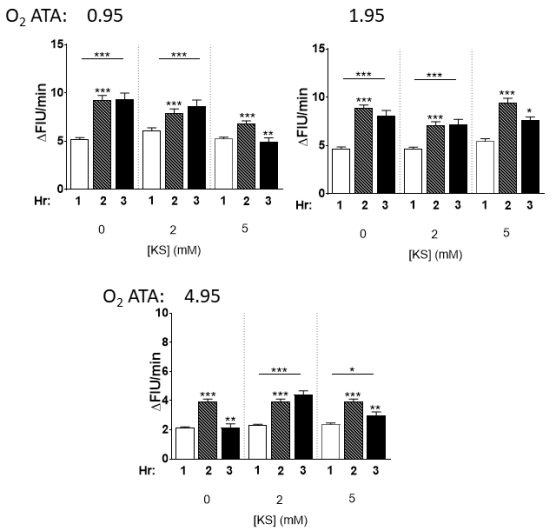
Cellular mechanisms of CNS O_2 toxicity (CNS-OT) during CO_2 retention and ketone metabolic therapy

P.I. / Jay B. Dean, Ph.D.

Background: Ketone metabolic therapy (KMT) delays onset of CNS-OT seizures (Sz) in rodents breathing HBO_2 by ~600%. Our goal was to determine the effects of KMT on brain cells that are implicated in the pathogenesis of CNS-OT; i.e., the caudal solitary complex (cSC) in the brain stem. The effect of CO_2 rebreathing are also of interest because it accelerates onset of CNS-OT during HBO_2, and has powerful effects in and of itself on the integrated cardio-pulmono-gastro-esophageal systems.

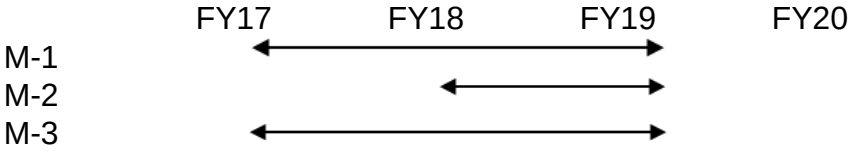
Naval & Scientific Benefits: Changes in inspired O_2 & CO_2 levels are limiting factors in Naval unique SPECWAR/SPECOPS diving operations and submarine operations. This project seeks to understand how O_2-CO_2 interact at the cellular & organismal levels in the context of diving & submarine medicine.



Effects of O_2 (0.95, 1.95 & 4.95ATA) ± ketone salts (KS: 2&5mM) on super-oxide production in cSC cells in rat brain slices based on changes in DHE fluorescence intensity per min (ΔFIU/min) during exposure to control 0.4 ATA O_2 (Hr 1, white bar), hyperoxia (Hr 2, grey bar) & hyperoxia + KS (Hr 3, black bar).

Objectives: 1) To study conditions that delay (KMT) CNS-OT at the cellular & organismal levels to improve our understanding of how therapeutic ketosis delays onset of CNS-OT (M-1). 2) To quantify how we measure the latency to Sz for assessment of mitigation strategies in the rodent model (M-2). 3) To incorporate CO_2 retention into physiological studies of CNS-OT and other Navy relevant adverse environments; e.g., DISSUB (M-3).

Milestone Tracker



FY19 Accomplishments, Discoveries, & Inventions

- KMT inhibits ROS production in cSC cells of the brain stem;
- 1st Sz in unanesthetized rats are variable, often difficult to detect, and likely originate in subcortical nuclei.
- CO_2 rebreathing disrupts REM sleep & inhibits gastric motility (in addition to ↑RONS during hyperoxia)

FY20 Goals

- In a new project 1) identify sites of Sz genesis during HBO_2 ± CO_2 using deep electrode telemetry in animals treated ±KMT; and 2) study the electrophysiology of neurons in deep nuclei involved in Sz genesis during HBO_2 ±KMT.

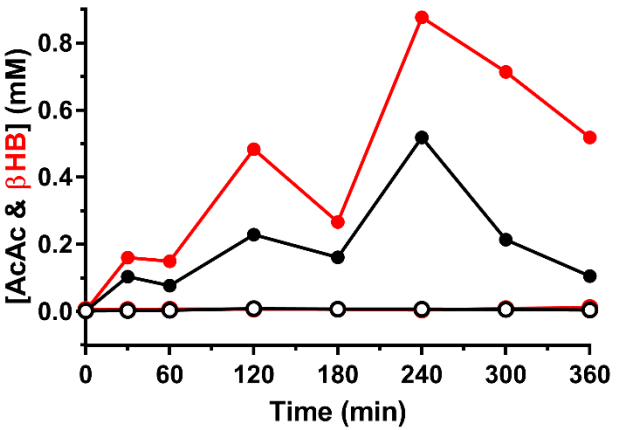
Principal Investigator Contact Email: jbdean813@gmail.com; jdean@health.usf.edu

An assessment of the ketone ester, R,S-1,3-butanediol acetoacetate diester [BD-$(AcAc)_2$], for the induction of ketosis and delay of CNS HBO_2 toxicity in swine

LT Geoffrey Ciarlone, PhD

Background: Clandestine U.S. Navy diving operations require the use of a closed-circuit rebreather utilizing pure O_2, which limits operational depth and time due to the toxic effects of O_2 on the central nervous system (i.e. seizures). The ketone ester BD-$(AcAc)_2$ has been shown to significantly delay these toxic endpoints in rodents, representing a promising mitigation strategy for a condition with limited treatment options.

Naval & Scientific Benefits: The acute use of BD-$(AcAc)_2$ for the delay of CNS HBO_2 toxicity will expand mission parameters and dive profiles for clandestine diving operations that would directly result in increased mission effectiveness, while maintaining or increasing diver safety, situational awareness, and comfort.



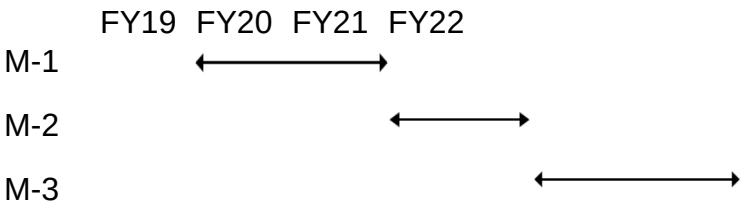
Mixed venous blood concentrations of the ketones acetoacetate (AcAc, black circles) and β-hydroxybutyrate (βHB, red circles) following oral administration of either water (open circles) or BD-$(AcAc)_2$ (1.25g/kg, closed circles) at t=0 min in 30kg swine (N=1/group). *Note negligible endogenous ketone production in control animals, as expected.

Objectives:

Aims 1 & 2: Determine the lowest effective dose (LED) of BD-$(AcAc)_2$ for induction of therapeutic levels of AcAc in blood and efficacy of LED for prolongation of seizure latency in 20kg swine

Aim 3: Assess the effects of BD-$(AcAc)_2$ on cardiorespiratory function

Milestone Tracker



FY19 Accomplishments, Discoveries, & Inventions

- Successful completion of pilot animals and GC/MS analysis to validate procedure and collection methods
- Executed LP-CRADA with Disruptive Enterprises, LLC for procurement of BD-$(AcAc)_2$

FY19-20 Goals

- Complete pilot studies and additional animals for Aim 1
- Use LED from Aim 1 to determine efficacy for prolongation of seizure latency at 5 ATA O_2 in Aim 2
- Begin determination of the effects of BD-$(AcAc)_2$ on cardiorespiratory function and exercise performance

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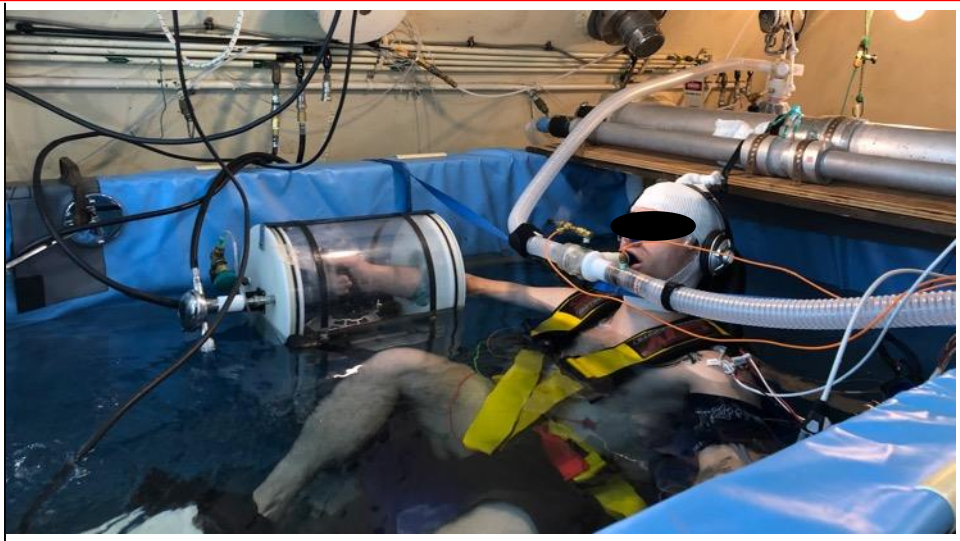
Ketogenic Diet for Reduction of CNS O_2 Toxicity in Working Divers

PI: Bruce J. Derrick, MD

Background: Central nervous system (CNS) oxygen toxicity remains a significant limitation to Navy 100% O_2 rebreather diving and O_2 decompression operations. The ketogenic diet (high fat, scarce carbohydrate, adequate protein) has been used to treat refractory epilepsy in children and some adults. Increased latency to O_2 toxicity seizure has been demonstrated in animals with elevated serum ketone levels. It is unknown if nutritional ketosis affects CNS O_2 toxicity in human divers.

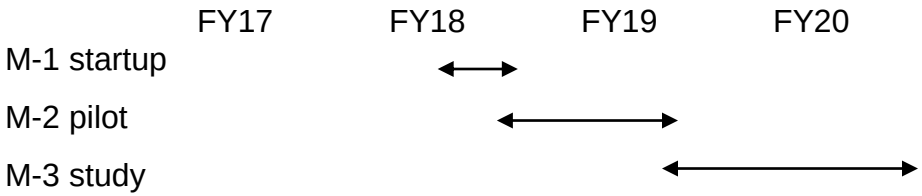
Naval & Scientific Benefits: This study could improve diver safety, lead to expanded operational limits for high PO_2 diving, add to our understanding of CNS O_2 toxicity physiology, and lead to advancements in decompression research.



Objectives:

- Determine if nutritional ketosis (NK) prevents or delays the onset of CNS O_2 toxicity in head-out working divers.
- Develop an effective protocol for inducing nutritional ketosis suitable for Navy divers.
- Evaluate the physiologic and cognitive effects of high PO_2

Milestone Tracker



FY18 Accomplishments, Discoveries, & Inventions

- Pilot study complete (first 10 subjects, 20 dives)

	CD (n=10)	KD (n=10)	P-Value
PX arrival BHB (mmol/L)	0.1 ± 0.1	0.8 ± 0.2	0.0002*
PX arrival - pre-dive BHB (mmol/L)	0.0 ± 0.1	0.6 ± 0.4	0.0012*
Lab BHB (mmol/l)	0.3 ± 0.2	1.7 ± 0.5	0.0126*
Dive Time Average (min)	47.2 ± 17.2	70.2 ± 28.3	0.0410*
Dive Time Median (min)	40.8	62.1	
Dive Time Range (min)	29.2 - 76.6	36.7 - 120	

FY19 Goals

- Addition of electrodermal activity (EDA) monitoring
- Begin study phase of 40 additional subjects (80 dives)

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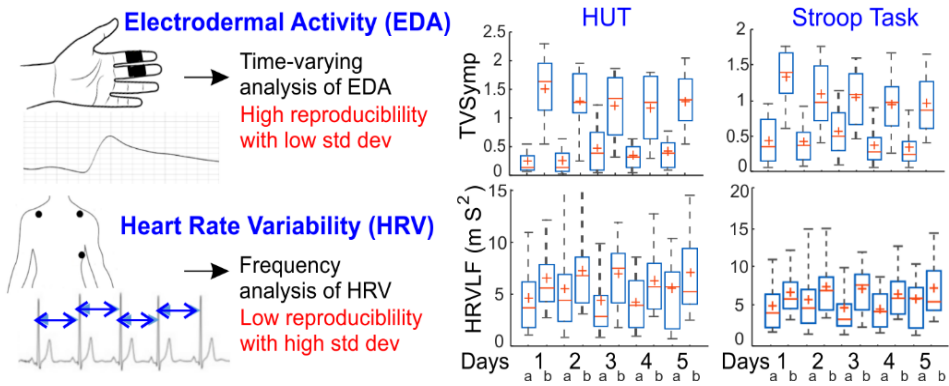
Feasibility of electrodermal activity for detecting seizures elicited by central nervous system oxygen toxicity under the water

Ki H. Chon

Background: The current work is to examine if electrodermal activity (EDA) can be used to detect and/or predict the onset of seizures caused by central nervous system oxygen toxicity in both dry and water immersion conditions. This study will provide methods for detection and/or prediction of seizures, the most adverse side effect that divers can get when pre-breathing oxygen to thwart decompression sickness.

Naval & Scientific Benefits: If EDA is sensitive to pre-seizure and seizure conditions with enough warning time to take action, the proposed approach has the potential to save divers' lives when the EDA sensor is used in conjunction with O2 prebreathing and ketogenic nutrition. EDA wearable systems for future deployment will be much practical than electroencephalographic sensors.



Reproducibility of frequency- and time-domain parameters of EDA to distinguish SNS activities from baseline. Left panels: Baseline and HUT measures. Right panels: Baseline and Stroop task measures of HRV and EDA for the five days. The letter "a" represents baseline measurements, and "b" represents test measurements. **HUT**: head-up tilt

Objectives: The first objective of the study is to determine the feasibility of EDA for detecting seizures using rats. The rats will allow us to explore HBO2 breathing at pressures higher than 3 Atmospheres Absolute, which causes a high seizure occurrence rate. The second objective is to evaluate the reliability of EDA in humans undergoing cognitive stress and mild CNS-OT. The protocol will elicit some CNS-OT manifestations, with either no or a low seizure occurrence rate.

