

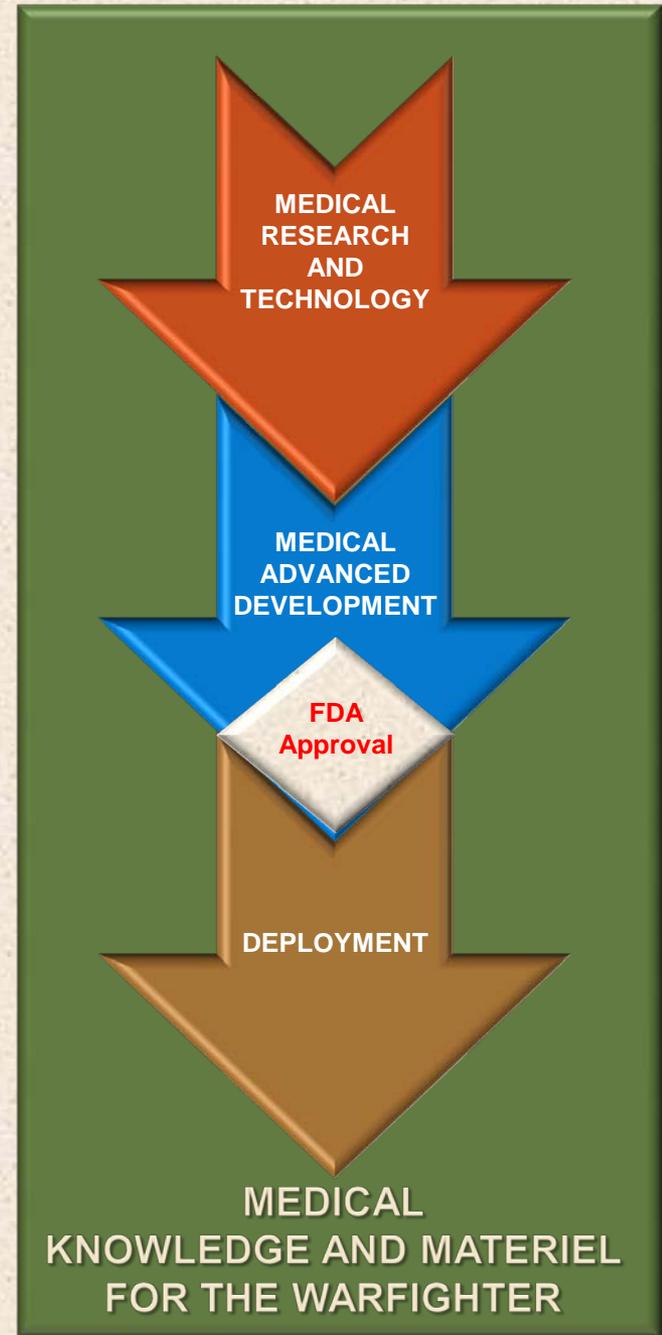


# U.S. ARMY MEDICAL RESEARCH & MATERIEL COMMAND (USAMRMC)

*Presented to*  
*Biomedical Technology Forum*

*By*  
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**Research Program**

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# USAMRMC MILITARY MEDICAL RESEARCH & TECHNOLOGY

## Responds to Threats to Service Member Health and Performance

### Endemic Disease Threats

- Parasitic Diseases
- Bacterial Diseases
- Viral Diseases

### Combat Injuries

- Hemorrhage
- Head Trauma
- Blast Injury

### Chemical/Biological Warfare Threats

- Bacterial Threats
- Viral Threats
- Toxin Threats
- Nerve Agents
- Vesicant Agents
- Blood Agents

### Operational Stressors

- Sleep Deprivation
- Traumatic Stress and Situational Stressors
- Physical Work Load
- Cognitive Burden & Operational Complexity

### Environmental Hazards

- Heat and Cold
- Altitude
- Toxic Industrial Chemicals & Materials

**Difficulties of Medical Command, Control, Communications, Computer, Intelligence, Surveillance and Reconnaissance (C4ISR)**

### Systems Hazards

- Laser
- Blast
- Biomechanical Insults and Stresses
- Noise



# CHANGING SCOPE OF THE MILITARY MEDICAL RDA MISSION

## Joint Battlefield Healthcare & Redeployment Rehabilitation



UNITED STATES ARMY MEDICAL RESEARCH AND MATERIEL COMMAND



Science & Technology Warfighter Performance (34)

