METRC

Major Extremity Trauma Research Consortium

2012 Annual Report

Contents

1 Letter from the Chair and the Director of the Coordinating Center

2 About METRC

6 Ensuring Quality Research

10 The METRC Registry

12 Ongoing Research

28 Sources of Funding

30 Looking Forward

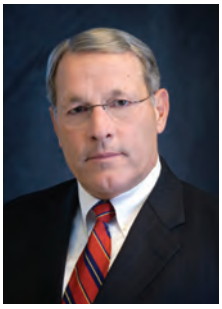
Appendices:

Appendix A – Participating Centers

Appendix B – Staff of the METRC Coordinating Center

Appendix C – Study Participation

METRC
Major Extremity Trauma Research Consortium



Dear Colleagues and Friends,

The METRC research program continues to grow. We are pleased by the ongoing progress of the Consortium and hope that all members take pride in our achievements to date.

We currently have five studies actively enrolling patients. Four additional studies are poised to commence enrollment by the end of 2012. While we recognize there is significant work before us, we remain optimistic about the potential for the Consortium to fundamentally change the way we care for the extremity trauma patient.

Over the past year, investigators from the University of Maryland collaborated with METRC to successfully compete for additional funding to investigate the effectiveness of high dose post operative oxygen therapy on the development of infection in high risk patients. Colleagues from San Antonio Army Medical Center and the Center for the Intrepid were also successful in obtaining funding to evaluate the impact of the IDEO brace on the recovery and functional outcomes of patients with severe lower limb trauma treated at three of our military medical centers. METRC is proud to be coordinating this study for the military.

Using METRC registry data, we submitted two abstracts to the 2012 OTA meeting. Both were accepted as poster presentations.

Of major importance this year was the initiation a major quality assurance program. In addition to generating monthly and quarterly data reports on all active studies, we have started to conduct site visits at our core centers to assess infrastructure, data quality and regulatory compliance. To date we have conducted site visits at 6 METRC Centers. We want to thank the centers we visited for their cooperation and enthusiastic response to the reviews – and particularly recognize the near perfect performance of the Wake Forest, Houston and Miami teams. We hope to complete all site visits in 2013.

We are proud of the work the Consortium has accomplished to date and look forward to the productive partnerships that will result from our initiatives.

Sincerely,

Michael J. Bosse, MD
Ellen J. MacKenzie, PhD

About METRC

Advancing Limb Trauma Care through Research

The Major Extremity Trauma Research Consortium (METRC) was established in September of 2009 with funding from the Department of Defense (DOD). It is comprised of a network of clinical centers and one data Coordinating Center that work together with the DOD to conduct multi-center clinical research studies relevant to the treatment and outcomes of orthopaedic trauma sustained in the military.

Improving outcomes through collaborative research

The overall goal of the METRC Consortium is to produce the evidence needed to establish treatment guidelines for the optimal care of the wounded warrior and ultimately improve the clinical, functional and quality of life outcomes of both service members and civilians who sustain high energy trauma to the extremities.

The need for a Consortium dedicated to improving outcomes following major limb trauma is evident. Approximately 82% of all service members injured in OIF/OEF sustain extremity trauma. Many are burdened with injuries to multiple limbs. Complex wound management, infection, bone loss, articular surface loss, blast-related extremity heterotopic ossification, segmental nerve loss, complete muscle tendon unit loss and compartment syndrome have been identified as critical challenges in caring for our wounded warriors. These challenges are only compounded by the needs in the post-acute and rehabilitation phases of recovery. Rigorous clinical research is sorely needed to address these challenges. This research must rely on a multi-disciplinary approach that combines the clinical insights of the military and civilian orthopaedic surgeons and rehabilitation specialists, the research acumen of a world renowned clinical research center and high volumes of patients with severe injuries that are treated at major Level I trauma centers and the military treatment facilities (MTFs). METRC is designed to meet these needs.

Anchored by a Data Coordinating Center at the Johns Hopkins Bloomberg School of Public Health and its Center for Injury Research and Policy, the Consortium includes 22 core Level I civilian trauma centers and 4 core MTFs – with the ability to expand patient recruitment to more than 30 additional satellite trauma centers. The Consortium works collaboratively with the DOD to:

1. *Continuously identify the most critical issues that challenge recovery from major orthopaedic trauma;*
2. *Develop and sustain a research infrastructure to support the conduct of multi-center research studies aimed at the rigorous evaluation of current standards of orthopaedic care;*
3. *Partner with basic scientists and engineers to facilitate the translation of new and emerging technologies into clinical practice;*
4. *Mentor young orthopaedic trauma surgeons and rehabilitation specialists in the design and conduct of clinical trials;*
5. *Contribute to the science of fracture and soft tissue repair;*
6. *Contribute to the science of conducting clinical trials in a challenging patient population and treatment environment.*

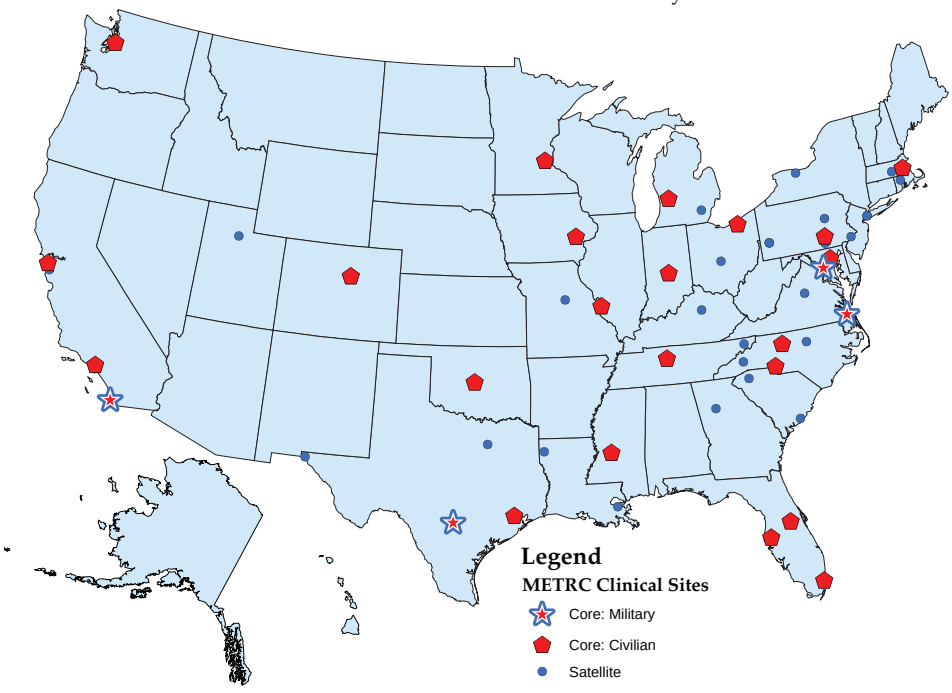
METRC is committed to conducting high quality clinical research that will make a difference in the lives of those who sustain major orthopaedic trauma. It does so by establishing a clinical research network that is dynamic and responsive to new clinical challenges or the emergence of new, promising novel therapies. The success of the Consortium depends on the identification of critical topics, the design of clinical trials that are sensitive to the realities of surgical patient research, rapid and high volume recruitment to those studies and excellent post-treatment follow-up. It also depends on the responsiveness of the network to specific centers and studies that are not meeting expectations and its ability to re-allocate resources and re-focus priorities accordingly.

Core funding for METRC is provided through the Orthopaedic Extremity Trauma Research Program (OETRP) (Award # W81XWH-09-2-0108) and a cooperative agreement with the DOD Peer Reviewed Orthopaedic Research Program (PRORP) of the Congressionally Directed Medical Research Program (CDMRP) (Award # W81XWH-10-2-0090).

The backbone of the Consortium consists of a dedicated group of core and satellite clinical centers located throughout the United States.

The Core Clinical Centers include 22 civilian trauma centers and the four military hospitals receiving the majority of major casualties, including Walter Reed National Military Medical Center (WRNMMC), San Antonio Military Medical Center (SAMMC), the Naval Medical Center in San Diego (NMCSD), and the Naval Medical Center in Portsmouth (NMCP). The civilian core centers are large, level I trauma centers with leading orthopaedic trauma programs and established research infrastructures. The core clinical centers are provided with resources to support METRC activities and participate in most trials sponsored by the Consortium. These centers were chosen on the basis of their volume of major extremity trauma cases, commitment to research, experience in participating in large multi-center studies, and academic qualifications.

The Satellite Clinical Centers are civilian trauma centers with an established orthopaedic trauma program. They are invited to participate in individual METRC studies to ensure adequate numbers and appropriate mix of patients. Their participation is supported by a payment provided for each patient screened, enrolled and successfully followed.

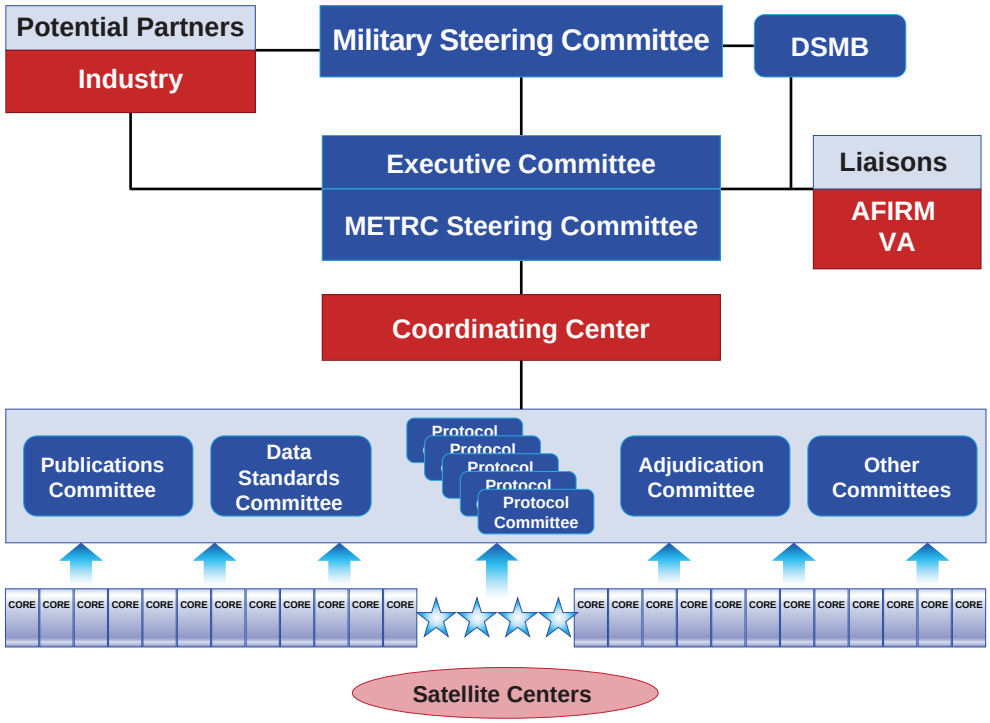


A current list of both core and satellite centers is provided in Appendix A at the end of this report.

