Vision Research Portfolio

Clinical and Rehabilitative Medicine Research Program
Congressionally Directed Medical Research Programs
Telemedicine and Advanced Technology Research Center
Department of Defense and Department of Veterans Affairs
Vision Center of Excellence
The mission of the U.S. Army Medical Research and Materiel Command (USAMRMC) is to provide medical knowledge and materiel lifecycle management to protect, treat, and optimize health and performance of military personnel across the full spectrum of operations. As part of its mission, the USAMRMC manages research focused on eye- and vision-related issues, principally through the offices of the Clinical and Rehabilitative Medicine Research Program, Congressionally Directed Medical Research Programs, and Telemedicine and Advanced Technology Research Center. There exists a great medical need for research in vision restoration and rehabilitation. Multiple studies have demonstrated that eye injury has affected a large number of wounded warfighters accounting for nearly 13% of all injuries (Joint Theater Trauma Registry database, January 2002 to June 2008). Much of the eye and vision research managed through these programs addresses the needs of the warfighter, other armed forces personnel, and the veteran population.

**CRMRP MISSION**
To focus on definitive and rehabilitative care innovations required to reset our wounded warriors, both in terms of duty performance and quality of life.

Janet Harris, R.N., Ph.D.
Colonel, U.S. Army
Director, CRMRP

**CDMRP MISSION**
To provide hope by promoting innovative research, recognizing untapped opportunities, creating partnerships, and guarding the public trust.

E. Melissa Kaime, M.D.
Captain, U.S. Navy
Director, CDMRP

**Clinical and Rehabilitative Medicine Research Program (CRMRP)**
The CRMRP concentrates on accelerating restorative and rehabilitative research, including eye- and vision-related projects, needed to reset wounded warriors, both in terms of duty performance and quality of life. The goal of the CRMRP is to plan, coordinate, and monitor the science and technology program focused on definitive and rehabilitative care to bring the best medical solutions and latest medical technologies to our wounded warriors. A Scientific Steering Committee (SSC) was developed to help the CRMRP establish program direction, priorities, and funding strategies for vision-related research. In addition, the CRMRP provides policy and process oversight for all clinical and rehabilitative medicine congressional programs managed by the CDMRP and TATRC.

**Congressionally Directed Medical Research Programs (CDMRP)**
The CDMRP manages congressionally directed peer-reviewed programs that solicit proposals through open competitions in an effort to find and fund the best research to eradicate diseases and support the warfighter for
the benefit of the American public. The CDMRP manages a total of 18 vision-focused research projects within its portfolio, for a total of approximately $28 million (M). These projects were funded through three separate congressionally directed programs, the Peer Reviewed Medical, the Psychological Health/Traumatic Brain Injury, and the Deployment Related Medical Research Programs.

Telemedicine and Advanced Technology Research Center (TATRC)

The TATRC manages congressionally mandated advanced technology projects including the identification, exploration, and demonstration of key technologies that will reduce the medical “footprint” and increase medical mobility while ensuring that warfighters have access to essential medical expertise and support wherever they deploy. Currently, the TATRC manages a total of 10 vision-focused awards within its portfolio, totaling approximately $43M. In fiscal year 2009 (FY09), the TATRC solicited research application submissions to the Peer Reviewed Vision Research Program (PRVRP) using congressionally directed appropriation for eye and vision research along with additional funds contributed by the CRMRP and the Combat Casualty Care Research Program. The PRVRP has identified 5 critical eye- and vision-related research areas and estimates that 10 grants will be awarded.

Department of Defense and Department of Veterans Affairs Vision Center of Excellence (DOD/VA VCE)

The DOD/VA VCE was established as a coordinated DOD and VA effort in response to the increase in vision injuries and diseases sustained by the men and women of members of the armed services to ensure the full spectrum of eye- and vision-related care is fully supported. Working with TRICARE, Military Health System, and other Centers of Excellence, the VCE will lead efforts to enhance collaboration between military and veteran eye care providers, provide guidance for clinical practice guidelines, and maximize patient-centered support close to home, unit, and family.
Eye Injury Statistics

- Operations Desert Shield and Desert Storm: 14% of warriors with battle injuries had ocular injury and/or disease.
  