Milestone Tracker

FY19 Accomplishments, Discoveries, & Inventions

- The work commenced in April 2019
- EDA showed to be sensitive to pain stimuli

FY19 Goals

- IRB approval for both animal and human studies
- Collect data for both animal and human studies
- Perform data analysis

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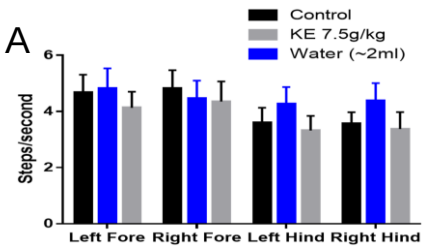
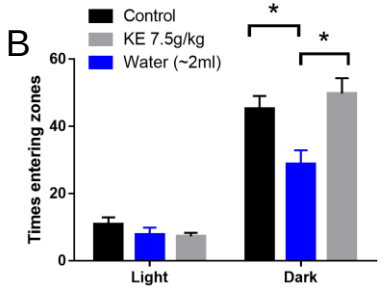
Optimizing Ketone Metabolic Therapy and Identifying Biomarkers for Mitigation and Prediction of CNS Oxygen Toxicity: Animal Studies

Dominic D'Agostino, PhD (PI)
Jay B. Dean (Co-I); Angela M. Poff (Co-I)

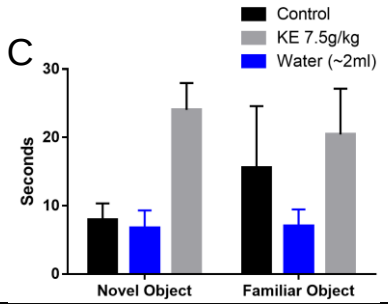
Background: Ketogenic metabolic therapy (KMT) is a novel potential mitigation strategy to delay Central Nervous System Oxygen Toxicity (CNS-OT) seizures in rats. However, the optimal ketogenic agent formulation, its effects on cognitive and motor performance, and its mechanisms of action remain largely unknown.

Naval & Scientific Benefits: Naval unique Special Warfare and Special Operations diving maneuvers and submarine operations are limited by the risk of developing CNS-OT. This is also a limitation for recreational divers & patients receiving hyperbaric oxygen therapy. This project seeks to evaluate the efficacy and mechanisms of KMT as a promising mitigation strategy for CNS-OT.



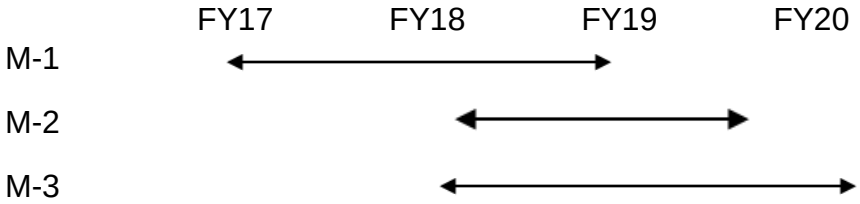


A) DigiGait, Steps Per Second – KE does not impair motor performance.
B) Light/Dark, Frequency Entering L/D Zones – KE is anxiolytic.
C) Novel Object Recognition, Latency to 1st Interaction –KE trend to improve learning & memory.



Objectives: 1) Optimize the formulation and dosage of ketogenic agent (KA) to delay CNS-OT that does not impair motor or cognitive performance. 2) Identify early physiological predictors of CNS-OT onset. 3) Study the mechanisms by which KMT delays CNS-OT onset.

Milestone Tracker



FY18 Accomplishments, Discoveries, & Inventions

- Behavioral analysis revealed that KE does not impair motor performance, exhibits anxiolytic effects and produces a trend towards improved learning & memory
- Ari et al., *Physiological Reports*, 2019 Jan;7(1):e13961.
- Ari et al., *BMC Anesthesiology;* 2018; 18:85
- Kovacs et al., *Front Behav Neurosci.* 2018, Feb 22;12:29.
- Ari et al., *JoVE*, 2019 Jan 7;(143).
- Established & optimized techniques required for Aim 3

FY19 Goals

- Publish KE effects on behavior + EEG monitored rats
- Complete Aim 2 KE dose optimization for CNS-OT
- Molecular mechanisms of KMT for CNS-OT

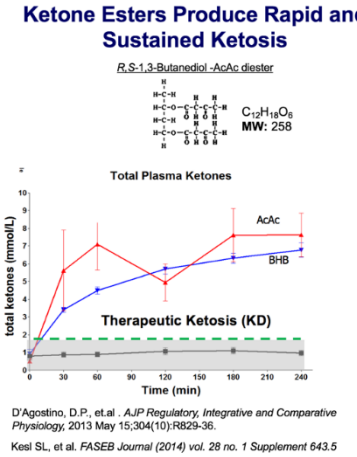
PI Contact Email: ddagosti@health.usf.edu

Human Fuel for Optimizing Cold Water Performance

Dr. Dawn Kernagis, Dr. Jeffrey Phillips, Dr. Peter Pirolli, Dr. Timothy Broderick

Background: Hypothermia adversely impacts undersea operator physical and cognitive performance. Given the high operational tempo and multilayered risks involved in cold water operations, maximized cognitive and physical performance is critical for operator safety and mission execution. A safe and tolerable approach to optimizing warfighter performance and resilience will be key for future Navy cold water operations.

Naval & Scientific Benefits: This project will evaluate the effect of ketone ester supplementation on a mission-relevant physical and cognitive task battery for undersea cold water operators



Objectives

M-1: Pharmacokinetic analysis of ketones with exercise

M-2: Develop and validate cold water task battery with WSRI

M-3: Assess the effect of ketone supplementation on mission-relevant physical and cognitive performance in cold water

M-4: Transition the performance task battery and KE supplementation to in-water testing

Milestone Tracker

	FY18	FY19	FY20
M-1	-------->		
M-2	---------->		
M-3		---------->	
M-4		----->	

FY18 Accomplishments, Discoveries, & Inventions

- Task development complete with WSRI
- IRB amendments complete for cold water task battery validation

FY19 Goals

- Complete cold water task battery validation (Complete)
- Complete ketone and cold water study (In Progress)
- Transition task battery to in-water testing

Principle Investigator: Dawn Kernagis, 850-202-4434, dkernagis@ihmc.us

Role of Oxygen Breathing on Carotid Body Sensitivity

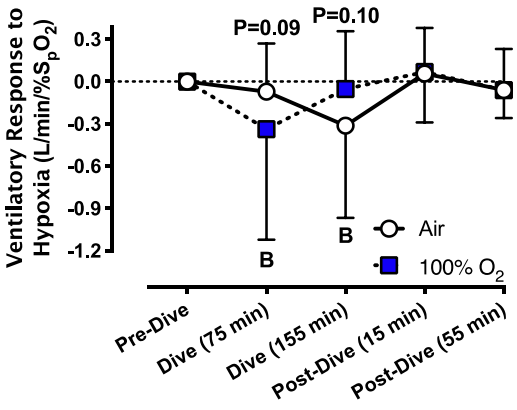
D Hostler, PhD and BD Johnson, PhD

Background: Many Navy divers have a reduced ventilatory response to hypercapnia, which leads to CO2 retention. The reduction in carotid body chemosensitivity might further exacerbate CO2 retention leading to both physiological and psychological symptoms. Additionally, CO2 retention increases the risk of decompression syndrome and oxygen toxicity. This may compromise diver health, performance, and increase the risk of diving accidents.

Naval & Scientific Benefits:

Our proposal will determine if carotid body chemosensitivity in humans is reduced following a dive. Ultimately, data from this study may provide insight into the mechanisms underlying oxygen toxicity in divers.

Specific Aim 1 Preliminary Results. Carotid body chemosensitivity to hypoxia data are presented (n=5).
B=different from Pre-Dive (P<0.05)
*=different from 100% O_2 dive (P<0.05)
Reported P values are between condition comparisons.

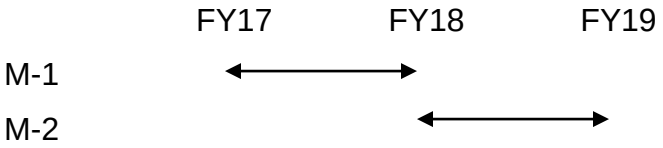


Objectives: We will address the following Specific Aims:

Specific Aim 1: Determine if carotid body chemosensitivity is altered during and following a simulated dive and determine if breathing 100% oxygen during a simulated dive alters carotid body chemosensitivity when compared to breathing 21% oxygen.

Specific Aim 2: Determine if cold-water immersion alters carotid body chemosensitivity.

Milestone Tracker



FY18 Accomplishments, Discoveries, & Inventions

- Presented interim results for Specific Aim 1
- Completed data collection for Specific Aim 1

FY19 Goals

- Submit manuscript for publication for Specific Aim 1 data
- Complete data collection for Specific Aim 2

Principle Investigators:

Dave Hostler, PhD, 716-829-6795, dhostler@buffalo.edu

Blair Johnson, PhD, 716-829-6789. blairjoh@buffalo.edu

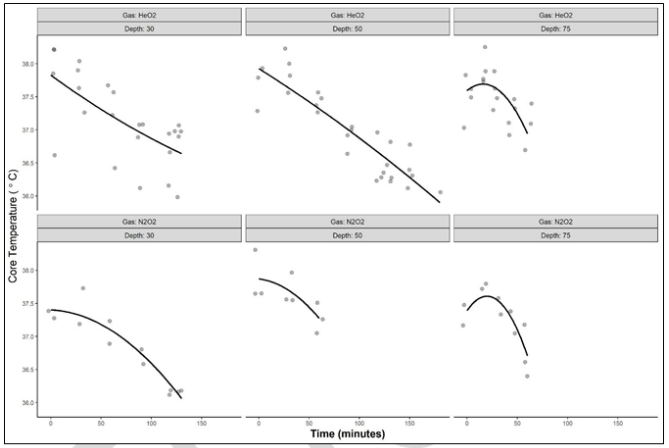
Evaluation of thermoregulatory differences in between insulative clothing options during cold water diving

Karen R. Kelly, PhD

Background: Military divers are exposed to the extreme environment of the open sea, including extreme pressure and temperature variability, all the while being charged with operational tasks. Perhaps the most pervasive environmental factor that affects military divers is cold exposure and puts not only the operator but the mission at risk.

Naval & Scientific Benefits: Data from this effort will provide unprecedented contemporary information on cold-water diving capabilities as a function of thermal protective clothing. This information can readily be disseminated across services and incorporated into the operational environment to enhance operational readiness and effectiveness in cold-water environments

RATE OF CORE TEMPERATURE CHANGE x GAS x DEPTH



Objectives:

1)To evaluate closed cell wetsuit for thermal protective capability during long duration cold-water exposure at various depths.

2)To measure changes in skin and core temperature, as well as, cognitive function during a mock arctic training scenario.

3) Develop reference table for thermal protection suit x dive duration x depth x water temp

4) Develop predictive equations for the determination of core, mean skin, hand/foot/finger and toe temperature changes based on dive depth and duration.

FY19 Goals:

- Expand on data set to develop requested reference table and predictive equation
- Secure additional funding to complete other requests from Group 3 that compliment this work and expand operational capabilities

Principal Investigator Contact Email:
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Measurement of Regional Heat Exchange Using Direct Regional Calorimetry in Resting Subjects Immersed in Cold Water

John Florian, PhD, James Campbell, PhD
Navy Experimental Diving Unit

NAVSEA
NAVAL SEA SYSTEMS COMMAND
Supervisor of Salvage & Diving

Background: Current thermal protection for Navy divers and Special Operations Forces (SOF) remains inadequate and is a limiting factor that adversely impacts diver safety and dictates mission capabilities. A gap exists in our understanding of the safest and most efficient means of applying heat to the diver, particularly when the power supply is limited.

Naval & Scientific Benefits: This work fills a clear void in our understanding of heat exchange in the underwater environment and is directly applicable to ongoing Navy thermal protection problems. The evidenced-based heating strategies (i.e., quantity and spatial distribution of heating) developed from this investigation can be incorporated into current and future thermal protection systems.

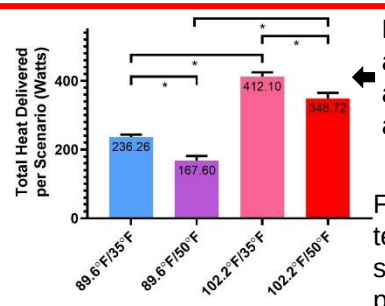

Fig. 1 - Heat energy delivered in all scenarios avoided termination criteria of hypothermia and avoided dangerously low skin temperatures associated with non-freezing cold injury.

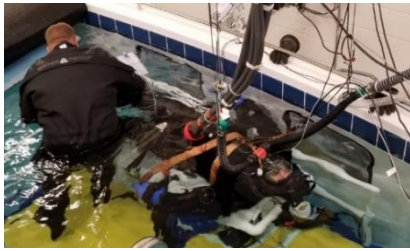

Fig. 2 – The tender and subject preparing for official immersion.

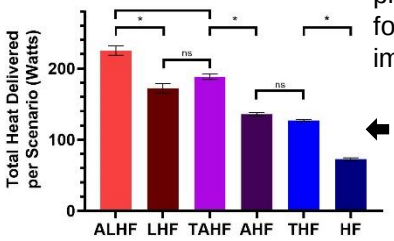

Fig. 3 - All scenarios of heat supply were safe and metabolic compensation occurred with lesser heat supplied. X-axis - A:arms, L: legs, T:torso, H:hands, F:feet supplied heat.

