Advanced Platform Technology (APT) Center
Louis Stokes Cleveland
Department of Veterans Affairs Medical Center (LSCDVAMC)

APT CENTER

TECHNICAL FOUNDATIONS
FOR CLINICAL INNOVATIONS

ANNUAL REPORT
January 1, 2005 – December 31, 2005

Annual Report
January 1, 2005 – December 31, 2005
Cleveland Advanced Platform Technology Center
Louis Stokes Cleveland Department of Veterans Affairs Medical Center

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A. SUMMARY OF YEAR

1. Mission of the Cleveland APT Center

Mission: *The Cleveland APT Center will develop advanced technologies that serve the clinical needs of veterans with motor and sensory deficits and limb loss to provide clinician-researchers within the Department of Veterans Affairs (VA) with new tools for rehabilitation, treatment and scientific inquiry that lead to independence and enhanced societal participation. We will accomplish this by collaborating with leading academic, industrial and clinical partners within and outside the VA system. The Cleveland APT Center will be a national leader in creating and delivering innovative products based on cutting edge technologies and a catalyst for the discovery and development of new technologies and techniques that can be employed in the rehabilitation process to provide independence for veterans and other individuals with disabilities.*

The primary strategy of the Cleveland APT Center is to bring the clinical needs of veterans to the attention of the engineers and scientists pursuing new and emerging technologies in order to apply them for the purposes of reducing disability, improving daily function and enhancing quality of life. Our approach is based on the fundamental assumption that there is considerable untapped potential in new technologies that could be brought to bear on solving the pressing, real world clinical needs of disabled veterans. In many cases, these technologies are being developed for non-medical purposes and their potential in rehabilitation has not yet been appreciated.

The purpose of the Center is to identify high priority rehabilitation needs and then match them with potential technological solutions. We will systematically gather, organize and analyze the needs of clinicians and potential consumers of assistive technologies before evaluating the portfolio of technologies at our disposal to see if possible solutions exist. Therefore, it is important that the Center maintain a broad base of collaborators in the various engineering and scientific disciplines. Where no potential matches between emerging technologies and clinical needs exist, the interactive process will facilitate the exploration of new approaches, techniques and technologies that might not otherwise have existed or been apparent.

It is critical to the mission of the Center that the platform technologies identified and developed become readily available to the veteran and accessible to clinician-scientists within the VA Healthcare System. Therefore, prototype devices and new technologies need to be developed in a manner that is consistent with the production and commercialization of medical-grade products. The Cleveland APT Center is organized to ensure that the technologies that result from our efforts are suitable for regulatory approval, are manufacturable and producible, and can be broadly disseminated. Our goals will be accomplished by performing design and prototype functions under structured quality control systems so that large-scale production can be outsourced to contract fabrication facilities or transferred directly to commercial partners.

2. Stated Goals and Objectives Achieved

Goals: The overall goals of the Cleveland APT Center are to:

1. Create an environment where the pressing clinical needs of clinicians and veterans with motor and sensory dysfunction and limb loss can be coherently represented to engineers and scientists developing advanced technology
2. Foster multidisciplinary interactions between clinician-scientists and device designers in order to find creative solutions to real-world rehabilitation issues
3. Design deployable and manufacturable rehabilitation products that address the unmet needs of veterans with disabilities
4. Facilitate production of new rehabilitation technologies for a wide variety of applications
5. Ensure access to the resulting rehabilitation products and disseminate them throughout the VA Healthcare System
6. Protect intellectual property and enable technology transfer to commercial manufacturers
7. Provide training opportunities for clinicians in rehabilitation engineering and technologists in rehabilitation science related to advanced technology
8. Support rehabilitation research at other Centers of Excellence by adapting the foundational technical platforms to meet their specific needs for advanced prosthetic systems and sensory aids

This section reports on the progress toward these goals completed in 2005. Center objectives established at the beginning of the reporting period are identified, followed by specific accomplishments and progress toward achieving them.

Objective 1: Establish key infrastructure and create an environment conducive to successfully achieving the stated goals of the Center.

Progress and Accomplishments:

- **Recruited Key Members of Senior Management Team**

  Three key members of the Senior Management Team, as identified in the Center Proposal, were recruited during this period: After an exhaustive search, highly qualified and experienced Director of Operations (S. Iveljic) and Quality Systems Manager (J. Burger) were hired and have successfully assumed their administrative responsibilities. An offer has been extended to the third key member of the Senior Management, the Senior Engineering Manager. The critical nature of this position and the specialized expertise that it requires necessitated a national search that elicited over 80 applicants. Of those applicants, only 10 were qualified for an interview. We anticipate filling this last key position on the Senior Management Team in the first quarter of 2006.

- **Secured Administrative Support Services**

  The services of an Information Technology (IT) Specialist and a Purchasing/Contract Specialist have been secured for the needs of the APT Center. The IT specialist (M.

Vibbert) administers our computer networks, designs and maintains our website and digital communication systems, and specifies, procures and installs computing resources for the Center. The Purchasing/Contract specialist (M. Washington) administers our local ordering and grants accounting system, processes Interagency Personnel Agreements (IPAs), and facilitates contracts for goods or services between the VA and outside entities for the APT Center. As originally proposed in the APT Center grant, these positions are shared with the administrative core of the Cleveland Functional Electrical Stimulation (FES) Center in order to take advantage of existing in-house expertise and established infrastructural processes. Recruiting for an Administrative Assistant dedicated exclusively to APT Center activities is ongoing.

- **Hired Dedicated APT Technical Staff**

  The technical staff serving APT Center projects was established through the recruiting and hiring of three full-time engineers dedicated to microfabrication, electronics design, as well as system integration and sensor development. Two Master's level Electrical Engineer (J. Dunning and J. Schnellenberger) and one Bachelor's level Biomedical Engineer (P. Fletter) joined the APT Center and are providing their technical expertise on a number of projects detailed below. A third engineer (J. Sakai) is dividing his effort between ongoing FES Center projects and support of new APT Center initiatives utilizing the advanced mechanical design and rapid prototyping facility in the Department of Mechanical and Aerospace Engineering at Case.

- **Acquired New Technical Capabilities**

  During the reporting period, the APT Center acquired two major pieces of research equipment: a twin screw microcompounder, and a new high resolution laser head for our advanced stero-lithographic assembly (SLA) machine housed in the rapid prototyping facility at Case. These devices significantly extend our previous abilities to create small quantities of new dynamic polymer materials, and to fabricate molds or mechanical parts with the micro-scaled features required for high density neural interfaces and other implantable devices, respectively.

- **Renovated Dedicated APT Center Space at the LSCDVAMC**

  We have acquired and are completing renovation of 1,225 square feet of space at the Louis Stokes Cleveland Department of Veterans Affairs Medical Center to serve as the central offices for the APT Center. Working space for five investigators and four full-time APT Center staff will be ready for occupancy in early 2006. In addition, we have completed a needs assessment and obtained preliminary architectural plans and interior designs for renovations to the Technical Development Laboratories (TDL) and Administrative Offices of the Cleveland FES Center on the Campus of Case Western Reserve University in order to accommodate APT Center personnel.

Objective 2: Establish a formal process for identifying and prioritizing the unmet clinical needs of veterans with disabilities and other potential consumers of advanced rehabilitation technologies.

Progress and Accomplishments:

- **Organized First Formal Needs Assessment Workshop**

  Our formal *Clinical Needs Assessment* effort was launched in 2005, led by the Medical Director (G. Creasey) and Director of Operations (S. Iveljic). Our first workshop will be held in the VA Learning Exchange. This is the first of a network of work laboratories being established in the VA Healthcare System of Ohio with the purpose of assisting VA staff to accelerate their work using a variety of techniques that facilitate collaborative learning and organizational change. The workshop has been planned with the assistance of Robert Means, Ph.D., the National Director for Education Research and Dissemination of Innovations in the VA Employee Education Service, assisted by nationally known consultants such as Nancy Dixon, Ph.D.

  Participants will include approximately 30 veterans, external researchers and rehabilitation clinicians, and representatives from the medical device industry, as well as APT Center staff and leadership. Appreciative inquiry and reiteration will be used to identify veteran needs in this workshop. Unmet clinical needs will be grouped using an affinity diagram. The grouped needs will then be prioritized using a criterion based scoring methodology formula incorporating the number of veterans affected, the severity of the need, and the time factor involved.

  By design, this preliminary effort will be small and local in nature and focus on motor system issues in order to refine the assessment process and prepare for future workshops engaging experts at a national level on a broader range of issues affecting the disabled veteran, including sensory loss and prosthetics.

  More details on our formal needs assessment effort are provided below in section **B. Project Reports**.

Objective 3: Communicate clinical imperatives to technologists, engineers and scientists and collaboratively identify suitable technologies for addressing them.

Progress and Accomplishments

- **Instituted Quarterly "All Hands" Investigators Meetings**

  To facilitate ongoing interactions between clinicians and affiliated APT Center scientists, we have established a quarterly Investigators Meeting that brings faculty and physicians together to discuss potential new projects and present updates on progress of existing projects. Part of each meeting is dedicated to a tutorial given by a clinician on a topic of particular relevance to the disabled veteran. Areas covered have included clinical issues related to organ, cavity or tissue pressure, prosthetics and orthotics, and telemedicine.

- **Sponsored Four Seminars and Outside Speakers**

  The APT Center assumed responsibility for co-sponsoring the Neuroprosthesis Seminar Series at Case Western Reserve University with the Cleveland FES Center. During the course of 2005, the APT Center organized lectures by visiting scholars pre-eminent in their fields of specialization as detailed below in section **D4: Sponsored Conferences and Workshops**. The platform-technology-related speakers included: Dr. Darrin Young, an affiliated APT Center investigator who discussed studies toward advanced technical approaches to rehabilitation for hearing loss; and. Dr. Joseph Rizzo, Director of the Boston VA RR&D Center of Excellence for Innovative Visual Rehabilitation, who delivered the capstone lecture of the series in December. Dr. Douglas Shire from Cornell University and the Boston Center accompanied Dr. Rizzo to tour APT Center facilities and explore potential collaborative projects with APT Center faculty. Barry Yomtov, the Lead Engineer on the retinal prosthesis project at Boston Center, also toured the APT Center and discussed possible collaborations.

  In addition to the monthly joint Neuroprosthesis Seminar Series at Case Western Reserve University, the APT Center also sponsored speakers in our weekly internal seminar program. Mr. Bradley Boggs from Goodrich Company presented his work on micro-electro-mechanical (MEMS) pressure sensors for medical applications, and Dr. Pedram Mosheni, another APT Center investigator in the Department of Electrical Engineering and Computer Science at Case described his work on sensing technology and wireless telemetry of cortical recordings. Both topics addressed high priority areas for the APT Center and were relevant to our overall mission as well as ongoing Center projects.

Objective 4: Implement design controls and quality assurance systems during the development process to expedite transfer of prototypes to human testing.

Progress and Accomplishments

- **Created New APT Quality System**

  One major achievement over the past year has been the initiation of our comprehensive quality management system for design and document control. Introduction of the Quality System occurred in October 2005 with the release of the first document in the system, Document Change Control. We have established the Document Control and Document Change Control area including secured storage for our documents. We have also purchased database software for control of our specifications and drawings (parts and vendors). A draft Quality Manual was written and distributed for final approval that specifies management level responsibilities in the quality system, including a) the quality related Center organization, b) responsibility and authority for quality, c) resources committed, d) quality system review policies, and e) quality planning. The Center quality operations were also specified in a draft Standard Operating Procedures collectively referred to as Level II quality documentation.

In addition, we have released documents and completed training of APT Center and various FES Center staff in quality procedures related to Control of Laboratory Notebooks, Control of Quality Records, and Design Control. This system will be applied to the first APT Center projects in early 2006, beginning with the Networked Neural Prosthesis (NNP) development program described below in section **B: Project Reports**. This system will be made available for any VA Center of Excellence interested in maintaining Food and Drug Administraion (FDA) compliance with its design activities and has recently been exported to the Cleveland FES Center which is adopting it for its internal quality control efforts.

Objective 5: Initiate new design and development efforts for components of our platform technology portfolio.

Progress and Accomplishments

- **Established Project Teams and Project Plans for 5 New APT Center Technical Development Efforts**

  Five new design and development projects were initiated with APT Center sponsorship in 2005. We have begun to pursue four (4) technical initiatives originally proposed in our Center grant application that address pressing rehabilitation issues such as chronic wound treatment, pressure and physiological monitoring for incontinence management and genitourinary health, manufacture of advanced interfaces with the nervous system, and unique dynamic materials for cortical recording. A fifth project dealing with advanced control techniques for myoelectric limb prostheses was conceived and initiated during the reporting period. Leaders for each design and development effort have been identified, project plans have been defined, and resources for start-up activities including professional staff, equipment and graduate student support have been allocated from APT Center funds. Center support is designed to prove of concepts, develop physical or functional prototypes, pilot new manufacturing processes, or otherwise generate preliminary data required for dedicated grant submissions to continue or complete development of each new product with independent external funding.

  Specifically, APT Center initiatives undertaken this year include:

  - Clinical needs assessment workshop to identify and prioritize the needs of patients with sensory and motor loss in order to focus research using existing or emerging technology.
  - A disposable bandage with integrated surface stimulator for the acceleration of chronic wound healing (i.e. the “Integrated Surface Stimulation Device” or ISSD).
  - Implanted pressure sensors and telemeters utilizing microelectromechanical system (MEMS) technology.
  - Implantable micro-miniature myoelectic signal (EMG) telemeters for advanced powered limb prostheses.

- Microfabrication techniques for producing high density electrode arrays out of unique materials for chronic implantation in high resolution neural interfaces.
- New biologically-inspired dynamic materials for cortical probes that can change mechanical properties to match those of the surrounding tissue to minimize chronic inflammatory response or damage to neural structures.

As described in our original grant application, the APT Center is also continuing to partner with the Cleveland FES Center on the ongoing effort to develop a radically new rehabilitation platform technology - the Networked Neural Prosthesis. All six of these projects and progress toward their completion are presented in detail in section **B4: Project Progress Notes**.