- Operations Iraqi Freedom and Enduring Freedom, August 2004 to October 2006: 21% of casualties with traumatic brain injury (TBI) had concomitant ocular trauma.
  

- Operation Enduring Freedom and Operation Iraqi Freedom, October 2005 to March 2008: 76% of patients with polytrauma and 75% of the patients with TBI self-reported visual symptoms.
  
  Optometry (2009) 80(8):419-24

- Operation Iraqi Freedom, December 2005 to April 2006: Concomitant cranial and ocular injuries were frequently seen in combat casualties. 32.7% of patients with cranial trauma had ocular trauma and 21.5% of patients with ocular trauma had cranial trauma.
  

- Operations Iraqi and Enduring Freedom, March 2003 to September 2006: 17% of casualties reported wearing ocular protection sustained an ocular injury and 26% of casualties who reported not wearing eye protection suffered an eye injury.
  

- Combat troops exposed to blast with a resulting mild TBI are at risk for visual dysfunction, and combat troops with polytrauma injuries are at risk for visual dysfunction and/or visual impairment. In the population with moderate to severe levels of TBI, 13% had an acuity loss of 20/100 to no light perception and 32.3% had visual field defects. In the population with mild TBI, 1.6% had an acuity loss of 20/100 to no light perception and 3.2% experienced visual field defects.
  

Prioritized Gaps

The CRMRP SSC identified the following needs in priority order:

1. Improve treatments for traumatic and war-related injuries and diseases to ocular structures and the vision system

2. Strategies for diagnosis, treatment, and mitigation of visual dysfunction associated with TBI and war-related injuries

3. Advanced technologies to restore vision

4. Epidemiological studies to understand mechanisms of injury and evaluate functional outcomes of strategies used to treat ocular and visual system injury

5. Improved ocular diagnostic capabilities, including imaging, electrodiagnostics, and biomarkers

6. Enhanced vision rehabilitation strategies
Research Investment

Combined, the CDMRP and TATRC are currently managing 28 eye and vision research projects spanning the range of scientific endeavors from basic to translational to clinical research, totaling about $71M in congressional appropriations. Additional research proposals that have been recommended for funding for FY09.
Eye injuries, especially corneal damage, are the result of trauma, infection, and chemical or thermal (including laser-induced) burns. Battlefield injuries to the eye mostly occur on the cornea and retina through trauma to the head- and laser-related exposures. These injuries are usually treatable but can lead to blindness because of collateral damage to tissues surrounding the injured area. The resulting state of significantly reduced visual function occurs from injury-induced inflammation, cell death, failure to regenerate or repair, and development of scar tissue. Developing effective treatments that would preserve vision will benefit not only United States military and support personnel at risk on the battlefield, but also the American public. Investigators funded by the CDMRP and TATRC are developing new preventive methods and novel therapeutic interventions to preserve vision.
Autonomic Biomarkers Military Vision Research Program
Darlene A. Dartt, Ph.D.
Schepens Eye Research Institute
FY00, 01, 04, 05, 06, 07, 08, and 09 $12.12M (TATRC)

The focus of this project is to develop new ways to preserve the vision of soldiers injured on the battlefield and to advance the frontier of vision technologies. To keep abreast of the needs of the military, the institute holds 2-day symposia biannually in which practicing military eye specialists discuss with the institute’s scientists the challenges that they encounter in caring for men and women in uniform. The institute’s scientists then design research programs in response to military needs. The outcome of this research that spans from laser damage to the retina and optic nerve regeneration to corneal bandages and enhanced displays is clinically targeted products with enormous potential for both military and civilian applications.

