

Current Principles of Facial Allotransplantation: The Brigham and Women's Hospital Experience

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Background: Facial allotransplantation is a revolutionary operation that has at last introduced the possibility of nearly normal facial restoration to patients afflicted by the most severe cases of facial disfigurement.

Methods: The facial transplantation team at Brigham and Women's Hospital evaluated more than 20 patients as potential face transplant recipients; of these, six became face transplant candidates and underwent full screening procedures. The team performed facial allotransplantations in four of these patients between April of 2009 and May of 2011. This is the largest clinical volume of facial transplant recipients in the United States to date.

Results: The authors have learned important lessons from each of these four unique cases and from the more than 20 patients that they have evaluated as potential face transplant recipients. The authors have translated lessons learned through direct experience into a set of fundamental surgical principles of the operation.

Conclusions: The authors' surgical principles emphasize safety, technical feasibility, preservation of functional facial units, and return of motor and sensory function. This article describes each of these principles along with their rationale and, in some instances, illustrates their application. (*Plast. Reconstr. Surg.* 131: 1069, 2013.)

Severe facial deformity often leads to impairment in facial function and social interactions and to discrimination, disability, depression, and body image and self-perception issues, all of which are detrimental to quality of life.¹⁻⁶ Facial deformity may be consequential to trauma, burns, high-voltage injury, malignancy, or congenital disease. Reconstructive surgery provides only partial restoration of appearance and function and thus falls short regarding its ability to restore quality of life to patients with severe facial defects. Over many decades, researchers have attempted to develop therapies to bestow a more normal appearance and function to disfigured patients that, if successful, would improve quality of life. Until the recent advent of facial allotransplantation, these research efforts had not met with outstanding success. Facial allotransplantation entered the clinical arena almost 7 years ago⁷ as the only therapy to replace missing or damaged

facial units such as the nose, lips, maxilla, and/or eyelids with functional and aesthetic equivalents. Reported outcomes clearly surpass those expected or achieved with conventional reconstruction.⁸⁻¹²

Planning a face transplant operation requires careful analysis of the recipient's facial defect, and meticulous design of the facial allograft. A facial transplantation is a highly dynamic, prolonged operation requiring multiple teams communicating seamlessly through its duration.¹³⁻¹⁵ The multidisciplinary members of our team, along with their roles in the screening, planning, perioperative, and postoperative phases of facial transplantation, have been previously described in detail.¹⁵ Our team has evaluated over 20 patients interested in undergoing facial transplantation; of these, six have been selected

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Table 1. Defect for Each Recipient and the Salvage Operation Planned

Recipient	Date Transplanted	Description of Facial Defect at the Time of Face Transplant Evaluation	Salvage Plan
1	April of 2009	Complex bony and soft-tissue defect of the midface; loss of nose, maxilla, and upper lip; reconstructed with anterolateral thigh fasciocutaneous free flap to separate the oral and nasal cavities	Repeated anterolateral thigh flap
2	March of 2011	Loss of most soft tissues of the face, eyelids, left eye, nose, lips, teeth, and large portion of temporoparietal scalp; reconstructed with bilateral latissimus serratus muscles and skin grafts	Split-thickness skin grafting of underlying latissimus and serratus muscles
3	April of 2011	Loss of nose, facial skin over the entire face, upper and lower lips (with remnants of orbicularis in the upper lip), bilateral lower lid ectropion; reconstructed with skin grafting over forehead and eyelids, and lateral arm flap for the neck, mandible, and lower lip	Split-thickness skin grafting of facial wound, with preservation of motor function
4	May of 2011	Loss of central facial tissues including the nose, eyelids, both eyes, maxilla, and both lips, with extensive scarring of the remaining face; reconstructed with anterolateral free flap for wound control, and nasal reconstruction with rib cartilage	Repeated anterolateral thigh flap to separate the oral and nasal cavities

as candidates for the procedure based on criteria previously described,¹⁶ and we have performed facial transplantation in four of these candidates over the past 3 years (Table 1).^{10,11} Thus, we are currently the institution with the most clinical experience in the United States. Through these four successful experiences, we have identified the set of surgical principles described below. These principles serve as the guidelines for our processes of planning and performing face transplant operations.

