revolutionize device sterilization in hospital and health care settings as well as shift the paradigm of the treatment of colonized and/or infected wounds.

DISCLOSURE/FINANCIAL STATEMENT: *Dr. Czeslaw Golkowski is President of SteriFreMed, Inc.*

Vascular Anatomy of Facial Units for Vascularized Composite Tissue Transplantation Design in a Large Animal Model: An in-Vivo and Radiological Study

Anita T. Mohan, MRCS BSc; Marissa Suchyta, BA; Basel Sharaf, MD, DDS; Karim Bakri, MBBS; Saad Alsubaie, MD; Gregory Michalak, PhD; Samir Mardini, MD

INTRODUCTION: A large animal model for composite face transplantation is necessary to better understand the immunologic processes and nerve regeneration. Current porcine models of facial transplantation fail to include all major branches of the facial nerve, and have not demonstrated long-term survival.1,2 A better understanding and detailed evaluation of vascular anatomy and microvascular territories in facial subunits and bone can help effectively develop a reliable porcine composite tissue flap model for experimental reconstructive or transplantation studies.

METHODS: Eleven 10kg domestic pigs were used for in-vivo studies. Vascular anatomy was assessed by Intra-operative anatomical dissections of 11 hemi-facial composite tissue flaps including the auricle. In addition Computed Tomographic Angiography (CTA) and Laser-assisted Indocyanine Green Fluorescence Angiography (LA-ICGFA) were used to assess vascular architecture preoperatively and flap perfusion. In addition, 8 cadaveric pigs were used for selective angiography of branches of the external carotid artery using a barium sulfate and latex mixture to provide detailed qualitative and quantitative analysis of the vascular territories using ultra-high resolution 3D CTA followed by a detailed anatomical dissection. Perforator distributions in facial subunits and the relationship of vascular territories to the facial nerve branches were documented.

RESULTS: A composite tissue flap of the hemi-face including the auricle was elevated and auto-transplanted in eleven 2 months old domestic pigs. Three pigs underwent preoperative CTA. We demonstrated two principal vessels supplying the hemifacial tissues: Internal maxillary artery (IMA) and superficial temporal artery (STA), with less significant contribution from the facial artery. Use of 3D volume rendering of the CTAs and the anatomical dissections demonstrated the vasculature and potential angiosomes of dominant and minor branches from the external carotid artery. We have been able to categorize facial subunit vascularity to delineate safe vascular territories for flap design in facial transplantation or reconstructive surgery.

CONCLUSION: We describe a new swine facial transplantation model with successful outcomes and reliable vascularity confirmed with anatomic, in-vivo CTA studies. Novel detailed vascular injection studies provide understanding of 3D vascular territories paramount to flap design, therefore enabling successful long-term modeling of hemi-facial composite tissue transplantation.

DISCLOSURE/FINANCIAL SUPPORT: *None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript.*

REFERENCES:

1. Kuo, Y. R., Shih, H. S., Lin, C. C., et al. (2009). Swine hemi-facial composite tissue allotransplantation: a model to study immune rejection. Journal of Surgical Research, 153(2), 268–273.
2. Gordon, C. R., Murphy, R. J., Coon, D., et al. (2014). Preliminary development of a workstation for craniomaxillofacial surgical procedures: introducing a computer-assisted planning and execution system. The Journal of craniofacial surgery, 25(1), 273.

Analysis of Acute Skin Rejection in Non-Human Primate Models of Face and Hand Allotransplantation

Zhi Yang Ng, MD; Alexandre G. Lellouch, MD; Matthew W. Defazio, BS; Harrison Powell, BS; David A. Leonard, MD, PhD; Zachary W. Heroux, BS; Josef M. Kurtz, PhD; Curtis L. Cetrulo, Jr., MD

INTRODUCTION: The incidence of acute rejection (AR) of the skin within the first year after hand or face transplantation is approximately 85% and up to 56% of patients experience multiple episodes[1]. Significant immunosuppression is

required to prevent allograft loss, and recent studies suggest that repeated AR episodes can lead to VCA dysfunction and loss[2]. The mechanisms underlying variability in AR presentation remain poorly defined however.

