

Reports of the Immunologic Management of the First Successful Combined Face and Whole-Eye Transplant



David L. Tran MD, Alay R Shah MD, Sachin R Chinta BS, Bruce E Gelb MD, Massimo Mangiola PhD, Daniel J Ceradini MD, Eduardo D Rodriguez MD DDS

Hansjörg Wyss Department of Plastic Surgery, NYU Langone Health, New York, NY

INTRODUCTION

- Since the first face transplant (FT) in 2005, significant strides have been made in our technical and immunologic understanding
- Coinciding with recent improved understandings of immunologic processes and rejection, whole-eye transplant (WET) can be revisited

Objectives:

1. Outline the first successful case of a combine FT-WET
2. Review immunologic management and early outcomes following success transplantation

METHODS

- Single-center prospective case report on the first combined FT-WET
- 46-year-old male who sustained a high voltage electrical injury resulting in severe facial injuries and left eye enucleation
- With a baseline cPRA of 32%, following identification of an appropriate donor, underwent combined FT-WET with optic nerve coaptation and immune induction via rituximab and anti-thymocyte globulin



Figure 1 Preoperative photos

RESULTS

Operative Details

- Operation time approximately 22 hours
- Total graft ischemia time of 2 hours and 59 minutes
- Initial induction immunosuppression consisted of thymoglobulin at 6mg/kg and 1000mg rituximab
- Direct optic nerve coaptation performed primarily
- Intraoperative administrated of isolated donor derived CD34+ hematopoietic stem cells at the nerve coaptation

Postoperative

- Mycophenolate, tacrolimus, and prednisolone were used as maintenance immunosuppression
- Now more than 300 days postoperatively, there have been no reports of acute rejection episodes after index operation or subsequent revision procedures
- No gross evidence of orbital rejection



Figure 2. Preinjury, postinjury, and post-reconstruction

DISCUSSION

- Following catastrophic craniofacial injury and globe loss, combine partial FT-WET restored anatomic facial features, oral competence, and external airway function (Figure 2).
- Postoperative examination of the eye demonstrates robust vascularization and a viable globe with healthy sclera, clear corneal surface, a round iris, and clear lens
- Induction agents were dosed as described (table 1). Maintenance therapy at our institution utilizes trough-based tacrolimus dosing dependent on POD from index operation

| Induction Agent | Dose   |
|-----------------|--------|
| ATG             | 6mg/kg |
| Rituximab       | 1000mg |

| Maintenance triple therapy | Dose       |
|----------------------------|------------|
| MMF                        | 1 mg q12hr |
| Tacrolimus                 | 4mg q12hr  |
| Prednisone                 | 30mg daily |