SURGICAL PRINCIPLE 1: SAFETY

Face transplantation is an elective operation aimed at enhancing quality of life and potentially bringing severely disfigured patients back to a nearly normal appearance and functional status, productive lives, and active participation in family and society. The clinical volume of face transplantations to date is small, and it is only expected to increase if the inclusion criteria can be safely broadened¹⁶ based on positive outcomes, one of which is safety. With regard to safety, we have identified two main factors that must be addressed comprehensively during the planning stages: preserving salvage options in case of facial allograft failure and lifelong immunosuppression and follow-up coverage.

Preserving Salvage Options in Case of Facial Allograft Failure

The longest follow-up peer-reviewed publication available on face transplantation dates to 5 years after the operation and reports some manageable complications not unlike those reported after solid organ transplantation, in addition to excellent function, patient satisfaction, and social reintegration.⁸ In spite of these encouraging results,

the long-term outcomes of face transplantation remain unknown, and although unlikely, allograft loss is always possible. It is important to have a robust salvage plan to execute in the unfortunate event of facial allograft loss; death is not an acceptable outcome of face transplant failure. The salvage plan must address safe coverage of the defect left after loss of the allograft, and it typically involves autologous skin graft or flap reconstruction. Discussions regarding the salvage plan must be carried out during the pretransplantation evaluation, and must include the patient and the physicians. These discussions must address the possibility that the outcomes of salvage might leave the patient in a functional and aesthetic state worse than the pretransplantation state. An example of a case where we applied the principle of preserving salvage options is the man depicted in Figure 1, *left*, who had suffered electrical burn injuries to the entire face 1.5 years before presenting for face transplantation consideration. During acute postinjury care, extensive débridement left the patient with exposed bone, which was then covered by bilateral muscle free flaps. The surgical plan we executed consisted of maintaining this muscle (Fig. 1, *right*), which can be regrafted in one operation should the transplanted face fail. Of note, burn patients present the most challenges for salvage: those with burns covering large surface areas or having a history of multiple reconstructive efforts may have depleted their donor sites. Within this context, embarking on extensive reconstructive efforts for the treatment of facial defects that have no known acceptable clinical solution can be unwise. Our recommended approach is to present the option of transplantation following basic wound control in this patient population.



Fig. 1. (Left) A full facial transplantation candidate at the time of initial evaluation. (Right) Orbital islands of skin were maintained to provide for lining behind planned ocular prostheses. Periorbital skin was maintained to substitute for missing intraoral lining.

Lifelong Immunosuppression and Follow-Up Coverage

Although not a surgical factor, ensuring that a plan is in place for the provision and financial coverage of lifelong immunosuppression and follow-up is imperative for the survival of the allograft. Before each face transplant operation and as an absolute criterion for inclusion, the Brigham and Women's Hospital team secured written authorization from the medical insurance providers of its four face transplant recipients with regard to lifelong coverage of posttransplant immunosuppression and follow-up. To date, coverage of transplant-related follow-up and immunosuppressive medications for all of these patients has proceeded without any issues. At the present time, compliance with immunosuppressive medications is absolutely necessary to reduce the incidence and intensity of rejection episodes; our team's psychiatry and social work members assess the patient's likelihood of compliance during the screening phase for facial transplantation,¹⁵ and patients who are deemed likely noncompliant are excluded from the intervention. The team has not observed issues of compliance with immunosuppressive medications in any of its four transplant patients. If rejection presents, medical treatment must be provided to prevent allograft loss. Finally, periodic monitoring is needed to minimize and address the serious side effects of immunosuppression.¹⁷⁻¹⁹ Of the four current Brigham and Women's Hospital face transplant recipients,

three have experienced single episodes of acute rejection in the months following the operation, all of which were successfully managed with methylprednisolone boluses administered in an inpatient setting and followed by steroid taper.^{10,11} None of the recipients has developed symptoms of chronic rejection. Finally, the team at Brigham and Women's Hospital, and other teams across the globe, are currently actively pursuing research aimed at safely minimizing or completely withdrawing immunosuppression in face transplant recipients by inducing donor-specific tolerance.

