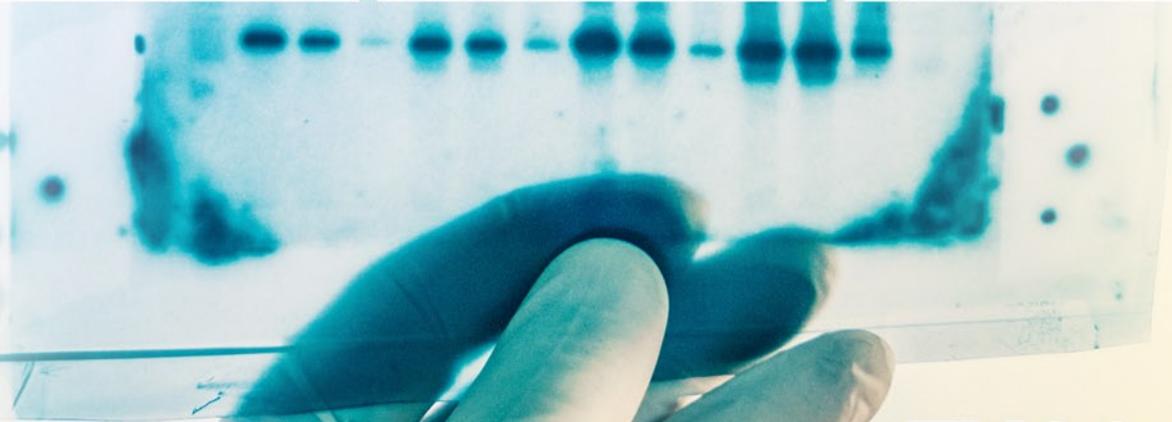


National Aeronautics and Space Administration



HUMAN RESEARCH PROGRAM

SEEKING KNOWLEDGE



FY2015
ANNUAL REPORT

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Background

Crew health and performance are critical to successful human exploration beyond low Earth orbit. Hazards include physiologic effects from radiation, hypogravity, and planetary environments, as well as unique challenges associated with the distance from Earth. The scientists and engineers of the Human Research Program (HRP) investigate and reduce the greatest risks to human health and performance, and provide essential countermeasures and technologies for human space exploration.

HRP delivers products and strategies to protect the health and safety of spaceflight crews and increase their productivity while living and working in space. Research is performed onboard the International Space Station (ISS), on the ground in analog environments that have features similar to those of spaceflight, and in laboratory environments. Data from these experiments further the understanding of how the space environment affects the human system. These research results contribute to scientific knowledge and technology developments that address the human health and performance risks from exposure to the hazards of exploration missions.

As shown in this report, HRP continues to make significant progress toward developing medical care and countermeasure systems for space exploration

missions which will ultimately reduce risks to crew health and performance.

Goal and Objectives

The goal of the Human Research Program is to provide human health and performance countermeasures, knowledge, technologies, and tools to enable safe, reliable, and productive human space exploration. The specific objectives of the HRP are:

- 1) Develop capabilities, necessary countermeasures, and technologies in support of human space exploration, focusing on mitigating the highest risks to crew health and performance. Enable the definition and improvement of human spaceflight medical, environmental and human factors standards.
- 2) Develop technologies that serve to reduce medical and environmental risks, to reduce human systems resource requirements (mass, volume, power, data, etc.) and to ensure effective human-system integration across exploration mission systems.
- 3) Ensure maintenance of Agency core compe-

tencies necessary to enable risk reduction in the following areas: space medicine, physiological and behavioral effects of long duration space-flight on the human body, space environmental effects, including radiation, on human health and performance and space human factors.

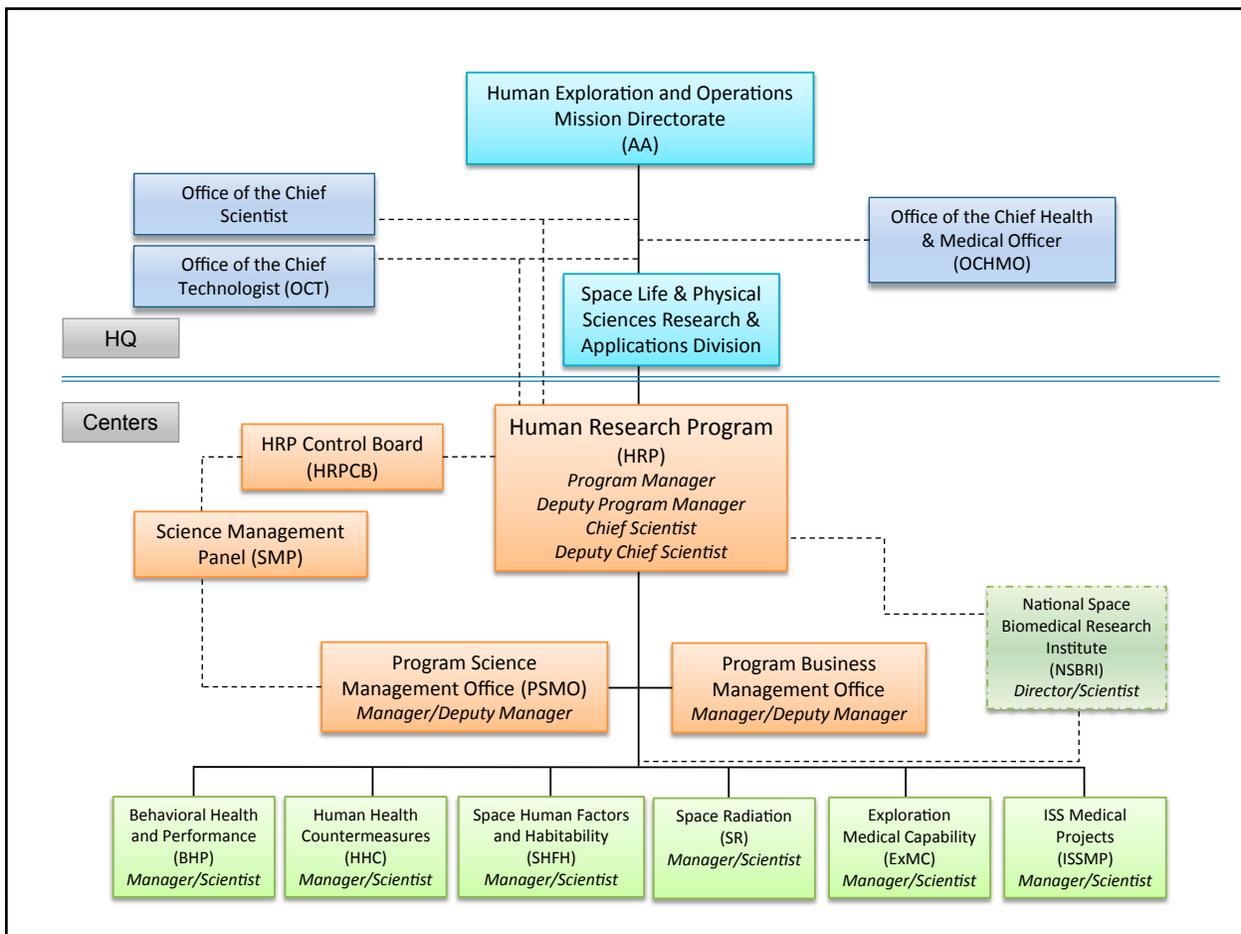
in the design, development, and operation of technological systems for exploration missions.

Program Organization

The HRP's organization is designed to support the goals of the Human Exploration and Operations Mission Directorate (HEOMD) and NASA's Office of the Chief Health and Medical Officer (OCHMO). To that end, HRP conducts research and develops technology that enables the OCHMO to establish and maintain NASA-wide human health and performance standards. Furthermore, HRP provides HEOMD with methods of meeting those standards

Organizationally, HRP resides within the HEOMD; however, the management of HRP is located at the Johnson Space Center and work is performed across multiple participating NASA centers. The HRP Program Manager and Deputy Manager lead all aspects of the program and the HRP Chief Scientist and Deputy Chief Scientist lead the science management and coordination.

As shown in the chart below, two offices support program, science and business management and provide integration across the Program. The Program Science Management Office (PSMO), and the Program Business Management Office provide coordination of HRP activities across all Program components.



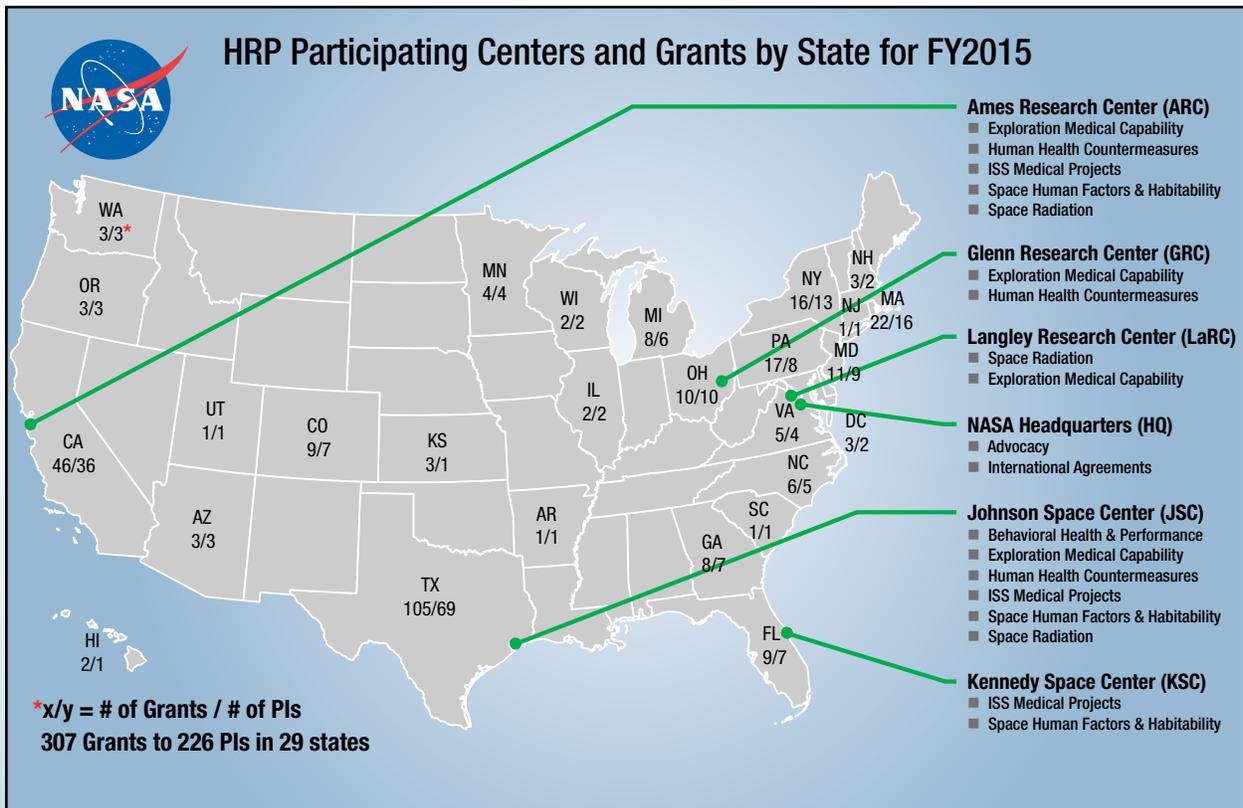
OVERVIEW

The PSMO maintains scientific integrity of the HRP's research, reviews and integrates science tasks, reviews the prioritization and implementation of flight and ground analog tasks, communicates research needs to other NASA programs and cultivates strategic research partnerships with other domestic and international agencies. The Program Business Management Office maintains all business functions for the Program, providing budget planning, integration and coordination with the HEOMD and across all Program components.

There are six Elements that comprise the Program and are focused to accomplish specific goals for investigating and mitigating the highest risks to astronaut health and performance. Of the six, five are research Elements and one, the International Space Station Medical Project, is a service element which provides the other Elements access to the ISS and ground-

based analogs. The research Elements include: Space Radiation, Human Health Countermeasures, Exploration Medical Capability, Space Human Factors and Habitability, and Behavioral Health and Performance. These Elements provide the HRP's knowledge and capabilities to conduct research to address human health and performance risks of spaceflight, and they advance the readiness levels of technology and countermeasures to the point where they can be transferred to the customer programs and organizations. As shown below, the HRP is a multi-center program, with research being performed across the nation.

Each research Element consists of related portfolios, projects and research tasks focused toward developing products that reduce the highest risks in that area. To learn more about the HRP Elements, please visit: <http://www.nasa.gov/hrp/elements>.



Partnerships and Collaborations

The HRP has a long history of collaborative work with universities, hospitals, and federal and international agencies for the purpose of sharing research facilities and multi-user hardware, and cooperation on research tasks of mutual interest.

The National Space Biomedical Research Institute (NSBRI), an institute funded by HRP, investigates the physical and psychological challenges of long-duration human spaceflight. Founded in 1997 through a NASA competition, NSBRI is a nonprofit research consortium that connects the research, technical, and clinical expertise of the biomedical community with the scientific, engineering, and operational expertise of NASA. NSBRI is located within the Baylor College of Medicine's Center for Space Medicine. For more information, visit www.nsbri.org.

The HRP also maintains collaborative relationships with international partners through various working groups. These relationships enhance the research capabilities of all partners and provide synergism of research efforts.

For more than a decade, HRP utilized bed rest facilities at the University of Texas Medical Branch in Galveston, Texas, to study changes in physiologic function associated with weightlessness. In FY2015, HRP closed their facilities in Galveston and began a new era in international collaboration. Future bed rest studies will be multi-lateral studies conducted in a new facility managed by the Deutsches Zentrum für Luft- und Raumfahrt (DLR) in Koln, Germany.

The NASA Space Radiation Laboratory (NSRL) at the Department of Energy's Brookhaven National Laboratory in Upton, New York, conducts research using accelerator-based simulations of space radiation.

Partnerships and Collaborations with Universities, Industries, and Government Agencies

| Examples of HRP Partnerships and Collaborations | Benefits to Exploration |
|--|---|
| National Space Biomedical Research Institute (NSBRI) | Investigates the challenges of long-duration human spaceflight and bridges the expertise of the biomedical community with the scientific, engineering, and operational expertise of NASA |
| US-Russian Joint Working Group (JWG) | Broaden ISS research and enhance opportunities for collaboration |
| Multilateral Medical Operations Panel (MMOP) | Multilateral hardware and data collaborations between ISS operations and HRP research. |
| Multilateral Human Research Panel for Exploration (MHRPE) | Permanent steering group for duration of ISS program. Integrates data and strategies from operations and research. Leverages existing processes among implementation groups. |
| International Human Space Flight Analog Research Coordination Group (HANA) | Coordinates isolation and confinement research in analog environments across the multiple international partnering agencies. |
| International Space Life Sciences Working Group (Canada, Japan, Germany, Ukraine, France, and the European Space Agency) | Encourages a unified effort among space life sciences communities around the world by coordinating the use of spaceflight and ground research facilities and identifying mutual interests and compatibilities |

OVERVIEW

| Examples of HRP Partnerships and Collaborations | Benefits to Exploration |
|---|--|
| National Institutes of Health, Department of Energy, Centers for Disease Control and Prevention, Department of Agriculture, Department of Defense | State-of-the-art research facilities, research activities, and technology development of mutual interest |
| Cleveland Clinic Center for Space Medicine | Provides collaboration and consultation regarding medical issues experienced during space flight and provides access to a network of more than 2,000 Cleveland Clinic physicians |
| University of Texas Medical Branch, Galveston, TX | Provides bed rest facilities to study changes in physiologic function associated with weightlessness |
| Department of Energy - Brookhaven National Laboratory | State-of-the-art facility conducts research using accelerator-based simulation of space radiation |
| Summa Health Systems | Provides collaborative research for advanced health care delivery to astronauts |
| European Space Agency (ESA) | Collaboration on the utilization of the Pulmonary Function System, MARES, and exercise research |
| Japan Aerospace Exploration Agency (JAXA) | Research on bone-related risks, auscultation capabilities, and utilization of environmental sampling |
| Institute for Biomedical Problems (IBMP) | Coordination of the One-Year Mission and functional performance Field Test Experiment and VIIP research |
| SHAPE America | Collaborating and co-promoting Train Like an Astronaut Project |
| University at Buffalo, Department of Epidemiology and Environmental Health | Space Act Agreement for collaboration on topics in pediatric obesity and program evaluation for MX and TLA |
| Destination Station, and ISS Program outreach and outreach feature press releases | Public dissemination of HREC information on the Human Challenges of Space Exploration |
| The Jamestown Resource Center | Collaboration on HREC content to be used for those with unique needs and their participation in the Train Like an Astronaut (TLA) activities |
| Let's Move! Initiative | TLA materials co-branded with this White House Initiative |
| International space agency education support with world-wide community partners and schools | Collaborative partnerships fostering the world-wide dissemination of HREC <i>Mission X: Train Like an Astronaut</i> physical and educational activities encouraging better nutrition and healthier lifestyles for children |



International Cooperation Enables One-Year Mission, Twins Study and Future Efficiencies

On March 27, 2015, NASA astronaut Scott Kelly and Russian cosmonaut Mikhail Kornienko began a yearlong mission onboard the ISS. Their flight was the outcome of three years of collaborative planning, training, hardware development, and certification.

The multilateral commitment to a yearlong ISS expedition began in 2012 in an effort to utilize the ISS more efficiently by optimizing the capabilities and resources of all ISS partners. In 2013, the Space Station Control Board chartered the Multilateral Human Research Program for Exploration (MHRPE) to coordinate joint research on future expeditions, starting with the ‘One-Year Mission.’ MHRPE developed schedule milestones and overarching principles for sharing of hardware, crewmember subjects, and data across international partners.

Through MHRPE, NASA and the Russian Federal Space Agency, Roscosmos, agreed to a coordinated program of collaborative research involving Kelly and Kornienko. The selection of Scott Kelly as the U.S. crewmember brought an unanticipated opportunity for systems biology, or “omics,” research into the effects of spaceflight by involving his identical twin brother, Mark. Both highly accomplished test pilots, they were selected into NASA’s astronaut corps

together in 1996. Mark retired from NASA in 2011 after flying on four Space Shuttle missions for a total of 54 days in space. Scott completed two Shuttle missions before changing course and becoming a long-duration ISS crewmember. His time in space after the yearlong expedition will be 516 days—almost 10 times longer than Mark’s total.

The direct comparison between the brothers promised to highlight differences associated with acute and chronic exposures to spaceflight factors by minimizing the biological variations normally found between unrelated subjects. Accordingly, a solicitation for the Twins Study was issued in September 2013.

An objective of the Twins Study is to investigate the interactions of biological information by mapping genes, proteins, and metabolites that are associated with spaceflight, thus integrating the various fields of genomics, proteomics, and metabolomics with respect to spaceflight responses. Ten proposals were selected in early 2014, making the Twins Study the first human spaceflight study to span the molecular, microbial, physiological, and cognitive domains of systems biology. For a list of these studies, see the table on page 17.

HRP support included implementing the science requirements, crew training, flight hardware certification, consent briefings, and sample and data col-

MAJOR PROGRAM-WIDE ACCOMPLISHMENTS



Scott Kelly (top) and his identical twin brother Mark Kelly (bottom) are interviewed at a National Press Club breakfast marking the halfway point for the One-Year Mission.

lection sessions for both participants. The One-Year Mission also required the use of novel hardware in space. Experiment-unique hardware was flight certified specifically for the joint U.S.-Russian Fluid Shifts investigation, which characterized changes in the fluid distribution in the body and its potential impact on intracranial and intraocular pressure and visual impairment. The study presented unique challenges with an extensive crew time commitment and the logistical difficulties of conducting operations in both the U.S. and Russian ISS segments.

At the end of FY2015, the One-Year Mission passed its halfway point with multiple outreach activities. Landing is planned for March 2, 2016—providing a mission duration of 340 days. In-flight data collection has continued, in spite of increased competition for crew time and the loss of three resupply vehicles. Results are expected after six months of postflight data collection followed by up to a year of analysis.

The improved processes and techniques developed as part of the Twins Study will increase the scientific return from future expeditions while decreasing the resources required. ISS Program managers intend to apply lessons learned from this yearlong mission to biomedical risk reduction research and technology development activities on all subsequent missions, regardless of their duration.

Crew Time Constraints Prompt Research Flight Queue Scrub

HRP is historically the single largest user of ISS crew time, apart from general maintenance and operations tasks. In the past year, HRP performed a thorough “scrub” of its queue of flight experiments due to increasing requests for crew time by other groups within NASA, as well as by the Center for the Advancement of Science in Space (CASIS).

HRP experiments require direct crew involvement as test subjects and often as operators. Many have schedule constraints; for example, they may require measurements at specific times. Therefore, adequate time would not be available to meet the objectives of all these groups with the flight queue as it existed a year ago. William Gerstenmaier, NASA’s Associate Administrator for Human Exploration and Operations, asked HRP management if it was possible to reduce crew time needs, and to what level.