The primary decision-making body of the Major Extremity Trauma Research Consortium (METRC) is the METRC Steering Committee, which is a representative body of the investigators and the U.S. Military. It provides ongoing oversight in planning and conducting each study sponsored by the Consortium and approves all study protocols. The Steering Committee meets monthly by WebEx-facilitated conference calls and in-person at least twice each year.

An Executive Committee serves as the agent of the Steering Committee in carrying out the day-to-day administrative responsibilities of the Consortium and Consortium-sponsored studies. The Consortium is supported by a network of Standing Committees, that include: (1) Publications and Presentations; (2) Data Standards; (3) Clinical Outcomes Adjudication; and (4) Study-Specific Protocol Committees.

A Military Steering Committee has been established by the DOD to (1) review progress of METRC; (2) provide advice and guidance on scientific and military relevance; (3) coordinate proposed projects with other military relevant orthopaedic trauma initiatives; (4) provide approval on all proposed Consortium studies prior to implementation; and (5) recommend areas of future study to the Consortium.



The Coordinating Center for METRC is located at the Johns Hopkins Bloomberg School of Public Health. The Coordinating Center works closely with the METRC Steering Committee to ensure that study protocols are appropriately designed, executed and analyzed. The Center is organized around three cores: (1) Protocol Development, Implementation and Monitoring; (2) Administration and Regulatory Affairs and (3) Informatics and Biostatistics. Resources of the Johns Hopkins Biostatistics Center are used to further support the data management and analysis activities of the Center. The Director, Deputy Director, Principal Biostatistician, and Principal Economist oversee the three core activities of the Coordinating Center. A list of key personnel of the Coordinating Center is available in the appendix as Appendix B.

JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH

The METRC Data Safety Monitoring Board (DSMB):

A DSMB was established for METRC and acts in an advisory capacity to the DOD and the METRC Steering Committee to monitor patient safety and evaluate the efficacy of the interventions under study. Dr. Marc Swiontkowski of the University of Minnesota is chair of the DSMB and serves as Medical Monitor. Other members of the board are listed here. The DSMB meets at least two times a year and more frequently as necessary.

METRC Data Safety Monitoring Board

Marc Swiontkowski, MD (CHAIR)
Department of Orthopaedics
University of Minnesota

Baruch Brody, PhD
Department of Philosophy
Rice University

Hans Kreder, MD, MPH
Department of Orthopaedics
Sunnybrook Health Sciences Centre

Stephen Walter, PhD
Department of Clinical Epidemiology & Biostatistics
McMaster University

Capt. Christopher Ayres USMC (Ret.)
OIF Combat Wounded
Northrop Grumman

Thomas Decoster, MD
Department of Orthopaedics
University of New Mexico Medical Center

Eli Powell, MD Col (Ret.)
Alaska Orthopaedic Surgery and Sports Medicine
Anchorage, AK

Ensuring Quality Research

METRC is committed to efficient and high quality research design and data collection. To this end, procedures have been put in place to document Consortium-wide and study-specific policies and procedures, facilitate communication across the Consortium, standardize approaches to data collection, and support rigorous continuous data quality assurance. These efforts are briefly described below.

Policies and Standard Operating Procedures (SOPs):

The policies governing METRC were developed in 2010 and are re-visited on a regular basis and amended as appropriate. They include polices on:

- Governance
- Approval and Initiation of Studies
- Conflict of Interest and Commitment
- Publications and Presentations
- Data Standards and Data Collection

In an effort to standardize the processes and procedures utilized by the Consortium, we have developed several Standard Operating Procedures (SOPs) and compiled them into a Manual of Operations (MOP) for METRC. These SOPS are distributed to all participating centers and made available on the website. Amendments to these SOPS are made as necessary.

METRC has developed Standard Operating Procedures (SOPs)

1. **METRC Overview and Policies**
2. **METRC Communications**
3. **Data Safety and Monitoring Board**
4. **Study Initiation**
5. **IRB Submission and Study Documentation**
6. **Clinical Site Certification**
7. **Patient Screening**
8. **Reporting Requirements**
9. **METRC Data Management**
10. **Patient Payments**
11. **Patient Follow-up**
12. **Case Report Form Management**
13. **HIPAA Compliance**
14. **Medical Care Costs Data**
15. **Data Quality Assurance**
16. **Clinical Site Monitoring**
17. **Research Coordinator Advisory Committee**
18. **Data Sharing Policies for METRC**

Facilitating Communication:

Several tools facilitate communications among members of METRC.

The METRC website includes sections that are password protected and accessible only by certified members of the METRC Consortium (www.metrc.org). This private part of the website is used to store and distribute all official Consortium documents and resources including: Consortium policies and SOPs, directories for all participating sites, investigators, and consultants, meeting agendas and minutes, METRC presentations, and other documents to support the work of the Consortium. A bulletin board facilitates communication among Consortium members. In addition, all materials related to specific studies can be accessed through the website. Posted for any given study are the protocol and master consent forms, recruitment materials, training presentations and videos, and case report forms (CRFs).

Web and video conferencing are a key component of the overall METRC communication strategy. Whenever possible, METRC meetings are conducted via web conferencing, which allows the sharing of documents, slide presentations, agendas, voting, private chat, audio and video. Monthly meetings of both the Steering Committee and the Site Research Coordinators are held via WebEx.

Monthly e-Newsletters are distributed to Consortium members providing them with a listing of upcoming meetings and trainings, summary of new materials posted to the website, FAQs of the month, and an update on the status of site participation.

Data Standards:

METRC has developed a Data Standards and Data Collection Policy that governs the development of case report forms (CRFs) and strategies for data collection. Core data elements are collected uniformly across all studies except in specific studies of limited scope. Collecting core data across studies, compare study populations and conduct secondary data analyses.

In addition to developing the core data elements to be collected across all studies, we are developing standard procedures for collecting data common to many (although not all) studies. Standards have been developed for measuring infection, fracture healing and functional performance.

Standard Data Collection across all METRC studies

1. **Patient Demographics**
2. **Socioeconomic Status**
3. **Usual Major Activity**
4. **Health Insurance**
5. **Psychosocial Predictors of Outcome**
6. **Smoking History**
7. **Height and Weight**
8. **Co-morbidities**
9. **Pre-Injury Health Status**
10. **General Injury Characteristics**
11. **Mechanism and Type of Injury**
12. **Functional Outcomes**

REDCap
Research Electonic Data Capture

The centerpiece of the METRC data management infrastructure is the Research Electronic Data Capture (REDCap) system hosted at the Coordinating Center. REDCap is a state of the art, metadata driven application for distributed data collection and data management in clinical studies. The REDCap data management functionality allows for a secure, web-based data entry system using most web browsers to access an internet-connected database server. The system permits both the Coordinating Center and clinical sites to have access to data as soon as they are entered, allowing for near-real-time recruitment reports and increased data entry availability and convenience for the clinical sites. The primary functions of the data system include the following features: registration of all candidates for the trial; randomization to study arms; entry of all study data forms; inventory, management, and editing of study data; maintenance of full audit trails of all data entry and editing; generation of real time performance reports. The REDCap data entry system also includes extensive data validation functionalities, including field level validation.

Continuous Quality Assurance:

Critical to the success of any multi-center trial or study is a robust data quality assurance plan. Quality assurance involves development and maintenance of proper attitudes among all investigators and research staff as well as the use of study designs that protect the results from treatment-related bias. Beyond these strategies, assurances depend on methods and procedures used for training, data collection and analysis. Paramount among these is the training and certification of study personnel involved in data collection, and the maintenance of those certifications throughout the trial. Additionally, data edits and audits are performed to ensure collection of quality data. The continuous and timely flow of data from the centers to the Coordinating Center is an essential prerequisite for maintaining data quality.

This past year we emphasized the development of monitoring and reporting mechanisms to ensure data quality control in all METRC studies. The following reports are generated by the Coordinating Center and distributed to the members of the Consortium:

- Study and Site Specific Monthly Data Quality Reports are distributed to the research coordinators and investigators at each of the participating sites. These reports summarize (for each site), the numbers of patients screened and enrolled by month and lists data errors or inconsistencies by study ID. Sites are required to respond to errors within two weeks.

- Study Specific Quarterly Reports are distributed to Consortium members. These reports include updates on overall and site specific recruitment and enrollment and compare actual enrollment against projected enrollment. The reports also summarize key information regarding types of patients enrolled, rates of follow-up and timeliness of data entry. These reports are reviewed carefully by the Protocol Committee for each study and actions taken as necessary to improve enrollment rates and data quality.

- DSMB Reports are generated at least two times each year and more often as requested by the DSMB. These reports consist of both open and closed reports and are used as a basis for discussion at the DSMB meetings. The DSMB also receives all quarterly reports.

This year we also began auditing study specific CRFs and formal on-site monitoring visits of METRC core sites that are actively recruiting patients into one or more studies. To date we have completed six of these visits. Two directors from the Coordinating Center spend one full day on-site reviewing study procedures and regulatory binders. They also audit CRFs and data entry for a sample of patients.