### Working Together

- Joint programs
- Service collaboration



### Help Reset the Force



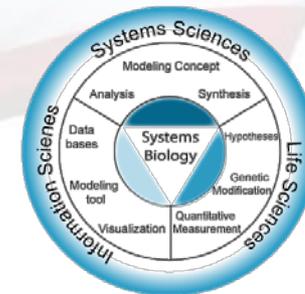
### Contemporary Health Threats

- Blast Injury
- Post Traumatic Stress Disorder (PTSD)
- Traumatic Brain Injury (TBI)
- Restoration and rehabilitation of Wounded Warriors



### Revolutionary Approaches

- Improved laboratory techniques (high performance computing, etc.)
- Systems biology
- Collaborative interdisciplinary research teams



# USAMRMC

## R&T Coordination – Coordinating Offices

(1) Basic Research, (2) Applied Research, and (3) Advanced Technology Development to **prove tech-base concepts** for medical products (drugs, biologics & devices) and information

**CHEMICAL & BIOLOGICAL DEFENSE  
PARTNERSHIP SUPPORT  
DIRECTORATE (PSD)  
LTC Nick Koterski**

**Interface with Defense Threat  
Reduction Agency (DTRA)**

- **Medical Biological Defense  
Research Program (MBDRP)  
Managed by DTRA**

- ▶ Vaccines and pre-treatments
- ▶ Small molecule therapies
- ▶ Next generation diagnostics
- ▶ Animal model development
- ▶ Broad-spectrum therapeutics

- **Medical Chemical Defense Research  
Program (MCCDRP)  
Managed by DTRA**

- ▶ Nerve agent pre-treatments
- ▶ Therapeutics for nerve agents
- ▶ Therapeutics for vesicant injury
- ▶ Diagnostic assays/technologies



Research Funds from DoD

**BLAST INJURY COORDINATING  
OFFICE – Mr. Mike Leggeri**

- **History:**

- ▶ Directed by Congress in FY06 National Defense Authorization Act
- ▶ Established by DoD Directive 6025.21E
- ▶ Secretary of the Army is Executive Agent
- ▶ USAMRMC is program coordinator

- **Mission:**

Coordinate DoD medical research programs focused on the prevention, mitigation, and treatment of blast injuries.

- **Key Accomplishments:**

- ▶ ID knowledge gaps to focus blast injury research programs across DoD, federal agencies, academia, and industry
- ▶ Developed funding requirements
- ▶ Established the Joint Trauma Analysis and Prevention of Injury in Combat (JTAPIC) Program - provides a coordinated approach to improve tactics, techniques, procedures, & materiel solutions to prevent blast injuries
- ▶ Strengthened collaboration between medical researchers and materiel developers to provide improved individual and combat vehicle blast protection systems



Research Funds from Many Sources

**ARMED FORCES INSTITUTE OF  
REGENERATIVE MEDICINE (AFIRM)  
COL Bob Vandre**

- A virtual organization of 27 universities and 230 scientists working with the US Army Institute of Surgical Research under a five-year cooperative agreement
- Expected to make major advances in the ability to understand and control the cellular response in wound repair and organ/tissue regeneration as well as designing and engineering new biomaterial scaffolds to guide the regeneration process
- Expected that this institute will be able to translate some of its technologies into patients within the five-year period

### Example of Tissue Regeneration



Right middle finger during an early stage of regrowth after an August 2005 accident cut off the tip.

After four months of healing.



**Product:** Extract of pig bladder for promoting healing and tissue regeneration.

**PI:** Dr. Stephen Badylak, University of Pittsburgh

Research Funds from Army, Navy, Air Force, NIH, and VA



# AFIRM Mission



- ➕ Discover, develop, and translate regenerative medicine technologies having both near term and far-term translation potential
- ➕ To provide cutting-edge medical capabilities to heal and reset our warriors who have catastrophic traumatic injuries and disabilities