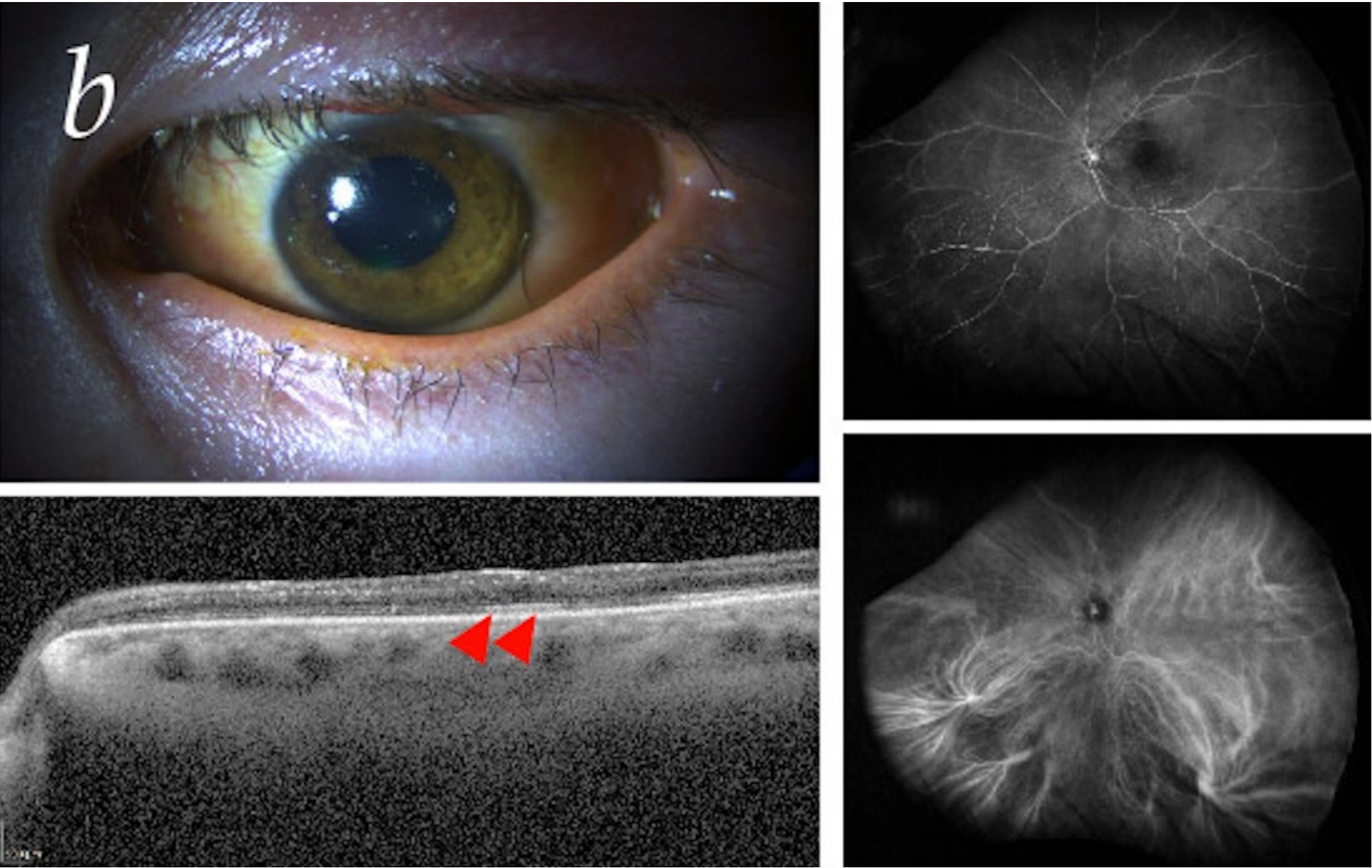


Figure 3. top left demonstrates healthy appearing globe; bottom left demonstrates retinal atrophy and ellipsoid zone attenuation; right panels demonstrate robust vascularity and choroidal flow

CONCLUSIONS

- While FT has become the standard of care at specialized centers for a small subset of devastating facial effects, eye transplantation has remained a formidable challenge due to anatomic complexity and questions regarding immunogenicity
- Here we describe our experience following the successful completion of the first combined partial FT-WET
- Immune regimens comparable to previously described protocols for FT not containing orbital components have demonstrated adequate immune control with no evidence of acute rejection episodes now more than 300d postop
- Inclusion of the optic nerve and orbital components did not increase the incidence of rejection episodes even after subsequent procedures for graft revision

