APT CENTER

WE BUILD TRANSLATION

FOURTH EDITION

SCIENTIFIC REPORT TO THE COMMUNITY

Professor Wen H. Ko (1923-2017)

Professor Wen Hsiung Ko was born in Fujian, China in 1923 and moved to the US in 1954. He married Christina in 1957 and lived in Cleveland until 2014 where they were leaders in the Cleveland Chinese community. He had an incredibly productive professional life for over 60 years. He was **a pioneer in microsensors, actuators, integrated microsystems, medical implants, telemetry, and packaging**.

Prof. Ko's career started at Case Western Reserve University (then known as Case Institute of Technology) where he received his M.S. in 1956 and Ph.D. in 1959. He was a **prolific researcher**, publishing more than 450 papers and conference abstracts and accruing 26 patents. He established and led the **Electronics Design Center**, an internationally recognized research center specializing in the development of microsensors and microsystems. After retiring in 1993 at the age of 70, he joined the emeritus faculty in the Electrical Engineering and Computer Science department, yet maintained an active research program that continued until Fall 2014.

As a mentor, he advised approximately 160 M.S. and Ph.D. students. His mentorship style was one of development and progress, with a sense of humor that held his hardworking group together in long, sometimes contentious meetings. Prof. Ko's lab has been described as "*a museum of the history of microelectronics and implantable medical devices, an archaeological dig where different layers represent unique epochs throughout his career.*"

Prof. Ko and his wife Christina at the White House for Christmas in 2013

Among Prof. Ko's many accomplishments include his founding of the Transducers Research Foundation and the Hilton Head Workshop series. Additionally, he was the recipient of many awards, including the Career Achievement Award at the Transducers International Conference and the Case Alumni Association's Meritorious Service Award.

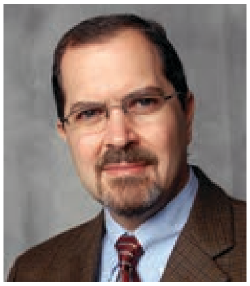
Prof. Ko joined the APT Center from its inception in 2005 and collaborated with many of our researchers, including Drs. Margot Damaser, Philip Feng (below with Prof. Ko), and Christian Zorman. While in his 80's, he was **awarded the first APT Center Innovation Incentive pilot grant**,

which helped him obtain a NIH R21 grant to develop a micropackaging technology for implantable micro devices and systems. He maintained a vast memory of all current and past research in the field and was innovative, creative, energetic, and persistent in his pursuit of his research.

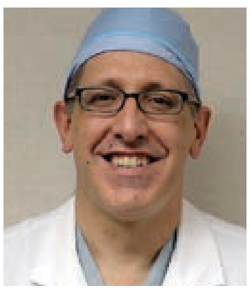
Prof. Ko died on Monday, December 4, 2017 in Palo Alto, CA at the age of 94. His spirit and intellect continued to be strong and curious up to the end, and he was surrounded by family in his last days. In appreciation of his contributions to the APT Center and in honor of his accomplishments, our summer student internship program has been renamed the Wen H. Ko Summer Internship Program. The program sponsors summer research for five undergraduate students.

To learn more about Prof. Ko's amazing life, visit **http://www.case.edu/ko-memorial**.

A LETTER FROM THE DIRECTORS



Ronald Triolo, Ph.D.



Gilles Pinault, M.D.

The Advanced Platform Technology (APT) Center is a National VA Rehabilitation Research & Development Center established January 2005 in collaboration with Case Western Reserve University that is focused on serving Veterans with sensorimotor dysfunction, cognitive impairment, or limb-loss using cutting edge technologies and rehabilitation techniques, and translating them from proof of concept to viable clinical options. Our research programs focus on four major areas: **Prosthetics and Orthotics, Health Monitoring and Maintenance, Neural Interfaces, and Enabling Technologies**.

Active partnerships with the Cleveland Clinic, University of Michigan, Cornell University and others have resulted in a cohesive, interdisciplinary network dedicated to the pursuit of clinically relevant and highly impactful assistive, restorative, or diagnostic technologies. Our investigators have secured external scientific, development, and translational research funding from local and federal granting agencies and industrial partners. This has resulted in peer-reviewed articles in the most prestigious journals, as well as innumerable positive stories in the lay press and popular media.

Our Core Investigators currently have 64 research projects as Principal Investigators, with an active portfolio valued at $13MM. In addition to our highlighted activities in this report, the APT Center was responsible for the Louis Stokes Cleveland VA Medical Center being designated as a new Innovation Site in the national VA Center for Innovation designed to overcome the challenges of translating innovations into practice. Also, our number of early career investigators has grown and four have been awarded Career Development Awards. Since our second competitive renewal in 2015, we have worked to implement new strategies to enhance communication, create opportunities for professional growth, expand our technical capabilities, and actively seek out and nurture new industrial interactions.

You are invited to share our passion for the research, technology and translational opportunities we work hard to achieve every day for the Veterans we serve.

Warm Regards

Ronald Triolo, Ph.D.
Executive Director

Gilles Pinault, M.D.
Co-Director

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APT CENTER AT A GLANCE

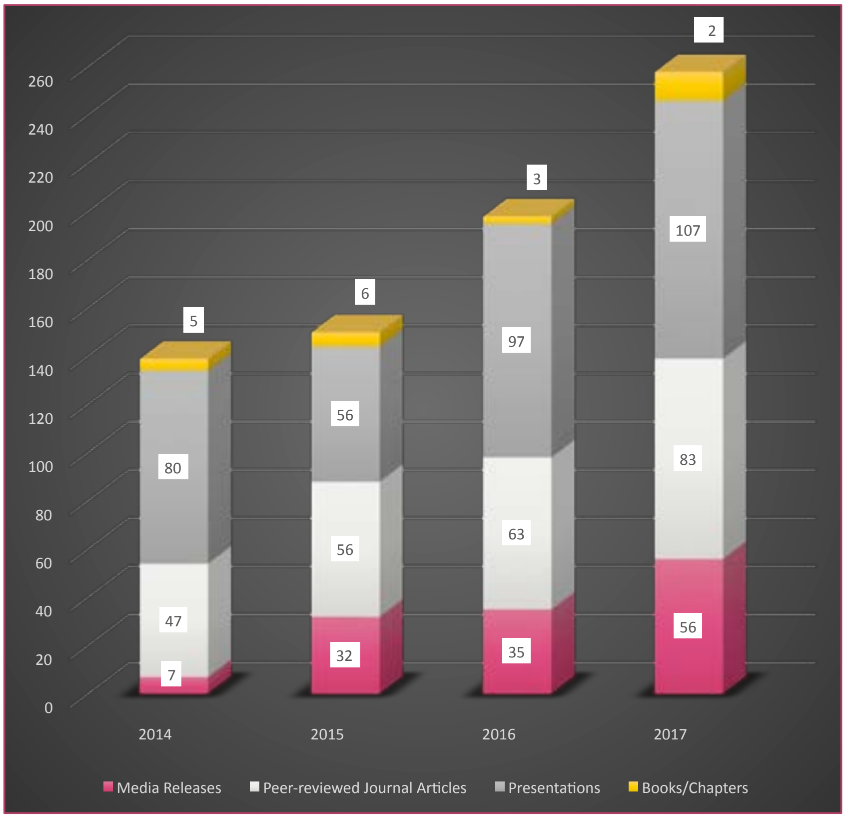
People

- 53 Scientists and Physicians
- 19 Engineers and Professional Support Staff
- 134 BS/MS/PhD/Post-Doctoral Trainees (2014-2017)