**1. Cranio-Facial Reconstruction**



**2. Healing Without Scarring**



**3. Limb and Digit Salvage and Reconstruction**



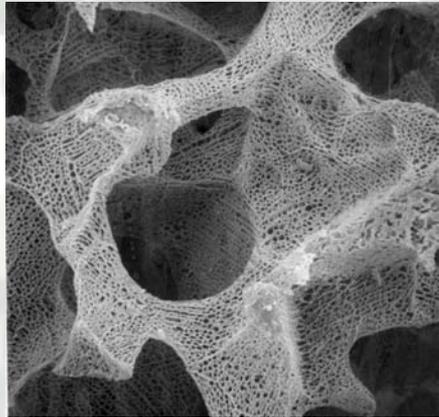
**4. Compartment Syndrome**



**5. Burn Repair**



# Approaches to Regeneration



**Scaffold**

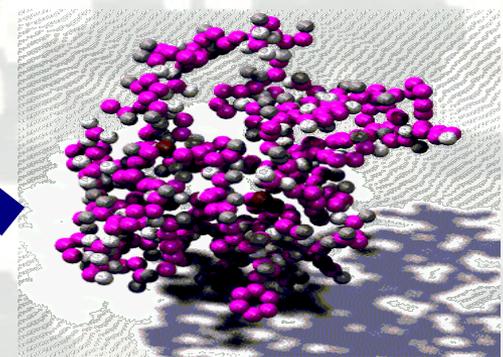


**Cell-based therapy**



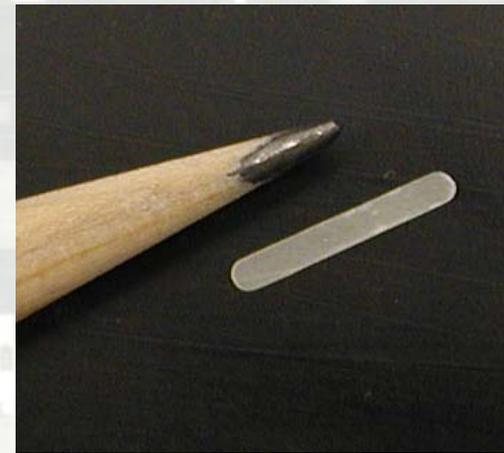
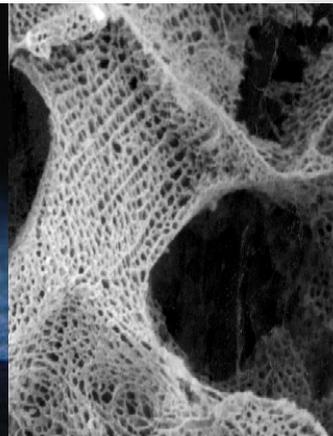
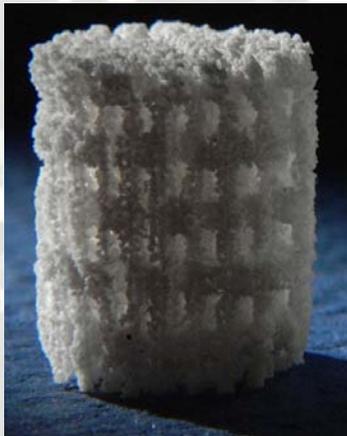
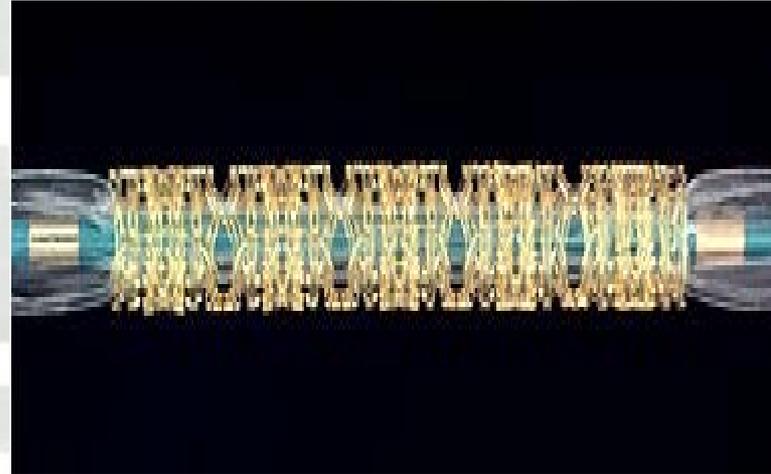
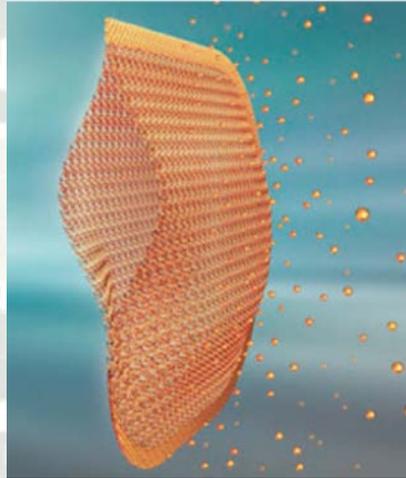
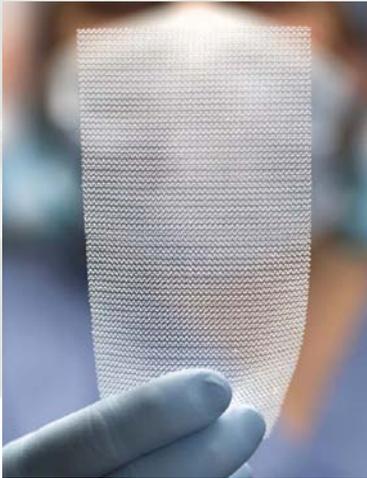
**Cell-Scaffold Hybrid**

