



Defense Health Program Research & Development Overview: Focus on Clinical & Rehabilitative Medicine & Genitourinary/Lower Abdomen Reconstruction

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Military Health System

- Four areas for continuous quality improvement enabled by Military Health System research and development
 - **Force Readiness**
 - Population Health
 - Quality Health Care
 - Cost Management
- Research and development in the Military Health System is the Department's fundamental and sustaining institutional means to **modernize the practice of military medicine and produce better health outcomes and lifestyles** for the 9.6 million DoD beneficiaries who are entrusted to our care.



**“Our men and women in combat; our wounded warriors; the chronically ill—
these are our priorities
and these Service members and families need our
greatest attention.”**

**Jonathan Woodson, M.D.
Assistant Secretary of Defense for Health Affairs**



Military Health System Strategic Goal

“The integrated Military Health System delivers a coordinated continuum of preventive and curative services to eligible beneficiaries and is accountable for health outcomes and cost while supporting the Services’ warfighter requirements.”

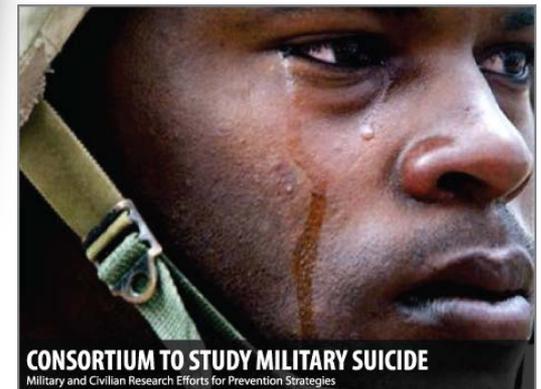
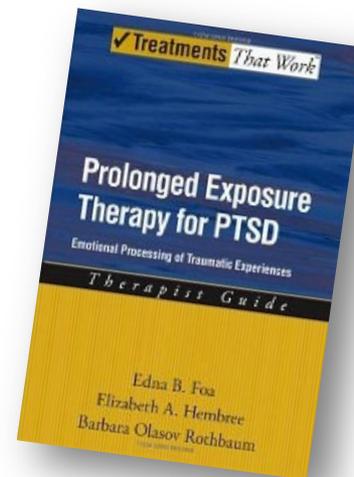


Research Strategy is based on the Continuum of Care Construct



Research & Development Objectives

- **Discover and explore** innovative approaches to protect, support, and advance the health and welfare of military personnel, families, and communities.
- Accelerate the **transition of medical technologies** into deployed products.
- Accelerate the **translation of advances in knowledge into new standards of care** for injury prevention, treatment of casualties, rehabilitation, and training systems that can be applied in theater or in the clinical facilities of the **Military Health System**.

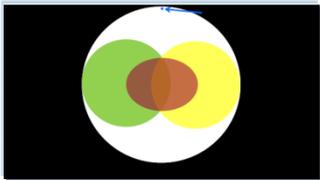




Investment Areas

Clinical & Rehabilitation Medicine

Regenerative Medicine
 Neuromusculoskeletal Injury
 Pain Management
 Sensory System Injury
 Rehabilitation Medicine
 Clinical Medicine
 Wound Management



Health Information Sciences and Medical Training



Combat Casualty Care

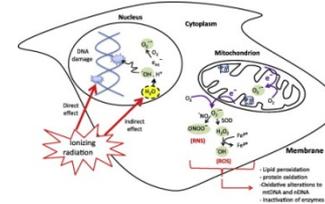
Moderate/Severe/Penetrating TBI
 Hemorrhage Control, Resuscitation and
 Blood Products (DP)
 Extremity Trauma, Tissue Injury,
 Craniomaxillofacial Injury, lung injury,
 and Burns
 EnRoute Care
 Health Monitoring and
 Diagnostic Technology

Military Operational Medicine



Mild Traumatic Brain Injury
 Injury Prevention and Reduction
 Psychological Health and Resilience
 PTSD and Suicide
 Physiological Health Environmental
 Health and Protection