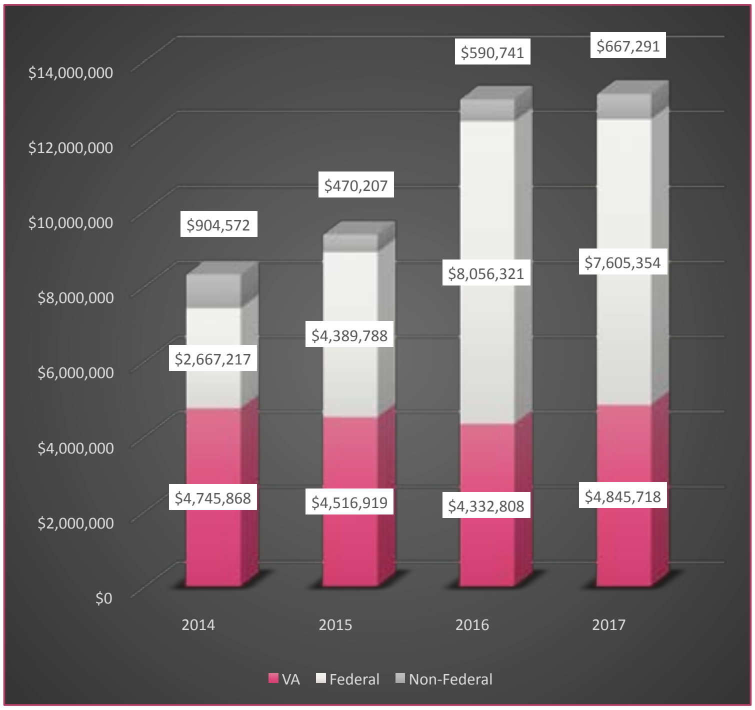
Innovations

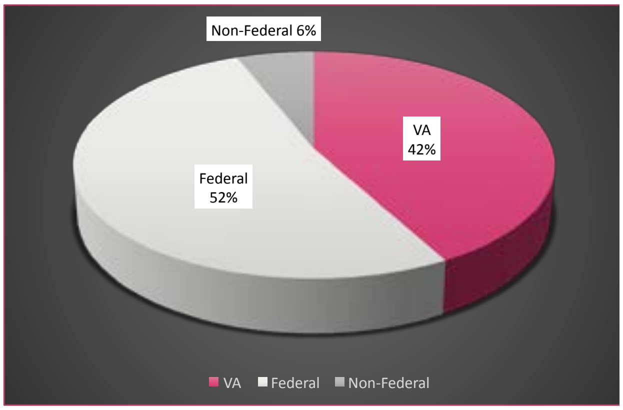
- 23 Invention Disclosures (2017)
- 34 Patent Applications (2017)
- 17 Total APT Center Patented Concepts and Prototypes

Information Dissemination FY 2014-2017



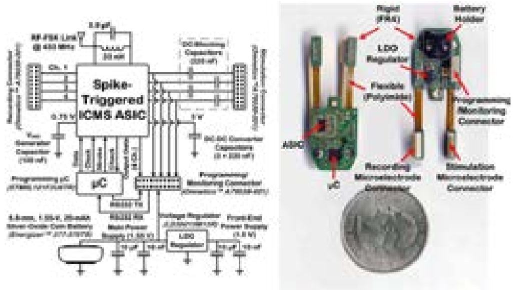
APT Center Cumulative Funding FY 2014-2017





Methods And Associated Neural Prosthetic Devices For Bridging Brain Areas To Improve Function

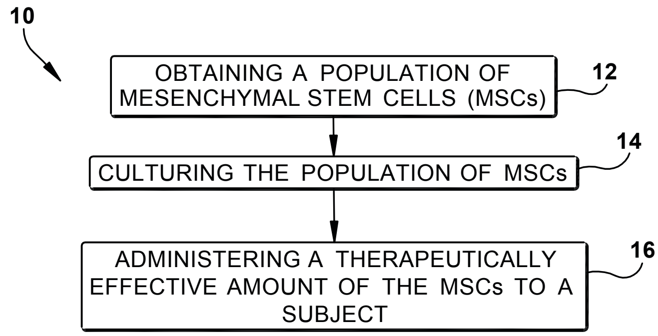
US Patent 9,008,780
Issued April 14, 2015
APT Center Inventor: Pedram Mohseni, Ph.D.



This patent relates generally to methods and associated neural prosthetic devices for bridging brain areas, between which there is substantially no effective communication, to restore or improve neurological function. The method forms an artificial bridge and establishes lasting communication between two neural sites, promoting functional recovery after brain injury. The neural prosthetic device (above) comprises an integrated circuit with recording channels, a processor unit, and stimulation channels.

Methods For Treating Genitourinary Disorders

US Patent 9,782,440
Issued October 10, 2017
APT Center Inventor: Margot Damaser, Ph.D.

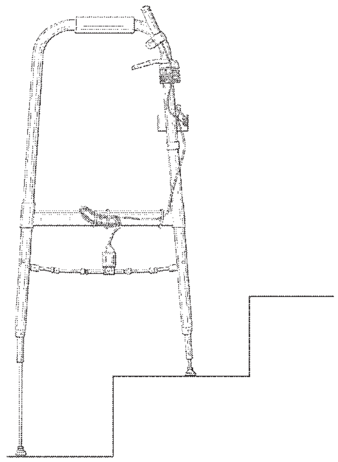


This patent relates generally to stem cells and methods for tissue repair and regeneration, and more particularly to mesenchymal stem cells, concentrated culture media therefrom, and related methods for treating or preventing genitourinary disorders, such as urethral and pelvic floor disorders. One of the therapeutic methods uses mesenchymal stem cells to promote structural and functional recovery of a dysfunctional organ or biological tissue associated with a genitourinary disorder.

Self Leveling Walker

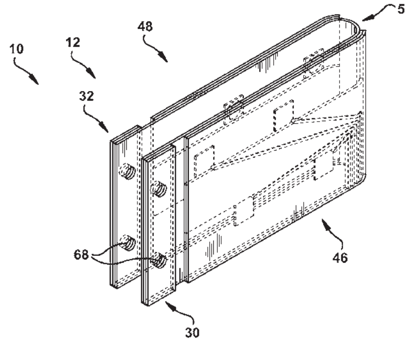
US Patent 9,119,757
Issued September 1, 2015
APT Center Inventors: Ronald J. Triolo, Ph.D., Thomas Bulea, Ph.D.

This invention relates to a self leveling walker to assist persons who have insufficient strength or movement in their legs when standing and walking on uneven surfaces, and for traversing ramps and stairs. The inventive self leveling walker includes a frame with a leveling assembly that adapts the length of the walker's four legs to keep the walker at a constant level. This allows the user to maintain an erect standing posture at all times, without the need to lean to accommodate uneven surfaces.



Implantable Cuff And Method For Functional Electrical Stimulation And Monitoring

US Patent 9,603,538
Issued March 28, 2017
APT Center Inventors: Dustin Tyler, Ph.D., Matthew Schiefer, Ph.D., Michael Miller, M.S., Ronald Triolo, Ph.D.



This patent relates generally to implantable biomedical interfaces, and more particularly to an implantable cuff for biological soft tissue that can be used as an electrode interface for selective stimulation and/or monitoring of nerve groups. The implantable cuff (above, folded in half) has at least one conductive segment in electrical communication with at least one conductor. The cuff, or "elastic collar," is configured around a nerve to deliver electrical stimulation or record electrical activity of the nerve.

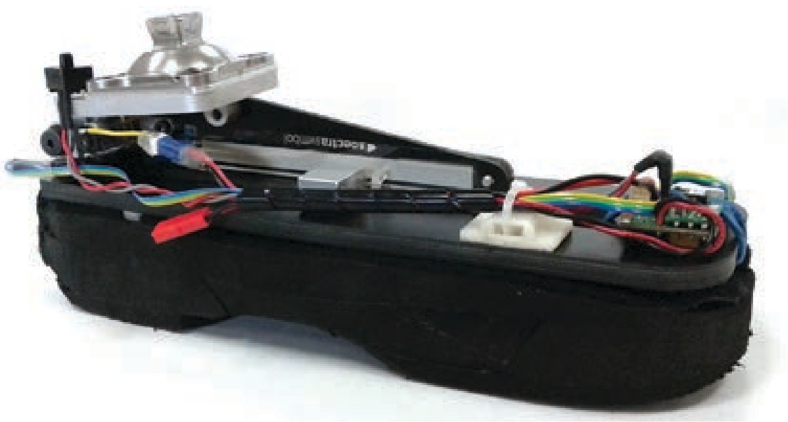
Wen H. Ko Summer Internship Program

The summer of 2017 marked the inaugural year for the APT-Summer Internship Program (APT-SIP) for undergraduate science, technology, engineering, and math students. Of the 16 applicants, 4 students were accepted into the 10-week program to participate in cutting-edge biomedical research projects under the mentorship of Drs. Jeffrey Capadona, Evon Ereifej, Matthew Schiefer, and Ronald Triolo. Dr. Schiefer led the program by coordinating opportunities and activities for the interns. They attended regular seminars at CWRU and had the opportunity to present posters and attend conferences. All interns have continued working in their respective mentor's lab. Three are now co-authors on APT Center publications and another had an abstract accepted to the Biomedical Engineering Society 2017 conference.

