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TITLE: Clinical Evaluation of Decellularized Nerve Allograft with Autologous Bone Marrow Stem Cells to Improve Peripheral Nerve Repair and Functional Outcomes

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14. ABSTRACT

The current award is a phase I safety study (n=12) evaluation of the synergistic effect of the co-treatments of a commercially available decellularized processed peripheral nerve allograft scaffold (Avance ® Nerve Graft, AxoGen, Alachua FL) with autologous bone marrow stem cells (BMSC) for the reconstruction of mixed peripheral nerve gaps between 3 and 7 cm in length. Each treatment separately has been shown to have an established safety record. Avance has been used in more than 10,000 surgeries without a reported adverse event. The current standard of care for nerve injury, the autograft, has significant limitations: the source and quantities of autologous tissue needed for repairs are limited, and when faced with severe trauma these donor sites are not viable due to concurrent injury. Use of a decellularized nerve graft mitigates concerns of donor site morbidity, decreases surgical time and has substantially equivalent outcomes. Augmenting the scaffold with the patient's own BMSCs may allow for point of care treatment with the potential to enhance the regenerative ability of the wound-healing environment. The proposed use of an existing commercially available scaffold with an autologous stem cell transplant, both with proven safety records, would establish a safety profile and provide a proof of principle for this type of approach.

15. SUBJECT TERMS
Avance nerve graft, autologous bone marrow stem cells (BMSC), nerve autograft, peripheral nerve repair

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Introduction

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Keywords

Avance® nerve graft, autologous bone marrow stem cells (BMSC), nerve autograft, peripheral nerve repair

Accomplishments

The study team at WRNMMC consented 4 patients and currently have 2 actively enrolled. Patients not currently in the study were due to one patient being lost to follow-up as he indicated that he will not be returning for the study and the other separated from the military.

The study team at BAMC consented a total of 10 patients and currently have 4 actively enrolled. Patients not currently in the study were due to one patient being lost to follow-up at the 18 month visit, two patients withdrawn due to nerve gaps exceeding 7 cm in length, one patient withdrawn due to not needing the nerve graft, one patient withdrawn due to an infection of the dorsi pedicle myofasciocutaneous flap causing the graft to be removed and one patient passing away due to an unrelated study event.

There were two reported unrelated serious adverse events at BAMC. Patient 009-SAM had an infection at the dorsi pedicle myofasciocutaneous flap causing the graft to be removed. The IRB was notified on October 25, 2018. Patient 005-SAM passed away on April 18, 2019 due to an unrelated study event. The IRB was notified on April 18, 2019.

Impact

Military combat injuries to the extremities from blast, fragmentary, and ballistic injury can result in a spectrum of musculoskeletal trauma to include injuries to the soft tissues, vessels, nerves, and bone. It has been reported that while body armor has decreased the mortality associated with combat trauma, there is actually an increase in severe traumatic injury to the upper extremity in the surviving warrior. The incidence and prevalence of extremity injury has been on the rise significantly in the 21st century, with 54% of all casualties seen to involve extremity injury in 2006 up from 22% just 3 years prior. Costlier still is the fact that 65% of inpatient care is devoted to such wounds which are known to have the highest long-term costs associated with them – both a drain on military medical resources. The proposed phase I safety study complements the ongoing DoD and VA areas of interest by decreasing the burden of wounded warriors in the short term by lessening length of rehabilitation, and in the long term by reducing recidivistic chronic ailments. Moreover, these wounded service members have often sustained injuries to multiple limbs, often deeming the autograft sites unviable. The recent availability of the only commercially viable peripheral nerve allograft (Avance®, AxoGen Inc.) presents an attractive alternative to harvesting autograft by offering numerous benefits to the patient, including decreased operative time and no donor site morbidity. Furthermore, while the efficacy of these options have already been documented, there are limitations on the expected level of recovery and on the length of discontinuity that can be treated. The addition of a Warriors own BMSC's is expected to further improve outcomes and has shown a long safety record and is a standard point-of-care procedure. This proposed phase I safety trial, has the potential for establishing a safety record for the synergistic effect of the allograft and autologous stem cells leading to the acceleration and translation of advances in knowledge into new treatment algorithms for combat related injuries through evidence-based practices for the peripheral nerve repair.

Changes/Problems

No key personnel changes occurred this past year. A new program manager for this award started in July 2018 and the clinical research nurse relocated to San Antonio, TX. He manages the study team from Bethesda, MD.

Products

No products have been generated to date.

Participants and Other Collaborating Organizations

WRNMMC, SAMMC and Cleveland Clinic and Curtis National Hand Center are all collaborating on this project. Work at both WRNMMC and SAMMC is managed through HJF directly. The subaward to the Cleveland Clinic is ongoing.

Special Reporting Requirements

None

Appendices

None