Advanced Platform Technology Center

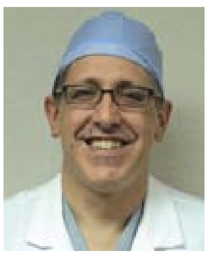
A VA Research Center of Excellence

THIRD EDITION

SCIENTIFIC REPORT TO THE COMMUNITY

W E B U I L D T R A N S L A T I O N

Ronald Triolo, Ph.D.



Gilles Pinault, M.D.

A Letter from the Directors

The APT Center focuses on the practical medical needs of veterans disabled by sensorimotor dysfunction, cognitive deficits, or limb loss. We create novel, cross-cutting assistive and restorative technologies within a structured framework that facilitates regulatory compliance, dissemination within the rehabilitation community and transfer to outside manufacturers. Our R&D and translational programs focus on **prosthetics and orthotics, wireless health monitoring and maintenance, neural interfaces** and emerging **enabling technologies**. To date, Center projects have concentrated primarily on developing new materials and microsystems for interfacing with the nervous system, repairing orthopaedic trauma and accelerating wound healing, replacing or restoring natural limb, sensory and organ system function, and both monitoring and promoting neurological, genito-urinary and vascular health.

Our primary strategy is to bring the medical needs of disabled veterans to the attention of scientists and engineers pursuing original work that could be brought to bear on solving the pressing, real world problems. Transdisciplinary collaborative teams identify needs in the clinical setting and shepherd potential technical solutions through the R&D process to translate them into interventions that can improve the health and well-being of individuals with disabilities and advance the medical knowledge and care practices of the entire nation.

Our active partnership between the Department of Veterans Affairs and the Schools of Medicine and Engineering at Case Western Reserve University, as well as numerous collaborations with University Hospitals Case Medical Center, MetroHealth Medical Center and the Cleveland Clinic among others, have resulted in a cohesive, interdisciplinary network of scientists and physicians dedicated to the pursuit of clinically relevant and highly impactful restorative technologies.

We dedicate this third edition of our Report to the Community to our friend and collaborator, Steven Garverick, Ph.D. Over the past seven years he worked tirelessly on several APT Center projects, including a wireless pressure monitor small enough to be inserted into the bladder wall via a cystoscope and a fully conformable, untethered surface electrotherapy delivery device for wound care and pain management. He took on these Herculean tasks with his typical technical brilliance, good humor, great patience, and extreme dedication. Until his sudden and unexpected passing, his interactions with other faculty, staff, and students alike were always characterized by quietly effective support and guidance directed to solving the many challenges inherent in medical device development and implementation. Steve's wisdom was invaluable, and he is sorely missed by all.

Please join us in the pages to follow as we invite you to share our passion for the research, technology and translational opportunities we work hard to achieve every day for the veterans we serve.

Best Wishes,

Ronald Triolo, Ph.D.

Gilles Pinault, M.D.

APT Center Research Sites

The APT Center is located on the premises of the Louis Stokes Cleveland Veterans Affairs Medical Center (LSCVAMC) and operates in partnership with Case Western Reserve University (CWRU) Schools of Engineering and Medicine. In addition, our investigators collaborate with clinicians and researchers located at University Hospitals Case Medical Center, MetroHealth Medical Center, and Cleveland Clinic Foundation (CCF) and numerous other institutions nationally. The Center capitalizes on significant local expertise in the areas of microelectronics, micro/nanofabrication, materials science and mechanics to address unmet needs of disabled veterans and the broader rehabilitation community.

APT Center Family

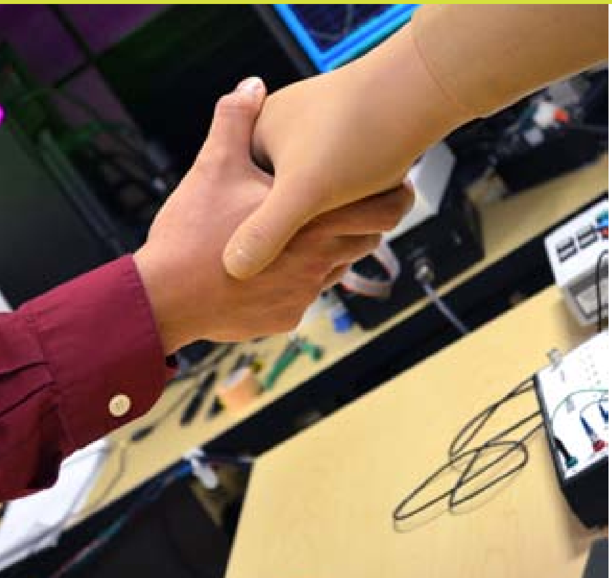
Personnel associated with the Center include more than 40 investigators, plus engineers, clinical staff, trainees and support specialists in regulatory affairs, quality systems and research administration. These individuals have successfully secured external scientific, development and translational research funding from private and public sources, including local and federal granting agencies and industrial partners, at an eight-to-one ratio to core Center dollars. At this writing, our active portfolio was valued to be in excess of $7 million, with a total of $40 million from 51 new projects since 2010. Investigators with the Center include multiple recipients of prestigious Presidential Early Career Awards for Scientists and Engineers (PECASE) and the NIH Director's Innovation Award, inductees of the American Institute of Medical and Biological Engineering (AIMBE), and VA Career or Senior Career Research Scientist awardees. Clinician-researchers associated with the Center include some of the "Best Doctors in America" as named by Cleveland Magazine and Best Doctors, Inc. Investigators with the Center have also produced innumerable peer-reviewed articles in the most prestigious journals (Science, Nature, Journal of Rehabilitation R&D, etc), have been invited speakers at national and international conferences and have generated more than 60 invention disclosures, where over 15 are patent-pending concepts and prototypes.

Sampling of APT Center Capabilities

- Circuit and software design - Digital and analog simulation and other development tools are available for integrated circuit layout, fabrication, and testing, as well as creation and verification of new software systems.
- Neural interfacing - We have more than 40 combined years of experience with devices that bridge the gap between neurobiology and engineering. We have the facilities, tools, and know-how to help design, develop, and test systems that communicate with and transfer to and from the peripheral or central nervous systems.
- Polymer and bioactive material development - New materials can be engineered on the molecular level to mimic biological functions or designed to interact and live with living tissue and biologic systems.
- Rapid prototyping - Computer controlled machining, 3D printing and additive manufacturing, and other processes reduce design to fabrication time.
- System validation and design control - We develop devices based on industry standard design controls.
- Professional engineering support and project management.
- Administrative support for intellectual property protection, regulatory affairs, and grant and contract management.

