## Transplant Roundup

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# Hand Transplantation:

The Benefits, Risks, Outcomes, and Future

The field of transplantation came to fruition in 1954 when Joseph Murray, an American plastic surgeon, performed the first kidney transplant in the world.<sup>1</sup> Subsequently, most early transplantations in the U.S. were of solid homogeneous organs. Then, in 1964, a hand transplant was performed in Ecuador on a sailor who had lost both arms in an explosion,<sup>2</sup> and the possibility of composite tissue allotransplantation (CTA) with heterogeneous tissues then emerged. However, the patient's graft was rejected and was explanted at week 3. The field was stagnant until the 1980s, when the discovery of calcineurin inhibitors improved immunotherapy and made limb transplantation viable. In 1999, a hand was transplanted with longterm success in Louisville, Kentucky,<sup>3</sup> reawakening interest in CTA and reconstructive transplantation. By 2009, 53 successful hand transplants had been performed worldwide.<sup>4</sup>

In reconstructive transplantation for catastrophic limb and tissue loss, a one-year graft-survival rate of 96% has been reported<sup>5</sup>—notable because upper-extremity transplantation is extremely complex. The steps include bone approximation and plating of both the radius and ulna, extensive vessel anastomoses, extensor and flexor tendon repairs, and limb innervation.

Hand and arm transplantation optimally restores full motor and sensory function. Investigators<sup>6</sup> reported better functional outcomes after tissue transplants than after using prosthetic devices: quantitative testing<sup>7</sup> in multiple recipients revealed that CTA methods enabled patients to resume most daily activities, including eating, driving, and writing.<sup>6</sup> In one registry,<sup>5</sup> all transplant recipients developed protective sensibility against pain, 90% regained tactile sensibility, and 82.3% achieved discriminative (fine) sensibility. However, the greatest benefit was improved quality of life, reported by 75% of recipients.<sup>5</sup>

Despite the benefits of CTA, debate continues on whether the potential for improving a patient's quality of life outweighs the risks: limb transplants are usually elective procedures, yet they necessitate intensive surgery and the same lifelong immunosuppressive therapy as do solid-organ transplants. Risks include opportunistic infection (chiefly cytomegalovirus), metabolic disorders such as diabetes mellitus and Cushing syndrome, and malignancies (skin cancers and lymphoproliferative disease).<sup>58,9</sup> The graft itself might also fail consequent to infection, acute rejection, intimal hyperplasia, or noncompliance with immunosuppressive medications.<sup>5</sup> Acute rejection, which reportedly occurs in 85% of recipients within the first year, typically manifests itself with cutaneous lesions.<sup>5,10</sup> Therefore, healthcare providers disagree about when and whether hand transplantation should be offered.<sup>11</sup> On the bright side, acute rejection can be reversed with prompt treatment, and we found no reports of graft-versus-host disease or chronic rejection in recipients of hand grafts.

Satisfactory survival rates after CTA indicate that the field of reconstructive transplantation will continue to expand. Risk reduction will be crucial, particularly in association with immunotherapy. The Baylor Comprehensive Hand Transplant Program team has developed a protocol for using donor bone marrow and stem cells to modulate the immune system in place of typical immunosuppression during clinical reconstructive transplantation. Success in these efforts may transform the care of patients who experience catastrophic limb loss.

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### References

- Murray J. Interview with Dr Joseph Murray (by Francis L Delmonico). Am J Transplant 2002;2(9):803-6.
- Gilbert Fernandez JJ, Febres-Cordero RG, Simpson RL. The untold story of the first hand transplant: dedicated to the memory of one of the great minds of the Ecuadorian medical community and the world. J Reconstr Microsurg 2018 Aug 31. [Epub ahead of print]
- Breidenbach WC, Gonzales NR, Kaufman CL, Klapheke M, Tobin GR, Gorantla VS. Outcomes of the first 2 American hand transplants at 8 and 6 years posttransplant. J Hand Surg Am 2008;33(7):1039-47.
- Thuong M, Petruzzo P, Landin L, Mahillo B, Kay S, Testelin S, et al. Vascularized composite allotransplantation - a Council of Europe position paper. Transpl Int 2018 Nov 2. [Epub ahead of print]
- 5. Petruzzo P, Lanzetta M, Dubernard JM, Landin L, Cavadas P, Margreiter R, et al. The International Registry on Hand and Composite Tissue Transplantation. Transplantation 2010;90(12):1590-4.

- Graham B, Adkins P, Tsai TM, Firrell J, Breidenbach WC. Major replantation versus revision amputation and prosthetic fitting in the upper extremity: a late functional outcomes study. J Hand Surg Am 1998;23(5):783-91.
- Carroll D. A quantitative test of upper extremity function. J Chron Dis 1965;18:479-91. Available at: http://www.swiss wuff.ch/images/adl/adl-pdf/carroll1965quantitativetestupperex-function.pdf.
- Petit F, Minns AB, Hettiaratchy SP, Mathes DW, Randolph MA, Lee WPA. New trends and future directions of research in hand and composite tissue allotransplantation. J Am Soc Surg Hand 2003;3(3):170-4.
- 9. Wu S, Xu H, Ravindra K, Ildstad ST. Composite tissue allotransplantation: past, present and future-the history and expanding applications of CTA as a new frontier in transplantation. Transplant Proc 2009;41(2):463-5.
- 10. Schneeberger S, Zelger B, Ninkovic M, Margreiter R. Transplantation of the hand. Transplant Rev 2005;19(2):100-7.
- Mathes DW, Schlenker R, Ploplys E, Vedder N. A survey of North American hand surgeons on their current attitudes toward hand transplantation. J Hand Surg Am 2009;34(5):808-14.