CDMRP

Department of Defense

Defense Health Program

Peer Reviewed Orthopaedic Research Program

Provide all Warriors affected by orthopaedic injuries sustained in the defense of our Constitution the opportunity for optimal recovery and restoration of function.

U.S. Army Medical Research and Materiel Command

CDMRP VISION

Transform health care for Service members and the American public through innovative and impactful research

MISSION

Responsibly manage collaborative research that discovers, develops, and delivers health care solutions for Service members, Veterans, and the American public

Congressionally Directed Medical Research Programs

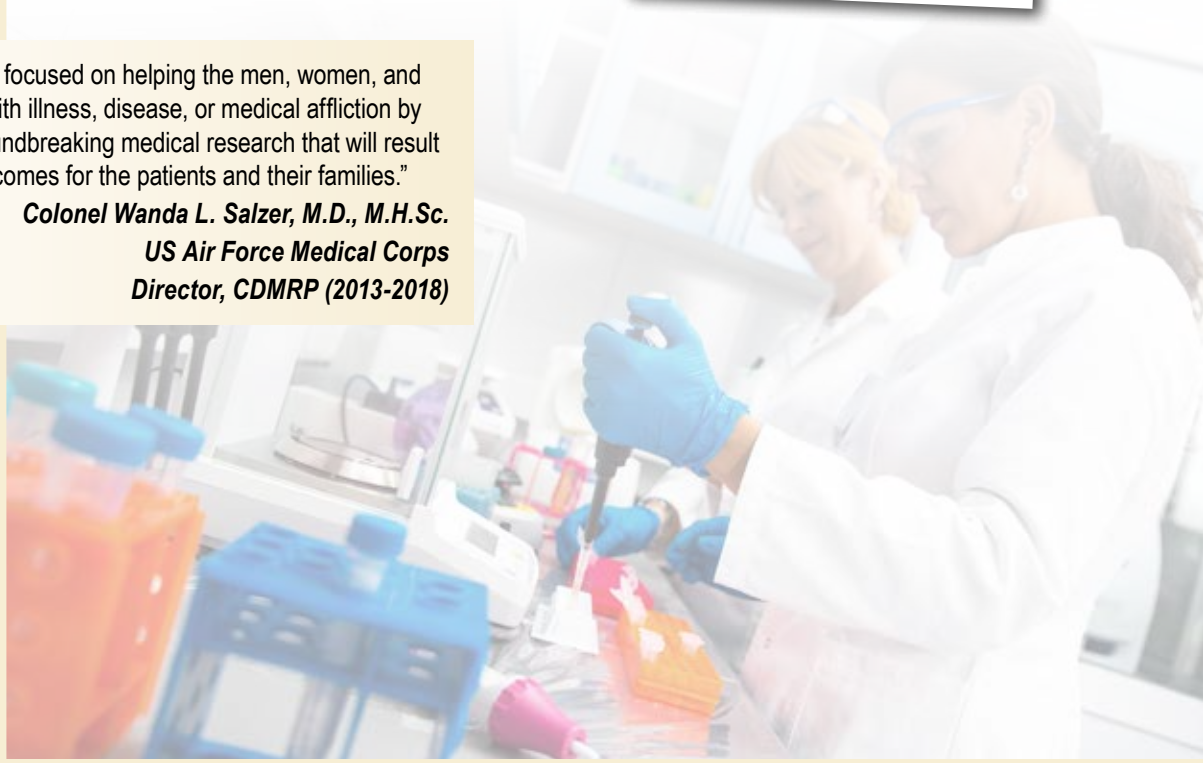
History of the CDMRP

The Congressionally Directed Medical Research Programs (CDMRP) was organized in fiscal year 1992 (FY92) from a powerful grassroots effort to secure a Congressional appropriation of funds for breast cancer research. This initiated a unique partnership among the public, Congress, and the military. The CDMRP has grown to encompass multiple targeted research programs and has received more than $11.9 billion in appropriations since its inception. Funds for the CDMRP are added by Congress to the Department of Defense (DoD) budget annually, with support for individual research programs allocated via specific guidance from Congress. The CDMRP executes programs such as the Peer Reviewed Orthopaedic Research Program (PRORP) on behalf of the DoD Defense Health Agency J9, Research and Development Directorate, which provides health support across the full range of military operations.

The CDMRP uses a two-tier review process for application evaluation, with both tiers employing dynamic interaction among scientists and disease survivors. The first tier of evaluation is a scientific peer review of applications measured against established criteria determining scientific merit. The second tier is a programmatic review conducted by a Programmatic Panel composed of leading scientists, clinicians, and consumer advocates that makes recommendations for funding based on scientific merit, adherence to the intent of the award mechanism, portfolio composition, and relevance to overall program goals.

"The CDMRP is focused on helping the men, women, and children living with illness, disease, or medical affliction by investing in groundbreaking medical research that will result in improved outcomes for the patients and their families."

Colonel Wanda L. Salzer, M.D., M.H.Sc.
US Air Force Medical Corps
Director, CDMRP (2013-2018)



Peer Reviewed Orthopaedic Research Program (PRORP)

VISION: Provide all Warriors affected by orthopaedic injuries sustained in the defense of our Constitution the opportunity for optimal recovery and restoration of function

MISSION: Address the most significant gaps in care for the leading burden of injury for facilitating return-to-duty by funding innovative, high-impact, clinically relevant research to advance optimal treatment and rehabilitation from musculoskeletal injuries sustained during combat and combat-related activities