Radiation Health Effects



Diagnostic Biodosimetry
 Countermeasures
 - Protection
 - Treatment

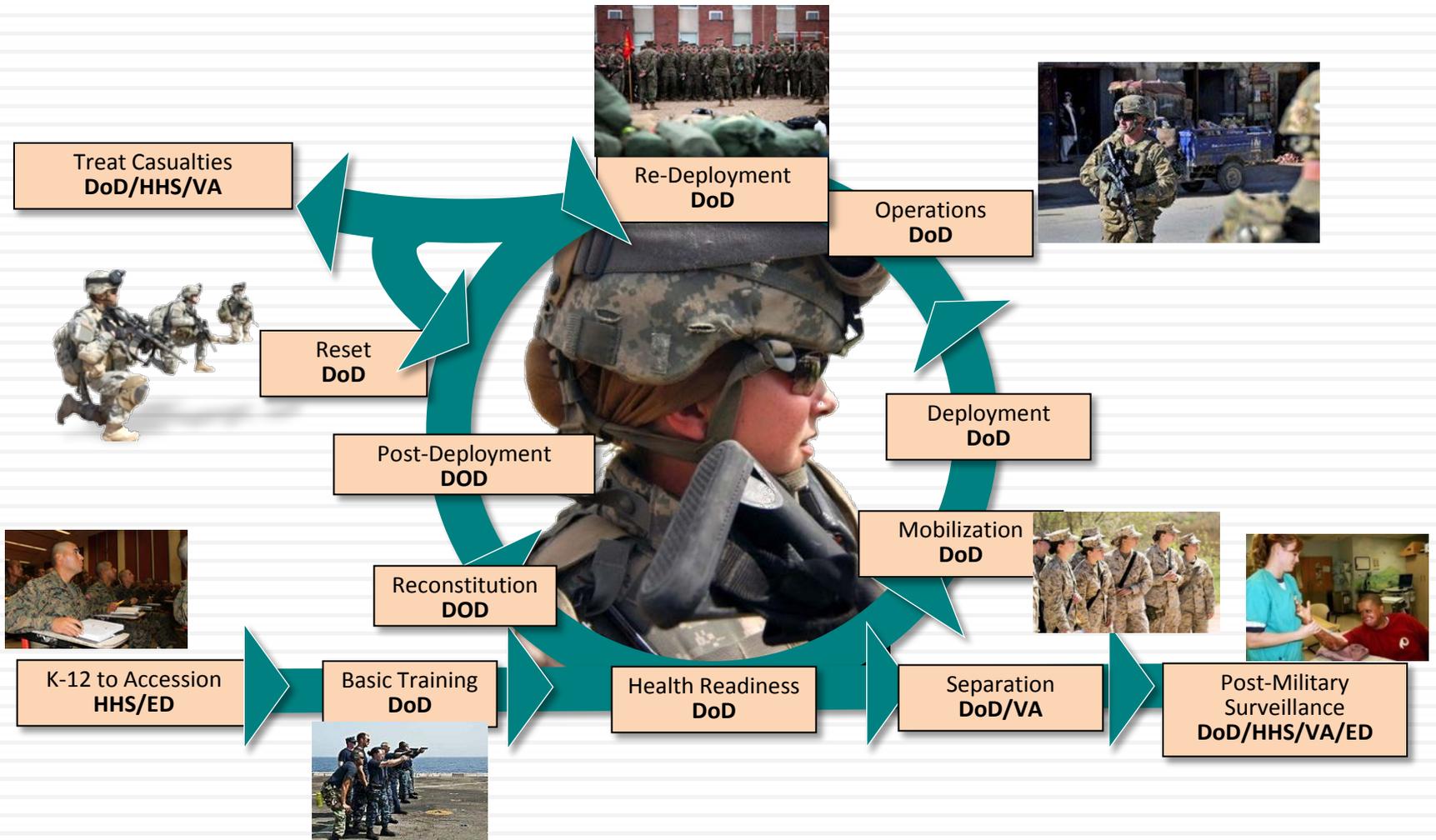
Mobile Health Applications
 Med-Surgical Simulation
 Technologies
 Live tissue replacement
 Skills Retention/Transference
 Re-entry

Infectious Diseases



Wound Infection
 - Prevention
 - Management
 - Treatment
 Pathogen Detection
 HIV Prevention
 H1N1 Diagnostics

Direction & Influences Drive Joint Integrated Planning





Focus Area: Clinical Medicine and Rehabilitation

Regenerative Medicine and Transplants:

- Improve speed of healing and decrease scarring
- Regenerate missing tissue and repair nerve gaps
- Improve functionality and appearance following craniofacial repair
- Develop architecture to integrate created tissue
- Reduce need for tissue rejection therapy
- Improve surgical approaches and limb/tissue function



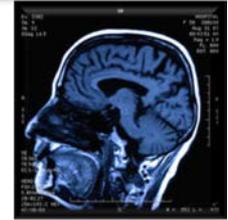
Neuromusculoskeletal Injury: (Incl. Amputee)