(L-R) Dr. Evon Ereifej, Dr. Brooke Odle, Helen Liu, Joshua Rosenberg, Vi Huynh, Dr. Matt Schiefer, Alex Wolkoff, Keying Chen, Keith Dona, Dr. Hamid Charkhkar, Dr. Naji Alibeji

APT Center Distinguished Lecture Series

In late 2016, we began the "APT Center Distinguished Lecture Series" to bring in experienced researchers focusing on research and rehabilitation efforts nationally. Presentations have included 1) control mechanisms of human locomotion and applications to robotics and powered prostheses and orthoses (see below), 2) devices to improve gait by exploiting biomechanical workarounds for lost function, and 3) neural culture platform that can be used to screen biologically-active surface coatings and mechanical properties in 3D.



Ankle-foot devices that retain the benefits of passive systems (low weight, height, complexity, and cost), while adding simple robotic features that improve versatility and adaptability across tasks. Courtesy of Dr. Peter Adamczyk

RECOGNITIONS & UPDATES

Recognitions

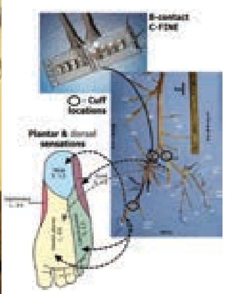
Dr. Jeffrey Capadona was named as one of Crain's Cleveland Business's "Forty under 40" of 2015 – an annual honor for 40 individuals under the age of 40 who are making positive changes to the Northeast Ohio business community. Dr. Capadona's expertise is in the development of bio-inspired and biomimetic materials to interface with biological systems.

Dr. Paul Marasco received the Presidential Early Career Award for Scientists and Engineers (PECASE) Award in 2016 - the highest honor bestowed by the U.S. government on outstanding scientists and engineers - from President Barack Obama. Dr. Marasco's research uses neural-machine-interfaces to provide touch and movement sensation to prosthetic limbs so that individuals with amputation feel like the devices are a part of their body. Past awardees: Drs. Jeffrey Capadona and Margot Damaser.

APT Center Investigators, **Drs. Ronald Triolo (2014)**, **Margot Damaser (2015), Eben Alsberg** and **Horst von Recum (2016)**, and **Jeffrey Capadona** and **Dustin Tyler (2017)**, were appointed to the prestigious College of Fellows of the American Institute for Medical and Biological Engineering (AIMBE) - the top 2% of the most accomplished and distinguished medical and biological engineers nationally and internationally – for outstanding contributions to their respective fields.

Project Updates

Drs. Ronald Triolo and **Dustin Tyler** progressed their peripheral nerve cuff electrodes from animal models into human studies with great success. With VA and NIH (NIBIB) funding, two participants paralyzed by spinal cord injuries are relearning to stand and walk with implanted neural stimulation systems utilizing the new Composite Flat Interface Electrode (C-FINE). One participant can now stand for more than 20 minutes and pedal a bike. Four upper or lower limb amputees are also benefiting from the C-FINE (see p. 4).



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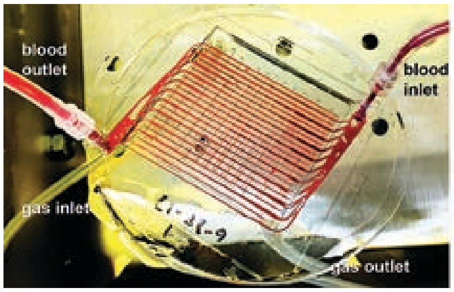
Dr. Joe Potkay's team continues to make progress on their microfluidic artificial lung research. The team has developed and applied the first comprehensive design optimization procedure for these devices, resulting in the most volume efficient device to date. They have further developed a new manufacturing technique that uses a cylindrical substrate, akin to roll-to-roll



manufacturing, that should enable large scale manufacturing. They continue to develop flow resistant biocompatible coatings and have initiated experiments in rabbits. Finally, Dr. Potkay's team has initiated a study to develop the world's first 3D printed microfluidic artificial lung.

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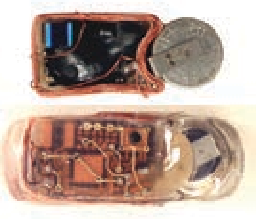
Drs. Margot Damaser, **Steve Majerus**, and **Hui Zhu** have developed a miniature, catheter-free, wireless, rechargeable pressure monitor that can sense continuous internal organ pressure for extended periods of time. The primary application is chronic ambulatory bladder pressure monitoring to treat urinary incontinence in spinal cord injured Veterans. The "Uromonitor" has been successfully tested in the bladder of a calf and demonstrated bladder pressure



recordings during unrestricted activities. This team has active collaborations with a major medical device manufacturing company to translate the technology into novel tools for more accurate diagnosis and treatment of bladder dysfunction.

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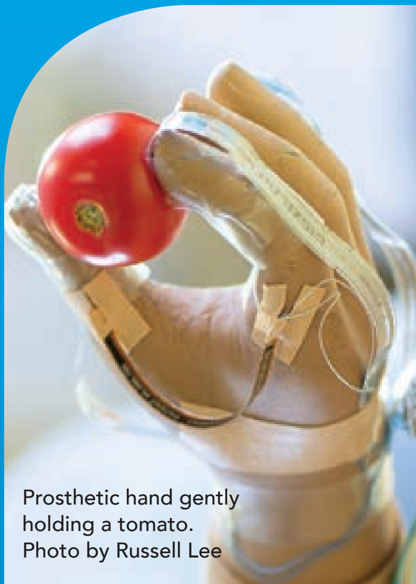
NSF has awarded **Drs. Roger Quinn, Musa Audu,** and **Ronald Triolo** a 3-year, $1 million grant to add automatic balance control for standing and walking to the prototype Hybrid Neuroprosthesis (HNP) being developed with Rudi Kobetic, MS. The HNP uses a "muscle-first" approach to restore walking in individuals paralyzed from a spinal cord injury and extends ongoing work to develop muscle-driven exoskeleton walking assist devices developed with VA support by Mr. Kobetic and his team.

■

Drs. Musa Audu and **Ronald Triolo** have received $678,338 from CDMRP SCIRP and $2.2M from NIH NINDS to continue and expand their prior VA funded project for 4 years to improve seated balance and trunk control after paralysis and determine the feasibility of a new comprehensive trunk posture and balance control system. Currently, they have 23 subjects and have shown that stimulating back and hip muscles can improve aspects of daily life, such as reaching, transferring, and propelling their wheelchairs.



Prosthetic hand gently holding a tomato.
Photo by Russell Lee

Principal Investigators:

Paul Marasco, Ph.D.

Ronald Triolo, Ph.D.

Dustin Tyler, Ph.D.

Funding Agencies:

Defense Advanced Research Projects Agency (DARPA)

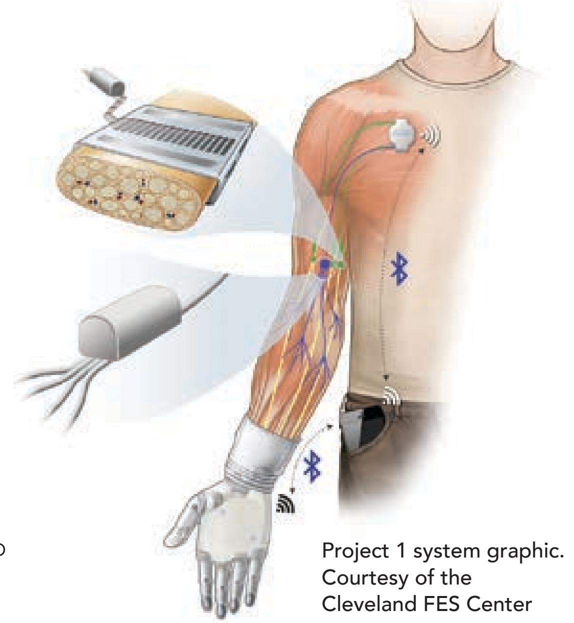
Congressionally Directed Medical Research Program Defense Medical Research and Development Program (CDMRP DMRDP)

Veterans Affairs, Rehabilitative Research and Development

Focusing on Sensory Feedback

While upper limb prostheses have come a long way, artificial arms and hands lack adequate sensory feedback. In 2014, the Defense Advanced Research Projects Agency (DARPA) launched the Hand Proprioception and Touch Interfaces (HAPTIX) program. The program aims to help restore full and natural functionality to wounded service members and veterans. To date, 46% of its budget has been awarded to APT Center Investigators. These are the three research projects receiving major contracts from DARPA:

PROJECT 1: Restoring Amputees' Sense of Touch – Dustin Tyler, Ph.D., serves as PI on a 5-year, $15.2 million project to develop a fully-implantable mobile prosthetic "iSens System" that uses electrical stimulation to provide amputees natural upper limb sensation. When amputees use their prosthetic to touch something, they actually feel it in their fingertips. When completed, the only external piece of hardware will be an iPod®-sized controller. Dr. Tyler also has a 4-year, $1 million grant from the VA RR&D for this project.