Molecular Solutions to Low Vision Resulting from Battlefield Injuries
Darlene A. Dartt, Ph.D.
Schepens Eye Research Institute
FY03 Investigator-Initiated Award $2.99M (CDMRP)

The intent of this study is to investigate the effect of battlefield trauma on corneal, retinal, and optic nerve function and on dry eye after refractive surgery with the goal of developing a molecular solution to prevent or reverse damage. The hypothesis is that targeted molecular interventions can preserve vision threatened by trauma-induced corneal and retinal inflammation, cornea and retina/optic nerve apoptosis, ocular surface dry eye after refractive surgery, and retinal degeneration.
Treatment of Laser-Induced Retinal Injury and Visual Loss Using Sustained Release of Intra-Vitreal Neurotrophic Growth Factors

Randy H. Kardon, M.D., Ph.D.
University of Iowa and Veterans Affairs
FY06 Investigator-Initiated Research Award $0.58M (CDMRP)

This study will test the treatment effect of sustained-release intra-vitreal neurotrophic growth factor(s) on the preservation and recovery of visual function and structure in a canine model of laser-induced retinal injury. The successful outcome will allow the development of an injectable treatment of laser-induced retinal damage to humans, even under battlefield conditions.

Intraceptor Interference of VEGF Pathways in Corneal Angiogenesis

Balamurali Ambati, M.D.
Medical College of Georgia
FY06 Investigator-Initiated Research Award $0.72M (CDMRP)

This proposal hypothesizes that intracellular autocrine loops are part of VEGF (vascular endothelial growth factor) signaling in the cornea. The goal of the project is to disrupt intracellular VEGF and VEGFR-2 expression, which may represent an important modality in treating disorders involving angiogenesis, in vascular endothelial cells in vitro and in the injured cornea in vivo. By exploring a novel avenue of anti-angiogenic therapy, this project will hopefully add to the therapeutic arsenal for corneal injury and transplant rejection, macular degeneration, and diabetic retinopathy.
**Improved Therapeutic Regimens for Treatment of Post-Traumatic Ocular Infections**

Michelle Callegan, Ph.D.
University of Oklahoma Health Sciences Center
FY06 Investigator-Initiated Research Award $0.90M (CDMRP)

The objective of this research is to identify effective therapeutic regimens that will prevent vision loss and inflammation during a *Bacillus* endophthalmitis infection. A number of therapeutic agents, drug combinations, and regimens will be tested to identify the most effective in preserving vision, arresting inflammation, and limiting intraocular damage.

**Molecular Blockade of Lymphangiogenesis in Promoting High-Risk Corneal Transplant Survival**

Lu Chen, M.D., Ph.D.
University of California, Berkeley
FY06 Investigator-Initiated Research Award $1.17M (CDMRP)

Normal cornea is transparent and absent of lymphatic vessels. However, lymphangiogenesis (LG; the development of new lymphatic vessels) is induced in the cornea after traumatic or inflammatory damages. LG is also a primary mediator of high-risk transplant rejection, of which there is little effective treatment to date. This research project investigates the effect of molecular blockade of LG on high-risk transplant survival after corneal injuries as a necessary step to the development of new therapeutic strategies.
Repair of Corneal Injury with Stem Cell-Based Bioengineered Tissue
De-Quan Li, M.D., Ph.D.
Baylor College of Medicine
FY06 Investigator-Initiated Research Award $0.90M (CDMRP)

The long-term objective of this research project is to bioengineer stem cell-based corneal constructs using human limbal epithelial progenitor cells (LEPCs). The goal is to use these LEPC-derived corneal constructs for therapeutic repair of corneal injury.

Identification of ABCG2 as a potential marker for corneal epithelial stem cells.

Optical Quality, Threshold Target Identification, and Military Target Task Performance After Advanced Keratorefractive Surgery
COL Kraig S. Bower, M.D.
Walter Reed Army Medical Center
FY08 Clinical Trial Award $1.42M (CDMRP)

The Warfighter Refractive Eye Surgery Program has been instituted to provide refractive surgery to deploying soldiers with a goal of eliminating the need for contacts and/or eyeglasses in battlefield conditions. This randomized, prospective study will determine the effect of two types of wavefront modalities (wavefront-guided and wavefront-optimized) performed with two types of laser refractive surgery (photorefractive keratectomy and laser-assisted in situ keratomileusis) on visual and military task performance. The safety and efficacy as well as measurement of objective image quality will be evaluated for the different techniques.
Treating Vascular Eye Diseases
Dean Y. Li, M.D., Ph.D.
University of Utah
FY08 Advanced Technology/Therapeutic Development Award
$2.99M (CDMRP)