Objective 6: Generate grant proposals and engage in collaborative studies with other VA Rehabilitation Research & Development (VA RR&D) Centers of Excellence.

Progress and Accomplishments

- **Submitted 6 VA Merit Reviews of which 3 were Center-to-Center Collaborative Proposals**

  We have been actively seeking support for research and development projects that respond to areas of high priority and special interest to disabled veterans such as chronic wound healing, advanced command-control systems for powered limb prostheses, and neural interfaces for sensory feedback in prosthetic applications. APT Center investigators generated a total of 6 grant submissions to the Department of Veterans Affairs in 2005, including three projects responding to the call for collaborations between Rehabilitation R&D Centers of Excellence. These accomplishments are summarized below in section **B1: Project Submissions**.

  We have directed considerable effort toward establishing collaborative projects within the VA Healthcare System with particular emphasis on developing close working relationships with other VA RR&D Centers of Excellence. To date we have participated in grant submissions with investigators from the Boston Center for Innovative Visual Rehabilitation ("Engineering the Neural Prosthesis-Tissue Interface Through Controlled-Release Polymers" - D. Shire and D. Tyler, Co-Principal Investigators), the Center of Excellence in Limb Loss Prevention and Prosthetic Engineering at the VA Pugent Sound Health Care System ("Neuromuscular Control of a Biomimetic Torsional Prosthesis" - G. Klute and R. Triolo, Co-Principal Investigators), and the VA Medical Center in Ann Arbor ("Evaluation of Telemedicine Technologies for Spinal Cord Injury" – C. Ho and J. Lowery, Co-Principal Investigators). Establishing active collaborative projects with other Centers of Excellence will continue to be a priority for us in 2006 and throughout the entire period of APT Center funding.

- **Submitted 5 Funding Applications to non-VA Agencies**

  In 2005, APT Center investigators submitted five (5) applications for funding to other non-VA agencies, including three (3) grant proposals to the National Institutes of Health (NIH), and two (2) White Papers to the Defense Advanced Research Projects Agency (DARPA). Accomplishments in this area are also further enumerated in section **B1: Project Submissions**. These submissions were primarily in support of the APT Center initiatives previously listed in the progress summary for **Objective 5**, as well as in section **B4: Project Progress Notes**. A majority of these applications are still in review with funding decisions pending.

- **Initiated New Collaborative Project with the University of Pittsburgh**

  In the last quarter of 2005, we established a new collaborative feasibility study with researchers at the University of Pittsburgh (D. Weber). The APT Center portion of the effort concentrates on the design and fabrication of multi-contact spiral nerve cuff recording electrodes to acquire sensory signals from the dorsal roots in a feline animal model. We have set design specifications and functional requirements of the devices in conjunction with our collaborators and are in the process of developing the fabrication techniques to produce a small quantity of recording electrodes for initial feasibility testing in Pittsburgh. As described in section **E2: Active Collaborations**, once the performance of the device is verified we plan to produce quantities sufficient to support ongoing funded projects in Pittsburgh dedicated to reconstructing the movement of a limb from afferent signals, the outcome of which should have applications for the control of neural prostheses or other assistive devices.

Objective 7: Significantly involve and begin training of at least one medical student, graduate student, and post-doctoral fellow.

Progress and Accomplishments

- **Recruited and Hired Post-Doctoral Fellow**

  Dr. Jeffrey Capadona joined the APT Center as a post-doctoral fellow under the mentorship of senior APT Center investigators (S. Rowan, D. Tyler and C. Weder). Dr. Capadona is a full-time VA investigator based in the Department of Macromolecular Science at Case Western Reserve University and is working in support of APTC initiatives in the areas of novel dynamic materials for rehabilitation applications. Dr. Capadona is in the process of completing an Associate Investigator award application and is rapidly becoming a key member of our faculty capable of developing and conducting his own independent research program within the APT Center.

- **Initiated Training of 6 Medical/Graduate Students**

  One M.D./Ph.D. student (T. Gifford), two candidates for Master's degrees in Electrical Engineering and Computer Science (D. Howe and B. Farnsworth), and three doctoral students in Biomedical Engineering (E. Arguello, M. Schiefer and J. Harris) at Case Western Reserve University have elected to pursue their academic training while

working on various aspects of APT Center projects. In addition, two students in the undergraduate program in Mechanical and Aerospace Engineering (E. Fetty and D. Lachut) at Case Western Reserve University are pursuing Senior Projects on the application of principles of rapid prototyping to the design and fabrication of high density neural interfaces.

Objective 8: Establish at least one significant alliance with a commercial partner for the production and marketing of resulting rehabilitation products.

Progress and Accomplishments

We have initiated or strengthened working relationships and entered strategic alliances with the following industrial partners:

- **Ardiem, Inc. (Indiana, PA)**

  We have allied with this manufacturer of human grade implantable medical devices to produce stimulating electrodes originally designed by the Cleveland FES Center. The devices can now be fabricated to our specifications according to protocols and work instructions generated by the APT Center. This will greatly facilitate our ability to provide these components to collaborators within the VA system. In addition, we are participating with Ardiem in the planning of a project with the Department of Defense for the development of advanced wireless systems for the control of powered limb prostheses.

- **NDI Medical (Cleveland, OH)**

  During this reporting period we started working with NDI Medical to jointly develop a clinical programming interface for a new generation of implanted pulse generators. The software platform will be used to edit patterns of stimulation for a variety of motor and sensory system applications.

- **Point Medical (Crown Point, IN)**

  We initiated a relationship with Point Medical to fabricate components of a new flat interface electrode.

- **Ethox, Inc. (Buffalo, NY)**

  This contract sterilization company has assisted us with establishing FDA compliant protocols for sterilizing, packaging and shipping various implantable components of neuroprosthetic systems.

3. Future Goals and Objectives

The long-term goals of the APT Center remain unchanged from our original plan as articulated in the Center grant proposal. Specific short-term objectives for 2006 are as follows:

1. Establish an APT Center governing board and convene at least one meeting of this advisory panel
2. Complete facility renovations at the Technical Development Laboratory and the Louis Stokes Cleveland Department of Veterans Affairs Medical Center for APT Center activities
3. Complete hiring of key personnel
    a. Engineering Manager
    b. Administrative and technical staff
4. Build capacity by submitting at least one associate investigator or career development award application for APT Center junior faculty
5. Conduct first two workshops in the Clinical Needs Assessment series
6. Implement the APT Center Quality System
    a. Finalize all Level 1 and Level 2 documents, including Quality Manual, Standard Operating Procedures, Organizational Charts and Policies
    b. Release all of the documents through the QS Document Control System
    c. Complete training on all QS documents to all APT Center personnel
    d. Assist the FES Center in implementing the Quality System for their projects
7. Transfer three ongoing development projects into the APT Center Design Controls
    a. Bring projects under the APT Center management
    b. Establish project teams
    c. Evaluate and formally approve project development plans
    d. Complete the initial phases of Design Controls up through Design Verification
    e. Submit at least one design dossier to FDA to apply for a Device Master File
8. Produce APT Center products and assure availability to collaborators
    a. Solidify relations with external contractors
    b. Formalize intellectual property arrangements with partner institutions
9. Secure leveraged funding for APT Center projects from at least two sources
10. Submit at least 5 manuscripts for publication in peer reviewed journals and 10 presentations at national conferences
11. Launch at least one new initiative in advanced prosthetics or other high priority area for the VA
12. Participate in one new collaborative project with clinical and/or research groups within the VA Healthcare System

4. Plan adjustments

Adjustments to the operations plan of the APT Center have been few and relatively minor. Delays in identifying and hiring the Senior Engineering Manager have resulted in the necessity of postponing the implementation of formal structured development schedules and production timelines for several existing FES Center products originally intended for transfer to the APT Center. These start-up transients are temporary since the position will be filled in the first quarter of 2006. The delay in start of this key member of the APT Center leadership team has also required us to continue to rely on the current management structure of the Technical Development Laboratory (TDL) of the Cleveland FES Center. This will also change in the first quarter of 2006 as the APT Center assumes responsibility for management of several design, development and production efforts as anticipated in our original proposal.

The delay in securing a Senior Engineering Manager for the APT Center has also made it necessary to maintain the TDL as a shared use facility jointly occupied by APT and FES Center staff and serving the technology development needs of both Centers, rather than transfer the facility in its entirety to APT Center management as originally proposed. Similarly, the NNP is being co-developed in a collaborative manner between the FES and APT Centers, rather than accruing primarily to APT as in the original Center proposal. This new arrangement has the advantage of allowing us to continue to work on FES-related projects that represent platform technologies with broad, cross-cutting applications in rehabilitation, without encumbering our ability to focus on new projects and products unrelated to electrical stimulation that serve the broader rehabilitation needs of the disabled veteran. In this way, we can continue to take full advantage of the synergies that exist between our Centers, including full and unrestricted access to the laboratory facilities and human resources that have already been established. In short, it should allow us to collaborate more effectively with other VA Centers of Excellence outside of the FES Center and be responsive to the technical needs of the larger VA community.

Finally, we have deviated slightly from our original intention to rely almost exclusively on post-doctoral fellows to advance APT Center technologies in favor of Master's trained professional engineering staff and pre-doctoral graduate students. While our current post-doctoral training experience has proven to be extraordinarily successful, this adjustment will enhance our ability to complete more projects on time and under budget as well as provide for continuity during transitions between projects. We still intend to recruit post-doctoral fellows in selected specialty areas as needed, but at a slightly reduced rate than originally anticipated.

B. PROJECT REPORTS

During the reporting period, APT Center investigators submitted a total of 11 applications for research funding to various federal and private agencies. Six (6) submissions were VA Merit Review applications, three (3) of which were proposed Center-to-Center Collaborative grants. Another three (3) grant applications were submitted to other federal agencies such as the National Institutes of Health (NIH), and two (2) White Papers were prepared for consideration

by the Defense Advanced Research Projects Agency (DARPA). Peer review of eight (8) of these opportunities is still in process, with funding decisions pending.

1. Project Submissions/Approvals (VA, Other Federal, and Private Funding)

	Status	Investigator	Title	Sponsor	Period	Total Request
1.	Review Pending	Bogie	Integrated surface electrical stimulation device for therapeutic applications[1]	NIH	7/06-6/08	$424,875
2.	Submitted	Bogie	Development of a reliable wound healing measurement protocol	VA RR&D	N/A	N/A
3.	Review Pending	Creasey	Electrical activation of afferent nerves to restore bladder function[2]	VA RR&D	4/06 - 3/09	$645,600
4.	Submitted	Ho (PI), Lowery (Co-PI)	Evaluation of telemedicine technologies for spinal cord injury	VA RR&D Center-to-Center Collaboration	N/A	N/A
5.	Submitted	Klute (PI), Triolo (Co-PI)	Neuromuscular control of a biomimetic torsional prosthesis[2]	VA RR&D Center-to-Center Collaboration	N/A	N/A
6.	Review Pending	Shire (PI), Tyler (Co-PI)	Controlled-release polymers for the neural prosthesis-tissue interface	VA RR&D Center-to-Center Collaboration	6/06 – 5/08	$250,000
7.	Review Pending	Tyler (PI)	Stimulus-responsive, mechanically-dynamic nanocomposite for cortical electrodes[1]	NIH	6/06 – 5/08	$424, 875

	Status	Investigator	Title	Sponsor	Period	Total Request
8.	Review Pending	Tyler (PI)	Neural interfaces for prosthetic command and sensory feedback[1]	VA RR&D	6/06 - 5/09	$722,400
9.	Review Pending	Zealear (PI) Tyler (Co-I)	Electrical stimulation of the bilaterally paralyzed larynx paced with respiration[1,2]	NIH	06/06 – 05/11	$590,904
10.	Review Pending	Weinstein (PI) Tyler (Co-I)	Enhanced neurite extension for neural prosthetic interfaces	DARPA	N/A	N/A
11.	Review Pending	Young (PI) Tyler (Co-I)	An implantable wireless neural interface for an insect-based microsystem[1]	DARPA	N/A	N/A
	Total VA			6	-	Pending
	Total Other Federal			5	-	Pending
	Grand Total			**11**	**-**	**Pending**

[1] See Section B.3 Project Progress Notes for a detailed description.
[2] In collaboration with The Cleveland FES Center.

2. Ongoing Funded Projects (VA, Other Federal, and Private Funding)

The APT Center participated in nine (9) ongoing projects funded by various sources in 2005 as summarized below.

	Status	Investigator	Title	Sponsor	Period	Total Award
1.	Completed	Creasey	Electrical treatment of reflex incontinence[2]	VA RR&D	4/02 - 3/05	$531,000
2.	Ongoing	Damaser	Research Career Scientist	VA RR&D	10/04 - 9/09	$306,250
3.	Ongoing	Kilgore	A novel waveform for electrical nerve conduction block[2]	VA RR&D	6/04 - 5/07	$922,231

	Status	Investigator	Title	Sponsor	Period	Total Award
4.	Ongoing	Peckham	Development of networked implantable neuroprosthesis[1,2]	NIH	3/05 - 2/10	$7,004,342
5.	Ongoing	Triolo	Center of Excellence, Advanced Platform Technology	VA RR&D	1/05 - 1/10	$4,250,000
6.	Ongoing	Triolo	Research Career Scientist	VA RR&D	10/02 - 9/07	$306,250
7.	Ongoing	Triolo	Enhancing neuroprosthesis performance with nerve cuff electrodes[2]	NIH	9/03-8/06	$1,128,525
8.	Ongoing	Triolo	A hybrid neuroprosthesis for mobility after paralysis from spinal cord injury[2]	DOD	3/05 – 2/09	$1,745,533
9.	Ongoing	Tyler (PI)	Dynamic laryngotracheal closure using BION technology[2]	VA RR&D	3/05-2/08	$441,400
	Total VA			6		$6,757,131
	Total Other Federal			3		$9,878,400
	Grand Total			**9**		**$16,635,531**

[1] See Section B.3 Project Progress Notes for a detailed description.
[2] In collaboration with Cleveland FES Center.