SURGICAL PRINCIPLE 2: TECHNICAL FEASIBILITY

Once started, the face transplant operation is subject to significant time constraints. From the instant the donor's facial allograft is removed from physiologic blood flow until the moment of anastomosis to the recipient's circulatory system and reestablishment of blood flow, there is only a 4-hour window of safety. Beyond this 4-hour window, the recovery of facial muscles is unclear. Only a decade ago, it was thought that a full facial flap including portions of the lateral cheek, ears, scalp, and forehead had to be anastomosed to multiple arteries on each side of the face to obtain adequate perfusion (Fig. 2).²⁰ Dissection of this much vascular territory is time consuming and requires inclusion of the parotid gland, which further enhances the complexity of inset. The time

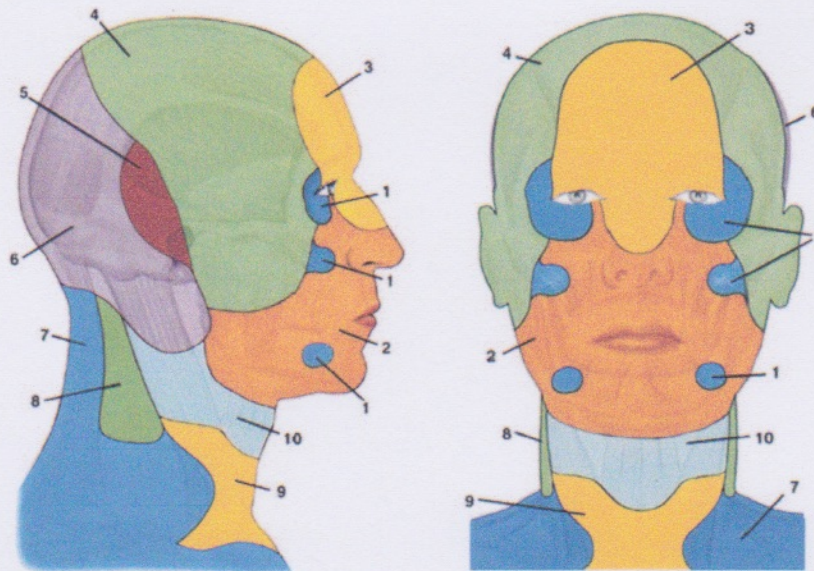


Fig. 2. The angiosome territories of the facial artery (2) are shown in frontal and profile views. The angiosome territories of the internal maxillary (1), facial (2), ophthalmic and internal carotid (3), superficial temporal (4), posterior auricular (5), occipital (6), transverse cervical (7), deep cervical (8), inferior thyroid (9), and superior thyroid (10) arteries are depicted in frontal and lateral views. Based on these angiosomes, it was thought that to perfuse a full facial flap including portions of the lateral cheek, ears, scalp, and forehead, multiple arteries had to be anastomosed on each side. We demonstrated that single anastomosis of the facial artery (2) on each side is sufficient to perform a full facial flap containing full cheeks, forehead, and partial scalp. (Reprinted with permission from Housemann ND, Taylor GI, Pan WR. The angiosomes of the head and neck: Anatomic study and clinical applications. *Plast Reconstr Surg.* 2000;105:2287–2313.)

needed for extensive dissection may interfere with the recovery of life-saving organs and may eliminate the future option of facial allograft recovery from donors who have died as a result of cardiac death, where the reperfusion window is even narrower. Therefore, in our patients, we pursued considerable simplification of the design of the anastomoses. In our recent series of full facial transplants, following extensive preoperative planning, we performed only single arterial anastomosis on each side of the face for three patients.¹⁰ We observed that only single-side anastomosis was adequate to achieve full perfusion of the full face allograft, but because of the high stakes of the operation, both sides were reconnected. In all three patients, we observed excellent blood flow without significant bleeding complications, and full revascularization within 5 to 10 minutes after retiring the clamps. One of the reasons we were confident of the success of this simplified approach was our preoperative imaging with computed tomographic angiography and magnetic resonance angiography, which allowed us to understand the intricacies of the vascular

anatomy of each recipient^{21,22} and identify the recipient's vessels that were suitable for anastomosis, thus minimizing the risks of critical blood loss and increased ischemia time, and minimizing venous outflow problems by preparing backup options, such as vein grafts. In addition, we had a plan should the allograft face not perfuse completely based on facial vessels alone. Our plan was not transplanting the recipient's forehead (the likely site of ischemia), but rather inseting the allograft at or above the level of the eyebrows. We therefore did not remove the skin from the forehead of any of our patients until after we observed excellent perfusion of the entire allograft and bleeding on its edges following anastomosis.