The main objective of this study is to develop a therapeutic approach that activates the novel endothelial receptor Robo4 signaling pathway for the treatment of vascular eye diseases such as age-related macular degeneration, diabetic macular edema, and diabetic proliferative retinopathy. This goal will be achieved by developing a biologic Robo4 agonist that is (a) effective in validated preclinical systems; (b) compatible with design and manufacturing processes required for pilot Good Manufacturing Practice-compliant production; and (c) capable of advancing to appropriate adsorption, distribution, metabolism, excretion, and toxicity profiles required for an Investigational New Drug application to initiate clinical trials. Additionally, this study will identify the downstream pathways and determine whether we can activate this pathway with small molecules.

Ocular Safety of Topical Naltrexone
Joseph W. Sassani, M.D., M.H.A.
Pennsylvania State University, Milton S. Hershey Medical Center
FY08 Clinical Trial Award $0.07M (CDMRP)

Previous research by this team in animal models of corneal epithelial defects has demonstrated that the opioid antagonist, naltrexone (NTX), expedites corneal epithelial wound healing without toxic effects. The goal of this Phase I clinical trial is to demonstrate the safety of the topical NTX dosage most likely to be used in the clinical setting. The successful outcome of this research will lead to a significant improvement in the treatment of corneal injuries in warfighters and their family members who suffer ocular trauma or in individuals with delayed corneal wound healing, such as diabetics.
Sealing Penetrating Eye Injuries Using Photoactivated Bonding and Corneal Protection for Burn Patients

Irene E. Kochevar, Ph.D.
Massachusetts General Hospital
COL Anthony Johnson, M.D.
Brooke Army Medical Center
FY08 Advanced Technology/Therapeutic Development and Translational Research Awards $2.42M (CDMRP)

This team of scientists and physicians is working collaboratively in the field of eye injury clinical research. The objective of the first research study is to decrease vision loss caused by penetrating wounds by employing a rapid, sutureless method to securely seal corneal, scleral, and eyelid skin injuries, photochemical tissue bonding (PTB). This study will identify laser parameters for effective sealing, evaluate healing after PTB treatment, minimize potential side effects, and increase knowledge of the bonding process, which may lead to further improvements.

The second study is focusing on preserving vision of patients recovering from severe facial burns by studying an improved method in the application of amniotic membrane to reduce development of corneal defects, inflammation, infection, and opacification in an animal model. The specific aims are to (1) Modify amnion to make it less susceptible to degradation while preserving its anti-inflammatory and healing properties, (2) Determine whether a photo-activated method for bonding amnion to the cornea provides a rational alternative to suturing, and (3) Combine amnion with a water-retaining layer of material to provide hydration to the corneal surface.

Determine advantages and disadvantages of attaching amniotic membrane to the ocular surface using photosensitized crosslinking. The amnion will be bonded to the sclera conjunctiva (A) or to the limbus (B) in a circumferential manner.
Both nonpenetrating and penetrating ocular injuries are highly prevalent and a major medical concern in the military and battlefield environment. The goals of the Eye PATCH research are to design and develop a bioengineered ocular bandage and adhesives for primary management of ocular trauma on the battlefield by a non-expert provider, as well as to develop a stronger membrane to guide ocular reconstruction following complex injury. It is expected that new membranes and adhesives with controlled mechanical and optical properties, and drug delivery capability will be synthesized and tested.