In carrying out this directive, the entire HRP portfolio of current and planned experiments using ISS crewmembers as test subjects was examined. Particular attention was paid to the following criteria in deciding whether an experiment truly needed to be performed on ISS: it must be relevant to the current priorities in the HRP Integrated Path to Risk Reduction; it should not request more test subjects than needed; and it must not be compromised by changes in procedures or medical operations.

Experiments were further examined for synergies wherein two or more studies could be combined to reduce resource requirements. Preference was given to experiments having the greatest impact on changing the posture of a given risk, and those with international partnerships.

Specific recommendations were made for missions through FY2018, when the availability of commercial crew vehicles would allow for an increased crew size. Long term recommendations were made to move

some experiments to alternative platforms such as analog bed rest, possibly with later validation on ISS.

As a result of this lengthy and sometimes painful process, five experiments were removed from the flight portfolio, and 14 were reduced in scope. Although these reductions may increase uncertainty in results or recommendations, HRP is now in a better position to perform research necessary to mitigate the major risks to human health and performance in space, in the short and long term.

Standing Review Board Site Visit at JSC: Four Strengths Noted

The NASA Standing Review Board (SRB) held its site visit August 17-19, 2015. The SRB is the board responsible for conducting independent reviews of a program or project and for providing objective, expert judgments. As a key element in NASA's strategic framework for managing space flight programs, SRBs help ensure appropriate program and project management oversight in order to increase the likelihood of mission success.

The SRB reported that HRP continues to meet Agency needs and commitments and has met the success criteria agreed to in the Terms of Reference. Four strengths, two issues, and four concerns were noted. The strengths highlighted HRP's Human Research Roadmap, Path to Risk Reduction (PRR), use of Customer-Supplier Agreements, and management of the risk of limited ISS and ground analog resources. The issues noted were on Program workforce vacancies and Space Radiation's PRR, which did not appear to meet agency needs for a decision on readiness for a Mars Design Reference Mission.

2015 HRP Investigators' Workshop Sets Another Attendance Record

The 2015 HRP Investigators' Workshop was held January 13-15 in Galveston, Texas. The theme of the workshop was "Integrated Pathways to Mars." This



HHC Element Scientist, Peter Norsk, MD, gives a presentation during the 2015 HRP Investigators Workshop.

year's workshop was preceded by a retreat for the Space Human Factors and Habitability Element and combined the Behavioral Health and Performance Working Group and the Space Radiation Element Investigators' Workshop. The meeting was the largest ever, with 917 registrants from five countries and 465 abstracts submitted.

The meeting is the primary venue for HRP and NSBRI researchers to share their findings. It included three plenary sessions, 46 discipline-specific sessions, and two poster sessions. Sessions included a flight analogs presentation by astronaut Serena Auñón, MD, a lunch talk on medical considerations for participants in commercial space flights, the NSBRI student poster competition and Pioneer Award. In the closing session, astronaut Stanley Love, PhD, gave an engaging talk about the difficulties involved with human exploration of Mars.

HERO Research Solicitations and Selections

The Human Exploration Research Opportunities (HERO) NASA Research Announcement (NRA) is a solicitation that remains open all year with research opportunities, or appendices, being issued as needed. In FY2014, HRP issued six appendices including NASA Flagship, NASA Omnibus, NSBRI, Ground-Based Studies in Space Radiobiology, Behavioral Health and Performance, Human Health Counter-

MAJOR PROGRAM-WIDE ACCOMPLISHMENTS

measures Topics, NASA Specialized Centers of Research (NSCOR) for Ground-Based Studies Assessing Cancer Risks from Space Radiation.

A NSCOR consists of a team of investigators who have complementary skills and who work together to answer a closely focused set of research questions with the goal of achieving overall research progress that is greater than the sum of the progress achievable by each project individually. The Space Radiation Element sponsors NSCOR teams covering multiple cancer types as well as one specifically focused on risks to the CNS from space radiation exposure.

In response to the 2014 appendices, HRP received 331 Step-1 proposals, 188 invited Step-2 proposals, and issued 43 new awards.

For the 2015 HERO NRA, HRP received 184 Step-1 proposals submitted in response to the Flagship, Omnibus, and NSBRI appendices, and invited 135 Step-2 proposals. Final NRA selections will be announced in April 2016.

The Artificial Gravity solicitation, released in July 2015, solicited proposals for exploring partial-gravity dose-response relationships in cells, animal models, parabolic flights, and computational models. Fifteen proposals were received in response to this solicitation. Peer review of proposals will occur in November, and final selections will be announced in December.

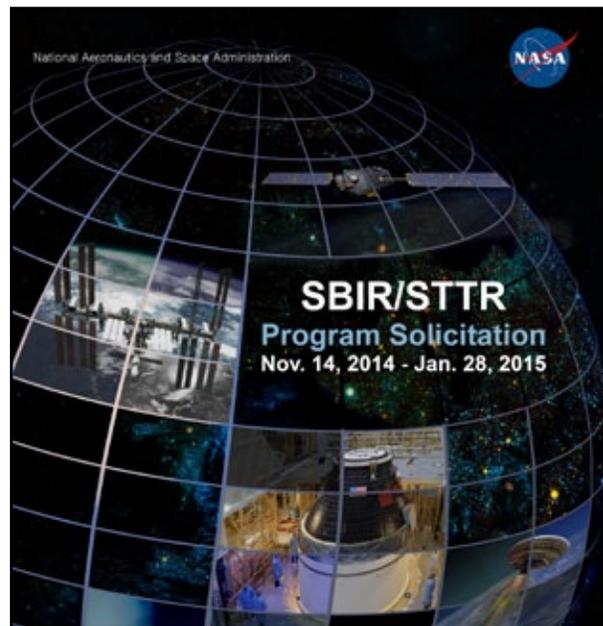
The International Life Sciences Research Announcement was released in September 2015 and solicited for research related to behavioral health and performance to be performed in the HERA. Final selections will be announced in May 2016.

SBIR Research Solicitations and Selections

Three NASA HRP 2015 Small Business Innovation Research (SBIR) Phase 1 awards were announced in April 2015: Cognitive Assessment and Prediction to Promote Individualized Capability Augmentation

and Reduce Decrement, Charles River Analytics, Inc.; Optical System for Monitoring Net Ocular Blood Flow, Physical Sciences, Inc.; Appraisal of Task Health and Effort through Non-Intrusive Assessments, SIFT, LLC.

In addition, two HRP SBIR topics awarded in 2012 were awarded Phase 2 awards in April 2015: STARwatch to Deliver Objective Sleep Measures for Spaceflight Operations, Pulsar Informatics, Inc. and A Low-Power Medical Oxygen Generator, TDA Research, Inc.



The SBIR program is a competitive 3-phase award system which provides small businesses with opportunities to propose innovations to meet specific research and development needs.

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Overview

The International Space Station Medical Projects (ISSMP) Element provides planning, integration, and implementation services for HRP research studies. ISSMP supports both spaceflight and flight analog research. Through the integration of these two efforts, ISSMP offers an innovative way to guide research decisions to meet the unique challenges of understanding the human risks to space exploration.

The objectives of ISSMP are to maximize the utilization of the ISS and flight analog environments and to develop and verify strategies to ensure optimal crew performance for exploration missions. The ISSMP also enables the development and validation of physical, pharmacologic, and nutritional countermeasures sponsored by HRP research Elements that influence mission success or crew health.

ISSMP supports HRP flight and flight analog research investigations by coordinating pre-, in-, and post-mission activities. Services provided by ISSMP include training of crewmembers and ground controllers; monitoring real-time experiment and hardware operations; and facilitating the transfer of data to research investigators.

ISSMP provides and sustains the Human Research Facility on board ISS, including hardware that enables

human research and is available to investigators who conduct human physiological research. ISSMP also facilitates the development and certification of new flight hardware and manifests consumables to ensure uninterrupted in-flight data collections and provides complete integration support for multiple flight vehicles including the Russian Soyuz and Progress, European, Japanese, and commercial launch vehicles. During flight research operations, ISSMP maintains the JSC Telescience Support Center (TSC). The TSC provides a focal point for real-time ISSMP operations and for remote investigators to monitor their experiments and acquire telemetry data.

Additionally, ISSMP coordinates with the ISS International Partners to develop integrated mission-specific science complements for flight investigations and to negotiate schedules, usage agreements, and crewmember participation.

The Flight Analogs Project (FAP) within ISSMP assists HRP researchers by characterizing current and potential spaceflight analogs, evaluating their relevance and similarity to spaceflight conditions, negotiating access and matching the characteristics of analogs to requirements for research. Examples of analog environments are head-down tilt bed rest, undersea habitats, isolation and confinement facilities, altitude chambers, and extreme environments such as remote desert test sites and Antarctic outposts.

FAP also manages and operates the Human Exploration Research Analog (HERA) located at JSC in support of NASA's HRP-sponsored research. The HERA facility offers a unique platform for conducting HRP isolation and confinement studies under controlled mission conditions.

The use of ground analogs, such as bed rest and HERA, are essential for HRP research efforts because access to resources required to conduct studies in space is very limited and the expense of flight studies is significantly greater than the expense of ground studies. Use of ground analogs allows participation by a greater number of subjects. Flight analog testing will become more and more critical to NASA to validate countermeasures, given the few opportunities to use flight platforms such as the ISS and the limited number of crewmembers per Expedition.

For details visit: <http://www.nasa.gov/hrp/elements/issmp>

FY2015 Activities and Accomplishments

Fiscal year 2015 was a successful year for the ISSMP and included the implementation of joint U.S.-Russian research investigations, the launch of the first one-year mission, and the start of the unique NASA Twins Study. ISSMP coordinated and optimized the flight research supporting ISS Increments 42-44. Research accomplishments include the completion

of four flight studies and continuation of 11 studies. Also in FY2015, nine new investigations began flight operations, and one investigation was under feasibility assessment and awaiting a future select-for-flight decision. Through early September 2015, ISSMP supported 343 in-flight sessions from the TSC, resulting in the use of 500 hours of dedicated human research on orbit. ISSMP also coordinated and conducted 11 informed consent briefings, 104 crew training sessions, and 331 preflight and 318 postflight baseline data collection sessions. Additionally, ISSMP provided support for the international partners by participating in 13 technical readiness reviews.



ISS One-Year crewmember Scott Kelly and Russian crewmembers Mikhail Kornienko and Gennady Padalka use the ISSMP developed ultrasound during the Fluid Shifts study.

INTERNATIONAL SPACE STATION MEDICAL PROJECTS ELEMENT

Current International Space Station Medical Projects Flight Investigations

| Investigation Title | Ops Title | Investigator | Subjects | |
|---|---------------------------|---|------------------------|------------------------------------|
| | | | Required | Participation Through Increment 44 |
| Investigations Continuing Flight Operations in Fiscal Year 2015 | | | | |
| NASA Biochemical Profile Project | Biochemical Profile | Scott Smith, PhD <i>NASA/JSC</i> | All USOS | 10 |
| Bisphosphonates as a Countermeasure to Space Flight Induced Bone Loss | Bisphosphonates (Control) | Adrian LeBlanc, PhD <i>Universities Space Research Association (USRA)</i> Toshio Matsumoto, MD, PhD <i>University of Tokushima</i> | 10 | 9 |
| Quantification of In-flight Physical Changes – Anthropometry and Neutral Body Posture | Body Measures | Sudhakar Rajulu, PhD <i>NASA/JSC</i> | 12 | 7 |
| Defining the Relationship Between Biomarkers of Oxidative and Inflammatory Stress and the Risk for Atherosclerosis in Astronauts during and after Long-Duration Spaceflight | Cardio Ox | Steven Platts, PhD <i>NASA/JSC</i> | 12 | 7 |
| Occupational Risk Surveillance for Bone: Pilot Study-Effects of In-Flight Countermeasures on Sub-Regions of the Hip Bones | Hip QCT | Jean Sibonga, PhD <i>NASA/JSC</i> | 10 | 11 |
| Risk of Intervertebral Disc Damage (IVD) After Prolonged Spaceflight | IVD | Alan Hargens, PhD <i>University of California San Diego</i> | 12 | 6 |
| Study of the Impact of Long-Term Space Travel on the Astronaut's Microbiome | Microbiome | Hernan Lorenzi, PhD <i>J. Craig Venter Institute</i> | 9 | 9 |
| Prospective Observational Study of Ocular Health in ISS Crews | Ocular Health | Christian Otto, MD <i>USRA</i> | 12 | 11 |
| The Effects of Long-Term Exposure to Microgravity on Salivary Markers of Innate Immunity | Salivary Markers | Richard Simpson, PhD <i>University of Houston</i> | 6 | 7 |
| NASA Biological Specimen Repository | Repository | Kathleen McMonigal, MD <i>NASA/JSC</i> | All | 42 |
| Integrated Resistance and Aerobic Training Study | Sprint | Lori Ploutz-Snyder, PhD <i>NASA/JSC</i> | 6 Control 12 Active | 4 Control 7 Active |

INTERNATIONAL SPACE STATION MEDICAL PROJECTS ELEMENT

| Investigation Title | Ops Title | Investigator |
|--|--------------------|---|
| Previous Investigations Included in One-Year Mission Data Set | | |
| Psychomotor Vigilance Test Self-Test on ISS | Reaction Self Test | David Dinges, PhD <i>University of Pennsylvania</i> |
| Sleep-Wake Actigraphy and Light Exposure on ISS12 | Sleep 1YM | Laura Barger, PhD <i>Brigham and Women's Hospital/Harvard Medical School</i> |
| Physiological Factors Contributing to Changes in Postflight Functional Performance | FTT | Jacob Bloomberg, PhD <i>NASA/JSC</i> |

| Investigation Title | Ops Title | Investigator | Subjects | |
|---|--------------|---|----------|------------------------------------|
| | | | Required | Participation Through Increment 44 |
| Investigations with Initial Flight Operations in Fiscal Year 2015 | | | | |
| Factors Contributing to Food Acceptability and Consumption, Mood and Stress on Long-term Space Missions | Astro Palate | Zata Vickers, PhD <i>University of Minnesota</i> | 8 | 1 |
| Individualized Real-Time Neurocognitive Assessment Toolkit for Space Flight Fatigue | Cognition | Mathias Basner, MD, PhD <i>University of Pennsylvania</i> | 6 | 5 |
| Recovery of Functional Sensorimotor Performance Following Long Duration Space Flight | Field Test | Millard Reschke, PhD <i>NASA/JSC</i> Inessa Kozlovskaya, MD <i>IBMP</i> | 15 | 3 |
| Effects of Long-duration Microgravity on Fine Motor Skills | Fine Motor | Kritina Holden, PhD <i>NASA/JSC</i> | 8 | 2 |
| Fluid Shifts Before, During and After Prolonged Space Flight and Their Association With Intracranial Pressure and Visual Impairment | Fluid Shifts | Michael Stenger, PhD <i>Wyle ST&E/NASA JSC</i> Scott Dulchavsky, MD, PhD <i>Henry Ford Health System</i> Alan Hargens, PhD <i>University of California San Diego</i> | 10 | 2 |
| Habitability Assessment of International Space Station | Habitability | Sherry Thaxton <i>Lockheed Martin/NASA JSC</i> | 6 | 1 |
| Spaceflight Effects on Neurocognitive Performance: Extent, Longevity and Neural Bases | NeuroMapping | Rachel Seidler, PhD <i>University of Michigan</i> | 13 | 3 |
| Assessing Telomere Lengths and Telomerase Activity in Astronauts | Telomeres | Susan Bailey, PhD <i>Colorado State University</i> | 10 | 3 |

INTERNATIONAL SPACE STATION MEDICAL PROJECTS ELEMENT

| Investigation Title | Ops Title | Investigator | Subjects | |
|---|----------------|---|----------------------|------------------------------------|
| | | | Required | Participation Through Increment 44 |
| Differential Effects on Telomeres and Telomerase in Twin Astronauts Associated with Spaceflight | Twins Study | Susan Bailey, PhD <i>Colorado State University</i> | 2 | 2 |
| Cognition on Monozygotic Twin on Earth | | Mathias Basner, MD, PhD <i>Univ. of Pennsylvania</i> | | |
| Comprehensive Whole Genome Analysis Of Differential Epigenetic Effects Of Space Travel On Monozygotic Twins | | Andrew Feinberg, MD, MPH <i>Johns Hopkins University</i> | | |
| Metabolomic And Genomic Markers Of Atherosclerosis As Related To Oxidative Stress, Inflammation, And Vascular Function In Twin Astronauts | | Stuart Lee, PhD <i>Wyle ST&E/NASA JSC</i> | | |
| The Landscape of DNA and RNA Methylation Before, During, and After Human Space Travel | | Christopher Mason, PhD <i>Cornell University</i> | | |
| Immunome Changes in Space | | Emmanuel Mignot, PhD <i>Stanford University</i> | | |
| Proteomic Assessment of Fluid Shifts and Association with Visual Impairment and Intracranial Pressure in Twin Astronauts | | Brinda Rana, PhD <i>University of California</i> | | |
| Biochemical Profile: Homozygous Twin control for a 12 month Space Flight Exposure | | Scott Smith, PhD <i>NASA/JSC</i> | | |
| Longitudinal Integrated Multi-Omics Analysis of the Biomolecular Effects of Space Travel | | Michael Snyder, PhD <i>Stanford University</i> | | |
| Metagenomic Sequencing of the Bacteriome in GI Tract of Twin Astronauts | | Fred Turek, PhD <i>Northwestern University</i> | | |
| Investigations Completing 6-Month Mission Duration In-Flight Operations in Fiscal Year 2015 | | | | |
| Physiological Factors Contributing to Changes in Postflight Functional Performance | FTT | Jacob Bloomberg, PhD <i>NASA/JSC</i> | 13 Shuttle 13 ISS | 7 Shuttle 14 ISS |
| Assessment of Operator Proficiency following Long-Duration Spaceflight | Manual Control | Steven Moore, PhD <i>Mount Sinai School of Medicine</i> | 8 | 8 |
| In-flight Demonstration of Portable Load Monitoring Devices – Phase I: XSENS ForceShoe™ | Force Shoes | Andrea Hanson, PhD <i>NASA/JSC</i> | N/A | N/A |

INTERNATIONAL SPACE STATION MEDICAL PROJECTS ELEMENT

| Investigation Title | Ops Title | Investigator | Subjects | |
|---|------------------------------|--|----------|------------------------------------|
| | | | Required | Participation Through Increment 44 |
| Behavioral Issues Associated with Long Duration Space Expeditions: Review and Analysis of Astronaut Journals | Journals | Jack Stuster, PhD <i>Anacapa Sciences, Inc.</i> | 10 | 11 |
| Investigations Initiating Flight Development Activities in Fiscal Year 2015 | | | | |
| Dose Tracker Application for Monitoring Crew Medication Usage, Symptoms and Adverse Effects During Missions | Dose Tracker | Virginia Wotring, PhD <i>Baylor College of Medicine</i> | 24 | 0 |
| Functional Immune Alterations, Latent Herpesvirus Reactivation, Physiological Stress and Clinical Incidence Onboard the International Space Station | Functional Immune | Brian Crucian, PhD <i>NASA/JSC</i> | 10 | 0 |
| Testing Solid State Lighting Countermeasures to Improve Circadian Adaptation, Sleep, and Performance During High Fidelity Analog and Flight Studies for the International Space Station | Lighting Effects | George Brainard, PhD <i>Thomas Jefferson University</i> Steven Lockely, PhD <i>Brigham and Women's Hospital</i> | 6 | 0 |
| Medical Consumables Tracking | Medical Consumables Tracking | John Zoldak <i>Zin Technologies/NASA GRC</i> | N/A | N/A |
| Inflight Pharmacokinetic and Pharmacodynamic Responses to Medications Commonly Used in Spaceflight | RX Metabolism | Virginia Wotring, PhD <i>Baylor College of Medicine</i> | 6 | 0 |

FLIGHT ANALOGS PROJECT

FY2015 Activities and Accomplishments

During the past year, the Flywheel portion of the 70-day Countermeasure and Functional Testing (CFT-70) ongoing bed rest study, initiated in 2012, was completed. This study, consisting of eight independent research studies each with individual goals, operated as one integrated research campaign. This maximized the scientific return from one group of test subjects, and minimized the overall amount of resources required.

In addition, a new bed rest study requiring 18 subjects was initiated in late FY2014 before the FARU was closed on December 31, 2014. This study focused on

the role of vascular compliance and increased dietary intake of sodium in the visual impairment/intracranial pressure syndrome. Subjects underwent 14 days of head-down tilt bed rest with half of the subjects being exposed to a diet higher in salt. Results from this study will demonstrate how an increased-sodium diet and vascular compliance are linked to changes in ocular structure and function.