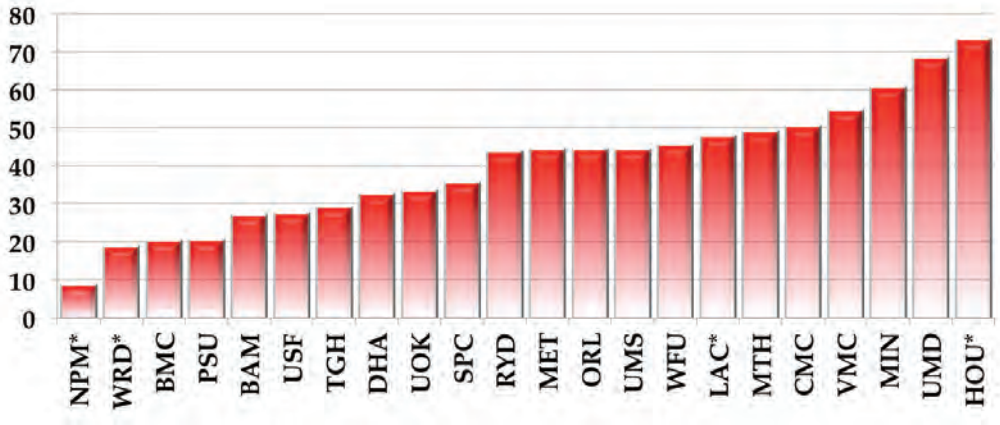
The METRC Registry

In 2010, a registry was established to assist the Consortium in determining the feasibility of future studies that could address critical research questions with adequate power. All core centers were asked to implement the registry and maintain the registry for at least 365 consecutive days. The registry contains a limited set of data on patients between the ages of 18 and 84 who were admitted with fractures requiring surgery of the upper or lower extremity, pelvis or acetabulum, and foot (calcaneus, talus or crush injuries only). Excluded from the registry are hip fractures in patients 60 years or older and fractures to the wrist, hand, ankle, clavicle, patella, and the foot other than calcaneus/talus/crush.

As of August 15, 2012, 22 of the 26 core civilian and military centers had implemented the registry and had entered cases for greater than 90 days; 18 of these centers have entered cases for at least 365 consecutive days. An additional 3 centers have just started to enter cases or are poised to begin; one center was unable to get the registry approved at its institution. A total of 11,972 patients have been registered across the 22 sites. These patients sustained a total of 15,043 fractures (mean of 1.26 fractures per patient).

As shown in the figure below, the average number of registry cases entered per month varies by site. Given temporal trends in the incidence of major trauma, estimates for the 4 sites contributing data for less than 365 days (indicated by the asterisk) may be biased.

Average Registry Cases Entered Per Month By Site



The table to the right provides annual estimates of the number of 'registry' fractures treated per site and over the 22 core sites who have been contributing to the registry for at least 90 days. The 22 sites together treat a total of 13,291 'registry' fractures each year (including 278 traumatic amputations). Over three quarters (77%) of all fractures are to the lower extremity. Nearly one quarter (23%) of all fractures are open and of the open fractures, 49% are Gustilo type III (33 % IIIA, 13% IIIB and 3% IIIC).

An estimated 436 amputations (traumatic and surgical) are registered annually across the 22 sites (54 to the upper limbs and 382 to the lower limbs).

The registry data have added value to the Consortium and its ability to plan for future studies. Patients with type III tibia fractures are the subject of several potentially competing METRC projects–driving the need for the addition of new centers. Despite a high number of upper extremity, pelvic, and femur fracture patients, these injuries are currently the focus of few METRC studies. This information is being used to design future research.

The registry has also afforded METRC the opportunity to compare the newly developed OTA Open Fracture Classification (OFC) with the Gustilo-Anderson Classification. At present, the Gustilo Classification is the most commonly used fracture classification system. It is well recognized, however, that a Type IIIB tibia fracture with no bone loss and only a 2x2 cm pre-tibial skin defect that is covered with a rotational flap is different from the Type IIIB fracture with severe contamination, a 5 cm bone defect and a soft tissue injury that removed most of the anterior compartment – requiring a free tissue transfer and bone defect reconstruction procedures. Recognizing this limitation of the Gustilo classification, the OTA developed a new Open Fracture Severity Classification that assigns the fracture an injury severity level in 5 domains: Bone Loss, Muscle Injury, Skin Injury, Arterial Injury and Contamination (J Orthop Trauma 2010; 24:457-465).

Annual Number of Registry Fractures by Upper and Lower Limb and OTA Code
(based on data as of July 31, 2012)

	Annual Number of Registry Fractures	
	Average Per Site	**Total for 22 Sites**
All Upper Limb Fractures	**135**	**2963**
Traumatic Amputations	2	42
Closed Fractures	96	2114
Open Fractures	37	807
Gustilo Type I or II	24	522
Gustilo Type III	13	285
Humerus	**64**	**1417**
11 A,B,C (% open)	24	536 (6%)
12 A,B,C (% open)	21	472 (22%)
13 A,B,C (% open)	19	409 (40%)
Radius/Ulna	**69**	**1504**
21 A,B,C (% open)	29	628 (28%)
22 A,B,C (% open)	40	876 (38%)
All Lower Limb Fractures	**470**	**10328**
Traumatic Amputations	11	236
Closed Fractures	357	7851
Open Fractures	102	2241
Gustilo Type I or II	47	1036
Gustilo Type III	55	1205
Pelvis /Acetabulum	**79**	**1729**
61 A,B,C (% open)	38	826 (5%)
62 A,B,C (% open)	41	903 (2%)
Femur	**144**	**3184**
31 A,B,C (% open)	41	900 (3%)
32 A,B,C (% open)	72	1593 (19%)
33 A,B,C (% open)	31	691 (32%)
Tibia	**195**	**4271**
41 A,B,C (% open)	63	1379 (13%)
42 A,B,C (% open)	79	1730 (49%)
43 A,B,C (% open)	53	1162 (33%)
Foot	**41**	**902**
81 A,B,C (% open)	13	296 (27%)
82 A,B,C (% open)	25	546 (19%)
83 A,B,C (% open)	3	60 (55%)

OTA Classification of Bone Loss and Muscle Injury Type IIIB Fractures Only
Source: METRC Registry (July 31, 2012)

		Muscle Injury (in 6 cases, degree of muscle injury could not be assessed)		
Bone Loss	**Total**	**Level 0**	**Level 1**	**Level 2**
Total	**378**	**61**	**185**	**132**
Level 0	**74**	23	37	14
Level 1	**160**	22	88	50
Level 2	**144**	16	60	68

Of all 378 fractures in the registry that were classified as Gustilo Type IIIB injuries, 23 patients had no bone or muscle loss (Cat 0) while 68 patients had both severe bone loss (Cat 2) and severe muscle loss (Cat 2). A total of 61 patients had minimal muscle injury (Cat 0) while 132 had the most severe muscle injury (Cat 2).

Based on these data it appears that the Gustilo Classification does not adequately reflect the variation in severity of high energy trauma.

Ongoing Research of the Consortium

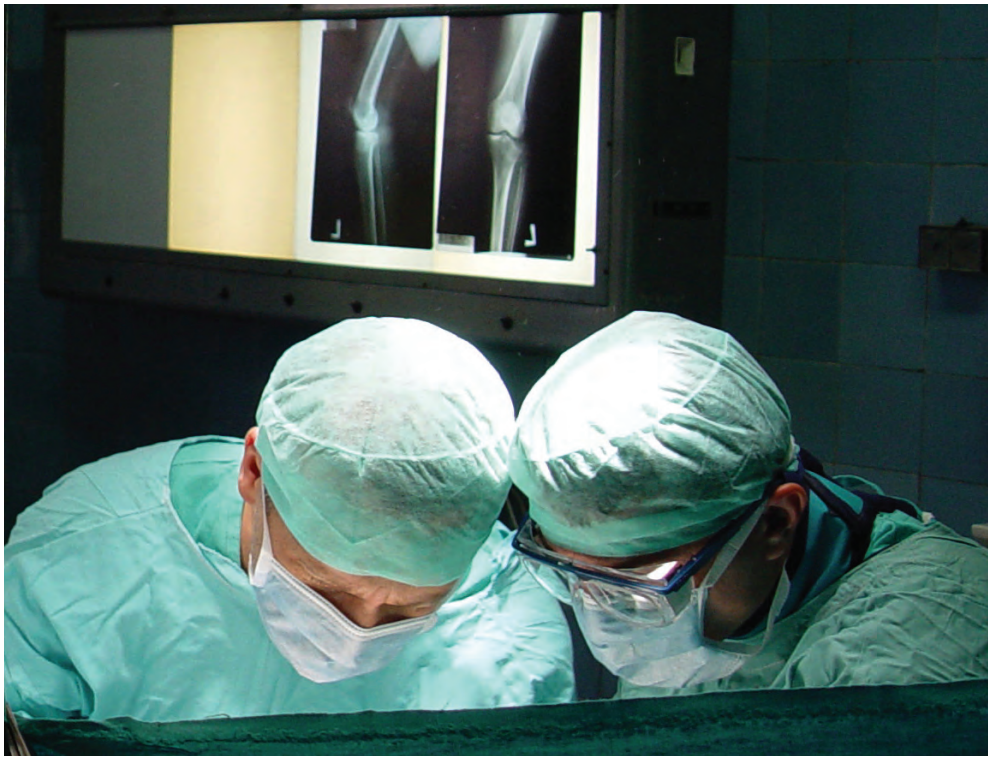
Research Cores have been established to facilitate the development of research priorities and identification of studies (see box). These are the priorities used by the METRC and Military Steering Committees in selecting and approving specific studies to be conducted by the Consortium. Each decision is made after careful consideration of the importance and relevance of the research question, integrity of the proposed study design, feasibility, and availability of funding (either through the core funds of the Consortium or through outside funding).

METRC encourages collaboration with industry in the evaluation of proprietary investigational agents under guidelines set forth by the Consortium. These guidelines, established to maintain the independence and scientific integrity of the Consortium, pertain to protocol development, data access, publication review and intellectual property. In particular, all industry sponsored studies must involve METRC investigators in protocol development and the final study protocol must be approved by the METRC Steering Committee. Collection and analysis of the data remain the responsibility of METRC and its Coordinating Center, independent of industry involvement.