Sampling of APT Center Technologies

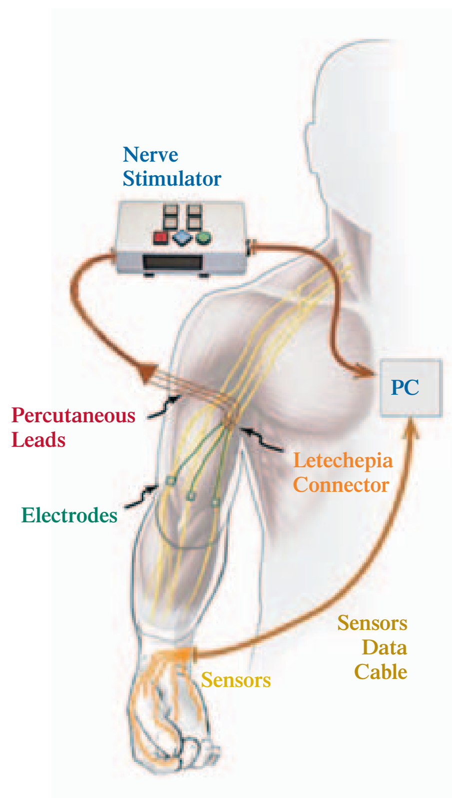
- Biosignal acquisition and processing, including emerging new technologies for electromyography (EMG), electroencephalography (EEG), and electroneurography (ENG).
- Implantable sensing, recording, stimulating and communication devices.
- Pressure, volume, acceleration, and other physical or chemical sensors.
- Portable computer controlled systems for surface and percutaneous stimulation.
- Stimulating and recording electrodes.



Natural Sensation for Amputees

Amputation is one of the most significant, non-fatal co-morbidities of combat. Upper extremity amputation is particularly devastating. Upper limb loss also affects a significant percentage of the civilian population. The loss of either one arm or two, results in functional deficits and decreased independence.

Investigators with the APT Center are pursuing a system that attempts to provide sensory feedback for the hand via a direct interface to the residual peripheral nerve. Sensors on a prosthetic hand control stimulation to electrodes around the nerves in the remaining portion of the amputated limb, which cause the nerves to transmit impulses to the brain that intended to be interpreted by users as tactile perceptions on their missing hands directly related to touch on the prosthesis.

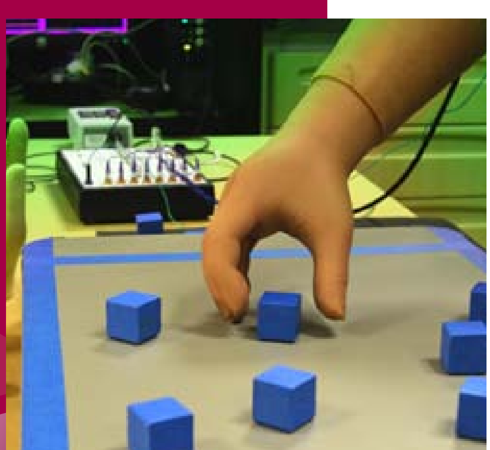


Results are promising in the first study subjects who described it as being equivalent to feeling a pulse with their index fingers. Sensory feedback increased awareness of the prosthetic hand immediately after turning the system on and improved the ability to grasp, hold and move small objects without looking at them in these preliminary studies. Furthermore, advanced stimulation techniques are reducing or eliminating the abnormal tingling sensation commonly reported with electrical stimulation. The devices have now been in place for more than a year and may be a viable option for long term restoration of somatosensory function in the future.

Principal Investigator:
Dustin Tyler, Ph.D.

Clinical Collaborators:
J. Robert Anderson, M.D.
Michael W. Keith, M.D.

Funding Agency:
Veterans' Affairs Rehabilitation Research and Development

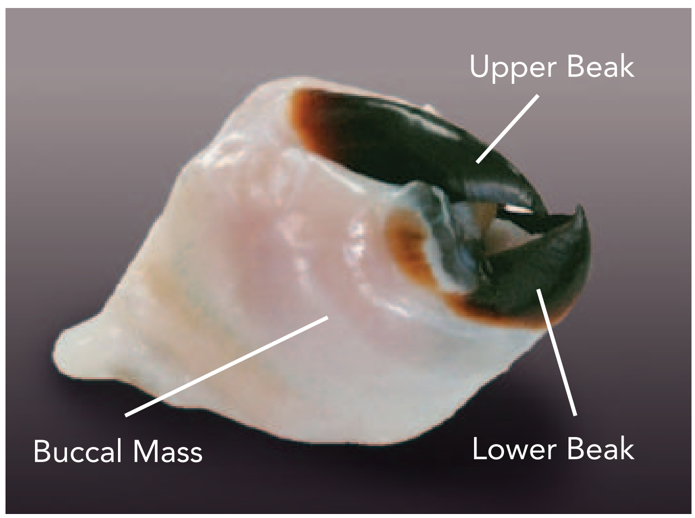


Bio-inspired Materials for New Prosthetic Liners

Although prosthetic limbs have undergone some remarkable advances in the last decade the weak link remains how artificial extremities are connected to the user's body. Low-tech straps, cuffs or sockets hold high-tech limbs in place, sometimes imperfectly. Attaching hard metal or plastic prosthetic components to the soft, vulnerable skin and muscle of the residual arm or leg is a recipe for discomfort, or worse, further injury and tissue damage. Our goal is to improve the interface between a veteran amputee and their prosthetic limb by developing a new material for prosthetic liners inspired by the 'shock absorber' function of a squid beak.

Principal Investigators:
Paul D. Marasco, Ph.D.
Stuart Rowan, Ph.D.
Jeffrey R. Capadona, Ph.D.

Funding Agency:
Veterans' Affairs APT Innovation Incentive Grant FY2013



A squid's beak is as hard and sharp as a razor blade embedded in soft tissue the consistency of Jell-O. The beak doesn't carve itself loose from the soft body of the squid, but becomes gradually less stiff and more supple from tip to base. The animal creates this natural damping mechanism, called a mechanical gradient, by subtly tweaking the mix of the beak's chemical ingredients.

The prototype material the APT Center team has formulated so far doesn't yet have the stiffness range of its natural counterpart. Its hardest area is five times that of its softest, while the tip of the squid's beak is 100 times harder than its base. The investigators are confident that they can ramp up the mechanical gradient and produce a new material that will revolutionize prosthetic suspensions and greatly improve device comfort, usability and safety.

