Extremity Injury

Characterization and Optimization of Auto-transplantation and Allo-transplantation of Free Composite Tissues for Reconstruction of Battlefield Injuries

Modern battlefield injuries often produce devastating extremity and craniofacial injuries, for example extremity and craniofacial injuries account for greater than 85 percent of all injuries in Operation Iraqi Freedom/ Operation Enduring Freedom (OIF/OEF). Current methods of reconstruction often fall short of restoring form and function. Surgical reconstruction of these injuries using free composite tissue auto-/allo-transplantation can be used to ameliorate ischemia/reperfusion injury and maximize reconstructive reliability; however, clinical adoption of vascularized composite allotransplantation (VCA) is limited by the need for systemic immunosuppression, with associated morbidity and mortality. Small-animal models lack the biological fidelity and preclinical relevance to enable translation of immunologic insights to humans. Large-animal models have been described; however, limitations persist, including the inability of heterotopic models to evaluate functional nerve regeneration, and the sensitivity of primates to toxicity of immunosuppressive drugs. Researchers from the US Army Institute of Surgical Research (USAISR) and 59th Medical Wing in collaboration with researchers from the Royal Centre for Defence Medicine, Birmingham, England the Department of Surgery at the University of Texas Health Science Center at San Antonio, and the University of Pittsburgh Medical Center developed a novel orthotopic porcine limb transplant model that has broad applicability and translational relevance to both immunologic and functional outcomes after VCA. In this model, pigs underwent amputation at a level corresponding to the mid forearm. Replantation or transplantation of grafts was performed by plate fixation of the radio-ulna, microsurgical repair of brachial artery and median nerve, and extensor and flexor tendon repairs. Viability of replants was monitored clinically and radiologically. Transplants were monitored for clinicopathologic signs of rejection. Animals mobilized freely postoperatively. The researchers found that replantations remained viable until the endpoint of 14 days. Transplants developed Banff Grade 4 Acute Rejection (AR) by postoperative day seven. Doppler sonography and angiography confirmed vascular patency. Serial biopsy specimens of skin and histopathology of replants at endpoint confirmed tissue viability and bone healing. In conclusion, an orthotopic load-bearing porcine forelimb VCA model was successfully established. Technical, procedural, and logistic considerations were optimized to allow model use for immunologic, bone healing, functional nerve regeneration, and other translational studies. This research was published in Plastic and Reconstructive Surgery in 2016[1] and is expected to improve reliability of Composite Tissue Allograft (CTA), providing translatable principles for immediate application to battlefield injuries in the expeditionary setting and for restoration of long-term near-normal form and function.

1 Fries, C. A., Villamaria, C. Y., Spencer, J. R., Rickard, R. F., Gorantla, V. S., & Davis, M. R. (2016). A Porcine Orthotopic Forelimb Vascularized Composite Allotransplantation Model: Technical Considerations and Translational Implications. Plastic and Reconstructive Surgery, 138(3), 461e–71e. https://doi.org/10.1097/PRS.0000000000002451