The goal of this study is to develop solutions for corneal wound repair. (1) A contact lens containing therapeutic agents to sterilize the wound, prevent infection, and aid in recovery can be applied to the cornea. The properties of the contact lens will act to physically hold the cornea together, as well as preclude the blink reflex from further exacerbating the wound until surgery can be performed. The lens will contain a drug delivery system that can administer therapeutic agents for up to 3 days. (2) Bioadhesive glue containing therapeutic agents to stabilize the cornea will be used by the military for “in the field” treatment of patients with disrupted or missing corneal tissue. This glue would hold the cornea together until the patient can reach a hospital. (3) Identification of proteins and measurement of their level of secretion by the eye during corneal trauma would lead to new therapeutic treatments for corneal injuries that occur in the field.
Retinal diseases specifically affect the retina, a layer of tissue at the back of the eye that is responsible for vision. These diseases also can affect the macula (area of central vision) or the fovea at the center of the macula. Many retinal diseases share common symptoms and treatments, but each has unique characteristics. In the industrialized world, retinal disease is the major cause of blindness, and currently there is no cure or treatment available for these patients. An estimated 1 million adults in the United States (which includes 160,000 veterans) are blind, approximately 2.3 million have low vision, a total of almost 3.3 million have impaired vision. (National Eye Institute, National Institutes of Health). Over the last 15 years, active military personnel have suffered from substantially increased risk of blindness, mostly from ocular blast injuries and laser-induced retinal injury. Investigators funded through the CDMRP and TATRC are using a variety of approaches to treat blindness. Some examples include the development of a microelectronic, implantable device designed to interface directly with the retina, microelectrodes that electrically stimulate the visual cortex in the brain, and a biocompatible, electrochemical implantable muscle stimulation system that would restore motion to paralyzed muscle in a painless and more natural manner.
**Sight Restoration by Electrical Stimulation of Visual Cortex via Arrays of Penetrating Microelectrodes**

Richard Norman, Ph.D. and Brad Greger, Ph.D.

University of Utah Moran Eye Center

FY05–FY07 $0.50M (TATRC)

This study is demonstrating proof of concept whereby the Utah Microelectrode Array will be used to potentially restore limited but useful vision in nonhuman primates. A systematic experimental approach is being employed to define the design parameters needed to implement a functional visual neural prosthesis, using behavioral responses to indicate what they perceive in response to patterned electrical stimulation of the cortex. Investigators will then determine the design parameters for a functional visual neural prosthesis and study its safety and efficacy.

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**Replicating Physiological Patterns of Activity with Prosthetic Stimulation**

Shelley Fried, Ph.D.

Boston VA Research Institute, Inc.

FY06 Investigator-Initiated Research Award $0.75M (CDMRP)

The hypothesis for this study is that specific morphological features and biophysical properties of the ganglion cell shape its response to electric stimulation. The goal is to develop methods to create specific patterns of activity in retinal ganglion cells with a prosthetic device that will replicate the patterns created by the normal retina in response to light.

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The sodium-channel band is coextensive with the region of low threshold. A: Threshold map of a DS (directionally selective) ganglion cell. The map includes threshold measurements over the soma/proximal axon region (right) as well as along more distal sections of the axon (columns in the middle and the left). The circle indicates the position of the soma. The lowest thresholds (blue) are offset from the soma. B: Overlay of the threshold map with the GFP (dye)-filled ganglion cell. Xs indicate the position of lowest threshold in each column and were aligned to the corresponding portion of the distal axon in the dye-filled cell. The region of lowest threshold corresponds to a location along the proximal axon. C: A higher-magnification view of the soma/proximal axon region from B (indicated by the rectangular box in B). The approximate center of the low-threshold region is spatially correlated with a dense band of sodium channels, localized to the proximal axon via immunochemical staining for PAN sodium antibody. This suggests that the band is the site of maximum sensitivity in response to electric stimulation and raises the possibility that the band is the site that “responds” to the electric stimulus. Scale bar in A, B, and C: 50 μm.
A Hybrid Electrochemical Microstimulator Implant for Denervated Muscles

Kimberly Cockerham, M.D.
VA Health Care System, Palo Alto
FY06 Advanced Technology: Product/Technology Down-Selection or Optimization Award $1.21M (CDMRP)

The long-range objective of this project is to develop a hybrid implantable microstimulator system that will act as a stimulus for denervated muscles, by mimicking the natural stimulation that occurs at neuromuscular junctions.