Investigations at the FARU in Fiscal Year 2015

| Investigation Title | Investigator | Subjects | | |
|---|--|----------|---------------------------|---|
| | | Required | Completed prior to FY2015 | Completed in FY2015 |
| Physiological Factors Contributing to Postflight Changes in Functional Performance: Bed Rest Analog Study (FTT) | Jacob Bloomberg, PhD NASA/JSC | 24 | 21 | 3 |
| Integrated and Resistance and Aerobic Training Study - Bed Rest (iRATS) | Lori Ploutz-Snyder, PhD USRA | 24 | 21 | 3 |
| Automated Detection of Attitudes and States through Transaction Recordings Analysis (AD ASTRA) Bed Rest Analog | Christopher Miller, PhD Smart Information Flow Technologies | 15 | 12 | 3 |
| Integrated and Resistance and Aerobic Training Study - Bed Rest (iRATS) with Flywheel | Lori Ploutz-Snyder, PhD USRA | 8 | 5 | 3 |
| FAP Standard Measures | Ronita Cromwell, PhD USRA | N/A | 13 | Collected on all long-duration subjects |
| Vascular Compliance | Steven Platts, PhD NASA/JSC | 18 | 4 | 8* |

*Eight subjects were studied before FARU closing. This investigation has been selected for flight and awaits mission assignment.

FARU Project Ends Operations After More Than 10 Years of Bed Rest Analog Research

December 2014 marked the conclusion of HRP's support of the Flight Analog Research Unit (FARU) at the University of Texas Medical Branch (UTMB) in Galveston, Texas. FAP was formed in 2004 primarily to establish and operate the FARU as part of the Human Health Countermeasures (HHC) Element. The project transitioned to be part of the ISSMP Element in FY2013.

Since the FARU's first study began data collection in August 2004, more than 160 subjects utilized the bedrest facility for studies lasting from a few days up to 3 months. All campaigns included a complement of principal investigator science as well as HHC Standard Measures. The table on the following page shows all campaigns performed at the FARU since 2004.



A Tendon Reflex test is performed on a bedrest subject in the NASA Flight Analog Research Unit (FARU) at University of Texas Medical Branch in Galveston, Texas.

Campaigns Conducted at the FARU

| Campaign | # of PI studies (up to) | Campaign Dates | | Subjects (N) |
|---|-------------------------|----------------|--------------|--------------|
| | | From | To | |
| Campaign 1: Immune Function and Steroidogenesis during Long-Duration Bed Rest | 2 | Aug 30, 2004 | Nov 21, 2004 | 3 |
| Campaign 3: Gender Differences | 6 | Feb 20, 2005 | Apr 14, 2010 | 23 |
| Campaign 2: Artificial Gravity Pilot Study | 6 | Feb 5, 2006 | Dec 23, 2006 | 15 |
| Campaign 5: Retention of Skeletal, Musculature and Postural Status with a Non-Invasive, Extremely Low Level Mechanical Signal: A Ground-Based Evaluation of Efficacy (C5: Vibe) | 1 | Apr 30, 2006 | Dec 23, 2007 | 18 |
| Lunar Analog Feasibility Study (Part 1 and 2) | 1 | May 13, 2008 | Jul 13, 2009 | 19 |
| Head Down Tilt 30-day | 4 | Oct 13, 2009 | May 13, 2010 | 12 |
| Campaign 9: Daily Bone Load Stimulus Study (C9: DBLS) | 3 | May 3, 2010 | May 21, 2010 | 0 |
| Integrated Resistance and Aerobic Training Study: 14-Day Bedrest Feasibility Study (iRATS14) | 2 | Nov 9, 2010 | Apr 27, 2011 | 9 |
| Campaign 17: Alternative Compression Garment Study (C17: ACG) | 2 | May 11, 2011 | Feb 12, 2012 | 16 |
| Campaign 11: Countermeasure and Functional Testing in Head-Down Tilt Bed Rest (C11: CFT70) | 8 | Jun 16, 2011 | May 7, 2014 | 29 |
| Campaign 11: Countermeasure and Functional Testing in Head-Down Tilt Bed Rest with Flywheel (C11: CFT70-Flywheel) | 7 | Nov 26, 2013 | Dec 18, 2014 | 8 |
| Effects of Long Duration Spaceflight on Venous and Arterial Compliance in Astronauts (NAVC) | 1 | Aug 26, 2014 | Dec 31, 2014 | 11 |

Comparison Report of Analog Capabilities: NEEMO and HERA

The NEEMO mission in July 2014 offered HRP a unique opportunity to perform a cross-analog comparison of NEEMO and HERA. A subset of seven studies previously conducted in both HERA and NEEMO were used to compare the two analog environments. The facility comparison that follows gives HRP insight into the similarities and differences between these two unique analogs, and the results can be used to guide the future implementation of HRP research.

Analog Comparison Study Findings

| | HERA Campaign 1 (7 Days - 2014) | NEEMO 18 (9 Days - Jul 2014) |
|-------------------|--|--|
| Research Focus | Research requirements and needs were prioritized; typically ensures good data return | Research was secondary and results in occasional loss of data or lack of compliance; data may not meet needs |
| Operational Focus | Operations simulated; crews seemed to take operational task performance less seriously | Operations were priority; work taken seriously and tasks treated as 'real' |
| Facility Fidelity | Reported at a similar level to NEEMO | Reported at a similar level to HERA |

INTERNATIONAL SPACE STATION MEDICAL PROJECTS ELEMENT

| | HERA Campaign 1 (7 Days - 2014) | NEEMO 18 (9 Days - Jul 2014) |
|---------------------------------|--|--|
| Crew Fidelity | Lower fidelity; astronaut-like enough to meet research needs | Primary benefit of NEEMO is astronaut participation; allows for more confidence in generalizability of results |
| Predictability of Access | Very predictable access allows longer term planning and more complex research designs | One-off missions focus on feasibility assessment and feedback, general case-study |
| Training Access | Higher level of access pre-mission; credited for higher compliance | Very limited access; questions about adequate time for training on research |
| Performance Data | Objective and subjective data available | Unavailable |
| Personnel Support | Reported high levels of support before, during, and after mission | Lower level than HERA; focus is operational needs; occasionally at expense of research |
| Technical Integration | Reported at a similar level to NEEMO | Reported at a similar level to HERA |
| Mission Input | Capability to introduce stressors, interventions, and manipulations to meet research needs | Very limited, generally unable to introduce manipulations, limited to existing operational scenario |

Completion of Second HERA Campaign

In FY2015, FAP completed its second HERA campaign of four 2-week missions. In this campaign, 12 studies and two operational tools were integrated. They examined teamwork, habitability, stress, fatigue, sleep deprivation, psychological and cognitive state, communication delays, sensorimotor function, and dietary and human factors reporting tools.

Each HERA mission consists of a crew of 4 subjects who participate in a high-fidelity exploration spaceflight analog mission. The mission scenario and tasking are highly crewmember-immersive and simulate the workload and pace of operations on the ISS and what would be expected during a long-duration exploration mission.



HERA Campaign 2 consisted of four 2-week missions simulating research and maintenance activities typical of spaceflight.

FY2015 Investigations Conducted in HERA

| Ops Name | Investigation Title | Investigator |
|---|---|---|
| Cognition | Individualized Real Time Neurocognitive Assessment Toolkit for Space Flight Fatigue | Mathias Basner, MD, PhD University of Pennsylvania |
| Workload Scale / Task Journaling | Using Real-Time Lexical Indicators to Detect Performance Decrements in Spaceflight Teams: A Methodology to Dynamically Monitor Cognitive, Emotional, and Social Mechanisms that Influence Performance | Eduardo Salas, PhD University of Central Florida |

INTERNATIONAL SPACE STATION MEDICAL PROJECTS ELEMENT

| Ops Name | Investigation Title | Investigator |
|-------------------|---|--|
| Team Role | Dynamic Team Role Allocation in Long Duration, Exploration Missions: Identification of Roles, Triggers, and Measurement Tools | Eduardo Salas, PhD <i>University of Central Florida</i> |
| Team Cohesion | Measuring, Maintaining, and Regulating Teamwork for Long Duration Missions in the Human Exploration Research Analog (HERA) | Steve Kozlowski, PhD <i>Michigan State University</i> |
| OCR | Optical Computer Recognition of Stress, Affect and Fatigue During Performance for Spaceflight | David Dinges, PhD <i>University of Pennsylvania</i> Dimitris Metaxas, PhD <i>Rutgers University</i> |
| Comm Delay | Protocols for Asynchronous Communication in Space Operations: Communication Analysis and Experimental Studies | Ute Fischer, PhD <i>GA Institute of Technology</i> |
| TPT | Development of an Objective Behavioral Assay of Cohesion to Enhance Composition, Task Performance, and Psychosocial Adaptation in Long-Term Work Groups | Peter Roma, PhD <i>Institute of Behavior Resources</i> |
| DebriefNow | Composing and Developing Resilient, Adaptive, and Self-Sustaining Teams for Long Duration Space Exploration | Scott Tannenbaum, PhD <i>Group for Organizational Effectiveness</i> |
| iSHORT | Habitability Ground and Analog Testing | Sherry Thaxton, PhD <i>Lockheed Martin</i> |
| Nutrition Tracker | Evaluation of the ISS Food Intake Tracker App | Sara Zwart, PhD <i>USRA</i> |
| Biomarkers | Biomarkers as Predictors of Resiliency and Susceptibility to Stress in Space Flight | Namni Goel, PhD <i>University of Pennsylvania</i> |
| Performance Task | Automation in Procedures: Guidelines for Allocating Tasks for Performance | Debra Schreckenghost, PhD <i>TRAClabs</i> |
| A2M | Advanced Acoustic Monitoring Characterization Study | Chris Allen, PhD <i>NASA</i> |
| Autonomy | Leadership Followership: Moving Beyond Traditional Leadership to Build Highly Functioning Autonomous Teams | Shawn Burke, PhD <i>University of Central Florida</i> |

‘Space Week in HERA’ Event Allows Astronauts to Evaluate Spaceflight Analog

In May 2015, four astronauts—two international and three with previous spaceflight experience—spent four days and three nights in HERA as an evaluation of the facility to support future training. In addition to conducting a series of tasks focused on ISS EVA operations, crew members engaged in seven hours of HRP-provided science and operational tools which yielded valuable feedback on their usability.

They also evaluated the fidelity of HERA as an analog for long duration missions and indicated that the

experience was similar to events encountered during an typical ISS increment. The Space Week in HERA event reinforced multiple elements of crew training using a realistic timeline and also provided crew members an opportunity to develop and practice expeditionary skills. The crew office is planning a second event in February 2016.

NSBRI Study Utilizes Unique :envihab Facility to Examine Cerebral Effects of CO₂

In FY2015, NSBRI deployed a team of American neurologists and scientists to conduct a two-week pilot demonstration experiment at :envihab, a newly built



A bedrest subject is examined in a head-down tilt orientation at the new :envihab facility in Germany. The facility allows for the study of subjects in a carbon dioxide enriched atmosphere.

specialized bedrest facility of the German Aerospace Center (DLR). The study, titled “Studying the Physiological and Anatomical Cerebral Effects of CO₂ and Tilt (SPACECOT), consisted of six male subjects and examined how the human brain adapts to increased levels of fluid inside the skull in combination with elevated CO₂ levels. These conditions may be experienced by astronauts living aboard the ISS and could be related to the vision changes that some crew have experienced. The study has implications for people on Earth who suffer from brain disorders, including elevated pressure on the brain.

Dorit Donoviel, PhD, NSBRI Deputy Chief Scientist and Industry Forum Lead, assembled the research team, led by Baylor College of Medicine neurologist Eric Bershady, MD. The team used state-of-the-art portable medical devices capable of monitoring brain physiology in real-time. These devices have the potential to transform brain health monitoring for patients on Earth. One such device is the Volumetric Induction Phase-Shift Spectroscopy (VIPS) device delivered by Cerebrotech Medical Systems.

The VIPS technology noninvasively and continuously monitors fluid shifts inside the brain that can arise from conditions such as progressive swelling or bleeding. Ornim Medical supplied a c-FLOW™ monitor, a noninvasive, continuous, real-time, easy-to-use brain blood flow monitor. Vittamed Corporation provided

a noninvasive quantitative absolute intracranial pressure meter.

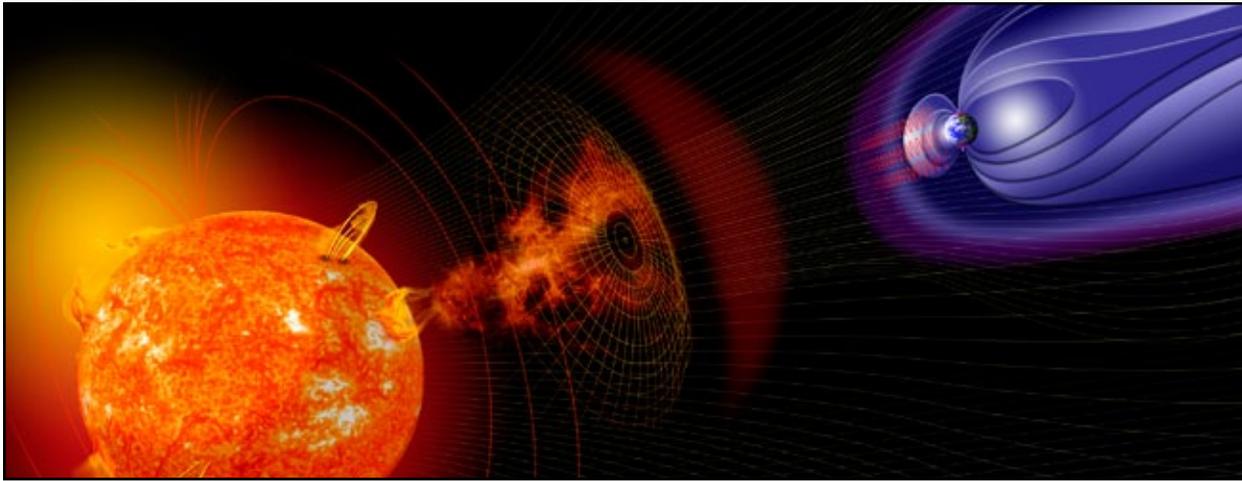
These innovative devices, along with sophisticated magnetic resonance imaging, will help detect neurological changes after prolonged exposure to simulated spaceflight conditions. In addition to the benefits of the research, this study was also valuable as an operational test of the :envihab facility, providing insight into how campaigns are managed at the facility as well as the unique capabilities of the facility such as providing CO₂ exposure. The insights gained and lessons learned will help inform future NASA bedrest and environmental studies planned for this facility.

FUTURE PLANS

The ISS and flight analog facilities will continue to play a critical role in the development, testing, and integration of both research investigations and hardware systems necessary to allow humans to further expand their presence in space. In FY2016, ISSMP looks forward to the conclusion of the NASA one-year mission and Twins Study on ISS with support for postflight operations.

FAP is planning four 30-day missions in HERA and assessing several new facilities including the :envihab facility in Germany. The :envihab offers several unique capabilities such as controlled carbon dioxide delivery systems, which may prove key in understanding the vision impairment/intracranial pressure syndrome, as well as a short-radius centrifuge that can be utilized in many different research areas. Also under evaluation are a number of analogs that can provide long-duration, isolated, confined, and controlled conditions, potentially including several Antarctic sites.

As the ISS Program transitions to commercial spaceflight to the ISS and support of larger crews, the ISSMP is uniquely positioned to support research studies, certify flight hardware, train crewmembers, and integrate the research required, to enable the safe exploration of space.



Overview

The Space Radiation (SR) Element is responsible for ensuring that crewmembers can safely live and work in space without exceeding acceptable radiation health risks. Outside the protection of Earth's magnetic field, space radiation can become a serious hazard to humans. The main sources of space radiation are galactic cosmic rays (GCRs), trapped particles that consist of protons and electrons trapped in Earth's magnetic field, and solar particle events (SPE). GCRs permeate interplanetary space and include high-energy, charged nuclei of elements ranging from hydrogen to iron.

At the cellular and tissue levels, these particles cause damage that is largely different from the damage caused by terrestrial radiation, such as X-rays or gamma-rays, because of their significantly greater ionizing power. Because of this difference, there are large uncertainties in quantifying biological response. Shielding against GCRs is much more difficult than shielding against terrestrial radiation because of the large masses required to stop primary GCR particles in space and the secondary particles generated in the shield material.

Health risks from space radiation may include an increased incidence of cancer, acute radiation syndrome, degenerative tissue damage manifested as health prob-

lems such as heart disease and cataracts, and early and late central nervous system (CNS) damage. Cancer risks pose the largest challenge for exploration. The uncertainties in cancer risk projection have large impacts on exploration mission designs, and they can affect NASA's ability to accurately assess mitigation measures such as shielding and biological countermeasures. There are also uncertainties about the dose thresholds, effects of radiation quality, and latency and progression rates for risks involving the CNS and cardiovascular system, that will affect mission designs. Research is needed to optimize radiation protection practices and countermeasures to prevent acute radiation syndromes from SPE.

Space Radiation study results contribute to human exploration by providing a scientific basis to accurately project and mitigate health risks from space radiation. Research in radiobiology and physics guides and supports risk assessment and protection strategies. The results provide tools for evaluating shielding recommendations for habitats and vehicles, as well as requirements for storm shelters and early warning systems for SPE. To read more about the Space Radiation Element, please visit: <http://www.nasa.gov/hrp/elements/srpe>

FY2015 Activities and Accomplishments

The Space Radiation Element completed another suc-

successful year of high-quality hypothesis-driven research through the efforts of many outstanding investigators across the country. Numerous experiments were conducted at the NASA Space Radiation Laboratory (NSRL) with support from a dedicated NSRL science staff. NSRL also served as the training site for the next generation of researchers at the 12th Annual Summer School. The 26th Annual Investigators' Workshop was completed, and the Central Nervous System Working Group was established to enhance the sharing of scientific research results and collaborations.

New research and investigators were selected from responses to the Human Exploration Research Opportunities (HERO). These researchers will work on understanding and mitigating the risks of cancer, cardiovascular disease, and in-flight and late effects on the central nervous system as well as systems biology and genomics, and validation experiments for the galactic cosmic ray simulator under construction at NSRL. Three new NASA Specialized Centers of Research (NSCOR) were selected to study the risks of cancer and adverse behavioral and cognitive outcomes as a result of exposure to space radiation.

Collaborative efforts continued with the Behavioral Health and Performance (BHP) and Human Health and Countermeasures (HHC) Elements to understand the combined effects of spaceflight on the central nervous system that affect behavior and the risk of cardiovascular disease and immune dysfunction.

In addition, a new website was developed to enhance scientific output by promoting the sharing of tissue samples that have already been irradiated, collected, and stored at principal investigators' institutions. In the future, SR will facilitate tissue sharing of samples to be collected, with arrangements planned before scheduled NSRL runs.

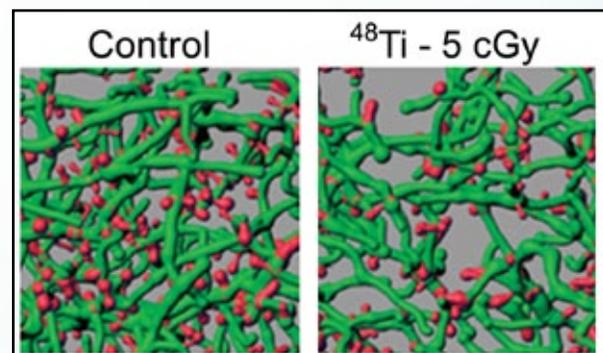
Facility upgrades at the NSRL to better simulate the mixed ion field of space are underway to support the future identification and validation of countermeasures against the risks of space radiation exposures.

SR also conducted three workshops focusing on galactic cosmic ray (GCR) simulation at the NSRL. The first workshop, held at NASA Langley Research Center, included physicists and radiobiologists from a variety of institutions. A second occurred during the NASA Space Radiation Investigators' Workshop and included participants from a broader variety of institutions. A third workshop, held at the Radiation Research Society meeting in Weston, Florida, was devoted to the issue of GCR simulation.

A NASA Technical Report was published, and two additional papers are being considered for publication in the journal *Life Sciences in Space Research*. The first paper outlines the technical requirements for a GCR simulator, and the second paper addresses broader issues that pertain to GCR simulation, such as the appropriate biology experiments and the advantages and disadvantages of GCR simulation.

NSRL Beam Campaigns Advance Radiobiological Research

Research conducted at the NSRL increases SR's understanding of the link between ionizing radiation and cell damage. Cells that are damaged and mutated by radiation exposure may affect astronaut health and performance. High-energy heavy-ion beams simulate the space radiation environment and SPE, and the facility is uniquely suited for ground-based research in space radiobiology, shielding, and dosimetry.



Exposure of mice to 50 milliGray doses of titanium ions results in a profound reduction of dendritic branches (green) and spines (red) 8 weeks after whole body irradiation.