Project 1 system graphic. Courtesy of the Cleveland FES Center

PROJECT 2: Evaluating Prosthetic Limb Technology – Paul Marasco, Ph.D., leads a 5-year, $2.5 million project to develop a suite of six clinically-relevant outcome metrics for advanced bi-directionally integrated prosthetic limbs that are rooted in cutting-edge technology. While prosthetic limb technology has undergone significant advancements in recent years, there is currently no standardized set of metrics to evaluate these technologies.

PROJECT 3: Re-establishing Natural Sensation for Lower Limb Amputees – Ronald Triolo, Ph.D., was awarded $1.7 million for a 4-year study to ascertain the feasibility of re-establishing how trans-tibial or trans-femoral limb prostheses interact with the environment that are indistinguishable from perceptions of the intact limb. This will give users better balance, prevent falls and enhance the ability to negotiate complex and unpredictable environments without conscious attention. Dr. Triolo recently received a 4-year, $2.5 million grant from CDMRP DMRDP for this project.

Project 3 subject indicating specific location of sensation felt in the foot after stimulation

A small robot that generates illusory perceptions of joint movement when applied to deep muscles

Principal Investigator:
Paul Marasco, Ph.D.

Funding Agencies:
Defense Advanced Research Projects Agency (DARPA)

National Institutes of Health

Veterans Affairs, Rehabilitative Research and Development

Getting the Mind to Accept Prosthetics

One of the biggest hurdles to advancement of prosthetics is not the actual devices, but the human mind. Kinesthesia, the sensation of movement, is difficult with prosthetics. How can the mind be made to accept prosthetic limbs as though they are real?

Paul Marasco, Ph.D., focuses on broad-based sensory neuroscience research to understand the mechanistic aspects and brain organizational properties of kinesthesia. His express goal is to develop a deeper systems-level understanding of the kinesthetic sense so that methodologies can be established to provide prosthetic limbs with a physiologically relevant sense of limb position.

Dr. Marasco has three primary projects related to kinesthesia:

- Developing a systems-level understanding of neural substrates, including peripheral receptors and brain organization, as well as mechanistic insight.
- Complex grip movement perception through active movement percepts and volitional neural motor control to create illusionary limb movement sensation. Upper limb amputees can determine prosthetic hand movement and closing point solely with kinesthetic illusionary input.
- A touch-integrated prosthetic limb for long-term home use is in development. The battery-powered, stand-alone system creates sensation in the thumb, fingers and palm (see photo below).

Educating Amputees on Self-Management Interventions

Principal Investigators:

Joseph M. Czerniecki, M.D., VA Puget Sound Health Care System

Aaron P. Turner, Ph.D., VA Puget Sound Health Care System

Cleveland Site Principal Investigator:

Clay M. Kelly, M.D.

Funding Agency:

Veterans Affairs, Rehabilitative Research and Development

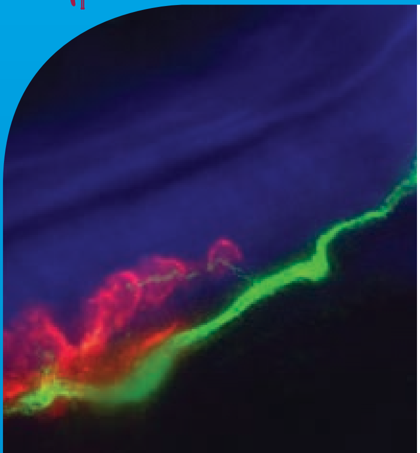
Patients in the VA Health Care System with lower extremity amputations are at high risk for morbidity, mortality, loss of function and reduced quality of life. One way to minimize those risks is for patients to become knowledgeable about and manage their condition.

The Promoting Amputee Life Skills (PALS) program is an 8-week self-management course that has been shown to help people with limb loss learn skills to improve their lives. This study is designed to evaluate and compare VETPALS, a group-based, modified version of PALS, to a second program involving individual patient education for patients with recent lower-limb amputation.

Clay M. Kelly, M.D., anticipates that the results of this 4-year study will be integrated into the VA Amputation System of Care, which incorporates the latest practices in medical rehabilitation management, rehabilitation therapies and prosthetic technology. The study has three primary aims:

- Determine the impact of a group-based self-management intervention on physical and psychological functioning for veterans with limb loss.
- Ascertain its impact on self-efficacy, patient activation, problem solving, quality of life and positive affect.
- Establish if VETPALS would be a valuable addition to the VA Amputation System of Care considering the interest and participation of patients, the challenges and solutions involved in implementing the program and participant feedback about their experiences in the program.

Monthly support group meeting for Veteran amputees



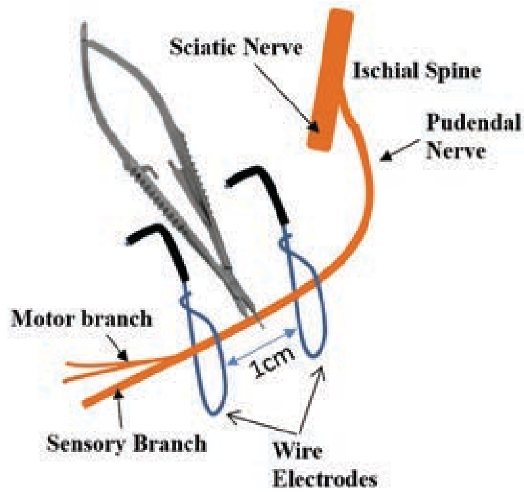
Fluorescent photo of urethral tissue – blue is striated muscle, green is nerve, and red is neuromuscular junction

Principal Investigator:
Margot Damaser, Ph.D.

Funding Agencies:
National Institutes of Health

Veterans Affairs, Rehabilitative Research and Development

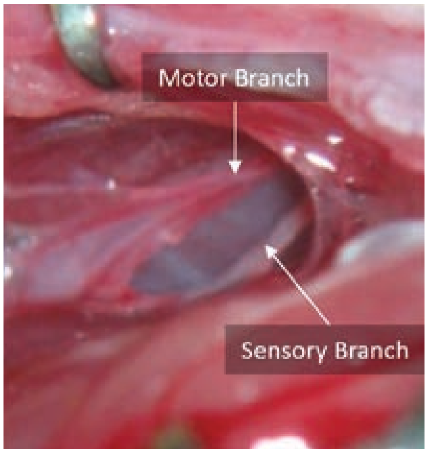
Finding a Treatment for Stress Urinary Incontinence

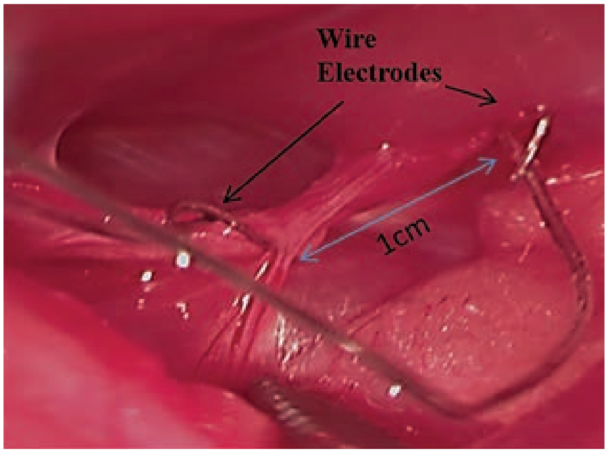


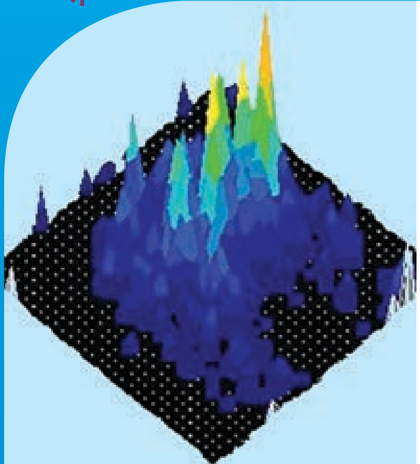
Stress urinary incontinence (SUI), the involuntary leaking of urine during physical movement or exertion, is a common condition, affecting approximately 15 million adult women in the United States. SUI greatly affects quality of life – simply laughing or coughing can lead to embarrassing urine leaks. In addition, more than $12 billion is spent annually on management of SUI.

