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Results From the John Glenn Biomedical Engineering Consortium

A Success Story for NASA and Northeast Ohio

Marsha M. Nall
Glenn Research Center, Cleveland, Ohio

Gerald J. Barna
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June 2009

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Vision and Plan

The John Glenn Biomedical Engineering Consortium was established by NASA in 2002 to formulate and implement an integrated, interdisciplinary research program to address risks faced by astronauts during long-duration space missions.

The consortium is comprised of a preeminent team of Northeast Ohio institutions that includes the following

(1) Case Western Reserve University (CWRU)—offers a Biomedical Engineering Program that is one of the top programs in the nation. MetroHealth Medical Center in Cleveland is part of the consortium through its affiliation with the CWRU School of Medicine.

(2) The Cleveland Clinic—excels as one of the top hospitals in the nation and has ranked number one in cardiac care in the U.S. for the past 14 years. The Clinic's Lerner Research Institute provides laboratory-based, translational and clinical research aimed at understanding the underlying causes of human diseases and developing new treatments and cures.

(3) University Hospitals Case Medical Center (UHCMC)—ranks nationally in numerous specialties with a rich history filled with medical innovation, leading-edge research, teaching, and a bedrock commitment to outstanding patient care.

(4) The National Center for Space Exploration Research (NCSER)—demonstrates superior capabilities in fluid physics, computational simulation, and instrumentation.

(5) NASA's Glenn Research Center (GRC)—has outstanding competency in interdisciplinary bioengineering for human systems along with exceptional spaceflight hardware development, sensors, diagnostics and computational modeling expertise.

The John Glenn Biomedical Engineering Consortium research is focused on fluid physics and sensor technology that addresses the critical risks to crew health, safety, and performance. Effectively utilizing the unique skills, capabilities and facilities of the consortium members is also of prime importance. Research efforts were initiated with a general call for proposals to the consortium members. The top proposals were selected for funding through a rigorous, peer review process. The review included participation from NASA's Johnson Space Center, which has programmatic responsibility for NASA's Human Research Program. Almost all of the projects initially selected involved collaboration among the consortium institutions, which ensured that the very best capabilities of the members were utilized in conducting the research. A board was established with senior executive membership from each institution. The board assures that the appropriate resources and capabilities of all members are utilized to achieve the goals of the consortium. The board also fosters a cooperative relationship between all member institutions. All of the projects selected for funding have been completed. Because of the success of the consortium, the member institutions have extended the original agreement to continue this highly effective research collaboration through 2011.

The Projects

The projects range in scope from delivery of prototype hardware to applied research that enables future development of advanced technology devices. Highlights of the completed projects are given below. They are discussed as one of two current Human Research Program areas of emphasis: Exercise Countermeasures and Exploration Medical Capability. Exercise Countermeasures provides requirements for optimized and validated exercise protocols and equipment that maximize benefits to the body, minimize crew time required for exercise, and minimize volume and mass requirements for exercise hardware. Exploration Medical Capability develops requirements and advanced technologies for clinical medical systems requiring little or no real-time support from Earth and a probabilistic analysis model of health care delivery during exploration missions.

Exercise Countermeasures

Exercise Prescription Monitoring and Feedback for Bone Mass Maintenance

Principal Investigator: Gail P. Perusek, M.S., GRC
Co-Investigators: Brad Humphreys, Ph.D., ZIN Technologies, Inc.
Marcus Just, Ph.D., ZIN Technologies, Inc.
Carlos Grodsinski, Ph.D., ZIN Technologies, Inc.
Peter R. Cavanaugh, Ph.D., D.Sc., Cleveland Clinic

Figure 1.—The enhanced Zero-Gravity Locomotion Simulator (eZLS) at NASA Glenn.

In space, astronauts exercise to counteract the detrimental physiological effects of spaceflight, including bone loss. The skeletal system adapts to mechanical loading by the "adaptive remodeling response." When mechanical loading is diminished (e.g., in magnitude, rate, duration), as during spaceflight, significant bone loss is observed in weight-bearing skeletal locations. Astronaut exercise prescriptions do not currently employ biometrics for quantifying accumulated mechanical loads in space, nor are astronauts monitored to evaluate actual versus prescribed dosage. The objective of this project was to develop a monitoring algorithm based on the daily load stimulus (DLS) theory of bone mass maintenance and implement this algorithm on biometric monitoring hardware to actively measure DLS dosage based on vertical ground reaction force and provide feedback to the test subject in real time. Results were demonstrated on the enhanced Zero-gravity Locomotion Simulator at NASA Glenn, which included supplying real-time feedback to the exercising subject. The DLS dosage interface was analogous to "filling a bucket." Progress was displayed on a computer screen indicating when the accumulated dosage was reached. The project resulted in significant advancement of a highly practical monitoring algorithm for prescribing daily load stimulus through quantifying foot reaction force. Using this approach, exercise sessions can be optimized and overall bone loss may be reduced. This project leveraged funding and resources from the other research projects funded through the National Space Biomedical Research Institute (NSBRI), a Small Business Innovative Research (SBIR) Phase 1 effort, and a flight experiment activity. The results may be applied to health care on Earth such as physical activity monitoring and osteoporosis prevention.