SURGICAL PRINCIPLE 3: PRESERVATION OF FUNCTIONAL UNITS

Although unprecedented to date, failure of facial allografts can occur. Failure may be acute



Fig. 3. This patient suffered high-voltage burn injuries to the face 11 years previously. Extensive conventional reconstruction yielded the results observed (*left*). Note that the patient is wearing a prosthetic nose. Oral competence could not be restored. The facial muscles of the forehead, cheeks, and eyelids were functional and therefore preserved. The allograft face was placed over the functioning facial bed, and only nerves that provide function to the lips were reconnected, yielding the results achieved (*right*), where 4 months after the transplant operation the patient was capable of facial expression, limited by receding swelling.

and caused by vascular compromise, or secondarily caused by acute or chronic rejection. Failure of the facial allograft would mandate surgical removal. Removal should preserve the patient's life and, if possible, lead to the same (i.e., not worse) postinjury, pretransplant state of function. However, as discussed earlier, return to the pretransplant state can be deemed unfeasible in some cases. This must be carefully discussed and disclosed to the patient as part of the informed consent process.

An attempt should be made to preserve the pretransplant functional units of the face, even if preservation increases the degree of complexity of the operations. For example, two of our four face transplant recipients had functional facial units that, if removed, would have significantly simplified their operation. Nevertheless, we strove to preserve these functional units in case the transplants should ever fail. In one of the patients, we preserved the functional soft and hard tissues of the chin, forehead, eyebrows, and eyelids, and designed a midface allograft

containing the nose, cheeks, and maxilla.¹¹ In another, we designed a full face allograft where the functional musculature of the forehead, cheeks, and eyelids was preserved, but the entire face was resurfaced, and the muscles and nerves that provide function to the lips were restored (Fig. 3).¹⁰ If the allografts of either of these two patients fail and are removed at any point in time, conventional reconstruction techniques can return these patients to a state of disfigurement and function similar to that after injury, before transplantation, but not significantly worse.

SURGICAL PRINCIPLE 4: FUNCTIONAL AND AESTHETIC REINTEGRATION

Recovery of facial sensation is faster when coaptation of proper sensory nerves is performed.¹⁰ With the exception of direct neurotization of the most central facial muscle-to-muscle connections, motor recovery is dependent on facial nerve coaptation. The speed of sensory

and motor recovery depends on axonal regrowth of the recipient's nerve past the coaptation site. This type of nerve regeneration proceeds slowly, at a rate of approximately 1 mm/day following an initial delay of 1 month,²³ and appears to be accelerated by tacrolimus immunosuppression.^{24,25} Neurorrhaphies should therefore be performed as close to the effector muscles as the anatomy allows, by minimizing the length of the donor portion of the nerves and/or maximizing the length of the recipient portion of the nerves. The previously described simplicity of the facial artery-based allograft fits well in the context of coapting individual branches of the facial nerve as close to the effector muscles as possible, thus facilitating targeted innervation of effector muscles.

We advocate for attempting neurorrhaphies in every instance when nerve stumps are present and healthy. If they are not, nerve grafts can be used to bridge distances. If nerves are not present and usable, and nerve grafting is not possible, nerve transfers based on our knowledge of head and neck reconstruction can be used. There has been substantial clinical experience with the use of cross-facial nerve grafts and nerve transfers (or crossovers) for facial reanimation in patients who lack proximal facial nerve segments suitable for coaptation but have intact distal neuromuscular pathways—patients whose anatomy mimics that of face transplant recipients, who have irrecoverable native facial nerves but pristine donor allografts. These techniques have been used for the treatment of both congenital and acquired facial paralysis, but the best results have been demonstrated in patients who undergo reanimation within 1 year of the onset of paralysis.²⁶ Cross-facial nerve grafting depends on intact distal branches of the facial nerve to provide the donor nerve for contralateral musculature. In transplant recipients with intact native buccal or mandibular branches, this remains an option. However, for patients with significant damage to native anatomy requiring coaptation of the facial nerve at the level of the trunk, these distal segments would be incorporated within donor allograft tissues and would themselves be downstream of facial nerve coaptations. In all cases, cross-facial nerve grafting involves long-segment nerve regeneration, given the length of graft required to reach from the ipsilateral to the contralateral portion of the face. As such, facial transplantation lends itself more readily to nerve transfers that used intact motor nerves from other tissues to power the facial nerve territory. When intact, the motor nerve to the masseter is