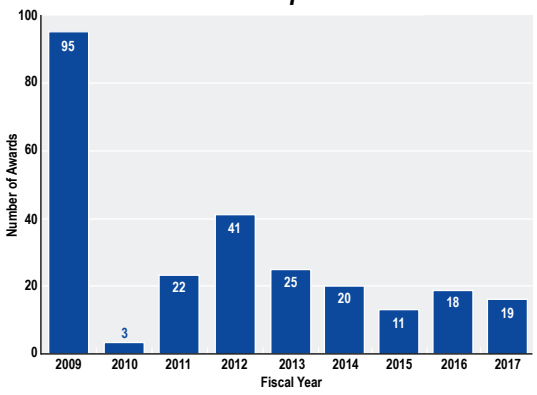
History of the PRORP

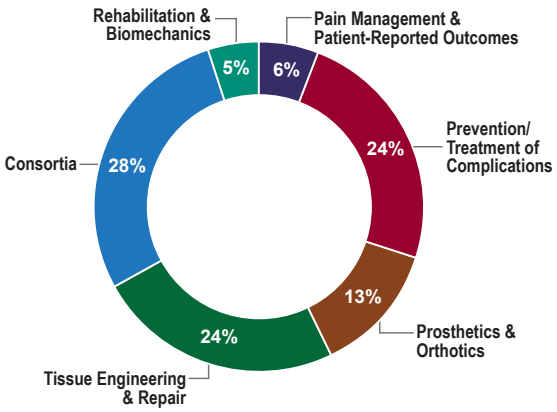
Over half of all combat injuries sustained during Operation Iraqi Freedom and Operation Enduring Freedom involve extremity injuries and orthopaedic-specific conditions secondary to battle injury, representing the largest source of long-term disability in returning Service members.[1] Since its inception in FY09, the PRORP has dedicated its Congressional appropriations, totaling $368.5 million (M), to supporting military-relevant orthopaedic research that also benefits the treatment and care of the general population (see figure at right). Many Service members involved in once-fatal incidents have been saved and/or resuscitated with the help of advances in care and materiel products derived from modern research, resulting in an increase in survivability. This increase in survivability has also resulted in an increased number of Service members and Veterans living with extremity injuries. Orthopaedic injuries sustained during combat-related activities tend to be distinct from those seen in the civilian setting, since they more frequently involve multiple limb trauma, open fractures, major tissue loss, and a high degree of wound contamination. In addition, these injuries are frequently sustained in harsh environments where access to optimal acute care can be limited.

Keeping in line with guidance from Congress regarding the scope of research funded by the PRORP, 254 awards have been supported by the program, focusing on topics such as prevention, treatment, rehabilitation, and prosthetics/orthotics, including three large consortia efforts (see figure at right). The clinical consortia efforts are designed to bring military patients, leading researchers, and military treatment facility (MTF) clinicians together with the infrastructure, patients, and expertise of highly qualified civilian organizations to form partnerships that will ultimately provide new solutions along the continuum of care for wounded Service members with orthopaedic injuries.

Fiscal Year	PRORP Congressional Appropriation
2009	$112,000,000
2010	$22,500,000
2011	$24,000,000
2012	$30,000,000
2013	$30,000,000
2014	$30,000,000
2015	$30,000,000
2016	$30,000,000
2017	$30,000,000
2018	$30,000,000
Total	**$368,500,000**

PRORP Awards per Fiscal Year





Overall Program Investment by Research Area for the PRORP, FY09–FY16

[1] Cross JD, Ficke JR, Hsu JR, et al. 2011. Battlefield Orthopaedic Injuries Cause the Majority of Long-Term Disabilities. *J Am Acad Orthop Surg;* 19:S1-S7.

Consumer Advocacy

A unique aspect of the CDMRP is the active participation of consumers throughout the program's annual cycle. Consumers work collaboratively with leading scientists and clinicians in setting the PRORP's program priorities, reviewing applications, and making funding recommendations. From the unique perspective gained through personal experience, a consumer, who is often a Service member who suffered a traumatic orthopaedic injury obtained on the battlefield, brings a sense of urgency and focus to all levels of decision-making. Consumers evaluate applications based on the potential impact and benefit to the patient population, encouraging funding recommendations that reflect the concerns and needs of the orthopaedic injury population, their families and caregivers, and the clinicians who treat them.

"There is appreciation for having a consumer reviewer at the table. The scientists and clinicians on the panel hear my point of view and they believe it. I am able to advocate for individuals with orthopaedic injuries at the user level."

—Edwin Salau
PRORP Consumer Peer Reviewer

Matt Anderson, PRORP Programmatic Panel Member

I've had a long, rocky road with my injury, starting after a landmine blast in Kandahar Province, Afghanistan, on October 16, 2010. I was the first landmine injury that did not result in some version of traumatic amputation on site. The five fasciotomies were a little different than the standard and included two in the tibialis anterior and soleus muscles, as well as three in my foot: one on the instep and two on the top of my foot. The instep required a skin graft from my thigh, and the adhesions are still painfully sticking around.

With the advent of the Intrepid Dynamic Exoskeletal Orthosis (IDEO) only months before, the doctors and physical therapists were confident that I'd be able to run again with the new ankle-foot orthotic (AFO). I can run for short distances, but anything longer than a few hundred yards is going to hurt a lot. However, I am able to put up 1,000 pounds on the leg press at the gym.

Some of the new issues I faced with the AFO were fitting into shoes and pants due to the IDEO that wrapped around my toes, heel, and ankle and up to the bottom of my knee. I did sustain pretty extensive peripheral nerve damage. I don't need pain medication for daily activities, but a hard workout is going to hurt. The lack of pain allows me to do a lot, but it also can lead to more injuries. During a 5k run in Colorado Springs, I noticed that I wasn't getting as much spring return from the IDEO, but kept running. The IDEO had broken on both sides of my ankle, and I had reshattered my calcaneous down to chicklets. That's another setback and another Taylor spatial frame.

Being a part of the PRORP panel gave me a lot of hope for continued improvement. The DoD PRORP addresses novel and cutting edge approaches to blast and battlefield trauma injuries to give our nation's Warriors the best recovery possible, allowing them to return to duty or, with more extensive injuries, to have a productive and active lifestyle. I have really enjoyed my time with the PRORP. It allows me to stay involved with cutting edge research that will positively affect future wounded Warfighters, as well as have an impact on civilian trauma and orthopaedic practices. The research funded through the PRORP positively affects both military and civilian orthopaedic treatment.