Core Research Areas

- **Bone Defect Reconstruction and Fracture Healing**
- **Prevention and Treatment of Acute and Chronic Infections**
- **Diagnosis and Treatment of Compartment Syndrome**
- **Wound Care and Closure**
- **Prevention and Treatment of Post-Traumatic Osteoarthritis (PTOA)**
- **Limb Salvage and Amputation Outcomes**
- **Post-Acute Care and Rehabilitation Outcomes**

METRC is currently funded to conduct 13 studies that address six of the seven core areas of research.



METRC studies are listed below, organized by the source of funding.

A list of participating centers in each of the studies is attached at the end of this report (Appendix C)

DOD OETRP
(core funding for METRC 1)

- **pTOG:** rhBMP-2 vs. autograft for critical size tibial Defects: A multicenter, randomized trial
- **FIXIT:** A randomized controlled trial of ring external fixation vs. locked IM nail as the definitive stabilization of Grade IIIB tibia fractures
- **BIOBURDEN:** Assessment of severe extremity wound bioburden at the time of definitive wound closure or coverage: correlation with subsequent post-closure deep wound infection

DOD CDMRP
(core funding for METRC 2)

- **OUTLET:** Outcomes following severe distal tibia, ankle and/or foot trauma: comparison of limb salvage vs. transtibial amputation
- **PACS:** Predicting acute compartment syndrome using optimized clinical assessment, continuous pressure monitoring, and continuous tissue oximetry
- **PAIN:** Comparing the efficacy of standard pain management vs. standard pain management combined with use of perioperative pregabalin or ketorolac in the treatment of severe lower limb fractures
- **TAOS:** Comparison of transtibial amputation with and without a tibia-fibula synostosis: A randomized controlled study
- **TCCS:** Using a collaborative care model to improve activity and quality of life following major extremity trauma

DOD PRORP Clinical Trial Awards

- **APS:** Novel therapy to reduce infection after operative treatment of fractures at high risk of infection: a multicenter randomized controlled trial (primary award to University of Maryland)
- **OXYGEN:** Supplemental perioperative oxygen to reduce surgical site infection after high energy fracture surgery (primary award to University of Maryland)
- **POvIV:** A prospective randomized trial to assess oral (PO) vs. intravenous (IV) antibiotics for the treatment of early post-op wound infection after plate fixation of extremity fractures (primary award to Vanderbilt University)

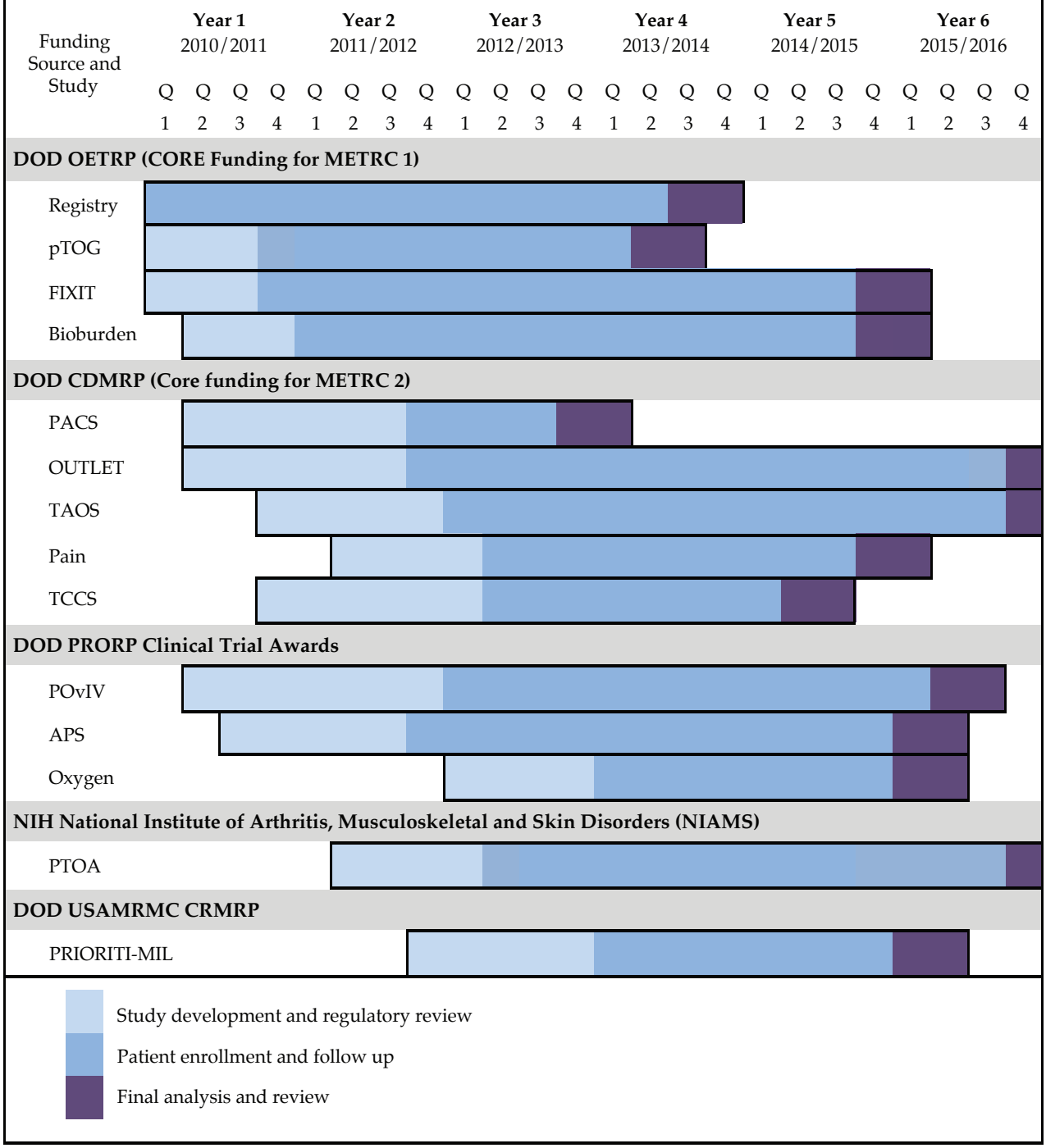
NIH National Institute of Arthritis, Musculoskeletal and Skin Disorders (NIAMS)

- **PTOA:** Multi-center investigation of the mechanical determinants of post-traumatic osteoarthritis (primary award to University of Iowa).

DOD USAMRMC CRMRP/TATRC

- **PRIORITI-MIL:** Patient response to an integrated orthotic and rehabilitation initiative for traumatic injuries in the military treatment facilities.

METRC Study Timelines



Each study currently funded by METRC is described in a one page brief that follows. For more information, visit the METRC website www.metrc.org

A Prospective Randomized Trial to Assess Fixation Strategies for Severe Open Tibia Fractures: Modern Ring External Fixators vs. Internal Fixation

The FIXIT Study

Sponsored by: DOD OETRP
Award Number: W8XWH-09-20108 (METRC 1)
PI/Protocol Chair: Robert O'Toole, MD

The FIXIT Study is enrolling patients:

- 19 sites approved for enrollment
- 4 sites pending DOD approval
- 3 sites pending local IRB approval
- 1 sites pending IRB submission
- **65 patients enrolled as of 9/1/12**

The overall goal of the FIXIT study is to compare the outcomes associated with the use of modern ring external fixators versus standard internal fixation techniques in treating severe open tibia shaft or metaphyseal fractures with or without a bone defect of any size. Primary outcomes include hospital readmission for a defined set of complications. Secondary outcomes include: infection (superficial or deep), fracture healing, limb function, pain intensity and interference, and patient reported functional outcome and quality of life. Cost of treatment (for the initial hospitalization and total one-year treatment costs) will also be ascertained, as well as patient reported satisfaction with fixation method and overall treatment.

A secondary objective will determine the percentage of Gustilo IIIB open tibia shaft fractures that can be treated successfully (i.e. without amputation) without a soft tissue flap secondary to the use of ring external fixators.

Study design: Multicenter, phase III prospective randomized controlled trial. Patients who refuse randomization will be eligible for a prospective cohort study.

Study duration: 5 years (6 month planning, 36 month accrual, 12 month final follow-up, 6 month analysis and writing). Participants will be followed for one year from the time of definitive treatment.

Sample size: 312 in randomized study (156 per arm) and 312 in observational study.

Number of study sites: 27 core and satellite centers.

Principal Inclusion criteria: All Gustilo Type IIIB and selected Gustilo Type IIIA diaphyseal or metaphyseal tibia fractures.

Protocol committee: R O'Toole, MD, M Bosse, MD, R Crichlow, MD, W Gordon MD, LTC J Hsu, MD, C Jones, MD, JS Reid, MD, J Sontich, MD, D Sietsema, PhD. From the Coordinating Center: E MacKenzie PhD, R Castillo PhD, G deLissovoy, PhD, D Scharfstein ScD, A Carlini, MS, L Reider, MHS.

rhBMP-2 vs. Autograft for Critical Size Tibial Defects: A Multicenter, Randomized Trial

The pTOG Study

Sponsored by: DOD OETRP
Award Number: W8XWH-09-20108 (METRC 1)
Co-PIs/Protocol Co-Chairs: Lisa Cannada, MD and Paul Tornetta, III MD

The purpose of this study is to compare the effect of recombinant human bone morphogenetic protein (rhBMP-2/ACS) versus autogenous iliac crest bone graft (ICBG) on rates of fracture healing in patients with critical size defects following tibial shaft fractures. We hypothesize that rhBMP-2 is a safe substitute for the patient's own bone in fracture healing. The primary outcome for this study is fracture union at 12 months post-injury. Secondary outcomes include infection, functional status and one year medical cost. rhBMP-2 is commercially available (Medtronic Sofamer Danek, Memphis TN). It is currently approved for use within the first 14 days in open tibia fractures treated with an intramedullary nail. The FDA has granted an Investigational Device Exemption (IDE) for use of rhBMP-2 in this study.

