AAHS/ASPN/ASRM Joint Outstanding Paper Session
(ASRM Abstracts Only)
Saturday, January 13, 2018, 11:00am – 12:00pm

11:40 AM - 11:45 AM
RM 205. **A Clinically Relevant Protocol Induces Tolerance to a Vascularized Composite Allograft Across Major Histocompatibility Barriers In A Large Animal Model**
University of Colorado, Aurora
Presenter: David Woodbridge Mathes, MD
Bruce Swearingen, MD(1), Scott Graves, PhD(2), Rainer Storb, MD(3) and David Woodbridge Mathes, MD(4)
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Background Vascularized Composite Allograft (VCA) transplantation is a clinical reality but its widespread application is limited by the need for chronic immunosuppression. We have developed a clinically relevant protocol based on non-myleoablative bone marrow transplantation platform. One barrier has been the need for the time required to pre-conditioning the recipient thereby limiting these protocols to living transplants. We have developed a protocol that uses a rapid stem cell mobilizer (AMD3100) that can mobilize cells in 6 hours after administration and combined that with our previously described protocol. **Methods** 7 DLA-haploidentical, recipients [Group I] received conditioning with 350cGy total body irradiation (TBI), AMD3100 mobilized donor stem cells, bone marrow aspirate, and VCA transplantation and a limited course of post-grafting immunosuppression (Mycophenolate Mofetil (MMF) 56 days/Cyclosporine (Csp): 70 days). 2 DLA-mismatched recipients [Group 2] received conditioning with 450cGy TBI, AMD3100 mobilized donor stem cells, bone marrow aspirate, and VCA transplantation with post-grafting immunosuppression (MMF 56 days, CSP, 70 days). We also added 28 days of Rapamycin to increase the T regulatory cell population. Donor cell chimerism was evaluated by PCR and allograft survival was followed clinically and histologically. **Results** Initial stem cell engraftment and donor chimerism were seen in all animals. Group 1 demonstrated tolerance to the transplants and engraftment off immunosuppression (POD 426, 265, 176, 131, 95). Two animals had pulmonary issues and were sacrificed before the cessation of immunosuppression (POD 59, 45). One dog lost donor cell chimerism at POD 70 and had a single rejection episode of the skin (POD 79) that resolved and has since gone on to maintain tolerance to the VCA (POD 176). Group 2 demonstrated donor cell engraftment and tolerance to the VCA (H910 POD 93, H912 POD 73). The most recent chimerism levels are H910 52.9% Granulocytes and 85.4% Lymphocytes and H912 26.7% Granulocytes and 53.4% lymphocytes. **Conclusion** This is the first clinically relevant protocol to induce tolerance in a large animal model across both a haploidentical and now a complete mismatches. This protocol can be completed with out the need for preconditioning and is applicable for cadaveric transplantation as the AMD3100 can be given to a brain-dead organ donor and the cell mobilized in 6 hours.

11:45 AM - 11:50 AM

RM 206. **Two Veins Reduce Muscle Free Flap Complications in Lower Extremity Reconstruction**

Wyss Department of Plastic Surgery, NYU Langone Medical Center, New York

Presenter: John T Stranix, MD

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Background: Venous insufficiency is the most common culprit behind free flap failure. Considering that the dependent position of the lower extremity predisposes to venous congestion at baseline, we investigated the effect of a second venous anastomosis on free flap outcomes in lower extremity trauma reconstruction.

Methods: Retrospective review of 806 lower extremity free flap reconstructions (1979-2016); 481 soft tissue flaps performed for below knee trauma reconstruction met inclusion criteria. Primary outcome measures were perioperative complications. Multivariable regression analysis controlled for: age, sex, time to coverage (<7 days, 8-90 days, >90 days), and flap type (muscle vs. fasciocutaneous).

Results: Lower leg injuries (n=361) were more frequent than foot/ankle (n=165), and muscle flaps predominated (n=362) compared to fasciocutaneous (n=119). Time from injury to coverage was divided into acute (<7 days, 29%), subacute (8-90 days, 40%), and chronic (>90 days, 32%). Single-vein outflow was more common (n=354) than two-vein (n=127). Two-veins were associated with fasciocutaneous flaps ($p<0.001$), foot/ankle injuries ($p=0.023$), and the subacute time period ($p=0.002$). Complications occurred in 191 flaps (39.7%): 71 takebacks (15%), 45 partial losses (9%), 37 complete losses (8%). Takeback indications were most commonly for venous congestion (48%), followed by arterial compromise (31%), unknown (10%), and hematoma (10%). Overall, regression analysis demonstrated two veins to be protective against complications (RR=0.628,$p=0.042$) and partial flap failures (RR=0.281,$p=0.019$). Interestingly, subgroup analysis by flap type demonstrated no effect of venous outflow type on fasciocutaneous flap outcomes. Among muscle flaps, however, two-vein flaps had fewer complications ($p<0.001$), takebacks ($p=0.047$), partial flap failures ($p=0.001$), and any flap failure ($p=0.012$). On regression analysis, muscle flaps with a second venous anastomosis were protected against complications (RR=0.366,$p=0.001$), partial flap failure (RR=0.078,$p=0.013$), and any flap failure (RR=0.361,$p=0.017$).

Conclusion: While two venous anastomoses reduced the overall risk of complications among lower extremity free flaps in our cohort, this finding was driven by the strong protective effect of two-vein outflow among muscle-based flaps. One-vein muscle flaps had 2.7 times higher risk of complications overall and a 12.8 times higher risk of partial flap failure. These results provide evidence for performing a second venous anastomosis when feasible, particularly among muscle flaps, for lower extremity trauma reconstruction.