Objectives:

1. Measure regional heat loss through direct calorimetry and heat flux during cold water immersion.
2. Determine effective quantity and distribution of regional heating applied in a garment for maintenance of body heat content during a simulated cold water mission scenario.
3. Develop heat distribution guidance based on water temperature and basic garment ensemble, and determine power requirements for a mission with divers at rest.

FY18 Accomplishments, Discoveries, & Inventions to date

- Successful experimentation Aug/Sept 2018: completed human study using tubesuit perfusion temperature (100F) immersed in 35F water.
- Optimal distribution of heat per zonal application is Arms, Legs, Hands & Feet. Wattage required was 225. A second best option was Legs, Hands, Feet with a required 172 Watts of heat.
- Hands and Feet/Fingers and Toes lose and gain heat equally per tubesuit temperature supplied and immersion water temperature. Extremities are most vulnerable to cold injury. The balance of function and dexterity vs. thermal protection is critical.

FY19 Goals

- Stand up next phase of Calorimetry – Cal X (exercise)
- Describe heat loss as a result of convection in real world scenarios of active vs. passive transport while immersed in cold water

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AI: Dr. James Campbell, NEDU, James.E.Campbell3.ctr@navy.mil

EPIDEMIOLOGICAL ANALYSES OF U.S. NAVY DIVER SEPARATION HEALTH ASSESSMENTS

PI - CDR Doug McAdams, MD, UMO, USN;
AI - Brian J. Maguire, Dr.PH

NAVSEA
NAVAL SEA SYSTEMS COMMAND
Supervisor of Salvage & Diving

Background: Navy divers face unique occupational stressors and extreme physical demands. These stressors include exposure to: hydrostatic pressures, extreme temperatures, contaminated water, dangerous marine life, underwater blasts, and noise. Health hazards include decompression sickness, oxygen toxicity, hypoxia, hypercapnia, arterial gas embolism, pneumothorax, hypothermia, and musculoskeletal injury.

Naval & Scientific Benefits: Military diving requires a higher level of physical fitness than many other military occupations. Identifying common illnesses and injuries among divers can help shape mitigation strategies for these health issues, thereby helping to preserve end strength, and potentially reducing permanent disabilities and early separations.

Milestone/Quarter	1	2	3	4
Access Naval Safety Center's Dive/Jump Reporting System (DJRS) data, identify divers	■			
Request data from VA	■			
Link available data		■		
Test relational databases			■	
Create analytical data set, analyze data				■
Produce report				■

Objectives: 1) Describe the overall health status of Navy divers upon separation. Catalog illnesses and injuries by prevalence. Identify correlations and potential risk factors for common or severe conditions. 2) Contribute to the ongoing population-based health study of Navy divers. 3) Contribute to a Navy diver SQL server database currently in the early stages of development.

Methods: Available data sources will capture the health records of approximately 10,000 current and retired U.S. Navy divers. The Naval Safety Center's Dive/Jump Reporting System (DJRS) will be used to identify divers and link to BUMED records. These combined records will be analyzed to catalog and report the health conditions and related diving history prevalent among divers upon separation from the Navy.

FY18 Accomplishments, Discoveries, & Inventions

- Naval Safety Center (NSC) – NSMRL MOU submitted for access to the pertinent NSC data.
- Documentation submitted to BUMED for access to diver health records.

FY19 Goals

- Report the overall health status of Navy divers upon separation from the Navy.
- Obtain access to the DJRS and BUMED records.
- Contribute data to the Navy diver SQL server database currently being developed.

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Optimizing performance during topside operations and diving at altitude

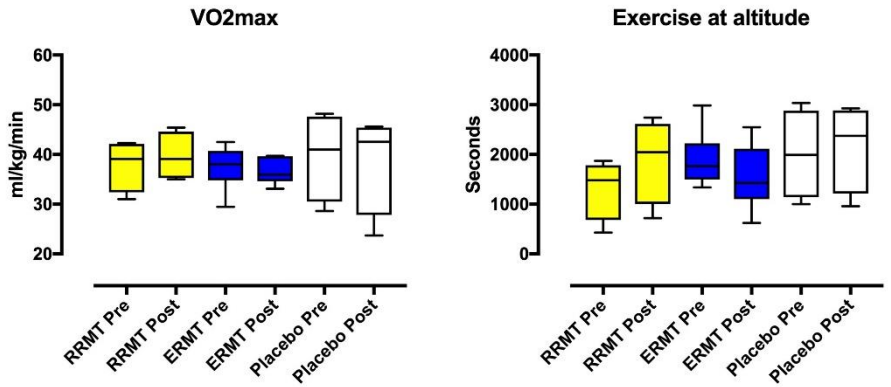
Dave Hostler, PhD

UNIVERSITY AT BUFFALO
CRESE
CENTER FOR RESEARCH & EDUCATION IN SPECIAL ENVIRONMENTS

NAVSEA
NAVAL SEA SYSTEMS COMMAND
Supervisor of Salvage & Diving

Background: US military ground operations can be conducted at medium and high altitude. Mission needs can require fighters to be flown immediately to altitude without time for adjustment or adaptation. One of the normal physiological compensations of altitude is hyperventilation. The increase in respiratory work provides some protection against altitude-related disease but can also impair performance due to respiratory muscle fatigue. Problems can quickly develop on land with exercise, but can also be seen underwater should diving activity be required.

Naval & Scientific Benefits: This project will investigate a simple field usable method for respiratory muscle training to enhance endurance during exertion at high altitude.



VO_{2max} at sea level and exercise time at 12,000' before and after RMT training. (RRMT = resistance RMT; ERMT = endurance RMT)

Objectives: This proposal will examine the effects of respiratory muscle training (RMT) on performance during topside operations at altitude and during diving at altitude. It will also explore the decompression strain that occurs after diving at altitude by assessing venous gas bubbling after diving at 3658 m (12,000 ft) of altitude..
The following aims will be addressed:
1) Determine if two forms of RMT improve exercise performance at a simulated altitude of 12,000 ft.
2) Determine the effects of pre-dive, altitude-induced physiological changes on diver performance at depth, and if this is modulated by RMT.
3) Explore the decompression stress associated with diving at altitude.

FY18 Accomplishments, Discoveries, & Inventions

- Technical issues with data collection at altitude solved
- Full cohort of Phase I subjects complete or on protocol
- Technicians trained on ultrasound procedures
- Phase II procedures being piloted

FY19 Goals

- Complete Phase I data collection
- Prepare Phase I manuscript
- Start and complete Phase II data collection
- Prepare Phase II manuscript
- Final report

Principal Investigator Contact Email: Dave Hostler, PhD, 716-829-6795, dhostler@buffalo.edu

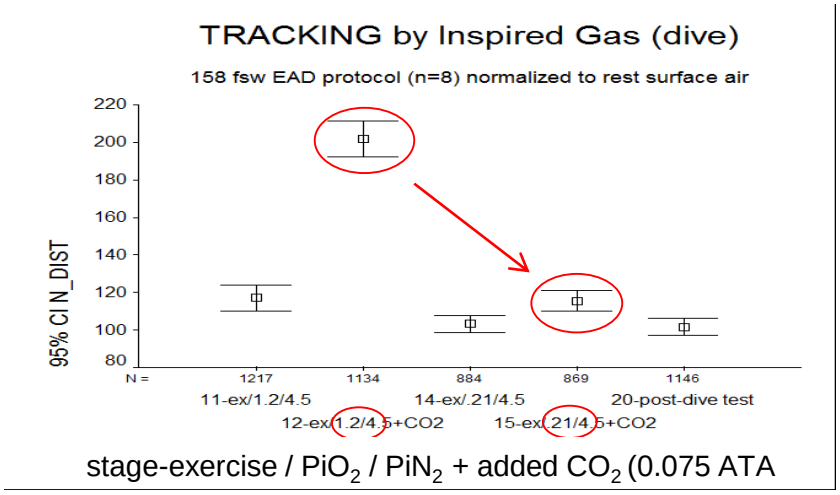
DOES HEART RATE VARIABILITY PREDICT IMPAIRMENT OF OPERATIONAL PERFORMANCE IN DIVERS?

JOHN J FREIBERGER, MD, MPH
Duke Center for Hyperbaric Medicine and Environmental Physiology
john.freiberger@duke.edu 919-684-6726

NAVSEA NAVAL SEA SYSTEMS COMMAND Supervisor of Salvage & Diving

Background: This application proposes to examine existing NAVSEA data from N0463A-12-C-001, “Hypercapnia: cognitive effects and monitoring”1 to validate or repudiate Heart Rate Variability (HRV) as an operational performance indicator and early warning sign for inert gas narcosis and oxygen toxicity. N0463A-12-C-001 is an ideal dataset to use to assess the utility of HRV because it was one of the largest and most detailed studies on diving narcosis to date. It contains extensive cognitive performance observations of extreme narcosis and possible oxygen toxicity.

Naval & Scientific Benefits: If HRV is shown to be a reliable operational performance predictor it could aid mission planning and reduce risk.



stage-exercise / PiO_2 / PiN_2 + added CO_2 (0.075 ATA

Objectives: The primary objective is to search for an HRV signal that reliably precedes severe narcosis and / or oxygen toxicity symptoms. We propose to compare HRV measures to the cognitive outcomes that were recorded under the 20 experimental conditions of N0463A-12-C-001

Milestone Tracker

	FY19	FY20
Prepare Data Sources for Analysis	⟷	
Assess the timing and association of HRV with Cognitive Testing Results	⟷	
Prepare Final Report	⟷	

FY19 Accomplishments, Discoveries, & Inventions

- collected and categorized outcome data (EKG, BP/HR, and cognitive testing) on the 42 subjects
- separated each subject's previous outcome data into bins corresponding to each of their their exposure stages (gases, depths added CO2, exercise).

FY20 Goals

- divide each 5 minute stage's outcome data into additional time segments corresponding to the first and last 2.5 minute segments (n=1144)
- manually complete the beat analyses and reviews of each EKG segment
- write and send the 1144 outcome and EKG files to Ki Chon, PhD for detailed HRV analysis
- write report

DATA SCIENCE-DRIVEN RESEARCH TO IMPROVE OPERATIONAL GUIDANCE AND HUMAN SAFETY FOR IMMERSION IN WARM WATER ENVIRONMENTS

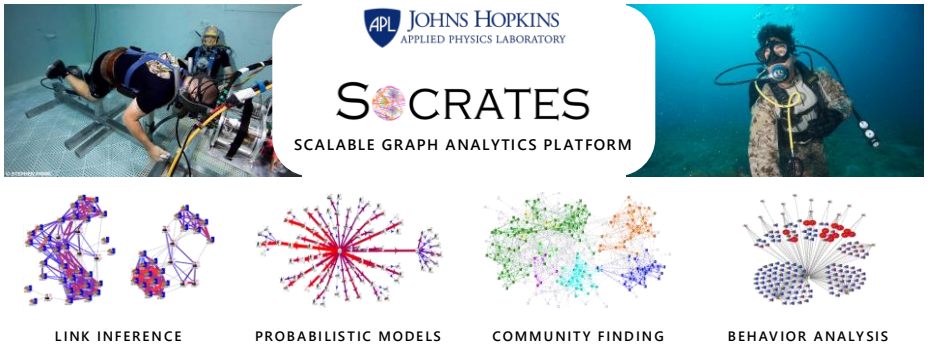
JOHNS HOPKINS APPLIED PHYSICS LABORATORY

Monique Beaudoin, PhD, Laura Cosentino,
Matthew Dinmore, PhD, Paul Nyquist, MD/MPH

NAVSEA NAVAL SEA SYSTEMS COMMAND
Supervisor of Salvage & Diving

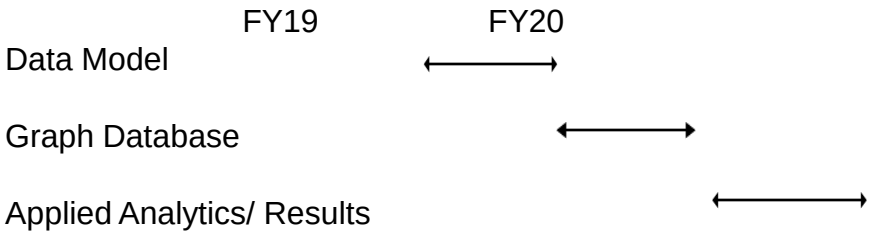
Background: Through Fleet operational requirements and research performed by Navy Dive biomedical institutions, the United States Navy established the need to improve the understanding, prediction, and mitigation of the physiological and cognitive effects of immersion. Over a period from 2001-2003, NEDU conducted extensive research to investigate effects and mitigation measures for human immersion in warm water environments.

Naval & Science Benefits: By improving the forecasting the effects of human immersion in warm water, the Navy may reduce risks and enable refinement of exposure guidance for diving.



Objectives: This study will apply advanced analytics technologies such as graph analytics and machine learning techniques to NEDU historical data to uncover new relationships between variables that may improve understanding of warm water immersion effects.

Milestone Tracker



FY19 Accomplishments, Discoveries, & Inventions

- Initiated data acquisition from NEDU Library Project in collaboration with NEDU Librarian and researchers
- Exploring other datasets
- Developing compendium of data and metadata attributes

FY19 Goals

- Dataset curation
- Data model development
- Graph database development

Principal Investigator Contact Email:
Monique.Beaudoin@JHUAPL.edu

DEVELOPMENT OF A PORTABLE DOUBLE-LOCK FLEXIBLE & COLLAPSIBLE RECOMPRESSION CHAMBER FOR CONDUCTING TREATMENT IN ACCORDANCE WITH NAVY TREATMENT TABLES TO 165 FSW

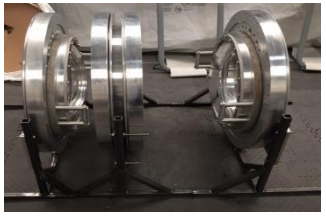
Principal Investigator: Stephen D. Reimers, PE

NAVSEA NAVAL SEA SYSTEMS COMMAND Supervisor of Salvage & Diving

Background:

A portable, collapsible, multi-occupant recompression chamber that meets Navy and PVHO requirements presently does not exist. This goal of this work is to develop a PVHO-compliant chamber that meets the needs of the Navy

Naval & Scientific Benefits: Provide greater safety in remote location diving operations by providing a lightweight, folding, multi-occupant, double-lock chamber system (3 persons with lock-in/lock-out capability) capable of supporting all standard Navy treatment tables that can be transported more easily than chambers built with existing technology.