A Harness for Use With Exercise Countermeasures

Principal Investigator: Peter R. Cavanagh, Ph.D., D.Sc., Cleveland Clinic
Co-Investigators: Gail Perusek, M.S., GRC
Carlos Grodsinski, Ph.D., ZIN Technologies, Inc.

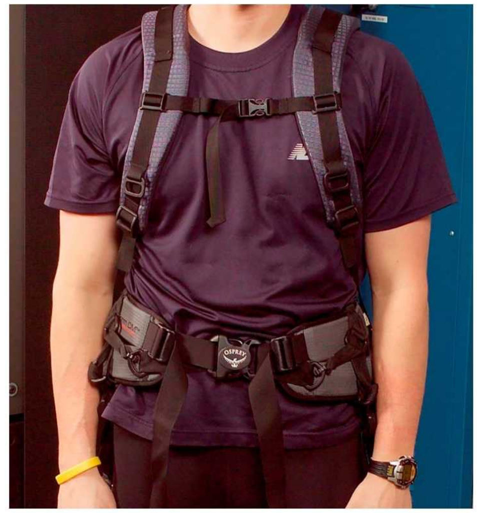

Figure 2.—Prototype harness developed under the John Glenn Biomedical Engineering Consortium.

Treadmill exercise has been used on orbit since early space shuttle flights because it has the potential to simultaneously benefit the neurovestibular, musculoskeletal, and cardiovascular systems. Extensive effort has been put forth toward the development of exercise countermeasures, yet bone continues to be lost on current International Space Station (ISS) missions and is a major concern for future exploration missions. A treadmill with vibration isolation (TVIS) has been a major component of the exercise hardware on the ISS. However, it has not proven to be a successful countermeasure. The key to the success of load-bearing exercise in space, such as treadmill running, is the application of loads to the crew member via a subject load device coupled to the body by a harness. ISS crew members frequently report discomfort from the current types of exercise harnesses, which makes the exercise protocols less effective. Experiments on the ISS have shown that this has resulted in low ground reaction forces on orbit (approximately 60 percent of 1 g loads), which is likely to be a major factor in the observed loss of bone mineral density in crew members. This project utilized valuable insights from the backpack industry for harness configuration and distributing loads to develop an improved harness. Based on preliminary consultation with industry experts, the harness was designed to minimize vertebral column loading. Form-fitting thermoplastic to mold the waist belt was used to better distribute loads to accommodate for individual differences, including gender. The project resulted in the advancement of a new, more comfortable harness design that is now being developed for flight testing on the ISS. Sensors to measure load distribution were developed during pilot testing of the prototype harness. This load sensing methodology will be used during the flight experiment to obtain comparisons of load and comfort between the new harness and the current U.S. ISS harness.

Development of a “Recompression Chamber” to Prevent Bone Loss in Space Through Exogenous Application of Acoustic Energy

Principal Investigator: Ulf Knothe, M.D., D.Sc., Cleveland Clinic
Co-Investigators: Dwight Davey, Ph.D., CWRU
Melissa Knothe Tate, Ph.D., CWRU

Developing countermeasures to prevent bone loss due to exposure to microgravity is a high priority in reducing risk for human space flight. The objective of this project was to develop and optimize a countermeasure for prevention of bone loss in microgravity based on exogenous application of acoustic energy. The first phase of the project identified the bandwidth and application regime necessary to enhance fluid flow and mass transport through the bone matrix and produce low-level diffuse microdamage in the bone matrix. This was done first in ovine bone samples and then in an ex vivo rat model. The ex vivo study showed the efficacy of the energy regime to produce low-level, diffuse microdamage in bone, mimicking that which occurs naturally through physiologic activity. In the second phase, the same energy regime was applied to rats in vivo and the rats were allowed to recover over a four-week period. This in vivo study showed that lithotripsy triggered a remodeling response in addition to significant bone apposition compared to untreated groups. In the final phase of the project, osteopenic, middle-aged rats were exposed to lithotripsy to evaluate the effectiveness of acoustic shock waves in counteracting bone loss due to simulated microgravity. Results showed, for the first time, that lithotripsy stimulates bone apposition and is a potential therapy to prevent bone loss associated with exposure to microgravity. This technique could also be used to prevent bone loss on Earth due to inactivity. This project effectively leveraged funds and equipment from other projects. Interest has been shown in exploring a commercial application of lithotripsy to prevent and combat osteopenia.