The pTOG Study is enrolling patients:

- 11 sites approved for enrollment.
- **6 patients enrolled as of 9/1/12**

Study design: Multicenter, phase III prospective randomized controlled trial.

Study duration: 3 years (18 month accrual, 12 month final follow-up, 6 month analysis and writing). Participants will be followed for one year from the time of bone graft.

Sample size: 50 (25 per treatment group).

Number of study sites: 11 core sites.

Principal Inclusion criteria: Patients 18-65 years old with an open diaphyseal tibia fracture with a circumferential bone defect of at least one centimeter in length compromising at least 50% of the circumference of the bone treated with an intramedullary nail.

Protocol Committee: L Cannada, MD, P Tornetta, III MD, M Bosse, MD, D Hak, MD, J Hsu, MD, C Jones, MD, S Morshed, MD, W Obremskey, MD, D Teague, MD, B Sangeorzan, MD, C Sagi, MD.
From the Coordinating Center: E MacKenzie, PhD, R Castillo, PhD, G deLissovoy, PhD, D Scharfstein, ScD, A Carlini, MS, L Reider, MHS.

Assessment of Severe Extremity Wound Bioburden at the Time of Definitive Wound Closure or Coverage: Correlation with Subsequent Post-Closure Deep Wound Infection

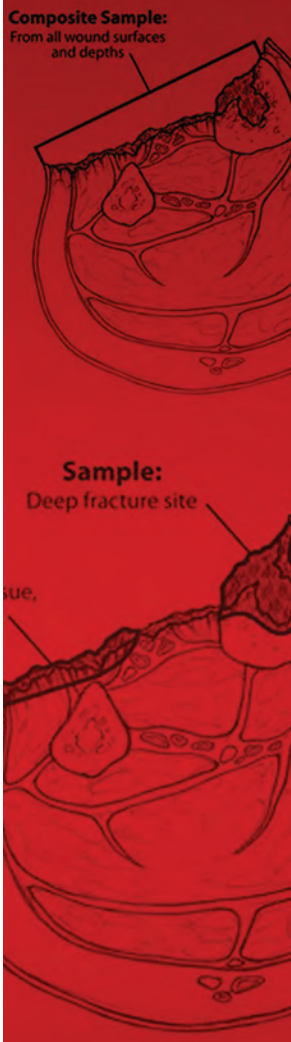
The BIOBURDEN Study

Sponsored by: DOD OETRP
Award Number: W8XWH-09-20108 (METRC 1)
PI/Protocol Chair: Michael Bosse, MD

The primary objective of this study is to characterize the contemporary extremity wound "bioburden" at the time of definitive wound coverage/ closure of severe extremity military and civilian wounds. We will analyze routine tissue samples collected as part of standard care employing both standard tissue culture microbiology and modern polymerase chain reaction (PCR) technologies. PCR analyses throughout this study will utilize the Ibis T5000 Biosensor System.

The BIOBURDEN study is enrolling patients:

- 21 sites approved for enrollment
- 4 sites pending DOD approval
- 4 sites pending local IRB approval
- 5 sites pending IRB submission
- **73 patients enrolled as of 9/1/12**



Secondary objectives of the study are to determine: 1) the correlation of the identified wound pathogens at the time of wound closure/coverage with subsequent deep wound infections; 2) the correlation of the PCR results with those obtained from standard hospital microbiology; and 3) the efficacy, if any, of antibiotics used in the care of the wound.

Study design: Multi-center, prospective cohort study.

Study duration: 3.5 years (2 year enrollment period, 1 year patient follow up and 6 month data analysis period). Participants will be followed for one year after injury.

Sample size: 600.

Number of study sites: 37 core and satellite centers.

Principal Inclusion criteria: All open Type III tibia fractures (plateau, shaft and pilon) requiring a second procedure following fixation, or traumatic transtibial amputations requiring delayed primary closure, skin grafting and/ or flap coverage.

Protocol committee: M Bosse, MD, LCDR J Carney, MD, G Ehrlich, PhD, LCDR, J Forsberg, T Miclau MD, C Murray, MD, A Pollak, MD, G Russell, MD, R Seymour, PhD, CDR J Toledano, MD, J Wenke, PhD, D Wilson, BA, CCRP. From the Coordinating Center: R Castillo, PhD, E MacKenzie, PhD, G deLissovoy, PhD, D Scharfstein, ScD, A Carlini, MS, M Zadnik Newell, ScD, MEd, OTR/L.

Predicting Acute Compartment Syndrome using Optimized Clinical Assessment, Continuous Pressure Monitoring, and Continuous Tissue Oximetry

The PACS Study

Sponsored by: DOD CDMRP
Award Number: W8XWH-10-2-0090 (METRC 2)
Co-PIs/Protocol Co-Chairs: Andrew Schmidt, MD and Michael Shuler, MD

The long-term objective of this research is to develop a tool that can aid clinicians in making a timely and accurate diagnosis of acute compartment syndrome (ACS) so that early fasciotomy can be done and unnecessary fasciotomy avoided. The immediate objective is to develop a model that accurately predicts the likelihood of ACS based on data available to the clinician within the first 48-72 hours of injury. Such data will include specific clinical findings, physiologic monitoring using muscle oxygenation measured with near-infrared spectroscopy (NIRS), continuous monitoring of intramuscular pressure (IMP) and perfusion pressure (PP), and serum markers of muscle injury (CPK levels).

The Master Protocol has been approved by the JHBSPH IRB and by DOD. Core and satellite centers are in the process of submitting the PACS protocol to their local IRB and DOD for approval:

- 5 sites approved to enroll
- 1 site pending DOD submission
- 2 sites pending local IRB approval
- 3 sites pending local IRB submission

Study design: Multicenter, prospective cohort study.

Study duration: 32 months (6 month planning, 6 month accrual, 6 month final follow-up, 8 month analysis and writing). Participants will be followed for six months after injury.

Principal Inclusion Criteria: Closed or open (Gustilo Type I, II or IIIA) tibial shaft or tibial plateau fractures, or severe soft tissue injuries or crush injuries to the lower leg resulting from a high-energy mechanism or gunshot wound.

Sample size: 200.

Number of study sites: 10 core sites.

Protocol committee: A Schmidt, MD, M Shuler, MD, M Bosse, MD, J Evans, MD, R Hayda, MD, R O'Toole, MD, T Walters, MD, J.R. Westberg.
From the Coordinating Center: E MacKenzie, PhD, R Castillo, PhD, G deLissovoy, PhD, D Scharfstein, ScD, A Carlini, MS, K Frey RN, MPH.

Outcomes Following Severe Distal Tibia, Ankle and/or Foot Trauma: Comparison of Limb Salvage vs. Transtibial Amputation Protocol

The OUTLET Study

Sponsored by: DOD CDMRP
Award Number: W8XWH-10-2-0090 (METRC 2)
PI/Protocol Chair: Michael Bosse, MD

The purpose of this study is to compare 18 month functional outcomes and health related quality of life (HRQoL) of patients undergoing salvage versus amputation following severe distal tibia, ankle and/or foot injuries with major soft tissue, bone and/or ankle articular surface loss. Functional outcomes and HRQoL will be measured using well established self-reported measures. Secondary objectives of the study are to 1) compare 18 month assessments of physical impairment using objective performance measures of agility, strength/power, speed and balance; and 2) to compare levels of participation that will be evaluated by rate and time to return to major usual activity and participation in light, moderate or vigorous recreational or sports activities.

The OUTLET study is enrolling patients:

- 5 sites approved for enrollment
- 5 sites pending DOD approval
- 7 sites pending local IRB approval
- 17 sites pending IRB submission
- **6 patients enrolled as of 9/1/12**

Study design: Multi-center, prospective longitudinal observational study.

Study duration: 51 months (30 month enrollment period, 18 month patient follow up and 3 month data analysis period).

Sample size: 464

Number of study sites: 34 core and satellite centers.

Principal Inclusion criteria: Patients with either (1) Gustilo type III distal tibia and foot or ankle fractures with fracture pattern consistent with one of OTA codes: 43B1.3, 43B2-B3, 43C, 44B, 44C, 81B2-B3, 82B, and 82C; (2) open or closed industrial foot crush injuries; or (3) open or closed foot blast injuries.

Protocol committee: M Bosse, MD, L Cannada, MD, W Gordon MD, C Jones, MD, G Klute, PhD, T Miclau, MD, S Morshed, MD, W Racette CPO, B Sangeorzan, MD, R Seymour, PhD, B Steverson RN, MHA, CCRP, R Teasdall, MD, CDR, J Toledano, M.D, J Wenke, PhD.
From the Coordinating Center: E MacKenzie PhD, R Castillo, PhD, G deLissovoy, PhD, D Scharfstein, ScD, A Carlini, MS, L Reider, MHS.

Comparison of Transtibial Amputation with and without a Tibia-Fibula Synostosis

The TAOS Study

Sponsored by: DOD CDMRP
Award Number: W8XWH-10-0090 (METRC 2)
Principal Investigator/Protocol Chair: Michael Bosse, MD

The TAOS protocol is pending approval from the JHSPH IRB.

Target date for enrollment is October, 2012.

The primary objective of this study is to compare levels of impairment and functional outcomes for patients undergoing a transtibial amputation and randomized to receive an end-bearing tibia-fibula synostosis (Ertl procedure) versus a standard posterior flap procedure (Burgess procedure). Secondary objectives of this study are to: 1) compare the fit and the alignment of the prosthesis together with levels of comfort and satisfaction; and 2) compare rates of re-hospitalizations for complications, resource utilization, and overall treatment costs for patients undergoing a below the knee amputation who are randomized to receive an end-bearing tibia-fibula synostosis versus a standard posterior flap procedure.

Study design: Multi-center, prospective phase III randomized clinical trial.

Study duration: 51 months (30 month enrollment period, 18 month patient follow up and 3 month data analysis period). Participants will be followed for 18 months after injury.

Sample size: 250 (125 per arm).

Number of study sites: Up to 35 core and satellite centers.

Principal Inclusion criteria: Transtibial amputation regardless of underlying injury.