Objectives:

- Develop an improved fabric clamp capable of reliably holding >5,500 lbs per lineal inch (384 psig burst pressure)
- Reduce weights to the extent possible with the goal of achieving a maximum single component shipping weight of 300 lbs, exclusive of packaging.
- Develop allowable damage criteria for the braid and bladder assemblies. Demonstrate non-catastrophic failure following penetration by two M16 rounds while fully pressurized. Develop a prototype field bladder patch kit.
- Achieve an 80 psig working pressure (MAWP) rating under the requirements of PVHO-1, Case 18.

FY19 Accomplishments, Discoveries, & Inventions

- Completion of all tests req'd for a PVHO-1 Case 18 MAWP rating of 75.1 psig (tests req'd to reach 80 psig pending)
- Clamp improved to consistently achieve non-slip performance at proof pressure of 360 psig.
- M16 test passed, patch kits demonstrated to work.
- Main Lock & Entry Lock weights, exclusive of packaging, reduced to 331 and 304 lbs respectively

FY20 Goals

- Development of controls, supporting systems & packaging
- Complete system factory testing
- Delivery of one complete pre-production system

Principle Investigator: Name, Phone #, Email

Stephen D. Reimers, MS, PE
703-229-1095, sreimers@pccii.com

Pulse Oximeter to Monitor Oxygen Levels in Rebreather Divers

Richard E. Moon / Rachel M. Lance

NAVSEA
NAVAL SEA SYSTEMS COMMAND
Supervisor of Salvage & Diving

Background: Rebreather diving has one of the highest fatality rates per man-hour of any activity in the world. The leading cause of death is hypoxia, typically from equipment or procedural failures. Hypoxia causes very few symptoms prior to causing loss of consciousness. A pulse oximeter is a device that uses light to measure the oxygen saturation level of the bloodstream.

Naval & Scientific Benefits: As of 2008, all Navy divers are trained on the UBA Mk 16 as part of dive training. However, these rebreathers also have multiple single-point failures that could lead to hypoxia. A pulse oximeter would provide an independent alarm system to detect low O_2 in the diver rather than in the rebreather.

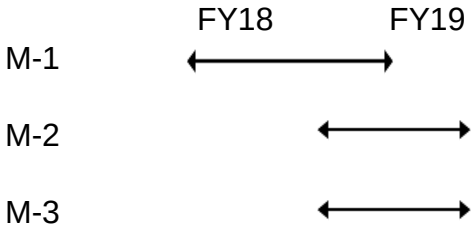
Objectives:

1) Develop COTS pulse oximeter for use underwater (NSWC PCD)

2) Characterize warning time provided to a diver (Duke)

3) Publish the scientific results (Duke) and enable transfer of technology (NSWC PCD)

Milestone Tracker



FY18 Accomplishments, Discoveries, & Inventions

- Made bracket to affix oximeter in full face mask (NSWC PCD)
- COTS oximeter into waterproof housing (NSWC PCD)
- Modification of full face mask and rebreather to allow procedures and measurements for the study (Duke)

FY19 Goals

- Screening of at least 30 test subjects
- Completion of 30 in-water studies of oximeter utility
- Processing and publication of data

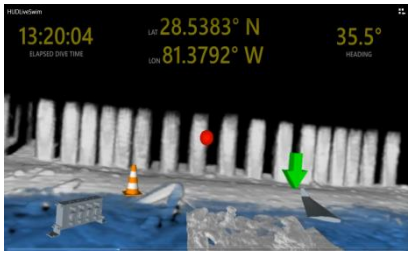
Principal Investigator Contact Email:
richard.moon@duke.edu

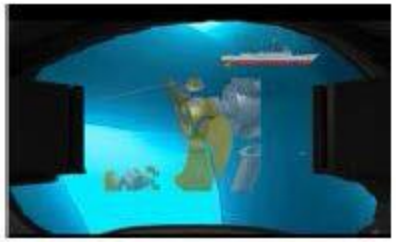
Divers Augmented Visual Device (DAVD)

P.I./Dennis Gallagher

Background: Military diving is regularly conducted in highly turbid and zero visibility environments in which standard visual displays and gauges are virtually useless. This has historically been a serious limitation to manned diving operations. See through head-up displays (HUDs) using emerging waveguide optical display technology is a potential solution to this limitation.

Naval & Scientific Benefits: If this technology can be effectively optimized and adapted for the military diving environment it will radically transform a dive mask/helmet into an immersive visual display interface capable of providing everything from life support data, to high resolution sonar imagery, to advanced underwater navigation displays, to 3D augmented reality displays.





MDSU-1 testing & evaluation

Objectives:

- Phase 1: Conduct RDTE on emerging waveguide optical display technology to develop see-through head-up display capability for the US Navy MK 20 FFM and KM-37 dive helmet
- Phase 2: Design a portable, prototype system that controls and sends data, video, sonar, and augmented reality from a topside system to the diver's HUD. Conduct in-water evaluations by military divers conducting design reference mission exercises.
- Phase 3: Rapidly transition the DAVD system to a Gen 1.0 production status via a Cooperative Research And Development Agreement (CRADA) with a diving equipment manufacturer.

FY18 Accomplishments, Discoveries, & Inventions

- ✓ Phase 2 prototype in-water evaluations conducted at NDSTC & MDSU-1.
- ✓ CRADA signed with Coda Octopus Group, Inc. and began joint development of Gen 1.0 production system.
- ✓ DAVD presented at Sea-Air-Space Expo 2018 & Undersea Defence Technology International Conference 2018.

FY19 Goals

- Complete development/manufacture of Gen 1.0 production systems.
- Conduct in-water evaluations by Navy divers at MDSU-2, First Responder Divers at Florida State University-Panama City, and NASA divers at Aquarius Habitat (NEEMO-23 Mission),.
- Complete technology transition.

Principle Investigator: Dennis Gallagher, 850/235-5417, dennis.g.gallagher@navy.mil

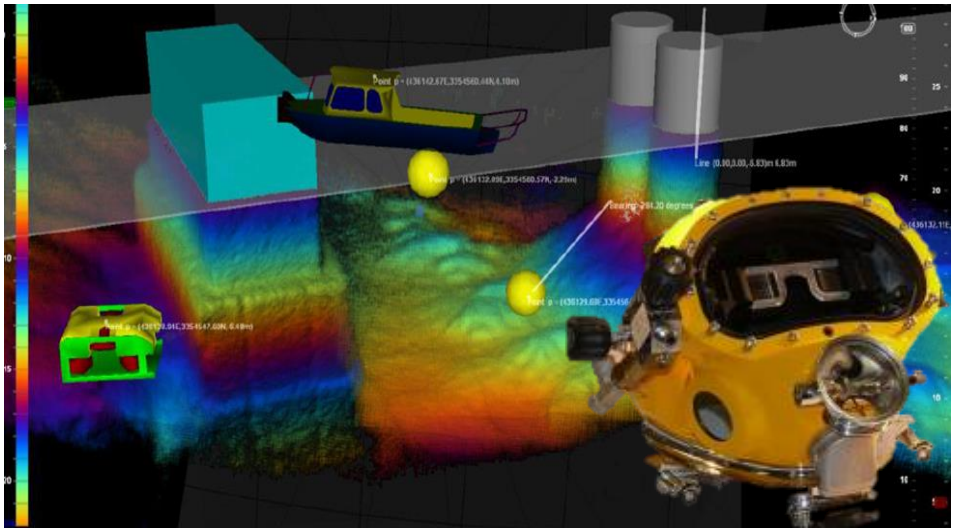
Diver Augmented Vision Device (DAVD)

NCRADA – NSWC PCD – 18-002

Blair Cunningham, President of Technology

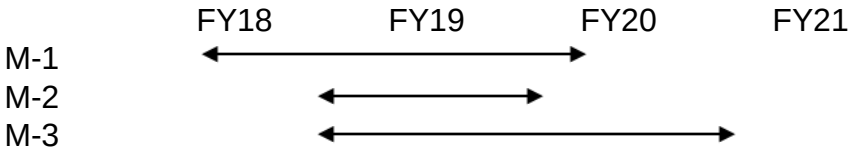
Background: Military and Navy diving operations are often conducted in near to zero visibility and hostile and challenging underwater environments. Spatial awareness and access to critical technical data and process for complex tasks are greatly diminished in these environments.

Naval & Scientific Benefits: Providing a vision platform for real-time 3D information underwater will enable safe spatial awareness for diving operations. Diver and Dive Master both see the live environment ensuring task and safety communication is specific and functional. This vision technology, coupled with high-resolution sensors and adaptive communication will help maximize safety, efficiency and accuracy of complex critical tasks.



Objectives: The key objective is to provide an easy to interpret mixed reality visual environment for all divers, controllers and observers on Navy dive missions. Utilizing latest 3D real-time sonar imagery – real-time situational awareness is provided to plan tasks, define routes, hazards and milestone objective pre-dive and quickly deploy dive assets in a safe, controlled and continuously observed environment.

Milestone Tracker



FY18 Accomplishments, Discoveries, & Inventions

- Prototype DAVD System Design Verification
- 3D Real-Time 1st and 3rd Person Imagery in DAVD with controlled environment,
- Redesign and verification of processor technology for “low” latency video imagery over 600ft subsea tether.

FY19 Goals

- Prototype “Production Ready” Gen.1 DAVD system
- 3D Head Tracker & Positioning (INS and Echoscope Acoustic Image Tracking) system
- 3rd Person Perspective Real-Time 3D Imagery

Principal Investigator Contact Email:
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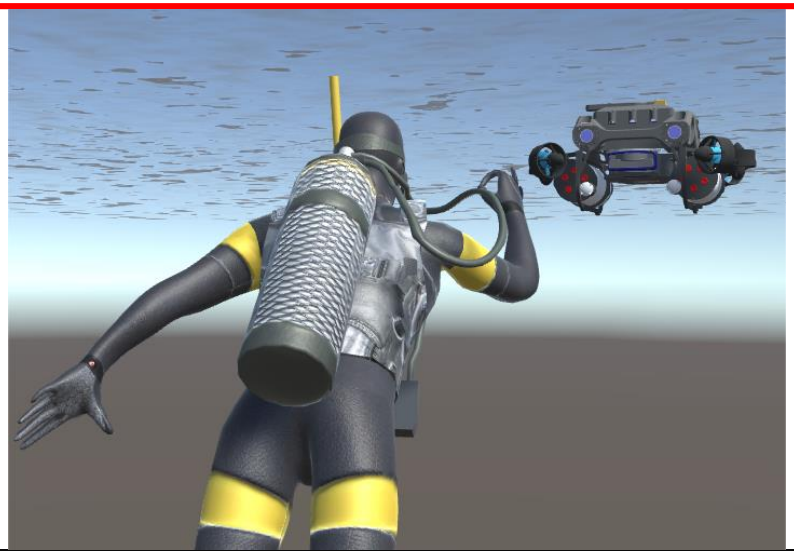
Advancing Diver-Robot Interaction Capabilities

prof. Nikola Mišković, Igor Kvasić

Background: The diver's dependency on technical life support equipment, limited navigation and communication capabilities makes the underwater a hazardous environment for humans. This project proposes and evaluates the feasibility of several human-robot interaction solutions which can facilitate diving operations and increase safety.

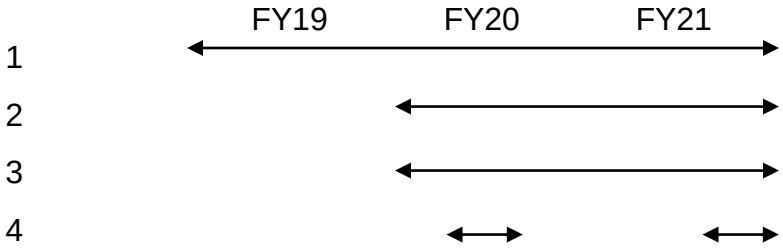
Naval & Scientific Benefits: The Adriatic project integrates high-level cognitive methods aimed at enhancing decision making speed and quality and detection of potentially hazardous situations. The robot platform design introduces game-changing diver-robot interfaces allowing divers to perform advanced and robust environmental sensing.



Objectives:

1. Diver-robot collaborative motion strategies
2. Posture and physiological parameter monitoring
3. Novel diver-robot communication methods
4. Diver-robot interaction feasibility evaluation.

Milestone Tracker



FY19 Accomplishments, Discoveries, & Inventions

- Diver-robot simulator
- Glove prototype for gesture recognition developed

FY19 Goals

- Autonomous underwater vehicle design and assembly
- Diver detection in sonar image
- Acoustic nano-modem prototype
- Hardware in the loop testing

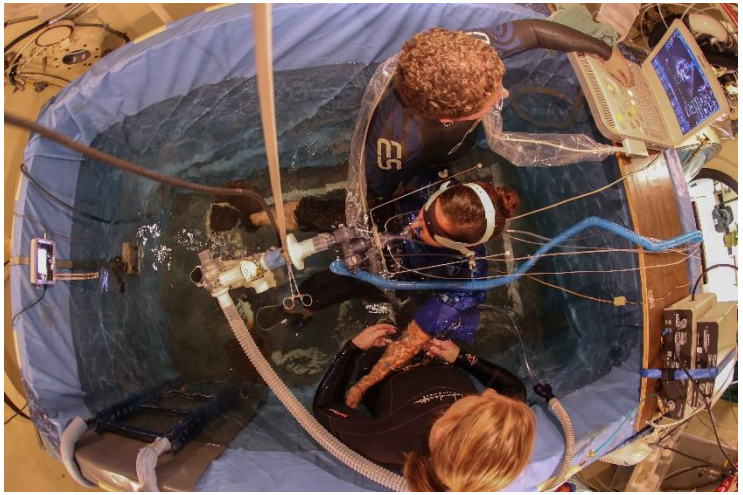
Principal Investigator Contact Email:
nikola.miskovic@fer.hr

Sildenafil for Prevention of Immersion Pulmonary Edema (SIPE)

P.I. Richard E. Moon

Background: At BUD/S approximately 40 cases per year (around 3%) have been reported, more commonly during winter, when it is observed in up to 5% of BUD/S trainees. Return to duty time can be up to 7 days. SIPE also affects other groups of highly fit individuals such as triathletes. In susceptible individuals it tends to recur, thus a preventive medicine would be useful for both Navy SEALs and civilians.