In FY2015, the NSRL science team and Space Radiation-funded principal investigators completed three successful beam campaigns. During these campaigns, 86 investigator teams conducted experiments on 11,000 biological specimens, including tissues and cells, and the facility provided more than 1000 hours of use. The results of the investigations are published in over 75 peer-reviewed articles in major journals such as *Cancer Research*, *Oncogene*, *Radiation Research*, *Stem Cells*, *Clinical Center Research*, *Journal of Neuroscience*, and *Neurology*.

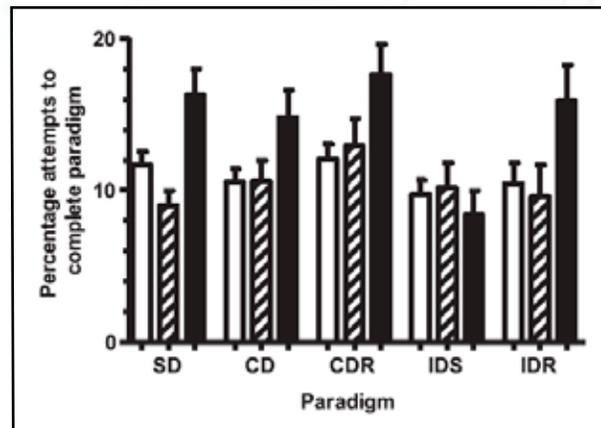
Studies Look at Behavioral Changes Associated with Radiation-Induced CNS Damage

CNS research led by Charles Limoli, PhD, University of California, Irvine, indicates that doses of space-like charged particles as low as 50–100 milliGray elicit robust, persistent changes in neuron structure and synapse number that reduce connectivity of neural networks.

Additionally, a study by Richard Britten, PhD, Eastern Virginia Medical School, showed these doses are associated with impairment of memory processes linked to the hippocampus and prefrontal cortex, as measured by “novel object recognition” and “object in place” behavioral tests. Socially mature male rats exposed to 1 GeV/n iron particles exhibited impairments in four out of five complex tasks in the “attentional set shift” battery three months after exposure.

Research findings by Patric Stanton, PhD, New York Medical College, have also highlighted the reduction of new adult neurons in the hippocampus and alterations in electrical properties of neurons associated with excitability and synaptic strength control, which may also impair neuronal network performance on mission timescales. The significance of these results to the morbidity of astronauts has not been explained but underlying structures and mechanisms share strong similarities between animal models and humans.

The CNS Evidence Report “Risk of Acute and Late



Socially mature male rats exposed to iron particles exhibited impairments in performing complex tasks. White bars are controls while hatched and black bars represent exposed rats.

Central Nervous System Effects from Radiation Exposure” was updated from the previous 2009 version and will be reviewed by the HRP Standing Review Panel in December 2015 before public release. A CNS Working Group was formed to consider in-flight and late effects on astronaut behavior and performance from exposure to the heavy ions found in space. The working group includes BHP personnel to facilitate the understanding of how radiation-induced changes might interact with behavioral disturbances caused or exacerbated by other space flight factors such as isolation, confinement, and sleep deprivation.

A commentary entitled “Potential for Central Nervous System Effects from Radiation Exposure During Space Activities Phase I: Overview” has been prepared by an expert panel of the National Council on Radiation Protection and Measurements. It is under final review and establishes expert opinion on the current status of evidence and strategies for estimating human risk. Based on this commentary, a Phase II full report will follow.

Together, these analyses will inform the process of risk estimation for CNS, which may require strategies different from the well-developed methods used to estimate the Risk of Exposure Induced Death (REID), applicable to cancer and other mortality risks.

New Web-Based Messaging Forum Expands Tissue-Sharing and Data Exchange

Space radiation research has developed a large body of experimental results describing the effects of high-linear energy transfer (LET) radiation on biological endpoints. Proposed studies are highly desirable when they make use of existing data sets that are directly relatable to past data sets and use existing tissue samples. To facilitate the use of existing or future data sets, SR has established an online messaging forum to promote radiobiological tissue sharing.

The Tissue Sharing Forum provides access to a database of investigator-stored tissue samples and enables both SR members and NASA-funded investigators to exchange information about stored and future radiobiological tissues available for sharing. Radiobiological investigators provide preliminary tissue information and the site administrator works with respective laboratories to keep the inventory list updated.

Investigators may use the messaging forum to review online data of available tissues, inquire about tissues posted, or request tissues for an upcoming study using an online form. Users are also strongly encouraged to use the forum for open exchange of information and offering of tissues. The forum also promotes group discussions and fosters collaboration for cost-effective tissue-sharing opportunities within SR.



The NASA Space Radiation Tissue Sharing Forum is an online messaging forum promoting tissue sharing and data exchange.

University Teams Collaborate Through the Center for Space Radiation Research (CSRR)

Deep-space travel is associated with exposure to space radiation, including protons and heavy ions that are moving at significant fractions of the speed of light and are therefore difficult or impossible to shield against. While high doses of protons are known to cause adverse acute health effects, the risk of acute effects from low proton doses is largely unknown. In addition, recent evidence from radiation exposures on Earth suggests that the heart and vasculature are more sensitive to ionizing radiation than was previously thought. These findings have raised concern about potential adverse cardiovascular effects from exposure to protons and heavy ions during deep-space exploration missions.

The NSBRI-led CSRR consists of teams drawn from four universities who are working to identify the acute health effects of low-dose proton exposures, as well as the cardiovascular health effects from protons and heavy ions. For the acute-effects studies, male mice were exposed to low doses of protons, which caused an increase in apoptotic, or programmed, cell death in the retina of the eye. The CSRR plans to next examine whether protons modify the retinal vasculature. Current investigations also include acute effects in the skin, bone marrow, and heart tissues.

The CSRR also studies degenerative effects on tissue, and has shown a reduction in numbers of bone marrow stem cells at two weeks after exposure to oxygen ions in a mouse model. Changes were also observed in the expression of hundreds of proteins in the heart at two weeks after exposure to 'light oxygen' or ¹⁶O ions. Alterations in cardiac function were also measured with high-resolution ultrasound three months after exposure. In addition, exposure to oxygen ions altered several markers of endothelial function in mouse heart and retinal endothelial cells in culture.

The CSRR is currently examining the effects of oxygen ions on the retinal vasculature, function and struc-

ture of the heart, and epigenetic changes in DNA, at time points up to nine months after irradiation. Lastly, the team members are measuring metabolites in urine samples as potential biomarkers of radiation exposure.

FUTURE PLANS

The effects of space radiation on astronauts represent a major limiting factor for long-duration human space missions beyond low Earth orbit. Of greatest concern are the effects of GCR from hydrogen to nickel in the approximate energy range of 10 MeV/n to 50 GeV/n.

To study the effects of GCR on biological systems, an active program involving facility and controls upgrades is underway at NSRL. Typical experiments have involved the use of single-ion beams at fixed energies; however, heavy-ion accelerator technology has now become feasible to accelerate a variety of beams with differing energies, with beam switching times sufficiently small to allow approximate simulation of the GCR spectrum. Such a simulation can take into account the important effects of light ions—defined as isotopes of hydrogen and helium—that are a major contributor to space radiation dose equivalent.

Upgrades required to simulate the GCR spectrum include the ability to produce a rapidly switchable ion source capable of delivering 6 to 12 ion species to the

experimental area. Magnets in the beam line will also be upgraded to deliver beams at 1.5 GeV/nucleon to better represent the energies in the natural GCR, and a reference field will be defined to include the rapid switching of H, He, O, Si, and Fe ions over multiple energies and to use well-designed absorbers. The laser ion source that generates ions for acceleration has been installed and is currently being used.

The facility modifications for high-energy research up to 1.5 GeV per nucleon were completed in FY2015. Additionally, the modifications of controls to enable rapid switching between ion species will be completed and tested in FY2016. More detailed descriptions of the field characteristics will be made available on the NSRL website as the upgrades progress.



In FY16, the NSRL will finish installation of new magnets allowing for beams up to 1.5 GeV/n.



Overview

NASA uses the term “countermeasures” to describe the strategies to keep astronauts healthy and productive during space travel and return to Earth. The Human Health and Countermeasures (HHC) Element is responsible for understanding the normal physiologic effects of spaceflight and developing countermeasures to those with detrimental effects on human health and performance. HHC provides the biomedical expertise for the development and assessment of medical standards, vehicle and spacesuit requirements, and countermeasures that ensure crew health during all phases of flight.

Preflight countermeasures involve physical fitness and exercise, and physiologic adaptation training. In-flight countermeasures include nutritional health, physical fitness, pharmaceuticals, and sensorimotor training protocols. Postflight countermeasures target rehabilitation strategies. Before they are flight-tested, candidate countermeasures and technologies are developed and refined using ground-based studies.

The HHC is composed of five portfolios: Vision and Cardiovascular, Exercise and Performance, Multi-System, Bone and Occupant Protection, and Technology and Infrastructure. To learn more, please visit: <http://www.nasa.gov/hrp/elements/hhc>.

FY2015 Activities and Accomplishments

In FY2015, HHC research contributions continued to add to the knowledge base addressing HRP risks. The science output, in terms of publications, consisted of 48 papers in peer-reviewed international science journals. About 2/3 of these articles were judged to have medium to high impact on the evidence base for HRP risks. Some of the publications with the greatest impact on the evidence base included: medication use by ISS crewmembers; the relationship between genotype, B-vitamin status, and spaceflight-induced ophthalmic changes; blood and fluid shift to the heart during spaceflight and the impact of this shift on circulation and blood pressure; definition of the optimal effect on blood pressure of the pre-landing fluid and salt loading procedure to mitigate postflight orthostatic intolerance; development of a hypobaric treatment model for decompression sickness; determination of which types of exercise are associated with prediction of astronaut fitness for spaceflight mission tasks; and mechanical loading as a countermeasure against radiation induced bone loss.

A paper published in the *Nature Microgravity* journal showed immune system alterations persist during long-duration spaceflight and this phenomenon, in the absence of appropriate countermeasures, has the potential to increase specific clinical risks for crewmembers during deep-space missions. The Pi-

lot Field Test, a study of neurovestibular and sensorimotor disturbances that occur immediately after return from the ISS, completed data collection in 18 crewmembers.

Another highlight in FY2015 was the completion of the first in-flight session in the Fluid Shift study using lower-body negative pressure on the ISS. Among HHC ground-based studies, data collection in the Energy Mobility study was completed. The data collected in Energy Mobility were repeated measures of metabolic costs of functional tasks in six different subjects in three different prototype spacesuits.

Finally, HHC advanced four compact exercise concepts for potential use in the Multipurpose Crew Vehicle for the EM-2 mission, scheduled to be the first crewed mission of Orion. The devices need to weigh less than 23 pounds and provide up to 350 pounds of resistance exercise and an aerobic exercise mode. A final selection of devices for further design maturation will occur in January 2016. An exercise concept for a Mars mission, the Hybrid Ultimate Lifting Kit (HULK), was demonstrated successfully on a parabolic flight. Highlights can be seen at: <https://www.youtube.com/watch?v=4j4n0Xr-LjQ>

VISION AND CARDIOVASCULAR PORTFOLIO

FY2015 Portfolio Overview

A variety of flight and ground studies in HHC's Vision and Cardiovascular Portfolio continue to explore changes in the eye, brain, and cardiovascular system that are hypothesized to result from spaceflight exposure. The Portfolio's three active flight studies—Fluid Shifts, Ocular Health, and Cardio Ox—are generating interesting preliminary data.

The Fluid Shifts experiment is quantifying body fluid redistribution before, during, and after spaceflight and testing for relationships between those findings and ocular changes. The study also investigates the ability of lower-body negative pressure (LBNP) to re-

verse or diminish the ocular and vascular effects of the headward fluid shift that occurs during microgravity.

The Ocular Health study is documenting the time course of observed structural and functional changes in the eyes over the preflight, in-flight, and postflight timeline and seeks to understand the long-term impact of spaceflight on ocular health.

The Cardio Ox investigation will investigate the effects of long-duration spaceflight on measures of oxidative and inflammatory stress and on measures of arterial structure and function to determine whether these changes are related. Cardio Ox is the first study of its kind to monitor the vascular status of astronauts for up to five years after their long-duration spaceflight mission.

Noninvasive Vittamed Meter Validated for Measurement of Intracranial Pressure (ICP)

NASA considers the visual impairment intracranial pressure (VIIP) syndrome a critical health risk for astronauts. This syndrome, which is associated with exposure to microgravity, manifests with changes in visual acuity and eye structures. In some cases, post-flight cerebrospinal fluid pressure—as measured by invasive spinal tap—was found to be elevated, suggesting that astronauts exhibiting this syndrome may have elevated intracranial pressure (ICP).



Principle Investigator Dr. Eric Bershad and a test subject demonstrate use of the Vittamed device while astronaut Dr. Mike Barratt observes.

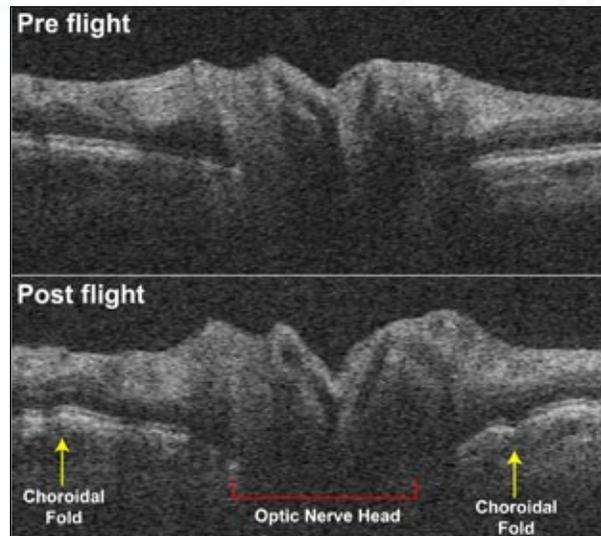
NASA seeks a safe, noninvasive method to quantitatively measure ICP in astronauts during spaceflight. To this end, NSBRI evaluated several emerging medical technologies and identified a promising device that uses ultrasound waves transmitted through the eye through a closed eyelid. The Vittamed ICP meter was invented in Lithuania and brought to the U.S. to be clinically evaluated. Eric Bershad, MD, and his team of neurocritical care specialists compared ICP values obtained by the Vittamed and simultaneous standard-of-care invasive pressure measurement with lumbar puncture.

Measurements made by the Vittamed meter had good agreement with those made by invasive methods across a wide range of skull pressures. A miniaturized version of the device is now approved for clinical use in the European Union, and Food and Drug Administration (FDA) approval is in progress. Not only will this technology be useful in monitoring brain pressures during spaceflight, but it will also be useful for patients on Earth.

Postflight Ocular Changes Demonstrated in OCT Study

After long-duration microgravity exposure, astronauts return with varying degrees of optic disc swelling and folds at the outer vascular layer of the retina. These changes at the back of the eye are clinically observed using ophthalmoscopy, but quantification based on these methods is subjective and variable. With clinical instrumentation such as optical coherence tomography (OCT), the back of the eye can be imaged and quantified with good repeatability.

The purpose of this study led by Dr. Nimesh Patel, from the University of Houston, was to quantify thickness changes of the optic nerve head (ONH) and surrounding retinal tissue in astronauts after long-duration ISS missions. Pre- and postflight OCT scans of 15 ISS astronauts were analyzed using custom software. For the astronauts studied, the total retinal thickness at the ONH, and up to 500 micrometers



An OCT image of the optic nerve of one astronaut, pre- (top) and postflight (bottom). Note the increase in thickness within the optic nerve head region and appearance of choroidal folds.

from the ONH rim margin, was thicker postflight. Similarly, in the same region there was an increase in thickness of the retinal nerve fiber layer, a layer containing cells whose axons are part of the optic nerve. Although there was thickening at the ONH, the position of the ONH relative to the surrounding tissue was deeper postflight.

Of the 30 eyes analyzed, only seven had greater than mild choroidal folds. These results would suggest that with microgravity exposure, mechanical forces on the optic nerve result in ONH edema and a thickening of the surrounding retinal tissue. Longitudinal studies are necessary to investigate the time course of these changes during flight, and resolution postflight, once astronauts are reexposed to gravity.

Volunteer Cancer Survivors Assist with Parabolic Flight Study of ICP

Astronauts experience changes in their vision during long-duration ISS missions. When humans stand upright on Earth, gravity pulls blood toward the feet, but when lying flat, blood distributes evenly throughout the body, especially toward the head. In a microgravity environment, the distribution of

blood is believed to shift slightly toward the brain. This hypothesis led NASA scientists to speculate that pressure inside the brain increases, causing compression and folding of the eye structures, which distorts vision. Moreover, it was thought that strength-based exercises and small increases in carbon dioxide in the ISS atmosphere would exacerbate the problem.

To begin to understand this complex issue, a team of NSBRI supported investigators performed a series of experiments that measured pressure inside the brain by accessing a special port placed in the heads of patients cured of leukemia. Pressure inside the brain was measured during changes in posture on Earth and during 0g parabolic flight. Measurements were also taken while subjects breathed increased carbon dioxide and during strength-based exercises.

These experiments showed that pressure inside the brain is quite low when one is sitting upright relative to lying flat on Earth. In microgravity, pressure inside the brain actually fell relative to when subjects lay flat on Earth, but remained substantially greater than the upright posture on Earth. Additional carbon dioxide did not affect pressure inside the brain. Strength-based exercise caused a dramatic rise in brain pressure when it was performed with a Valsalva maneuver; however, breathing in during the contraction proved a simple and effective countermeasure.

The ultimate conclusions from these experiments were that microgravity does not cause prolonged pathological increases in brain pressure. However, the absence of gravity on the ISS means that pressure inside the brain would be at a level that is persistently above the normal upright posture on Earth where humans typically spend two-thirds of the day.

Fluid Loading Study Published in *Aerospace Medicine and Human Performance Journal*

Understanding the effects of altered gravity on human cardiovascular function during spaceflight is of critical importance to the maintenance of astronaut



Pressure is measured inside the brain of a leukemia survivor during parabolic flight. The subject has an intraventricular catheter implanted in her brain for drug delivery during cancer treatment. Her volunteerism provides a unique opportunity to invasively measure ICP during microgravity conditions.

health and safety. When returning to Earth after extended exposure to weightlessness, some astronauts experience postflight orthostatic intolerance such as difficulty standing or light-headedness. The current countermeasure for postflight orthostatic intolerance is fluid loading, which restores lost plasma volume by having crewmembers ingest salt tablets and water before reentry.

HRP researchers at Ames Research Center conducted an experiment to better understand the effects of fluid loading on orthostatic intolerance and on the time course of changes in physiological response during head-down-tilt (HDT) simulated microgravity. The 16 study participants were subjected to two 6-hour exposures—with and without fluid loading—to HDT. Pre- and post-HDT stand tests of orthostatic tolerance were given. In addition, relevant physiological measurements were recorded: heart rate, blood pressure, peripheral blood volume, total peripheral resistance, and impedance cardiography. Echocardiography measures of stroke volume and cardiac output were also recorded. This study was led by Dr. Patricia Cowlings from the Ames Research Center.

The results showed that fluid loading produced significant increases in mean arterial pressure measured

between hours one and three of HDT. The results also showed that the best physiological indicator of susceptibility to fainting was a decrease in blood pressure at three hours after fluid loading. Nonsignificant trends of multiple cardiovascular responses showed similar time profiles.

These findings show that to minimize orthostatic intolerance, the optimal time for crewmembers to begin fluid loading is between one and three hours before reentry. The large amount of individual variability suggests that fluid loading alone may not be an adequate countermeasure for all crewmembers. These results are reported in the January 2015 issue of *Aerospace Medicine and Human Performance*.

EXERCISE AND PERFORMANCE PORTFOLIO

FY2015 Portfolio Overview

The Exercise and Performance Portfolio addresses risks such as impairment of crewmembers' control of the spacecraft and of their immediate exit from the vehicle because of sensorimotor alterations associated with spaceflight. Additionally, the Portfolio addresses the risk of reduced physical performance due to diminished aerobic capacity and impaired performance due to reduced muscle mass, strength, and endurance.

In FY2015, the Portfolio completed bed rest analog evaluation of the Multi-Mode Exercise Device (M-MED), with findings to inform requirements for advanced exercise concepts and their development for exploration missions. In addition, researchers concluded a key study, led by Dr. Thomas Barstow from Kansas State University, that will inform the establishment of a new minimum aerobic fitness threshold to complete mission tasks.

Flight and analog Functional Task Test (FTT) analyses revealed the importance of supplementing current in-flight exercise countermeasures with in-flight balance training.

Functional Task Test Study Complete and Final Report Submitted

FY2015 marked the completion of the FTT study and submission of the final report. The goal of the study, led by Jacob Bloomberg, PhD, of the JSC Neuroscience Laboratory was to determine the effects of spaceflight on performance of functional tests that are representative of critical exploration mission tasks and to identify the key physiological factors that contribute to decrements in performance.

