reconstituted the recipients' hemopoietic and lymphoid lineages. Furthermore, VBMT accelerated the recovery of complete hematopoietic population and maintained the normal bone marrow histology of the femur grafts. Similarly, the spleen index in VBMT group was much higher than that in control animals.

CONCLUSION: Vascularized femur transplantation may provide an alternative method for bone marrow transplantation and can be used as a research tool to aid the study of roles of bone marrow in vascularized composite allografts.

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Defining The Role Of Skin And Mucosal Biopsy In Facial Allotransplantation.

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PURPOSE: The implications of allograft skin and mucosal biopsy findings on classification of rejection and treatment remain unclear. The purpose of this study is to review the histology and clinical episodes of rejection in a face transplant recipient to define data driven reasoning to obtain skin and mucosal biopsy in monitoring for acute rejection.

METHODS: Following facial allotransplantation, scheduled surveillance allograft skin and mucosal biopsies were obtained. Clinical concern for acute rejection prompted biopsies off schedule. Compilation of biopsy results, Banff grading, immunosuppression, and clinical correlation were critically reviewed for a 2-year follow up.

RESULTS: A total of 39 biopsies at 21 time points were obtained for analysis including both allograft skin (n=21) and mucosa (n=18). The patient had 3 episodes of acute rejection warranting treatment. Discordance between skin and mucosa occurred in 55.6% of biopsies (p=0.01). Mucosa concordance with the clinical evaluation occurred in 38.9% of biopsies (p=0.02), and skin concordance with clinical evaluation was present in 81% of biopsies (p=0.01).

CONCLUSIONS: The clinical utility of mucosal biopsy remains elusive. Our experience suggests that mucosal biopsies or skin biopsies, alone, should not drive the decision-making process in treatment. Skin biopsies are more likely to confirm clinical suspicion of rejection than mucosal histology. Data from other institutions is lacking, and future reporting may help elucidate the role of mucosal and skin biopsy in facial allotransplantation.

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Development of a Brain Body Interface for Upper Limb Reanimation: Selective Muscle Activation with a Chronically Implanted Nerve Cuff Electrode on the Sciatic Nerve

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PURPOSE: Spinal cord injury results in devastating loss of motor control. However, cortical signals of motor intention above the injury, and lower motor neurons below remain intact. Currently, brain-machine interface (BMI) systems, which rely on implanted cortical electrodes to control the movment of an artificial limb or computer cursor, have demonstrated the potential to bypass injury and return lost motor function. We propose that a brain-body interface (BBI), where cortical signals are fed directly into paralyzed muscles, may offer some distinct advantages over BMI. This approach acknowledges current limited understanding of cortical representation and instead aims to harness the brain's plasticity in order to re-organize neural connections and "re-learn" how to move the limb. Our overarching aim is to demonstrate restoration of voluntary motor function in a non-human primate (NHP) using cortically driven functional electrical stimulation (FES) of peripheral nerves with implantable nerve cuff electrodes. We have developed a highly selective, reversible paralysis model to simulate spinal cord injury in the upper extremity in a NHP. The aim of this portion of the study was to demonstrate selective fascicular stimulation of murine and rodent sciatic nerves using acute and chronically implanted, polyamide nerve cuff electrodes in preparation for implantation into the NHP spinal cord injury model. The NHP model will require the placement of the electrodes on small nerve branches (1-2mm) analogous in size to the rodent sciatic nerves.

METHODS: 8-channel polyamide stimulating cuff electrodes were wrapped around the sciatic nerves of adult Sprague Dawley rats (n=5) and C57 Black 6 mice (n=5). Cuff electrodes were connected to a Tucker-Davies stimulation/recording system. Electromyography (EMG) needle electrodes were inserted into the tibialis anterior (TA) and gastrocnemius (G) muscles to record muscle activity. Single pulses and pulse

trains were delivered to the various channels of the cuff while pulse parameters, including pulse amplitude and width, were systematically varied. Following successful demonstration of selective fascicular stimulation in non-survival surgeries, stimulating nerve cuff electrodes and EMG recording electrodes were implanted chronically in the rat to assess the stability of the equipment.

RESULTS: Muscle activity was recorded in all animals. In 9 animals, we successfully obtained muscle recruitment curves as a function of stimulation amplitude. Depending on channel activation, we were able to show selective activation of tibial and common peroneal fascicles and therefore selective recruitment of G and TA muscles respectively. Following 30 days of chronic implantation in the rat, successful selective stimulation and recording was still possible.

CONCLUSION: We have successfully shown that selective fascicular stimulation can be achieved using implantable cuff electrodes in sub-1mm nerves and over prolonged periods. Following implantation of an epicortical recording array in the NHP, we intend to use these nerve cuffs to deliver cortically recorded signals of motor intention directly to peripheral nerves of the upper limb. By activating this system during reversible paralysis achieved with selective nerve blocks, we aim to show that, through mechanisms of cortical learning and plasticity, the NHP is able to regain control of limb movement.

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The Impact and Mechanisms of Antibody-Mediated Rejection in Vascularized Composite Allotransplantation

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PURPOSE: The immediate clinical management of devastating tissue injuries often requires multiple blood transfusions and/or skin allografts as life-saving interventions for patients suffering from severe trauma. However, the consequent formation of alloantibodies (anti-HLA IgG Abs) after these procedures is a great barrier facing patients who wish to receive definitive treatment in the form of reconstructive transplantation as sensitization currently stands as a major contraindication for vascularized composite allotransplantation (VCA). The role of donor-specific antibodies (DSA) and mechanisms of antibody-mediated rejection (AMR) in VCA are still largely unknown. These phenomena must be understood in an effort to provide reconstructive transplantation options to the large population of sensitized patients in need of VCA.

METHODS: Major histocompatibility-mismatched Dark Agouti (RT1Aa) donors and Lewis (RT11) recipients were utilized to examine the effect that sensitization to donor antigens has on the rejection scheme of VCA. Lewis rats were sensitized with 1.5 x 1.5 cm full-thickness skin grafts from Dark Agouti donors and after 30 days received orthotopic hind-limb transplantation. Serum antibody titers, tissue biopsies, and clinical observations were obtained and analyzed with regards to rejection kinetics and processes.

RESULTS: Serum antibody titers after skin graft sensitization peaked in Lewis recipients at post-operative days 10 and 14 for IgM and IgG respectively. All sensitized rats (n=6) in the control group receiving no immunosuppression rejected their hind limb grafts within 4-5 days after transplantation, while non-sensitized control rats rejected their grafts within 9-10 days ($p<0.05$). Treatment of non-sensitized recipients with tacrolimus (0.5 mg/kg) resulted in rejection-free long-term graft survival (>30 days), whereas the same treatment regimen given to sensitized recipients resulted in accelerated allograft rejection around POD 10. Immunofluorescence and immunohistochemical staining showed that IgG and C4d were present in the epidermis, dermis, and capillaries in hind limb allografts recovered from sensitized control rats 3 days after transplantation. In contrast, non-sensitized rats showed only very isolated IgG or C4d dermal staining at 3 days postoperatively.

CONCLUSIONS: Sensitized recipients reject VCA in an accelerated manner as compared to non-sensitized recipients. Additionally, antibody-specific markers of rejection such as IgG and C4d deposition appear at earlier time points in sensitized recipients as compared with non-sensitized controls. Treatment with standard immunosuppressive agents proves to be insufficient in stifling the rejection processes caused by DSA.