Naval & Scientific Benefits: Many BUD/S candidates who experience SIPE become SEALs, thus there are many SIPE-susceptible operational Special Warfare personnel, who might be called upon to perform a mission-critical task. A prophylactic medication with few side effects and no adverse exercise performance effects would be useful.



Objectives:

- Complete a randomized placebo-controlled study of 20 SIPE-susceptible volunteers to test the effectiveness of a standard dose of sildenafil for prevention of SIPE in susceptible individuals.

Milestone Tracker

	FY18	FY19	FY20
IRB approval	→		
Test 10 subjects		→	
Test remaining 10 subjects			→

FY18 Accomplishments, Discoveries, & Inventions

- IRB approval obtained.

FY19 Goals

- Complete studies of 10 SIPE-susceptible volunteers.

Principal Investigator:
Richard Moon, MD
Tel: 919-684-8762
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STEM Outreach: Design of a Passive Water Sampler

Richard E. Moon / Rachel M. Lance

Background: Little guidance exists to tell working divers if a site is contaminated. Traditional water samplers take one sample at one location in the water column and require expertise to avoid contaminating that sample. A simple, low-cost sampler would allow collection and preservation of water throughout the water column for analysis without expertise.

Naval & Scientific Benefits: This sampler will collect water samples and assess the pathogens to which divers have been or will be exposed. Current methods allow for later analysis of the sample to inform medical diagnosis and treatment, and future projects would allow on-site assessment of contamination. The project will also introduce motivated young students to scientific research opportunities with the DoD.

Current chemical sampler
Expensive
Requires multiple days

Current biological sampler
Cheap…
But requires expertise

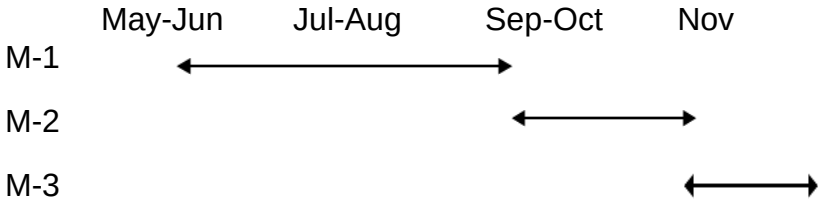
Objectives:

M-1: Students design and manufacture prototypes

M-2: High school outreach program to use samplers in local body of water

M-3: Report and publish

Milestone Tracker (FY19)



FY19 Goals

- Hire three engineering undergraduate students
- Students design samplers and build working prototypes
- Manufacture enough samplers to use for high school STEM outreach field trip

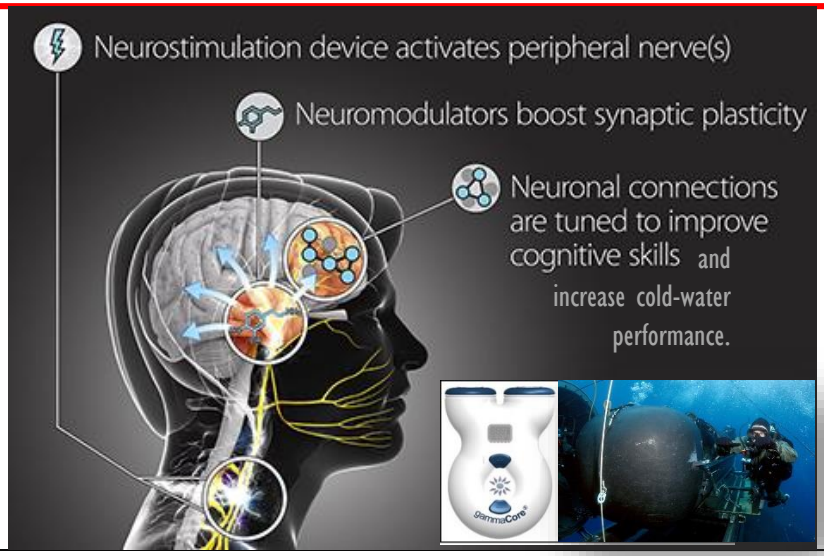
Principal Investigator Contact Email:
richard.moon@duke.edu

Biotechnology to Improve Cold Water Operator Performance

Dr. Jake Howard / Dr. Timothy Broderick

Background: Hypothermia is one of the top risks for undersea special operations. Hypothermia adversely impacts undersea operator physical and cognitive performance. The response to cold-water stress includes thermogenic, autonomic, and cardiovascular components. Transcutaneous vagal nerve stimulation (tVNS) could reduce the physical and cognitive impacts associated with prolonged cold-water operations.

Naval & Scientific Benefits: This project will evaluate biotechnologies that could improve undersea operator cold water performance, and quantify the performance benefits of using a technology such as tVNS.



Objectives

M-1:Conduct undersea operator task analysis and develop a pool-based task battery to evaluate cold water technology ✔☐

M-2: Validate cold water task battery ✔☐

M-3: Identify transcriptional signatures of hypothermia and response to biotechnology countermeasures

M-4: Evaluate tVNS in performance of operationally relevant tasks in cold water pool-based experiments

Milestone Tracker

	FY18	FY19	FY20
M-1	---------->		
M-2		---------->	
M-3		--------->	
M-4		---------->	

FY18 Accomplishments, Discoveries, & Inventions

- Mission-relevant cold water task battery developed

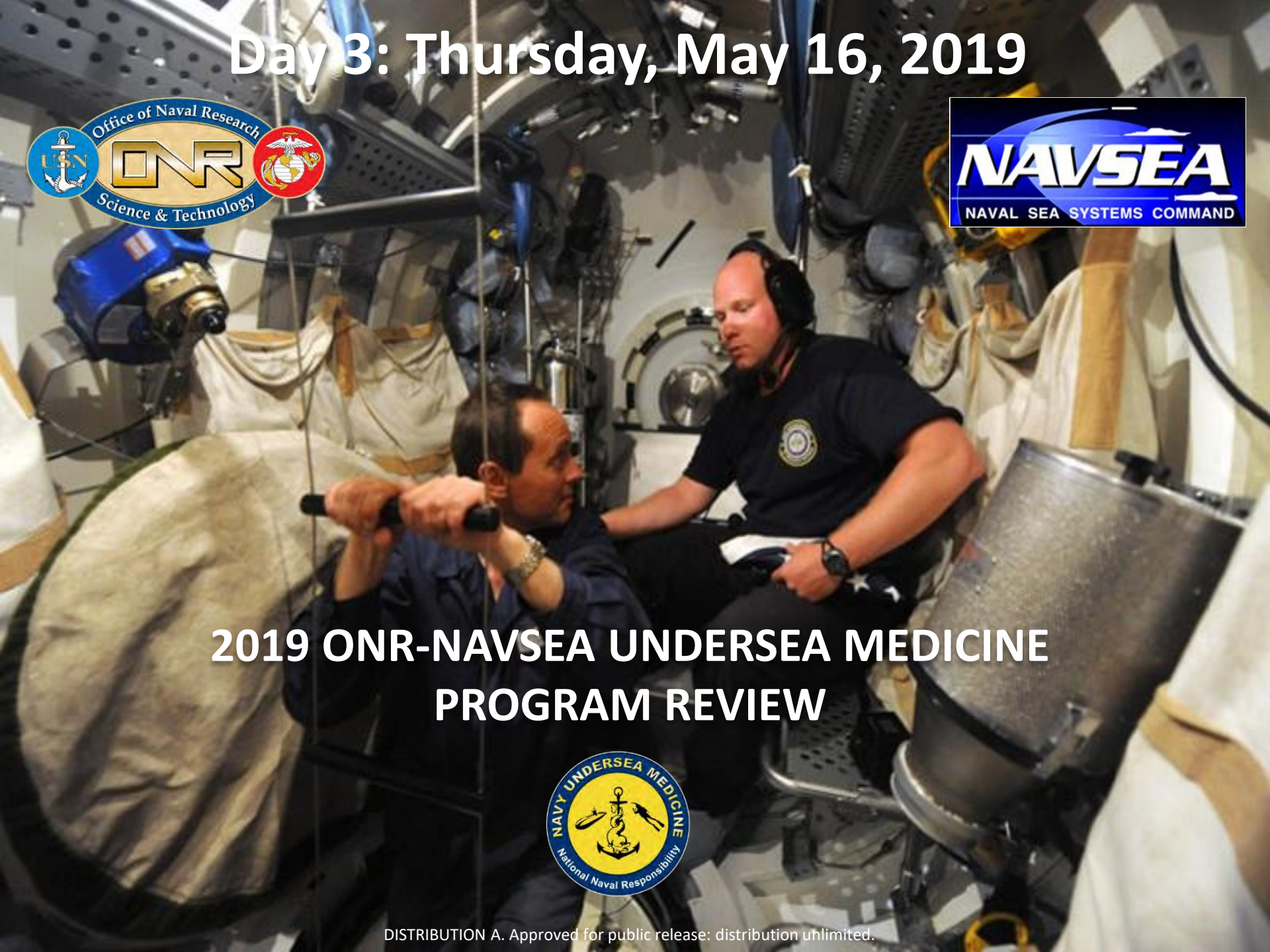
FY19 Goals

- Cold water task battery validation (Completed)
- Collect blood samples and define transcriptional response to cold water and ketone ester supplementation (In Progress)
- Transition DARPA tVNS success to ONR cold water studies using our validated cold water task battery (07/19)
- Classified biotechnology assessment by Dr. Howard (07/19)

Project WSU PI: Dr. Jake Howard, jake.howard@wright.edu

Project IHMC Lead: Timothy Broderick, tbroderick@ihmc.us

Day 3: Thursday, May 16, 2019



2019 ONR-NAVSEA UNDERSEA MEDICINE PROGRAM REVIEW

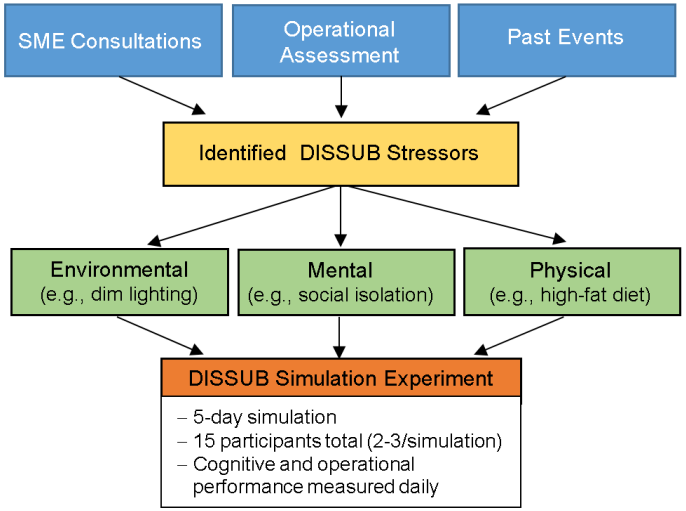
Effects of Disabled Submarine Stressors on Submariner Cognition

Paul Reinhart, Ph.D.; Sarah Chabal, Ph.D.;
Alexia Bohnenkamper, B.S.; Emily Moslener, B.S.

NAVSEA
NAVAL SEA SYSTEMS COMMAND
Supervisor of Salvage & Diving

Background: In a disabled submarine (DISSUB) scenario submariners must make life-or-death survival decisions including how to minimize casualties and when to await rescue versus attempt escape. Past research has worked to improve survival outcomes by minimizing the physiological effects of a DISSUB environment, but attention has not been paid to submariners' cognitive performance under these conditions.

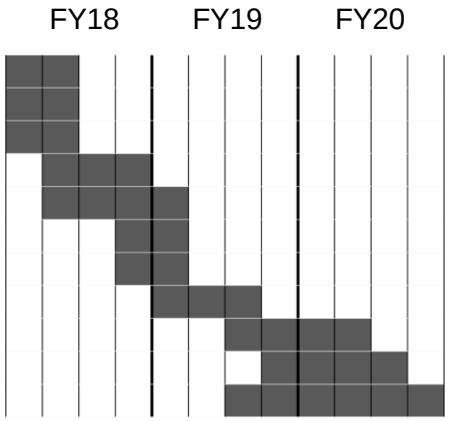
Naval & Scientific Benefits: This work explores how DISSUB stressors affect submariners' cognition and their ability to successfully operate in a DISSUB scenario. The knowledge gained will serve as a foundation with which future work will be able to target specific areas of need for the development and validation of countermeasures.



Year 2 Objective: Conduct empirical research to evaluate submariners' cognitive performance under the stressors present in a DISSUB scenario.

Milestone Tracker

A.1 Knowledge elicitation
A.2 Survivor training
A.3 Review of incident reports
B.1 Literature search
B.2 Report writing
C.1 Knowledge gap selection
C.2 Study design
C.3 Scientific review/IRB
C.4 Data collection
C.5 Data analysis
C.6 Writing of reports



FY19 Accomplishments, Discoveries, & Inventions

- Two technical reports identifying potential stressors present in a DISSUB scenario and reviewing their potential cognitive effects are currently undergoing review or in final preparation.
  - We discovered that little is known about how DISSUB-like stressor exposure (i.e., constant exposure for up to 7 days) will affect cognition.
- Human-subjects research protocol has been developed to explore the cognitive effects of a DISSUB simulation, and all data collection will be concluded by the end of FY19.