For more than two decades, Margot Damaser, Ph.D., has investigated female pelvic floor disorders, including SUI. This current project will assess the use of electrical stimulation of the pudendal nerve to promote neuroregeneration and functional recovery from SUI as a consequence of childbirth injury. Vaginal delivery can damage both the pudendal nerve, which innervates the external urethral sphincter (the primary muscle responsible for urinary continence), and the sphincter itself. Dr. Damaser hypothesizes that the damaged sphincter cannot produce enough neurotrophins to help regenerate the damaged pudendal nerve, causing the sphincter to atrophy from lack of use. By the time the nerve regenerates and re-innervates the muscle, there is less muscle to help maintain continence. Dr. Damaser's past studies found that daily stimulation is more effective than twice a week.

This study will also focus on the specific neurotrophins that are upregulated in the pudendal nerve after stimulation. Future projects will study whether pelvic or vaginal stimulation will suffice instead of the current method of applying stimulation at the site of the nerve.







Seated pressure distribution mapping: yellow/orange indicates high levels of pressure under left gluteal region

Principal Investigator:
Kath Bogie, D.Phil

Funding Agencies:
Congressionally Directed Medical Research Programs (CDMRP) Spinal Cord Injury Research Program (SCIRP)

Craig H. Neilsen Foundation

Toward Individualized Care and Prevention of Pressure Injuries

Pressure injuries (PrI) are serious complications causing staggering costs and human suffering, especially for those with a spinal cord injury (SCI). PrI development soon after injury will slow or even stop the progress of SCI rehabilitation and increases the risk for recurrent PrI development. This has a devastating and continuing effect on the affected individual's overall health and quality of life.

Kath Bogie, D.Phil, has led studies to develop health maintenance technologies for tissue health, wound management, and wheelchair seating for two decades. Currently, Dr. Bogie has two projects focused in the clinical management of PrI in Veterans with SCI.

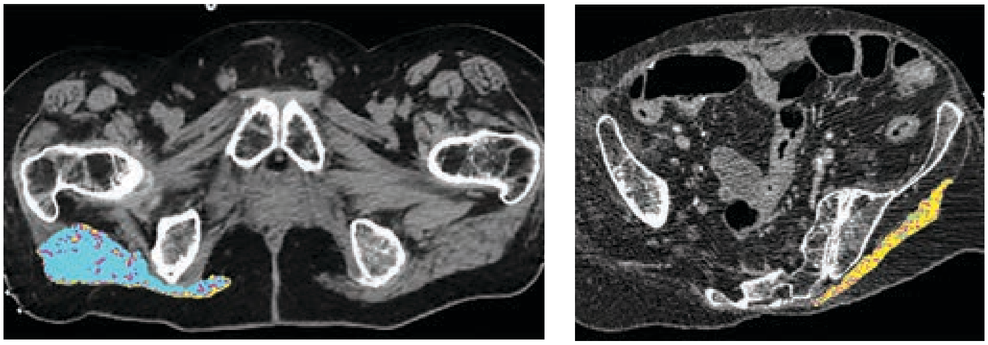
Project 1: Establish a model of biomarkers for PrI development risk by investigating risk factors and evaluating relationships between muscle quality and tissue resilience under applied loads. This study has discovered the following:

- Muscle composition impacted skin and muscle blood flow in those with > 15% gluteal intramuscular fat under the ischial tuberosities (see CT scans below). Those with higher levels of intermuscular fat were more likely to have a history of severe PrIs.
- Blood tests revealed that FAPB4 is seen in those with fattier tissues (> 20%).

Project 2: Develop and test the Spinal Cord Injury Pressure Ulcer and Deep tissue injury (SCIPUD+) Resource, a multi-domain database and healthcare tool to assess risk factors and provide personalized PrI prevention care planning. This study has discovered the following:

- Demographic factors that increase the propensity for PrI include complete SCI, divorce/living alone, Caucasian (vs. African-American), and using an air mattress or cushion (vs. standard firm mattress).
- Predictive factors for readmission include a longer duration of injury, poorly controlled spasticity, sub-optimally managed neurogenic bowel, and use of manual wheelchairs.

These studies will decrease treatment costs and enable clinicians to develop clinical care plans for PrI prevention, including the most appropriate pressure relief regimes, lifestyle changes, and selection of support surfaces. Ultimately, this research will be applicable to all individuals at risk for PrI development and could even make routine home monitoring of PU risk simple.



Gluteal muscle composition of two individuals with SCI: (left) 78.9% muscle, (right) 77.3% fat

Examples of SIG-Blocks

Principal Investigator:
Kiju Lee, Ph.D.

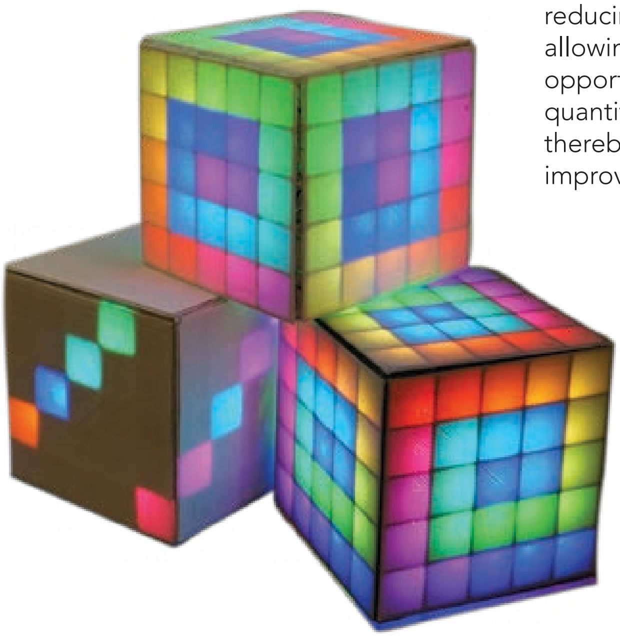
Funding Agencies:
APT Center's Steven Garverick Innovation Incentive Program

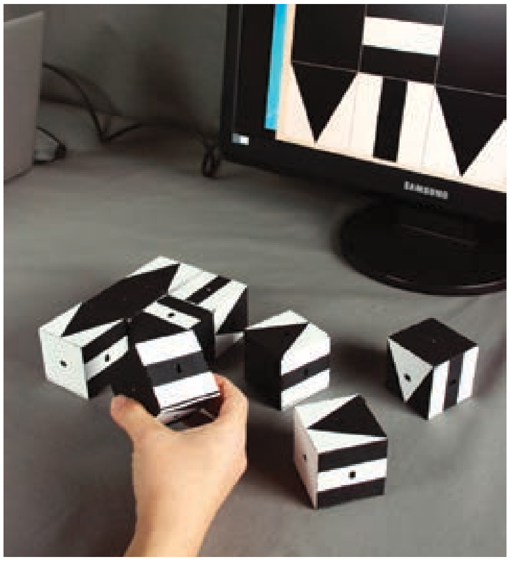
National Science Foundation

Assessing TBI Patients Through Games

Traumatic brain injury (TBI) is a principal cause of death and disability, affecting more than 2 million Americans and costing an estimated $76 billion in medical expenses annually. Early diagnosis of TBI, followed by rehabilitation interventions, is essential to increasing long-term survival and improvement of symptoms. However, assessing the symptoms and severity of TBIs requires a blend of cognitive, social, behavioral, emotional and physical assessments due to the high complexity of the injury.

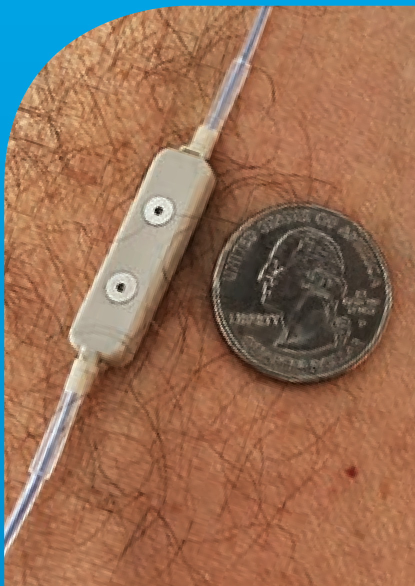
Kiju Lee, Ph.D., helped develop TAG-Games – a tangible game interface consisting of a set of sensor-integrated geometric blocks (SIG-Blocks) and a user interface. TAG-Games allow for play-based assessment of an individual's cognitive, motor control and learning skills. The games enable remote and real-time monitoring of a player's performance and behavior via wireless communication between the SIG-Blocks and the host computer through a user interface (above).