used because of its proximity, and produces the best results. In patients with damaged masseteric nerves, extrafacial nerves may be used, such as the glossopharyngeal, accessory, phrenic, or (most commonly) hypoglossal nerve. These coaptations can be performed using partial or complete proximal nerves; the entire nerve may be used or, after intraneural dissection, 20 to 50 percent of proximal nerve axons may be coapted to the allograft facial nerve to restore function to facial nerve territory muscles. Functionally, results are suboptimal. There is loss of function of the donor nerve, with the majority of patients undergoing hypoglossal nerve transfer demonstrating some degree of ipsilateral tongue atrophy.²⁷ In addition, this technique does not easily allow for targeted reconnection of distal nerves, relying only on a single proximal nerve segment to innervate all desired facial nerve territory musculature. If the donor nerve is coapted at the level of the facial nerve trunk, movement that is generated postoperatively is therefore characterized by significant synkinesis. Spontaneous and undesired movements, such as eye-closing with attempted smile require, further interventions and therefore make this avenue of treatment undesirable. Nonetheless, in facial transplant recipients with absent facial nerves, these techniques represent plausible treatment options when incorporating and reinnervating donor tissues.

Finally, integration of the facial allograft with the best aesthetic result is often in direct competition with the preservation of functional units and unscarred facial skin. Better aesthetic results are generally accomplished when larger areas following aesthetic units are resurfaced.²⁸ As we do not know at the present time what the future may bring with regard to overall survival of the allograft, we believe that the patient has to be consulted to make an informed decision. The level of risk acceptance can be quite different in various patients, and ultimately each individual should have the autonomy to decide.

CONCLUSIONS

Facial allotransplantation is a single operation that can provide nearly normal restoration to severely disfigured patients that, before the advent of this revolutionary intervention, were limited to undergoing multiple staged reconstructions and suboptimal functional and aesthetic results. Experience with four operations and over 20 patients evaluated for facial transplantation has highlighted the importance of surgical safety,

which must include planning for exit options (i.e., salvage plans in case of allograft failure); simplification of vascular anastomoses; preservation of uninjured, functional facial units over aesthetic considerations; and advocating for functional reintegration of the allograft through maximized attempts at proximal neuroorrhaphies and use of nerve grafts and/or nerve transfers. Finally, we acknowledge that the outcomes of the first series of face transplant interventions in the world are still young (<7 years), and that much is yet to be learned about the long-term outcomes of this intervention. As our experiential knowledge in this field increases, we vow to modify our principles and protocols toward optimum patient safety, satisfaction, and functionality.

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PATIENT CONSENT

Patients provided written consent for the use of their images.