I currently serve on the board of directors for the Salute Military Golf Association. I also advocate for Tee It Up For the Troops, the Military Warriors Support Foundation, Patriot Point, and the Yellow Ribbon Fund.

Rickey Williams, PRORP Consumer Peer Reviewer

I served as a United States Army Fire Chief. My medical odyssey began in January 2009, when I was helping pressure-wash some military vehicles. While coming off the back of a vehicle, I accidentally grazed my left thigh, leaving not much more than a surface scratch. I did not think much about it and continued working. The next day, I started to feel a bit bad, but assumed that I was just really tired and needed to rest. Forty-eight more hours went by. Then it became clear to me that I was not tired; I was sick. I was sent to Brooke Army Medical Center in San Antonio, where it was discovered that the scratch on my thigh from 3 days ago was inflamed, and the inflammation was growing and killing all of the surrounding tissue as it expanded. It was determined that I had necrotizing fasciitis, commonly known as flesh-eating bacterial infection. After a lot of drugs, debridements, and a skin graft, I was sent home to continue healing; however, I never fully healed and began to suffer other medical abnormalities, such as blood clots. This went on for about 18 months before the blood clots fully took over and choked off blood flow to my limbs, which required amputation of both legs below the knee and my left arm above the elbow.

I learned about the DoD PRORP through the Amputee Coalition of America. I am humbled to serve as a consumer reviewer on the prosthetic and orthotic panels and give firsthand commentary regarding how future devices will impact the lives of Soldiers and civilians alike. With each meeting that I attend, my admiration grows for the dedicated and professional scientists that are committed to trying to understand what it's like to be the end user of the science. They are receptive to what the consumers say regarding their experiences and value those shared expressions.

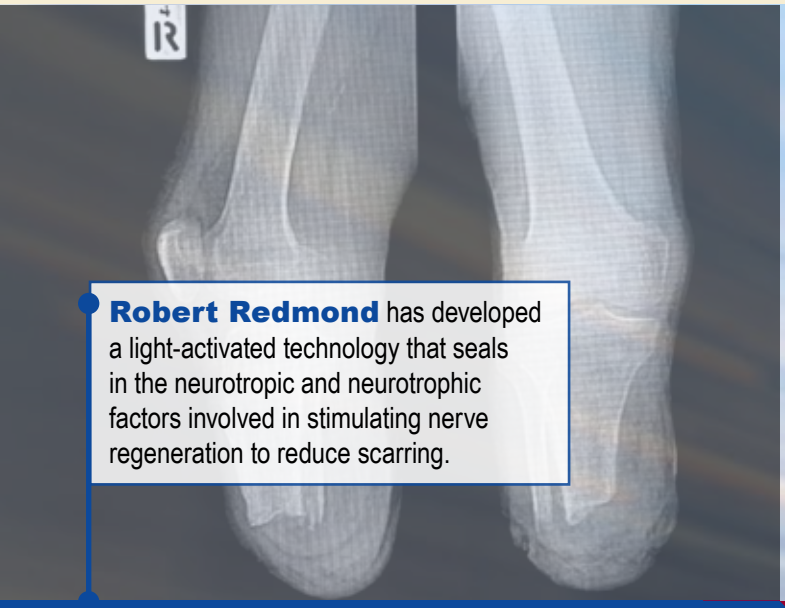
Maxwell Ramsey, PRORP Consumer Peer Reviewer

After being wounded in action on March 1, 2006, my journey of recovery has been similar to many other amputees at Walter Reed National Military Medical Center. The overarching factor in my recovery has been a determination to be highly functional with my prosthetic leg. Even though it was tiresome having to trudge through the day with a socket, I wore my prosthetic leg for 14 to 18 hours each day. I remained in the Army for a couple of years after sustaining my injury, jumping out of planes for the 101st Airborne Division's Parachute Demonstration Team, before retiring from the Army in 2009. Currently, I am a participant in a Phase I human study of percutaneous osseointegrated prostheses, and my journey has taken a turn I never could have imagined. My daily activity level has increased to the point that I barely think about my missing leg at all. In fact, my "sound" limb is in worse shape to some degree.

Serving as a consumer reviewer for the DoD PRORP has been an exhilarating experience. I like listening to and participating in the academic discussions. The overall idea of the DoD PRORP is important, and I would like to see a similar environment replicated outside of government solicitations. In addition, I would like to see an environment that helps facilitate more public-private partnerships to advance more orthopaedic research projects toward Food and Drug Administration (FDA) approval.

I have made it a point to excel in my recovery efforts and have managed to remain as highly functional as possible with my prosthetic leg. When I'm not working as a writer for a media outlet in the mobile technology space, covering products and industry events, I enjoy supporting large cat preservation efforts, participating in politics, Pilates, boxing cardio, and, of course, playing with gadgets.

Near-Term Impact of PRORP-Funded



Robert Redmond has developed a light-activated technology that seals in the neurotropic and neurotrophic factors involved in stimulating nerve regeneration to reduce scarring.

Robert Guldberg developed a tool for microCT scanning of surface roughness and exposed bone to determine the early effects of potential therapeutics.

Steven Svoboda is investigating the impact of biomarkers expressed during cartilage turnover following acute joint injury in an effort to identify novel techniques to detect patients at risk for subsequent injury and early onset post-traumatic osteoarthritis (PTOA).

Potential New Treatments

Wesley Thayer and **Curt Deister** developed three surgical instruments that can capture, manipulate, size, and position severed nerve ends for repair with polyethylene glycol as the sealant instead of potentially nerve-damaging sutures.

Matthew Carty is developing a novel biological interface for lower limb amputees that will provide greater control of the residual limb after amputation, resulting in improved function and overall health outcomes.