The three main goals of Dr. Lee's project are to 1) evaluate the existing technology platform on people with TBI, 2) develop two new TAG-Games and a new user-friendly software interface for clinical applications of personalized cognitive assessment and rehabilitation and 3) assess the games' technical functionality, usability, clinical effectiveness and market potential.

TAG-Games can serve as an alternative or supplemental assessment tool to address some of the challenges of traditional TBI assessment and rehabilitation tools. TAG-Games technology is fully autonomous and can be administered remotely, reducing clinician time and costs and allowing for broadened rehabilitation opportunities. It also offers improved quantity and quality of measurable data, thereby decreasing human errors and improving assessment outcomes.



Principal Investigator:

Douglas Shire, Ph.D.

Funding Agency:

Veterans Affairs, Rehabilitative Research and Development

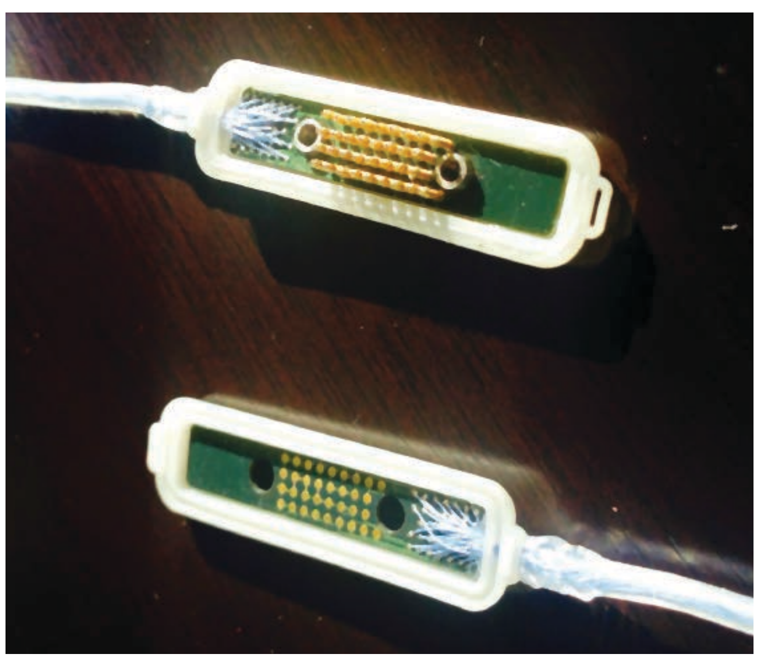
Creating Connections in Medical Devices

As implantable medical devices become more sophisticated and interact with different tissues in the body, researchers are working to improve their durability and versatility. These devices often comprise an electrode or other stimulation or recording lead that connects tissue to a module containing electronics. APT Center Investigators are focused on designing implantable, custom-microfabricated connectors that not only facilitate interconnections, but are smaller than many of the current ones available. These connectors are used in between the implanted electronics and the electrodes so that components in contact with sensitive nerve tissue are not disturbed if the system needs a repair or an upgrade.

Douglas Shire, Ph.D., along with Dustin Tyler, Ph.D. and graduate student Brian Sanner, have created a high-density connector (above, closed; below, open) containing 34 pins that is about the size of a quarter. The size of the connector and amount of channels will allow versatility for future interconnections. The design and materials have been refined and improved and the next phase will entail additional tests to qualify the device with the FDA for use in humans.

One of the primary patient populations that could benefit are people with motor nerve dysfunction due to stroke, incomplete spinal cord injury or multiple sclerosis. The simple design of this multi-channel, high-density connector can have a great impact on patients by enhancing the safety of their implanted system.

The photos here are of a High-Density In-Line 32-channel implantable connector that was developed under a VA RR&D SPiRE award. This type of connector improves the safety and inter-operability of any system they are used with, since it eliminates the need to explant an entire neurostimulator system in the event of a malfunction. Existing in-line connectors are far more bulky and not very practical for systems with large numbers of leads.



Gold microelectrodes on the polymer nanocomposite substrate

Principal Investigators:

Evon Ereifej, Ph.D.

Allison Hess-Dunning, Ph.D.

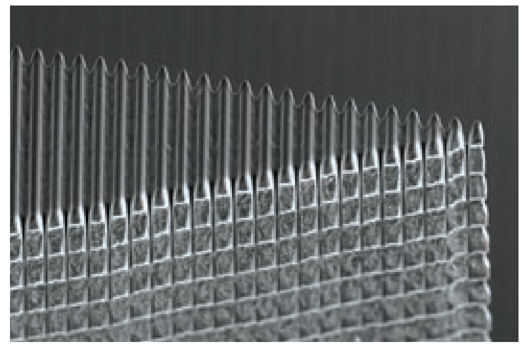
Funding Agency:

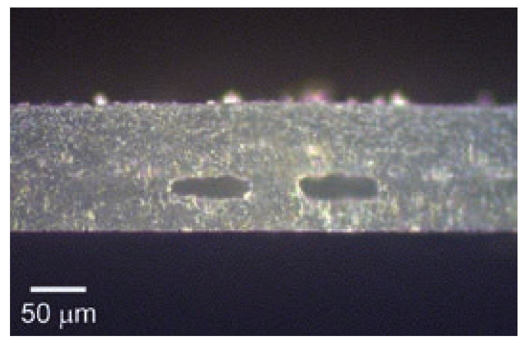
Veterans Affairs, Rehabilitative Research and Development

Highlighting Our Early Career Investigators

PROJECT 1: Improving Neural Electrode Biocompatibility
– Evon Ereifej, Ph.D.

Dr. Ereifej's research project will determine if combined therapeutic administration of Resveratrol and topographical patterning of microelectrode surfaces (see photo top right, after topographical patterning) can additively improve the quality and stability of neural recordings obtained from intracortical microelectrodes. This could lead to improved signal quality and consistency of the electrical signals recorded and used by patients to communicate with computers and control robotic limbs. This project facilitates Dr. Ereifej's long-term career goal of becoming a leading investigator in studying diseases, injuries and disorders of the nervous system in order to find therapeutic and medical device treatments that aid the wellbeing and longevity of patient lives.

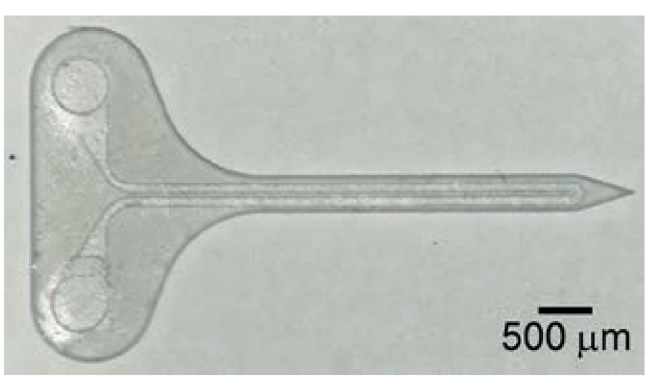




A slice through the microfluidic probe

PROJECT 2: Flexible Multi-Sensory Mode Neural Devices for Neurochemical Control
– Allison Hess-Dunning, Ph.D.

Dr. Hess-Dunning's research project will establish a microfabrication-based approach to integrate a mechanically-adaptive polymer nanocomposite with the functions required for preventing and treating the biological tissue response to neural implants. Currently, there is no practical technique to track tissue response activity at the implant-tissue site before encapsulation has occurred, at which point damage to the biotic-abiotic interface may be irreversible. The nanocomposite will release a controlled, sustained small amount of anti-inflammatory agents highly localized to the region surrounding the implant. These capabilities can then be combined and integrated with microelectronic systems to sense and control the local neuroinflammatory response. The long-term goal of Dr. Hess-Dunning's 4-year study is to develop advanced, multi-functional neural interfaces for localized interaction with the biological environment.



Nanocomposite-based probe with a micromolded, microfluidic channel running through it

Assessing Blood Coagulation Rapidly


Graphic by Grace Gongaware

Principal Investigators:

Pedram Mohseni, Ph.D.