REFERENCES

1. Bjordal K, Kaasa S, Mastekaasa A. Quality of life in patients treated for head and neck cancer: A follow-up study 7 to 11 years after radiotherapy. *Int J Radiat Oncol Biol Phys*. 1994;28:847–856.
2. Gamba A, Romano M, Grosso IM, et al. Psychosocial adjustment of patients surgically treated for head and neck cancer. *Head Neck* 1992;14:218–223.
3. van der Wouden JC, Greaves-Otte JG, Greaves J, Kruij PM, van Leeuwen O, van der Does E. Occupational reintegration of long-term cancer survivors. *J Occup Med*. 1992;34:1084–1089.
4. Bonanno A, Esmali B, Fingeret MC, Nelson DV, Weber RS. Social challenges of cancer patients with orbitofacial disfigurement. *Ophthal Plast Reconstr Surg*. 2010;26:18–22.
5. Tartaglia A, McMahon BT, West SL, Belongia L. Workplace discrimination and disfigurement: The national EEOC ADA research project. *Work* 2005;25:57–65.
6. Kauvar DS, Wolf SE, Wade CE, Cancio LC, Renz EM, Holcomb JB. Burns sustained in combat explosions in Operations Iraqi and Enduring Freedom (OIF/OEF explosion burns). *Burns* 2006;32:853–857.
7. Devauchelle B, Badet L, Lengelé B, et al. First human face allograft: Early report. *Lancet* 2006;368:203–209.
8. Petruzzo P, Testelin S, Kanitakis J, et al. First human face transplantation: 5 years outcomes. *Transplantation* 2012; 93:236–240.
9. Lantieri L, Meningaud JP, Grimbert P, et al. Repair of the lower and middle parts of the face by composite tissue allotransplantation in a patient with massive plexiform neurofibroma: A 1-year follow-up study. *Lancet* 2008;372:639–645.
10. Pomahac B, Pribaz J, Eriksson E, et al. Three patients with full facial transplantation. *N Engl J Med*. 2012;366:715–722.
11. Pomahac B, Pribaz J, Eriksson E, et al. Restoration of facial form and function after severe disfigurement from burn injury by a composite facial allograft. *Am J Transplant*. 2011;11:386–393.
12. Siemionow MZ, Papay F, Djohan R, et al. First U.S. near-total human face transplantation: A paradigm shift for massive complex injuries. *Plast Reconstr Surg*. 2010;125:111–122.
13. Pomahac B, Bueno EM, Siemionow M. Donor facial composite allograft recovery operation: Cleveland and Boston experiences. 2012;129:461e–467e.
14. Pomahac B, Nowinski D, Diaz-Siso JR, et al. Face transplantation. *Curr Probl Surg*. 2011;48:293–357.
15. Bueno EM, Diaz-Siso JR, Pomahac B. A multidisciplinary protocol for face transplantation at Brigham and Women's Hospital. *J Plast Reconstr Aesthet Surg*. 2011;64:1572–1579.
16. Pomahac B, Diaz-Siso JR, Bueno EM. Evolution of indications for facial transplantation. *J Plast Reconstr Aesthet Surg*. 2011;64:1410–1416.
17. Vicari-Christensen M, Repper S, Basile S, Young D. Tacrolimus: Review of pharmacokinetics, pharmacodynamics, and pharmacogenetics to facilitate practitioners' understanding and offer strategies for educating patients and promoting adherence. *Prog Transplant*. 2009;19:277–284.
18. Kasiske BL, Snyder JJ, Gilbertson DT, Wang C. Cancer after kidney transplantation in the United States. *Am J Transplant*. 2004;4:905–913.
19. Kasiske BL, Snyder JJ, Gilbertson D, Matas AJ. Diabetes mellitus after kidney transplantation in the United States. *Am J Transplant*. 2003;3:178–185.
20. Houseman ND, Taylor GI, Pan WR. The angiosomes of the head and neck: Anatomic study and clinical applications. *Plast Reconstr Surg*. 2000;105:2287–2313.
21. Soga S, Pomahac B, Mitsouras D, et al. Preoperative vascular mapping for facial allotransplantation: Four-dimensional computed tomographic angiography versus magnetic resonance angiography. *Plast Reconstr Surg*. 2011;128:883–891.

22. Soga S, Ersoy H, Mitsouras D, et al. Surgical planning for composite tissue allotransplantation of the face using 320-detector row computed tomography. *J Comput Assist Tomogr*. 2010; 34:766–769.
23. Tinel J. *Les Blessures Des Nerfs. Sémiologie Des Lésions Nerveuses Périphériques Par Blessures De Guerre*. Paris: Masson; 1916.
24. Gold BG, Katoh K, Storm-Dickerson T. The immunosuppressant FK506 increases the rate of axonal regeneration in rat sciatic nerve. *J Neurosci*. 1995;15:7509–7516.
25. Lyons WE, George EB, Dawson TM, Steiner JP, Snyder SH. Immunosuppressant FK506 promotes neurite outgrowth in cultures of PC12 cells and sensory ganglia. *Proc Natl Acad Sci USA* 1994;91:3191–3195.
26. Iñigo F, Ysunza A, Rojo P, Trigos I. Recovery of facial palsy after crossed facial nerve grafts. *Br J Plast Surg*. 1994; 47:312–317.
27. Shipchandler TZ, Seth R, Alam DS. Split hypoglossal-facial nerve neuroorrhaphy for treatment of the paralyzed face. *Am J Otolaryngol*. 2011;32:511–516.
28. Gonzalez-Ulloa M, Castillo A, Stevens E, Alvarez Fuertes G, Leonelli F, Ubaldo F. Preliminary study of the total restoration of the facial skin. *Plast Reconstr Surg (1946)* 1954;13: 151–161.

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