Prevention of Complications

Jennifer M. Wolf is investigating the impact of Vitamin D in the prevention and progression of PTOA.

Andrzej Fertala is testing the efficacy of a novel anti-fibrotic antibody to prevent post-traumatic joint stiffness leading to osteoarthritis.

Cecilia Giachelli is engineering an osteoclast system as a local cell therapy for the prevention and/or regression of heterotrophic ossification.

Projects

Advances in Prosthetics

Harold Sears developed a slip detection function for the Motion Control (MC) Electric Terminal Device and the MC Hand prosthetic that automatically increases grip force when socket "slip" is detected.

Gregory Ara Dumanian is developing a surgical nerve transfer procedure to provide amputees with more intuitive control of upper limb prostheses.

Joan Sanders is developing a portable bioimpedance monitor system that enhances understanding of limb fluid volume and the variables that affect it.

Stefania Fatone developed the Northwestern University Flexible Sub-Ischial Vacuum Socket, an assisted prosthetic socket for enhanced prosthetic care and functional performance for transfemoral amputees.

Gordon Hirschman developed a thermoelectric module to provide temperature and moisture management for prostheses of all types with minimal lifestyle changes.

Harold Sears developed a water-resistant End Terminal Device 2 for upper extremity prosthetic use with multiple grasping patterns.

Gregory Ara Dumanian is conducting a clinical trial to determine whether the long-term outcomes of targeted reinnervation provide amputees more control of upper limb prosthetics.

"The PRORP focuses specifically on the care of the combat injured Service member, from basic science through randomized clinical studies. This research is conducted not only within the military, but with partnerships with many elite academic centers and private research entities. It focuses not only on the acute injury of the patient, but also the reconstructive care, rehabilitative care, and psychological care of the patient. An additional benefit of the research being done is that several of the techniques and developments have been translated to the care of non-combat-related injuries that occur in civilian trauma, thus benefiting not only those in the military."

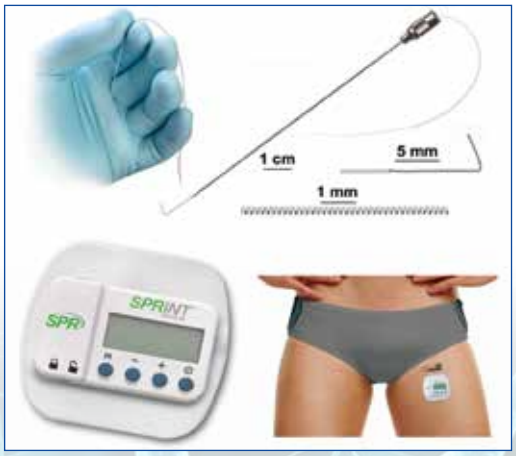
—Romney Andersen, PRORP Chair

Funding Breakthrough Research

Improving Functional Outcomes of Combat-Injured Warfighters by Relieving Post-Amputation Pain

Joseph Boggs, Ph.D., SPR Therapeutics, Inc. (a portfolio company of NDI Medical, LLC)

A significant number of Service members living with combat-related traumatic amputations suffer from moderate to severe post-amputation pain. Unfortunately, many do not find relief from current therapies on the market, resulting in a significant number of these individuals not being able to return to maximum function and optimal fitness. Peripheral nerve stimulation (PNS) is a promising non-opioid approach to pain management, but PNS systems have traditionally been limited by lead migration and the invasiveness of device implantation surgeries. In FY12, the PRORP awarded Dr. Joseph Boggs with a Clinical Trial Award (CTA) to study percutaneous PNS using the SPRINT® PNS System (SPR Therapeutics, Inc., Cleveland, OH; https://www.sprtherapeutics.com), which is designed to reduce the risk of complications and enable delivery of stimulation without surgery. In a previous study, the percutaneous PNS system provided pain relief and improved functional outcomes in at least 75% of amputees. The therapy involves the insertion of a fine-wire coiled lead through an introducer needle to target one or more peripheral nerves. A review conducted to compare the use of a coiled versus non-coiled design found that percutaneous leads used for neurostimulation of the peripheral nervous system have a much lower risk of infection with a coiled design compared with non-coiled leads. The goal of the CTA was to collect data on the safety and effectiveness of the percutaneous PNS therapy in improving functional outcomes by alleviating pain in individuals with major lower limb amputations. The project has successfully achieved its goal of demonstrating clinically and statistically significant reductions in post-amputation pain and pain interference from use of the percutaneous PNS system.



"Of all combat casualties, >75% sustained at least one orthopaedic injury. These combat-related orthopaedic injuries are often complex, open fractures with concomitant soft-tissue and muscle loss. Additionally, over 1,600 wounded Warriors have lost nearly 2,300 limbs in the recent conflicts. The PRORP has strived since its inception in 2009 to identify and support military, Veterans Affairs, industry, and civilian research of exceptional scientific merit on optimizing the recovery and restoration of function for military personnel with combat or combat-related orthopaedic injuries. The PRORP is uniquely positioned to identify the critical gaps in military neuromusculoskeletal care that will benefit our wounded military Service members and conserve the strength of our fighting force. While the focus of PRORP research is targeted to the orthopaedic and rehabilitation care of military Service members, it is expected that these research findings will benefit the general population. The PRORP encourages multidisciplinary collaboration between military, other governmental, and civilian personnel to leverage their individual expertise and augment the number of patients enrolled in clinical trials so that requisite sample sizes are met. The benefits of maintaining this military-civilian partnership is the ability to investigate and draw meaningful conclusions to the major gaps in orthopaedic and rehabilitation research defined by the military."