Seated Balance and Trunk Control with Implanted Neuroprostheses

Principal Investigators:
Musa Audu Ph.D.
Ronald Triolo, Ph.D.

Clinical Collaborators:
Gilles Pinault, M.D.
Stephen Selkirk, M.D.

Funding Agencies: Veterans' Affairs Rehabilitation Research and Development; Department of Defense

Spinal cord injury (SCI) can result in paralysis of the core trunk and hip musculature which compromises the ability to stabilize the torso while reaching, resist disturbances to sitting balance, and efficiently propel a manual wheelchair, thereby limiting the ability to work, engage in social or leisure activities, and assume an independent and productive lifestyle. There is evidence that stimulation of the trunk and hip extensor muscles can positively alter seated posture, extend bimanual reach, restore erect sitting, and improve wheelchair propulsion mechanics at slow speeds and on level surfaces. However, the benefits of low levels of continuous stimulation seem to disappear during dynamic movements that either require more stiffness of the core, or modulation of stimulus timing and intensity.

Our objectives for this translational research project are to expand the functionality of neuroprostheses for seated posture and balance by appropriately varying activation of the trunk and pelvis muscles with the intended task automatically without conscious effort by the user. This has the potential to maximize the physical and functional benefits and make them more robust and generalizable to a large segment of the SCI population.

There are a number of goals for the next phase of the project, yet the most important is synchronizing stimulation to the trunk and hip muscles with the manual wheelchair propulsion cycle via the voluntary activity of the intact shoulder muscles.

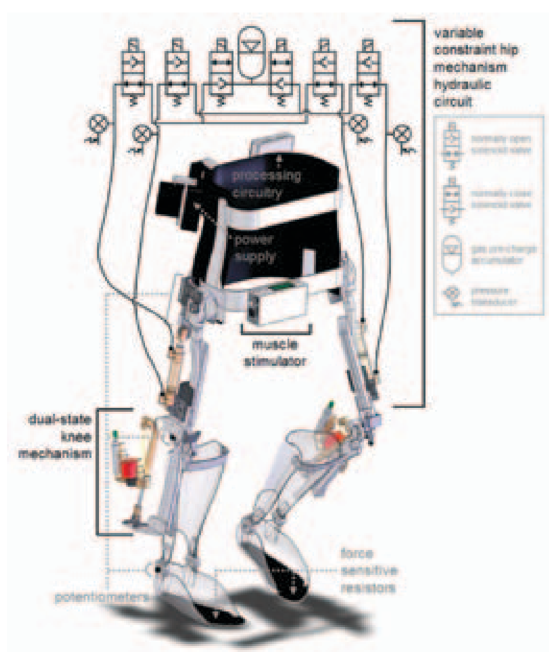
Left is reaching without trunk and hip stimulation; right is reaching with stimulation.

Advanced Exoskeletons for Independent Mobility

Paralysis, muscle weakness, and lack of coordination are common consequences of combat related injury to the central nervous or musculoskeletal systems that can prevent a return to active duty or independent performance of essential activities of daily living. APT Center Investigators continue to improve the design, fabrication and testing of the bracing systems consisting of unique electromechanical joints that lock and unlock in coordination with voluntary or stimulated muscle contractions to restore or assist independent walking and upright mobility.

A first generation prototype neuromechanical gait assist system combined electrical stimulation to the paralyzed lower extremity muscles with a controllable hydraulic exoskeleton for standing, walking, and stair climbing for individuals with spinal cord injuries. The system consisted of computer controlled hydraulic knee and hip mechanisms that allowed the lower extremity joints to either move during walking or be fixed during weight bearing to let the muscles rest. The system showed the potential to improve the stability and posture of individuals with paraplegia as compared to walking with electrical stimulation alone, and also reduce user effort and increased walking speed when compared to standard reciprocal braces.

The project is advancing the design to make it self-contained and suitable for independent use and clinical testing outside the laboratory. Efforts are directed toward reducing the size and weight of the exoskeleton, repackaging the electronics and refining the control system to include natural coupling of hip and knee motion and damping of knee flexion during loading. These improvements should improve foot-floor and step clearance during walking and stair climbing, and provide smoother and more natural gait and stair descent. Completion of this project may define a new means to overcome physical barriers and manage uneven terrain, thus enabling ambulation in a wide variety of physical environments to improve access.



Principal Investigators:
Ronald Triolo, Ph.D.
Rudi Kobetic, M.S.

Clinical Collaborators:
Gilles Pinault, M.D.
Stephen Selkirk, M.D.

Funding Agencies: Veterans' Affairs Rehabilitation Research and Development;
Department of Defense

Affordable Modular Pressure Relief Seat Cushions

Principal Investigator:
Kath Bogie, Ph.D.

Clinical Collaborator:
Steve Mitchell, OTR/L, ATP

Funding Agency:
Veterans' Affairs Rehabilitation Research and Development

APT Center Investigators are developing a low-tech, high-performance product they hope will help prevent pressure ulcers for the more than 25,000 veterans with spinal cord injuries, and for all others in the U.S. and worldwide who are long-term wheelchair users.

The product is a seat cushion. The basic idea is not new – there are "high-performance" models already on the market. The APT Center innovation lies in the common and inexpensive materials used and simplicity of design that could make maintenance and customization quick and easy, ultimately saving significant time and money.

The up-front cost should be low due to the cushion materials, and ongoing costs should be reduced because the design is modular – so that if one part fails, it can be replaced without having to throw out the whole cushion. The annual cost of the new cushion is expected to be around $57 per year, compared to $128 for existing commercial products. Preliminary analysis suggests that a customer could entirely replace every component of the proposed cushion several times and still have a more cost-effective solution than anything else on the market.

APT Investigators are currently testing the cushions with a machine that creates heat and water vapor while applying pressure, mimicking the sweat and temperature that the cushions will endure under real world conditions.

Wireless Implantable Bladder Pressure Monitor for Continence and Urinary Health

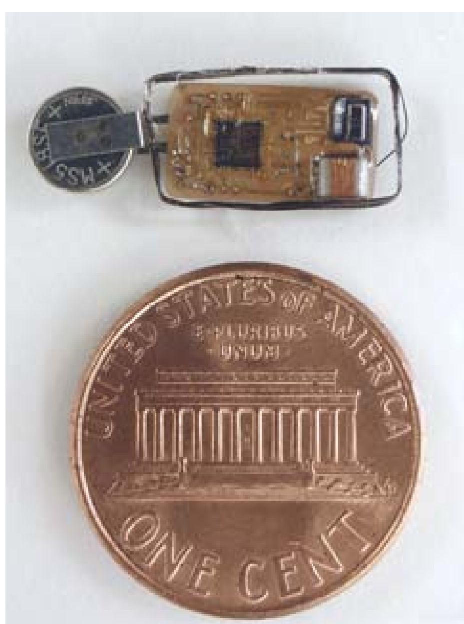
Principal Investigator:
Margot Damaser, Ph.D.