3. Project Progress Notes

The APT Center investigators led or actively participated in numerous ongoing projects in 2005, and either initiated or assumed principal roles in the eight (8) projects described below. Only projects in which The APT Center supplied core resources in support of project staff, or access to the necessary infrastructure and research resources, are summarized. In all cases, Center support was allocated to obtain the preliminary data required prior to submitting future grant applications to continue the research and development efforts. Detailed summaries of the status of each project, including plans for publication and future funding opportunities, are provided. These projects would be prohibitively difficult or impossible to pursue without the unique environment and contributions of the APT Center.

Project #1: Clinical Needs Assessment

Principal Investigators: Graham Creasey, M.D., and Suzana Iveljic, M.B.A.

Description

The APT Center places high priority on developing technology that is clinically relevant. This project consists of using systematic processes to acquire an accurate, thorough picture of the needs of veterans that may be addressed by advanced technologies and can be used in focusing research in the direction most beneficial to the veteran by increasing his/her independence and enhancing societal participation. These processes collect and examine information about issues and then utilize that data to determine priority goals, to develop a plan, and to allocate funds and resources. Veterans, external researchers and rehabilitation clinicians, and representatives from the medical device industry, as well as APT Center Co-Investigators and Leadership are included in gathering data. Both structured and informal data gathering techniques are employed. Structured techniques include focus groups, surveys, and expert panels; informal techniques include user-engineer and clinician-engineer interaction, web-based methods, and unsolicited feedback obtained at conferences and scientific meetings.

Objectives

The main objective of this project is to identify and prioritize the needs of veterans that may be solvable by applying new and emerging technologies in the short, medium, and long-term. A secondary objective is to learn the most effective techniques for obtaining this data.

Research Plan

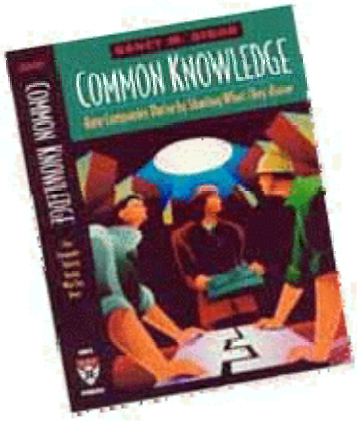
Surveys provide general impressions and direction but not enough detail to develop specific technological applications. Consumers have difficulty trying to define the “next step” technological device and it is rare that consumers can express their needs in a way that is translatable to technical specifications. Our best successes come from having those involved in technical design and development converse and interact directly with consumers during their regular activities. Interactions such as these enable critical design specifications that might otherwise go unnoticed be identified. Therefore, we plan to use focus groups, workshops, expert panels, and direct interaction at the foundation of our research plan. Once we obtain a relatively whole picture of the technological needs, we can follow-up and supplement with surveys, web-based information gathering, and observation to fill in details, provide feedback, and complete our assessment.

Methodology

A series of workshops will be held at the Cleveland VAMC Learning Exchange over the next two years. This location was chosen due to its reputation as an innovative, flexible, and high performance work laboratory equipped with technology that supports creative work processes. The facility includes: Smartboard technology for multi-user collaboration; PC Tablets with handwriting and voice recognition; E-Beams to capture notes and graphics from whiteboards; Multi-site display and quick-time reproduction; and BOSE amplified sound systems to enhance the learning process.

The Cleveland VAMC Learning Exchange also brings skilled facilitation to the table. Robert Means, Ph.D., who is responsible for creating the Learning Exchange is the National Director of Research and Dissemination of Innovations in the VA Employee Education Service and has many years of experience in educational research including a previous position as the Chief Employee Education Officer for the VA Headquarters in Washington, D.C.

Nancy Dixon, Ph.D., is also advising on these workshops; she is an author and consultant working with clients to create effective ways to share knowledge across organization boundaries. Dr. Dixon has studied knowledge transfer systems in organizations around the world and based on that study has constructed a framework that helps organizations determine the type of system that best leverages each different type of knowledge. That framework is the subject of her book *Common Knowledge: How Companies Thrive by Sharing What They Know* (Figure 1).



Many of the systems she describes rely primarily on person-to-person interaction and others combine personal interaction and technology.

Figure 1. Common Knowledge.

In addition to using state-of-the art facilities and highly qualified consultants, the methodology driving the agenda of the workshop has been used in over 35 projects in 15 Veterans Integrates Service Networks (VISNS) encompassing 65 Veteran's Health Administration (VHA) Veterans Affairs Medical Centers (VAMCs), Community Based Outpatient Clinics (CBOCs), the Veterans Benefit Administration (VBA) and National Cemetery Administration (NCA) organization, and within National Headquarters. Water Cooler Logic© (WCL) has been developed within the Department of Veterans Affairs in close collaboration with social scientists at Water Cooler Logic Inc. It is a method of qualitative discovery, research, and social intervention that integrates the aims and principles of change management with organizational learning. WCL builds on the realities of the social dimension of work, learning, and knowledge. It also

recognizes and leverages the largely unrecognized contributions of informal work and learning.

The three phases of WCL are:

a. "Discovery" – observing and talking with those who are potential users of the technology or who will be affected by it.

b. "Co-design" – initially using divergent thinking to scan a wide range of options, followed by convergent thinking to classify and group the resulting possibilities into practical solutions and products.

c. "Deep implementation" – evaluating prototypes while maintaining a willingness to revise, adjust, and amend the process. This recognizes the iterative nature of development whereby feedback refines the design and corrects misconceptions or unintended consequences.

While the workshops are based on WCL, we are also using other techniques such as Appreciative Inquiry that was developed by David Cooperrider and his colleagues at the Case Weatherhead School of Management in Cleveland. This is a process that reduces premature judgment and engages an entire system in an inquiry as to what works in an organization.

Finally, other proven supplemental methodologies such as surveys and web-based information gathering will be used to reaffirm our findings and provide for insight into other exploratory areas.

Milestones

The first workshop is scheduled for February 2006 and the second for September 2006. The website is scheduled to go live in the first quarter of 2006.

Project #2: Integrated Surface Electrical Stimulation Device for Therapeutic Applications

Principal Investigator: Kath Bogie, D.Phil.

Co-Investigators: Steven Garverick, Ph.D. & Christian Zorman, Ph.D.

Staff/Students: Jeremy Dunning, M.S.; Jonathon Sakai, B.S.; & Daniel Howe, B.S.

Project Description:

The overall goal of this project is to develop an integrated surface stimulation device (ISSD) combining the use of advanced materials, fabrication techniques and design together with a simple, user-friendly communication interface in a novel medical device

costing less than $100. It consists of a flexible substrate and battery and custom integrated circuitry integrated into a conforming occlusive dressing. The device can be applied over a chronic wound as a bandage (for days or weeks at a time) and deliver therapeutic electrical currents to accelerate healing without cables, and other external electronics. The device can then be simply removed, disposed of, and replaced to continue treatment. The ISSD will be a therapeutic electrical stimulation device that achieves high efficacy and safety *and* high acceptance by both clinicians and user.

The initial objective is to investigate use of the ISSD for **treatment of chronic ischemic wounds**; however multiple therapeutic applications in acute clinical care and rehabilitation would be positively affected by utilization of electrical stimulation (ES) as a platform modality. This project will thus provide the basis for the further development of a novel surface stimulation platform technology with the potential for widespread clinical utility both within the VA Health Care system and in other health care settings.

Objectives

a. To establish the proof of concept for the ISSD through the design and preliminary testing of a prototype device
b. To implement use of the ISSD in our current ischemic wound animal model.

Research Plan & Methodology

A prototype ISSD is being designed that meets the primary functional requirements that it be capable of delivering ES treatment using pre-defined stimulation patterns safely and reliably for periods up to 7 days (Figures 2 and 3). In addition the device is flexible and durable. All stimulation system components are integrated into a low-profile, lightweight device that can be 'worn' by the user in a similar manner to a standard-type occlusive wound dressing. The proposed integrated surface stimulation device (ISSD) will thus combine ease of clinical use and reliability with complete patient mobility.

The basic initial design will incorporate forward compatible upgradeability. The open architecture will allow the potential for functional expansion such as multi-channel stimulation and biofeedback sensor capability. This will be based on the second core concept that the device will comprise an integrated power supply and pre-programmable stimulator/control system mounted on the upper face of a flexible polymeric 'backbone'.

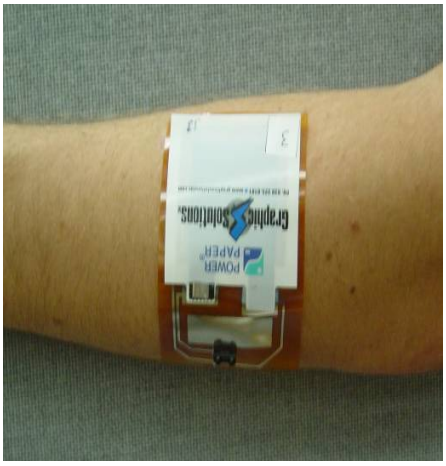


Figure 2. Flexible prototype deployed on forearm.

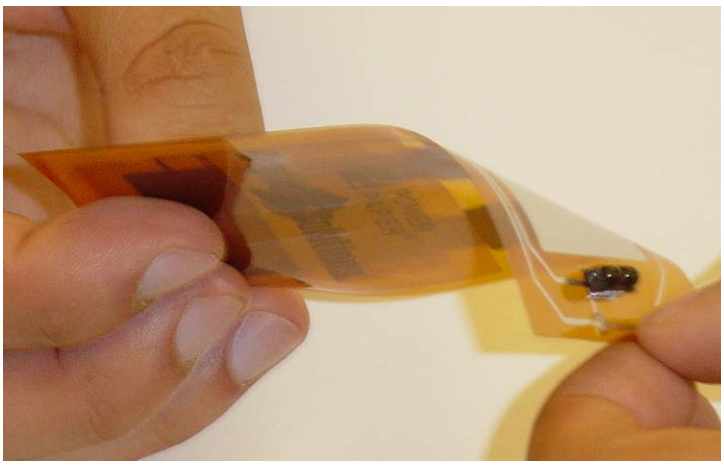


Figure 3. Flexible prototype with major device components.

Testing of all components of the system will be performed to insure their performance and reliability. Bench testing and *in vitro* testing will be performed prior to *in vivo* testing in the rabbit model.

Following bench testing the flexible ISSD will be implemented in our animal wound model and the effects of ES wound therapy will be evaluated using a randomized controlled study design.

Preliminary Results

A prototype ISSD has been fabricated on a rigid printed circuit board (PCB) substrate for use in development and testing of the device. An external communications protocol is under development which will allow two-way communication to both control the stimulation variables and download information on wound status.

Milestones

Complete evaluation of the individual components of the ISSD is scheduled for third quarter of 2006, with benchtop testing of a working prototype to follow in early 2007. By mid 2007 we anticipate initiation of animal testing, which will result in information necessary to optimize the design of the integrated circuit by the end of the year. Preparation for production and qualification for human testing would follow.

Future Grant & Publication Plans

In addition to the NIH grant application reported in **B1: Project Submissions/Approvals,** the following grant application to an internal program for research initiation at our institutional partner, Case Western Reserve University, is in preparation. Submission is anticipated for January, 2006:

In-situ, Wireless Microenvironment Monitor for Healing in Surface Wound. Co-PI with SL Garverick.

Application to: Case Western Reserve University Presidential Research Initiative, Jan 2006. Request: $80,000. Study period: July 2006 – June 2007.

Project # 3: Wireless Intracavity Micro-Manometer (WIMM)

Principal Investigator: Margot Damaser, Ph.D.

Co-Investigators: Graham Creasey, M.D., Chris Zorman, Ph.D., Darrin Young, Ph.D., & Steve Garverick, Ph.D.

Staff: Paul Zaszczurynski, B.S., Paul Fletter, B.S.

Description

This project is aimed at designing, prototyping, and testing an insertable or implantable device for measuring pressure in internal body cavities (the wireless intra-cavity micro-manometer or WIMM). It will wirelessly transmit data to an external collection unit as well as to other devices for networking and control purposes. The device will be miniaturized to fit the smallest desired biological environment. This type of device does not currently exist in the market for a broad application of organs. It has potential application for diagnosis and treatment of urological, gynecological, gastrointestinal, pulmonary, and cardiac conditions. The most likely application is for those conditions for which diagnosis or treatment can be improved by relatively long-term monitoring of localized pressure during activities of daily living. Such conditions include chest pain of noncardiac origin, urinary incontinence, and pulmonary edema. In addition, this device could act as a sensor to alert the patient of the need to perform an action (catheterize the bladder to void or perform daily bowel routine) or could interface with an electrical stimulation or other system to provide feedback control.

Objectives

The objectives of this project are to design, prototype, and test a wireless intra-cavity micro-manometer (WIMM) (Figure 4). The seed funds from APT center are being used to design, prototype, and perform initial *ex vivo* testing of the device. We will apply for external funding for further re-designs, re-prototypes, and in vivo animal testing of the device.

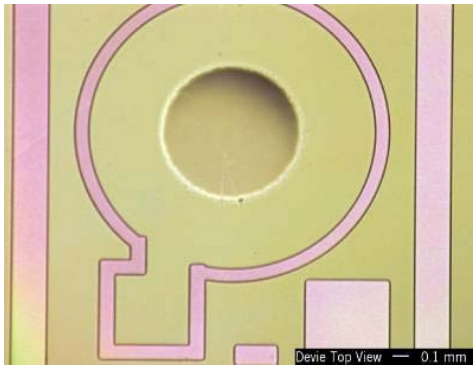


Figure 4. Example Implantable Wireless MEMs-based pressure sensor.

Research Plan & Methodology

Regular design discussions are being held currently. Preliminary testing of radiofrequency transmission through saline are being performed in order to select antennae design prior to miniaturization. Saline is being used as an *ex vivo* surrogate for the abdominal cavity. Preliminary *ex vivo*

testing of the effect on pressure measurement of a device placed under the mucosa in an example organ (the bladder) will be conducted in the near future.