**All major scientific approaches to tissue regeneration are utilized in the development of regenerative therapies for the wounded service member**



**Bioactives**

# Representative Technologies: Biomimetic, resorbable tissue scaffolds

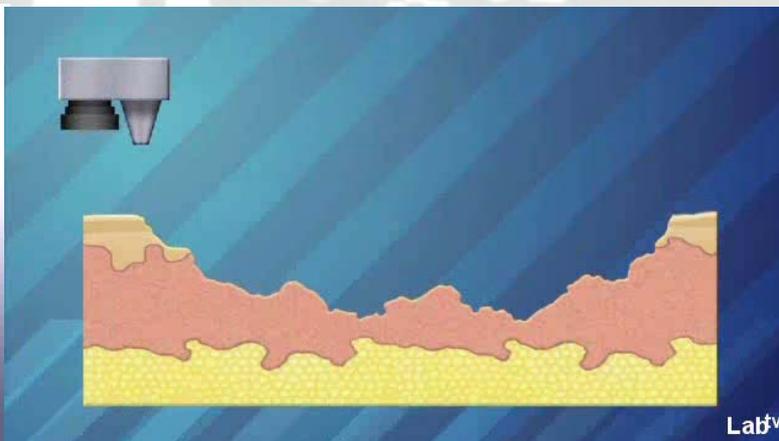
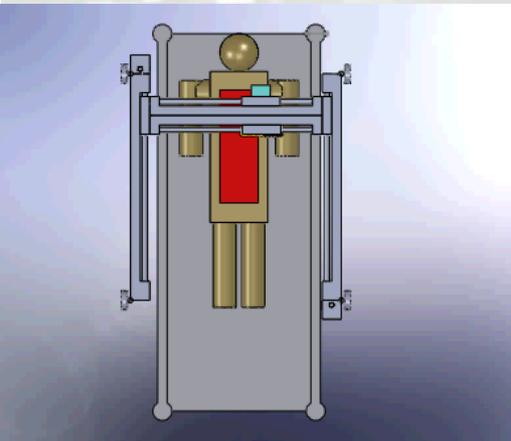


**Nerve, Bone, Other Connective and Soft Tissue**



# Representative Technologies: Skin Printer

- **Goal:** Because severely burned patients need skin and need it fast, development based on ink jet printer technology device to “print” skin directly on burns is underway.
- The system will include a scanner to determine the size and depth of the burn.
- **PI:** James Yoo





# Representative Technologies: Injectable and Implantable Engineered Soft Tissue for Trauma Reconstruction

- **Goal:** Injectable and/or implantable soft tissue substitute resulting in sustained shape and volume over time to provide precise shape of facial features after craniofacial injury.
- Based upon biomaterial scaffolds comprised of silk, collagen, and hyaluronic acids, along with autologous cellular elements.
- First clinical trial will be an initial study on the use of autologous adipose derived stem cells in a lipoaspirate scaffold. During the coming year, we will determine the optimal combination of biomaterials for the clinical therapy
- **PI:** Peter Rubin



**Athymic mice sacrificed 6 weeks after injection with lipoaspirate mixed with GFP labeled ASCs (n=6). Tissues formed subcutaneously were exposed, excised and measured with water displacement method. A. lipoaspirates mixed with  $2 \times 10^6$  ASCs. B. lipoaspirates alone C. Tissues harvested after 6 weeks. Left: lipoaspirates with ASCs, Right: lipoaspirate without ASCs**