The FTT consisted of seven functional tests and a corresponding set of interdisciplinary physiological measures targeting the sensorimotor, cardiovascular, and muscular adaptations associated with exposure to spaceflight. Shuttle and ISS crewmembers, as well as subjects who experienced 70 days of head-down-tilt bed rest—with and without exercise—were tested before and after spaceflight and bed rest. The bed rest analog allowed researchers to investigate the impact of body support unloading on performance, in the absence of alterations in vestibular function associated with spaceflight.

It was shown for all subjects that functional tasks having a greater demand for dynamic control of postural equilibrium showed the greatest decrement in performance. These changes in functional performance were paralleled by similar decrements in sensorimotor tests



Subject performing a functional task in the FTT study.

designed to specifically assess postural equilibrium control. Bedrest and spaceflight subjects experienced a similar pattern of deficits in functional tests with balance challenges and sensorimotor tests designed to evaluate postural stability, indicating that body support unloading experienced during spaceflight plays a central role in postflight alterations of functional task performance and balance control.

Bed rest subjects who performed a high-intensity interval-type resistance and aerobic training program—while still in bed—showed significantly improved lower-body muscle performance relative to bed rest controls and spaceflight subjects. However, resistive and aerobic exercise alone was not sufficient to mitigate decrements in functional tasks that require dynamic postural stability and mobility. These results demonstrate the importance of supplementing current in-flight exercise countermeasures with preflight sensorimotor adaptability training and in-flight balance training to mitigate decrements in balance and gait control.

Standardized Preflight Exercise Tests to Predict Performance During Lunar EVA

The spaceflight environment elicits a variety of physiological adaptations, such as spaceflight deconditioning, which manifests upon return to gravity and may inhibit a crewmember's ability to complete extravehicular activities (EVA). A concern with long-duration spaceflight is not only the ability of crewmembers to function while they are in space, but also their capacity to endure the physical demands on them at landing. Researchers considered two questions: Is the decreased aerobic exercise capacity after microgravity a primary concern for mission safety? Also, what is the minimum level of fitness required, particularly after long-duration missions, to complete EVA on a planetary body?

Scientists in the Department of Kinesiology at Kansas State University, led by Thomas Barstow, PhD, are studying what measurements best predict the ability



A test subject traverses a rock wall obstacle during the "Standardized 'Pre-flight' Exercise Tests to Predict Performance during Extravehicular Activities in a Lunar Environment" study.

of a subject to complete a series of tasks simulating those that an astronaut might engage in at a destination such as the Moon or Mars. Subjects completed a series of field tasks that included a 10-kilometer walk/run back, transfer of weighted cylinders, and a circuit consisting of 6 stations: ladder climb, agility cones, stair climb, rock wall climb, equipment lift, and step-entry where subjects stepped over hurdles and ducked under chest-level poles.

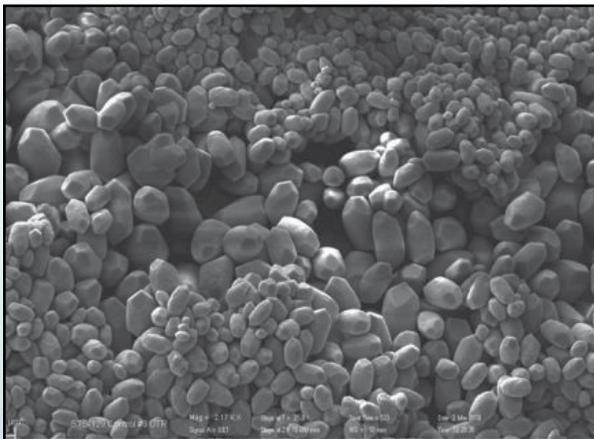
Laboratory tests revealed that the best predictors of performance time were critical speed and critical power for legs or arms followed by peak aerobic capacity (VO_{2max}). Critical speed and power represent the highest running and arm-crank exercise intensity that can be sustained for at least 20-30 minutes, and typically represent approximately 75-85% VO_{2max} . These results will help NASA form a new minimum aerobic fitness threshold for critical power, speed, and VO_{2max} , which may be used to evaluate astronaut physical capacity for these types of tasks.

Study Examines Effects of Microgravity on Mouse Inner Ear Otoconia

Mammals use the inner-ear otolith organs to detect gravity, and they use this information in spatial orientation and balance control. The otolith organs consist of ciliated mechanosensitive hair cells surmounted by biomineral crystalline deposits of calcium carbonate (CaCO_3) called otoconia, which provide mechanical loading of the hair cells. Because the density of otoconia is related to otolith sensitivity and their biomineralization is not static, changes in gravity load put them at risk of structural remodeling.

In a microgravity environment, such as spaceflight, it is argued that the organism counters loss of gravity by increasing CaCO_3 production, thereby increasing otolith mass, and this action is seen as an attempt to increase the “system gain.” Upon reentry into a gravity environment, this remodeling response is maladaptive and might have negative impacts on cognitive and functional performance of the crew, such as motion sickness; spatial disorientation; under- or overshooting when reaching for an object; gaze nystagmus associated with dizziness and vertigo; and decreased balance stability, including an inability to perform a simple heel-to-toe walk without falling.

The objective of the Otoconia study, led by Rich-



A scanning electron microscope image of rodent otoconia. These small crystallized deposits of calcium carbonate in the inner ear are crucial for balance control in mammals.

ard Boyle, PhD, at NASA ARC, was to investigate whether the structure of otoconia is remodeled by the intensity and duration of gravity loading. Electron microscopic and focused ion beam milling techniques were applied to images of the otoconia mass obtained from mice subjected to 90 days of ISS weightlessness, mice subjected to 90 days of 2g centrifugation on the ground, and mice flown on Space Shuttle missions STS-133 and STS-135.

Images from ISS showed a clear restructuring of individual otoconia with increased mineral deposition and mass, whereas their 2g counterparts showed a decrease in otoconial mass. Conversely, after the shorter Shuttle exposures to weightlessness the otoconia appeared to be normal. Therefore, long-duration exposure to spaceflight may induce adaptive mechanisms that lead to structural alterations in peripheral end-organ transduction of motion, contributing to performance disturbances.

Multi-Mode Exercise Device (M-MED) Validated During 70-Day Bed Rest Study

The Multi-Mode Exercise Device (M-MED) is an NSBRI prototype exercise device that allows both resistance and aerobic exercise using a single device. A unique aspect of the M-MED flywheel ergometer is its inherent design to generate resistance during both the lengthening and shortening components of exercise in a gravity-independent manner. In FY2015, a



A test subject performs a squat exercise using the M-MED prototype which allows for both aerobic and resistive exercises using a single device.

70-day head-down-tilt bed rest study was completed using the M-MED, and included a comparison of 34 bed rest subjects who performed no exercise with two other groups who exercised.

One of the exercise groups in the study performed traditional ISS-like exercise using a treadmill, cycle, and several resistance exercise machines. The other exercise group performed rowing and several resistance exercises, all on the M-MED. Subjects in the exercise groups exercised six days a week, with three nonconsecutive days of resistance and aerobic exercise alternating with three days of aerobic-only sessions.

Control—bed rest-only—subjects showed a relatively linear decline in VO_2 max during bed rest, resulting in an approximate 25% reduction immediately post bed rest. Both traditional exercise subjects and M-MED subjects showed an initial decline followed by an improvement such that by the end of the bed rest period they had returned to baseline. Control subjects showed a nearly linear decline in muscle cross-sectional area during bed rest, resulting in nearly a 10% decrease in quadriceps size and 26% decrease in calf size. Exercise and M-MED subjects maintained cross-sectional area of the upper leg, and mitigated calf loss relative to controls.

Initial results indicate that during bed rest the M-MED exercise program resulted in improved performance relative to controls on muscle strength, size and endurance, cardiovascular fitness, and balance and gait control. Importantly, these findings also indicate that M-MED training did not differ in effectiveness from the exercise performed on traditional equipment, suggesting that it is possible to use a single device to protect against muscle atrophy and cardiovascular deconditioning during long-duration exploration-class missions.

With respect to functional tasks, balance, and gait control, the M-MED subjects performed similar to or slightly worse than subjects performing traditional exercise. Therefore the flywheel holds promise, but

needs additional development before its capability to contribute to a sensorimotor countermeasure can be ascertained.

MULTISYSTEM PORTFOLIO

FY2015 Portfolio Overview

The HHC Multisystem Portfolio encompasses research on a diverse set of physiological system risks, including nutrition, immunology, pharmacology, extra vehicular activity (EVA), decompression sickness (DCS), and exploration atmosphere. Each discipline team focuses on identifying spaceflight impacts that contribute to the unified picture of intersystem dynamics and develops countermeasures aimed at increasing the quality of human health and performance during spaceflight.

Energy Mobility Study Provides Comparison of Three Future Suits

Spacesuit mobility is commonly verified by looking at the range of motion achievable at a single joint. While a person inside a spacesuit can achieve a given range of motion for a certain movement, this has limited predictability as to how they will perform during suited operations. The primary goal of the Energy Mobility study was to determine if a more functional test of mobility could be used as a complement to the isolated range-of-motion tests.

Investigators Jason Norcross of JSC's EVA Physiology Laboratory and Shane McFarland from JSC's Advanced Space Suit Laboratory measured energy expenditure of six suited subjects while performing physically demanding functional tasks including walking, stair climbing, sidestepping, and relocating objects.

Two prototype planetary surface EVA spacesuits the Mark III Technology Demonstrator (MKIII) and the Rear Entry I (REI) Suit were evaluated. An enhanced-mobility launch, entry, and abort suit, the Constel-



The Energy Mobility study measured energy expenditure during physical tasks as an indicator of suit mobility. Pictured here, a test subject in the MKIII suit is performs a functional task test which simulates typical motions.

lation Program Demonstrator (Demon), was also evaluated. Each subject performed the test battery two to three times per suit.

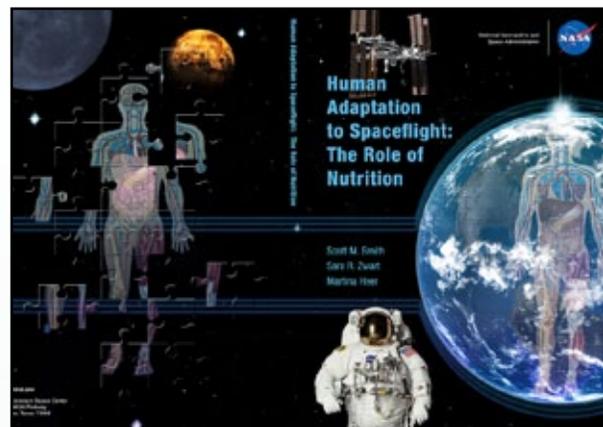
Initial results showed similar energy expenditure in the MKIII and REI, but the REI trended lower for the stair climb and sidestep because it was almost 30 pounds lighter. The Demon suit, the least mobile but lightest of the three, resulted in much higher energy expenditure for every task, indicating that suit mobility affects energy expenditure to a greater degree than suit mass.

These data will optimize future study designs using more costly but flight-like reduced-gravity analogs such as the Active Response Gravity Offload System and the Neutral Buoyancy Laboratory. Finally, results will inform a draft set of functional suit mobility requirements using time and energy expenditure as the outcome metrics of performance.

New Book Published by HRP – Human Adaptation to Spaceflight: The Role of Nutrition

In FY2015, HHC nutrition researchers published a textbook that provides readers with a comprehensive look at the role of nutrition in human adaptation to spaceflight. The approach of this book differs from a previous book published in 2009 by the same laboratory. The new book begins with an illustrated review of the tools used to evaluate nutritional status during spaceflight, including food intake tracking, body mass determinations, and methods for blood and urine collection. Each subsequent chapter highlights a physiological system, showcasing the role of nutrition in that system and what is known—or not known—about the interaction of those systems with nutrition data accumulated from years of spaceflight and ground analog studies. Topics include energy metabolism, muscle, bone, hematology, cardiovascular physiology, kidney physiology and renal stones, ophthalmology, immunology, oxidative stress, and pharmacology.

The book was published by and is available for purchase from the Government Printing Office, but is also available for free download from <http://www.nasa.gov/hhp/education>. Also available are PDFs of the 2009 book, *Nutritional Biochemistry of Space Flight*, and the *Space Nutrition* book aimed at intermediate school



Human Adaptation to Spaceflight: The Role of Nutrition cover, highlighting the nature of research, putting puzzle pieces together to see the larger picture.

students. These two textbooks provide an easily accessible version of the Nutrition Evidence Report, an HRP product reviewed by the Institute of Medicine. A significant addition to the new book is the inclusion of many findings from ISS research, in particular those from the Nutritional Status Assessment protocol completed last year.

■ BONE PORTFOLIO

FY2015 Portfolio Overview

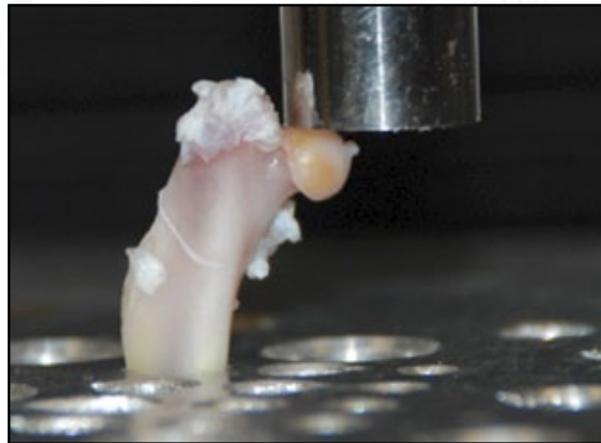
The Bone Portfolio pursues innovative methods to increase understanding of musculoskeletal adaptation to space by optimizing the use of modeling for fracture assessment and for bone mass, maximizing the use of preclinical studies, and exploring new measures of bone quality through the recently formed Finite Element Task Group.

An Intervertebral Disk (IVD) workshop convened in August of 2015 to share findings on multiple studies, including the corroboration of ultrasound and MRI imaging to characterize spaceflight-induced spinal changes, changes in spinal morphology and causal factors related to postflight back pain, and an increased risk of postflight disc herniation.

Benefits of Bisphosphonates May Extend to Later Microgravity Exposure

Bisphosphonates are prominent osteoporosis drugs used to treat postmenopausal women. A limited number of ISS crewmembers have taken bisphosphonates as part of musculoskeletal countermeasures. In general, the anti-resorptive effects of these drugs persist beyond treatment end. The current study was devised to utilize the well-established adult rat unloading ground-based analog to simulate two successive missions with bisphosphonates administered for only the first unloading exposure.

The primary goal of the study, led by Harry Hogan, PhD, from Texas A&M, was to test whether protec-



A new study used rodents and tested the strength of hip bones after administration of bisphosphonates. In the photo, the femoral neck region is stressed until failure to gauge bone strength.

tive effects of bisphosphonate treatment given during the first unloading period would extend to a second unloading exposure, with a period of reambulation recovery in-between. An additional goal was to compare two bisphosphonates, alendronate and zoledronate, in this two-mission scenario.

Rats were unloaded for 28 days, allowed to recover with weight bearing for 56 days, and then unloaded again for 28 days. Each animal was given a CT scan every 28 days during the study to monitor bone density and related variables. Results for bone density indicated that protective effects for both alendronate and zoledronate did indeed extend to the second unloading period, but to varying degrees. Zoledronate was much more potent than alendronate in not only mitigating or preventing losses, but also actually enhancing skeletal measurements above those of controls. This enhancement was most prominent for the first unloading exposure period.

Femur bones were harvested at the end of the study and loaded to failure in mechanical testing. Breaking strength of the femoral neck was higher for zoledronate-treated animals only, again reflecting the superior potency of this agent. In addition, bone cell activity was measured using fluorochrome labels, which allow calculation of bone formation rates. Bone formation

rates generally increase rapidly when unloaded animals return to weight bearing, but this response was dampened or delayed for the animals that had taken bisphosphonates. The main finding from this study is that bisphosphonate treatment generates protective effects that do indeed continue after administration of the drug ceases and extend into the second unloading period, but the risk-to-benefit ratio for astronauts is not yet defined.

Intervetebral Disc (IVD) Study Suggests Increased Risk of Postflight Spinal Injuries

A report published in 2010 highlighted a 4.3 fold higher incidence of Herniated Nucleus Pulposus (HNP) in astronauts and suggested that astronauts are at a greater risk for HNP compared to a non-flying, control population. Despite this evidence, it was not clear of the role that spaceflight played in physiological events that led to postflight injuries.

For optimal planning of exploration class missions, studies are required to describe changes to individual vertebral units of the back. Researchers seek an understanding of which changes are most likely to contribute to the risk, when the risk is most likely to occur and when an intervention is best implemented. The IVD Study successfully demonstrated the ability of an astronaut to use the current ISS ultrasound



An ISS crewmember performs a spinal ultrasound scan as part of the IVD study. Long duration spaceflight crews may be at an increased risk of postflight spinal injury.

unit, to generate real-time, diagnostic quality images of the intervertebral disc.

The pre- and postflight measures by the IVD Study revealed possible risk factors for postflight back injury and pain, which include muscle atrophy and increased fatigability, loss of spinal curvature, increased spinal bending stiffness, bony endplate irregularities and bone marrow inflammation.

Additionally, a data mining effort revealed 51 HNP cases in 330 astronauts from the last 50 years. This suggests an effect of spaceflight for increasing the risk of HNP in the first three months after spaceflight. The risk declines to background hazard levels by one year after return. Notably, while the causality of spaceflight to HNP is still an open issue, the data provide support for potential mitigation strategies and establishes a requirement for further data acquisition.

TECHNOLOGY & INFRASTRUCTURE PORTFOLIO

FY2015 Portfolio Overview

The Technology and Infrastructure Portfolio consists of three projects that augment the risk mitigation and countermeasure development of HHC. These three projects include the Advanced Exercise Concepts (AEC) Project, the Digital Astronaut Project (DAP), and the Artificial Gravity (AG) Project.

The AEC Project establishes requirements for exercise equipment to provide the countermeasures prescribed for astronauts within the constraints imposed by the space vehicle.

The DAP develops computational models of physiological systems affected by spaceflight and physiological simulations that help quantify health, safety and performance risks. DAP produced three significant advances in FY2015.

The AG Project conducts research to characterize and validate the use of AG as an effective countermeasure

for multiple physiological systems and enabling analyses of countermeasure studies. This research provides future vehicle designers a “tradespace” for developing appropriate physiological countermeasures in a complex physiological environment.

MPCV Exercise Prototype Preliminary Downselect and Parabolic Flight Testing

The AEC Project passed several key milestones in support of Multi-Purpose Crew Vehicle (MPCV) exercise concepts technology. AEC support included development and preliminary downselection of candidate concepts and support of the MPCV EM-1 Critical Design Review.

NASA’s Integrated Exercise Working Group reviewed six exercise device concepts for MPCV, and based on the concepts’ ability to meet requirements, a downselect committee recommended four device concepts for maturation for human-in-the-loop testing. These devices will be evaluated against key performance parameters established with stakeholders. After testing, the selected concept will be further developed under sponsorship of HRP for human efficacy testing, and delivered to MPCV for subsequent flight hardware development beginning in FY2017 for use on the MPCV EM-2 mission.

The AEC team also completed a parabolic flight campaign with a representative exercise concept to



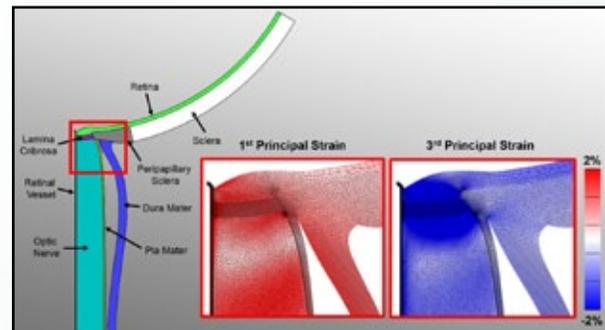
Parabolic flight-testing of a ‘balance challenge’ platform to inform a sensorimotor requirement for an MPCV exercise device.

determine operational volume and dynamic interface loading to MPCV. The team completed both aerobic and resistive exercises in 0g. In addition, three sensorimotor countermeasure exercise “balance challenge” concepts were tested with inputs from the Neurovestibular Lab to inform a new sensorimotor exercise requirement for MPCV. These data are crucial for understanding the feasibility of exercising on MPCV and advancing the exercise device design.

DAP Team Expands Model Analysis to Include Ocular Tissue Changes and Bone Loss

Some astronauts experience persistent visual degradation after long-duration spaceflight, potentially from cephalad fluid-shift pressures acting on ocular tissue. DAP researchers performed finite element and lumped parameter modeling seeking quantification of relevant ocular tissue changes. Their results showed that peak tensile and compressive strains in the lamina cribrosa, anterior optic nerve, and retina increased with the increase in pressure. Combined with numerical probabilistic analysis, the model also demonstrated that individual mechanical properties of tissues may be risk factors for development of pathology as a result of the larger strains that are found in microgravity than on Earth.