Clinical Collaborators:
Donna Hansel, M.D.
Hui Zhu, M.D.

Funding Agency:
Veterans' Affairs Rehabilitation Research and Development

Numerous neurological conditions result in an overactive bladder and uncontrolled leakage of urine. This control of urine leakage is of major importance as spinal cord injury patients are susceptible to pressure ulcers. These ulcers may become infected from the urine and lead to more serious body infections and potentially death.

Investigators with the APT Center have designed a miniature, implantable, catheter-free, wireless, rechargeable pressure monitor to provide long-term information about the state of the bladder. This new tool should enable physicians and researchers to obtain data related to bladder pressures without the inconvenience and infection risk of chronically indwelling catheters, or need for repeated catheterizations. The wireless pressure monitor will be inserted into the bladder cystoscopically, using a standard clinical urological procedure, and will reside long term behind the urothelial lining of the bladder, potentially reducing the risk of urinary stone formation. In the future, this device could enable conditional electrical stimulation to reduce unwanted bladder activity, an improvement over the continuous open-loop stimulation methods currently available. Testing of the wireless implantable pressure monitor in animals is currently underway while first human trials are being planned.



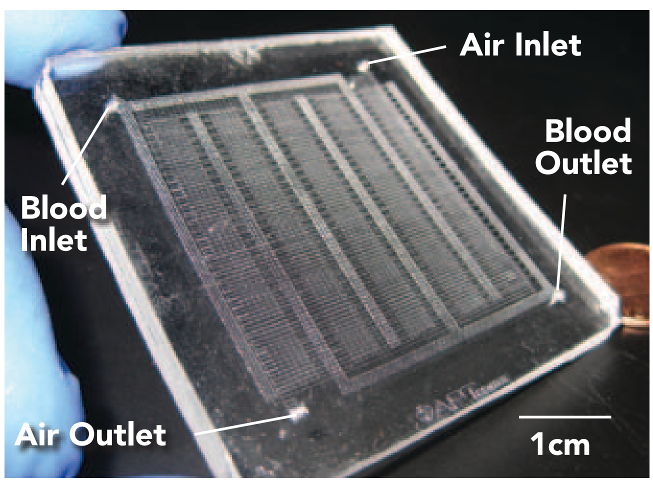
The unpackaged wireless pressure monitor prototype is shown to demonstrate the size of the device and the on-board circuitry that was designed to reduce power consumption and increase efficiency.

Microfabricated Portable Artificial Lung

Chronic obstructive pulmonary disease affects approximately 16% of veterans, which makes it the fourth most prevalent disease in the VA population and very costly to the VA health care system. Operations Enduring Freedom and Iraqi Freedom veterans were exposed to chemicals known to cause respiratory conditions, and over 2.3 million veterans reported having some form of "lung trouble." Investigators with the APT Center are addressing the need for the first truly portable, biocompatible artificial lung capable of both long and short term respiratory support to improve the rehabilitation and daily functioning of individuals with chronic lung disease. Existing artificial lung technologies are too limited in their gas exchange efficiency, biocompatibility and size to fully realize this potential.

The artificial lung technology pioneered by APT Center Investigators has potential to drastically improve the outcome of pulmonary rehabilitation by: 1) Enhancing gas transfer performance, 2) Extending device lifetime, thus enabling long-term treatment, and 3) Increasing portability to enable ambulatory care and greater quality of life. The device also has the potential to provide lung rest for patients with pulmonary disabilities, serve as a bridge to transplant for patients with chronic lung disease and lung cancer, and eventually lead to the development of the first implantable artificial lung for semi-permanent support.

Our artificial lung technology has the highest efficiency of any device to date. We have also developed a surface modification that improves blood compatibility and will enable use of the device in acute clinical applications. Planning for initial animal experiments is underway.



A photograph of the artificial lung showing blood and air inlets and outlets and the microfluidic channels comprising the device. A penny is shown in the background for scale. The artificial lung contains blood channels that are similar in size to those in the natural lung.

Principal Investigator:
Joseph Potkay, Ph.D.

Clinical Collaborators:
Brian Cmolik, M.D. Erik van Lunteren, M.D.

Funding Agency:
Veterans' Affairs Rehabilitation Research and Development

Diagnosing Balance Impairments Following Mild Traumatic Brain Injury

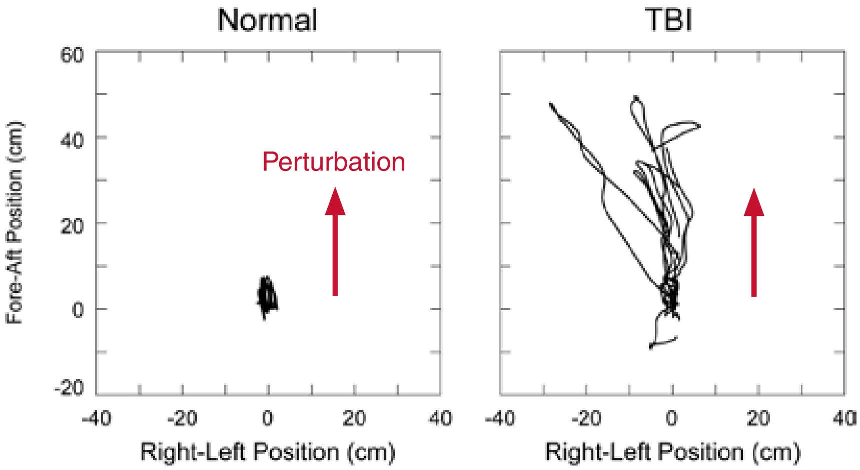
Principal Investigator:
Mark Walker, M.D.