# Current AFIRM Clinical Trials

1. Hand transplants (accelerated with Congressional Special Interest funding)
2. Face transplants
3. Use of porcine extracellular matrix to regenerate limb muscle form and function (accelerated with JIEDDO/OTT funding)
4. Engineered Skin Substitute (ESS) to treat >50% TBSA burns
5. Autologous skin cell spraying to treat burn injuries with less scarring (ReCell®)
6. Autologous fat injections to reduce severity of burn scarring (AFT)
7. Skin graft stretching to reduce degree of scarring
8. Segmental nerve gap regeneration using a novel nerve scaffold biomaterial (2010 new start)
9. Safety and efficacy of allogeneic skin substitute for burn coverage (2010 new start)
10. Bandage for Improved healing and scar reduction (2010 new start)

## OTT\* contributions (2010 new starts) to AFIRM investigators

- Autologous skin cell spraying to repair excessive scars
- Nanoscale Ca PO<sub>4</sub> scaffolds for craniomaxillofacial repairs
- Allogeneic Cultured Human Dermal Fibroblasts injections to remodel facial scars

## BTI\*\*

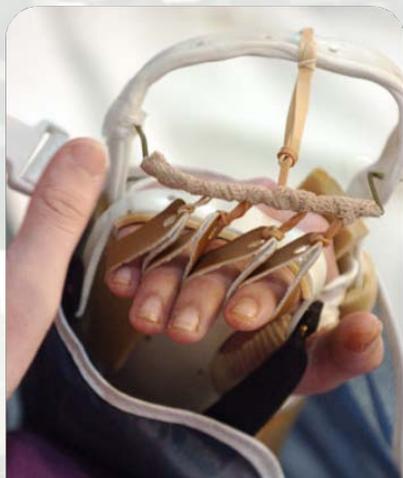
- Autologous Adipose Derived Stem Cells For Soft Tissue Reconstruction After Facial Trauma



# Clinical Trial: Hand Transplantation as a Treatment For Combat Injuries Involving Hand or Forearm Loss



- **Goal:** Protocol for treatment of forearm or hand loss by transplantation with local immunomodulation
- **Status:** Enrollment at approved sites is currently underway
- **PI-** Andy Lee, U. Pitt



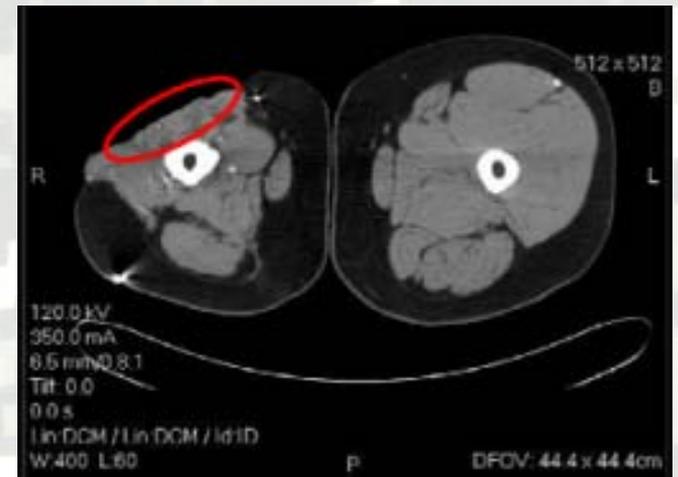


# Muscle Regeneration



**Novel application of extracellular matrix to encourage regeneration of large muscle**  
**PI: S. Badylak, U. Pitt**

**CT scan showing 10% increase in quadriceps mass (red circled area) at 4 months post surgery.**





# ReCell Skin Cell Spray



Courtesy Avita Medical

- A regenerative device that uses patient's own cells to treat burns, wounds and chronic skin defects.
- Goal: FDA approval & the first Class I efficacy data w/ long-term outcome data

PI- J. Holmes,  
Wake Forest and Avita Medical



Avita Medical has received approval from the FDA to begin its US clinical trial for ReCell spray-on skin. The company claims it to be the first regenerative device enabling surgeons to treat burns, wounds and chronic skin defects using the patient's own cells (December 2009 Press Release)

# Engineered Skin for Burn Treatment



**A small sample of a patient's skin is digested and seeded onto a resorbable matrix, then treated to grow into a full thickness sheet of engineered skin.**

