Immune Tolerance for Surgical Transplantation of the Hand or Face

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INTRODUCTION: The use of composite tissue allografts (CTA) has become a clinical reality with the successful transplantation of hand, abdomen, and face. The survival of these transplants is dependent on immunosuppression. The future of the clinical application of CTA transplantation is dependent on the establishment of immune tolerance that would allow for the elimination of the need for immunosuppression.

We have previously demonstrated that tolerance to CTA can be achieved when transplanted after the establishment of mixed chimerism (MC). In clinical CTA transplantation there is little time available for recipient conditioning. The purpose of this research was to develop a large animal model for the simultaneous transplantation of hematopoietic stem cells (HSC) and CTA using our established MC protocol.

METHODS: Four transplants were performed across MHC matched, minor mismatch barrier. All dogs received 200 cGy of radiation on the day of transplant and underwent a CTA transplant (myocutaneous rectus) with intraoperative injection of HSC. All dogs were treated with post-grafting immunosuppression (35 days of cyclosporine and 28 days of Mycophenolate Mofetil). The animals were followed for donor chimerism and underwent routine biopsies. Finally, they were followed for the expression of FoxP3, TGF-B, IL-10, Granzyme B in the CD3+ cell populations from their blood, transplant muscle and skin.

RESULTS: Three of four dogs still have detectable donor cell chimerism in the peripheral blood. However, the longest surviving dog, lost chimerism after pod 84. Despite the loss of the donor cell chimerism the CTA has remained stable without any signs of rejection. The level of Foxp3 decreased in the peripheral blood but was stable in both the skin and muscle.

CONCLUSION: This study demonstrates simultaneous transplantation of HSC and CTA is feasible and leads to tolerance to the CTA.

Preliminary Report on the PSEF Venous Thromboembolism Prevention Study (VTEPS): Validation of the Caprini Risk Assessment Model in Plastic and Reconstructive Surgery Patients

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INTRODUCTION: In 2008, the Venous Thromboembolism Prevention Study (VTEPS) was funded by the Plastic Surgery Educational Foundation to evaluate the effectiveness of chemoprophylaxis in prevention of postoperative venous thromboembolism (VTE) in patients undergoing aesthetic and reconstructive procedures. The five center study consortium includes: the University of Michigan, University of Pittsburgh, St Paul’s Regions Hospital, University of Texas-Southwestern, and University of Washington. Using a retrospective cohort design, VTEPS will compare rates of VTE and postoperative hematomas in patients receiving postoperative low molecular weight heparin with rates in historic controls who received no chemoprophylaxis. As of August, 2010, VTEPS has data for approximately 2800 patients, with a planned study accrual of 4000.

METHODS: Preliminary analyses of the controls were conducted to 1) evaluate the incidence of VTE in patients without chemoprophylaxis and 2) validate the Caprini Risk Assessment Model in plastic surgery patients. Data for control patients from March 2006 to June 2009 were included. Inclusion criteria were Caprini score ≥ 3 and inpatient surgery under general anesthesia. Dependent variables included symptomatic deep venous thrombosis (DVT) or pulmonary embolism (PE) within the first 60 post-operative days and time to DVT or PE.

RESULTS: In 1126 control patients, overall VTE incidence was 1.69%. For patients with Caprini scores >8, 11.3% had a VTE. Patients with Caprini scores >8 were significantly more likely to develop VTE when compared to patients with scores of 3-4 (OR 20.9, p<0.001), 5-6 (OR 9.9, p<0.001), or 7-8 (OR 4.6, p=0.015) (Figure 1). Among patients with scores >6, VTE risks extended well beyond 30 days. (Figure 2).
CONCLUSION: In these preliminary analyses, the Caprini RAM effectively risk-stratified plastic and reconstructive surgery patients for VTE risk. In higher risk patients, there was no evidence that VTE risk is limited to the immediate post-operative period. Final results for VTEPS are expected in early 2011.

Figure 1: Rates of VTE in the first 60 post-operative days by stratified Caprini score (N=1126).

Figure 2: Kaplan Meier analysis examining time to VTE by stratified Caprini score (N=1087).