—COL (ret.) Philip Belmont, PRORP Co-Chair, FDA Division of Orthopaedic Devices

Prevention of Post-Traumatic Contractures with Ketotifen

Kevin Hildebrand, M.D., University of Calgary

Recently, the military reviewed extremity injuries in war and determined that joint stiffness and contractures were a major complication that limits function. Approximately 200,000 elbow fractures or dislocations occur in adults each year in the United States, and up to 30,000 individuals require surgery due to loss of elbow motion. Recent studies have shown that joint contractures result from a myofibroblast-mast cell-neuropeptide axis of fibrosis in the joint capsule, the critical structure limiting joint motion. Dr. Kevin Hildebrand and his research team sought to determine whether Ketotifen, a mast cell stabilizer that has been used in the treatment of chronic asthma for over 30 years, could reduce joint contracture severity. Using a rabbit model of post-traumatic contractions, it was determined that Ketotifen prevents growth factor release and decreases contracture severity by 50%. Importantly, decreases in the number of myofibroblasts, mast cells, neuropeptide-containing nerve fibers, and measures of fibrosis in the joint capsule were also observed. Based on these findings and with support from an FY14 PRORP Clinical Trial Development Award, Dr. Hildebrand designed a Phase III multicenter randomized control trial. Dr. Hildebrand and his team built the necessary infrastructure to conduct the trial and report findings. Dr. Hildebrand was then awarded an FY16 PRORP Clinical Trial Award to support the execution of a Phase III clinical trial to determine the optimal dosage and efficacy of Ketotifen in preventing post-traumatic elbow joint contractures. Findings from these studies can aid in the development of a potential new therapy for joint fibrosis and contracture that repurposes an established drug for a new indication.

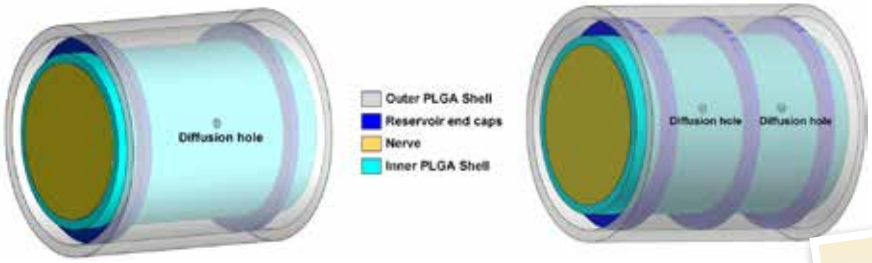
A Novel Nerve Conduit with a Diffusion-Controlled Drug Reservoir to Treat Peripheral Nerve Injuries

Jay Agarwal, M.D., (pictured far right) University of Utah

Peripheral nerve injuries, commonly caused by traumatic incidents, often result in paralysis, chronic pain, and neuropathies in patients. Standard treatment for peripheral nerve injuries frequently involves the use of nerve autografts and conduits; however, these procedures have limited success, particularly when repairing nerve gaps greater than 10mm. The use of a nerve conduit as a drug delivery system for neurotropic factors (NTFs) that enhance axonal outgrowth across nerve gaps has been explored and has met with challenges, including the ability to release adequate amounts of the NTFs over an extended period of time and the ability to change or add NTFs to the drug delivery system.

With support from an FY12 Idea Development Award, Dr. Jay Agarwal and his research team designed and constructed a novel nerve conduit that contains a diffusion-controlled drug reservoir. The drug reservoir is located between two concentric tubes made from biodegradable material. The diffusion of the drug(s) into the lumen is controlled by the size of the hole(s) placed in the inner conduit. Dr. Agarwal and his team successfully constructed devices that could release therapeutic levels of nerve growth factor (NGF) for 30 days. These NGF-loaded devices were implanted across 15mm nerve gaps in a rat sciatic nerve injury model and were found to improve muscle weight, myelinated nerve growth, and neuromuscular junction connectivity when compared to devices without NGF.

Using this device allowed the controlled release of growth factors, which enhanced peripheral nerve regeneration across nerve gaps. Using in vivo models, Dr. Agarwal and his team plan to evaluate the efficacy of this device compared to autograft, as well as the potential to use this device to deliver multiple drugs simultaneously.



PRORP Clinical Consortia: Facilitating

The PRORP supports high-impact research through multiple mechanisms including, notably, two complementary clinical consortia, each designed to provide new solutions along the continuum of care for wounded Warriors with orthopaedic injuries. The partnerships within each consortium are intended

Major Extremity Trauma and Rehabilitation Consortium

The Major Extremity Trauma Research Consortium (METRC), led by Dr. Ellen MacKenzie of Johns Hopkins University and Dr. Michael Bosse at Carolinas Medical Center, was initially established in September 2009 with funding from the DoD and the Orthopaedic Extremity Trauma Research Program. Two separate follow-on awards, funded by the PRORP, were made to the METRC, which provided support for the consortium to expand in both size and scope (2010; METRC 2) and to incorporate several rehabilitation focus areas (2015; METRC 3). With the newest award in 2015, the METRC's historically acute care focus shifted, leading to the newly titled Major Extremity Trauma and Rehabilitation Consortium (METRC).

