

Hyperbaric Sub-Normothermic *ex-vivo* Perfusion Delays the Onset of Acute Rejection in a Porcine VCA Model

Lin C. Wang, MD; Sharon D. Lawson, MD; C. Anton Fries, MA, MRCS; Michael R. Davis, MD

Disclosure/Financial Support: None of these authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript.

INTRODUCTION: Vascularized composite allotransplantation (VCA) offers superior functional recovery following devastating maxillofacial and upper limb injuries compared to traditional reconstructive techniques. Here, we evaluate the efficacy of a novel sub-normothermic (SN) *ex-vivo* perfusion strategy using hyper-oxygenated University of Wisconsin (UW) solution to mitigate reperfusion injury (RI) and the onset of acute rejection in a porcine VCA model.¹ Minimizing RI by optimizing allograft preservation strategies could improve early VCA outcomes, and reduce dose, frequency, and duration of immunosuppression.

MATERIALS AND METHODS: Heterotopic gracilis myocutaneous flap transplants were performed into the necks of Yorkshire swine recipients, mismatched for one swine leucocyte antigen. Group 1 (controls, n=8) received allotransplants without additional flap treatment. Group 2 (experimental, n=8) flaps were perfused *ex-vivo* with hyper-oxygenated UW for five hours at 20°C in a hyperbaric chamber at 3 atm before transplantation. Without systemic immunosuppression, flaps were monitored daily for clinical evidence of rejection and biopsied for immunohistopathological analysis. Serum was sampled for markers of immune injury secondary to RI.

RESULTS: Control flaps experienced Banff² Grade 1 rejection at a mean of 6.4 days (SD=0.52), and Grade 4 rejection at a mean of 10.5 days (SD=2.6). The experimental flaps showed a statistically significant delay in the onset of Grade 1 rejection at 13.7 days (SD=0.52, p<0.05). At the experiment's conclusion (Day 15), 75% of the experimental flaps showed no evidence of Grade 4 rejection.

CONCLUSION: Hyperbaric SN perfusion significantly delays the onset of acute rejection in the absence of systemic immunosuppression. This technology has potential utility in the field of solid organ transplantation and VCA, and could expand the donor pool dramatically. Furthermore, *ex-vivo* normalization of tissue physiology may reduce antigen presentation and acute rejection phenomena in allotransplantation.

REFERENCES:

1. Villamaria CY, Rasmussen TE, Spencer JR, Patel S, Davis MR. Microvascular porcine model for the optimization of vascularized composite tissue transplantation. J Surg Res. 2012Nov;178(1):452-9
2. Zdichavsky M, Jones JW, Ustuner ET, et al. Scoring of skin rejection in a swine composite tissue allograft model. Surg Res. 1999Jul;85(1):1-8