Funding Agency:
Department of Defense

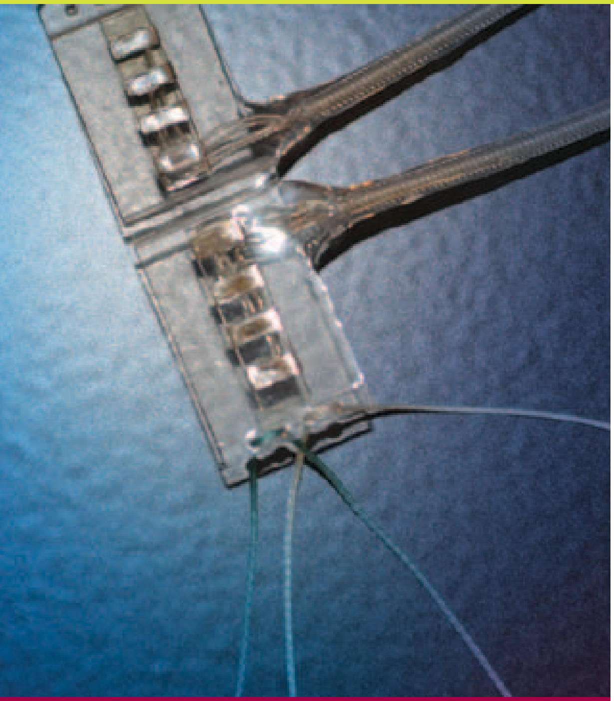
Chronic balance impairment is a known pathological condition of both civilian and military traumatic brain injury (TBI), however little is known regarding its underlying mechanisms. APT Center Investigators are combining a detailed assessment of walking and balance with measures of vestibular function (the parts of the inner ear and brain that process the sensory information for controlling balance and eye movement) to determine whether there are injuries to specific neural structures that may explain TBI-related disequilibrium.

Veterans of the Iraq and Afghanistan conflicts with disequilibrium who had experienced a mild TBI (mTBI) due to blast and/or blunt head trauma exhibit specific and repeatable deficits in standing and walking stability when compared to a similar group of veterans with mTBI without balance problems. They tend to sway more, especially when standing with eyes closed and on a surface that is not firm, and they have more difficulty keeping their balance when disturbed.

These important findings show it may be possible to demonstrate a measurable physiological correlate to the chronic symptom of disequilibrium after mTBI. These quantifiable physiological measures may provide a more robust record of injury that can be followed over time and used to optimize treatment and document the effectiveness of various therapies. Lastly, this ability to quantify TBI-related neurological deficits precisely may be important for making decisions regarding return to normal activities and assessing the risk of repeat injury.



In the figure above, the left panel shows the range of sway in a subject without mTBI and the right panel the sway in a veteran with mTBI and imbalance, after a forward perturbation.



New Technologies for Communicating with Peripheral Nerves

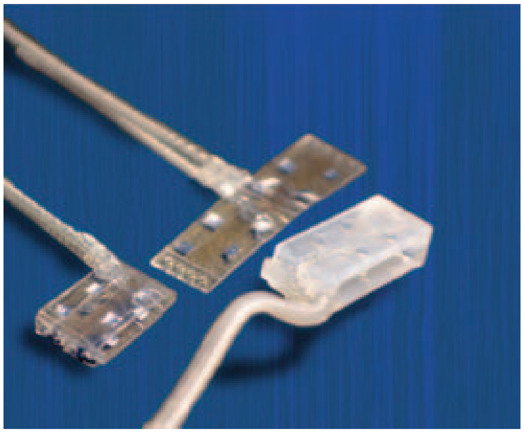
Principal Investigators:
Ronald Triolo, Ph.D.
Dustin Tyler, Ph.D.

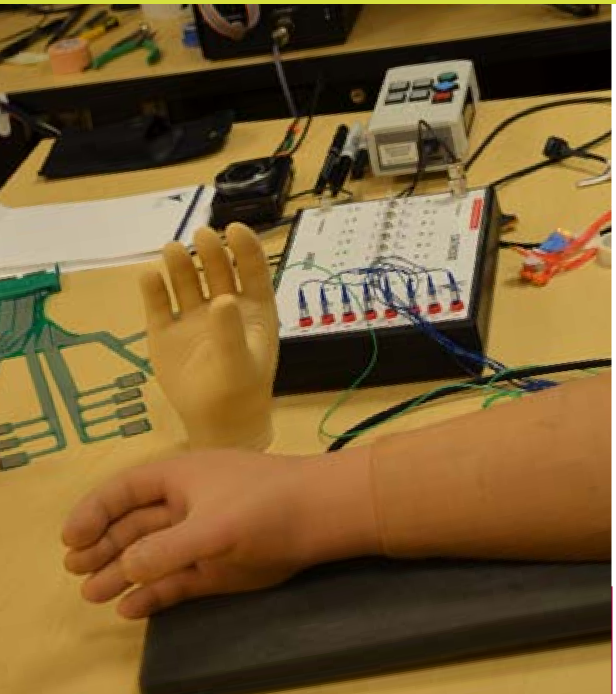
Clinical Collaborators:
James Anderson, M.D.
Harry Hoyen, M.D.
Gilles Pinault, M.D.

Funding Agencies:
National Institutes of Health;
Veterans' Affairs Rehabilitation Research and Development

Effectively exchanging information with the peripheral nervous system is important for many advanced therapeutic and prosthetic applications of neurotechnology. Activating fascicles within or detecting the natural activity of sensory or motor nerves requires intimate contact between recording or stimulating electrodes and the target neural structure. Peripheral nerve cuff electrodes should achieve this while being as small and flexible as possible to match the compliance of the nerve and minimize the potential of neural injury or tissue damage. APT Center Investigators have developed and tested a new electrode with regionally patterned stiffness to direct the reshaping the nerve's cross section for improved selectivity. It is compatible with microfabrication techniques, and is significantly smaller and more flexible than prior designs to allow it to bend and move with the nerve.

The nerve cuff has a multi-layer structure consisting of thin, narrow pieces of a stiff, biocompatible polymer sandwiched between thin, flexible silicone sheets. The embedded polymer bars are compatible with metal deposition microfabrication techniques, allowing for a high number of densely spaced contacts. In bench tests, the cuff maintained a diameter greater than required by industry standards for ensuring adequate blood flow and preventing neural injury. Animal tests confirmed that the new design is biocompatible and results in no appreciable changes to the nerve structure or function, even when placed in tight anatomical locations near the joints. Nerves with cuffs remained healthy and conducted impulses normally after months of implantation. Stimulation thresholds were stable over time and consistent with other nerve cuffs. Future plans are to use this new neural interface in both upper and lower extremity applications for restoring natural sensation to amputees and standing, stepping and arm movements to individuals with paralysis.