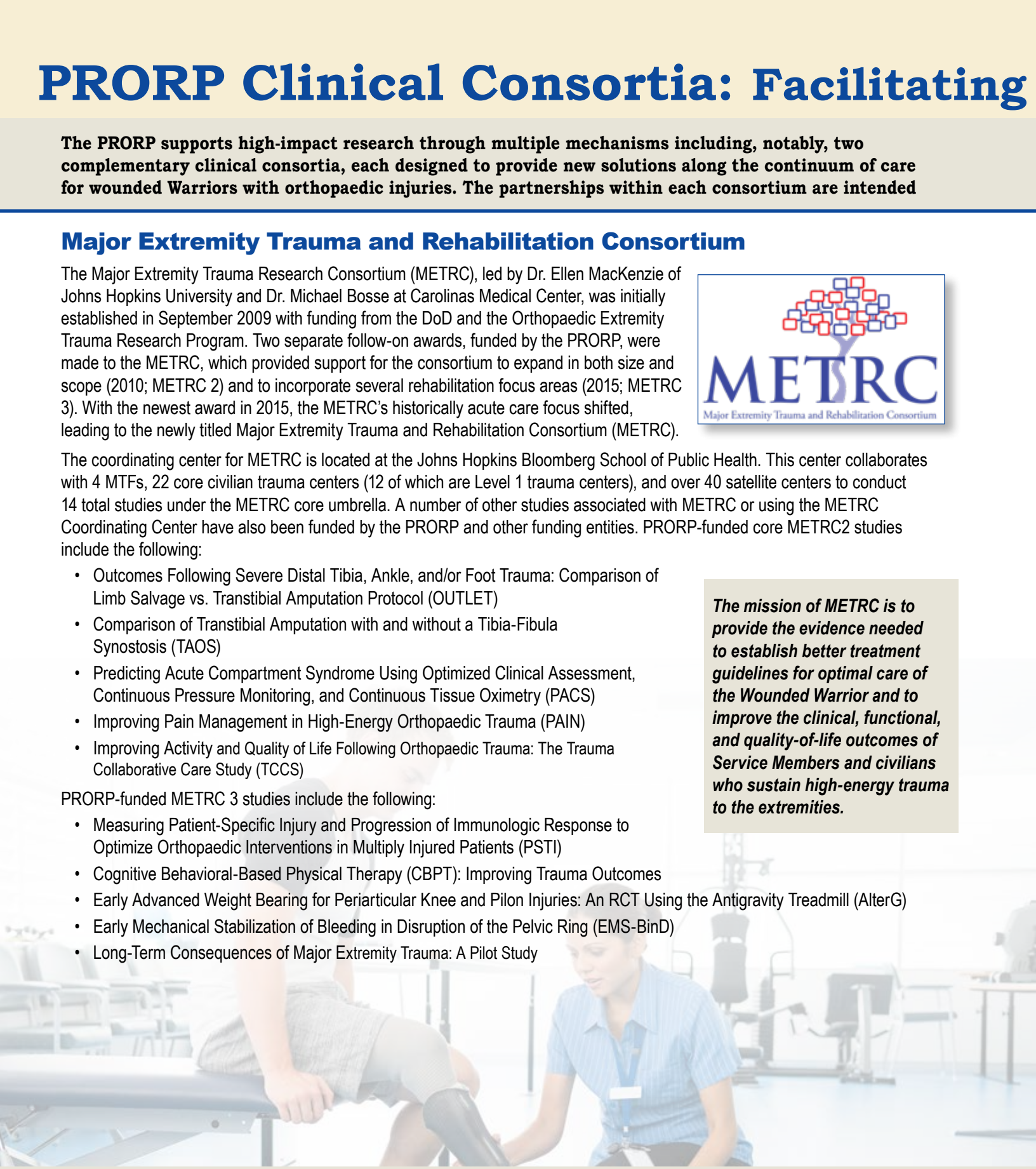
The coordinating center for METRC is located at the Johns Hopkins Bloomberg School of Public Health. This center collaborates with 4 MTFs, 22 core civilian trauma centers (12 of which are Level 1 trauma centers), and over 40 satellite centers to conduct 14 total studies under the METRC core umbrella. A number of other studies associated with METRC or using the METRC Coordinating Center have also been funded by the PRORP and other funding entities. PRORP-funded core METRC2 studies include the following:

- Outcomes Following Severe Distal Tibia, Ankle, and/or Foot Trauma: Comparison of Limb Salvage vs. Transtibial Amputation Protocol (OUTLET)
- Comparison of Transtibial Amputation with and without a Tibia-Fibula Synostosis (TAOS)
- Predicting Acute Compartment Syndrome Using Optimized Clinical Assessment, Continuous Pressure Monitoring, and Continuous Tissue Oximetry (PACS)
- Improving Pain Management in High-Energy Orthopaedic Trauma (PAIN)
- Improving Activity and Quality of Life Following Orthopaedic Trauma: The Trauma Collaborative Care Study (TCCS)

The mission of METRC is to provide the evidence needed to establish better treatment guidelines for optimal care of the Wounded Warrior and to improve the clinical, functional, and quality-of-life outcomes of Service Members and civilians who sustain high-energy trauma to the extremities.

PRORP-funded METRC 3 studies include the following:

- Measuring Patient-Specific Injury and Progression of Immunologic Response to Optimize Orthopaedic Interventions in Multiply Injured Patients (PSTI)
- Cognitive Behavioral-Based Physical Therapy (CBPT): Improving Trauma Outcomes
- Early Advanced Weight Bearing for Periarticular Knee and Pilon Injuries: An RCT Using the Antigravity Treadmill (AlterG)
- Early Mechanical Stabilization of Bleeding in Disruption of the Pelvic Ring (EMS-BinD)
- Long-Term Consequences of Major Extremity Trauma: A Pilot Study



More information regarding these studies and their results can be found at http://metrc.org.

Collaborative Partnerships

to bring military patients, leading researchers, and MTF clinicians together with the infrastructure, patients, and expertise of highly qualified civilian organizations in concerted studies to impact military orthopaedic and rehabilitative medicine.

Bridging Advanced Developments for Exceptional Rehabilitation Consortium

The Bridging Advanced Developments for Exceptional Rehabilitation (BADER) Consortium, led by Dr. Steven Stanhope of the University of Delaware, was established in 2010 with funding from the PRORP to support the advancement of orthopaedic rehabilitation research capabilities at DoD MTFs and Department of Veterans Affairs (VA) sites. The BADER Consortium helps strengthen a research-intensive culture at each MTF and works in concert with them to conduct high-impact research studies and help establish self-sustaining research enterprises at these sites, with DoD and VA employees serving as Principal Investigators in research projects. BADER Consortium studies have helped change patient care in rehabilitation at many of these facilities, including the prescription of devices for optimal running gait. BADER has conducted eight clinical research projects totaling $7.7M and supported 32 projects for the DoD/VA. To date, the consortium has generated 56 published abstracts and 15 published manuscripts and has obtained grants to fund an additional 7 projects.