Exercise devices in exploration vehicles must be much smaller than the Advanced Resistive Exercise Device (ARED) currently used on the ISS. This realization



A finite element model of ocular tissues and strains resulting from analyses of varying pressures. Individual tissue mechanical properties may be risk factors for developing the visual impairment and intracranial pressure syndrome.

causes concerns that such devices will not provide sufficient stimuli for maintaining physiological health. DAP developed biomechanical models of squat, heel raise, and single-leg squat exercises performed on the Hybrid Ultimate Lifting Kit (HULK), a smaller exploration exercise device prototype, to calculate localized muscle and bone loading profiles that cannot be measured directly. In FY2015, DAP provided the first quantitative comparison between exercise forces produced by ARED and HULK.

DAP also delivered an updated bone physiology model for estimating femoral neck bone loss during skeletal unloading, without exercise, for up to 180 days. Additionally, DAP coupled a finite element model of the femur with a daily load stimulus algorithm to quantify the effect of exercise on preserving bone mineral density. The model has been verified and validated for predicting bone maintenance in healthy adults as a result of walking and running in Earth gravity, as well as for astronauts after long-duration spaceflight.

FUTURE PLANS

Looking forward, HHC researchers will focus future work on developing an integrated countermeasure suite for exploration-class missions. In FY2016, researchers will initiate a comprehensive spaceflight study to test an integrated sensorimotor and neurovestibular countermeasure suite. The goal is to effectively mitigate neurovestibular disturbances caused by spaceflight, because they may prevent unassisted egress of astronauts from the space vehicle after emergency landings.

New flight studies are planned for FY2016, such as the further characterization of the immune system in space with the Functional Immune Study, and the Pharmacology Study, which for the first time will characterize the effects of spaceflight on pharmacodynamics and pharmacokinetics. Additionally, the first studies of the effects of artificial gravity on various physiological variables are expected in FY2016.



Overview

Human exploration of the moon, Mars, and other destinations beyond Earth's orbit will present significant new challenges to crew health. During exploration missions, crews will need medical capabilities to diagnose and treat injury or disease. Providing capabilities that overcome these challenges will require new health care systems, procedures, and technologies to ensure the safety and success of exploration missions.

The Exploration Medical Capabilities (ExMC) Element develops medical technologies for in-flight diagnosis and treatment, as well as data systems to maintain and protect patients' private medical data. These data systems also aid in the diagnosis of medical conditions, and act as repositories of information that support relevant NASA life science experiments.

ExMC physicians and scientists develop models to quantify the probability that a medical event will occur during a mission. Personnel also define procedures for treating an ill or injured crewmember without having access to an emergency room and with limited communications with ground-based personnel for consultation and diagnostic assistance. To read more about the ExMC Element, visit <http://www.nasa.gov/hrp/elements/exmc>

FY2015 Activities and Accomplishments

In FY2015, ExMC achieved many of its research and technology development objectives to help NASA better manage medical risk during an exploration-class mission. A prototype medical data management system, the Exploration Medical System Demonstration (EMSD) project, was successfully ground tested and consideration of a larger, more integrated next-generation system is already underway. The Medical Consumable Tracking (MCT) system to determine usage rates for medical consumables was built using radio frequency identification (RFID) technology and delivered to JSC.

Of note, over the past year ExMC reevaluated its strategic approach on how to understand and manage the medical risks posed by exploration-class missions. This effort culminated in the development of a new gap structure for research and development and highlights the need for an integrated approach to managing medical risk.

ExMC's relationships with other government entities and academia, and its mentoring of both graduate and undergraduate-level students continued through FY2015. Through use of the Small Business Innovative Research (SBIR) mechanism, ExMC has continued to foster collaborative partnerships with members of industry.

ExMC Gap Restructure Complete

In FY2015, ExMC reorganized the gap structure for research and development efforts used to minimize the risk of medical issues for future crews. The new structure consolidated 21 gaps from the old model into 13 gaps. This structure breaks apart the elements of the deliverable medical system and identifies where operational needs drive technology development, and where that development can feed back into the operational structure—in a systematic and iterative approach.

ExMC divided the work into three divisions: Operations Research, Information Resources, and Technology Development. Each division holds specific categories of medical issues identifying a need, and the needs were then assessed to determine gaps. Once the gaps were defined, it was critical to identify which deliverables within each gap send information to other gaps and which are principal to guide the overall systems development.

This new structure will help combine isolated research lines into an Exploration Medical System to be integrated with future vehicles to maximize medical capabilities in the face of limited resources.

Exploration Medical System Demonstration (ESMD) Project Ground Tests Complete

NASA's plans to travel increasingly farther from Earth impose unique medical care challenges that must be addressed to ensure astronaut health and safety. These exploration missions, and the vehicles associated with them, will levy strict constraints on in-flight medical care. With long communication delays, future astronauts will require advanced medical systems to assist in autonomous data collection and decision making.

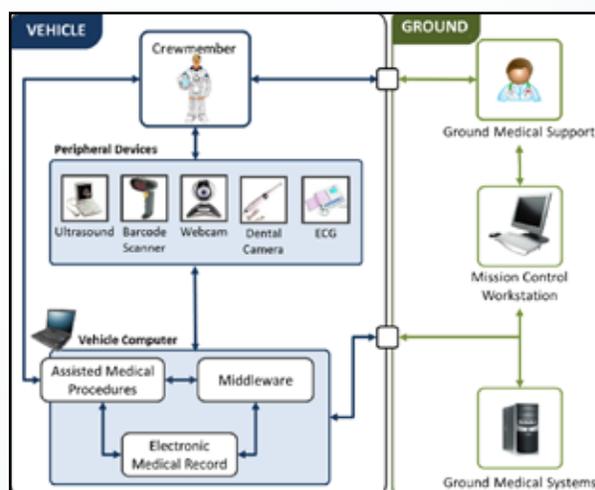
ExMC addressed this need through the development of the ESMD project—a prototype in-flight medical data management system for exploration missions. ESMD was successfully ground tested in FY2015.

The ESMD integrates currently disparate medical technologies and information tools, such as an electronic medical record (EMR), assisted medical procedure system, and various medical devices.

With the ESMD system, crewmembers can retrieve historical medical information, view interactive instructions for standard medical procedures, and save patient- and device-generated medical data, all through a single, intuitive user interface. Using a combination of text, images, and videos, these procedures provide explicit instructions, resulting in expeditious medical care treatment and more judicious use of medical consumables.

The integration of medical devices into the system provides an automated and secure method of transferring data into the patient's onboard EMR. The result is a reduction in risk of corruption or accidental loss and, ultimately, higher confidence in data integrity, a necessity for both onboard and ground medical personnel.

Providing future astronauts with an intuitive medical interface will yield a better standard of care by reducing reliance on ground medical personnel and improving onboard treatment outcomes.



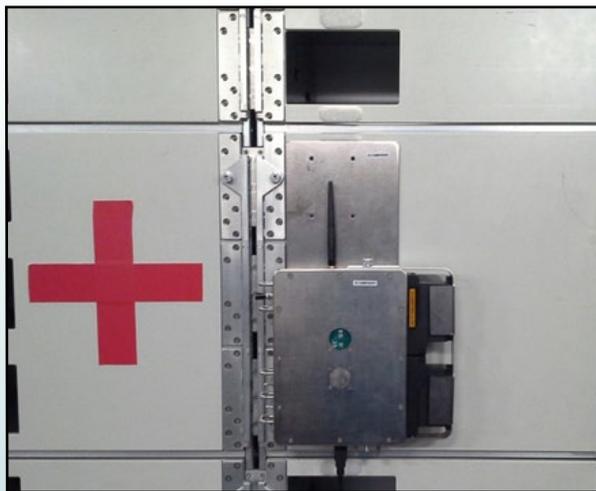
The ESMD project integrates disparate medical devices and provides astronauts with interactive medical procedures in a single interface.

RFID Medical Consumables Tracking Suite Ready for ISS: Destroyed On SpaceX CRS-7

Tracking the usage of medical resources on ISS and correlating items used with the astronaut using them is not currently performed on ISS. With the increased likelihood of a medical incident on longer exploration missions, tracking medications and consumables in the preparation phase for space flights of longer duration allows the medical community to understand what supplies are essential. Exploration missions have limited stowage mass and volume available and there is a risk of not being able to adequately treat an ill or injured crewmember because of a shortfall or misallocation of medical resources.

The Medical Consumables Tracking (MCT) system is designed to address these inventory issues. The system utilizes an RFID system comprised of a reader and a transponder to track medications and medical consumables. Each item has an RFID tag and the system tracks which supplies are onboard and which are consumed. This information is considered private medical data—only the flight surgeon will know which astronaut has taken medications or used consumables.

MCT successfully completed its System Acceptance



The MCT uses radio frequency identification (RFID) technology to track the use of medical consumables removed from an ISS medical locker.

Review and the hardware was delivered to JSC for launch on the SpaceX CRS-7 mission. Unfortunately, MCT was destroyed with the loss of the SpaceX vehicle. Efforts are currently underway to build a new MCT and launch it on a future vehicle.

FUS Ultrasound Project Passes Final Integration Review with GE Collaboration

The Flexible Ultrasound System (FUS) is a technology development project that addresses NASA's gap in noninvasive diagnostic capability for imaging of internal anatomy on future exploration missions. Because it is portable, has low power consumption, and avoids the use of ionizing radiation, ultrasound is the technology of choice for internal imaging.

State-of-the-art clinical ultrasound is difficult to adapt to novel custom scans and therapeutic algorithms. The FUS Project addresses this gap by introducing advanced research-level system access into a clinical



The GE Vivid E95 ultrasound serves as the platform for the FUS Project. Researchers are tailoring both the hardware and software to better meet spaceflight needs.

diagnostic scanner. It also expands the functionality of the system with additional hardware capabilities and provides ultrasound imaging and therapies simultaneously with a single integrated system.

The FUS Project conducted a successful final integration review in July 2015. This review involved the integration of the FUS platform research interface; the modality software development environment; auxiliary hardware, including the quantitative ultrasound (QUS) acoustic transducer; and ultrasound modalities developed by NSBRI researchers. Modalities currently under development are kidney stone detection and manipulation, bone density via QUS, and monitoring of intracranial pressure by imaging the optic nerve and ocular globe with 3D ultrasound.

The FUS final integration review was preceded by a technical critical design review with the developer of the FUS platform, GE Health Care. They used GE's recently released product, the E95 clinical platform, as the basis for the FUS. The FUS preserves the FDA status of the clinical interface of the E95 while integrating the research interface or portal. This portal gives investigators the ability to control acoustic transducers and imaging parameters to develop new and improved modalities.

Small Business Innovative Research Status

ExMC actively manages a variety of Small Business Innovative Research (SBIR) awards. These awards maximize medical technology development by leveraging funds from other governmental programs. ExMC currently has four active Phase II SBIR awards under contract management.

The “Next Generation Oxygen Concentrator for Medical Scenarios” will use vacuum swing adsorption technology to concentrate oxygen from cabin air for exploration-class missions. This technology will minimize the risk of fire by decreasing the likelihood of the cabin environment becoming enriched with additional oxygen. The “Medical Suction Capability”

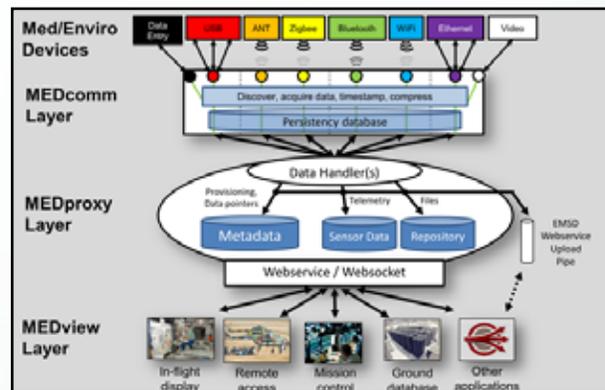
award will develop a solid/liquid/gas phase separator that uses an absorbent material bonded to foam to capture solids and fluids and allow gas to escape. This technology will drastically reduce the volume required when using medical suction, by eliminating the gas volume and leaving only solid and liquid matter.

The “Smart Phone Blood-based Diagnostics” technology uses cell phone optics and lateral flow assays to identify a variety of blood biomarkers. This technology could reduce the mass, volume, and power required to perform a blood analysis during an exploration mission.

The “Low Gravity Drug Stability Analyzer” advances the hardware design of a spectral analyzer that determines whether a drug still has enough active ingredient to be useful. This technology will be useful when the duration of an exploration mission exceeds the stated shelf life for a variety of medications.

Delivery of SpaceMED Middleware for Seamless Integration of Biomedical Data

Numerous biomedical and environmental monitoring devices have been deployed aboard the ISS, enabling assessment of heart rate, blood pressure, ultrasound imagery, CO₂ and radiation levels, and many other variables. However, nearly all of these de-



Various devices and sensors (top row) use different networking protocols making interoperability problematic. The SpaceMED prototype seeks to integrate the data from these devices to facilitate analysis and curation.

VICES are made by different manufacturers and hence were never designed to operate together, synchronize data streams, or coordinate with decision-support or therapeutic devices. As a result, most in-flight data is first sent to ground controllers for time-consuming data curation. This concept of operations will need to change for exploration missions, as communication delays would prohibit timely access by ground controllers to medical and environmental data.

With support from NSBRI, a team led by Gary Strangman, PhD, at Massachusetts General Hospital and Harvard Medical School have developed a prototype platform called SpaceMED—for Spaceflight Medical and Environmental Devices. The prototype seamlessly integrates disparate biomedical and environmental sensors and effectors, as well as future procedure-guidance, decision-support, and therapeutic systems. The SpaceMED v2.2 software was delivered to ExMC for potential deployment in multiple spaceflight scenarios, from a 2-person rover to a space station or a planetary base.

The platform operates by continuously “listening” for new devices being turned on or plugged in, and automatically collects, synchronizes, stores, and communicates data without human intervention. All data—both live and archived—can be accessed through a Web-based interface by astronauts during flight, or by authorized users in any location with Internet access. SpaceMED has proven capable of handling at least 10 clinical electrocardiography recordings simultaneously, providing more-than-sufficient performance for all design reference missions, and is also designed to integrate with ExMC’s EMSD software.

Results of First Clinical Test of Feasibility of Ultrasound to Reposition Kidney Stones

Nearly 1 in 11 Americans are affected by kidney stones which can cause severe pain due to urinary blockage. Astronauts are at increased risk of developing kidney stones because of dehydration, bone loss from the low-gravity environment, and medications



UW researchers have developed a novel, noninvasive ultrasound technique capable of moving kidney stones of all sizes.

used in space; therefore, this is considered a human health risk for exploration space missions. NSBRI has supported the development of an ultrasound-based technology to detect and to reposition kidney stones. Using this new technology, doctors are able to move stones by applying a handheld probe to the skin and aiming ultrasound waves at the stone. Astronauts could move a small stone out of the kidney to pass naturally, or dislodge an obstructing stone to relieve pain and delay or avoid surgery.

A clinical test of the feasibility of ultrasonic propulsion to treat stones was completed in FY2015 with a combination of NIH and NASA/NSBRI funding. The research team lead by Hunter Wessells, MD, of the University of Washington (UW), enrolled fifteen patients at UW Medical Center. Ultrasound images and a pain questionnaire were completed before, during, and after “pushing” of the stones.

Kidney stones were moved in 14 of 15 subjects. Of 43 stones observed, 65% showed some movement while 30% were displaced to a new location. The largest stone moved was 10 millimeters. Stones were moved in a controlled direction, such that 4 patients passed 30 fragments retained after prior stone treatment using lithotripsy—a process using shockwaves to break-up stones. Investigators concluded that ultrasonic propulsion can safely and effectively reposition kidney stones and aids passage of fragments. This technology is being integrated into the NASA Flexible Ultrasound System.

FUTURE PLANS

ExMC is developing an operations concept to define the strategies and capabilities needed for an exploration-class mission, in parallel with its reorganization of the gap structure. A foundational component of ExMC's plans for the future will be the development of a medical system architecture that can incorporate information from multiple sources, transform data, and integrate data with query capability, and also enables augmented clinical decision support.

ExMC also anticipates delivery of the first phase of the Medical Optimization Network for Space Telemedicine Resources (MONSTR). MONSTR is comprised of medical conditions of potential concern for exploration missions, and information on the relative priority of resources required for both diagnosis and treatment. The goal of the MONSTR project is to provide an objective, quantified approach to determine where ExMC should focus its research and technology efforts over the next several years.

Also in FY2016, ExMC expects final delivery of a FUS platform along with the initial research to be performed on that system. Additionally, ExMC anticipates completion of an external review of the Integrated Medical Model, a decision-support tool useful to spaceflight mission planners and medical system designers for assessing risks and optimizing medical systems. The intent is to transition IMM as an operational product to the Crew Health and Safety Program within NASA.

ExMC recently partnered with the Canadian Space Agency to bring the Astroskin, developed by Carré Technologies, to the Human Exploration Research Analog as a technology demonstration. Astroskin is an autonomous medical monitoring system, which consists of an intelligent garment for the upper body and a headband fitted with sensors, and associated software and technology that measure vital signs, sleep quality and activity level of the wearer.

Finally, several SBIR awards have been issued related to next-generation medical hardware to reduce human risk during exploration-class missions, and ExMC plans to continue building on these small business relationships.

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Overview

The Space Human Factors and Habitability (SHFH) Element consists of three main research portfolios: Advanced Environmental Health (AEH), Advanced Food Technology (AFT), and Space Human Factors Engineering (SHFE).

The AEH portfolio focuses on understanding the risk of microbial contamination to crew health and safety, quantifying the virulence changes of microorganisms in response to prolonged microgravity exposure, and establishing permissible limits for exposure to potential toxins such as lunar and celestial dust. AEH countermeasures include use of new technologies and improvements in spaceflight operations to monitor and prevent contamination. In addition, AEH makes recommendations for future requirements to protect environmental quality, food, and crew health.

The AFT portfolio focuses on reducing the mass, volume, and waste of the entire integrated food system to be used during exploration missions, while investigating methods to extend the shelf life and acceptability of food items to five years. AFT also researches bioregenerative solutions as a component of the overall food system, and investigates not only food quality, stability, and nutrition, but also the technologies for food preparation and storage.

The SHFE portfolio establishes human factors standards and guidelines that govern the interaction of the human system with hardware, software, procedures, training, and the spacecraft environment. SHFE provides improved design concepts for advanced crew interfaces and habitability systems, methods for measuring performance of humans and human-system combinations, including robotics and automation.

SHFE also provides validated human models for determining and predicting the effects of interface designs on human performance and safety. Examples include occupant protection during the dynamic phases of spaceflight such as landing. SHFE also facilitates development of tools, metrics, and methodologies for use in implementing, assessing, and validating standards and requirements.

To learn more about the SHFH Element, please visit: <http://www.nasa.gov/hrp/elements/shfh>

FY2015 Activities and Accomplishments

SHFH had another successful year, increasing research collaborations with other HRP Elements as well as with other programs such as Space Biology. A number of new research studies were initiated in the areas of microhost, human-computer integration, training, and occupant protection.

This year's strategic planning included establishing requirements for ground-based analog environments for future efforts, and identifying integrated, multi-disciplinary research topics for the human system interaction design (HSID) risk. SHFH continued interactions with the Department of Defense (DoD) Human Factors Engineering Technical Advisory Group (HFETAG) and Human Systems Community of Interest (HS COI), to identify and align the research roadmaps.

AEH PORTFOLIO

FY2015 Portfolio Overview

AEH encompasses the risk of adverse health effects due to alterations in host-microorganism interactions as well as exposure to dust and volatile compounds encountered during space exploration. In FY2015, research on the host-microorganism interactions risk focused on continuation of the solicited spaceflight study "Study of the Impact of Long-term Space Travel on the Astronaut's Microbiome." Testing was completed for six of nine test subjects, and the last subject is expected to complete flight operations during FY2016.

A new one-year task was initiated as part of the NASA Research Announcement (NRA), and it is expected to provide key insights into which species of microorganisms may acquire altered virulence characteristics during spaceflight. Additionally, a new three-year task was selected as part of the NRA that will evaluate reactivation of cytomegalovirus in a ground-based spaceflight analog environment.

A one-year solicited study was completed that evaluated a human infection model analog using the nematode *Caenorhabditis elegans* (*C. elegans*). The study provided interesting findings, but the data suggests that *C. elegans* cultured in the NASA Rotating Wall Vessel spaceflight analog is not a sufficient model to indicate which organisms may alter their virulence in response to spaceflight.

Additionally, AEH updated the celestial dust research plan to reflect the revised definition of the lunar dust permissible exposure standard. Future efforts will focus on assessing health and performance risks associated with exposure to dusts and volatiles during missions to other destinations. In addition, dust researchers developed a preliminary assessment of the potential health risks from exposures to perchlorate and other chemicals associated with Martian dust.