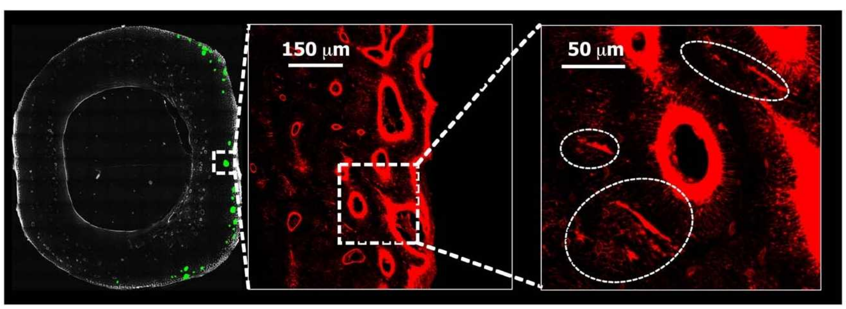

Figure 3.—Microdamage throughout the cortex of the cross section resulting from the application of acoustic energy to cortical bone blocks.

Two-Photon Microscopy for the Assessment of Countermeasures in Bone Loss

Principal Investigator: Greg A. Zimmerli, PhD., GRC
Co-Investigators: David G. Fischer, Ph.D., GRC
Marius Asipauskas, Ph.D., NCSER
Melissa L. Knothe Tate, Ph.D., CWRU

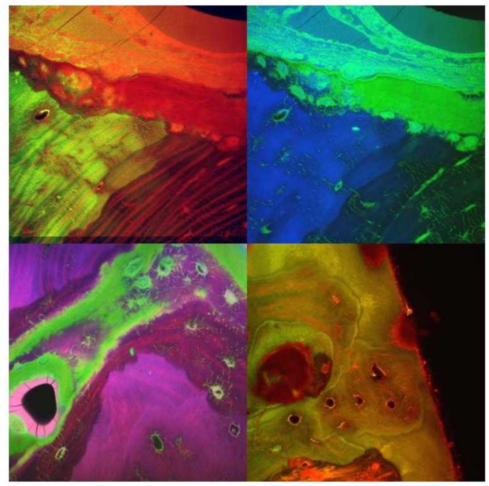

Figure 4.—Image gallery of spectrally resolved, false color, two-photon image of bone tissue stained with basic fuchsin.

Bone loss in weight-bearing skeletal locations during long-duration spaceflight is a serious issue for astronauts. Data from NASA's crewed missions indicates that astronauts experience a significant reduction in bone mass density (BMD) due to exposure to microgravity. It is also of concern for long stays under partial gravity conditions such as on the surface of the Moon and Mars. Analysis suggests that the weight-bearing bones of an astronaut returning from a 30-month mission to Mars could have the equivalent BMD of an 80-year-old person. Because of its dense, optically opaque structure, bone tissue is a particularly challenging subject for white light imaging or fluorescence microscopy. This project investigated the quality of bone imaging provided by two-photon fluorescence microscopy compared to traditional confocal fluorescence imaging. Fresh frozen human femur and tibia samples were prepared and imaged using a custom-built two-photon microscope and a confocal microscope. The two-photon imaging technique showed distinct advantages including better signal and contrast when imaging 50 percent deeper into the bone tissue, a significantly better penetration depth, and advantageous spectral resolution characteristics compared to traditional confocal imaging techniques. This project demonstrated the benefit of using two-photon microscopy to understand the underlying mechanisms of bone changes by studying cellular activity in a living animal, in real time. In addition, the project conducted research to better understand in-vitro bone cell cultures and the regulation of expressed proteins. In particular, the gene regulation effect that fluid flow has on osteoblasts was examined.

Portable Unit for Metabolic Analysis (PUMA)

Principal Investigator: Daniel L. Dietrich, Ph.D., GRC
Co-Investigators: Nancy D. Piltch, Ph.D., GRC
Marco E. Cabrera, Ph.D., CWRU
Peter M. Struk, Ph.D., NCSER
Richard D. Pettegrew, Ph.D., NCSER

Figure 5.—PUMA headgear.