Milestones

We are presently conducting high level sensor design which should be complete in the first quarter of 2006. This part of the project has minimal cost beyond salaries supported by the APT Center. We will prototype the sensor in early 2006. This part of the project has the as of yet unknown costs of producing a PC board prototype. We will conduct bladder testing *ex vivo* in the spring and summer of 2006. This part of the project has moderate to low costs beyond salaries as the equipment for bladder testing exists in Dr. Damaser's laboratory and fresh pig bladders can be obtained inexpensively from a slaughterhouse.

Project # 4: Wireless Implantable EMG Microsystem

Principal Investigator: Darrin Young, Ph.D.

Co-Investigator: Ronald Triolo, Ph.D.

Staff/Students: Bradley Farnsworth, B.S.

Description

This project focuses on developing a subcutaneously implantable sensing and telemetry microsystem for electromyographic (EMG) or myoelectric signals (MES) that can be interfaced with an external transceiver module, housed in or on a prosthetic socket. The prototype system will sense EMG signals from the muscles remaining in the amputated limb and transmit them out of the body to the external receiver for analysis and adaptive control. The external unit can also transmit RF power to the implanted system. Because commercially available myoelectrically controlled powered prostheses rely on EMG signals acquired from the surface of the skin via recording electrodes embedded in the socket, they are prone to problems that can significantly degrade signal integrity and prosthesis performance. The microsystem configuration we are developing (tiny wireless sensing elements placed subcutaneously directly on the target muscles) should significantly reduce movement artifact and obviate other factors that are known to adversely impact the operation of myoelectric prostheses. In essence it will decouple the issues related to socket fit and alignment (including perspiration, variable contact with the skin surface, inability to utilize a liner, etc.) from issues related to EMG signal acquistion. The transcutaneous EMG sensing and telemetry microsystem is expected to substantially enhance the biomimetic performance of myoelectrically controlled powered prosthetic limbs for veteran amputees. The proposed prototype development can potentially be incorporated into existing upper and lower limb prosthetic systems.

Objectives

The objective of this project is to design and implement an implantable EMG sensing and telemetry microsystem, which can be interfaced with an external transceiver module housed in a residual limb-prosthetic socket.

Research Plan & Methodology

The electronic building blocks required for the proposed implantable wireless EMG sensing microsystem will be first designed and optimized using a computer-based circuit simulation program. The finalized design will be fabricated using a commercial complementary metal oxide semiconductor (CMOS) process with an estimated chip dimension of 3 mm x 2 mm x 0.3 mm. The fabricated chips will first be protected by several layers of sputtered or evaporated nitride or other insulating films to achieve a thin pin-hole-free moisture barrier. These surface coatings will then be selectively removed by applying a photoresist masking layer, which is a standard material in semiconductor micro-fabrication process, followed by a photolithograph step to expose the bonding pads. The integrated circuit (IC) chips then will be attached to a thin flexible printed substrate for wire bonding and interfacing with EMG electrodes. A medical-grade polymeric layer will be applied over the bond wires for protection and insulation. The final packaged module will be interfaced with muscles of interest for electrical performance characterization and system evaluation.

Preliminary Results

We have successfully characterized the wireless link for remote RF powering and data telemetry. RF power can be converted to achieve 3V/1mA to supply the implantable electronics. Data telemetry with 1 Mbps has been demonstrated. These capabilities far exceed the requirements for the control of existing myoelectric limb prostheses.

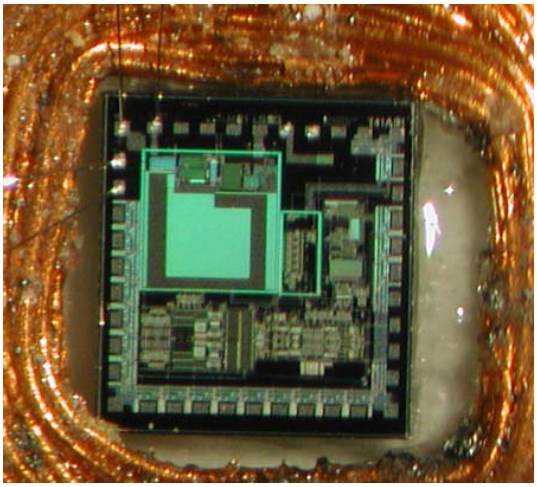


Figure 5. Prototype wireless telemeter.

Milestones

We plan to develop a fully functional prototype wireless implantable EMG sensing microsystem within one year. Once performance of the prototype is verified, we will package the device for implantation and initiate in vivo animal testing. This will be followed by interfacing the prototype circuitry to an existing myoelectric prosthesis, essentially substituting the microsystem for the socket-based surface recording. Finally, issues related to fabrication and qualification for human use will be addressed.

Future Grant & Publication Plans

We plan to submit a VA grant application including the proposed implantable wireless EMG sensing microsystem development as one of the research tasks. The research results will be published in conferences and journals.

Project # 5: Design, Development and Fabrication of Polymer Microstructures

Principal Investigators: Christian Zorman, Ph.D., & Dustin Tyler, Ph.D.

Staff/Students: Jeremy Dunning, M.S., Allison Hess, B.S., Varun Keesara, B.S.

Description

The APT Center is currently pursuing the design and development of innovative technologies that will yield advanced polymer materials for neural interfaces, micro-electromechanical systems (MEMS) and implantable systems for biosignal acquisition and wireless transmission for the control of prostheses and other assistive devices. This particular effort proposes to merge two of these activities, namely advanced polymer materials and MEMS technology by developing polymer-based neuro-interface devices made using MEMS-based microfabrication techniques.

Objectives

To develop baseline fabrication techniques for polymer micromachining using the tool set in the Microfabrication Laboratory (MFL) at Case Western Reserve University for the fabrication steps and a neural electrode array structure as the demonstration vehicle.

Research Plan & Methodology

The methodology used in this study follows procedures commonly used to evaluate new MEMS materials. For the Liquid Crystal Polymer (LCP) devices, structures were fabricated from commercially-available LCP sheets cut for mounting on Silicon (Si) wafers. Platinum (Pt) electrodes were fabricated on the base sheet, after which a cover sheet was thermally laminated onto the base. The cover sheet was then patterned and etched to reveal the final structure. Process development involved using a batch of wafers, some of which were extracted from the process sequence at various strategic points to evaluate key processing steps. Fabrication of polynorborene-based devices followed a process quite similar to conventional photoresist processing. This was possible because the formulation of polynorborene that we used was photodefinable. Process development in this case followed the same strategy used in LCP process development.

Preliminary Results

To date, flexible electrode structures fabricated using multilayered LCP laminants and polynorborene polymers were successfully fabricated (Figure 6). Various fabrication processes were evaluated and an optimized fabrication sequence was identified for

each polymeric material. It was found that LCP, while exhibiting superior moisture absorption properties, was much more challenging to micromachine, requiring vacuum lamination and two-step etching to make the structure. Because our vacuum wafer bonder was down for repair, we were forced to use atmospheric bonding, which greatly reduced the fabrication yield and affected the etching process. Polynorborene, to our knowledge **never before used in biomedical applications**, proved to be photodefinable, thus greatly simplifying the processing steps required to fabricate a multilayered structure that incorporates Pt electrodes. Initial biocompatibility studies suggest that the material is acceptable, however, a much more extensive study is currently underway.

Figure 6. Microfabricated polymer-based neural electrode array structures: (A) LCP structure, and (B) polynorborene structure.

Milestones

At present, we plan to continue the development of polymer processing capabilities as the needs of the Center dictate. Since the last fabrication run was completed, the wafer bonding tool has been repaired. During the first quarter of 2006, we plan several attempts at wafer-scale vacuum lamination using this tool. We also plan to conduct an extensive biocompatibility study of polynorborene during the first half of 2006. The aforementioned work was completed by a graduate student who will be graduating in January 2006. We will begin training of a replacement student who will be responsible for further developing the processing capabilities as part of her Master's thesis.

Future Grant & Publication Plans

Aspects of this work will be included in an upcoming Biomedical Research Partnership (BRP) proposal to the NIH (D. Durand, PI) to make neural electrodes based on LCP. Two abstracts describing the aforementioned work have been submitted to MEMS conferences to be held in 2006.

Publications anticipated in 2006 include a paper summarizing the in vitro assessment of the cytotoxcicity of *Avatrel*® (Polynorborene) targeted for the Journal of Biomedical Materials Research.

Project #6: Stimulus-Responsive, Mechanically-Dynamic Nanocomposite for Cortical Electrodes.

Principal Investigator: Dustin Tyler, Ph.D.

Co-Investigators: Jeffrey Capadona, Ph.D., Christoph Weder, Ph.D., Stuart Rowan, Ph.D.

Staff/Students: James Harris, M.S.

Description

The proposed project will develop the first examples of a new class of polymer nanocomposites that reversibly and dynamically alter their mechanical characteristics in response to an external stimulus. While many polymers alter their mechanical properties, the proposed materials are novel in that they change in direct proportion to the stimulus and are reversible, hence can be controlled. These advanced polymeric materials are scientifically novel and are expected to significantly contribute to the development of many advanced devices and applications in medical technology. The first application targeted here is a “smart” substrate for cortical electrodes. The proposed polymer nanocomposites will be engineered to exhibit a high Young’s modulus, or stiffness, and tensile strength to facilitate implantation of the electrodes into the cortex. Once the device is in place, the material will respond to the chemical environment of the cortex, changing the Young's modulus to match the surrounding tissue and thus becoming “mechanically invisible” to minimize chronic tissue response.

This will be the first demonstration of a mechanically dynamic and reversible, chemo-responsive synthetic material that can change its stiffness on a physiological time scale. We will establish the basic macromolecular engineering principles and demonstrate their feasibility in an important first application that represents an intriguing “prototype” because it only requires a single switching event under very well defined conditions. The general design principles established in this project can then be extended to other biomedical applications in which the mechanical properties can be changed in a controlled and reversible manner.

This development effort is highly significant as there is an unmet need for mechanically-dynamic material, which will enable development of a wide range of biomedical devices that will significantly and positively impact Veteran care. Such applications could include dynamically compliant stress transducers, orthopaedic and prosthetic devices with controllable joint stiffness, conformal matching of socket mechanical properties, neuromimetic electrodes for neural interfaces, obstructive sleep apnea (OSA) devices that dynamically stiffen the airway at night and are compliant during the day, implants for erectile dysfunction, vocal fold implant to stiffen paralyzed folds for speaking and open the folds for breathing, dynamic loading elements in implants, dynamic implantable connectors with minimal stiffness to connect and disconnect and rigid to prevent disconnect, and biodynamic sensors.

Further, this material will allow other investigators to devise many new and as yet unimagined applications.

Cortical electrodes have demonstrated their potential for significant improvement in human health and quality of life, but have not yet achieved a satisfactory mechanical or molecular match with cortical tissue for long-term use. By matching tissue mechanical characteristics, we intend to investigate whether the tissue response to the electrode can be reduced, thus providing a stable long-term interface with cortical neurons. In this application, the material is only required to change mechanical properties once, demonstrating the feasibility of a mechanically-dynamic material in a relatively straightforward system, paving the way for future development of devices with substantial clinical impact.

Objectives

a. *To fabricate mechanically dynamic, nanocomposite polymers*

The focus of this effort is to establish the basic chemistry and processing methods to produce the polymer nanocomposite, and understand its material composition and behavior. The specifications of the prototype material will be guided by its targeted use as a neuromimetic cortical electrode. This will require a material that is initially stiff to allow for insertion of the electrode into the cortex and rapidly changes to match the compliance of the cortical tissue. The materials resulting from this objective, and related materials developed based on the blueprints that result, would serve as a basis for many neural, orthopedic, and other device applications.

b. *To determine biocompatibility and tissue response to nanocomposite*

The objective is to demonstrate and understand the *in-vivo* behavior of the materials as they are developed. These studies will be performed in parallel to drive the development of the nanocomposite based on *in-vivo* behavior of the material. We will test the hypothesis that a mechanically matched material will minimize the astrocytic response and improve the interface between the cortical neurons and the electrode.

Research Plan & Methodology

To accomplish the first objective, high-aspect ratio, nanoscale cellulose "whiskers" are harvested from tunicates. These fibers are chemically functionalized and dispersed in a polyethelene-oxide substrate. The chemistry and interaction of the fibers are be quantified using scanning electron microscopy and dynamic mechanical analysis methods. As materials with varying mechanical properties are produced, this series of materials will be characterized for their properties in the initial "stiff" configuration and "flexible" configuration after immersion in artificial cerebral spinal fluid (ACSF) at 37 ^{o}C. Experiments over extended periods in ACSF will explore the behavior expected as a chronic implant in cortical tissue. At the conclusion of this aim, we expect to have developed an understanding for the structure-property relationship of a series of nanocomposites, in particular with respect to the range of change in modulus that can be realized, the effect of material composition and processing, and the effects of various metal ions and their concentrations on the material behavior. The result will be a catalogue of the most promising nanocomposites.

To accomplish the second objective, the most promising nanocomposites will be implanted chronically in the rat cortex. The tissue response will be characterized using fluorescent immunohistochemistry and light microscopy tools. The durability of the polymer will be assessed by mechanical testing of removed components. At the end of the proposed studies, we expect to have preliminary data to support further development of a cortical electrode with electrical contacts.

Preliminary Results

To date, research efforts have been made towards the first objective of fabricating mechanically dynamic nanocomposite polymers.

Stimuli-Responsive Filler-Filler Interactions: Our group has already established the procedures to isolate gram-quantities of cellulose whiskers. In preliminary experiments in which the cellulose whiskers were decorated with hydroxy and sulfate groups, the feasibility of chemo-mechanical switching of the filler-filler interactions has been unequivocally demonstrated. We have shown the gelation of a dilute suspension of tunicate whiskers upon addition of Magnesium^{2+} (Mg^{2+}), indicating an increase in fiber-fiber interactions (Figure 7). Significantly, we have demonstrated the reversible nature of this interaction through the addition of ethylenediaminetetraacetic acid (EDTA) which sequesters the Mg^{2+} and returns the reinforced gel to an aqueous solution. This experiment supports our hypothesis that polymer/whisker nanocomposites will be 'stiff' in the presence of high concentrations of divalent cations such as Mg^{2+} or Calcium^{2+} (Ca^{2+}). We surmise (*vide infra*) that once inserted in the cortex, which features a much higher concentration of monovalent ions than divalent ions, these divalent ions would be replaced, leading to a reduction of the interaction between the whiskers, and convert the material to a 'softened' state.