AFT PORTFOLIO

FY2015 Portfolio Overview

The AFT Portfolio mitigates the risk of performance decrement and crew illness due to an inadequate food system and seeks to provide crews with adequate nutrition for all of NASA's current design reference missions. This mitigation is accomplished through the investigation of methods and technologies that ensure the safety, nutritional content, acceptability, and shelf life of the space food system.

In FY2015, the "Effect of Processing and Storage on Nutrition" and "Pick and Eat Salad Crop Testing" studies were completed.

Space Food Meets Most Nutrient Requirements After Three Years of Storage

Long-duration spaceflight will require the crew to subsist for years on supplied provisions; therefore, space food must provide adequate nutrition for support of crew health and performance. AFT researchers tested 109 space food items during three years of room-temperature storage to determine the capability of the current food system to provide sufficient nutrition. The goal, after processing of food items, was to determine initial concentrations of micronutrients and how those concentrations changed over time.

The researchers found that vitamin stability after processing depended on the micronutrient, the food matrix, and the processing method. Only four mi-

cronutrients—potassium, calcium, vitamin K, and vitamin D—had inadequate levels in the diet initially. The levels were not caused by degradation but by limited occurrence in space foods. Significant storage degradation occurred with vitamin A, vitamin C, thiamin, and vitamin B6. Because of the prevalence of vitamins A and B6 in many categories of foods and high initial concentrations, only the degradation of thiamin and vitamin C have significance to overall nutritional delivery.

Nutrition countermeasures for potassium, calcium, thiamin, vitamin C, and vitamin K could include changing the processing method, fortifying foods, or reformulating food items to have more stable food matrices. Vitamin D is already supplemented through a pill. Cold storage of space food to suspend vitamin degradation is also an option.

Optimizing Nutrition: Study Investigates Bioactive Compounds in Space Food

Bioactive compounds, like flavonoids, have great physiological significance; their health benefits are continually reported. For long-duration missions, the presence of dietary bioactive compounds in food provisions would likely promote overall crew health.

Foods high in lycopene, lutein, or omega-3 fatty acids are present in the current spaceflight food system as demonstrated by chemical analysis. However, sterol availability is below the recommendation. New shelf-stable foods, such as Turkish Fish Stew, were successfully developed to address gaps in provisioning of bioactive compounds.

The storage stability of bioactive compounds varies with each compound and the storage temperature. Limited storage data suggests that some bioactive compounds, like lycopene, lutein, marine omega-3 fatty acids, and rice sterols, plateau at some equilibrium concentration. Anthocyanin stability is closely related to storage conditions, as is lutein stability in leafy vegetables. Sterol stability in nuts seems to relate

to storage duration but not temperature.

It is not yet known whether bioactive compounds will remain stable over for the five years required for a Mars mission. The functionality exists only if the chemical stability of the compounds sustains the beneficial structure for a long shelf life.

Tomatoes and Peppers: Beginning of a Pick-and-Eat Salad Crop System for Spaceflight

The capability to grow nutritious, palatable pick-and-eat salad crops has the potential to provide bioavailable nutrients; enhance the diet; and reduce launch mass. HRP researchers at Kennedy Space Center have identified candidate dwarf tomato and pepper fruiting crops and cultivated them in controlled environment facilities. These facilities mimic the temperature, humidity, CO₂, and light levels found in the “Veggie” vegetable-production system on the ISS.

Plants in the study were assessed for their growth habit and the number and size of fruit produced. Harvested fruits were weighed, freeze-dried, and analyzed



KSC researchers have identified various species of tomatoes and peppers as part of a future pick-and-eat crop grown in the ISS Veggie chamber.

for nutrients of interest. Cultivars were down-selected on the basis of growth and nutrition. Fresh tomatoes and peppers from top candidates underwent sensory analysis at JSC. Characteristics evaluated included flavor, texture, color, and aroma.

Test data will help determine the next crops to be grown in Veggie. The results of this study will be used in a jointly funded HRP-Space Biology research grant to test impacts of red and blue light ratios and fertilizer composition on yield, nutritional quality, and flavor of ISS fresh produce. These studies support plans to implement an operational pick-and-eat salad system for astronauts on ISS and future vehicles.

SHFE PORTFOLIO

FY2015 Portfolio Overview

In FY2015, the SHFE Portfolio worked to develop and approve the NASA Human System Risk Board (HSRB) risk for human factors: risk of inadequate human-system interaction design (HSID). This effort combines all five SHFE risks into one HSRB risk, and will help ensure that the appropriate level of human-centered design, development, and research is undertaken for exploration-class space vehicles.

Two SHFE research projects were completed in FY2015: work on metrics for measuring human-robot system performance, and generalizable methods of allocating work for human-automation systems. In response to the NASA Research Announcement “Human Exploration Research Opportunities,” five new research tasks were awarded in the areas of electronic procedures, training, task analysis, and lighting.

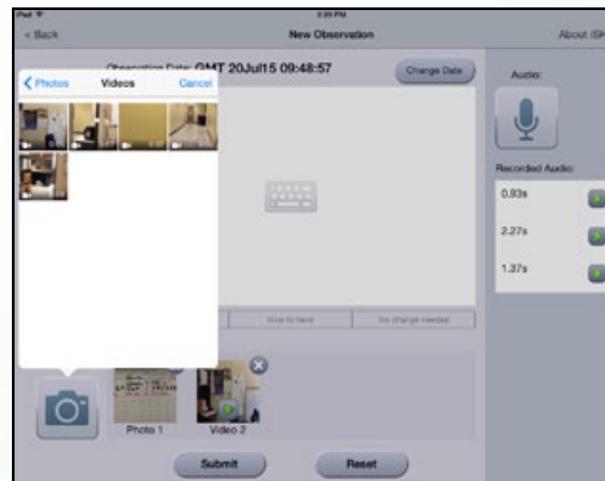
Research progress was made in a number of areas. Two human factors studies began data collection on the ISS One-Year Mission: ISS Habitability, and Fine Motor Skills. The Habitability Advisory Board, which consists of representatives from the crew office, design engineers, and other stakeholders, was formed and began work. The ‘Playbook’ planning tool, which

provides a platform for future research on crew autonomy for deep-space mission operations such as crew self-scheduling and plan execution, was successfully tested in NASA analogs and on ISS.

Two Human Factor Studies Included in ISS One-Year Mission Research

Space human factors research is typically accomplished in laboratories, mockups, and analogs. However, in FY2015, two human factors studies, ISS Habitability, led by Sherry Thaxton, PhD, and Fine Motor Skills, led by Kritina Holden, PhD, were included in the complement of the ISS One-Year Mission investigations. These studies were also the first to utilize custom iPad applications for space-based research.

In the first study, the team documents habitability observations near real-time using the Space Habitability Observation Reporting Tool (iSHORT), an iPad application that allows crewmembers to capture photos, video, audio, and text to document positive and negative aspects of their living and working environment. The insight gained from this study will be available to designers of future vehicles and habitats for exploration missions, resulting in designs that will lead to improved crew performance and comfort.



A screenshot from the iSHORT. The app provides a method for crewmembers to document habitability concerns and includes video or audio annotations.



Scott Kelly, a 1-Year Mission crewmember, tests his fine motor skills using an iPad app as part of the Fine Motor Skills study.

The second study examines the effects of long-duration microgravity and gravitational transitions on fine motor skills. Extended exposure to microgravity leads to muscle deconditioning, but data on the impact of such exposure on fine motor skills is incomplete. Research is necessary to be sure that after an exploration-class mission, crewmembers will be able to accurately and efficiently use their computer-based devices.

The team is using four iPad-based tasks—pointing, dragging, shape tracing, and pinch-rotate—to study the effects of long-duration spaceflight on fine motor skills. Future crewmembers will depend on these skills to complete their computer-based mission objectives.

Human Performance Data Project Provides Focal Point for Research Data

The spaceflight operations and research communities lack a comprehensive understanding of the factors affecting human performance in spaceflight. Investigating human performance using data from current operations may help inform future HRP research. The Human Performance Data Project (HPDP), led by Jurine Adolf, PhD, is identifying operational data, metrics, and measures that might benefit scientists and managers in the pursuit of solutions to reduce or mitigate HRP tracked risks and gaps.

The HPDP has documented existing, derivable, and potentially collectable metrics that can be used to improve human and human-system performance, reduce costs, minimize risk, and maximize resultant outcomes. A resource was then created that serves as a focal point for researchers, designers, and engineers to share these documented sources of data and metrics.

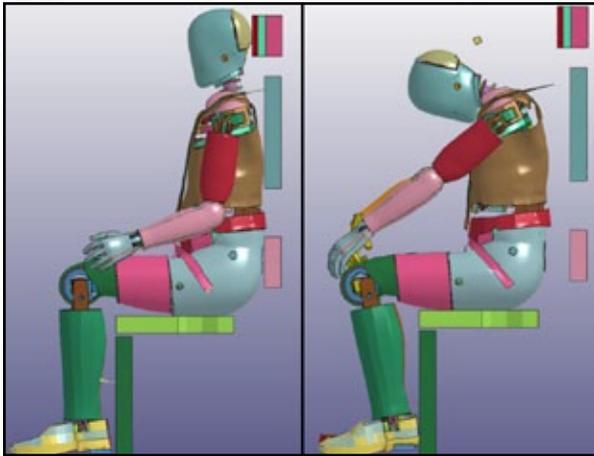
Rather than duplicating the existing databases spread across NASA, this resource includes database names, purposes, types of data stored, points of contact (POCs), intended audiences, and required permissions or approvals for access. Such a resource provides visibility and knowledge of existing data sources across the agency.

The data can be used to inform research to focus on solving operational issues and challenges, inform and enhance operations to maximize crew time efficiency and safety, and inform design decisions for future human exploration programs. The HPDP repository resource includes information regarding: NASA's Life Sciences Data Archive, Lifetime Surveillance of Astronaut Health, Generic Robotics Training, and Crew Notes and Command Errors Database.

Occupant Protection Project Performs Data Mining and Modeling Utilizing THOR Model

The goal of the Occupant Protection Project, led by Mike Gernhardt, PhD, is to develop occupant protection standards for NASA that would apply to all future crewed spacecraft. In FY2015, the team conducted testing with human volunteers and anthropomorphic test devices (ATDs)—also known as crash test dummies—to relate human and ATD responses during spaceflight-like dynamics.

The team validated a finite element model (FEM) for the Test Device for Human Occupant Restraint (THOR) ATD and developed injury assessment reference values (IARVs) for spinal force and chest deflection. To optimize the THOR FEM, the model was run under the same conditions as the ATD in



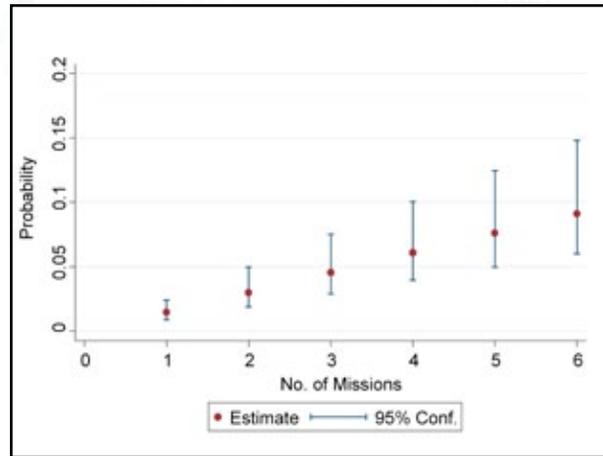
The Occupant Protection Project validated the THOR models using a variety of datasets including crash test 'dummies' and cadavers. The figure above illustrates a frontal impact.

one spinal and one frontal impact. The flexible joints in the upper and lower thorax and the pelvis flesh properties were altered to give the best FEM response in both loading directions. The FEM was validated by running it in different spinal and frontal loading conditions and comparing its responses to the ATD's.

A combination of sub-injurious human volunteer data from the U.S. Air Force Collaborative Biomechanics Data Network, injurious cadaveric tests and human exposures, along with match-paired tests with the THOR ATD and validated FEM were used to develop IARVs for THOR spinal force and chest compression. The data gained from this data mining and modeling will help inform design decisions for new programs and reduce required human testing for validation of initial or modified designs.

Data Mining Project Examines 50 Years of Spaceflight to Predict Risk of HNP

The Occupant Protection Project's study "Disc Herniation," led by Jeffrey Somers, investigated whether spaceflight increases the risk of herniated nucleus pulposus (HNP). A previous study reported that the risk of developing an HNP was higher in U.S. astronauts who had flown at least one mission than in those who had not yet flown. However, the study



HNP probability within one year of landing was estimated to increase with more missions. Due to low sample size, the accuracy of this estimate decreases as the missions flown increase.

did not account for the potential cumulative effect of multiple missions.

The team analyzed reports and dates of first HNP occurrences from 330 U.S. astronauts who took part in 745 space missions spanning 55 years. Of the 745 missions that took place before crewmembers' first-diagnosed HNP, 58 were "long-duration" and 98 were capsule landings. Analysis of 51 HNP cases suggested that the risk of HNP was higher in the first three months after spaceflight; however, the risk declines to background hazard levels by one year after return.

There was no strong evidence that flight duration, landing vehicle, gender, height, weight, body mass index, or a history of high-performance jet aircraft piloting had an effect on HNP risk. Notably, while the causality of spaceflight to HNP is still an open issue, the data provide support for potential mitigation strategies and establishes a requirement for further data acquisition.

Because this was an observational study, it is difficult to separate the effects of the many factors that affect HNP risk or to claim causality. Confounding factors include variable timing for long-duration and capsule-landing missions, changes in criteria for astronaut selection since the pre-Shuttle era, HNP time

of incidence being recorded at the time of diagnosis, rather than time of occurrence, and the possibility that effects of improved spaceflight deconditioning countermeasures obscured the risk of HNP. Supplementing the data with HNP reports from other International Partners as well as data from the IVD Study could offer more insight into these effects.

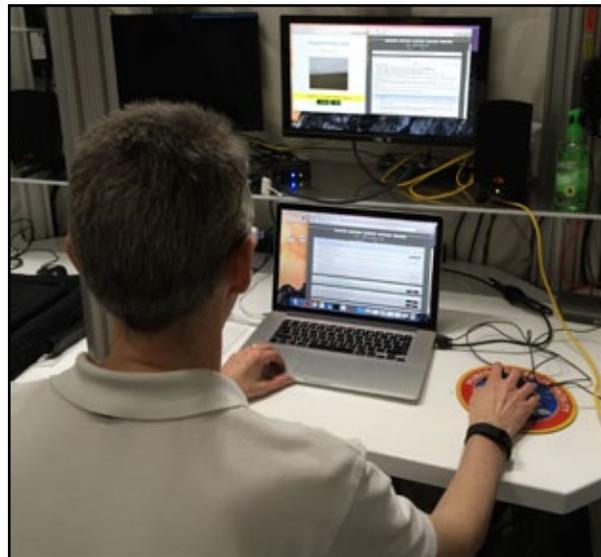
PRIDE Procedure Automation Testing During HERA Campaign 2

As missions move deeper into space and communication latency increases, strategies for carrying out tasks must shift. Astronauts will be unable to depend on real-time support from flight controllers and controllers will not be able to perform procedures in the same way they do for the ISS. This change threatens to increase astronaut workload, decrease efficiency, and increase the risk of suboptimal task execution. Automation is an important resource for adapting to the deep-space environment; however, it must be effectively integrated with the human crew it supports.

The NSBRI project “Automation in Procedures: Guidelines for Allocating Tasks for Performance,” led by Debra Schreckenghost of TRAClabs, completed a study during HERA Campaign 2. In this campaign, four crew members lived and worked in the habitat for two weeks and performed daily activities that simulated a mission to a near-Earth asteroid.

For this study crewmembers used the Procedure Integrated Development Environment (PRIDE) automation software to control simulated habitat systems for temperature, carbon dioxide removal, and power distribution. Each crewmember performed seven one-hour sessions using the PRIDE software. PRIDE uses a single procedure for both manual execution and machine automation. Thus, all automated interaction with the habitat is displayed as human-comprehensible procedures, making automated actions more transparent and predictable to users.

This study evaluated strategies for partial automation



A HERA crewmember uses the PRIDE software during Campaign 2 to control simulated habitat systems.

of procedures and their effect on human-automation performance. Evaluations included how users apply automation when multitasking with electronic procedures and whether these strategies improve work efficiency; how accurately users perform tasks when procedures are partially automated; and how users detect and resolve issues when operational conditions do not match the procedure as written.

Preliminary results suggest that using partial automation of a procedure can improve work efficiency over manual execution of the same procedure, indicated in small timing reductions. Greater efficiency gains are expected when automation frees time for users to do manual tasks concurrently with procedure automation, or to supervise multiple concurrent procedures executing automatically.

Results from this study and a precursor study suggest that software designed for procedure automation under normal conditions can also support problem solving when automation fails because procedure conditions do not hold. Further, these results indicate that once such problems have been observed, many users can use procedure automation to anticipate and prevent them.

Customized Refresher and Just-in-Time Training for Long-Duration Crews

Astronauts on long-duration missions will face critical and complex tasks for which they were not trained or their training is not current. In addition, crew time is a valuable resource, so onboard training efficiency is of prime importance. In FY2015 researchers, led by Stephen Robinson, PhD, from the University of California, Davis (UC Davis), are reviewing in-flight training techniques to bring astronauts up to readiness levels, after a significant period has passed since their final ground training.

Researchers are addressing both in-flight refresher and just-in-time training and are testing the hypothesis that customized crew training can be more efficient than traditional, generic training. The research considers two spaceflight-appropriate tasks, one requiring the repair of a complex electromechanical system, and the other requiring manual control of a simulated ISS robotic arm.

At UC Davis, engineering students replicate astronaut tasks and learn to repair simulated spacecraft systems while their performance is evaluated for time and accuracy. The objective is to choose training techniques



UC Davis engineering students perform complex repair tasks, similar to those astronauts face in-flight, as part of a study examining training techniques.

and materials that result in the best possible repair for the least time spent preparing.

Similarly, at the Michigan Institute of Technology, students are learning to accomplish complex tasks with a simulated space robotic arm. Together, these studies will bring new insights into developing training for long-duration spaceflight crews so they may accomplish their missions safely.

FUTURE PLANS

In FY2016, SHFH will continue current ISS flight experiments in the areas of microbiome, habitability assessment, fine motor skills, and body measures. New ground-based solicitations will be initiated in the areas of human-computer interface, human-automation/robotic integration, occupant protection, crewmember microhost, and the risk of inadequate mission, process, and task design.

SHFH plans to strengthen collaborations with other HRP Elements, external organizations, and international partners. This will allow the identification of research in progress and possibly allow influence of research plans to promote a mutual benefit. In addition, SHFH is committed to increasing interaction with the other NASA Program Offices and technology development projects to ensure smooth and effective implementation of research findings and transition of the tools and products to operational use.

Other major activities in FY2016 will include identifying innovative ways to select practical and affordable SHFH-related standard measures onboard the ISS, and systematically capturing operational data to enable retrospective data analysis research, even beyond the ISS lifespan. In addition, SHFH will increase the number of its solicitations to promote multidisciplinary research and will document and communicate to the human research community best practices for developing payload systems to facilitate higher-quality science and crew well-being.

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Overview

The Behavioral Health & Performance (BHP) Element manages a research portfolio related to characterizing and mitigating three human health and performance risks, including the Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders (“BMed Risk”), the Risk of Performance and Behavioral Health Decrements Due to Inadequate Cooperation, Coordination, Communication, and Psychosocial Adaptation within a Team (“Team Risk”), and the Risk of Performance Decrements and Adverse Health Outcomes Resulting from Sleep Loss, Circadian Desynchronization, and Work Overload (“Sleep Risk”).

Long-duration missions beyond low Earth orbit will require crews to adapt to increasingly autonomous operations in isolated, confined, and extreme environments. The distance and duration of these missions will be unprecedented. Crews will face challenges such as prolonged separation from home, extended periods of monotony mixed with times of heavy workload, and altered day-night/light cycles. Other risk factors such as radiation may also further lead to adverse behavioral and performance outcomes.

BHP uses a combination of laboratory, flight- and ground-based analogs to address risks. Spaceflight analogs, such as the Human Exploration Research

Analog (HERA), provide optimal platforms through which to address specific research questions, particularly when the ISS is not entirely analogous to what is anticipated for future exploration such as limited or no communication with home.

To read more about the Behavioral Health and Performance Element, please visit <http://www.nasa.gov/hrp/elements/bhp>.

FY2015 Activities and Accomplishments

In FY2015, BHP investigators completed several experiments on the ISS and in high-fidelity ground analogs. Flight investigations included evaluations of cognition and sleep-wake cycles during the one-year ISS mission. The “Journals” experiment, which systematically documents behavioral issues associated with long-duration missions, was also extended for the one-year mission. These investigations will yield unique insight into behavioral health and performance for long-duration spaceflight.