FY20 Goals

- Analysis of final data set and generation of reports

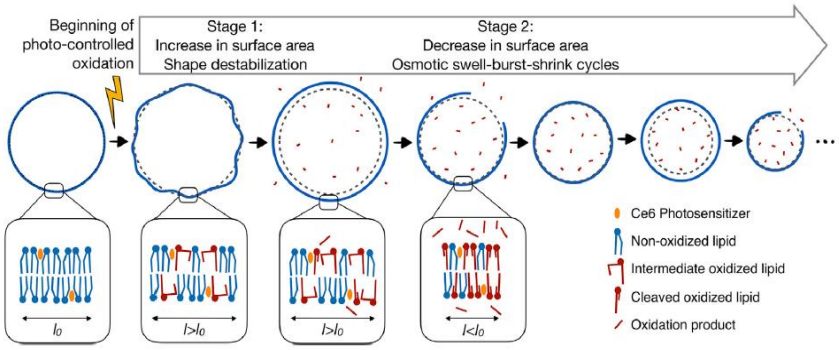
Principal Investigator: Sarah Chabal, Ph.D., sarah.a.chabal.civ@mail.mil
Project Lead: Paul Reinhart, Ph.D., paul.n.reinhart.ctr@mail.mil

Non-equilibrium thermodynamics of biological membranes

Padmini Rangamani

Background: This proposal seeks to answer a fundamental question in biomembranes research – how do lipid bilayers form and repair pores? Understanding the behavior of biologically derived materials under different conditions of repair and growth is critical for our ability to understand the response of cells to osmotic stresses.

Naval & Scientific Benefits: One of the constant stressors in undersea environments is high pressure -- using our models, we will be able to predict how membranes and cells respond to different pressure environments. The work proposed here is also of interest to the Applied and Computational Analysis Program at the Office of Naval Research, and the Center for Biomolecular Science and Engineering at NRL.



Schematic of the proposed mechanism of the effect of lipid unsaturation on membrane permeability (Bour et al, Biophys J

Objectives: The project has three main goals, all centered around understanding how membranes respond to osmotic stress.

Aim 1: Identify the dynamics of swelling and pore formation in single component artificial giant unilamellar vesicles (GUVs) under osmotic differentials.

Aim 2: Identify the dynamics of swelling and pore formation in multicomponent artificial GUVs under osmotic differentials.

Aim 3: Assess vesicle growth by lipid incorporation in membrane hydrophobic interfaces.

FY18 Accomplishments, Discoveries, & Inventions

- Publication on surfactant effects on lipid membrane dynamics
- Follow up study on lipid membrane permeability and oxidation.

FY19 Goals

- Work on Aim 3, to study membrane repair
- Mitochondrial membrane dynamics
- Develop the framework for mitochondrial fission

Principal Investigator Contact Email:
prangamani@ucsd.edu

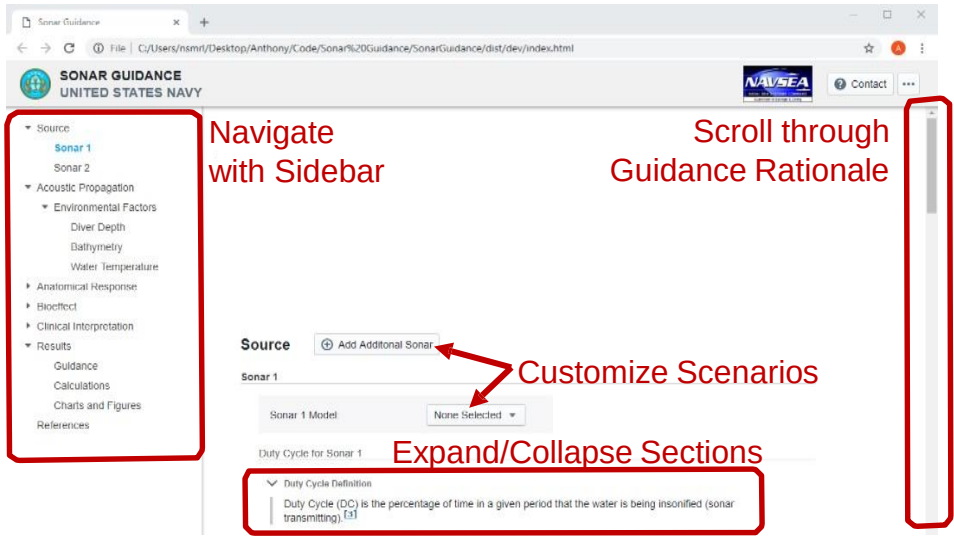
DEVELOPMENT OF AN INTERACTIVE SOFTWARE APPLICATION TO PROVIDE RECOMMENDATIONS FOR HUMAN EXPOSURE TO UNDERWATER NOISE

Brandon M. Casper, Ph.D., Matthew A. Babina

NAVSEA NAVAL SEA SYSTEMS COMMAND
Supervisor of Salvage & Diving

Background: The Navy's expanding use of UUVs is increasing the likelihood of diver exposure to active acoustic technologies. The standard operating procedures for determining safe exposures to active underwater acoustic sources are to: (1) refer to Appendix 1A of the US Navy Diving Manual, or (2) contact NAVSEA 00C for situations not specifically described in the manual. An automated software application could streamline generating guidance.

Naval & Scientific Benefits: Use of our proposed application will allow NAVSEA 00C to independently implement NSMRL's approach to generate standoff recommendations, hastening guidance to the fleet.



Objectives: The objective of this project is to streamline the guidance process and, thus, improve the mission-tailored support that Navy diving operations receives from NAVSEA 00C and NSMRL. To accomplish this objective, we will develop an interactive software application (App) that will provide recommendations for human exposure to underwater noise. The App will function by analyzing user input (e.g. frequency, sound level, environment) and output a standoff range that is scalable based on mission parameters and level of acceptable risk.

FY19 Accomplishments, Discoveries, & Inventions

- Investigation of existing acoustic guidance literature
- Update database of existing NSMRL underwater acoustic bioeffects experimental data
- Completion of a deployable software App to provide standoff guidance for known sonars.
- Begun development of sonar standoff recommendation App.

FY19 Goals

- Complete software prototype of standoff recommendation App

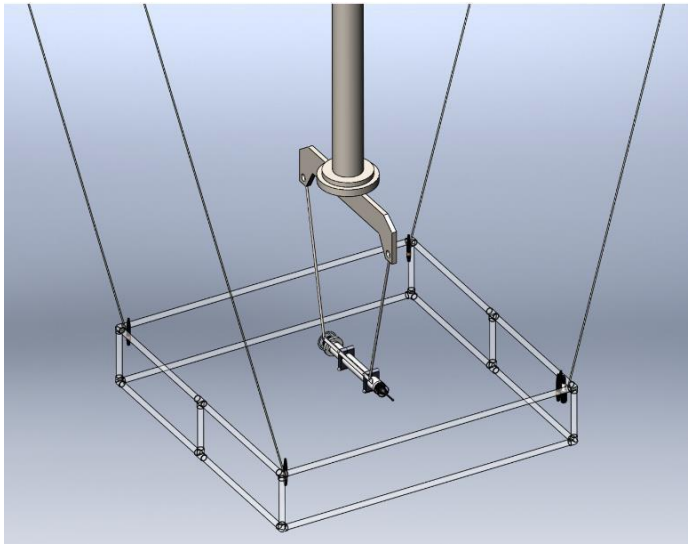
Principal Investigator: Brandon M. Casper, 860-694-3391, Brandon.m.casper4.civ@mail.mil

DEVELOPMENT OF A METHODOLOGY FOR CHARACTERIZATION OF ACOUSTIC TECHNOLOGIES OF NAVAL UUV EXISTING AND FUTURE ASSETS

Brandon M. Casper, Ph.D., Matthew A. Babina

Background: Ongoing development of underwater acoustic communications and scanning sonar systems and increasing deployment of UUV technologies have resulted in NAVSEA 00C to provide mission-tailored acoustic guidance more frequently. Such acoustic technologies may operate at frequencies and levels that have physiological/psychological effects on nearby divers. A consistent challenge in generating safe underwater sound exposure recommendations is a lack of standard acoustic data collection methods employed by vendors.

Naval & Scientific Benefits: The creation of a standard vendor-implemented acoustic testing methodology would greatly simplify the generation of safe acoustic exposure recommendations.



Objectives: The objective of this project is to establish a standard data collection methodology that UUV and active acoustic technologies vendors can utilize to collect the acoustic data necessary for the determination of diver safety. The data will facilitate characterizing the acoustic properties of their sonar and/or acoustic data modems. The purpose of this effort is to standardize the necessary data needed to provide informed guidance to the fleet when divers/swimmers are interacting with these technologies.

The approach includes (1) development of an acoustic testing setup that will allow vendors to collect their own data, (2) obtaining representative active acoustic equipment to test, and (3) documentation of the data collection procedures.

FY18/19 Accomplishments, Discoveries, & Inventions

- Characterizing the acoustics of the sonar technologies
- Begun writing the documentation for collecting information on active acoustic technologies
- Identified and procuring acoustic modem technologies

FY19 Goals

- Characterize acoustics of commercial acoustic modem systems
- Develop documentation of methodology for vendors

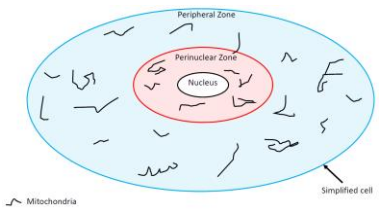
Principal Investigator: Brandon M. Casper, 860-694-3391, Brandon.m.casper4.civ@mail.mil

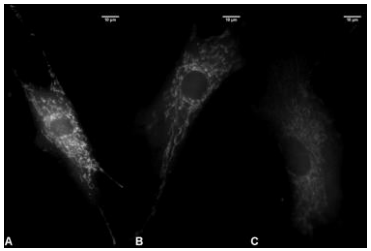
Mitochondrial Stress and Cellular Protection in Undersea Medicine

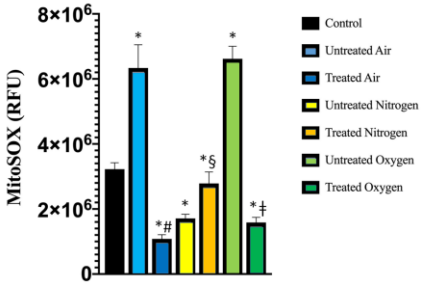
David M. Eckmann, PhD, MD

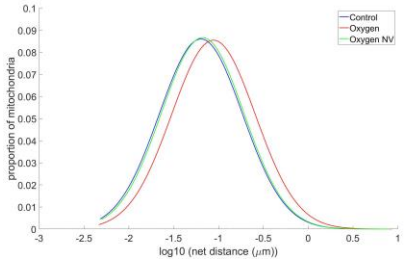
•**Background:** Degradation of normal mitochondrial function including aberations of mitochondrial bioenergetic capacity and mitochondrial dynamics (e.g., motility, fusion, fission) can occur with hyperoxic exposure or decompression from hyperbaric conditions. Altered mitochondrial function can lead to cellular bioenergetic failure, which can integrate into organ dysfunction or death. This may be amenable to mitochondrial-directed therapy provided to at-risk or exposed individuals.

•**Naval & Scientific Benefits:** Understanding mitochondrial dysfunction in decompression or hyperoxic exposure and potential molecular therapies or prophylaxis including breathing gas admixture is critical to developing new countermeasures for operational stress exposures.









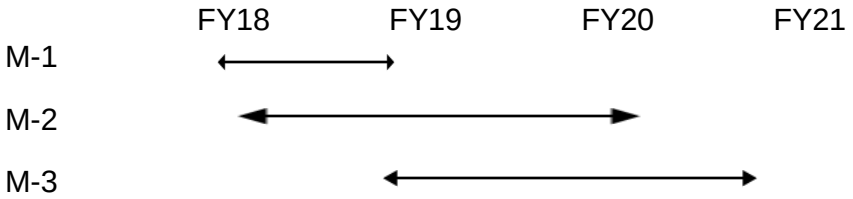
Objectives:

•M1: Develop methods to assess regional intracellular bioenergetics.

•M2: Quantify effects of hyperoxia/decompression exposures on mitochondrial bioenergetics and dynamics.

•M3 Quantify effects of mitochondrial-directed therapy on cellular bioenergetics following hyperoxia/ decompression.

Milestone Tracker



FY18 Accomplishments, Discoveries, & Inventions

- Study of intracellular compartmentalization of bioenergetics completed, accepted for publication
- Study with vascular smooth muscle cells and exogenous mitochondrial directed therapy completed
- Additional studies with mitochondrial molecular therapy published and submitted for publication.

FY19 Goals

- Complete experiments with neurons
- Initiate experiments with another cell line and additional mitochondrial molecular therapy
- Publish results

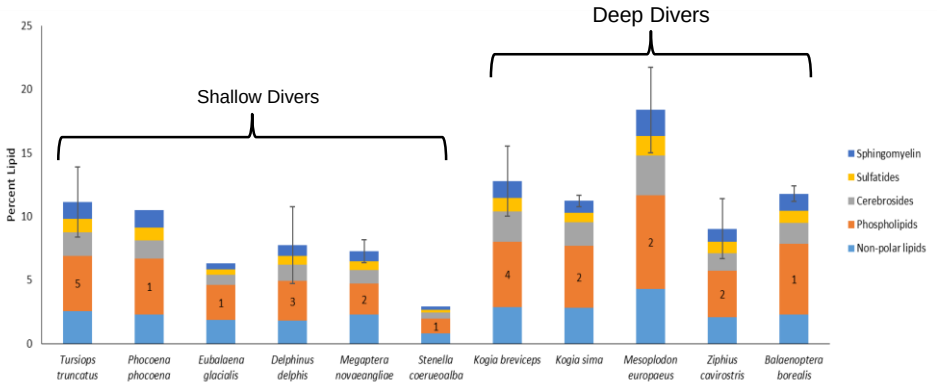
Principle Investigator: Dr. David M. Eckmann, 215-746-1482
eckmanndm@uphs.upenn.edu

Lipid composition and nitrogen solubility of the spinal cord and brain: comparisons between diving and terrestrial mammals to provide insight into Type II DCS.