It is critical to keep astronauts safe, healthy and physically fit during long-duration missions. Metabolic monitoring of astronauts can provide essential data during activities including exercise and extravehicular activity (EVA). However, stringent requirements for accuracy, weight, volume and portability pose significant challenges for devices needed to provide the essential metabolic data. The Portable Unit for Metabolic Analysis (PUMA) Project developed an innovative device that measures the six key quantities (oxygen, carbon dioxide, flow, temperature, pressure, and heart rate) needed to evaluate human metabolic function. PUMA is a battery-powered, self-contained device capable of measuring metabolic function at rest, during exercise, in clinical settings, or in the field. The device transmits data wirelessly to a laptop computer. It offers significant advantages over currently available portable units including superior measurement technology and highly time-resolved measurements of all relevant quantities, which eliminates the timing issues present in other devices. The integration of gas concentration profiles to obtain breath-by-breath analysis provides more accurate information than the single concentration per breath measurement obtained by other units. Also, the placement of essential sensors is closer to the mouth than other units. PUMA uses superior oxygen sensor technology with faster response, negligible drift, and no sensitivity to carbon dioxide (compared to currently available portable units). The project developed and evaluated three generations of the PUMA unit incorporating improvements from generation to generation. Human subject testing was conducted through a series of tests at the exercise physiology laboratories located at UHCMC and at NASA Johnson. PUMA has also been tested in the NASA Extreme Environment Mission Operations (NEEMO) underwater Aquarius habitat. NASA has applied for a patent for the PUMA device. Numerous opportunities exist for application to improve health care on Earth where basic physiological measurements are required including occupational fitness evaluations and training as well as dietary, nutrition, weight loss, and exercise studies.

A MicroSensor Array for Exercise and Health Monitoring

Principal Investigator: Gary W. Hunter, Ph.D., GRC
Co-Investigators: Daniel M. Laskowski, Ph.D., RPFT/CCRC
Raed A. Dweik, M.D., Cleveland Clinic
Chung-Chiun Liu, Ph.D., CWRU
Joseph R. Stetter, Ph.D., Transducer Technology, Inc.
Darby B. Makel, Ph.D., Makel Eng., Inc.
Benjamin J. Ward, Ph.D. Makel Eng., Inc.

The objective of this project was to develop a miniaturized metabolic gas monitor system for use in astronaut feedback during exercise and in astronaut health monitoring. The results contribute to reducing astronaut health risks in areas such as diminished cardiac and vascular function and reduced muscle mass, strength and endurance. The project team fabricated, tested, and delivered an integrated breath-monitoring sensor system that included an array of gas microsensors, a data acquisition and display unit, a sample pump, and a mouthpiece. The core species monitored were carbon dioxide and oxygen along with other species including carbon monoxide, nitrogen oxides (NO, NO_2), hydrogen sulfide, pH, and temperature. Team members at Makel Engineering Inc. and the Cleveland Clinic completed significant miniaturization of the testing system and performed complete system characterization, including patient testing. Testing demonstrated that high temperature oxygen and carbon dioxide sensors provide the functionality required for a breath monitoring system. The results outline a system for exercise feedback and personal health monitoring for use on Earth or in space. The type of sensor system developed through this project may be used in the future as a replacement for the traditional lab rack-sized equipment currently used. The collaboration established through this project led to a recent State of Ohio Third Frontier Award to develop a breath sensor system (starting with nitrogen oxide measurements) for home health applications that focus on asthma patients. This involves the Cleveland Clinic, Makel Engineering, The Ohio State University, and CWRU.

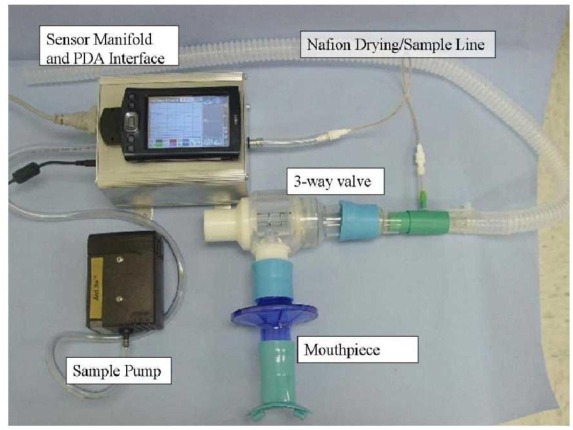

Figure 6.—Breath sensor system.

Exploration Medical Capability

Project "Rescue" for Diagnosis and Treatment of Cardiac Dysrhythmia

Principal Investigator: David W. York, GRC
Co-Investigator: David S. Rosenbaum, M.D., CWRU, MetroHealth System
Chief Engineer: Michael A. Mackin, GRC

Figure 7.—Researchers will test this prototype of the heart monitoring system for ambulatory patients with arrhythmia symptoms.