The BADER Consortium will improve the quality of life for Warfighters who suffer significant limb injuries in combat through orthopaedic rehabilitation research conducted at several military and civilian research institutions across the country.

Core PRORP-funded BADER Consortium projects include the following:

- Improving Step-to-Step Control of Walking in Traumatic Amputees
- Prosthetic Leg Prescription (ProLegRx): What Is the Optimal Stiffness and Height of a Running-Specific Prosthesis?
- Sustainable Benefits of a Power Ankle Prosthesis for Transtibial K2 and K3 Ambulators
- Development of an Assessment Toolbox to Measure Community Reintegration, Functional Outcomes, and Quality of Life After Major Extremity Trauma
- Maximizing Outpatient Rehabilitation Effectiveness (MORE)
- Characterization of Prosthetic Feet for Weighted Walking in Service Members with Lower-Limb Amputation

Surgical Timing and Rehabilitation Trial

The Surgical Timing and Rehabilitation (STaR) Trial, led by Dr. James Irrgang of the University of Pittsburgh, is a multi-site clinical trial that will provide scientific evidence to optimize both surgical care and rehabilitation for military and civilian patients with multiple ligament knee injuries (MLKIs). MLKIs represent a spectrum of injury that can create multiple serious complications during treatment. The timing of care for these injuries has typically resembled the treatment of anterior cruciate ligament reconstruction surgery; however, there is little evidence to support this practice. The consortium-like trial is comprised of two separate but complimentary studies that will determine the most optimal times for surgery and post-operative rehabilitation to increase the rate of return for individuals with MLKIs to their preinjury physical function and level of activity. The first aim is to determine the combined effects of early versus delayed timing of surgery and rehabilitation on the time it takes an individual to return to their pre-injury status and activity. The second aim is to investigate the effects of early versus delayed rehabilitation. In order to provide the support structure and scientific evidence needed to address the scientific question, the University of Pittsburgh has brought together a robust governance structure and highly accomplished research study team. Research participants will be recruited at a total of 25 clinical sites comprised of 5 U.S. military facilities, 17 U.S. civilian sites, and 3 Canadian sites. The PRORP funded the STaR Trial, which was submitted in response to the FY16 PRORP Integrated CTA mechanism, in 2017.

Strategic Direction

The orthopaedic field is vast; it includes topics in training, prevention, tissue engineering, pain control, surgical techniques and care, comorbid injuries/conditions, rehabilitation, prosthetics, etc. A reflection of the state of the science in any given topic area changes rapidly. The PRORP has funded research in all of the aforementioned topics and many others. In order to keep abreast of the ever-changing research landscape and clinical environment (both for the military and civilians), program staff solicit input from experts in several disciplines and across the Service branches who serve on the PRORP Programmatic Panel and Government Steering Committees. In addition, the PRORP works with various Joint Program Committees and other federal partners. The PRORP also routinely monitors research supported by other funding agencies, including the National Institutes of Health, Defense Advanced Research Projects Agency, and VA, to coordinate research funding and priorities across organizations, eliminate research duplication, and ensure that efforts are complimentary in order to best address knowledge and capability gaps.

The PRORP maintains the Congressional intent of the program and continues to support militarily relevant orthopaedic trauma research to benefit Service members, Veterans, and the general public. Instructions from Congress clarified that the program's appropriations must focus on battle-related injuries, as these injuries are often heterogeneous and complex in nature and frequently involve multiple limb trauma, open fractures, major tissue loss, and a high degree of wound contamination.[2] Additionally, these battle-related injuries are sustained in harsh environments where access to optimal care can be limited. Importantly, findings obtained from PRORP-supported research are also applicable to and can benefit the civilian population.

The PRORP has supported and will continue to support research that addresses the needs of the nation's injured Warfighters and Service members, the needs of the military surgeons and medical personnel who are charged with their care and well-being, and the changing military needs of potential conflicts. The PRORP Programmatic Panel, composed of representatives from the military Services, VA, and other government, academic, and clinical practice, as well as the patient community, annually assesses the current research environment related to the short- and long-term care of orthopaedically injured patients and also reviews emerging technological developments in the field. In addition, the PRORP works with other DoD and federal organizations, as well as non-federal organizations, to ensure that all parties are working together to close identified capability gaps. Other agencies and organizations that invest in orthopaedic research, training, and rehabilitation include, but are not limited to, the VA; Association of Bone and Joint Surgeons; National Institute of Arthritis and Musculoskeletal and Skin Diseases; American Academy of Orthopaedic Surgeons/American Association of Orthopaedic Surgeons; Clinical and Rehabilitative Medicine Research Program; Combat Casualty Care Research Program; Defense Advanced Research Projects Agency; and Orthopaedic Research and Education Foundation. Although not all inclusive, additional organizations involved in orthopaedic research are included in the Helpful Resources section of this document.

The orthopaedic care field has benefited from many successes; however, many challenges still exist that prevent some injured patients from returning to their pre-injury level of fitness. Key challenges in military medicine as it relates to the orthopaedic field include identification of best practices for trauma care in a prolonged field care setting; optimization of point-of-injury care to minimize or eliminate long-term complications; evaluation of rehabilitation strategies to increase return-to-duty and return-to-work rates; development of interventions that predict and treat compartment syndrome; prevention of wound infection when access to care is limited; translation of advancements in neural-controlled prosthetics; and many others. The research field's ability to address these challenges has a direct impact on the readiness of the U.S. military, the rehabilitation and reintegration of our Veterans, and the clinical care of patients in the general public.

The PRORP Strategic Plan provides the framework for which current and near-future research investments will be made. The Programmatic Panel will continue to meet annually to review the current state of the science, priorities of the military, and immediate clinical needs in order to confirm that these priorities are still relevant and to refine the plan as needed.