Thin Film, High-Density Peripheral Nerve Cuffs

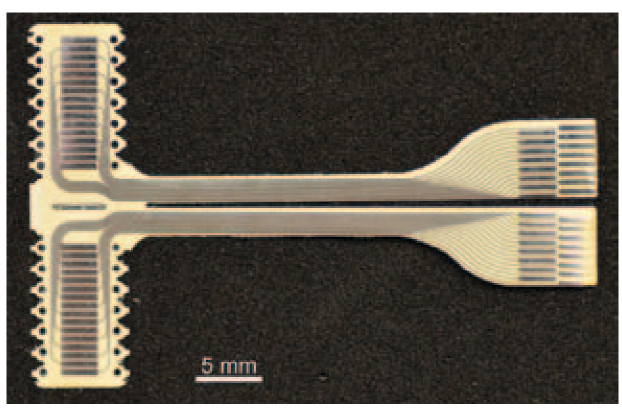
A microfabricated, mechanically-flexible, high-density peripheral nerve cuff is being developed to improve nerve stimulation selectivity and functional control for motor and sensory applications. In this device, high-density conductive features are formed on a flexible liquid crystal polymer (LCP) substrate using photolithography and thin-film deposition, which are part of the microfabrication technology. The cuff materials and design were chosen to facilitate long-term device reliability in vivo.

Each microfabricated peripheral nerve cuff has 32 stimulating electrode contacts. Devices can be prepared for connection to external electronics by bonding discrete wires to individual connection contact pads, then encapsulating the bonds for electrical insulation and moisture resistance. The cuffs are folded along the centerline, and secured closed along the edge.

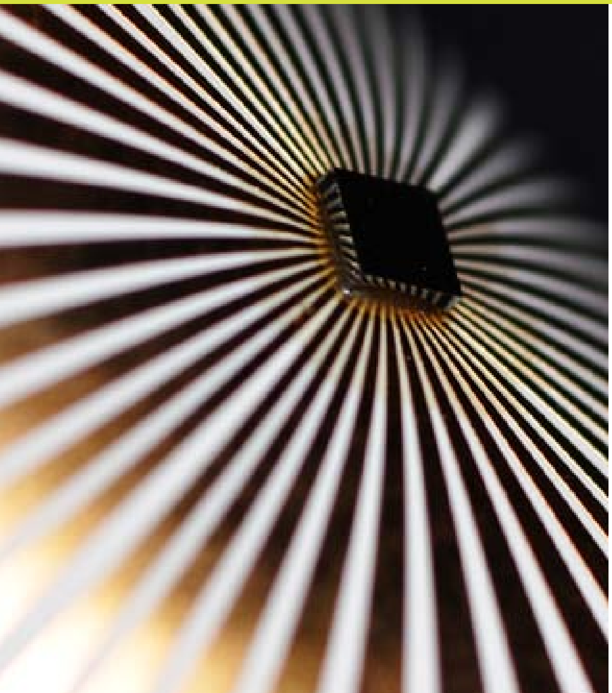
The high-density peripheral nerve cuffs have been used in both acute and chronic non-human primate experiments. A 32-contact LCP-based cuff implanted on the medial nerve was able to selectively activate four muscles acutely, and the cuff remained functional throughout 4 months of testing. During this time, 25 of the contacts displayed a median reduction in electrode-tissue interface impedance of 72%, indicating good biocompatibility and lack of tissue damage or excessive encapsulation. Further development of this technology for interfacing with complex neural structures like the human sciatic nerve is currently underway.

Principal Investigators:
Allison Hess, Ph.D.
Dustin Tyler, Ph.D.

Funding Agency:
National Institutes of Health



32-contact, microfabricated peripheral nerve cuff for electrical stimulation. The electrode contacts are on the left side of the photograph, while the connection pads are staggered on the right.



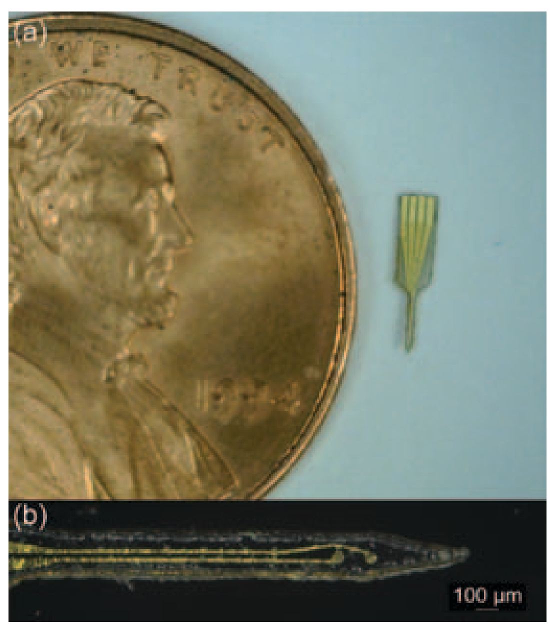
Dynamic Intracortical Probes

Interfacing to the cerebral cortex requires cortical probes to be stiff for insertion, but flexible chronically to avoid repeated trauma and potential damage to the brain. Investigators with the APT Center have developed such an intracortical microprobe based on a bio-inspired, mechanically-adaptive polymer nanocomposite (NC) for brain-machine interface applications. The NC is stiff when dry and becomes more flexible as cerebral spinal fluid permeates it after implant. This probe is designed to be used to study the relationship between implant mechanics, the neuroinflammatory response, and the long-term quality and reliability of neural recordings. The overall goal is to systematically identify the optimal neural probe design and materials for long-term neural recording reliability.

The process for fabricating NC-based neural microprobes with up to four electrode recording sites on a single device has been developed that combines laser-micromachining, thin-film deposition, photolithography, and wet and dry etching steps. Preliminary bench and in vivo evaluations of the probes are encouraging, with no evidence of delamination after accelerated soak tests and documented ability to record unit spikes during acute animal experiments.

Principal Investigators:
Jeffrey Capadona, Ph.D.
Allison Hess, Ph.D.
Dustin Tyler, Ph.D.

Funding Agency:
National Institutes of Health



(a) Four-contact NC probe next to a penny, as a size reference. The large rectangular contact pads are at the top of the device, and the electrode contacts are near the tip of the narrow shank.

(b) Close-up view of the shank of a two-contact NC probe, with the gold traces and electrode contacts visible.