Synchronized test environment controls all equipment precisely and helps reduce the error introduced from human intervention.
Optimization of Microelectronic Methods to Produce an Implantable Retinal Prosthesis to Treat Blindness

Joseph Rizzo, M.D.
Massachusetts Eye and Ear Infirmary, Harvard Medical School
FY06 Advanced Technology: Product/Technology Down-Selection or Optimization Award $1.24M (CDMRP)

This project focuses on developing a retinal prosthesis that may be used to treat several forms of retinal blindness that are currently untreatable, including blindness caused by battlefield laser injury to the retina, and military-related, blast-induced blindness. The implantable prosthetic will be a microelectronic device designed to interface directly with the retina. This device will: (1) Capture visual images, (2) Communicate the images to electronic components that interface with the retina, and (3) Selectively deliver electrical pulses to the retina to create vision. It intends to permit "customizable" adjustments to accommodate the unique visual needs of each patient and improve their quality of life.

Engineered Eyelid Muscle Replacement: Orbicularis Oculi

Cathryn Sundback, Sc.D.
Massachusetts General Hospital
FY08 Hypothesis Development Award $0.25M (CDMRP)

A severely damaged human eyelid muscle (orbicularis oculi) prevents eyelid closure, resulting in dry, painful, irritated eyes and potential blindness. This research will focus on engineering a functional model of a human eyelid muscle using innovative methods to address the complexities of muscle architecture and contractile function while enfolding vascularization and innervation. Fiber-based scaffolds to support myoid formation will be fabricated, tested for biocompatibility, and validated in muscle tissue maturation and contractility studies. If successful, this research will lead to translational large animal and human trials.

Graphic images of the designs of the Boston Retinal Implant Project. Left: Glasses support a small camera (red arrow) that collects visual images. Middle: A wire (white arrow) extends along the length of the sidebar to an external processing unit (not shown). Also embedded are two "primary" radiofrequency (RF) coils (yellow arrow). Right: The "secondary" RF coils (yellow arrow) are positioned just behind the circumference of the cornea. The titanium case (white arrow) provides a hermetic environment for the integrated circuit chip. The electrode array enters the eye through a small slit (red arrow) in the sclera.

Engineered skeletal muscle Engineered skeletal muscle encapsulated in biodegradable mesh scaffold
Telemedicine, a rapidly developing application of clinical medicine, has the ability to provide interactive multidisciplinary health care, utilizing modern technology and telecommunications. As diagnosis and treatment of many ophthalmologic diseases are not widely available in rural communities, telemedicine technologies can help deliver these important services. Additionally, mobile technologies would enable wireless and/or remote monitoring of a person’s health and/or environment, from the battlefield to the hospital to the home. By reducing barriers to eye care, telemedicine facilitates both early detection and appropriate and timely referral for treatment. Investigators funded through the TATRC are developing telemedicine systems to aid the distance diagnosis of complicated ocular diseases.
Tele-ophthalmology: Enhancing Care and Education for Military Medicine

Robert Sergott, M.D.
Wills Eye Institute
FY05–FY09 $8.089M (TATRC)

The focus of this researcher is to establish a cost-effective platform that will rapidly diagnose patients with common, costly diseases such as diabetes mellitus and other complicated ophthalmologic problems. Patients attending participating medical and endocrinology clinics will be screened with non-mydriatic, 45 degree fundus photography. The same technology will be used for the online education resource and the ophthalmology imaging academy distance learning programs.

The “Wills without Walls” solution promotes continuing medical education during wartime by providing secure, worldwide access to focus multimedia material in all ophthalmic subspecialties.
Comprehensive Visual Field Test and Diagnosis System for Acute and Routine Assessment of Vision, Visual Acuity, and Contrast Sensitivity in Military Environments

Wolfgang Fink, Ph.D.
California Institute of Technology
FY08 Advanced Technology/Therapeutic Development Award $0.38M (CDMRP)

The goal of this study is to develop and implement an innovative, noninvasive, Internet-based (or Intranet-based for field deployment) test and diagnosis system for the assessment, identification, characterization, and automated classification of visual field defects caused by operations in military environments. This system also will have database capacity for storing the testing data, which would enable patient follow-up over time.