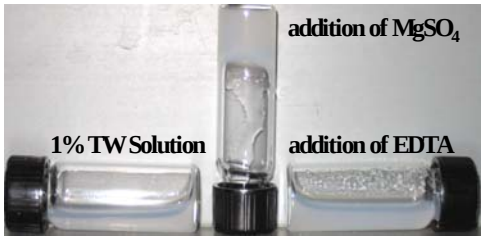


Figure 7. Picture of an aqueous tunicate whisker suspension before (left, liquid), after (middle, gelled) addition of $MgSO_4$, and after addition of EDTA (right, liquid).

Nanocomposite Fabrication: Recently, using dynamic mechanical thermal analysis (DMTA), we have demonstrated that 50:50 ethylene oxide–epichlorohydrin (EO/EPI) matrix copolymer films containing cellulose whiskers display approximately a 30-fold increase in modulus compared to the neat EO/EPI matrix (Figure 8). A moderate water swelling of approximately 24% w/w was observed regardless of whisker filler content. The swelling did not affect the mechanical properties of the neat matrix polymer without whiskers. The addition of 10% whiskers increased the modulus of the neat film by approximately 10-fold due to whisker to whisker interactions, while swelling reduced the film modulus by one-half. The addition of 1% Magnesium Sulfate$_4$ ($MgSO_4$) in the film increased the modulus by another factor of 2 as the Mg^{2+} induced greater whisker-whisker cross-linking. When swollen, solvation shields the Mg^{2+} and decouples the whiskers, resulting in a decrease of modulus back to the same level as the addition of 10% whiskers only. This process can be cycled between high modulus and low modulus. It must be clear that the mechanism of modulus

change in the nanocomposite is related to coupling and decoupling of a whisker matrix and differs from a hydrogel which expands the polymer matrix. This provides greater opportunity for engineering the modulus range and the switching mechanisms.

We have also shown that significant levels of Mg^{2+} ion migrated into the polymer matrix in high [Mg^{2+}] solution. These levels of Mg^{2+} ions had no effect on the mechanical properties of the neat polymer matrix without whiskers. Therefore, we are confident that ions will migrate into and out of the film and that the mechanical properties are modulated and dynamically switchable based on whisker-whisker coupling controlled via Mg^{2+} coordination.

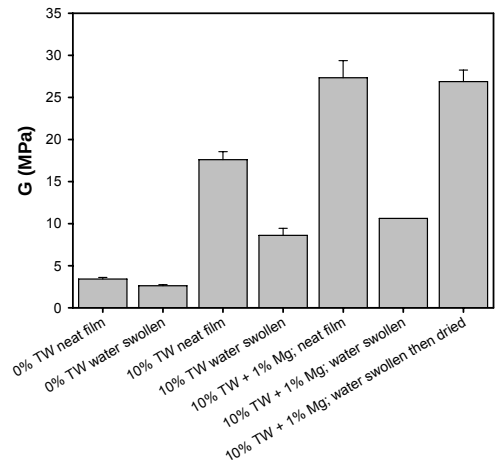


Figure 8. Young's modulus and swelling of 50/50 EO-EPI composites with 0 or 10% tunicate whiskers (TW) and 0 or 1% $MgSO_4$. Percentage above the bars represents % water uptake (w/w) at equilibrium.

While this interaction is both dynamic and reversible, it is important to note that the interactions shown in these preliminary experiments do not maximize the full potential of the nanocomposite system. In the preliminary system, the dynamic reinforcement of whiskers via Mg^{2+} is believed to be mediated by the solvation of the whiskers and Mg^{2+} ions in a water-swollen system. No effort has yet been made to control the pH of the whiskers to maximize ion/whisker interactions. Similarly, *the whiskers used in these initial studies are unmodified beyond hydrolysis during extraction from the tunicate*. They, therefore, have minimal levels of acid groups to further facilitate coordination with the Mg^{2+}. Based on these two proposed modifications alone, we feel that we can achieve at least two-four orders of magnitude higher Young's modulus, which would result in an estimated "stiff" modulus on the order of 100 GPa. Additionally, we anticipate that this general processing scheme - with appropriate modifications - will be universally applicable to all of the proposed target materials.

Recently, we have successfully modified the cellulose fibers to present acid groups along the backbone of the cellulose polymer in controlled densities. We are currently characterizing the degree of modification of the cellulose, and the effects of variable salt concentrations and pH on filler-filler interactions. We expect these optimizations of the whiskers to add several orders of magnitude to the range we have already demonstrated. With this newly characterized system, we will be poised to create a series of stimuli-responsive nanocomposites which should meet the mechanical goals outlined above.

Milestones

By the third quarter of 2006 we expect to be able to fabricate a series of materials with a dynamic range of at least three orders of stiffness. By the end of the year, preliminary *in-vivo* testing will be underway followed by full scale animal trials in 2007.

We anticipate animal testing to be complete by mid 2008, demonstrating proof of the concept.

The resources required to complete this work include a post-doc trainee to develop and explore the chemistry and synthesis of the nanocomposite material, constituent raw materials, testing instrumentation time, a graduate student to characterize the materials, and costs of animal trials. NIH funding mechanisms are currently being sought to provide continuity of these resources.

Future Grant & Publication Plans

An NIH - R21 proposal is currently in review. Upon successful completion of this APT Center pilot study, we will submit and R01 for device development and animal trials using the new material. VA Merit Review funding and clinical trials are anticipated in 5-10 years.

These preliminary results should result in the preparation and submission of three manuscripts:

1. Nature, *Mimicking Sea-cucumber's Skin: Mechanically-Dynamic, Stimulus-Responsive Nanocomposites*

   This paper will outline the synthesis and fabrication, as well as the mechanical testing and characterization of our dynamic nanocomposites.

2. Journal of Biomedical Materials Research**,** *In Vitro Evaluation of the Cytotoxicity of Mechanically Dynamic Cortical Implant Materials*

   This paper will be a summary of the *in vitro assessment of the cytotoxicity* of the novel nanocomposite material, as well as the *in vitro* assessment of the electrode insertion into mimetic brain tissue (gelatin).

3. To be determined**,** *In Vivo Evaluation of the Mechanically Dynamic Cortical Implant Materials*

   This paper will summarize the *in vivo* evaluation of the acute and chronic implant studies with electrodes fabricated from our nanocomposites.

Project # 7: Networked Neuroprosthesis

Principal Investigator: P. Hunter Peckham, Ph.D.

Co-Investigators: K. Kilgore, Ph.D.; R. Triolo, Ph.D. & R. Kirsch, Ph.D.

Staff: Brian Smith, B.S.

Description

Neuroprosthetic devices are powerful tools providing functional enhancement for individuals with central nervous system disorders, such as spinal cord injury and stroke. Life sustaining and improving functions such as breathing, standing/stepping,

reaching/grasping, and bladder/bowel function have been demonstrated, and some systems are commercially available. Existing implanted neuroprosthetic systems utilize considerable external powering and signal processing, and each system is customized to the specific application for which it was intended which severely limits progress in the field and delays introduction of new technology to the end user. Our project addresses this issue through the development of a networked neuroprosthetic system (NNPS). The NNPS is based on a network of small implanted modules, distributed throughout the body, and linked to a centralized power source.

We will realize a first configuration of the NNPS in individuals with spinal cord injury to provide enhanced grasp/release. This human feasibility study will provide the foundation for broader clinical application of the NNPS. We believe the NNPS is a revolutionary contribution to the field of neuroprosthetics since it is easily configured for current and anticipated neuroprosthetic applications, accommodates new innovations by participants in the field, eliminates external components, and can be implemented using minimally invasive surgical techniques.

Objectives

The implant design we propose is based on a network of small implanted modules, distributed throughout the body - the Networked Neuroprosthetic System (NNPS). Primary powering will be provided from an implanted rechargeable battery that will be recharged via a transcutaneous RF link. Each module will contain local processing capabilities in order to minimize the communication rate between modules, and will be programmable through a transcutaneous link. A variety of modules will be developed to the prototype stage, including: muscle-based stimulation, nerve cuff stimulation, biopotential signal sensing, body segment orientation measurement, and body movement command transduction.

Research Plan & Methodology

The system utilizes modules that provide various sensing and stimulation functions, linked together by an intrabody network, enabling reconfiguration for multiple applications or expandability within a particular individual. Each local module contains local processing capabilities in order to minimize the communication rate between them, and can be programmed through a transcutaneous link. The modules are connected to the network through a single four conductor lead that distributes power and provides a data link to each module, thus simplifying clinical implementation by simplifying lead routing through the body. Network communication utilizes the industry standard controller area network (CAN) protocol. The NNPS receives power from a single implanted lithium ion battery that is rechargeable through a central transcutaneous link.

Preliminary Results

To date we have focused our efforts on those critical aspects of the NNPS design concept that required new knowledge and/or techniques. We have evaluated and modeled several network topologies based upon safety, reliability, performance, ease of implementation, and the ability to upgrade. We have selected a network topology

and identified a network communication protocol. We have simulated a physical layer implementation for the internal network that will simplify the segment bus interconnect mechanism. We have modeled component assemblies and have mocked-up critical components for evaluation. Three dimensional models of the packaging for stimulation and sensing modules have been fabricated, along with the "Access Port" which provides power, control and communication functions (Figure 9). System level specifications have been generated and available battery technologies have been thoroughly evaluated. We have selected technologies that are cutting edge yet are attainable within the scope of the project timeframe. We have assembled the necessary industrial, academic and clinical partnerships in order to complete the design and fabrication of the NNPS.

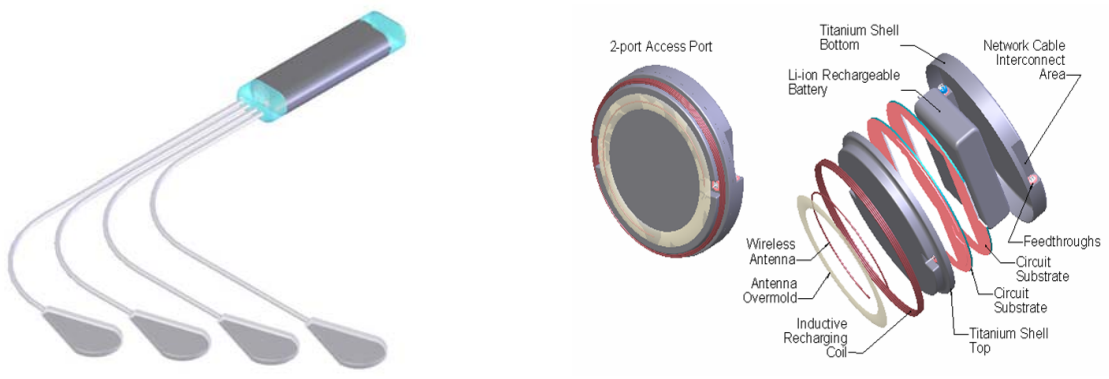


Figure 9. Implanted NNP components: (A) Four channel stimulation module. (B) Power and communications "access port."

Milestones

In the first half of 2006, we will prepare a physical mock-up of a complete system to test the communication protocols. All circuitry for power/communication/control, sensing and stimulation modules will be operational and ready for bench top evaluation. Design of capsules will follow. Later next year we will finalize the circuitry for inductive recharging of the power source incorporated into the "Access Port",as well as the wireless communication circuitry and protocol between the "Access Port" and external programming device. Plans for 2007 include the design of enclosures and cabling, which should lead to animal trials in 2008. IRB submission and initial human human implementation of the NNPS is targeting to begin in 2009.

Future Grant and Publication Plans

Two paper submissions are planned for 2006. One manuscript will describe the configuration and design details of the NNP targeted for a technical journal such as the IEEE Transactions on Neural Engineering and Rehabilitation Engineering. The second paper will review general design principles for implanted neural prostheses. The target journal for this review/tutorial has yet to be determined.

4. Project Milestones

Project Milestones are incorporated into each project progress note above.

C. CAPACITY BUILDING

The APT Center has 41 total staff members, including 10 graduate and post-doctoral trainees. 13 are Senior-level researchers, 4 are Mid-level researchers and 3 are Junior-level researchers. Of our 20 researchers, 8 are in mentoring programs. The support staff totals 11. New staff were added in all categories since this was our first year of operation.