Evi Stavrou, M.D.

Michael Suster, Ph.D.

Funding Agencies:

American Heart Association

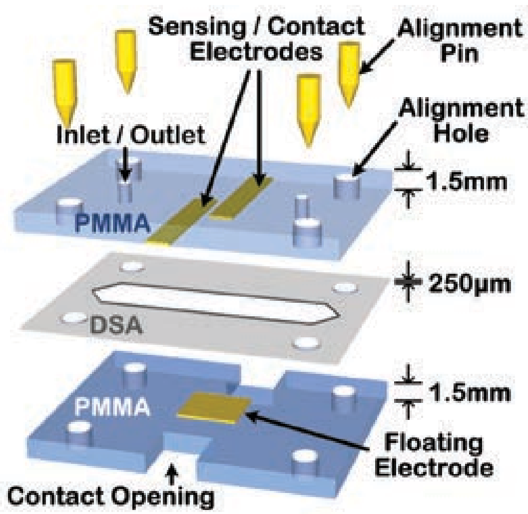
APT Center's Steven Garverick Innovation Incentive Program

Case-Coulter Translational Research Partnership

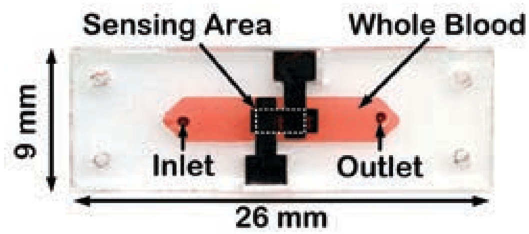
Case School of Engineering's San Diego-based Wireless Health program.

APT Center Investigators developed a portable sensor (the ClotChip) that can assess the clotting ability of blood in 15 minutes – 95 times faster than current methods. From only a single drop of blood, the device can determine 1) if a patient in trauma is on a blood thinner medication and 2) the effectiveness of anticoagulation therapy. This knowledge can expedite treatment in the home, emergency room or on the battlefield and can be of great benefit in early assessment of trauma-induced coagulopathy, surgical bleeding risk and coagulation risks to rapidly guide clinical decisions.

Currently, obtaining information on a patient's blood clotting ability requires specialized laboratory testing conducted by trained personnel that is time-consuming, labor-intensive and expensive. In preliminary tests, the ClotChip not only provided results faster than traditional testing (>1 day for results), but was also more sensitive and provided information on the entire blood coagulation process at the point-of-care.

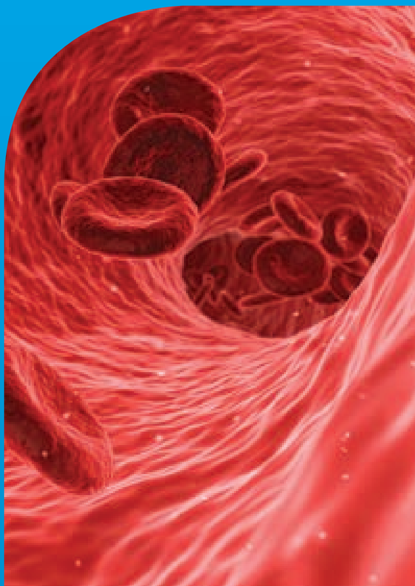


Fabrication drawing of the ClotChip sensor



The ClotChip sensor (test strip)

Pedram Mohseni, Ph.D., developed the ClotChip dielectric microsensor with fellow researcher Michael Suster, Ph.D., using pilot funds provided by the APT Center's Steven Garverick Innovation Incentive Program. Upon development, the research team brought the device to fellow APT Center Investigator Evi Stavrou, M.D., a staff physician and director of the Anticoagulation Clinic at LSCVAMC, as well as scientists and engineers from Case Western Reserve University, including APT Center Investigator Umut Gurkan, Ph.D., and clinicians at LSCVAMC and University Hospitals. ClotChip technology has been patented and licensed to Cleveland-based company XaTek, and clinical trials of its safety and efficacy are being planned to support FDA approval for marketing and commercialization.



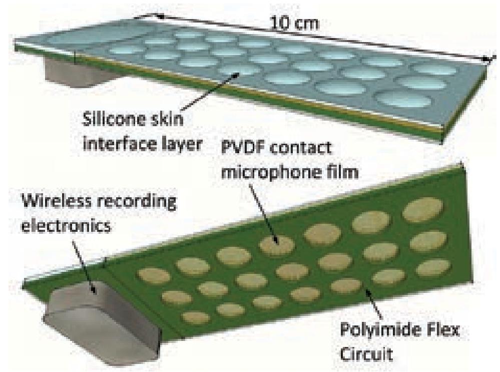
Highlighting Our Early Career Investigators

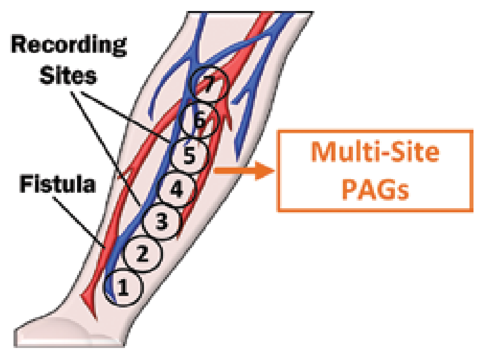
Screening Vascular Access Patency in Hemodialysis Patients – Steve Majerus, Ph.D.

Principal Investigator:
Steve Majerus, Ph.D.

Funding Agencies:
APT Center's Steven Garverick Innovation Incentive Program

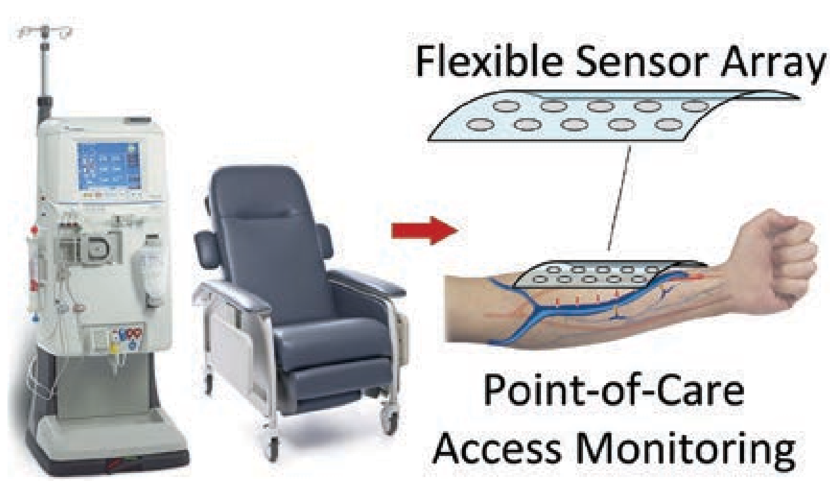
Veterans Affairs, Rehabilitative Research and Development





The Veterans Health Administration (VHA) cares for more than 35,000 veterans with kidney failure – and this number is increasing due to the clinical trend of providing dialysis therapy over prolonged patient lifespans. Long-term dialysis success and cost depends on maintaining the health of a patient's vascular access (a connection between an artery and a vein permitting high blood flow for dialysis). APT Center research includes clinical experiments to evaluate new approaches for non-invasive screening of hemodialysis vascular access patency.

Dr. Steve Majerus is investigating new techniques to rapidly screen vascular access patency in hemodialysis patients using the sounds of blood flow known as phonoangiograms (PAGs). Algorithmic calculation of PAG signal properties can detect subtle changes in blood flow sounds caused by vascular access dysfunction. PAGs may be recorded non-invasively with stethoscopes or a new multi-site flexible sensor array. This research will help answer hypotheses about the feasibility and reproducibility of non-invasive monitoring methods, and will demonstrate new technologies that could enable clinical application. These techniques could enhance the quality of life for veterans on chronic dialysis and reduce the financial impact of regular vascular access surveillance on the VHA.



Pilot Mark Muhn with the Gold medal

Sponsors:

Advanced Platform Technology Center, LSCVAMC

Case Western Reserve University

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City of Cleveland Heights

Laboratory for Bionic Integration

MetroHealth Medical Center

National Institutes of Health, NINDS

University Hospitals, Department of Orthopaedics

Veterans Health Administration Research & Development

The World's First Cybathlon, or "Cyborg Olympics"

On October 8, 2016, Team Cleveland, a research team led by Ronald Triolo, Ph.D., gained worldwide attention for its cutting-edge electrical stimulation work at the first-ever Cybathlon in Zurich, Switzerland. Team Cleveland won the gold medal in the bike race, one of six events for disabled individuals, using the latest assistive technologies.