Protocol committee: M Bosse, MD, L Cannada, MD, W Ertl, MD,W Gordon, MD, C Jones, MD, G Klute, PhD, T Miclau, MD, S Morshed, MD, W Racette CPO, B Sangeorzan, MD, R Seymour, PhD, B Steverson RN, MHA, CCRP, R Teasdall, MD, CDR, J Toledano, MD, J Wenke, PhD.
From the Coordinating Center: E MacKenzie PhD, R Castillo, PhD, G deLissovoy, PhD, D Scharfstein ScD, A Carlini, MS, L Reider, MHS.

Improving Pain Management in High Energy Orthopedic Trauma:

The PAIN Study

Sponsored by: DOD CDMRP
Award Number: W8XWH-10-2-0090 (METRC 2)
PI/Protocol Co-Chairs: Renan C. Castillo, PhD and Srinivasa N. Raja, MD

The protocol for the PAIN study has been approved by the FDA. The protocol is currently pending approval from the JHBSPH IRB.

Target date for enrollment is December, 2012.

The objective of this study is to definitively resolve questions regarding the use of multimodal pharmacologic pain management for orthopedic trauma patients in the context of a multicenter, randomized clinical trial. We will test whether adjunctive analgesic therapy during the pre and peri-operative period, in addition to standard of care pain management, can improve overall pain control and pain related outcomes without increasing analgesic related side effects. Participants will be randomized into three groups: (Group 1) standard pain management plus up to two weeks of oral placebo, plus intravenous and oral placebo for 48 hours at each surgical procedure; (Group 2) standard pain management plus up to two weeks of oral non-steroidal anti-inflammatory drugs (meloxicam) plus intravenous ketorolac and oral placebo for 48 hours at each surgical procedure; or (Group 3) standard pain management plus up to two weeks of oral pregabalin, plus intravenous placebo and oral pregabalin for 48 hours at each surgical procedure.. Patients will be followed for 12 months to study readmissions for complications, and to assess pain, functional outcome, and medical costs. Our overall hypothesis is that perioperative pain management will result in improved pain control, shorter hospital stays, and lower opioid consumption, but have equivalent levels of complications as standard of care pain management.

Study design: Three-arm, double blind, randomized, placebo controlled Phase III clinical trial.

Study duration: 4 years (12 month planning, 18 month accrual, 12 month final follow-up, 3 month analysis and writing). Participants will be followed for one year from the time of definitive treatment.

Principal Inclusion Criteria: Isolated, unilateral, Grade I &II open or closed pilon (distal tibial plafond) or calcaneus fractures requiring operative treatment with fixation.

Sample size: 450 (150 per arm).

Number of study sites: Between 25 and 35 core and satellite sites.

Protocol Committee: S Raja, MD, D Anderson, PhD, K Archer, PhD, MAJ B Goff, DO, A Gottschalk, MD, PhD, D Hak, MD, T Higgins, MD, M Holden, C Jones, MD, L Marsh, MD, R O'Toole, MD, G Russell, MD, B Sangeorzan, MD, P Tornetta, MD, H Vallier, MD, S Wegener, PhD.
From the Coordinating Center: R Castillo PhD, E MacKenzie PhD, G deLissovoy, PhD, D Scharfstein ScD, A Carlini, MS, K Frey RN, MPH.

Improving Activity and Quality of Life Following Lower Extremity Trauma: The Trauma Collaborative Care Study

The TCCS

Sponsored by: DOD CDMRP
Award Number: W8XWH-10-2-0090 (METRC 2)
Protocol Co-Chairs: Stephen Wegener, PhD and Ellen MacKenzie, PhD

The TCCS protocol has been approved by the Steering Committee.

Target date for JHBSPH IRB submission is September, 2012.

Target date for enrollment is March, 2013.

The overall objective of this study is to develop and evaluate the effectiveness of the Trauma Collaborative Care (TCC) in improving outcomes following major extremity trauma. The TCC intervention has three multi-modal components: 1) the Trauma Survivors Network (TSN) – an integrated approach to provide efficient access to information, peer support, and self-management training; 2) training of providers to promote patient use of TSN Program services and use of clinical guidelines for the management of psychological co-morbidities and; 3) the use of a 'Recovery Coach' to motivate use of services and promote communication between providers and patients. Primary outcomes include: patient reported assessments of function, depression and post traumatic stress (PTSD). The study will be powered on a binary composite measure of these three patient oriented outcomes. Secondary outcomes include pain, health related quality of life, and return to usual major activity, and the intermediate outcome measures is self-efficacy. Following a baseline assessment during the index hospitalization, all outcomes will be measured at 6 and 12 months following injury.

Study design: Multicenter cluster design.

Study duration: 4 years (18 month planning, 12 months developing TCCI, 12 month accrual, 12 month final follow-up, 6 month analysis and writing). Participants will be followed for one year from the time of injury.

Principal Inclusion Criteria: Ages 18 – 60 years inclusive, Patients treated surgically for one or more orthopaedic injuries with initial admission to the trauma service of the participating hospital and a length of stay >=5 days or >= 3 days with planned readmission for additional procedures

Sample size: 900 (450 per arm).

Number of study sites: 12 core sites.

Protocol Committee: S Wegener, PhD, M Bosse, MD, R Crichlow, MD, R Hymes, MD, C Jones, MD, D Sietsema, PhD, RN, H Vallier, MD. From the Coordinating Center: E MacKenzie, PhD, R Castillo, PhD, A Bradford, PhD, C Boult, MD, G deLissovoy, PhD, D Scharfstein ScD, A Carlini, MS, K Frey RN, MPH.

Supplemental Perioperative Oxygen to Reduce Surgical Site Infection After High Energy Fracture Surgery

The Oxygen Study

Sponsored by: DOD CDMRP PRORP
Award Number: W8XWH-09-20108
PI/Protocol Chair: Robert V. O'Toole, MD MSME

The protocol for this study is currently being developed.

The overall goal of this study is to to assess the efficacy of Supplemental Perioperative Oxygen in the prevention of surgical site infections. Supplemental Perioperative Oxygen is a low cost and readily available technology that could be easily disseminated to trauma centers across the country. A pilot study completed at the PI's institution yielded very provocative results with a 46 % reduction in surgical site infection in the high dose oxygen group. This effect was consistent across varying types of fractures. The results of the proposed trial have the potential to significantly reduce the incidence of infection after orthopedic trauma and make a major impact on the care of wounded soldiers and civilians.

Study design: Phase III clinical trial.

Study duration: 3 years (6 month start up, 18 months of recruitment, 6 months follow up, 6 months analysis and writing)

Sample size: 800 (400 per arm).

Number of study sites: 27 core and satellite centers.

Principal Inclusion criteria: High-energy tibial plateau, pilon and calcaneous fractures treated operatively with pate and screw fixation.

Protocol committee: To be determined.

A Prospective Randomized Trial to Assess PO versus IV Antibiotics for the Treatment of Early Post-op Wound Infection after Plate Fixation of Extremity Fractures

The POvIV Study

Sponsored by: DOD CDMRP PRORP
Award Number: W81XWH-10-2-0133
PI/Protocol Chair: William T. Obremskey, MD, MPH

Patients with post-operative infections routinely receive up to six weeks of intravenous antibiotic therapy following surgical debridement. However, a growing evidence base suggests oral antibiotic therapy is equally effective, results in a reduced risk of complications, and lowers medical costs. The equivalence of oral versus intravenous therapy to treat wound infection after plate fixation of extremity fractures has not been definitively established in a randomized clinical trial. Given the cost and risks associated with outpatient intravenous antibiotic therapy, and in light of the data on bioavailability, joint and bone penetration, and efficacy of oral antibiotics, this randomized clinical trial comparing the two treatment approaches will add greatly to the body of knowledge in treating these difficult infections. The trial's primary hypothesis is that the efficacy of oral antibiotic therapy (PO) is not inferior to intravenous antibiotic therapy (IV) for the treatment of infection after fracture plate internal fixation

The Master Protocol has been approved by the JHBSPH IRB and by the DOD. Core and satellite centers are in the process of submitting the protocol to their local IRB and DOD for approval. This study is being initially rolled out in 5 sites:

- 0 sites approved for enrollment
- 4 sites pending DOD approval
- 1 site pending local IRB approval
- 30 sites pending IRB submission

Study design: Phase III randomized controlled clinical trial.

Study duration: 4 years (6 month planning, 24 month accrual, 12 month follow-up, 6 month analysis and writing). Participants will be followed for 12 months following diagnosis of infection.

Sample size: 600 (300 per arm).

Number of study sites: 35 core and satellite sites.

Principal Inclusion criteria: Patients with long bone fractures (femurs, tibias, fibulas of the legs, and humeri, radii, ulnas of the arms) treated with a plate that will be retained until union, and diagnosed with a wound infection within six weeks of definitive fixation.

Protocol committee: W Obremskey, MD, MPH, J Anglen, MD, K Archer, PhD, DPT, M Bosse, MD, M Fleming, MD, M Holden, CDR J Keeling, MD, T Miclau, MD, S Morshed, MD, MPH, LTC C Murray, MD, A Schmidt, MD, T Talbot, MD, MPH, P Tornetta, III, MD, H Vallier, MD.
From the Coordinating Center: R Castillo PhD, E MacKenzie PhD, G deLissovoy, PhD, D Scharfstein ScD, A Carlini, MS, M Zadnik Newell, ScD, MEd, OTR/L.

Novel Therapy to Reduce Infection after Operative Treatment of Fractures at High Risk of Infection: A Multicenter Randomized Controlled Trial

The APS Study

Sponsored by: DOD CDMRP PRORP
Award Number: W81XWH-10-2-0134
PI/Protocol Chair: Robert O'Toole, MD

The APS study was submitted to the FDA for review on June 25, 2012.

Target date for JHBSPH IRB submission is October, 2012.

Target date for enrollment is December, 2012.