Serious cardiac rhythm disturbances have been recorded on several occasions during spaceflight. Cardiac dysrhythmia may pose a risk during long-duration spaceflight and is therefore being addressed by NASA's Human Research Program. Project "Rescue" developed a system of prototype hardware and software to aid in the detection and diagnoses of serious cardiac dysrhythmia. The system includes the ability to capture and display near real-time electrocardiogram (ECG) data locally (e.g., on board a spacecraft) and remotely (e.g., on Earth) using Embedded Web Technology (EWT). The system provides detection and diagnostic information using EWT, which was first developed at NASA Glenn for other applications. A team from MetroHealth worked with NASA personnel to establish appropriate protocols and research objectives for the measurement of T-wave alternans and ECG parameters, which are potential indicators for susceptibility to ventricular fibrillations and other potentially life-threatening arrhythmias. MetroHealth also provided the services of nurses with specialized training in T-wave measurements to prepare test subjects and ground baseline data acquisition for a series of microgravity flight tests in the KC-135 research aircraft. Analysis of the test data by MetroHealth confirmed that the T-wave alternans test provides accurate data during microgravity flight. Based on project success, clinical trials of the technology were initiated by MetroHealth. A potential commercial partner has expressed interest in the system, pending the outcome of clinical trials. NASA and MetroHealth have applied for a patent on the technology. Components of Project "Rescue" can also be used with other projects, such as PUMA, to collect, transmit, manipulate and store data.

A Dual-Track Actuated Treadmill in a Virtual Reality Environment: A Countermeasure for Neurovestibular Adaptation in Microgravity

Principal Investigators: Susan E. D'Andrea, Ph.D.
Brian Davis, Ph.D., Cleveland Clinic
Co-Investigator: Jay G. Horowitz, Ph.D., GRC

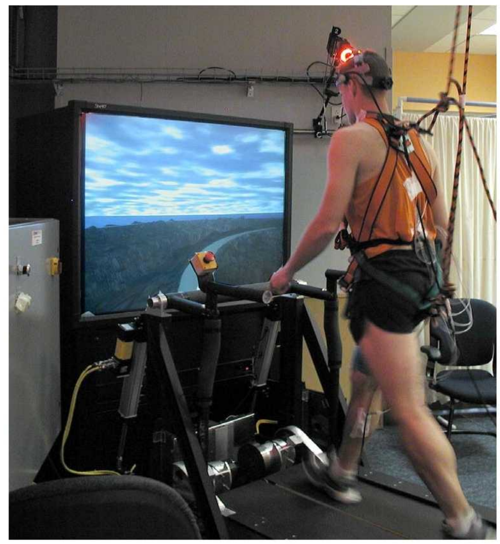
Figure 8.—Subject on Dual Track Treadmill with Virtual Reality.

The neurovestibular system is primarily responsible for balance and stabilization. The microgravity environment alters the cues given to the human neurovestibular system, resulting in sensory conflicts during reentry and post flight. This can cause crew members to suffer from disabling vertigo, oscillopsia, sudden loss of orientation, and overall decreased ability in standing and performance. Countermeasures are needed to eliminate these effects and assure crew safety and performance. A sophisticated dual-track treadmill was developed and utilized in conjunction with a virtual reality environment to potentially mitigate these deleterious effects. Extensive instrumentation was utilized in rigorous biomechanical testing that involved 24 human subjects. It was found that by increasing the input stimulus to the body (specifically, movements of the head), the treadmill forces the user to consistently activate his/her balance reflexes. Test results demonstrated the potential for the dual-track, actuated treadmill device with virtual reality to help alleviate the postural and balance disturbances after exposure to microgravity. In addition to utilization for NASA's exploration missions, this instrumented treadmill could be an effective tool for rehabilitating patients on Earth suffering from balance disorder or other problems involving the neurovestibular system.

Integrating Noninvasive Technologies to Enable Effective Countermeasures During Prolonged Space Travel

Principal Investigator: Rafat R. Ansari, Ph.D., GRC
Co-Investigator: Marco E. Cabrera, Ph.D., CWRU

Figure 9.—Space goggles concept for monitoring astronaut health.

Effective monitoring of astronaut health and the early detection of potential issues are critical for long-duration space missions. This project investigated the development of optical sensors for noninvasive, quantitative medical evaluations of the eyes, skin, and brain. These sensors could ultimately be integrated into a head-mounted device for monitoring and evaluating astronaut health, similar to a pair of goggles. The device would be equipped with a suite of optical biosensors for noninvasive and quantitative medical evaluations. Efforts included continuing work on a new technology for the early detection of cataracts that was developed and validated for clinical use at the National Institutes of Health (NIH). This technology is being used in clinical trials of anticataract drugs that have the potential of being used by people on Earth as well as by astronauts. A noninvasive sensor for glucose monitoring through the eye was developed with the potential for management of diabetes and other systemic diseases on the ground. A laser-Doppler flowmeter for measuring blood flow in the eye to address changing hemodynamic conditions under reduced gravity was developed and tested under low gravity conditions in the KC-135 aircraft. It has been adapted for measuring blood flow in distal finger tips to study the causes of injury to an astronaut's fingers during extravehicular activity. The project included the evaluation of existing technology (near-infrared spectroscopy) and its potential application in exercise-related studies for astronauts and children. The technology may also be applied for use in the intensive care unit. Because of the successes achieved, these efforts will now move to the clinical domain at the University of Texas/Texas Medical Center in Houston.