[2] Department of Defense Appropriations Bill, 2008, Report of the Committee on Appropriations. 2007. United States House of Representatives, 110th Congress, 1st Session. House Report 110-279. Available at https://www.gpo.gov/fdsys/pkg/CRPT-110hrpt279/html/CRPT-110hrpt279.htm.

Strategic Goals and Priorities

In order to construct a PRORP investment strategy (see next section) that aligns with the program's vision and mission, as well as the Congressional intent for the PRORP, the Programmatic Panel members sought to identify unanswered basic, translational, and clinical research questions in the field of orthopaedics. The Programmatic Panel members identified seven short- and long-term research priorities (listed below) in which the PRORP will invest through the solicitation of innovative and impactful research in the future (contingent upon the availability of future appropriations). These priorities will present as program focus areas in future solicitations for research applications.

1. Development of basic science animal models that replicate injuries or conditions that are challenging in a prolonged field care scenario
    a. Establishment of advanced diagnostics and therapeutics in ischemia reperfusion injury and compartment syndrome using the newly established prolonged field care animal models
2. Evaluation of promising clinical interventions for durability in a far-forward environment, as close as possible to the point of injury, including the following:
    a. Methods to prevent and/or control combat extremity wound infections (e.g., for long bone open fractures)
    b. Development of novel wound protectants
    c. Improved methods for acute pain control
    d. Advancing surgical interventions to earlier roles of care
3. Discovery of interventions and/or rehabilitation strategies that can facilitate early return to duty for common musculoskeletal injuries, including the following:
    a. Development of offloading and stability devices (e.g., braces and casting) for ligamentous injuries/small extremity fractures
    b. Development of optimal nonsurgical and/or surgical strategies, tools, and delivery parameters to improve functional outcomes for both immediate and eventual return to duty
    c. Development of protective equipment for treatment of non-severe, common battlefield musculoskeletal injuries
4. Translation of early research findings in surgical care topic areas to large animals and/or humans to move the research toward clinical trials and clinical practice
5. Identification of best practices to address rejection and failure of percutaneous osseointegrated prosthetic limbs
6. Development of innovative treatment pathways and technologies to optimize complex orthopaedic injury/extremity trauma management and minimize long-term disability
7. Development of advanced tissue regeneration therapeutics for the restoration of traumatically injured extremity tissues

Investment Strategy

Funding allocation and award mechanisms to be solicited by the PRORP will reflect the types of research (basic, translational, or clinical) that the program plans to fund, based on the needs of the field and the amount of funds appropriated to the program by Congress. For FY18, the PRORP released three program announcements to help address the identified PRORP research priorities: the ARA, CTRA, and CTA.

The ARA supports applied research projects focused on advancing optimal treatment and restoration of function for individuals with musculoskeletal injuries sustained during combat or combat-related activities. Although the ARA allows basic and animal research, it is not intended to support fundamental basic research without specific application toward knowledge or tangible products. Focus areas for the FY18 ARA include topics in animal model development, device development, wound infection, and tissue regeneration. Future solicitations for the ARA will depend on the outcomes of funded research projects in the listed focus areas in order to maintain a balanced PRORP research portfolio.

The CTRA supports translational clinical research that may or may not be ready for a full-scale clinical trial. Funded projects are expected to impact the immediate and long-term standard of care, as well as contribute to evidence-based guidelines for the evaluation and care of military or Veteran patients with orthopaedic injuries. Focus areas for the FY18 CTRA include topics in treatment techniques and outcomes, wound infection, surgical care, and tissue regeneration. Future solicitations for the CTRA will depend on the outcomes of current research projects in areas of interests to the orthopaedic field or PRORP.

The CTA differs from the CTRA in that the CTRA allows clinical research projects, whereas the CTA is restricted to clinical trials only. Intended to support rapid implementation of clinical trials that can bring life-saving and -changing interventions to patients, the FY18 CTA will support research projects in surgical techniques and outcomes, rehabilitation techniques and outcomes, acute pain, improved surgical interventions, and tissue regeneration. Future solicitations for the CTA will be based on then-current research environment assessments to ensure the PRORP continues to move promising interventions into clinical practice.

This investment strategy will be re-evaluated and updated as necessary during the program's annual Vision Setting meeting. The PRORP plans to continue its commitment to addressing the identified short- and long-term research priorities by funding basic applied research, clinical studies and trials, and expansions on prior/early-stage research investments via funding opportunities that include the ARA, CTRA, and CTA.

Measuring Progress

The PRORP will continue to monitor the outcomes of PRORP-funded research and their impact on the field. The following metrics, categorized into short-term and mid-term outcomes, will help the PRORP assess progress made toward addressing the identified unanswered research questions and research priorities:

Short-term outcomes (3-5 years)

Measurable by evaluating the amount of funding invested in each strategic goal and tracking contributions to the scientific and clinical community, including publications, patents, products, and clinical trials, which will vary based on the stage of the research project.

Mid- and long-term outcomes (6+ years)

Measurable by evaluating the proportion of funded investigators receiving additional awards to continue successful research, production of commercialized products, and changes in standard of care (e.g., clinical practice guidelines, evidence supporting specific treatment recommendations), point-of injury-care, return-to-duty rates, and quality of life.

"Serving on the PRORP Programmatic Panel provides an invaluable opportunity for interagency communication. My service on this Panel is a key element of ongoing efforts to ensure that the research funded by PRORP and VA is complementary, not duplicative, and works together to best advance the health care and lives of our Service members and Veterans."

—Brian Schulz,
Department of Veterans Affairs,
PRORP Programmatic Panel Member

Address the most significant gaps in care for the leading burden of injury and for facilitating return to duty by funding innovative, high-impact, clinically relevant research to advance optimal treatment and rehabilitation from musculoskeletal injuries sustained during combat or combat-related activities

For more information, visit
http://cdmrp.army.mil
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