Three-dimensional depiction of the central visual field obtained with the 3D Computer-automated Threshold Amsler Grid test (CTAG). The x-axis and y-axis denote the horizontal and vertical tested visual field dimension in degrees from central fixation, respectively. The z-axis displays the measured contrast sensitivity across the tested visual field area. Depicted is the visual field typical of a case of macular degeneration.
Anthro-Centric Multisensory Interface for Vision Augmentation/Substitution (ACMI-VAS)

Anil K. Raj, M.D.
Florida Institute for Human and Machine Cognition
FY09 $0.20M (TATRC)

This study will use the Brain Port® array held against the tongue to indicate high-resolution visual information from in front of the user (i.e., foveal vision). A wider field of view will be presented on the abdomen by the Video Tact™ to provide contextual and registration information relative to the tongue “foveal” information. The Torso Tactile Interface will display a low resolution 360 degree representation of the visual environment to enable the user to detect motion and other changes in the visual environment (i.e., peripheral vision) using an array of infrared range sensors worn on the head. Proper use of the ACMI-VAS system will require an orientation session during which the participant is taught how to use the displays. The participants will be able to move their heads to kinematically control the dynamic system (i.e., pan and tilt) to learn to accurately interpret this novel feedback stimuli.

Dr. Raj tests the BrainPort tongue vision system.
Centers of Excellence (COEs) are generally established to bring together multidisciplinary research teams to promote research leading to improved diagnostics and therapies resulting in improved quality of life for affected individuals. The vision portfolio managed by the TATRC includes awards for centers focused on accelerating the solution of major overarching questions that will have a significant impact on the prevention, detection, diagnosis, and/or treatment of eye- and vision-related issues.
National Eye Evaluation Research (NEER) Network for Clinical Trials in Retinal Degenerative Diseases

Stephen Rose, Ph.D.
National Neurovision Research Institute
FY06–FY09 $10.43M (TATRC)

Retinal degenerative diseases are a family of inherited pathologies with the ultimate consequence of photoreceptor apoptosis and severe visual impairment, frequently resulting in blindness. The focus of this study is to establish a network of five clinical treatment and evaluation centers to study retinal degenerative diseases. The network advances the science of therapeutic and preventive interventions for inherited orphan retinal degenerative diseases and dry age-related macular degeneration through conducting clinical trials.

Center for Ophthalmic Innovation (ONOVA)

Byron Lam, M.D.
Bascom Palmer Eye Institute
FY08–FY09 $3.80M (TATRC)

The focus of this effort is to establish a COE with four focus areas: (1) Telemedicine, (2) Ophthalmic Biophysics (for example, artificial cornea, implants to treat traumatic injury, novel methods of drug delivery, and laser effects on eye tissue), (3) Molecular Ophthalmology (biomarkers, molecular diagnostics and therapeutic targets, cellular therapies and tissue engineering, gene therapy, and genomics), (4) Inherited Eye Disease.
Proficiency in ophthalmic surgical skills remains vitally important because training surgeons outside of the operating room may reduce errors inside the operating room. Traditionally, residents have obtained and fine tuned their surgical skills and techniques working on the eyes of animals. Ophthalmic surgical simulators enable the surgeon to practice intraocular surgical techniques with the use of instruments that feel and function much like their real world counterparts. Training can include basic surgical techniques and enables trainee surgeons to become familiar with handling rare cases and possible complications. Using a surgical simulator, a trainee can repeatedly experience live tissue reactions that occur during surgery. The virtual ocular environment realistically depicts the anatomical structure and three dimensionality of the intraocular space, as well as the physical behavior of delicate tissues. Investigators funded through TATRC are developing ophthalmic surgical simulators that would enhance patient safety and improve patient care.
Virtual Mentor Cataract Surgery Trainer
John Loewenstein, M.D.
Massachusetts Eye and Ear Infirmary
FY07 $0.20M (TATRC)

The focus of this study is to develop a content-based curriculum to teach cataract surgery through virtual means. Computer-based and interactive, the proposed curriculum would pose common conceptual problems to the resident, thereby challenging critical thinking abilities in a variety of stressful, yet not uncommon surgical situations. The Virtual Mentor would include a library of video links that both demonstrate expert techniques as well as discuss in depth various details of each simulated scenario.