**PI: S. Boyce, Cincinnati Children's Hospital**

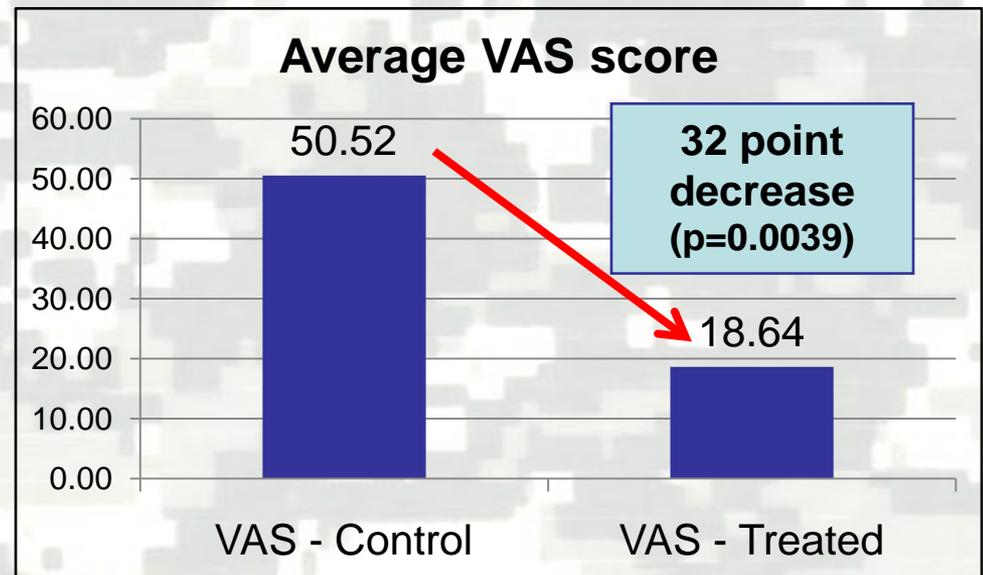


# Skin Bioreactor

- ⊕ PI: Sang-jin Lee
- ⊕ **Goal:** *in vitro* tissue expander system that permits a rapid increase in surface dimensions of donor skin while maintaining tissue viability for subsequent skin transplantation. This system was successfully tested and validated on human skin samples.
- ⊕ Consistently able to double the surface area of donor skin within 2 weeks while maintaining cell viability and showed viable graft take, in animals, when implanted on a recipient dermal bed.
- ⊕ Completed design and built a clinically applicable bioreactor system.
- ⊕ Defined clinical trial strategy.