Sliver Sensor: A Microminiature Monitor for Vital Electrolyte and Metabolite Levels With Adaptability, Self-Checking Capability, and Negligible Power Requirements

Principal Investigator: Miklos Gratzl, Ph.D., CWRU
Co-Investigator: Koji Tohda, Ph.D., CWRU

Understanding changes in human physiology during space missions is important to maintaining astronaut health and safety. The Sliver Sensor is a novel device that was conceived, developed and tested for in vivo monitoring of glucose and electrolytes in the interstitial fluid of astronauts during spaceflight. In addition to increasing basic understanding of metabolic changes in space, the device could also be critical in identifying and handling certain medical emergencies. The minimally invasive, micro miniature Sliver Sensor is placed just under the skin. Individual optical sensing capsules in the device change color with changes in concentration of glucose and basic electrolytes. The changes in color are read by an external watch-like device. The optical coupling eliminates the need for wires or optical fibers crossing the skin. In vivo biocompatibility studies on rats were conducted and the sensors were found to be biocompatible for at least 28 days. On Earth, the device can be used to monitor electrolytes in the blood of critically ill patients and for diabetes management. An industry sponsored project enhanced the research conducted under this project. An award was received from the Coulter-Case Translational Research Partnership for complete in-vivo testing of the developed device. Pre-clinical trials are expected to occur in the near term.

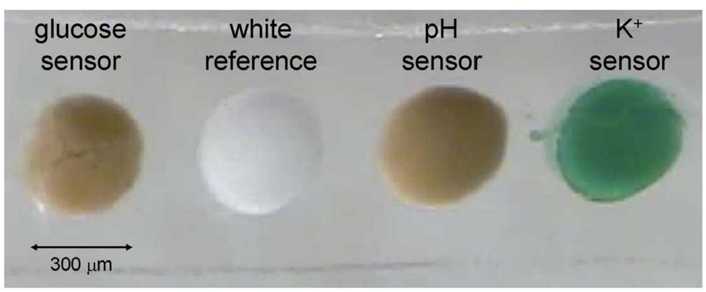

Figure 10.—An optical glucose, pH and K+ sensor together with optical white reference.

A High-Resolution Portable Ultrasonic Imaging System

Principal Investigator: Shuvo Roy, Ph.D., Cleveland Clinic
Co-Investigators: Aaron Fleischman, Ph.D., Cleveland Clinic
Noel Nemeth, Ph.D., GRC
Ken Goldman, Ph.D., H-Cubed, Inc.

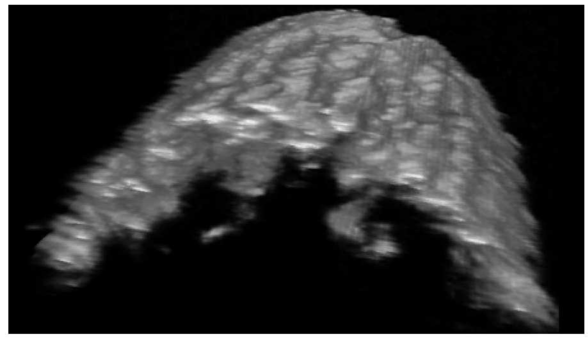

Figure 11.—Volume renderings of the ultrasound three-dimensional image.

Developing small ultrasonic imaging systems is important to diagnose skin and bone problems in space because other imaging technologies are not compatible with spaceflight. The objective of this project was to develop a portable, high-resolution ultrasonic imaging system for accurate diagnosis and monitoring of skin and bone conditions of astronauts. Specific bone conditions of interest included bone loss and fracture detection. A system was developed using 4 mm-diameter polyvinylidene fluoride (PVDF) focused ultrasonic microtransducers. Prototypical transducers had a 40 MHz center frequency with a fractional bandwidth of 60 percent. High-resolution imaging of human cancellous bone was successfully demonstrated using a bone specimen excised from a cadaveric human calcaneus. The bone was scanned in increments of 0.1 mm using a high-precision motorized stage. Amplitude of the received signal was detected along the scan lines and converted into image density. Then, regular visualization methods applied. Ray casting with blending was used for three-dimensional (3–D) volume rendering. This project demonstrated that high-frequency focused ultrasonic microtransducers can be used to image bone in both fundamental and harmonic imaging modes. Overall, the technical accomplishments have established the feasibility of ultrasound imaging for examining bone microstructure. With additional development, the PVDF microtransducers can be integrated into a portable ultrasound imaging system, which can applied to the diagnosis of fractures and bone loss in astronauts on space missions. On Earth, the availability of portable ultrasound systems can enhance clinical diagnosis for application in remote telemedicine, which is currently encumbered by expensive and bulky equipment. The focused ultrasonic transducer has also been used to examine coronary tissue with high-resolution for advanced plaque detection and characterization. Two large medical device companies are currently engaged in license discussions for potential commercialization of the transducer design/manufacturing for intravascular ultrasound (IVUS) imaging applications.