Ocular Trauma Microsurgery Simulator
Joseph Sassani, M.D.
Pennsylvania State University Hershey Medical Center
FY09 $0.214M (TATRC)

This project is developing a prototype microsurgical simulator that will have the following characteristics: portable, easily constructed and repaired utilizing “off-the-shelf” hardware components; flexible in terms of hardware and software so as to be able to simulate a variety of ocular and nonocular microsurgical procedures; cost effective; and a software architecture sufficiently open to encourage the writing of programs by multiple parties. The team will develop a hardware and software platform capable of simulating surgical procedures such as the microsurgical repair of traumatic wounds of the ocular cornea and sclera. Moreover, this platform will be easily adapted to simulate other types of microsurgery such as vascular and neural repairs. Future research will include the development of a commercially viable finished product of the hardware and the expansion of the library of simulation programs and the range of input devices.
Sensitive and accurate methods to evaluate and follow damage to retina, optic nerve, and visual centers of the brain are needed. Investigators funded through the CDMRP and TATRC are developing and improving technologies to diagnose and evaluate eye damage. Additionally, the CDMRP is managing awards that use eye function as a diagnosis for traumatic brain injury (TBI). These studies will hopefully develop a device that can diagnose attention and memory problems caused by concussion. An accurate and rapid measure of attention is essential in military operations to prevent injury and re-injury, to detect TBI, and to distinguish TBI from post-traumatic stress disorder (PTSD) and fatigue. Studies will also characterize and define the temporal window of brain vulnerability to repeated blast overpressure.
Brain Vulnerability to Repeated Blast Overpressure and Polytrauma

Joseph B. Long, Ph.D.
Walter Reed Army Institute of Research
FY07 Intramural TBI Investigator-Initiated Research Award $1.02M (CDMRP)

Using a preclinical rat model of blast overpressure, this study will evaluate and compare the cumulative effects of single and multiple air blast exposures on acute physiological responses, visual acuity, and neurobehavioral and histopathological outcome measures. Repeated exposures to blast overpressure of differing intensities with varied interblast intervals will also be used to identify a temporal window of brain vulnerability to repeated blast overpressure. Data from this study will provide a critical first step in establishing a rational risk guideline.

Vision Integrating Strategies in Ophthalmology and Neurochemistry (VISION)

Thomas Yorio, Ph.D.
University of North Texas Health Science Center
FY09 $2.80M (TATRC)

This study plans to (1) develop and characterize mouse models of (a) optic nerve crush, (b) retinal ischemia/reperfusion, and (c) chronic pressure elevation and generate defined and quantifiable end points for examining damage to the retina, optic nerve, and visual centers of the brain; (2) use microarray technology to identify pathways involved in damage to the retina, optic nerve, and visual centers of the brain in all three mouse models of traumatic ocular injury; and (3) initiate neuroprotection studies in the optic nerve crush and retinal ischemia/reperfusion models.

Phase I of the study is quantifying the damage to the retina, optic nerve, and brain vision centers by developing mouse models of (a) optic nerve crush, (b) retinal ischemia/reperfusion, and (c) chronic pressure elevation.

Eye-Tracking Rapid Attention Computation

Jamshid Ghajar, M.D., Ph.D.
Brain Trauma Foundation, Inc.
FY07 TBI Advanced Technology-Therapeutic Development Award $4.64M (CDMRP)

This project is designed to develop an eye-tracking device that will quickly diagnose subtle attention deficits that occur in TBI. The proposed device may also be able to help diagnose and distinguish between TBI, PTSD, simple fatigue, and aging.

New Developments for Injury Evaluation
Clinical and Rehabilitative Medicine Research Program
For more information, visit https://crmrp.amedd.army.mil/ or contact at crmrp@amedd.army.mil or 301-619-8932

Congressionally Directed Medical Research Programs
For more information, visit http://cdmrp.army.mil or contact at CDMRP.PublicAffairs@amedd.army.mil or 301-619-7071

Telemedicine and Advanced Technology Research Center
For more information, visit http://www.tatrc.org or contact at marketingdirector@tatrc.org or 301-619-7927

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