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Orthopaedic Research Society
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WORKSHOP 8

The Armed Forces Institute of Regenerative Medicine: Its Structure, Operations, and Goals

Organizers:

Michael J. Yaszemski, MD, PhD

Speakers:

Michael J. Yaszemski, MD, PhD

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Translational Bone Regeneration Strategies

George F Muschler, MD, Cleveland, OH

AFIRM is charged with addressing a broad range of challenges facing injured service members. Among these challenges are problems which threaten the salvage of injured limbs, specifically bone defects, nerve defects, muscle and soft tissue defects, vascular injury and deficiency, as well as compromise from burns and scarring.

Segmental defects in long bones represent a particularly challenging clinical problem, particularly in injuries which are incurred in high speed motor vehicle accidents and in the setting of military trauma (high energy projectiles and blast injury). These injuries are almost universally associated with both bone deficiency as well as regional loss of muscle and soft tissue planes, vascular compromise, and scarring resulting from the initial injury and from prior surgical procedures.

Recent advances in bone grafting materials, allografts, ceramic or collagen/ceramic scaffolds, addition of autogenous marrow-derived cells, BMPs, vascularized bone transplantation, and distraction osteogenesis have all been shown to have clinical value in a variety of settings. Each of these modalities have been used in treating complex defects, however, none provide a means of rapid and predictable bone regeneration in the complex bone defects.

AFIRM has established an open network of highly collaborative laboratories devoted to advancing the field of bone grafting in the setting of bone defects. AFIRM has initiated a systematic process for competitive assessment of scaffolds, cell sourcing and processing strategies, growth factor delivery. This effort is designed to provide rapid screening and comparison of available therapeutic options, evaluate combination therapies which have not been systematically assessed clinically, specifically for use in addressing the challenge of large segmental bone defects facing the injured service member and victim of severe trauma.

A staged approach is used. Initial characterization and comparison of materials and strategies is performed in the canine femoral multidefect model, in 10 mm in diameter and 15 mm long cylindrical. Outcome is assessed at 4 weeks both using microCT and histology. Materials and combinations which perform with superior efficacy in this screening model are then advanced for competitive assessment in more stringent settings which incorporate soft tissue defects and regional scarring that better reflect the physiological environment of segmental bone defects.

AFIRM's work is intended to inform surgeons regarding the likely biological value or futility of combined therapy strategies; to guide the development, selection and optimization of strategies for regeneration of bone defects; and bring forward new therapeutic strategies for clinical assessment which are most likely to offer a severely injured service member improved rate of recovery, overall outcomes and successful return to productive life.

Armed Forces Institute of Regenerative Medicine

US Warriors' Burden of Extremity Injuries and Research Directions

Colonel James Ficke, MD, Brooke Army Medical Center

US Armed Forces have faced sustained combat operations for the past 9 years in Afghanistan and Iraq. In relation to over 90% survival rates from war injuries, over 16,000 of our Warriors have sustained injuries of sufficient severity to require evacuation out of the combat zone. During this same period, even greater numbers have sustained non-battle injuries resulting in long term loss of function. While these injuries are due to a variety of mechanisms, over 60% involve the extremities. Furthermore, these injuries account for nearly 70% of direct health care costs, and result in permanent disability. A recent study demonstrated that among a cohort of 1333 battle injuries evacuated, the resource-related cost of this conflict is in excess of one billion dollars over the lifetime of those serving and injured. In fact, six of the ten most common reasons Warriors are medically discharged are related to musculoskeletal injuries. A detailed analysis of these patients with respect to specific diagnoses for basis of unfitness confirmed that the causes are related to orthopaedic injuries in the areas mentioned above in over 70% of individuals, even when evacuated for abdominal or chest injuries. In summary, if the patient survives, their far greatest obstacle to return to a functional life will be their extremity injuries.

The Armed Forces Institute for Regenerative Medicine has a mission to inquiring into these causes, and advancing our current state of science of burn repair; wound healing without scarring; craniofacial reconstruction; as well as specific extremity injuries requiring limb reconstruction, to include regeneration or transplantation; treating the sequelae and prevention of extremity compartment syndromes; and associated muscle or nerve loss. This presentation will address the current burden of extremity war injuries, and the greatest challenges faced by clinicians treating these challenging injuries. These challenges include post traumatic arthritis, segmental bone and soft tissue destruction that includes volumetric muscle loss, extremity infections. Limb salvage programs often lead to extensive and costly treatment with eventual requests for delayed amputation. With the desired endstate to return to optimum function, it is imperative to determine objective outcomes for these injuries compared to amputation.

These individuals are tactical athletes, who aspire to return to the highest level of function, yet are limited by the current methods of treatment, and concepts of rehabilitation medicine. They have very high expectations, and deserve the best we can offer. The Armed Forces Institute of Regenerative Medicine, in partnership with the Department of Defense, and existing clinical research programs such as the Orthopaedic Extremity Trauma Research Program, and the Major Extremity Trauma Research Program is uniquely positioned to answer these imposing challenges.