In Vivo Bioluminescent Molecular Imaging With Application to the Study of Secretory Clusterin, a Potential Biodosimeter During Space Exploration

Principal Investigator: David L. Wilson, Ph.D., CWRU
Co-Investigators: David A. Boothman, Ph.D., UHCMC, CWRU
Andrew Rollins, Ph.D., CWRU

Assuring that crews can live and work safely in the radiation environment of space during extended missions is vital for human exploration. A key element of maintaining astronaut health is the development of technology to monitor the effects of space radiation on astronauts. An In Vivo Molecular Imaging Device for Measurement of Radiation Effects was developed for measuring radiation exposure. The project team successfully constructed an imaging-based, biological radiation dosimeter using a reporter to produce a specific protein. Using this unique imaging instrument, the team performed cellular and animal testing to show that the bioluminescence signal responded to radiation exposure in a predictable way. This demonstrated the potential for future development of a new class of instruments to measure the effects of space radiation on astronauts. This imaging instrument helped gather critical preliminary data for large infrastructure and conventional research proposals. The consortium award was an important cornerstone for obtaining a series of successful proposals totaling more than $11 million, which stimulated substantial growth within the CWRU imaging program. In addition, there have been publications and research awards from NIH that were made possible with this device. The instrument was also the first in vivo molecular imaging device for small animals demonstrated in Northeast Ohio.

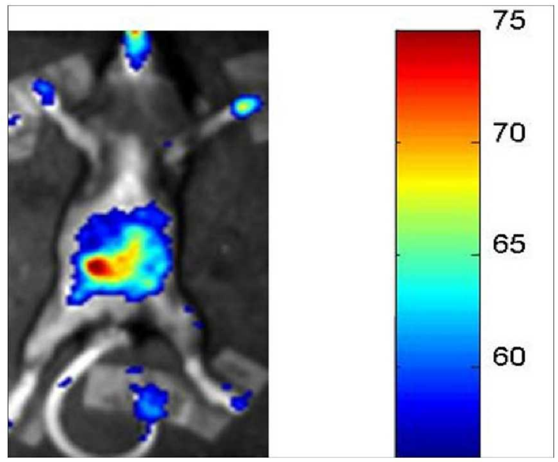

Figure 12.—In vivo imaging of transgenic mouse.

Rapid Design and Simulation Tools for Space-Bound Biochip Devices

Principal Investigator: Arnon Chait, Ph.D., GRC
Co-Investigators: Emily Nelson, Ph.D., GRC
David Jacqmin, Ph.D., GRC
Mohammad Kassemi, Ph.D., NCSER
Charles Panzarella, Ph.D., OAI
Marianne Zlatkowski, Ph.D., CWRU

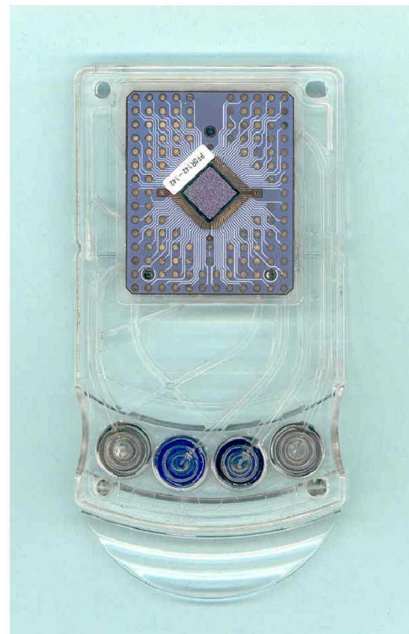

Figure 13.—Nanogen's DNA/RNA electrically addressable microarray.

A biochip is a collection of miniaturized test sites on a surface area usually smaller than a fingernail. The test sites, or microarrays, can perform many biological tests at the same time. A biochip can quickly perform thousands of biological reactions and are rapidly becoming critical for genetic, toxological, protein and biochemical research. Biochips could provide unique, miniaturized on board diagnostic systems and treatment devices for long-duration NASA missions. However, there are significant challenges when using biochips in a microgravity environment. The Rapid Design and Simulation Tools for Space-bound Biochip Devices Project developed a numerical simulation environment for customizing and optimizing biochips for microgravity operations. Microgravity-unique physics and biological sensing requirements were extensively tested using leading commercial off-the-shelf simulation codes to assess the best candidates to serve as a generalized simulation environment. The ACE+ code had the best combination of embedded capabilities for the project. Customized codes were developed in-house for specific microgravity physics effects involving free surface behavior, bubble dynamics, and automated biochip optimization environment. Numerous studies encompassing biochips and microgravity operations were completed and generalized tools were developed. An ACE+ based optimization environment for microfluidic devices was demonstrated with follow-on work by a vendor (via SBIR funding) and is now a commercially available tool. In addition to the collaboration among consortium members, additional partnerships were established with NASA's Marshall Space Flight Center, the Jet Propulsion Laboratory, Sandia National Laboratory, industry and academic institutions.