- Address psycho-social recovery aspects
- Improve rehabilitation for limb salvage and spinal injury patients
- Exercise and fitness systems and strategies
- Improved orthotics, prosthetics, robotics to improve extremity function
- Incorporate neural interface/feedback



Sensory Systems: (Vision/Hearing/Balance)

- Repair damage to the eye and visual system
- Restore hearing
- Treat tinnitus
- Improve diagnostics
- Rehabilitate TBI-associated sensory dysfunction



Pain Management:

- Strategies for Acute and Chronic Pain Management in Battlefield and resource-limited environments
- Strategies for Acute and Chronic Pain Management in Non-Deployed Settings
- Identification of Pain Generators
- Strategies for Identifying and Addressing Biopsychosocial Aspects of Pain





Focus Area: Regenerative Medicine

- **Extremity Regeneration:** Restoration of form and function to lost or damaged hard and soft tissues of the extremities
- **Craniomaxillofacial Regeneration:** Restoration of form and function to lost or damaged hard and soft tissues of the craniomaxillofacial region
- **Skin Regeneration:** Repair or regeneration of the skin after thermal injury with the aim of healing with subjectively and relatively less scar tissue
- **Composite Tissue Allotransplantation and Immunomodulation:** The transfer of composite tissue that may include skin, muscle, bone and nerve as a "replacement part" for tissues compromised by trauma
- **Genitourinary / Lower Abdominal Reconstruction:** Restoration of form and function to lost or damaged soft tissues of the pelvic and urogenital region



Armed Forces Institute of Regenerative Medicine (AFIRM I)

- **Two consortia working together with the U.S. Army Institute of Surgical Research (~340 scientists / students / technicians)**
 - Wake Forest – Pittsburgh University (WFPC) Consortium
 - Rutgers University – Cleveland Clinic (RCCC) Consortium
 - Over 60 academic institutions or hospitals and 24 industrial partners
 - 114 investigators – 30% of which are clinicians
- **Total 5-yr funding of >\$300M**
 - \$100M US Government funding from DHP, Army, Navy, Air Force, VA, and NIH
 - \$68M Matching funds from state governments and participating universities
 - \$109M in pre-existing research projects directly related to the AFIRM
 - DHP has supplemented more than \$23M for clinical trials since 2008



Strategy: Leverage the S&T investments for translation into Clinical Trials using AFIRM mechanisms



AFIRM II Genitourinary/Lower Abdomen Reconstruction

- Genitourinary and lower abdominal reconstruction efforts should focus on pelvic and urogenital reconstruction.
 - Pelvic reconstruction efforts should focus on promoting technologies that address injury to the anus.
 - Urogenital reconstruction efforts should focus on promoting technologies that address injury to genitalia (penile, scrotal, urethral tissues), perineal tissue, and bladder.



Composite Tissue Transplantation / Immunomodulation

- The limitation of conventional reconstructive treatment for severe injury and lost tissue sustained by a warfighter has prompted research into new treatment protocols
- Transplantation of large tissue units (hands / face) benefits a limited number of service members. The ability to transplant smaller tissue units would increase the potential to address a larger patient population
 - Limitation: Side effects outweigh benefits in younger, relatively healthy patient populations afflicted by traumatic injury
 - Targeted capabilities for Composite Tissue Allotransplantation (military need):
 - Improved prevention and treatment of transplant rejection
 - Optimization of graft function and prolongation of graft survival
 - Reduction or elimination of drug toxicities and adverse effects of anti-rejection therapies through drug minimization and improved tolerance induction



Composite Tissue Transplantation / Immunomodulation

- What is the program status?
 - 7 active projects
 - Highlights: 6 clinical studies funded
 - AFIRM – Hand transplantation clinical demonstration
 - AFIRM – Face transplantation clinical demonstration
 - AFIRM – Tol101 phase I / IIb clinical trial
 - DHP – Face transplantation clinical demonstration
 - DHP - Hand Transplant with belatacept phase I clinical trial
 - DHP – Tolerance induction in hand transplantation clinical demonstration

 - 4 face transplants performed to date, 3 additional patients funded
 - 8 hand transplants performed to date, 12 additional transplants funded

 - DHP Restorative Transplantation Research (RTR) cooperative agreement program announcement released October 3, 2012, \$15M
- Strategy
 - Greater interest in immunomodulation and tolerance induction technologies
 - Transplantation of smaller composite tissue units