REFERENCES

1. Bourne D, Li Y, Komatsu C, et al. Whole-eye transplantation: a look into the past and vision for the future. *Eye (Lond)* 2017; **31**(2): 179-84.
2. Bourne RRA, Flaxman SR, Braithwaite T, et al. Magnitude, temporal trends, and projections of the global prevalence of blindness and distance and near vision impairment: a systematic review and meta-analysis. *The Lancet Global Health* 2017; **5**(5): e888-e97.
3. Kemer RS, Cavatini D, Gelb BE, et al. Facial Transplantation for an Irreparable Central and Lower Face Injury: A Modernized Approach to a Classic Challenge. *Plast Reconstr Surg* 2018; **144**(2): 264e-83e.
4. Rami EP, Alfonso AS, Berman ZP, et al. The First Successful Combined Full Face and Bilateral Hand Transplant. *Plast Reconstr Surg* 2022; **150**(2): 414-28.
5. Saini M, Ceradini DJ, Levine JP, et al. Total Face, Eyelids, Ears, Sculp, and Skeletal Subunit Transplant: A Reconstructive Solution for the Full Face and Total Scalp Burn. *Plast Reconstr Surg* 2016; **138**(1): 205-19.
6. Ponnambazh S, Prabaz, Eriksson E, et al. Three patients with full facial transplantation. *N Engl J Med* 2012; **366**(8): 715-22.
7. Lantieri L, Grimbert P, Ortonne N, et al. Face transplant: long-term follow-up and results of a prospective open study. *Lancet* 2016; **388**(10052): 1398-407.
8. Olson D, Olson D, Iltis M, Hestoniguchi N, Cengiz M, Alvar J. Face allotransplantation for various types of facial disfigurements: A series of five cases. *Microsurgery* 2018; **38**(8): 834-43.
9. Siemionow M, Papay F, Alan D, et al. Near-total human face transplantation for a severely disfigured patient in the USA. *Lancet* 2009; **374**(9585): 203-9.
10. Knochkelet R, Siemionow M, Ophir A, et al. Youngest Composite Full-Face Transplant: A Model for "Facultured Composite Allotransplant" in Younger Populations. *Ann Plast Surg* 2022; **89**(5): 564-72.
11. Lagro M, Chaya BF, Brydges HT, et al. Technical Feasibility of Whole-eye Vascular Composite Allotransplantation: A Systematic Review. *Plast Reconstr Surg Glob Open* 2023; **11**(4): e4946.
12. Zor F, Karagoz H, Kapucu H, Kulachi V, Janjic JM, Gorantla VS. Immunological considerations and concerns as pertinent to whole eye transplantation. *Current Opinion in Organ Transplantation* 2019; **24**(6).
13. Zor F, Polat M, Kulachi V, et al. Demonstration of technical feasibility and viability of whole eye transplantation in a rodent model. *J Plast Reconstr Aesthet Surg* 2015; **72**(10): 1640-50.
14. Eilenberg D, Shi J, Jain S, et al. Impediments to eye transplantation: ocular viability following optic-nerve transection or enucleation. *Br J Ophthalmol* 2009; **93**(9): 1134-40.
15. Bravo NG, Garofalo MD, Johnson AR, Lee BT. Development of a New Large-Animal Model for Composite Face and Whole-Eye Transplantation: A Novel Application for Anatomical Mapping Using Indocyanine Green and Liquid Latex. *Plast Reconstr Surg* 2020; **145**(1): 67e-75e.
16. Siemionow M, Bozkurt M, Zor F, et al. A New Composite Eyeball-Prioriorbital Transplantation Model in Humans: An Anatomical Study in Preparation for Eyeball Transplantation. *Plast Reconstr Surg* 2018; **141**(4): 1011-6.
17. Brydges HT, Onuh OC, Chaya BF, et al. Combined Face and Whole Eye Transplantation: Cadaveric Rehearsals and Feasibility Assessment. *Plast Reconstr Surg Glob Open* 2023; **11**(11): e5409.
18. Saini M, Cavatini DJ, Hazen A, et al. Total Face, Eyelids, Ears, Sculp, and Skeletal Subunit Transplant Cadaver Simulation: The Culmination of Aesthetic, Craniofacial, and Microsurgery Principles. *Plast Reconstr Surg* 2016; **137**(5): 1569-81.
19. Gelb BE, Diaz-Silco JR, Hana NM, et al. Absence of Rejection in a Facial Allograft Recipient with a Positive Flow Crossmatch 24 Months after Induction with Rabbit Anti-Thymocyte Globulin and Anti-CD20 Monoclonal Antibody. *Case Rep Transplant* 2018; **7**(6): 7001072.
20. King KY, Goodell MA. Inflammatory modulation of HSCs: viewing the HSC as a foundation for the immune response. *Nat Rev Immunol* 2011; **11**(10): 685-92.
21. Bryukhovetsky AS, Bryukhovetsky IS. Effectiveness of repeated transplantations of hematopoietic stem cells in spinal cord injury. *World J Transplant* 2015; **5**(3): 110-28.
22. Hasempour M, Sanyalov AA, Kobayashi S, Ashara T. CD34 positive cells as endothelial progenitor cells in biology and medicine. *Front Cell Dev Biol* 2023; **11**: 1128134.
23. Robson AG, Prishman LJ, Grigg J, et al. ISEV Standard for full-field clinical electroretinography (2022 update). *Oec Ophthalmol* 2022; **144**(3): 165-77.
24. Odum JV, Bach M, Ringel M, et al. ISEV standard for clinical visual evoked potentials (2016 update). *Oec Ophthalmol* 2016; **133**(1): 1-9.
25. Le Bihan D, Turner R, Zeffiro TA, Cuendod CA, Jezzard P, Bonneret V. Activation of human primary visual cortex during visual recall: a magnetic resonance imaging study. *Proc Natl Acad Sci U S A* 1993; **90**(24): 11802-5.
26. Niranjana A, Christie IN, Solomon SG, Wells JA, Lythgoe MF. fMRI mapping of the visual system in the mouse brain with interleaved snapshot GE-EPI. *Neuroimage* 2016; **139**: 337-45.
27. Baete SH, Yutzy S, Boada FE. Radial q-space sampling for DS. *Magn Reson Med* 2016; **76**(3): 760-80.