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<sup>1</sup>Scott M. Tintle, MD

<sup>2</sup>Juyu Tang, MD

<sup>3</sup>L. Scott Levin, MD, FACS

<sup>1</sup>Walter Reed National Military Medical Center, Oakton, VA, USA

<sup>2</sup>Xiangya Hospital Central-South University, Changsha 410008, PR China

<sup>3</sup>University of Pennsylvania, Philadelphia, PA, USA

# A Rat Model for Elbow Allotransplantation

## Introduction

There is no durable solution for end stage elbow arthritis in the young active patient population. Potential surgical solutions to include elbow debridement, resurfacing arthroplasty, non-vascularized allograft elbow transplantation, and total elbow replacement have not proven to be the successful long term solution to this problem. In the current patient with end stage elbow arthritis or elbow destruction as a result of injury, infection or failed arthroplasty, the only viable solution is often surgical arthrodesis, or resection arthroplasty leaving a patient with a minimally useful extremity with minimal to no motion. An ideal replacement for these patients with elbow joint destruction would be a living joint allogeneic transplant that exactly matches the dimensions and structural properties of the missing joint. The purpose of this study was to create an animal model for elbow joint vascularized composite allotransplantation. (VCA)

## Methods

We developed an animal model for VCA of the elbow joint in rats. Microvascular elbow VCA was performed in 9 rats across a major histocompatibility barrier. 3 rats were treated with full dose immunosuppression consisting of cyclosporine until sacrifice. 3 rats were provided with 10 days of immunosuppression and then the cyclosporine was stopped. Finally, 3 rats were utilized as a control and were given no immunosuppression. Joint mobility and weight-bearing capability were assessed throughout 90 days of life. Pedicle patency, bone blood flow, and histologic analysis were performed at the time of sacrifice.

## Results

In the cyclosporine group, forelimb activity was gradually recovered over the postoperative 90 days. The operated extremity was utilized in daily activities such as ambulating and eating. There was little to no range of motion or utilization of the limb in the cyclosporine taper or the control groups. The vascular pedicles were patent at the time of sacrifice in the cyclosporine-treated group but not in the remaining groups. Micro-CT scan performed 3 months following the transplants revealed union at the bone junctions and the elbow joint appeared grossly normal upon sacrifice in the cyclosporine treatment group only. Incomplete healing was observed in the other two groups, and the elbow joints were grossly destroyed. Flow cytometry of blood samples obtained on days 14, 30, 60 and

90 showed no recipient cell chimerism in any of the groups. Histologic examination of the elbow joints is currently being performed.

## Discussion

We have provided an animal model for elbow VCA. In our cyclosporine-treated rats we have shown that animals regain near normal function of their forelimbs after bone union and maintain grossly normal elbow cartilage. Without cyclosporine treatment, both our control groups and the short term cyclosporine group rejected their allotransplants.

## Significance

No current model for elbow allotransplantation currently exists. This model will help further the study of the potential for this type of transplantation in the future. Significant progress with immunosuppressive regimens is necessary prior to making this a clinical reality, and it is therefore important that an animal model be established.

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## References

1. Lanzetta M, et al. Second report (1998-2006) of the International Registry of Hand and Composite Tissue Transplantation. *Transpl. Immunol.* 18, 1-6 (2007).
2. Petruzzo P, et al. The International Registry on Hand and Composite Tissue Transplantation. *Transplantation* 90, 1590-1594 (2010).
3. Raichle KA, et al. Prosthesis use in persons with lower- and upper-limb amputation. *J. Rehabil. Res. Dev.* 45, 961-972 (2008).
4. Bhaskaranand K, Bhat AK, Acharya KN. Prosthetic rehabilitation in traumatic upper limb amputees (an Indian perspective). *Arch. Orthop. Trauma Surg.* 123, 363-366 (2003).
5. Millstein SG, Heger H, Hunter GA. Prosthetic use in adult upper limb amputees: a comparison of the body powered and electrically powered prostheses. *Prosthet. Orthot. Int.* 10, 27-34 (1986).
6. Stürup J, et al. Traumatic amputation of the upper limb: the use of body-powered prostheses and employment consequences. *Prosthet. Orthot. Int.* 12, 50-52 (1988).
7. Pinzur MS, et al. Functional outcome following traumatic upper limb amputation and prosthetic limb fitting. *J. Hand Surg.* 19, 836-839 (1994).
8. Wright TW, Hagen AD, Wood MB. Prosthetic usage in major upper extremity amputations. *J. Hand Surg.* 20, 619-622 (1995).
9. Harvey ZT, et al. Advanced rehabilitation techniques for the multi-limb amputee. *J. Surg. Orthop. Adv.* 21, 50-57 (2012).
10. Kuiken TA, et al. Targeted muscle reinnervation for real-time myoelectric control of multifunction artificial arms. *JAMA.* 301, 619-628 (2009).
11. Grob M, et al. The psychological impact of severe hand injury. *J. Hand Surg. Eur. Vol.* 33, 358-362 (2008).
12. Errico M, Metcalfe NH, Platt A. History and ethics of hand transplants. *JRSM Short Rep.* 3, 74 (2012).