# A Novel Device to Minimize Cutaneous Scar Formation After Surgery

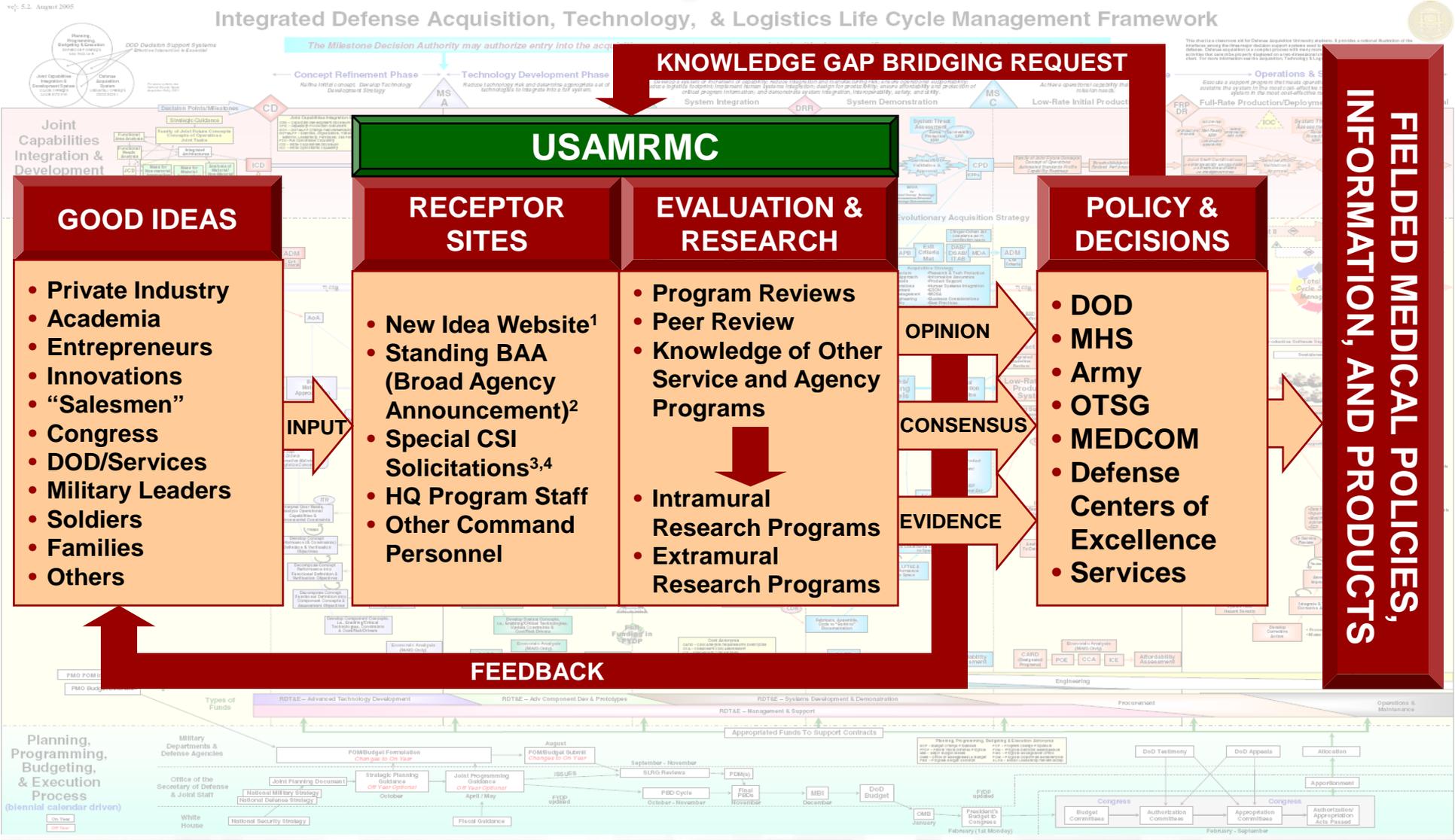
- ➕ Preliminary Pilot trial in humans post-abdominal surgery (n=9) show safety and dramatic efficacy of stress-shielding device



PI- G. Gurtner, Stanford Univ

# USAMRMC Medical R&T Good Ideas to Fielded Medical Policies, Information, and Products

## Integrated Defense Acquisition, Technology, & Logistics Life Cycle Management Framework



### GOOD IDEAS

- Private Industry
- Academia
- Entrepreneurs
- Innovations
- "Salesmen"
- Congress
- DOD/Services
- Military Leaders
- Soldiers
- Families
- Others

INPUT

### RECEPTOR SITES

- New Idea Website<sup>1</sup>
- Standing BAA (Broad Agency Announcement)<sup>2</sup>
- Special CSI Solicitations<sup>3,4</sup>
- HQ Program Staff
- Other Command Personnel

### EVALUATION & RESEARCH

- Program Reviews
- Peer Review
- Knowledge of Other Service and Agency Programs
- Intramural Research Programs
- Extramural Research Programs

OPINION

CONSENSUS

EVIDENCE

### POLICY & DECISIONS

- DOD
- MHS
- Army
- OTSG
- MEDCOM
- Defense Centers of Excellence
- Services

FIELDED MEDICAL POLICIES, INFORMATION, AND PRODUCTS

### FEEDBACK



# Partnership Resources

- √ Clinical and Rehabilitative Medicine Research Program-  
<https://crmrp.amedd.army.mil/>
- √ AFIRM - <http://www.afirm.mil/>
- √ Grants announcements- <http://grants.gov>
- √ Broad Agency Announcements-  
[http://www.usamraa.army.mil/pages/baa\\_forms/User/login.cfm](http://www.usamraa.army.mil/pages/baa_forms/User/login.cfm)
- √ SBIR/STTR- <http://www.acq.osd.mil/osbp/sbir/solicitations/>
- √ Federal contract solicitations- <https://www.fbo.gov/>
- √ Ideas-[http://www.usamraa.army.mil/pages/products\\_ideas/user/login.cfm](http://www.usamraa.army.mil/pages/products_ideas/user/login.cfm)
- √ CDMRP- <http://cdmrp.army.mil/>
- √ TATRC- <http://www.tatrc.org/>