Regenerative Medicine Portfolio – Transition Activities

Focus Area	A				B		C		Funds (\$M)	
	TRL 1	TRL 2	TRL 3	TRL 4	TRL 5	TRL 6	TRL 7	TRL 8		TRL 9
Extremity Regeneration		1 2 1	9 1 49	7 4 4 1	1 1	1				AFIRM = 24.6 DHP = <u>82.8</u> Total = 107.4 # projects = 83 % of portfolio = 51
Cranio-maxillofacial Regeneration		1	1 5	4 7 2	1 2	2		1		AFIRM = 17.4 DHP = <u>22.4</u> Total = 39.8 # projects = 26 % of portfolio = 19
Skin Regeneration		2	5 3 2	4 5 3 5	1 3 2 1	2 1 2		2		AFIRM = 28.2 DHP = <u>15.8</u> Total = 44.0 # projects = 43 % of portfolio = 21
Composite Tissue Transplantation / Immunomodulation				1	1	1 1 2				AFIRM = 4.8 DHP = <u>14.0</u> Total = 18.8 # projects = 7 % of portfolio = 9
Genitourinary / Lower Abdominal Reconstruction	<i>Included as a focus area in AFIRM II program</i>									
									Total Effort (\$M) = 210.2	



BACK UP



Dismounted Traumatic Amputees

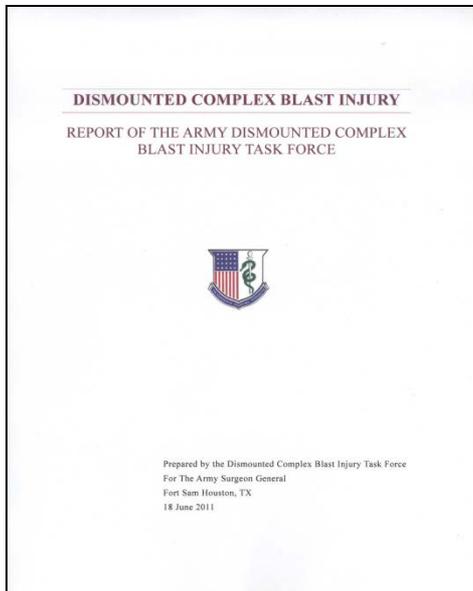
Dismounted Complex Blast Injury (DCBI)

“An injury caused by an explosion, occurring to a Service Member while dismounted in a combat theater that results in amputation of at least one lower extremity at the knee or above, with either amputation or severe injury to the opposite lower limb, combined with pelvic, abdominal, or urogenital injury.”

(Report of the Army Dismounted Complex Blast Injury Task Force, 28 April 2011, page 6)

Non-Dismounted Complex Blast Injury Amputee (Non-DCBI Amputee)

Any Service member who had at least one limb amputation that occurred above the foot or above the hand that was the result of a blast-event experience occurring during ground operations (i.e., not in a vehicle) that did not meet the definition for DCBI.



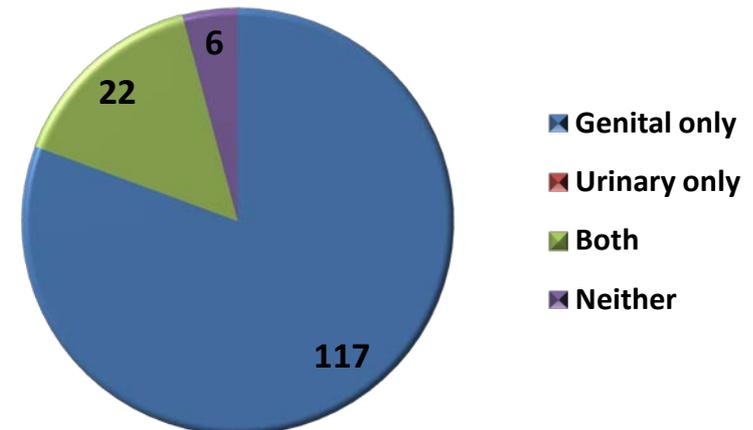
<http://www.armymedicine.army.mil/reports/DCBI>



Dismounted Traumatic Amputees

- DCBI is a relatively infrequent event, with rates between 1 and 8%
- Approximately 58% of all the traumatic amputations for the time period under study (January 1, 2010 to June 1, 2012) fail to meet the criteria for DCBI
- While not meeting the criteria for DCBI, approximately one out of three non-DCBI traumatic amputees sustain a concomitant genital and/or abdominal injury (202 cases reported for the same period)

Frequency of Urinary and Genital injury among those meeting DCBI definition
January 1, 2010, to June 1, 2012
(Urinary injury includes kidney, bladder, and ureter)



Data adapted from presentation by Mary Clouser et al., 2012 MHSRS conference, data extracted from Expeditionary Medical Encounter Database (EMED)