MATERIALS AND METHODS: 8 cynomolgus monkeys received either an orthotopic hand (n=2) or heterotopic face VCA (n=6) from MHC-mismatched donors following induction with anti-thymocyte globulin. Postoperatively, triple immunosuppression – tacrolimus, mycophenolate mofetil, methylprednisolone – was maintained for up to 120 days before bone marrow transplantation (BMT) was performed. Protocol biopsies of VCA skin were performed at 30-day intervals for histopathology and flow cytometric analysis of resident skin leukocyte populations; VCA-resident cells were differentiated by H38 status (mouse antihuman HLA class I monoclonal antibody that cross reacts with cynomolgus monkeys) for donor or recipient derivation. Clinical AR was treated with steroids and further biopsies were taken for histologic confirmation; corresponding anti-donor responses were evaluated by mixed lymphocyte reaction (MLR) and allo-antibody formation.

RESULTS: Up to three episodes of AR (from POD 14, Banff I to II) developed while recipient animals were maintained on triple immunosuppression. Corresponding flow cytometric analyses demonstrate > 80% of skin-resident T lymphocytes (CD4+, CD8+) within VCA dermis were of recipient origin, suggesting rapid immigration of various lineages into the VCA. These observations coincided with the first episode of AR in fully mismatched recipients but haplomatched animals remained rejection-free. All but one episode of AR were successfully treated. No allo-antibodies were detected and anti-donor responses by MLR were comparable to that against third-party. Following BMT, mixed chimerism was detected and enabled immunosuppression withdrawal. However, this was transient and once lost, clinical AR developed and nearly 100% of both dermal and epidermal lymphocytes were recipient-derived.

CONCLUSION: We report a clinically-relevant model for studying AR in VCA. Our results suggest that further understanding of the relative importance of MHC differences in transplant pairs may lead to differences in outcomes for VCA recipients maintained under standard immunosuppression. Immunosuppression-free tolerance of non-hematopoietic antigens in composite tissues can be achieved, but require additional strategies to achieve stable, rather than transient mixed chimerism following BMT.

DISCLOSURE/FINANCIAL SUPPORT: *Supported by the Reconstructive Transplantation Research Consortium grant W81XWH-13-2-0062. None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript.*

REFERENCES:

1. Petruzzo P, Lanzetta M, Dubernard JM, Landin L, Cavadas P, Margreiter R, et al. The International Registry on Hand and Composite Tissue Transplantation. Transplantation. 2010;90:1590–1594
2. Unadkat JV, Bourbeau D, Afrooz PN, Solari MG, Washington KM, Pulikkottil BJ, et al. Functional outcomes following multiple acute rejections in experimental vascularized composite allotransplantation. Plast Reconstr Surg. 2013;131:720e-30e

Immunomodulation in Vascularized Composite Allotransplantation – Preliminary Results in a Non-human Primate Model with Tocilizumab

Zhi Yang Ng, MD; Alexandre G. Lellouch, MD; Matthew W. Defazio, BS; Zachary W. Heroux, BS; Jigesh A. Shah, DO; Josef M. Kurtz, PhD; Curtis L. Cetrulo, Jr., MD

INTRODUCTION: Tolerance in vascularized composite allotransplantation (VCA) remains elusive and patients are faced with a lifetime of immunosuppression and associated risks. Tocilizumab (anti-IL-6 receptor monoclonal antibody) is currently FDA approved for use in rheumatoid and idiopathic arthritis. It mitigates inflammation, reduces the incidence of GvHD, and is potentially protolerogenic. We investigated the utility of a short course of tocilizumab in a non-human primate model (NHP) of facial VCA to achieve prolonged survival and/or tolerance.

MATERIALS AND METHODS: VCAs were transplanted into MHC-mismatched NHPs (n=4) after induction with anti-thymocyte globulin. Post-operative maintenance consisted of triple immunosuppression (FK506, methylprednisolone, MMF) before further conditioning (irradiation, lymphocyte depletion) in preparation for costimulatory blockade-based donor bone marrow transplantation (DBMT) on POD 60. Tocilizumab was administered on the day of DBMT, and at weekly intervals thereafter for