Mark Muhn piloted the bike, winning the 750-meter race against 11 cyclists in just under three minutes – more than a minute faster than the closest competitor. Muhn suffered a high-thoracic spinal cord injury in a skiing accident in 2008 and is paralyzed from the chest down. He approached the APT Center in 2011 to volunteer in research. "I've been trying to get up and walk ever since I've been in the wheelchair," says Muhn. "One way or another, I was going to find new technology and give it a shot."

Neural stimulation provided Muhn that shot. Using implantable neural stimulators connected to muscles that send pulses of electricity into nerves, paraplegic patients such as Muhn can stand up, balance, take steps and perform other routine tasks. Team Cleveland, which includes engineers, medical staff and researchers, prepared Muhn and one other athlete for more than a year-and-a-half for the Cybathlon.

Members of Team Cleveland and pilot Mark Muhn at the Cybathlon

Pilot Mark Muhn and Dr. Ronald Triolo on the winner's podium. Photo by Nicola Pitaro.

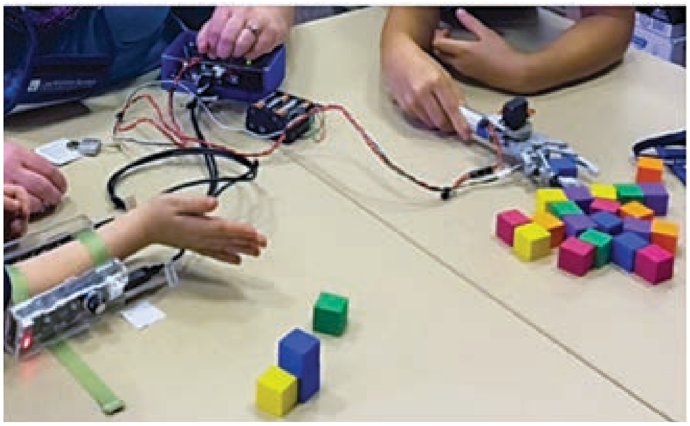
More important than winning gold at the appropriately nicknamed "Cyborg Olympics" was the attention gained for assistive technologies for people with disabilities. "It helps humanize the technology," says Dr. Triolo. "People can understand what a race is. They don't need to completely appreciate how sophisticated the technology is or the details of the design."

Soon after returning home from Zurich, Team Cleveland was back at work again, continuing to make strides in neural stimulation technology and help more patients improve their quality of life.

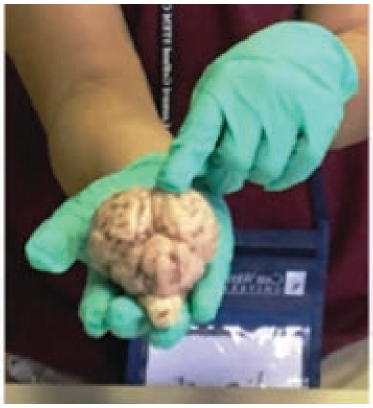
A student using the spikerbox

Mean Green STEM Machine

The Mean Green STEM Machine Program is an after-school program for students aged 7-12 designed to introduce students to various science, technology, engineering and math (STEM) disciplines and careers. APT Center students created a 2-hour neuroscience workshop that included using an EMG-powered robotic claw to manipulate objects, identifying structures in pre-dissected sheep brains, and using a "spikerbox" to listen to the neural signals generated by touching a dissected cockroach leg. Dr. Ronald Triolo donated a game called Mindflex that involves wearing a headset that reads brain waves to levitate a small ball and steer it through an obstacle course.



Picking up blocks using the EMG-powered robotic claw



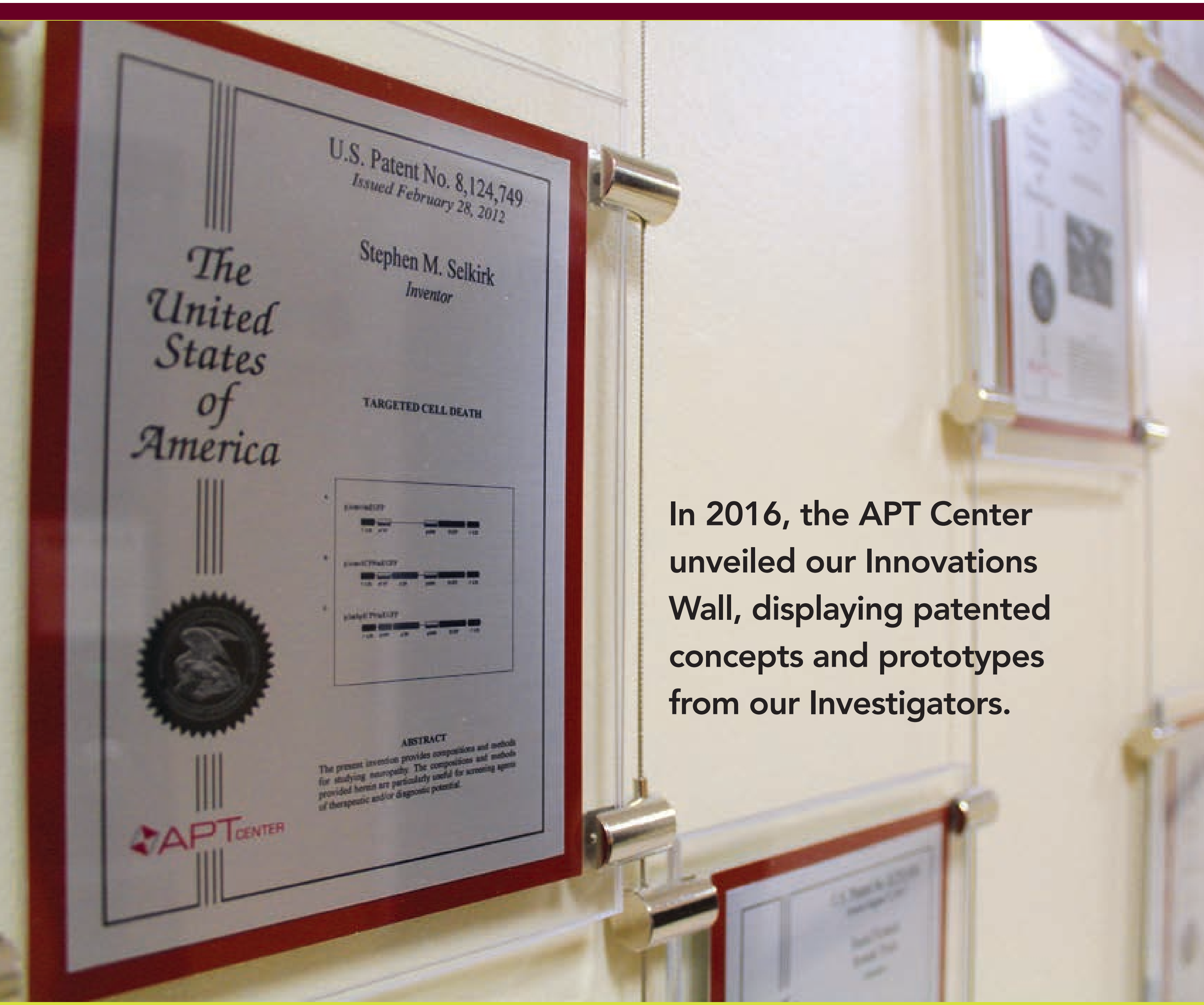
Identifying structures in a pre-dissected sheep brain

LSCVAMC's Take Our Daughters and Sons to Work Day

Researchers at the APT Center hosted 7-12th grade students of LSCVAMC employees throughout the day and spoke with those interested in becoming engineers about why they decided on that career path, what classes they take in school, and other information about their education journey. The students learned the capabilities of the Motion Study Laboratory which is equipped to monitor exercise, measure muscle strength and endurance and collect biomechanical data related to all types of human motor performance. Researchers also demonstrated the robotic claw and Mindflex described above.

APT CENTER

WE BUILD TRANSLATION



In 2016, the APT Center unveiled our Innovations Wall, displaying patented concepts and prototypes from our Investigators.

Louis Stokes Cleveland Veterans Affairs Medical Center
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