Heather N. Koopman (PI), Hillary L. Glandon (presenter)

•**Background:** Marine mammals are adapted for diving but may nonetheless succumb to an imbalance in N_2 gas dynamics when their normal diving regime is interrupted. Despite having high lipid content, there are little data on variation in spinal cord lipid composition between diving and terrestrial mammals, nor how the various components might interact with N_2 gas. The substantial amount of vascular surrounding the spinal cord of marine mammals, compared to non-diving groups, may mean additional potential for interaction with N_2 gas given the proximity and extent of blood flow.

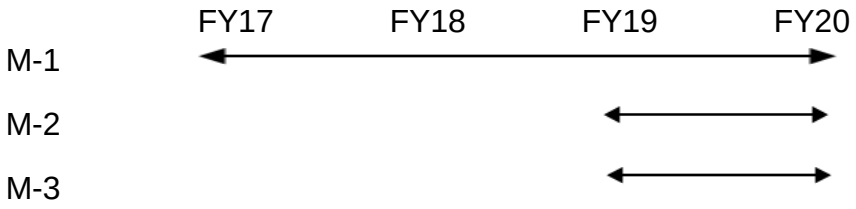
•**Naval & Scientific Benefits:** This study will provide insight into the mechanisms behind spinal cord injuries, possible methods of protection in diving scenarios, and risks of altered dive behavior.



Percent lipid of cervical spinal cord samples from 11 species of marine mammals. The height of the bars represents average percent lipid by species, error bars are standard deviation, and numbers are sample size. The colors are the percent of each lipid class. Cervical spinal cord tissue of shallow divers contained significantly less lipid than the cervical spinal cord of deep divers (P=0.0008), but no significant differences in lipid class composition were observed.

Objectives: This project will (M-1) determine the lipid content and lipid class composition of the spinal cord, spinal nerves and brain of diving mammals for comparison with data from the domestic pig and (M-2) quantify nitrogen solubility in these tissues. Also, (M-3) determine the potential for gas exchange in the spinal cord and tissues will be examined for evidence of bubble formation and/or histopathologic changes.

Milestone Tracker



FY18 Accomplishments, Discoveries, & Inventions

- Lipid content and lipid class composition from spinal cord (N=75), spinal nerves (N=55), and brain tissue (N=24) of 11 species of marine mammals (N=24 individuals) and the domestic pig (N=6) were quantified, with detailed sampling conducted on 5 species of marine mammals.
- A more accurate and precise method for lipid class quantification (HPTLC) was developed and utilized successfully to separate and quantify the above tissues.

FY19 Goals

- Quantification of nitrogen gas solubility of the above tissues.
- Begin characterization of spinal cord vasculature in marine & terrestrial spinal cord samples (**delayed by Hurricane Florence*).

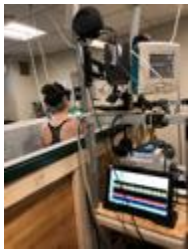
Principal Investigator Contact Email: Dr. Heather N. Koopman, 910-962-3471, koopmanh@uncw.edu

Autonomic Activity and Water Immersion

BD Johnson, PhD

Background: The autonomic nervous system reflexively controls many physiological systems, including the cardiovascular and respiratory systems. Water immersion attenuates circulating catecholamines, but it is not known if sympathetic nerve activity is altered. Furthermore, it is not known how the autonomic system responds to additional environmental challenges (i.e. hyperoxia, hypercapnia, exercise, cold) during water immersion.

Naval & Scientific Benefits: Understanding autonomic activity during water immersion is key to understanding diving physiology and developing potential countermeasures to protect divers from adverse physiological responses to the environmental conditions that they are exposed to.



Custom built rapid filling water immersion tanks will allow us to perform complex physiological measurements, such as muscle sympathetic nerve activity, during the studies.

Example of an integrated neurogram of muscle sympathetic nerve activity taken during a sympathoexcitatory maneuver.

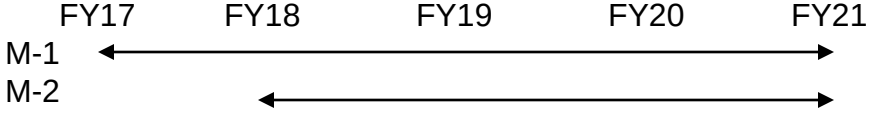
Example of radial nerve miconeurography. The white flag is attached to an electrode inserted into the radial nerve to assess muscle sympathetic nerve activity.

Objectives:

Specific Aim 1: Determine if sympathetic nerve activity is altered by breathing hyperoxic air compared to air breathing during both thermoneutral and cold water immersion conditions.

Specific Aim 2: Determine if sympathetic nerve activity is altered by breathing hypercapnic air compared to air breathing during both thermoneutral and cold water immersion conditions.

Milestone Tracker



FY18 Accomplishments, Discoveries, & Inventions

- Custom built rapid filling water immersion tanks
- Purchased equipment
- Began data collection for Specific Aim 1

FY19 Goals

- Continue data collection for Specific Aim 1
- Begin data collection for Specific Aim 2
- Present interim findings at national conferences

Principle Investigator:

Blair Johnson, PhD, 716-829-6789, blairjoh@buffalo.edu

Exploration Of Medical Response Strategies To Optimize Survival Of Escapees From A Disabled Submarine

Surg Cdr Lesley Whybourn / NSMRL

NAVSEA
NAVAL SEA SYSTEMS COMMAND
Supervisor of Salvage & Diving

Background: Survival in a Disabled Submarine (DISSUB) event depends upon many variables, one of which is a rapid and appropriate medical response, with assets capable of providing various levels of medical care in a complex and remote mass casualty situation. Examining the epidemiological features of DISSUB events and formulating reliable estimates of casualties and threats to the Health Service Support system are critical to effective planning of medical resource requirements.

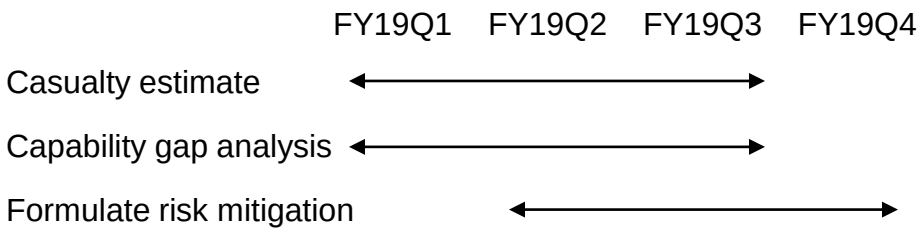
Naval & Scientific Benefits: Further work to address identified shortfalls in DISSUB survival & medical response capability is a Joint Force, DoN & SUBFOR priority objective. The project is of wider relevance to and offers opportunities for collaboration with Allied Forces.

Method of egress	Incidents and vessel type		Numbers attempting	Survivors	Last event
Surface abandonment	Nuclear	4	291	207	2003
	Diesel-electric	31	736	685	1988
	Total	**35**	**1027**	**892**	**2003**
Escape	Nuclear	2	92	85	1989
	Diesel-electric	9	212	135	1988
	Total	**11**	**304**	**220**	**1989**
Rescue	Nuclear	0	0	0	N/A
	Diesel-electric	1	33	33	1939
	Total	**1**	**33**	**33**	**1939**

Method of international DISSUB survivor egress since 1939

Objectives: To undertake a critical review of the likely biomedical evolution and existing medical response capability in DISSUB escape scenarios to inform (1) a casualty estimate, (2) a capability gap analysis and (3) recommendations for risk mitigation. This work extends an FY17 work effort that focused on DISSUB rescue and surface abandonment.

Milestone Tracker



FY18 Accomplishments, Discoveries, & Inventions

- Progression of TR publication approval for FY17 work effort
- DISSUB R&D paper presented at SMERWG Winter Meeting
- Initiation of FY19 work effort on receipt of funding 27 Nov 18

FY19 Goals

- Secure TR publication approval for FY17 work effort
- Complete casualty estimate and capability gap analysis
- Formulate recommendations and submit report

Principal Investigator Contact Email:
Lesley.a.Whybourn.fm@mail.mil

UNIVERSITY AT BUFFALO
CRESE
CENTER FOR RESEARCH & EDUCATION IN SPECIAL ENVIRONMENTS

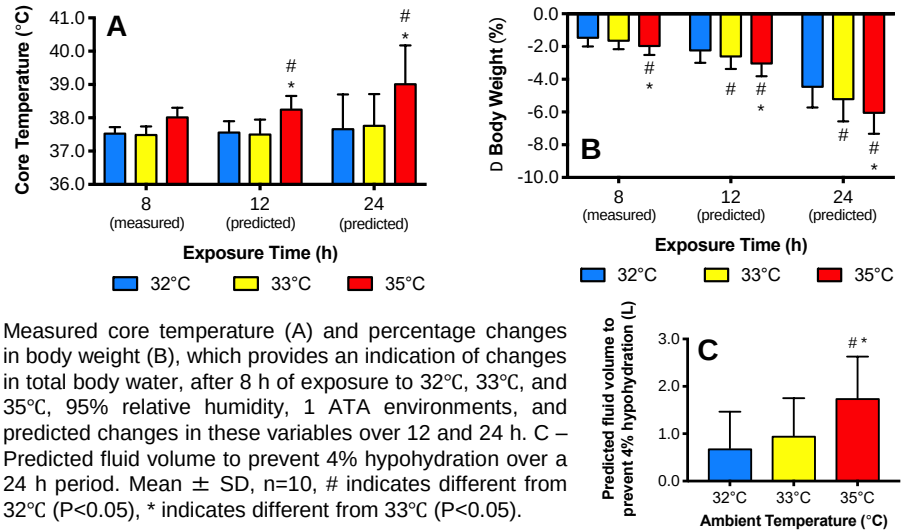
Hyperthermia and hypohydration in a disabled Pressurized Rescue Module

ZJ Schlader PhD, D Hostler PhD, BD Johnson PhD

NAVSEA
NAVAL SEA SYSTEMS COMMAND
Supervisor of Salvage & Diving

Background: Humidity and air temperature are predicted to quickly rise during a blower failure in a Pressurized Rescue Module (PRM). The resulting thermal environment can, in theory, become dangerous very quickly. There are no models, or data to base then on, capable of accurately predicting the magnitude of hyperthermia and/or hypohydration in a very humid and warm environment for up to 24 h.

Naval & Scientific Benefits: Safe deployment of a PRM is dependent on understanding and mitigating any challenges if failures were to occur. This project will inform the Submarine Guardbook as it relates to the management of environmental conditions likely to occur onboard a disabled submarine.



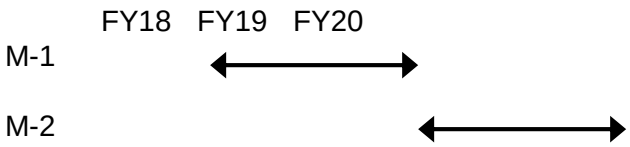
Measured core temperature (A) and percentage changes in body weight (B), which provides an indication of changes in total body water, after 8 h of exposure to 32℃, 33℃, and 35℃, 95% relative humidity, 1 ATA environments, and predicted changes in these variables over 12 and 24 h. C – Predicted fluid volume to prevent 4% hypohydration over a 24 h period. Mean ± SD, n=10, # indicates different from 32℃ (P<0.05), * indicates different from 33℃ (P<0.05).

Objectives:

1. (Aim 1): Determine the magnitudes of hyperthermia and hypohydration incurred in a warm and humid disabled PRM scenario at 1 ATA for up to 24 h.

2. (Aim 2): Identify the magnitudes of hyperthermia and hypohydration incurred in a warm and humid disabled PRM scenario at 20 fsw for up to 24 h.

Milestone Tracker



FY18 Accomplishments, Discoveries, & Inventions

- Completed data collection on 10 participants for Aim 1.
- The worst case predicted fluid volume required to prevent 4% hypohydration (a reasonable estimate for severe hypohydration) over a 24 h period is ~1.8 L

FY19 Goals

- Complete data collection for Aim 1
- Begin data collection for Aim 2
- Complete data analysis for Aim 1

Principle Investigator: Name, Phone #, Email

Zachary J. Schlader PhD, 716-829-6794, zjschlad@buffalo.edu

School of Medicine and Public Health
UNIVERSITY OF WISCONSIN-MADISON

Improving Safety of Submarine Escape and Rescue from Shallow Depth

Marlowe Eldridge, MD / Aleksey Sobakin, DVM, PhD

NAVSEA
NAVAL SEA SYSTEMS COMMAND
Supervisor of Salvage & Diving

Background: Experimental decompression findings in a large animal model (i.e. sheep) are essential for understanding serious DCS and developing practical risk management procedures to improve safety in submarine escape and rescue. Potentially fatal decompression outcomes require the ethical use of an animal model to investigate the risk, course, natural history of serious DCS, and efficacy of DCS treatment modalities.

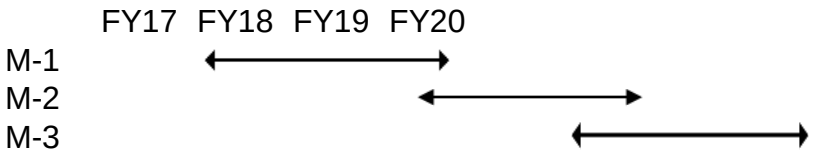
Naval & Scientific Benefits: With our current uncertainty of serious DCS risk under accelerated decompression from 70 fsw with 90 min oxygen pre-breath and 30 or 60 min surface interval, field officers need better information for operational decisions warranted in a DISSUB event.

Sheep drop-our pressure, fsw	Incidence of DCS during 30 and 60 min surface interval, %				
	DCS Type I	Limb bends	CNS-DCS	RDCS	Lethal
60 fsw (90 OPB, 60 min SI)	100	100	0	0	0
70 fsw (90 OPB, 30 min SI)	100	100	0	0	0

Objectives:

1. Accelerated decompression from prolonged hyperbaric exposure at 70 fsw for 24-h.
2. Evaluating the potential benefits of 90 min O_2 pre-breathing (OPB) before drop out decompression.
3. The clinical progression and minimization of DCS during 30 or 60 min surface interval (SI).