The treatment of high-energy military fractures continues to result in poor outcomes and be associated with high rates of infection. Local antibiotic delivery systems associated with fracture hardware have the potential to reduce complications by lowering infection rates in these patients. Although there is strong theoretical and animal study data as well as some promising preliminary clinical data regarding the use of local antibiotics to reduce infection, it is not yet clear that Antibacterial Plate Sleeves will perform better than treatment without Antibacterial Plate Sleeves in a rigorous head-to-head clinical trial. Our hypothesis is that the use of Antibacterial Plate Sleeves for fractures at high risk for infection will reduce infection rates and therefore improve outcomes compared to standard treatment. The results of this trial have potential to reduce surgical site infection in both the military and civilian patients, and improve patient outcomes from these potentially devastating injuries.

Study design: Phase III randomized controlled multicenter trial.

Study duration: 4 years (12 months planning and regulatory approval, 18 month accrual, 12 month final follow-up, 6 month analysis and writing). Participants will be followed for 12 months.

Sample size: 800 (400 per arm).

Number of study sites: 25-35 core and satellite sites.

Principal Inclusion criteria: Tibial plateau and pilon fractures initially treated in a staged fashion and then treated definitively with plate and screw fixation more than 5 days later after swelling has resolved; and calcaneus fractures initially treated in a splint or with limited percutaneous fixation or both, and then definitively more than 5 days later with plate and screw fixation after swelling has resolved.

Protocol committee: R O'Toole, MD, D Chan, MD, M Graves, MD, D J Hak, MD, MBA, LTC J Hsu, MD, M Joshi, MD, J Langford, MD, H Mir, MD, N Rao, MD, Z Roberts, MD, D Sietsema, PhD, RN, D Tsukayama, MD, D Wilson, BA, CCRP.
From the Coordinating Center: R Castillo PhD, E MacKenzie PhD, G deLissovoy, PhD, D Scharfstein ScD, A Carlini, MS, M Zadnik Newell, ScD, MEd, OTR/L.

Multicenter Investigation of the Mechanical Determinants of Post-Traumatic Osteoarthritis

The PTOA Study

Sponsored by: National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
Award Number: 1R21AR061808-01
PI/Protocol Co-Chairs: Lawrence Marsh, MD and Donald D Anderson, PHD

The PTOA study has been designed to be carried out as part of the PAIN protocol. The PTOA/PAIN study has been approved by the FDA. The protocol is currently pending approval from the JHBSPH IRB.

Target date for enrollment is September, 2012.

A growing body of evidence supports the theory that the intensity of the original joint trauma (injury severity) is one of the most important factors contributing to post-traumatic osteoarthritis (PTOA). Colleagues at University of Iowa have developed techniques to measure the fracture severity and validated them in surrogate bone specimens, cadavers, and in an initial patient series. The severity metric correlates strongly with PTOA development. In this multi-center pilot and feasibility study, we will eliminate an important barrier to improving treatment of articular fractures and subsequently decreasing the burden of PTOA. Mechanical metrics of acute injury severity and of contact stress challenge will be further validated, and extended to a large and geographically diverse group of patients with tibial pilon fractures treated using a range of current techniques. Making these techniques widely available for clinical research will help lay the foundation for the development of the next generation of treatment strategies for the prevention of PTOA.

Study design: Multi-center, prospective cohort study.

Study duration: 45 months (9 month planning, 18 month accrual, 18 month final follow-up, 6 month analysis and writing). Participants will be followed for one year from the time of definitive treatment.

Sample size: 150.

Number of study sites: Between 25 and 35 core and satellite sites.

Principal Inclusion criteria: Isolated pilon (distal tibial platform) fractures requiring operative treatment with fixation at the discretion of the treating surgeon.

Protocol committee: S Raja, MD, D Anderson, PhD, K Archer, PhD, MAJ B Goff, DO, A Gottschalk, MD, PhD, D Hak, MD, T Higgins, MD, M Holden, C Jones, MD, L Marsh, MD, R O'Toole, MD, G Russell, MD, B Sangeorzan, MD, P Tornetta, MD, H Vallier, MD, S Wegener, PhD.
From the Coordinating Center: R Castillo PhD, E MacKenzie PhD, G deLissovoy, PhD, D Scharfstein ScD, A Carlini, MS, K Frey RN, MPH.

Patient Response to an Integrated Orthotic and Rehabilitation Initiative for Traumatic Injuries

The PRIORITI-MIL Study

Sponsored by: DOD CRMRP/TATRC
Award Number: W81XWH-12-2-0032
Co-PI/Protocol Chair: LTC Joe Hsu, MD and Ellen MacKenzie, PhD

The protocol for this study is currently being developed.

The objective of this study is to examine the benefits of an integrated orthotic and rehabilitation program that incorporates the Intrepid Dynamic Exoskeletal Orthosis (IDEO) with a rigorous physical therapy regimen, but designed for scalability in the military environment. Specifically, the Patient Response to an Integrated Orthotic and Rehabilitation Initiative for Traumatic Injuries (PRIORITI–MIL) program will build on the principles of the program developed by the Center for the Intrepid (CFI) described above with two fundamental differences. First, the IDEO will be centrally fabricated at one facility and individually fitted by orthotists on staff at the military treatment facilities. Second, service members will undergo scheduled evaluations of physical performance measures and health outcome measures to compare function and well being before and after the intervention. We hypothesize that the PRIORITI program will be associated with improvements in short-term and long-term functional performance and patient reported measures of outcome and quality of life.

Study design: Multicenter before-after program evaluation where participants serve as their own controls.

Study duration: 3 years (6 month planning, 12 month accrual, 12 month final follow-up, 6 month analysis and writing).

Sample size: 85 Participants.

Number of study sites: 3 Military centers.

Principal Inclusion criteria: Patients who are currently two or more years out from a traumatic unilateral lower extremity injury below the knee at or below the knee, who are able to bear weight and who have chronic muscle weakness and/or limited range of motion at the ankle that translates into functional deficits that interfere with daily activities and overall quality of life.

Protocol committee: LTC J Hsu, MD, M Bosse, MD, D Dromsky, MD, W Gordon, MD,
From the Coordinating Center: E MacKenzie PhD, R Castillo PhD, G deLissovoy, PhD, D Scharfstein ScD, A Carlini, MS, M Zadnik Newell ScD, MEd, OTR/L.

Funding Sources

The activities of METRC are currently funded exclusively by federal grants. Core funding for METRC is provided through the Orthopaedic Extremity Trauma Research Program (OETRP) (Award # W81XWH-09-2-0108) (METRC 1) and a cooperative agreement with the DOD Peer Reviewed Orthopaedic Research Program (PRORP) of the Congressionally Directed Medical Research Program (CDMRP) (Award # W81XWH-10-2-0090) (METRC 2). These awards provide funding for specific studies and support the infrastructure of the Consortium. Four of our METRC Investigators have successfully obtained individual grants that use the METRC consortium as a foundation for the research. These individuals are the prime recipients of the awards (three from DOD CDMRP, one from NIH NIAMS and one from Clinical and Rehabilitative Medicine Research Program (CRMRP) but they subcontract with the Coordinating Center to help with the design, implementation, and analysis of the studies. These subcontracts also provide funding to support the participation of METRC Centers in the study. A summary of these awards (total amounts) is provided to the right.

Overview of 6-Year Budget - METRC Coodinating Center

	METRC 1	METRC 2	UMd PRORP #1	UMd PRORP #2	Vanderbilt University PRORP	University of Iowa R21	CRMRP/ TATRC
Personnel - MCC	3,135,912	4,547,195	309,725	315,964	572,502	57,135	327,180
Non Personnel Costs	674,127	1,522,474	52,522	61,267	43,362	2,353,752	75,732
Equipment and Major Supplies	375,000	2,941,858	3,375		85,176		280,000
Core Civilian Centers							
Direct Costs	6,505,639	10,040,449					
Indirect Costs to Centers	2,950,823	4,737,484					
Patient Enrollment Costs	1,755,000	3,296,000	1,440,000*	1,345,000*	1,380,000*	75,000*	
Core MTF Centers							
Direct Costs	2,243,281	1,659,333					1,139,560
Indirect Costs to Centers	446,413	330,207					238,624
Satellite Center Enrollment							
Patient Enrollment Costs	735,000	925,000					
Total Direct Costs	18,821,195	30,000,000	1,805,622	1,722,231	2,081,040	136,195	2,061,096
IDC on the Direct Costs (IDC to JHU)	2,678,425	8,657,995	117,731	233,883	225,736	87,165	438,904
Total Award	21,499,620	38,657,995	1,923,353	1,956,114	2,306,775	223,360	2,500,000

**These amounts may be used to support patient enrollment in either cores, military training facilities or satellite centers*

Looking Forward

Next year will be a busy one for METRC. All currently funded projects will be in the field and we will begin to realize the full potential of the Consortium. In addition to assuring that studies are rolled out in a timely manner, we will focus attention on the following activities:

- We will continue to monitor sites to ensure high quality data and compliance with regulatory requirements;
- We will publish all active METRC trial protocols in appropriate open access, peer-reviewed, online journals;
- The METRC registry will be expanded to include nerve injuries and other injuries of interest not currently included in the registry;
- The public face of the website will be enhanced to provide resources for study participants and their families, including educational materials, links to appropriate web resources, and research updates.
- Practice Surveys relevant to study questions under investigation will be distributed to all METRC investigators and their partners. The primary goal of these Practice Surveys is to document variation in knowledge, beliefs, and practices among orthopaedic trauma surgeons in the United States. A secondary goal is to prospectively assess the impact of METRC research projects on clinical practice.

We continue to cultivate new research ideas that address the priorities of the DOD and the Consortium. Currently under discussion are studies to:

- ✔ Compare the performance of a new custom energy-storing ankle foot orthosis (AFO), the Intrepid Dynamic Exoskeletal Orthosis (IDEO) with the standard of care typically received by civilian limb salvage patients (PI: LTC J Hsu, MD);
- ✔ Investigate the effect of local adjuvant antibiotics on wound infection rates in the surgical treatment of high-energy thoracolumbar spine fractures and dislocations) (PI: J Patt, MD, MPH);
- ✔ Evaluate the safety and efficacy of an antibiotic-loaded chitosan sponge delivery system used adjunctively for the prevention of infections in open fractures and severe extremity wounds (PI: M Bosse, MD);
- ✔ Use METRC as a platform for assessing the reliability and responsiveness of the Patient-Reported Outcomes Measurement Information System (PROMIS®) for measuring outcomes following orthopaedic trauma (PI: R Castillo, PhD).