High-fidelity analogs serve as an important platform for BHP’s risk-reduction strategy. During the past year, four missions were conducted in the Human Exploration Research Analog (HERA). Crews of four lived and worked in HERA for 14 days under spaceflight-like stressors, including sleep deprivation, work overload and underload, and communication

delays with the habitat mission control. The BHP investigations in HERA incorporated evaluations of cognitive performance, individual well-being, and team cohesion and performance.

BHP research studies completed this past year include an assessment of sleep medications' effect on neurocognitive performance at abrupt awakening, recommendations for composing and developing teams for long-duration exploration missions, and laboratory validation of a comprehensive cognitive measure. Follow-on work between BHP, NASA operations, and study investigators will ensure that study results inform operationally relevant deliverables for future spaceflight.

|| SLEEP RISK PORTFOLIO

Sleep Medication Ground Study Benefits Current ISS Crewmembers

Astronauts often experience difficulty sleeping in spaceflight. To address this, individualized strategies are needed to support spaceflight crews, as well as ground crews responsible for managing mission operations. Although FDA-approved, short-acting sleep medications serve as a primary countermeasure for sleep disruption in space, they have not been evaluated for their effects on cognitive performance upon awakening. Alarm-based awakenings occur at a rate of about six times per year on the ISS, requiring astronauts to immediately think and react.

A collaborative study between BHP researchers and the JSC Space Medicine Division led by NASA flight surgeon Smith Johnston, MD, used a double-blind, placebo-controlled, crossover design. The 34 participants included astronauts, astronaut candidates, flight directors, mission controllers, and physicians. Subjects were evaluated in a controlled ground setting for the effects of commonly used sleep medications on a range of neurocognitive performance functions at abrupt awakening and hours later at terminal awakening.



Two commonly used sleep medications—zaleplon and zolpidem—were used in a ground study to determine the effects on performance.

Relative to placebo, a dose of 10 mg zaleplon—a prescription sleep medication—modestly, but transiently, increased vigilance and working-memory errors. A dose of 5 mg zolpidem transiently reduced cognitive processing speed and working-memory performance. In contrast, 10 mg zolpidem for sleep resulted in large negative effects on virtually all cognitive performance outcomes both immediately after awakening and 30 minutes later. However, there were substantial inter-individual differences in vulnerability to effects from the different sleep medications, with some participants experiencing mild to severe performance deficits while others had no deficits.

This finding highlights the feasibility of using this study protocol to personalize the sleep medications astronauts use in space and to educate them on avoiding performance deficits if they are awakened abruptly after ingesting a sleep medication. Astronauts already benefit from this protocol aboard the ISS.

The protocol can also be used to evaluate the compounding effects of other medications. The results enrich the fatigue management training program for astronauts and ground crews, and inform the human system health and medical standards and requirements for future missions.

Study Uses Blue Light for Optimal Circadian Adaptation and Performance Improvements

Tuning the spectral characteristics of light has the potential to be a safe, nonpharmacological countermeasure to reduce the risk of circadian misalignment and performance deficits during space flight. These benefits can be achieved either by enhancing blue light to increase circadian resetting and alerting responses or depleting blue light to minimize alertness before sleep. NSBRI-funded researchers developed a Dynamic Lighting Schedule (DLS) to determine the timing of these settings to optimize circadian adaptation, improve alertness and performance, and enhance sleep.

Researchers, led by Elizabeth Klerman, MD, PhD, of Brigham and Women's Hospital, conducted a series of inpatient 8-day randomized clinical trials in a high-fidelity spaceflight analog that simulated the ISS lighting environment, sleep patterns, and work schedule. The study examined the use of the DLS with a gradual 8-hour phase advance shift in sleep-work schedules compared to deployment during an abrupt 'slam' shift of the sleep-wake and work schedule.

The first experiment assessed the effect of continuous exposure to the DLS, whereas the second experiment assessed the effects of intermittent exposure. Data col-



Sleep research has shown that blue-enriched light can help alleviate decrements due to sleep/work schedule-shifting and disruptions to circadian rhythms.

lection has been completed for both experiments and data analysis is ongoing. Preliminary analysis shows there was no statistical difference in phase shifting between gradual and abrupt shift protocols.

B-MED RISK PORTFOLIO

Software Tool Evaluates Cognitive Performance On ISS

Sustained, high-level cognitive performance is important for successful space missions, given the challenging environmental, physiological, and psychological stressors that may affect brain functions. A computerized cognitive test battery, named Cognition, was specifically designed for the astronaut population. It was developed at the University of Pennsylvania and consists of ten brief, validated neuropsychological tests that survey a range of cognitive functions related to spaceflight stressors.

The research study has two phases: the first, completed in FY2015, focused on establishing norms and in the second phase, Cognition was deployed to the ISS. Cognition was also deployed in several environments that mimic the stressors of long-duration exploration missions including HERA and three Antarctic research stations. Additionally, the Cognition project was selected to participate in the One-Year ISS mis-



Scott Kelly uses the Cognition software to evaluate cognitive performance. This tool was also used in other extreme environments such as the HI-SEAS and Antarctic research stations.

sion, as well as NASA's Twins Study. The success to date demonstrates the feasibility of Cognition as a tool for research, and possibly for in-flight operations.

Several validation efforts are underway to demonstrate the sensitivity of Cognition to common spaceflight stressors such as increased levels of CO₂. Preliminary analyses have shown Cognition to be sensitive to the effects of sleep deprivation, and a validation study is also underway to compare the test battery on iPad and Windows platforms with other measures commonly used in spaceflight operations.

While this project seeks to deliver tools for spaceflight, Cognition could also be a valuable in many workplaces where high performance is required and identification of cognitive performance decrements is important for safe operations.

TEAM RISK PORTFOLIO

Study Uses Automated Analysis of Communications to Determine Crew Attitudes

The Automated Detection of Attitudes and States through Transaction Recordings Analysis (AD ASTRA) study, led by Chris Miller, PhD, of Smart Information Flow Technologies, assessed individual and team psychosocial states and attitudes through automated analysis of textual data. Astronauts' journals have long proven a rich data source for experiences and attitudes, and many interpersonal communications are already recorded during mission operations. Automating the assessment of such sources expands the amount of data that NASA researchers have available to improve astronauts' psychosocial health and performance, while reducing the number of surveys astronauts must complete.

This study tested various text analysis techniques. The primary technique examined word counts in relevant categories such as group dynamics, and evaluation of length of sentences and semantic analysis for similarity and positive or negative sentiment detection.



During HERA campaigns, the AD ASTRA study used automated analysis of communications to gauge crew attitudes.

Analysis was performed first on historical mission transcripts and publicly available in-flight astronaut diaries or blogs, and later in three different spaceflight analog studies including Bed Rest Study Campaign 11, and the HI-SEAS and HERA missions.

Results show that automated diary analysis can reliably replace some attitude and emotion surveys. Analyses correlated significantly with subjects' ratings of their emotional positivity and focus on the past, present, or future. Correlations between attitudes about the study, physical well-being, and focus on self and others were also statistically significant.

When compared to daily human observers, automated evaluation did a better job of predicting subjects' survey responses. Potential applications of these results include a self-advisory tool for crewmembers; a "power level" and "team comfort or routine" indicator for tracking group dynamics; and an aid for researchers to identify attitudes and topic-focused information from crew debriefing sessions.

JSC Team Debrief Method Extended to MSFC and Astronaut Candidate Class

A recent team debriefing research study, led by Kim Smith-Jentsch, PhD, from the University of Central Florida, demonstrated a 50% reduction in certification time for JSC flight controllers. The results from



JSC flight controllers use TDT during simulations to reinforce training, increase performance and reduce certification time.

this study were used to develop a team debrief method and teamwork model for JSC's Flight Operations Directorate (FOD), a model now known as Team Dimensional Training (TDT).

This debriefing method targets four teamwork skills essential to effective team performance and functioning: information exchange, communication delivery, leadership/followership, and supporting behaviors and has been implemented in flight controller simulations. FOD continues to work toward broader implementation of the technique and is modifying it for their particular needs to realize the full benefit.

While the TDT methodology was originally studied at JSC, it was transitioned in FY2015 to multiple NASA centers. Instructors were trained in team dimensional training at the Marshall Spaceflight Center (MSC) in Alabama, home of NASA's payload mission control.

In addition, the astronaut candidate (ASCAN) class of 2013 was trained on the TDT method. Implementing TDT across multiple groups will ensure a consistent approach across NASA, reinforce training and debriefing best practices going forward, and offer the potential to improve performance on current missions and future exploration missions.



In a recent study, the NEEMO 19 crew used the DebriefNow software as a team debriefing exercise.

DebriefNow Software Helps Develop Resilient, Self-Sustaining Teams

One of the most promising countermeasures for sustaining resilience during a space mission is the use of periodic team-led debriefs. An analysis of past studies showed that, on average, teams that debrief outperform others by more than 20%. The Group for Organizational Effectiveness team, led by Scott Tannenbaum, PhD, studied team resilience through debriefing using DebriefNow, a software tool for targeted team debriefings.

In FY2015, results were reported from several empirical studies that used the DebriefNow tool. The countermeasure prompted team members with questions about team- and resilience-related factors such as sleep, privacy, and communications with mission control. The tool then produced a customized discussion guide used by the team to discuss concerns, confirm what was working well, and identify any needed adjustments.

In a study of 48 student teams in a tightly controlled lab setting, teams using the debriefing countermeasure demonstrated greater resilience, and in turn performed better. In a usability study of two NASA Extreme Environment Mission Operations (NEEMO) crews, astronaut participants reported the tool was

easy to use, stimulated constructive conversations, and would be beneficial during future space missions.

In FY2015, the research was extended to four crews during 14-day missions in the HERA habitat. The crews indicated the tool helped them identify where adjustments were needed and helped them improve how they worked and lived together. Empirical analyses of the data from the FY2014 crews also revealed a positive effect of debriefing on crew-rated team performance.

Collectively, the results show that team debriefing is an effective countermeasure and demonstrate the benefit of allocating time and tools for self-guided debriefs during future missions.

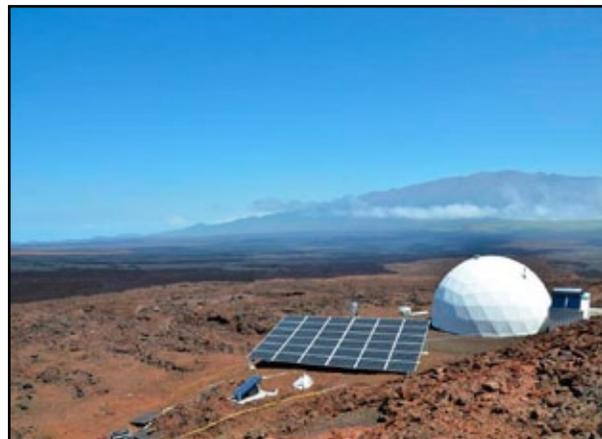
FUTURE PLANS

In FY2016, BHP's risk reduction research will be implemented on the ISS and in high-fidelity ground-based analogs. Also, improvements in spaceflight operations, based partially on previous BHP research, will come to fruition. The ISS will receive new Solid State Lighting Assemblies (SSLAs) in August 2016, which will allow circadian-related research to be conducted and may improve crew behavioral health. The SSLAs will be installed in phases, beginning with ISS Node 2 and individual crew quarters. With the new SSLAs in place, studies will begin that will include measures of urinary melatonin, cognitive performance, and sleep-wake actigraphy. BHP will also complete data collection for its one-year ISS study.

For the 30-day HERA missions starting in FY2016, a suite of BHP studies will examine a broad array of topics. Additionally, in late FY2016 data collection will be completed on the Long Duration Team Functioning study. This one-year mission, the third of three missions, will inform the key contributors to team function and performance over long durations. The study utilizes the Hawaii Space Analog and Simulation (HI-SEAS) habitat, a unique Mars analog.

FY2016 will also see continued data collection for a BMed risk characterization study in five Antarctic stations.

BHP will award new studies in areas such as individualized stress training countermeasures, sensory stimulation and augmentation, team selection, and training and culture. A solicitation is currently in progress for integrated behavioral health testing in the European Space Agency's :envihab facility, and BHP will contribute to other interdisciplinary efforts investigating multi-omics, biomarkers, workload, and integrated human physiological and behavioral effects of spaceflight. These studies will identify key risk triggers and inform countermeasures such as training and technology/tool development, to close knowledge gaps and meet key milestones on the pathway to risk reduction.



The HI-SEAS Habitat is a Mars analog utilized by the University of Hawaii to conduct a study on Long Duration Team Functioning. It is located at approximately 8000 ft elevation in an abandoned quarry on the northern slope of Mauna Loa, Hawaii. A crew of six live and work in the 36-foot diameter geodesic dome for a full year.

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Overview

The Human Research Program supported a number of education and communication initiatives in FY2015 across multiple NASA centers and the National Space Biomedical Research Institute (NSBRI). Additionally, HRP Elements helped support education initiatives including research internships, post-doctoral programs, and summer institutes for interns. Within HRP, the Human Research Engagement and Communications (HREC) Project is committed to engaging and informing the general public about NASA's human health and performance research and technology development.

Mission X Addresses Childhood Obesity with Exercise and Nutrition

Mission X 2015 (MX15) began the second phase of the multi-year international fitness and nutrition campaign "Mission X: Train Like an Astronaut." This phase spans MX15-MX17. The World Health Organization has designated childhood obesity as one of the most serious public health challenges of the 21st century. The promotion of nutrition, physical activity, and a healthy lifestyle is the best solution to this largely preventable problem.

The challenge to "train like an astronaut" helps to motivate participants to exercise more and, in some

cases, inspires less motivated individuals to engage in activities they normally would not even try.

Astronaut Samantha Cristoforetti, MX15 Ambassador, opened the challenge with a special message to participants from the ISS. For MX15, NASA spans the globe with 12 partner space agencies, almost 40,000 participants, and over 800 teams in 28 countries. The teams are guided and encouraged by nearly 2,000 adults and 65 international partner institutions. More than 92,000 participants have experienced Mission X since it began with Phase I in FY2012.

In 2015, MX15's Team USA encompassed almost 5,000 participants in 14 states and Puerto Rico. Team USA's closing events were held, via Google Hangouts, with team leaders and participants in three time zones. Special guests for the events included astronauts Shannon Walker and Tom Marshburn.

In preparation for MX16, the project has partnered with the State University of New York at Buffalo's Department of Epidemiology and Environmental Health to expand the project's expertise in pediatric obesity. This partnership seeks innovative ways to help children and their families increase their daily physical activity, improve their understanding of good nutrition, and become excited about human space exploration. For more information about MX, go to <http://trainlikeanastronaut.org>.



During FY2015, students from 28 countries took part in the Mission X: Train Like an Astronaut fitness challenge.

NSRL Summer School: Training the Next Generation of Space Radiation Investigators

The 12th annual Space Radiation Summer School was held at the NASA Space Radiation Laboratory (NSRL), located at the Brookhaven National Laboratory in Upton, NY, from May 28 to June 20. Sixteen students were selected from about 50 applicants. The school, sponsored by the Space Radiation Element, provides a “pipeline” of researchers aiming to tackle the challenges of harmful radiation exposure to humans who will travel on space exploration missions.

A student selection committee screened the applicants, with one of the most important criteria being the expectation that students would pursue a career in space radiation and help NASA address space radiation issues. Twelve of the students came from institutions in the United States, and four from Germany and Italy. The students’ backgrounds covered broad areas of radiation biology, biophysics, and nuclear physics. Most of the students were at graduate level studying for advanced degrees, and five students were at the postdoctoral level. Nine of the students were women and seven were men.

The summer school included an intensive lecture and laboratory program including expert lectures on radiation interactions with matter, accelerators, radiation dosimetry, systems biology, leukemia, apoptosis, mutagenesis, neurogenesis, and dose rate



Future space radiation investigators participate in NASA’s 12th Annual Radiation Summer School at the NSRL facility.

effects. About thirty visiting lecturers from across the nation provided classroom instruction and engaged in question-and-answer sessions with the students. Invited guest lecturers included the Space Radiation Element’s Chief Scientist, the author of *Radiobiology for the Radiologist*, the Chief Radiation Safety Officer from the Space Radiation Analysis Group at JSC, and a representative from the United Kingdom Medical Research Council.

Students also participated in an intensive hands-on experimental program at the NSRL. Extensive training occurred on how to prepare cell cultures and mouse models for experimental irradiation using the high-energy heavy-ion beams at the facility. Students received detailed training in four areas: using the gamma H2AX assay as a marker of double-strand breaks, using flow cytometry techniques for cell counting, the use of cell survival curves, and using the NSRL beams to understand the physics of beam interactions with materials. Many past summer school students are now fully engaged in space radiation careers and writing original research papers in space radiation.

RTO Team Develops Videos and Webpages Showcasing Twins and One-Year Mission

The Human Research Engagement and Communications Research to Outreach (RTO) Project develops and produces content about HRP research, utilizing various communications strategies, methodologies,

tools, and vehicles. The intent is to inspire, educate and inform the general public about the challenges of human space flight and HRP work, through feature stories, videos, website development, media partnerships, and workshops. HRP principal investigators and NSBRI researchers collaborate, provide guidance, and serve as primary subject matter experts for all RTO content. The ISS Program Science Office, and the NASA Headquarters and JSC External Relations and Public Affairs offices support the story development process with reviews, dissemination, and amplification of the products.

RTO developed the HRP One-Year Mission (<http://www.nasa.gov/1ym>) and Twin Studies (<http://www.nasa.gov/twins-study>) web pages for media and the general public. These pages highlight key investigations, summarize research goals and long-duration spaceflight effects, and provide media resources.

RTO personnel also worked with *Time* Magazine, CNN, and other media to explain the challenges of sending humans on deep-space missions to Mars and other long-duration destinations. During the first three quarters of the year, the One-Year Mission and Twin Studies websites had combined views of over 41,000. RTO stories, videos, images, and additional information about HRP may be found at <http://www.nasa.gov/hrp>.

NSBRI Fellowship Program Ends after More than a Decade of Fostering Scientists in Space Biomedical Research

Since beginning in 2004, the NSBRI First Award Fellowship program has awarded fellowships to 63 talented young scientists. Under the guidance of this program they conduct space-related biomedical or biotechnological research that supports the goal of protecting astronaut health during long-duration spaceflights.

The program offers young scientists the opportunity to manage their own space-related biomedical



An advertisement for the NSBRI First Award Fellowship Program, featured in Times Square in New York City, New York

research projects while continuing to learn from experienced faculty mentors. Participants join one of NSBRI's seven science and technology teams and are able to interact with some of the nation's leading researchers in their respective fields.

NSBRI has solicited applications for the First Award Program annually; however, FY2015 was the last year the program was offered. After a research announcement in February 2015, applicants prepared proposals with the support of a mentor, and all proposals were evaluated by a peer-review panel.

Thirty proposals were received by June 5th and in August a committee convened to make recommendations for funding. In September, nine new First Award fellows were selected for a one-year fellowship, and all accepted their awards.

Since inception, First Award Fellows have generated 386 peer-reviewed articles, 14 book chapters, 792 invited abstracts or presentations, and seven invention disclosures.

NSBRI Mentored Research Program

NSBRI's Mentored Research Program in Space Life Sciences is conducted at both Texas A&M University and Massachusetts Institute of Technology (MIT). Students in these programs work toward a PhD that focuses on space life sciences. The mentored research



A Texas A&M University PhD student participates in the NSBRI Mentored Research Program.

program provides an array of support to participants, including a defined curriculum, research supervision, mentoring, community forums, and funding to enable future careers in the space life sciences.

The PhD program at MIT trains graduate students in space life sciences, biomedical engineering, medical sciences, and space medicine for a broad range of possible career opportunities. It provides students with a combination of science and engineering coursework, clinical experiences, space-related research apprenticeships, and thesis research options at MIT, Harvard, and associated hospitals.

The training program is part of the Division of Health Sciences and Technology's Medical Engineering and Medical Physics PhD program. The program is led by Laurence Young, ScD, who is MIT's Apollo Program Professor of Astronautics and a member of NSBRI's Sensorimotor Adaptation team.

Students at Texas A&M University who participate in the PhD program earn a Certificate in Space Life Sciences while obtaining a doctoral degree in genetics, kinesiology, nuclear engineering, or nutrition, or an MD or PhD in medical sciences from the Texas A&M University Health Sciences Center Graduate School of Biomedical Sciences. Joanne Lupton, PhD, and Nancy Turner, PhD, lead the program at Texas A&M.

Each year, young scientists in the Mentored Research Program participate in a 10-week summer enrichment program in Houston. The program includes a week of space life sciences lectures followed by a nine-week research assignment in a NASA laboratory at Johnson Space Center, Ames Research Center, or Glenn Research Center.

To date, 35 graduate students have received NSBRI support through this initiative. Since the program's inception, 12 students have completed their doctorates and secured positions in industry, academia, or government. Graduate students of the program have also produced 103 peer-reviewed articles, one book chapter, 214 invited abstracts or conference presentations, and one invention disclosure.

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