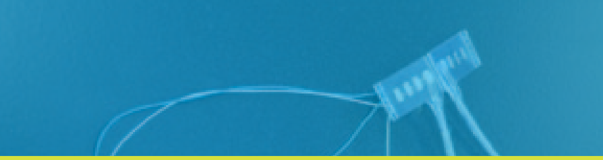
Effects of Anti-oxidants on performance of Brain-computer Interfaces

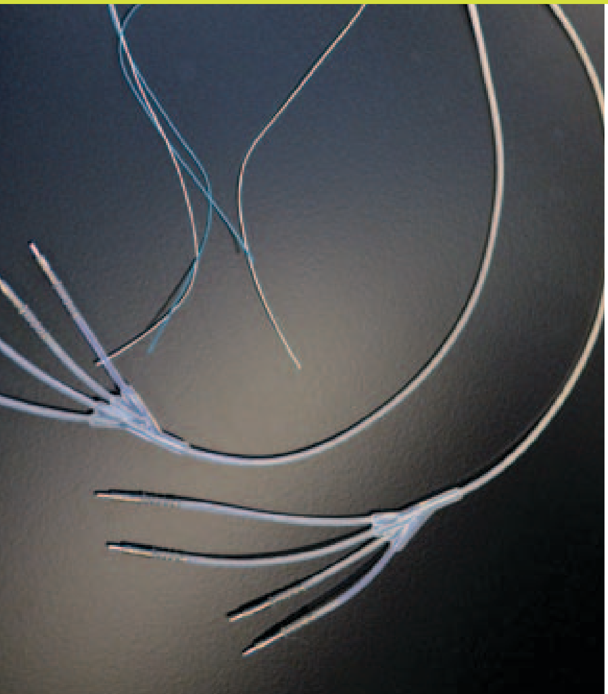
Principal Investigator:
Jeffrey R. Capadona, Ph.D.

Funding Agencies:
Veterans' Affairs Rehabilitation Research and Development;
Presidential Early Career Award for Scientists and Engineers;
Department of Biomedical Engineering Case School of Engineering at Case Western Reserve University;
The Medtronic Graduate Fellowship

Investigators with the APT Center are exploring simple and effective means to improve the quality and stability of neural recordings obtained from intracortical microelectrodes, which are components of the brain-computer interfaces that may allow individuals to use volitionally-controlled thoughts to control an external device, such as a computer cursor, a robotic arm, or one's own muscles. The majority of research in brain-computer interfaces has been directed at patients with SCI and Amyotrophic Lateral Sclerosis (ALS), who would benefit greatly from robust and reliable cortical recording technology. Yet, several biological mechanisms can lead to the premature failure of existing interfaces. Over time, neurons nearest to the microelectrode die off or get pushed away, so the ability to isolate large amplitude spikes of individual neurons declines so the ability of the patient to communicate with the computer diminishes. For this reason, we are developing a robust understanding of the time course of microelectrode-mediated neurodegeneration around the implant site. Further, we have shown that oxidative stress is a key component of the neuroinflammatory response to microelectrodes, and that oxidative stress correlates with neuron viability.

We have shown that the neuroinflammatory response to intracortical microelectrodes directly relates to the instability of neural recordings. The initial administration of resveratrol, a naturally-derived anti-oxidant, temporally reduces microelectrode-mediated oxidative stress, preserves neuron viability, and facilitates stable neural recordings. Our results imply that combinatorial therapies that include anti-oxidant treatment or coatings might be able to preserve the viability of cortical recordings and ensure extended use of brain-computer interfaces beyond what is currently possible.





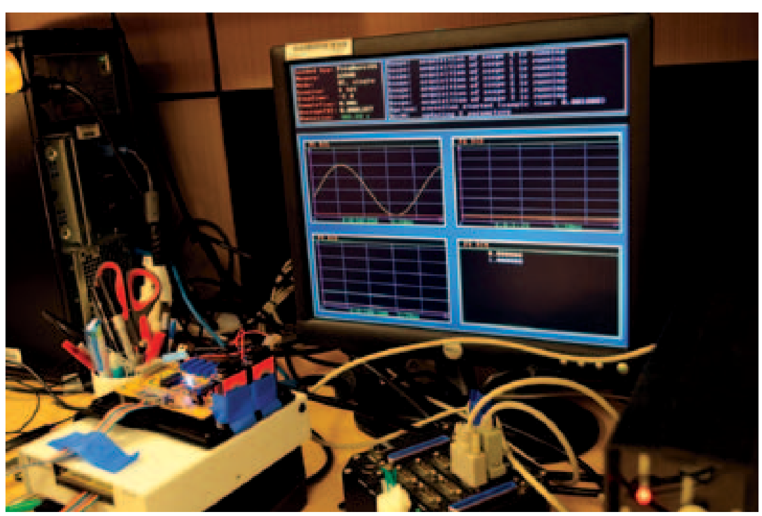
Model-driven Design of Optimal Electrodes and Stimulation

Principal Investigators:
Matthew Schiefer, Ph.D.
Dustin Tyler, Ph.D.
Ronald Triolo, Ph.D.

Funding Agency:
National Institutes of Health

Research with human volunteers is essential to establishing the performance of neural interfaces. However, there are far more design options and configurations than are possible to test experimentally in humans. Computer simulations offer an alternative method to evaluate and select the most effective design options for clinical application.

APT Center Investigators are applying finite element method computer models to simulate the complicated spread of electric current throughout realistic, histologically-derived, 3D representations of human nerves. Biomechanical models are also being combined with these neural models to predict the functional outcomes that can be expected at the muscle or joint level. Using statistical methods, the optimal size, shape, number and distribution of contacts and within a nerve cuff electrode can be determined. These computer simulations have allowed the cuff to be appropriately designed for each target nerve, balancing the engineering and manufacturing constraints with the clinical requirements. This *in silica* technique has been applied to the human femoral to restore the knee extension needed for standing, and the human sciatic, tibial, and common fibular nerves to restore the ankle motion needed for walking. In the upper extremity similar modeling techniques have employed genetic algorithms to maximize the ability to generate finger and wrist motion with a minimal number of contacts. The results of both of these simulation-driven studies have been confirmed experimentally, further documenting that use of computer simulations can accelerate the rate and reliability of translating technologies into clinical trials.



Developing Polymer Muscle Substitutes

Over 3 million patients per year are diagnosed with neurological disorders that result in significant muscle weakness. No currently available orthotic device can improve the muscle strength of individuals with such progressive neuromuscular diseases. A number of wearable robotic exoskeletons actuated by electric motors are on the market, but their size, weight, cost, and power requirements are significant impediments to daily use and might actually accelerate the deterioration of the proximal musculature.