Milestone Tracker



FY18 Accomplishments, Discoveries, & Inventions

- Decompression from 70 fsw, 90 min OPB, and 30 min SI.
- Decompression from 60 fsw, 90 min OPB, and 60 min SI.
- The incremental report has been submitted

FY19 Goals

- Decompression from 70 fsw, 90 min OPB, and 60 min SI.
- Complete data set analysis
- Submit a completion report

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Co-PI Contact Email:
sobakin@wisc.edu

Lightweight Atmospheric Diving Suit - N13A-T029

N. Jared Keegan – Midé Technology

TPOC: Sandra Chapman, Ph.D. – ONR Undersea Medicine

Background: Atmospheric Diving Suits (ADS) are hard shell suits that provide a single atmosphere internal pressure such that a diver can ascend and descend very deep under water without the hazards associated with traditional diving methods (i.e. decompression sickness). Current ADS are essentially one man submarines; are difficult to deploy due to their large size, and have limited maneuverability at depth. The goal of this project is to develop new joints, a more functional arm and suit.

Naval & Scientific Benefits: A lightweight maneuverable ADS will be more easily deployed and used by Navy Divers in a broad number of mission types. Improving the task set for an ADS will allow less dependence on costly, long insertion time diving operations (such as Saturation Diving)

Midé Joint Prototype and Robotic Test Arm During High Pressure Testing at NSWC PCD

ADS Elbow Joint Prototype in new Test Arm

Low Pressure testing of new Test Arm (Elbow Joint + Rotary)

Objectives: Phase II Objective is to create a new joint design, which will allow the ADS diver to move in a more natural motion than current ADS joints allow.

Phase II Option II work is to create a full test appendage featuring revised Mide joint.

Milestone Tracker

	FY17	FY18	FY19	FY20
M-1 (Elbow)	←	→		
M-2 (Arm: Elbow + Rotary)		←	→	
M-3 (Revised Arm – High Pressure Eval)			←	→

FY18 Accomplishments, Discoveries, & Inventions

- Developed a multi-degree of freedom test arm
  - Custom made rotary joints
- Created new low-pressure test tank at Mide
- Designed, built and tested first test arm featuring membrane elbow joint and custom/crude rotary joint (low pressure)
- Building rotary joint test method (high pressure)

FY19 Goals

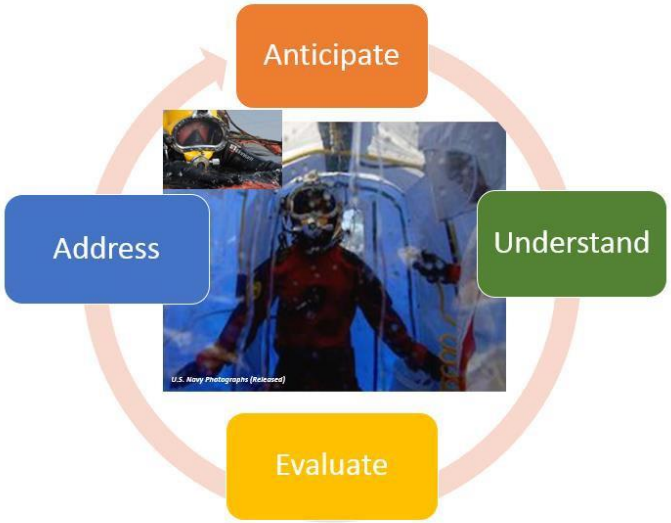
- Developing re-designed membrane joint (internals), and revised lower torque rotary joint for testing.
- Revise test arm, incorporate grasper
- Complete low and high pressure testing (unmanned)

Principle Investigator(s)

Mide: Dr. Marthinus vanSchoor, tienie@mide.com,781-306-0609

CONTAMINATED WATER RESEARCH
PI: K.C. Sorensen, R.D. George, P.C. Sims / NIWC PAC

Background: Water pollution is a global issue. With few exceptions most water bodies contain some level of contaminant (biologic and/or chemical). Domestically, some of the highest levels are associated with types of waterbodies our troops would frequent for routine operations. As a result potential exposure during both day-to-day operations and special mission critical operations poses a serious concern to divers. The ability to evaluate and address the potential threat, via improvements to sensors and PPE equipment, continues to improve. Yet, our ability to anticipate and understand the threat remains a critical issue.



Objectives: Combined efforts hope to address the following:

1. Provide CWD community framework to evaluate sites and risk
2. Understand legacy pollutant vs. current site conditions
3. How to address site specific or emergent COCs
4. Enable dive scenarios to be defined by site specific characteristics
5. Provide platform for key stake holders to collaborate and communicate

Naval & Scientific Benefits: Provide relevant information, to allow for accurate and rapid decision making giving user enhanced situational awareness & added protection.

Prior FY Accomplishments, Discoveries, & Inventions

- Development of limited scenario driven guidance tool
- T&E COC detection technology
- Development of pathogen based detection capability
- Development of machine learning tools

FY19 Goals

- Develop framework focused on state of knowledge as relates to relevant dive operations.
- Workshop focused on developing solutions for addressing CWD issues that are scientifically based, realistically achievable, and designed to protect diving personnel

Principal Investigator Contact Email: Dr. Kara C. Sorensen, 619-553-1340, sorensek@spawar.navy.mil

Transfer of Duke Dive Trial Data to U.S. Navy

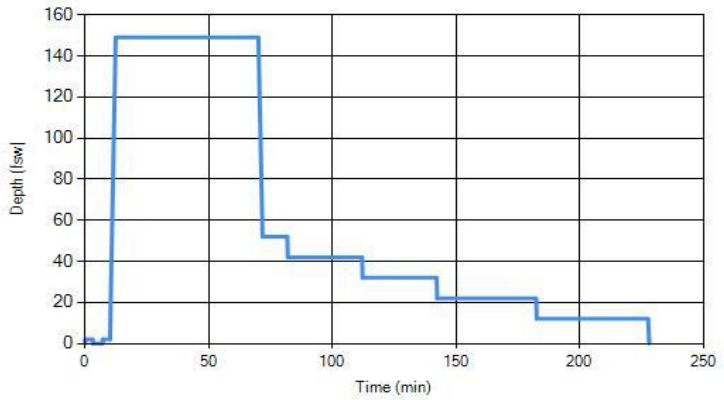
Laurens E. Howle, Ph.D., P.E.

Duke
MECHANICAL ENGINEERING & MATERIALS SCIENCE

NAVSEA
NAVAL SEA SYSTEMS COMMAND
Supervisor of Salvage & Diving

Background: Decompression studies (or non-decompression studies that required decompression) have been conducted at the Duke Hyperbaric Center from the late 1960s to present. Some, particularly the earliest, could not be done today due to safety concerns or funding limitations, and some were statistically underpowered by current analytical standards.

Naval & Scientific Benefits: Human dive trial data in the ANMRI format is presently used for calibrating and evaluating probabilistic decompression sickness (DCS) models by the USN and other organizations. The addition of the dive trial data from this project, when combined with data currently in USN use will improve statistical power and model fit of DCS models.



MK15 dive trial 297. This profile had 1 immersed, exercising human exposure with an outcome of DCS. The DCS symptom onset times were T1 = 227.55 min and T2 = 238.0 min.

Objectives: The objective of this project is to consolidate these studies in ANMRI dive profile format with DCS case descriptions and transfer these data to the USN for use in probabilistic DCS model calibration and evaluation. The data, when combined with existing USN human dive trial data, will expand the scope of existing decompression studies, improve statistical power, and might aid investigation of factors affecting DCS risk.

Milestone Tracker

	FY17 FY18
Convert and Transfer Dive Trials	⟷

FY18 Accomplishments, Discoveries, & Inventions

- Transferred 5 volumes detailing 5 dive studies carried out by the Duke Hyperbaric Center.
- Transfer 1 volume detailing a dive study conducted by Divers Alert Network.
- Added perceived severity index data to the USN NMRC 99-02 dive data.

Principal Investigator Contact Email:
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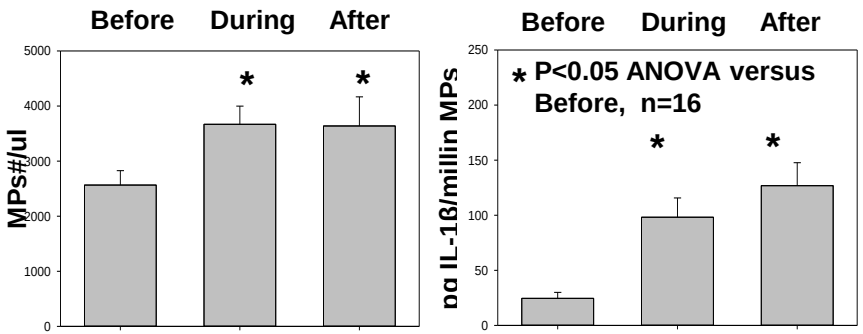
Microparticles, platelet-neutrophil aggregation and decompression sickness

Stephen R. Thom, M.D., Ph.D./ Univ. of Maryland

Background: This project is centered on the hypothesis that circulating microparticles (MPs, 0.1- 1 µm diameter vesicles produced by all vascular cells) are the proximal cause for organ injuries following decompression stress because they initiate an inflammatory response.

Naval & Scientific Benefits: Goals are to improve knowledge of DCS pathophysiology, treatment and prophylaxis. We have advanced to demonstrate that MPs and inflammatory changes occur in human divers and animals during the dive, thus some potential pathological changes occur before decompression *per se*. We are investigating several FDA-approved agents that abrogate decompression injuries without recompression treatment.

MPs containing high concentrations of IL-1β are generated in human divers exposed to 30 msw



Objectives: (1) Elucidate the mechanisms for evolution of MPs by various stimuli.(2) Evaluate methods to ameliorate MPs-induced injuries. (3) Determine the fate of MPs *in vivo*.

Milestone Tracker (publications)

FY 2017

J Neurotrauma 33: 168, 2016
Am J Physiol 310: R596, 2016
Fr Rad Biol Med 101: 154, 2016
Atherosclerosis 256:115-122, 2017
Neuroinflammation 14(1):47, 2017
Fr Rad Biol Med 106: 406, 2017
J Appl Physiol 123: 297, 2017

FY 2018

Exp Lung Res 43: 175, 2017
J Biol Chem 292: 18312, 2017
Sci Rep. 5;7(1):16929, 2017.
Am J Physiol 315(4):R759, 2018
J Appl Physiol 125: 1339, 2018
J Appl Physiol 2018 Aug 16. doi: 10.1152

FY 2019

Microvasc Res. 123:58, 2018
J Appl Physiol (1985). 2019 Feb 14. doi: 10.1152

FY18 Accomplishments, Discoveries, & Inventions

- Changes in human divers are comparable to mouse model.
- Many pathological events occur at pressure.
- Injuries seen on decompression can be abrogated by pharmaceuticals that block IL-1β, and also by hyperbaric oxygen that inhibits high-pressure induced inflammasome formation,

Future Plans

- Evaluate alternative pharmaceutical treatments that appear to inhibit MPs and IL-1β such as gelsolin.
- Evaluate blood-borne changes in human divers who have undertaken provocative diving and those suffering DCS.

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Diver Biometric Device (DBD) using Novel Physiological Sensors

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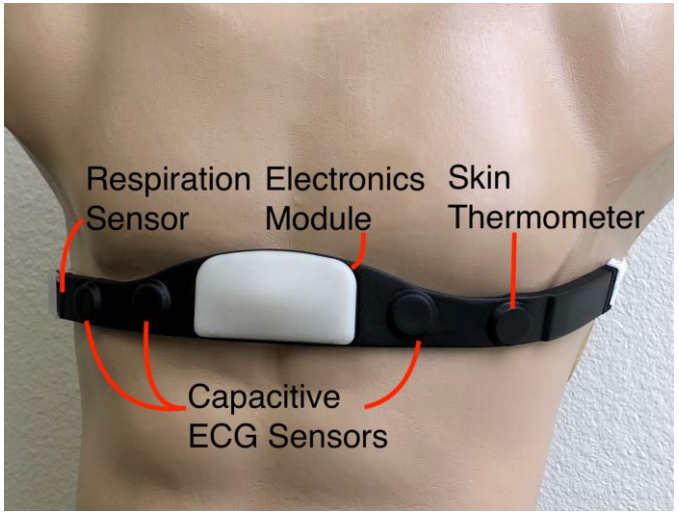
Background: The Diver Biometric Device (DBD) is a wearable suite of non-invasive sensors that aims to enable medical research and operational health assessment for the purpose of providing an indication of diver health status. DBD currently includes ECG, respiration, and skin temperature.

Naval & Scientific Benefits: The DBD is intended for use in a variety of operating conditions, including controlled laboratory environments, studies in open water, during training of Navy divers, and even for field health and performance monitoring. As no integrated underwater physiological monitoring capability currently exists, development of the DBD is expected to advance current research and monitoring capabilities of the Navy.



Phase II SBIR Objectives:

- Design and build a functional DBD prototype
- Record ECG, respiration, and skin temperature in salt water
- Evaluate prototype on divers in 10 m deep salt water pool and open ocean
- Develop and implement basic biometric algorithms
- Evaluate complete prototype on divers at a Navy lab

Options:

Design and integrate core temperature capability
Design and integrate pulse oximetry capability
Evaluate revised prototype on divers at a Navy lab

FY18 Accomplishments, Discoveries, & Inventions

- High quality ECG and respiration acquired on 3 different subjects wearing wetsuits at 10 m using testbed system
- Designed and fabricated first DBD prototype with next generation of ECG sensors
- Implemented a preliminary R-peak detection algorithm

FY19 Goals

- Evaluate DBD prototype in pool and open ocean
- Build 1-3 more DBD units
- Activate project Options to develop pulse oximetry and core temperature capabilities

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