1. Current APT Center Staff

Category	Last Name	First Name	Degree	Position
Senior Investigators	Creasey	Graham	M.D.	Medical Director
	Damaser	Margot	Ph.D.	Investigator
	Garverick	Steven	Ph.D.	Investigator
	Kilgore	Kevin	Ph.D.	Associate Director
	Kirsch	Bob	Ph.D.	Investigator
	Peckham	P. Hunter	Ph.D.	Investigator
	Rimnac	Clare	Ph.D.	Investigator
	Rowan	Stuart	Ph.D.	Investigator
	Ruff	Robert	M.D., Ph.D.	Investigator
	Stahl	John	M.D., Ph.D.	Medical Consultant
	Triolo	Ronald	Ph.D.	Center Director
	Weder	Christoph	Ph.D.	Investigator
	Young	Darrin	Ph.D.	Investigator
Mid-level Investigators	Bogie	Kath	D. Phil.	Investigator
	Ho	Chester	M.D.	Investigator
	Tyler	Dustin	Ph.D.	Associate Director
	Zorman	Christian	Ph.D.	Investigator
Junior Investigators	Capadona	Jeffrey	Ph.D.	Investigator
	Drake	James	A.S.	Investigator
	Mohseni	Pedram	Ph.D.	Investigator
Staff	Burger	James	B.S.	Quality Systems Manager
	Dunning	Jeremy	M.S.	Engineering Staff
	Flannery	Kevin		B.S. Student
	Fletter	Paul	B.S.	Engineering Staff
	Iveljic	Suzana	M.B.A.	Director of Operations
	Sakai	Jonathan	B.S.	Engineering Staff
	Schnellenberger	John	M.S.	Engineering Staff
	Smith	Brian	B.S.	Engineering Staff
	Vibbert	Marie	B.S.	IT Specialist

Category	Last Name	First Name	Degree	Position
	Washington	Merien		Administrative Staff
	Zaszczurynski	Paul	B.S.	Engineering Staff
Trainees	Arguello	Edward	B.S	Ph.D. Student
	Farnsworth	Bradley	B.S.	M.S. Student
	Fetty	Eric		B. S. Student
	Gifford	Tyler	B.S.	M.D./Ph.D. Student
	Harris	James	M.S.	Ph.D. Student
	Hess	Allison	B.S.	M.S./Ph.D. Student
	Howe	Daniel	B.S.	M.S. Student
	Keesara	Varun	B.S.	M.S. Student
	Lachut	Derek		B.S. Student
	Schiefer	Matthew	B.S.	Ph. D. Student

2. ***OOA Pre-Doctoral Fellows***

   N/A

3. ***Career Development Awardees***

   Rowan, Stuart J., NSF Career Award 2002-2007

4. ***Research Career Scientists***

   Name: Damaser, Margot S., Ph.D., Louis Stokes Cleveland VA Medical Center
   Dates: 10/1/2004-9/30/2009
   Award Amount: $306,250

   Name: Triolo, Ronald J., Ph.D., Louis Stokes Cleveland VA Medical Center
   Dates: 10/1/2002-9/30/2007
   Award Amount: $306,250

5. ***Other Research Fellow Programs***

   A. Post-doctoral

   (1) **Capadona**, Jeffrey Ph.D.
   Mentor(s): Dustin J. Tyler, Ph.D.; Christoph Weder, Ph.D.; Stuart J. Rowan, Ph.D.; Ronald J. Triolo, Ph.D.
   Project Title: Stimulus-responsive, mechanically-dynamic nanocomposite for cortical electrodes

   B. Pre-doctoral

   (2) **Arguello**, Edward
   Mentor: Dustin J. Tyler, Ph.D.
   Project Title: Regeneration enabled FINE Electrodes

(3) **Farnsworth**, Bradley
Mentor: Darrin Young, Ph.D.
Project Title: Wireless Implantable EMG Microsystem

(4) **Fetty,** Eric
Mentor: Dustin J. Tyler, Ph.D.
Project Title: Development of Rapid Prototype Processes for Fabrication of Implanted Devices

(5) **Gifford**, Tyler
Mentor: Ronald J. Triolo, Ph.D., Dustin J. Tyler, Ph.D.
Project Title: Biocompatibility of Polynorborene

(6) **Harris**, James
Mentor: Dustin J. Tyler, Ph.D.
Project Title: Stimulus-responsive, mechanically-dynamic nanocomposite for cortical electrodes

(7) **Hess,** Allison
Mentor: Christian A. Zorman, Ph.D.
Project Title: Design, development and fabrication of polymer microstructures

(8) **Howe**, Daniel
Mentor(s): Kath Bogie, D.Phil, Steven Garverick Ph.D
Project Title: Integrated surface electrical stimulation device for therapeutic applications

(9) **Keesara,** Varun
Mentor: Christian A. Zorman, Ph.D.
Project Title: Design, development and fabrication of polymer microstructures

(10) **Lachut,** Derek
Mentor: Dustin J. Tyler, Ph.D.
Project Title: Development of Rapid Prototype Processes for Fabrication of Implanted Devices

(11) **Schiefer,** Matthew
Mentor(s): Dustin J. Tyler, Ph.D., Ronald Triolo, Ph.D.
Project Title: Enhancing Neuroprosthesis Performance with Nerve Cuff Electrodes

6. Advisory Board Members –

As noted in **Section A.3 Future Goals and Objectives**, an *Advisory Council* consisting of representatives from the Department of Veterans Affairs (the ACOS of Research and Chief of Spinal Cord or Rehabilitation Medicine Services), the Chairs of the affiliated academic departments of the Case Schools of Engineering and Medicine, and representatives from the medical device and prosthetics/orthotics industry will be empanelled to assist the senior leadership of the Center with continuing program evaluation. A formal, written report detailing an objective assessment of the performance of the Center in achieving its goals will be generated by the body on an annual basis. We are targeting our first meeting in Q3 2006.

D. INFORMATION DISSEMINATION –

APT Center investigators and staff contributed to 22 peer-reviewed journal articles which appeared or were accepted for publication in 2005. Six (6) additional manuscripts were submitted or were under revision during the same reporting period. The Center also produced 53 presentations, conference abstracts, posters or platform lectures in 2005, and Center investigators participated in the organization and conduct of five (5) national and international workshops and scientific or clinical conferences. These activities complement our own efforts at sponsoring weekly internal seminars and a monthly Neuroprosthesis Seminar Series for external speakers. Our investigators filed **one new invention disclosure** and were issued **one new patent** during the period for APT Center related technologies. Furthermore, APT Center leadership were active in five community outreach organizations and two media releases. All of these activities are summarized below.

1 – Presentations

1. **Bogie KM**, Wang X, Sun J. LASR: A new analytical tool to increase information retrieval from complex images. Proc. *Joint XXth Congress of the International Society of Biomechanics and 29th Annual Meeting of the American Society of Biomechanics*, Cleveland, July 31-Aug 5, 2005.
2. **Bogie KM**, Banks PG, Washington M, Stubblefield AM, Ho CH. Is Volume a True Gold Standard for Wound Size Measurement? *Arch. Phys. Med. Rehabil*., 86(9), e16, 2005.
3. Ho CH, **Bogie KM**, Banks PG, Sakai J, Washington M, Stubblefield AM. Pulsatile Lavage as an Adjunct Hydrotherapy Treatment for Pressure Ulcers: A Randomized Controlled Trial. *Arch. Phys. Med. Rehabil.*, 86(9), e38, 2005.
4. Wang X, Sun J, **Bogie K**. Mining Huge-p-Small-n Data and New Image Registration Procedures, 2005 Proceedings of the American Statistical Association, Biometrics Section, Alexandria, VA: American Statistical Association: *To be published*

5. Petrie TA, **Capadona JR**, and García, AJ. Fibronectin-mimetic Surfaces Directing $\alpha_5 ß_1$ Integrin-Mediated Adhesion, Signaling, and Proliferation. *Society For Biomaterials (SFB). Pittsburgh, PA. 2006.*

6. Petrie TA, Gallant ND, **Capadona JR**, and García AJ. Micropatterned Surfaces Directing alpha5beta1 Integrin-Mediated Adhesion. *Materials Research Society (MRS).* Boston, MA. 2005.

7. **Capadona JR**, Collard DM, and García AJ. Biomimetic surfaces that promote extracellular matrix assembly and up-regulate cell proliferation. *Society For Biomaterials (SFB).* Memphis, TN. 2005.

8. **Ho CH.** A Novel Topical Oxygen Treatment for Chronic Difficult-to-heal Wounds – *American Paraplegia Society 50th Annual Conference*, Las Vegas, NV.

9. Banks PG, Bogie KM, Washington M, Stubblefield AM, **Ho CH.** Fluid Volume Measurements: The Gold Standard? *Wound Healing Society 2005 Annual Meeting & Exhibition*, May 18-21, Chicago, Illinois.

10. **Mohseni P.** and Najafi K, "A battery-powered 8-channel wireless FM IC for biopotential recording applications," in *Dig. Tech. Papers IEEE Int. Solid-State Circuits Conf. (ISSCC'05),* pp. 560-561, San Francisco, CA, February 6-10, 2005.

11. **Mohseni P**. "Single-chip wireless microsystems for multichannel neural biopotential recording," *Cleveland Functional Electrical Stimulation (FES) Center Seminar Series,* Cleveland, OH, October 12, 2005.

12. **Mohseni P**. "Wireless FM microsystems-on-chip for multichannel biological-electronic interfacing," *Dept. of Electrical Engineering, University of Hawaii,* Honolulu, HI, April 7, 2005.

13. **Mohseni P**. "Wireless FM microsystems-on-chip for multichannel biological-electronic interfacing," *Dept. of Electrical Engineering, Columbia University,* New York City, NY, March 30, 2005.

14. **Mohseni P**. "Wireless FM microsystems-on-chip for multichannel biological-electronic interfacing," *NSF-ERC Weekly Seminar Series, Center for Wireless Integrated MicroSystems (WIMS), University of Michigan,* Ann Arbor, MI, March 22, 2005.

15. **Mohseni P**. "Wireless FM microsystems-on-chip for multichannel biological-electronic interfacing," *School of Electrical Engineering and Computer Science, Oregon State University,* Corvallis, OR, March 14, 2005.

16. **Mohseni P**. "Wireless FM microsystems-on-chip for multichannel biological-electronic interfacing," *Dept. of Electrical and Computer Engineering, University of Minnesota,* Minneapolis, MN, March 7, 2005.

17. **Mohseni P**. "Wireless FM microsystems-on-chip for multichannel biological-electronic interfacing," *Dept. of Electrical Engineering, University of Washington*, Seattle, WA, February 24, 2005.

18. **Mohseni P**. "Wireless FM microsystems-on-chip for multichannel biological-electronic interfacing," *Dept. of Electrical Engineering and Computer Science, Case Western Reserve University*, Cleveland, OH, February 15, 2005.

19. **Ruff RL.** *Case Western Reserve University Geriatrics Grand Rounds* – "Research Challenges in the Treatment of Older Veterans with Amputees" Cleveland, OH, February 11, 2005.

20. **Ruff RL.** *Prevention of Amputee Care Team (PACT) National Meeting* – "VA Rehabilitation Research Related to Amputees" Phoenix, AZ, April 26, 2005.

21. **Ruff RL.** *Case Western Reserve University, Department of Neurology Grand Rounds* – "War Related Nervous System Injury Emerging from Operations Enduring Freedom/Iraqi Freedom" Cleveland, OH November 4, 2005.

22. **Triolo, RJ.** Advanced Platform Technology Center, *VA Rehabilitation R&D Center Directors Meeting*, Palo Alto CA, October 24-25, 2005.

23. **Triolo, RJ.** Perspectives on Research Priorities for Neuroprostheses for Standing and Walking after Spinal Cord Injury, *Department of Defense, Integrated Research Team: Neuroprostheses for the Soldier and Society*. Del Mar, California, October 10-12, 2005.

24. Gustafson K, Grinberg Y, Stone M, **Triolo RJ.** Quantification of Human Sciatic Nerve Anatomy: Implications for Neural Prostheses Utilizing Nerve Cuff Electrodes, *2005 Neural Interfaces Workshop*, Bethesda MD, September 2005.

25. To C, Kobetic R, **Triolo RJ,** Kirsch RF. A Hydraulic Approach to the Development of a Variable Reciprocating Hip Mechanism for the Reciprocating Gait Orthosis," *2005 Neural Interfaces Workshop*, Bethesda MD, September 2005.

26. Nataraj R, **Triolo R,** Kirsch R, Audu M, Kobetic R. Artificial Neural Network Prediction of Center of Pressure from Trunk Acceleration Inputs during Perturbed Human Bipedal Stance, *XX Congress of the International Society of Biomechanics*, Cleveland OH, August 2005.

27. Dutta A, Kobetic R, **Triolo R.** EMG Based Triggering and Modulation of Stimulation Patterns for FES Assissted Ambulation – A Conceptual Study, *XX Congress of the International Society of Biomechanics*, Cleveland OH, August 2005.

28. To C, Kobetic R, **Triolo R**, Kirsch R. A Hydraulic Approach to the Development of a Varaible Reciprocating Hip Mechanism for the Reciprocating Gait Orthosis, *XX Congress of the International Society of Biomechanics*, Cleveland OH, August 2005.

29. Schiefer MA, **Triolo RJ,** Durand DM, Tyler DJ. Modeling Selective Stimulation with a FINE for Standing Neuroprosthetics," (2005), *10th Annual Conference of the International Functional Electrical Stimulation Society*, Montreal Canada, July 2005.

30. Schiefer MA, **Triolo RJ,** Durand DM, Tyler DJ. Modeling Selective Stimulation with a Flat Interface Nerve Electrode for Standing Neuroprosthetic Systems," *2nd International IEEE/EMBS Conference on Neural Engineering*, Washington DC, March 2005.