Please continue to continue to check our website www.metrc.org to monitor the progress of our activities.

Appendix A

Participating Centers

MILITARY TREATMENT FACILITIES

San Antonio Military Medical Center, BAM
Principal Investigator: LTC Joseph R. Hsu, MD

Walter Reed National Military Medical Center, WRD
Principal Investigator: LTC Wade T. Gordon, MD

Naval Medical Center Portsmouth, NPM
Principal Investigator: LCDR Robert Gaines, MD

Naval Medical Center San Diego, NSD
Principal Investigator: CDR James E. Toledano, MD, MC, USN

CORE CIVILIAN SITES

Boston Medical Center, BMC
Principal Investigator: Paul Tornetta, III, MD

Carolinas Medical Center, CMC
Principal Investigator & Chair of the METRC Consortium: Michael J. Bosse, MD

Denver Health and Hospital Authority, DHA
Principal Investigator: David J. Hak, MD, MBA

Florida Orthopaedic Institute / Tampa General & St. Joseph's Hospitals, FOI
Principal Investigator: Roy W. Sanders, MD

Hennepin County Medical Center / Regions Hospital, MIN
Principal Investigators: Andrew H. Schmidt, MD & Peter A. Cole, MD

LAC + USC Medical Center, LAC
Principal Investigator: Jackson Lee, MD

MetroHealth Medical Center, MET
Principal Investigator: Heather A. Vallier, MD

Orlando Regional Medical Center, ORL
Principal Investigator: Joshua R. Langford, MD

OrthoIndy / Methodist Hospital, MTH
Principal Investigator: Walter Virkus, MD

Orthopaedic Associates of Michigan / Spectrum Health, SPC
Principal Investigator: Clifford B. Jones, MD

Penn State University M.S. Hershey Medical Center, PSU
Principal Investigator: J. Spence Reid, MD

St. Louis University Hospital, STL
Principal Investigator: Lisa K. Cannada, MD

University of California at San Francisco, USF
Principal Investigator: Theodore Miclau, III, MD

University of Iowa Hospitals & Clinics, UIA
Principal Investigator: J. Lawrence Marsh, MD

University of Maryland R Adams Cowley Shock Trauma Center, UMD
Principal Investigator & Co-Chair of the METRC Consortium: Andrew N. Pollak, MD

University of Miami Ryder Trauma Center, RYD
Principal Investigator: Gregory A. Zych, DO

University of Mississippi Medical Center, UMS
Principal Investigator: Robert A. McGuire, MD

University of Oklahoma Medical Center, UOK
Principal Investigator: David Teague, MD

University of Washington / Harborview Medical Center, UWA
Principal Investigator: Bruce J. Sangeorzan, MD

UT Health: The University of Texas Health Science Center at Houston, HOU
Principal Investigator: Milan K. Sen, MD

Vanderbilt University Medical Center, VMC
Principal Investigator: William T. Obremskey, MD, MPH

Wake Forest University Baptist Medical Center, WFU
Principal Investigator: Robert D. Teasdall, MD

SATELLITE CENTERS

Allegheny General Hospital, AGY
Principal Investigator: Gregory Altman, MD

Barnes-Jewish Hospital at Washington University, BJH
Principal Investigator: William M. Ricci, MD

Duke University Hospital, DUK
Principal Investigator: Robert D. Zura, MD

Emory University, EMU
Principal Investigator: William M. Reisman, MD

Geisinger Health System, GMC
Principal Investigator: Michael Suk, MD, JD, MPH, FACS

Greenville Memorial Hospital, GHS
Principal Investigator: Kyle J. Jeray, MD

Inova Fairfax Hospital, IFH
Principal Investigator: Robert A. Hymes, MD

Louisiana State University Health Sciences Center, SHV
Principal Investigator: Massimo Morandi MD, FACS

Louisiana State University, LSU
Principal Investigator: Peter C. Krause, MD

Medical University of South Carolina, MSC
Principal Investigator: Langdon A. Hartsock, MD

Mission Hospital, ASH
Principal Investigator: Harold M. Frisch, MD

Mountain States Health Alliance, JCM
Principal Investigator: Robert M. Harris, MD

New York University Hospital for Joint Diseases, NYU
Principal Investigator: Kenneth A. Egol, MD

Ohio State University Medical Center, OSU
Principal Investigator: Laura Phieffer, MD

Hospital for Special Surgery & New York Presbyterian Hospital, NYP
Principal Investigator: David L. Helfet, MD

Rhode Island Hospital, Brown University, RIH
Principal Investigator: Roman A. Hayda, MD

Stanford University Medical Center, STN
Principal Investigator: Julius A. Bishop MD

Texas Tech University Health Sciences Center, ELP
Principal Investigator: Amr A. Abdelgawad, MD

University of Kentucky, UKY
Principal Investigator: Brandon T. Bruce, MD

University of Massachusetts Medical Center, UMA
Principal Investigator: Judith A. Siegel, MD

University of Michigan Hospital, UMI
Principal Investigator: James A. Goulet, MD

University of Missouri/University Hospital, UMO
Principal Investigator: Gregory J. Della Rocca, MD, PhD

University of Pennsylvania, PEN
Principal Investigator: Samir Mehta, MD

University of Pittsburgh, PIT
Principal Investigator: Andrew R. Evans, MD

University of Rochester, ROC
Principal Investigator: John T. Gorczyca, MD

University of Texas Health Science Center, San Antonio, SAN
Principal Investigator: Animesh Agarwal, MD

University of Texas Southwestern Medical Center, UTX
Principal Investigator: Adam J. Starr, MD

University of Utah, UUT
Principal Investigator: Thomas F. Higgins, MD

University of Virginia Medical Center, UVA
Principal Investigator: David B. Weiss, MD

York Hospital / WellSpan Health, YRK
Principal Investigator: Thomas DiPasquale, DO, FACOS, FAOAO

Appendix B

Staff of the Coordinating Center

Ellen J. MacKenzie, PhD, Director

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Gregory deLissovoy, PhD, MPH, Principal Economist

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Steve Samudrala, MS, Programmer Analyst

Chanen S. Chavis, BA, Research Assistant

CORE: Protocol Development, Implementation & Monitoring

Lisa Reider, MHS, Director

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Lauren Allen, MA, Study Manager

Susan Collins, MSc, Study Manager

Tara Taylor, MPH, Study Manager

CORE: Administration and Regulatory Affairs

Rachel Holthaus, MS, CIP, Director

Cathy Epstein, Administrative Assistant

Tracy Russo, Financial Manager

Appendix C

Site Participation and Status by Study

Data as of August 31, 2012

Participation Confirmed | NOT Participating | Sites Not Yet Determined

	Registry	pTOG*	FIXIT	BIOBURDEN	POvIV*	PACS*	OUTLET	TCCS*	TAOS*	APS	PAIN	PTOA	Oxygen	PRIORITI_MIL*
CORE Sites														
BMC	ENR	ENR	ENR	ENR										
CMC	ENR	ENR	ENR	ENR	DOD		ENR	LOC						
DHA	ENR	ENR	DOD	PRE		PRE	PRE	LOC						
HCM	ENR		ENR	ENR		ENR	DOD	LOC						
HOU	ENR		ENR	ENR		ENR	ENR	LOC						
LAC	ENR			DOD		PRE								
MET	ENR		ENR	ENR	DOD		LOC	LOC						
MTH	ENR		ENR	ENR			PRE	LOC						
ORL	ENR		ENR	ENR			DOD							
PSU	ENR		ENR	ENR			PRE							
RYD	ENR		ENR	ENR			LOC							
SPC	ENR	ENR	DOD	ENR			LOC	LOC						
STL	ENR	ENR	ENR	LOC			PRE							
TGH	ENR	ENR	ENR	ENR			DOD	LOC						
UIA			DOD	LOC			LOC							
UMD	ENR		ENR	ENR	LOC	DOD	LOC	LOC						
UMN	ENR			ENR										
UMS	ENR		ENR	ENR		ENR	PRE							
UOK	ENR	ENR		ENR			ENR							
USF	ENR	ENR	ENR	ENR	DOD		LOC							
UWA	ENR	ENR		LOC			DOD							
VMC	ENR	ENR	DOD	ENR	DOD	ENR	ENR	LOC						
WFU	ENR		ENR	ENR		LOC	ENR	LOC						
Military Treatment Centers														
BAM	ENR	ENR	ENR	DOD		LOC	ENR							
WRD	DOD		LOC	DOD			PRE							
NPM	DOD		DOD	ENR			PRE							
NSD	DOD		LOC	DOD			PRE							
Satellite Centers														
AGY	**New Satellite Center**													
ASH	**New Satellite Center**													
BJH							PRE							
DUK			DOD	PRE										
ELP			ENR	ENR			ENR							
EMU														
GHS							PRE							
GMC	**New Satellite Center**													
IFH				PRE				LOC						
JCN	**New Satellite Center**													
LSU				ENR										
MSC							PRE							
NYP	**New Satellite Center**													
NYU														
OSU														
PEN							PRE							
PIT							ENR							
RIH				ENR			LOC							
ROC				DOD										
SAN			LOC	LOC										
SHV	**New Satellite Center**													
STN	**New Satellite Center**													
UKY				ENR			PRE							
UMA														
UMI														
UMO							PRE							
UUT				ENR										
UVA							PRE							
UTX	ENR		PRE	PRE										
YRK	**New Satellite Center**													

For participating sites: **PRE** = site is preparing submission to local IRB; **LOC** = Local IRB approval is pending; **DOD** = DOD approval of site is pending; **ENR**= site is approved for enrollment.

* Number of Centers that can participate is restricted: **pTOG** – Study approved for 11 sites; **POvIV** – Study to be initially rolled out at 5 sites; **PACS** – Study approved for 10 sites; **TCCS** – Study approved for 12 sites; **PRIORITI** – Study approved for 3 Military Treatment Facilities.