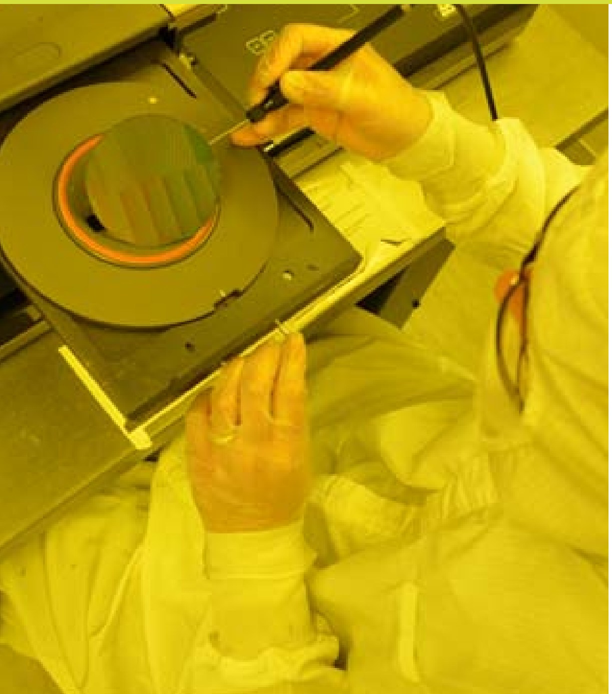
Both muscle atrophy from disuse with muscle destruction from overuse will both cause muscle loss and further weakness. Our group has started to develop lightweight, flexible exoskeletons, using "smart" biomimetic polymer actuators that might eventually help a user maintain the steady-state between disuse atrophy and overuse destruction, thus potentially altering the course of the disease and increasing the time over which natural muscle mass can be retained. APT Center Investigators envision a new class of external orthoses that can be as light and comfortable as a piece of clothing, while still able to generate the assistive power necessary to amplify user strength and coordinate complex muscle movements.

The most crucial step in creating these novel exoskeletons is the development of lightweight, biomimetic polymer actuators that can function as "artificial muscles" within the orthoses. This project involves designing and fabricating these artificial muscles. Our preliminary research indicates that dielectric elastomers may be the best class of materials to duplicate the properties of natural muscle, and thermoplastic polyurethanes are four times more electromechanically powerful than any other commercially available dielectric elastomer. After optimizing these electrically active polymers, the goal is to incorporate the artificial muscles into lightweight and dynamic orthotic devices that can generate supplemental power to assist in the completion of voluntary movements, or provide controlled resistance for rehabilitation and reconditioning exercise, without causing muscle damage.

Principal Investigator:
Rahila Ansari, M.D., M.S.

Clinical Collaborators:
Robert Ruff, M.D.

Funding Source:
Lubrizol



Micropackage Technology for Implantable Microsystems

Principal Investigator:
Wen H. Ko, Ph.D.

Clinical Collaborator:
Margot Damaser, Ph.D.

Funding Agency:
National Institutes of Health

Implanted medical devices containing active electronics currently need to be hermetically sealed in titanium or ceramic packages, which limit their size, mechanical flexibility and integration with biological tissues. Investigators with the APT Center are developing unique nonhermetic (not airtight), biocompatible micropackaging approaches based on the engineering of novel multilayer materials and thin film coatings.

The encapsulation we are developing is typically thinner than 250 μm (micromilimeters) and adds minimal volume to the system being packaged. The multilayer thin film approach allows flexible wires and electrode arrays to be inserted within the same thin flexible protective coating as any rigid integrated circuits and components to eliminate the weak points of traditional feed-throughs and cable connections. Our approach also produces soft, smooth outer layer that is mechanically and biochemically compatible with the tissue and may reduce the potential for irritation or rejection responses with movement of application of local pressure.

The non-hermetic micropackage technology we have developed thus far exhibits an accelerated life time of up to 5 years. Biocompatibility testing is similarly encouraging with all animals surviving the one month implantation period with no acute histological problems or pathologies observed at explant.

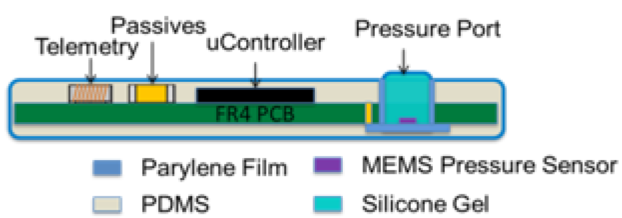
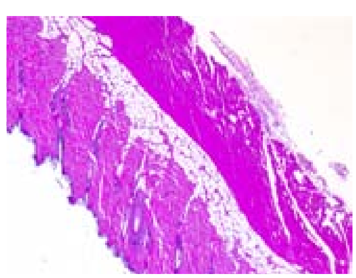
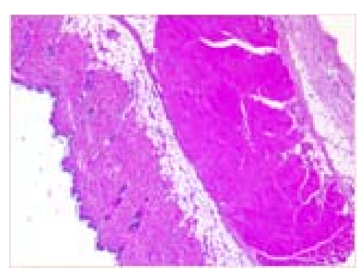


Diagram of the packaged pressure telemetry device.





The two pictures show great similarity in the morphology of the tissues. Left is the control group of healthy skin. Right is the tissue around the implant. The pathological examinations showed normal tissue response to the implant; no evidence suggesting foreign body giant cell reaction, no scar formation, and no inflammation.

CARE/DETECT and the Caren System Equipment

– Tools for enabling technology

The APT Center was instrumental in obtaining and installing $3.8M worth of new high tech capital research equipment from the State of Ohio through two projects (CARE: "Clinically Applied Rehabilitation Engineering" and DETECT: "Diagnostic Engineering Technologies for Evaluating Connective Tissues") at the LSCVAMC and its partner institutions (CWRU, CCF and Austen BioInnovation). One key piece of new equipment is a 3D-Bioplotter from EnvisionTEC that can fabricate biocompatible tissue scaffolds from a wide array of materials, from soft hydrogels over polymer melts to hard ceramics and metals. Additional new facilities include state-of-the-art equipment for tissue processing and histology, real time PCR (polymerase chain reaction), and additive manufacturing, microfabrication and 3D printing.

The CARE project, obtained the funding and completed the installation of the first Motek CAREN virtual reality rehabilitation system in a non-military facility in the United States. The CAREN system is an immersive virtual reality environment consisting of a 6-degree of freedom moving platform with an embedded treadmill, wrap around projection screens, integrated complete motion capture system, and virtual human model. Physically located adjacent to the LSDVAMC on the campus of CCF, this system is designed to allow sophisticated probing of the neuro-musculo-skeletal, vestibular and motor control systems and pursuit of innovative rehabilitation strategies designed to enhance community integration.

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Funding Agency:
Ohio Third Frontier Program,
State of Ohio

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