31. Huynh JC, Zobenica NS, Broniatowski M, and **Tyler D.**, Reduction of Aspiration through Stimulation of the Recurrent Laryngeal Nerves: A Chronic Analysis – *Neural Interfaces Workshop*, Besthesda, Maryland, September 2005.
32. Polasek K, Kirsch R, Hoyen H, Keith M, and **Tyler D.** Intraoperative Testing of Selective Nerve Cuff Electrodes for Neuroprostheses, presented at *Research ShowCase*, Cleveland OH, April 2005.
33. Polasek K, Kirsch R, Hoyen H, Keith M, and **Tyler D.** Intraoperative Testing of Selective Nerve Cuff Electrodes for Neuroprostheses, presented at *Neural Engineering Research Lectures*, Cleveland OH, June 3, 2005.
34. Polasek K, Kirsch R, Hoyen H, Keith M, and **Tyler D.** Intraoperative Testing of Selective Nerve Cuff Electrodes for Neuroprostheses, presented at *NIH Neural Prosthetics Workshop*, Bethesda MD. September 2005.
35. Polasek K, Kirsch R, Hoyen H, Keith M, and **Tyler D.** Chronic Human testing of Nerve Cuff Electrodes for an Upper Extremity Neuroprosthesis, presented at *Case Biomedical Engineering Research Day*, October 15, 2005.
36. Polasek K, Kirsch R, Hoyen H, Keith M, and **Tyler D.** Intraoperative Testing of Selectivity of Spiral Nerve Cuff Electrodes, presented at *IEEE Conference on Neural Engineering*, Washington D.C., March 2005.
37. Polasek K, Hoyen H, Keith M, Kirsch R, and **Tyler D.** Intraoperative Testing of Selectivity of Spiral Nerve Cuff Electrodes, presented at *10th Annual Conference of the International FES Society*, Montreal, Canada, July 6-9, 2005.
38. Schiefer MA, Triolo RJ, Durand DM, **Tyler DJ.** Models of Selective Stimulation with a Flat Interface Nerve Electrode for Standing Neuroprosthetic Systems, *ShowCASE* (highlight of research at Case Western Reserve University). 2005.
39. Schiefer MA, Gustafson KJ, Triolo RJ, Durand DM, **Tyler DJ.** Models of Selective Stimulation with a Flat Interface Nerve Electrode for Standing Neuroprosthetic Systems, *28th Annual Biomedical Graduate Student Symposium*. 2005.
40. Schiefer MA, Triolo RJ, Durand DM, **Tyler DJ.** (2005) Modeling Selective Stimulation with a FINE for Standing Neuroprosthetics, *Neural Engineering and Rehabilitation Day*, Cleveland, OH. 2005.
41. Schiefer MA, Triolo RJ, Durand DM, **Tyler DJ.** Modeling Selective Stimulation with a FINE for Standing Neuroprosthetics, *BMES Annual Conference*. 2005.
42. Schiefer MA, Gustafson KJ, Triolo RJ, Durand DM, **Tyler DJ.**Modeling Selective Stimulation with a FINE for Standing Neuroprosthetics, *BME Research ShowCASE*. 2005.
43. Broniatowski M, MD, FACS, Grundfest-Broniatowski S, MD, FACS, Tucker HM, MD, FACS, **Tyler DJ.** PhD, The Case For Electronic Manipulation Of The Larynx In Voice Disorders, London UK *Royal Academy of Music*, London, Sept. 2005.

44. Chaimanonart N, Suster M, and **Young DJ.** Two-Channel Data Telemetry with Remote RF Powering for High-Performance Wireless MEMS Strain Sensing Applications, the technical proceeding of the *IEEE Sensors Conference,* Irvine, CA, October 2005.

45. Lu CK, Qu H, Xie HK, **Young DJ.** CMOS MEMS Accelerometer for Long-Term In Vivo Real-Time Small Animal Biological Monitoring, the technical proceeding of the *IEEE Sensors Conference,* Irvine, CA, October 2005.

46. **Young DJ.** and Ko WH, Wireless Strain Sensing Microsystem, *technical proceeding of the 5th Emerging Information Technology Conference (EITC 2005),* Taipei, Taiwan, R.O.C, August 2005.

47. Cong P, Olszens K, **Young DJ,** and Ko WH, Implantable Blood Pressure Monitoring of Small Animal for Advanced Biological Research, *the 13th International Conference on Solid-State Sensors, Actuators and Microsystems*, Seoul, Korea, June 2006, pp. 2002-2005.

48. Suster M, Chaimanonart N, Guo J, Ko WH, and **Young DJ,.** Remote-Powered High-Performance Strain Sensing Microsystem, *the 18th International Conference On Micro Electro Mechanical Systems*, Miami Beach, Florida, January 2005, pp. 255-258.

49. **Young DJ.** Wireless Strain Sensing Microsystem Technology, presented at *Southeast University,* Nanjing, China, 9-6-2005.

50. **Young DJ.** Microsystem Technology for Totally Implantable Cochlear Prosthesis, presented at *National Cheng Kung University,* Tainan, Taiwan, R.O.C., 8-18-2005.

51. **Young DJ.** Wireless Strain Sensing Microsystem, presented as a plenary session talk at the 5th Emerging Information Technology Conference, *National Taiwan University*, Taipei, Taiwan, R.O.C., 8-18-2005.

52. **Young DJ.** Microsystem Technology for Totally Implantable Cochlear Prosthesis, presented at Neural Prosthesis Seminar at *Case Western Reserve University*, Cleveland, Ohio, 7-15-2005.

53. **Young DJ.** Strain Sensing Microsystem with Remote RF Powering and Data Telemetry, presented at ECE Department Seminar, *Carnegie Mellon University*, Pittsburgh, Pennsylvania, 3-18-2005.

2 - Publications Published or Accepted for Publication

1. **Bogie KM,** Ho CH, Terris DD. *Clinical evidence for new pressure ulcer treatment modalities.* Long-Term Care Interface, 43-47, June 2005.

2. **Bogie KM**, Bader DL. *Susceptibility of spinal cord injured individuals to pressure ulcers.* Pressure Ulcer Research, Eds: Bader D, Bouten C, Colin D, Oomens C. Springer-Verlag, 73-88, 2005.

3. **Bogie KM,** Wang X, Triolo RJ. *Long term prevention of pressure ulcers in high risk individuals: a case study of the use of gluteal neuromuscular electrical stimulation.* Arch Phys Med Rehabil, accepted for publication.

4. **Capadona, JR,** Petrie, TA, Fears, KP, Latour, RA, Collard, DM, and García, AJ, *Surface-Nucleated Assembly of Fibrillar Extracelluar Matrices*. Adv. Mater. 2005; 17; 2604-2608.

5. Bhadra N, **Kilgore KL**. *High-frequency electrical conduction block of mammalian peripheral motor nerve.* Muscle Nerve. 2005 Dec;32(6):782-90.

6. Bryden AM, **Kilgore KL**, Kirsch RF, Memberg WD, Peckham PH, Keith MW. *An implanted neuroprosthesis for high tetraplegia*, Top Spinal Cord Inj Rehabil, 10(3):38-52, 2005.

7. Wenzel BJ, Boggs JW, Gustafson KJ, **Creasey GH**, Grill WM. *Detection of neurogenic detrusor contractions from the activity of the external anal sphincter in cat and human.* Neurourol Urodyn. 2005 Oct 14; [Epub ahead of print] PMID: 16224800 [PubMed - as supplied by publisher].

8. Bhadra N, Grunewald V, **Creasey GH**, Mortimer JT. *Selective activation of the sacral anterior roots for induction of bladder voiding*. Neurourol Urodyn. 2005 Oct 14; [Epub ahead of print] PMID: 16224799 [PubMed - as supplied by publisher].

9. **Mohseni P**, Najafi K, Eliades SJ, and Wang X, *Wireless multichannel biopotential recording using an integrated FM telemetry circuit,* IEEE Trans. Neural. Syst. Rehab. Eng., vol. 13, no. 3, pp. 263-271, September 2005.

10. **Mohseni P** and Najafi K, *A 1.48-mW low-phase-noise analog frequency modulator for wireless biotelemetry*, IEEE Trans. Biomed. Eng., vol. 52, no. 5, pp. 938-943, May 2005.

11. Sivakova S, Bohnsack DA, Mackay ME, Suwanmala P, **Rowan SJ**. *Utilization of a Combination of Weak Hydrogen-Bonding Interactions and Phase Segregation to Yield Highly Thermosensitive Supramolecular Polymers.*J Am Chem Soc. 2005 Dec 28;127(51):18202-18211. PMID: 16366573 [PubMed - as supplied by publisher].

12. Sivakova S, Wu J, Campo CJ, Mather PT, **Rowan SJ.** *Liquid-Crystalline Supramolecular Polymers Formed through Complementary Nucleobase-Pair Interactions.* Chemistry. 2006 Jan;12(2):446-456. PMID: 16240319 [PubMed - as supplied by publisher].

13. **Rowan SJ.** *Metallomesogens.* Angew Chem Int Ed Engl. 2005 Aug 5;44(31):4830-2. No abstract available. PMID: 16052667 [PubMed - in process].

14. **Rowan SJ,** Beck JB. *Metal-ligand induced supramolecular polymerization: a route to responsive materials.* Faraday Discuss. 2005;128:43-53. PMID: 15658766 [PubMed].

15. Iyer PK, Beck JB, Weder C, **Rowan SJ.** *Synthesis and optical properties of metallo-supramolecular polymers.* Chem Commun (Camb). 2005 Jan 21;(3):319-21. Epub 2004 Dec 10. PMID: 15645023 [PubMed - in process].

16. J Knutson, M Audu, **R Triolo**. *Interventions for mobility and manipulation after spinal cord injury: a review of orthotic and neuroprosthetic options,* Topics in Spinal Cord Rehabilitation – (Accepted for publication, November 2005).

17. K. Amankwah, **R.J. Triolo**, R. Kirsch, M. Audu. *A Model Based Study of Passive Joint Properties on Muscle Effort During Stance*, Journal of Biomechanics – (Accepted for publication, August 2005).

18. CS To, RF Kirsch, R Kobetic, **RJ Triolo**. *The Feasibility of a Functional Neuromuscular Stimulation Powered Mechanical Gait Orthosis with Coordinated Joint Locking*, IEEE Transactions on Neural Systems and Rehabilitation Engineering 13(2):227-235, 2005.

19. Butter JY, Crenshaw BR, **Weder C**, Hecht B. *Single-Molecule Spectroscopy of Uniaxially Oriented Terrylene in Polyethylene.* Chemphyschem. 2005 Dec 19; [Epub ahead of print] PMID: 16363013 [PubMed - as supplied by publisher].

20. **Weder C.** *Synthesis, processing and properties of conjugated polymer networks.* Chem Commun (Camb). 2005 Nov 21;(43):5378-89. Epub 2005 Oct 12. PMID: 16261222 [PubMed - in process].

21. Steinhart M, Zimmermann S, Goring P, Schaper AK, Gosele U, **Weder C**, Wendorff JH. *Liquid crystalline nanowires in porous alumina: geometric confinement versus influence of pore walls.* Nano Lett. 2005 Mar;5(3):429-34. Erratum in: Nano Lett. 2005 May;5(5):995. PMID: 15755089 [PubMed - indexed for MEDLINE].

3 - Publications Under Review or in Revision

1. **Bogie KM,** Wang X, Fei B, Sun J*. Getting more out of pressure mapping: a new technique for interface pressure analysis* submitted to IEEE Trans Biomed Eng, Nov 2005.

2. Bhadra N, Gustafson KJ, Bhadra N, **Kilgore KL**. *High Frequency Alternating Current Block of the Feline Pudendal Nerve*, in revision, J Neural Engineering.

3. Gustafson K, Neville J, Syed I, Davis JA, **Triolo RJ**. *Fascicular Anatomy of the Human Femoral Nerve: Implications for Neural Prostheses Utilizing Nerve Cuff Electrodes*, Clinical Anatomy - (submitted, September 2005).

4. Suster M, Guo J, Chaimanonart N, Ko WH, and **Young DJ**, *A High-Performance MEMS Capacitive Strain Sensing System*, submitted to IEEE Journal of Microelectromechanical Systems.

5. Chaimanonart N, Suster MA, Ko WH, and **Young DJ**, *Two-Channel Data Telemetry with Remote RF Powering for High-Performance Wireless MEMS Strain Sensing Applications*, submitted to IEEE Sensors Journal.

6. Zurcher MA, **Young DJ**, Trang T, Megerian CA, Ko Wh, *Ossicular Chain Vibration Coupled to MicroElectroMechanical Accelerometer for a Totally Implantable Cochlear Prosthetic Microsystem*, submitted to IEEE Journal of Biomedical Engineering.

4 - Sponsored Conferences and Workshops

1. **Damaser, MS. – Panel Moderator,** *New Techniques for Monitoring and Diagnosing Voiding Function.* This panel includes 1 talk on *Novel methods of Bladder Volume Measurement.*
2. **Triolo RJ. - Organizing Committee,** *XXth Congress of the International Society of Biomechanics (ISB) & 20th American Society of Biomechanics (ASB)* , Cleveland OH - August 2005.
3. **Triolo RJ. - Chair,** Functional Electrical Stimulation platform session*, XXth Congress of the International Society of Biomechanics,* Cleveland OH – August 2005.
4. **Triolo RJ. - Organizing Committee,** *7th Symposium on Footwear Biomechanics (Technical Interest Group of the International Society of Biomechanics)*, Cleveland OH, August 2005.
5. **Young DJ. - Technical Program Committee,** *2nd International Workshop on Networked Sensing Systems*, San Diego, California, USA, 2005.

Neural Prosthesis Seminar Series

The APT Center jointly hosts the Neural Prosthesis Seminar Series with the Cleveland FES Center. Lectures are held once to twice a month during the fall and spring, and the program is a public educational forum on topics related to rehabilitation. Speakers are active in the national/international community of rehabilitation research and development of assistive technologies. Speakers invited to Cleveland to participate are provided with an excellent opportunity to experience our research environment, which often results in research collaborations. Funding for the Neural Prosthesis Seminar Series is provided by the Buckeye Chapter, Paralyzed Veterans of America and the Department of Veterans Affairs. We also co-organize a weekly seminar series for internal communication. Seminars conducted during the reporting period are listed below.

Date	Speaker	Affiliation	Topic
July 15, 2005	Darrin Young, Ph.D.	APT Center, Case Western Reserve University	Microsystem technology for totally implantable cochlear prosthesis
October 12, 2005	Pedram Mohseni, Ph.D.	APT Center, Case Western Reserve University	Sensing technology and wireless telemetry of cortical recordings
November 16, 2005	Brad Boggs, M.S.E.E.	Goodrich Company	Micro-electro-mechanical (MEMS) pressure sensors for medical applications
December 16, 2005	Joseph Rizzo, M.D.	Boston VA RR&D Center of Excellence for Innovative Visual Rehabilitation	Retinal prosthesis project

5 - Transferred (Commercialized/Patented Technology)

- **Invention Disclosures Filed**
  - **Zorman, Christian A. -** Integrated Surface Stimulation Device, 11/15/05.
- **Patents Filed**
  - **Damaser, Margot S. -** US Patent application submitted May 2005: *Intravesicular Bladder Volume Measuring Device.*

6 - Community Activities

1. **Press Release** - January, 2005. APT Center awarded.
2. **VA Research Currents** - March, 2005. APT Center awarded.
3. **Ruff, RL -** Medical Advisory Boards of the National MS Society and Myasthenia Gravis Foundation of America.
4. **Ruff, RL -** Board of Directors and Medical Board Director for the Ohio Chapter of the MGFA.
5. **Triolo, RJ** – Board Member, **RePlay *for Kids.***

   RePlay for *Kids* is a 501(c)(3) tax-exempt non-profit organization of volunteers who repair and adapt toys and assistive devices for children with disabilities in Northeast Ohio. **RePlay *for Kids*** provides these services at no cost for non-profit organizations that provide medical, educational, or recreational resources for children with disabilities in the

Northeast Ohio area. Most of these organizations have limited resources and often cannot afford to replace devices that have broken, and do not have the technical knowledge or time available to repair the devices. **RePlay *for Kids*** can provide these services, therefore increasing the number of functioning toys and assistive devices available for children with disabilities.