Controlled-Release Microsystems for Pharmacological Agent Delivery

Principal Investigator: Shuvo Roy, Ph.D., Cleveland Clinic
Co-Investigators: Aaron Fleischman, Ph.D., Cleveland Clinic
Christian Zorman, Ph.D., CWRU
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Effectively administering pharmacological agents is a key capability needed to ensure the health of astronauts during space missions. Miniature, implantable microsystems for the controlled release of pharmacological agents offer the potential for both research investigations into health problems of astronauts as well as for their immediate treatment. The unique drug delivery system investigated in this project is based on diffusion through nanoporous membranes that are fabricated using micromechanical systems (MEMS) techniques. Diffusion through the porous membrane is a function of pore size (5 to 100 nm in diameter), which can be designed to achieve different rates of release for a given pharmacological agent. Continuous drug delivery through a slow infusion while maintaining the right therapeutic concentration of the drug in the patient's body enables better control and eliminates the need for repeated injections. The project's key challenges to make this highly advanced concept a reality included ensuring structural integrity of the device, particularly fracture reliability and maintaining predictable fluid flow characteristics. Both of these challenges were successfully addressed. The project focused on nanoporous silicon membranes, but also explored fabrication of silicon carbide membranes. The project established the feasibility of developing robust silicon nanoporous membranes with appropriate pore size distribution for use in controlled release microsystems. The underlying technology from this project has potential for use in ultra filtration applications such as generating medical grade water and in developing a bio-artificial kidney that can be used instead of dialysis. The kidney project has been funded through a recent NIH three-year grant to the Cleveland Clinic.

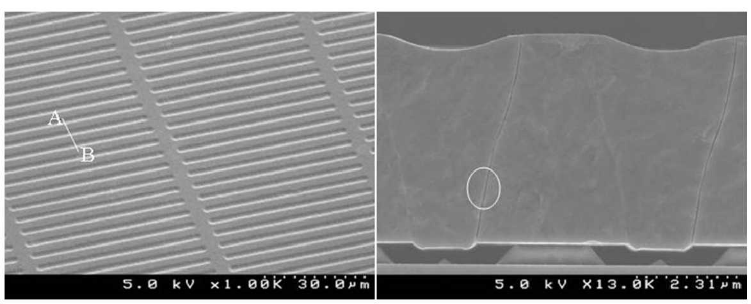

Figure 14.—Top and cross-sectional view of a nanoporous membrane matrix.

The Outcome

The John Glenn Biomedical Engineering Consortium projects have provided significant contributions to NASA by developing technologies to address critical risks affecting the safety, health and performance of astronauts during long-duration space missions. The projects have developed new diagnostic devices and potential methods for reducing the harmful effects of exposure to space. The consortium has also served as a pathfinder and model for interdisciplinary, multiinstitution collaboration. Additional collaborations have resulted from the successful experiences of the consortium. The consortium has served as a cornerstone for establishing NASA Glenn and Northeast Ohio as an integral part of NASA's Human Research Program.

In addition to the benefits to NASA, many of the devices and techniques investigated may improve health care on Earth. There has been significant interest in commercializing products from several consortium projects, potentially contributing directly to economic development in the biosciences. The John Glenn Biomedical Engineering Consortium continues to contribute to NASA's mission and the vitality of Northeast Ohio.

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14. ABSTRACT
The John Glenn Biomedical Engineering Consortium was established by NASA in 2002 to formulate and implement an integrated, interdisciplinary research program to address risks faced by astronauts during long-duration space missions. The consortium is comprised of a preeminent team of Northeast Ohio institutions that include Case Western Reserve University, the Cleveland Clinic, University Hospitals Case Medical Center, The National Center for Space Exploration Research, and the NASA Glenn Research Center. The John Glenn Biomedical Engineering Consortium research is focused on fluid physics and sensor technology that addresses the critical risks to crew health, safety, and performance. Effectively utilizing the unique skills, capabilities and facilities of the consortium members is also of prime importance. Research efforts were initiated with a general call for proposals to the consortium members. The top proposals were selected for funding through a rigorous, peer review process. The review included participation from NASA's Johnson Space Center, which has programmatic responsibility for NASA's Human Research Program. The projects range in scope from delivery of prototype hardware to applied research that enables future development of advanced technology devices. All of the projects selected for funding have been completed and the results are summarized. Because of the success of the consortium, the member institutions have extended the original agreement to continue this highly effective research collaboration through 2011.

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