6. **Tyler, DJ** – School BME Visitor Committee.
7. **Tyler, DJ** – Chair BME Subcommittee for Case High School Scholarship Committee.

7 - Other information Dissemination Activities

Information Dissemination			
Element	**Target**	**Purpose**	**Progress**
Annual report	Lay and consumer groups	Public relations and general education purposes	The VA annual report is completed and will be reformatted and revised for general educational purposes.
Quarterly Progress Reports	Technical professionals and Center stakeholders	Update all Center Investigators and affiliates on program progress	Quarterly Investigator Meeting minutes have been serving this purpose and additional progress reports would be duplicative.
Center Website	Consumer & clinical or technical professionals	Information clearinghouse for all Center related activities	The Center Website is about 75% complete and is expected to go live Q1, 2006.
Private list-serves and bulletin boards	Center Investigators and staff	Internal communication for ongoing project level management	We have established four list-serves. • The entire center • The investigators • The staff • The students
Professional society meetings	Rehabilitation & technical professionals	Transfer knowledge regarding Center discoveries, methods or products and solicit professional input and external advice	We are scheduled to present at Case Western Reserve University's Research Showcase on April 5th and 6th, with further plans to exhibit and present at other scientific meetings.
Special Issue of *JRRD*	Rehabilitation professionals, consumers	Contribute to scientific foundation of rehabilitation science and engineering.	Discussion with the editor regarding the potential for a special issue occurred.

E. RESEARCH COLLABORATIONS

1. Summary of Clinical Interface –

The APT Center is fundamentally a technology center that designs, develops, and produces enabling technologies that are clinically relevant. We consciously strive to share our technology within and outside of the VA system. Examples of Clinical Interfaces include:

- Veteran population affected – The new and emerging technologies we are developing may potentially be used to positively affect a significant proportion of the veteran population. Veterans with sensory deficits or motor impairment as a result of spinal cord injury (SCI), stroke, traumatic brain injury or other central nervous system damage or disease would benefit from clinical application of our technology. Veterans with limb loss would benefit from better mechanical and cybernetic interfacing of advanced prostheses. Veterans with impairment of special senses such as hearing and vision may benefit from further standardization of technology platforms.

- Active clinical participation in our leadership team – Graham Creasey, M.D., serves as our Medical Director and is a member of the leadership team which sets the direction and operational goals for the Center. Chester Ho, M.D.; Robert Ruff, M.D.; and John Stahl, M.D.; are clinical advisors to the center.
- Multi-disciplinary research teams – Most of our research teams are lead by both a clinician and engineer. In addition to these team members, all teams have technical staff assigned.
- Work environment – Several of our laboratories are located immediately adjacent to clinical areas, allowing immediate contact between clinicians and engineers for discussion of issues such as needs definition, development and testing of prototypes, and definitive solution dissemination.
- Clinical Needs Assessment – The clinical needs assessment actively involves clinicians and consumers in identifying and prioritizing needs which then shape our research focus. These workshops also include leaders in the field of biotechnology which allow for a broader market perspective of the clinical applications.
- Investigator Meetings - To facilitate ongoing interactions between clinicians and affiliated APT Center scientists, we have established a quarterly Investigators Meeting that brings faculty and physicians together to discuss potential new projects and progress on existing projects. Part of each meeting is dedicated to a tutorial given by a clinician on a topic of particular relevance to the disabled veteran. Areas covered have included clinical issues related to organ, cavity or tissue pressure, prosthetics and orthotics, and telemedicine.
- Sponsored Conferences – We are in the process of organizing special sessions at clinical conferences (American Paraplegia Society, etc.) to identify barriers to deployment of existing technologies and acceptance by the medical community.
- LSCDVAMC – A center research staff member is a participant each week in the spinal cord injury rounds, and regular presentations are made to the clinical staff.

- Neural Prosthesis Seminar Series – This seminar series discussed in **D4: Sponsored Conferences and Workshops,** has both technical and clinical speakers with an opportunity for networking immediately following the event.
- Technical Evaluation Team – An internal team consisting of investigators, senior engineers, and clinicians that triages potential solutions. The team allows for ongoing open discussion between those who are familiar with clinical needs and those who are familiar with capabilities of the technology.

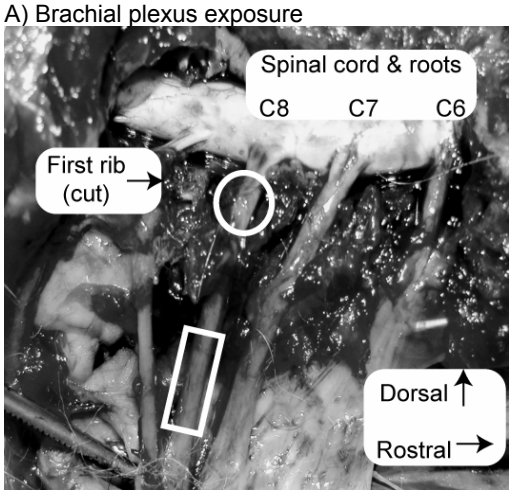
2. Active Collaborations

We have engaged in 2 active collaborations during the reporting period and are in the process of pursuing other collaborative projects that will advance our mission and that of the Rehabilitation RR&D Service. We continue to collaborate with the Cleveland FES Center on several projects which have been described elsewhere, such as the Networked Neural Prosthesis. In this report we focus on new and developing collaborations, rather than the ongoing pre-existing projects already mentioned.

- **New Collaborations**
  - **NDI Medical (Cleveland OH):** As previously mentioned in section **A2: Stated Goals and Objectives Achieved**, we are actively collaborating with NDI Medical to develop the clinical programming platform for a new 8-channel multi-purpose implantable pulse generator (IPG). The clinical interface will allow the rapid specification and modification of stimulation patterns to be delivered by the IPG so that its operation can be efficiently customized for the unique needs of each implant recipient by a clinician. The programmer is being designed to our specifications by NDI and will reside on a handheld computer (i.e., Palm) and communicate wirelessly to the IPG. This clinical interface represents a critical component of a new system that will form a technical platform for clinical trials of neuroprostheses for hand grasp, standing, stepping and other motor or sensory dysfunctions resulting from traumatic brain or spinal cord injury, stroke or multiple sclerosis.

- **University of Pittsburgh (D. Weber, Ph.D.):** The purpose of this collaboration is to study the afferent activity associated with limb movement and attempt to reconstruct the motion generating in order to derive control signals for prostheses and better understand the sensory system for interventions dealing with pain or sensory loss. The APT Center is developing the basic infrastructure and technical resources required to record sensory neuronal activity from primary afferent neurons during acute experiments with anesthetized cats that will be performed at the University of Pittsburgh. While microelectrodes record single unit activity from neurons in the dorsal root ganglion (DRG). Compound electroneurogram (ENG) signals will be recorded from a multicontact spinal nerve cuff electrode designed and produced by the APT Center located approximately 2 cm distal to the DRG (see Figure 11A). Spike-triggered averaging will then isolate single-unit activity in the nerve cuff ENG. The APT Center spiral nerve cuffs (see Figure 11B) have 5 pairs of contacts equally spaced along their length with the central (3rd) and outermost electrodes (1st and 5th) connected together to serve as the common reference for differential recording from the active (2nd and 4th) contacts. The advantage of this design is that the distance (D) between the active electrodes can be precisely measured or specified during fabrication, which allows nerve conduction velocity (CV) to be calculated based on the time delays (Δt) between the occurrences of negative peaks in the action potentials recorded on the active contacts. The CV measurements for each DRG afferent will be used to determine the afferent's receptor classification (e.g. group I, group II). Electrodes of this type are not available commercially and represent platform technologies that the APT Center can customize for specific research and clinical applications.

A) Brachial plexus exposure



B) Conduction velocity measurement from ENG

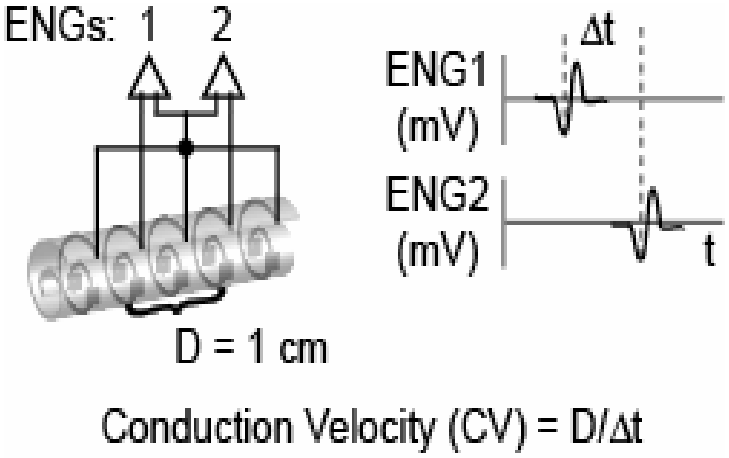


Figure 10: (A) Surgical exposure of cat cervical spinal cord and roots (C6-C8) and brachial plexus showing placement of DRG probe (circle) and nerve cuff (box). (B) Measurement of nerve conduction velocity from a pair of ENG recordings obtained from a 5-pole nerve cuff.

- **Collaborative Projects Under Development**
    - **VA HSR&D Center for Practice Management & Outcomes Research (Ann Arbor, MI):** The primary objective of this collaboration would be to evaluate the efficacy of providing telemedicine consultations to referring providers of care spinal cord injury (SCI) patients. Establishing such a collaborative relationship between the VA RR&D Advanced Platform Technology Center in Cleveland and the HSR&D Center in Ann Arbor would promote the design and conduct of other studies for evaluating rehabilitation technologies in clinical settings.
    - **VA RR&D Center for Innovative Visual Rehabilitation (Boston, MA):** The primary objectives of this collaboration would be to explore new drug eluting coatings for implantable devices that reduce inflammation and promote integration with the tissue. Devices that need to interact directly the nervous system, such as the retinal prosthesis being developed in Boston Center and other neural interfacing technologies being explored by the APT Center, would be targeted initially but would lead to more generalizable materials and techniques. The specific aims of this collaboration would include: 1) synthesizing photopolymerizable hydrogels capable of eluting added compounds such as steroids and nerve growth factors when added to implanted electrode arrays; 2) demonstrating a reduction in local tissue reactions (e.g. gliosis and high-resistance fibrotic encapsulation) to the presence of microfabricated electrode arrays coated with steroid-laden gels vs. uncoated controls using histology studies in the central and peripheral nervous systems; 3) demonstrating enhanced growth of neurites toward microfabricated electrode array surfaces coated with gels that elute neurotrophic factors (e.g. BDNF, CNTF) versus uncoated controls, again via histology studies in the central and peripheral nervous systems; and 4) studying the histologic response of tissue to the presence of coated electrodes containing gels bearing both neurotrophic and anti-inflammatory factors to determine if the effects resulting from their presence compete or superpose.
    - **Defense Advanced Research Projects Agency (DARPA), Telemedicine & Advanced Technology Research Center (TATRC), Ardiem Medical Inc. (Indiana, PA) and Walter Reed Army Medical Center:** The APT Center has been exploring the potential for a collaborative project with the Department of Defense (DARPA, TATRC), medical device manufacturers (Ardiem) and the United States Army's Amputee Center at Walter Reed Army Medical Center to research and develop advanced prosthetic systems that incorporate state-of-the-art command and control interfaces and direct sensory feedback for traumatic limb loss. The APT Center would facilitate the integration of existing implantable technologies with a wireless interface that would allow more natural control of the movements of myoelectric prosthetic limbs, as well as provide sensory information to the nervous system via the high density electrode arrays that we are developing out of new polymer materials with MEMS-based fabrication techniques. This collaborative project would focus on evaluation and

training, natural control of myoelectric limbs, and sensory feedback and would involve continued interactions with the Cleveland FES Center.

- **Center of Excellence in Limb Loss Prevention and Prosthetic Engineering (Seattle, WA):** We are exploring the potential for collaborating with the Seattle Center to further the development and eventual clinical application of our implantable micro-miniature EMG telemeter. In particular, the goal of a collaborative effort would be to develop a myoelectrically controlled torsional pylon for a trans-tibial amputees that allows safe and effective turning. The specific aims of this collaborative study would be to 1) determine whether residual limb EMG signals can be used to distinguish straight from turning gait, 2) finalize the design of the micro-miniature implantable EMG transceiver system and validate it for human use, 3) develop a pylon with adaptable torsional characteristics, and 4) specify a torsional control system using both environmental (limb accelerations and turning velocities) and biological (EMG data from the residual limb) signals. The Centers' personnel represent an ideal mix of engineering and medical expertise as rehabilitation physicians, orthopaedic surgeons, prosthetic and orthotic specialists, and bioengineers working together on cross-disciplinary research.
- **Vanderbilt University (Nashville, TN):** The central hypothesis of this proposal is that synchronization of stimulation of the posterior cricoarytenoid muscle for vocal fold abduction with the respiratory cycles will improve the performance of neuroprostheses for treating chronic vocal fold medialization. The hypothesis of the sub-contract is that a flat interface nerve electrode (FINE) electrode on can record the ENG activity of the phrenic nerve and adequately predict respiration. This will be the primary control source for the full system that is the subject of the studies in the parent proposal.