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Complex facial reconstruction by vascularized composite allotransplantation: The first Belgian case[☆]

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KEYWORDS

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Summary *Introduction:* Complex injuries to the central part of the face are difficult to reconstruct with the current plastic surgery methods. The ultimate one-staged approach to restore anatomy and vital facial functions is to perform a vascularized composite allotransplantation (VCA).

Methods: A 54-year-old man suffered from a high-energy ballistic injury, resulting in a large central facial defect. A temporary reconstruction was performed with a free plicated antero-lateral thigh (ALT) flap. Considering the goal to optimally restore facial function and aesthetics, VCA was considered as an option for facial reconstruction. A multidisciplinary team approach, digital planning, and cadaver sessions preceded the transplantation.

Results: A digitally planned facial VCA was performed involving the bilateral maxillae, the hard palate, a part of the left mandible, and the soft tissues of the lower two-thirds of the face. Due

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to meticulous preparations, minimal adjustments were necessary to achieve good fitting in the recipient. At week 17, a grade 4 rejection was successfully treated; sensory and motor recovery was noted to occur from the fourth postoperative month. Several serious infectious and medical problems have occurred until 15-months postoperatively; following that, the clinical situation has remained stable. Two years postoperatively, the patient and his family are very satisfied with the overall outcome and social reintegration in the community is successful.

Conclusion: The first face transplant in Belgium (#19 worldwide) was successful because of a meticulous 3-year preparation by a large multidisciplinary team. In our experience, preparatory cadaver dissections and three-dimensional (3D) computed tomographic (CT) modeling were valuable tools for an optimal intraoperative course and good alignment of the bony structures. Continuous long-term multidisciplinary follow-up is mandatory for surveillance of the complications associated with the immunosuppressive regime and for functional assessment of the graft.

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Introduction

Vascularized composite allotransplantation (VCA) represents the essentiality of reconstructive surgery where defects are repaired with anatomically identical structures.¹ After laryngeal transplantations^{2,3} and hand and forearm transplantations in the 1990s,⁴⁻⁶ allotransplantation of the face was introduced in 2005.⁷ In patients with major defects in the central part of the face due to trauma or congenital defects, it is very difficult to obtain good functional and esthetic results with traditional pedicled or free autologous flaps especially if the orbicularis oculi and oris muscle functions are lost. In selected cases, a VCA of the face offers the only possibility to restore vital facial functions such as breathing, swallowing, mastication, speech, and nonverbal communication in a single procedure.⁷⁻¹⁴

We report on the first Belgian face transplantation (#19 worldwide) performed in December 2011 at the Ghent University Hospital. The purpose of this article is to share our experience on performing a facial VCA with the use of 3D digital planning.

Methods

The patient

A 54-year-old man suffered a facial ballistic trauma resulting in a major defect of the lower two-thirds of the face, including soft tissues, maxillae, both eyes, the floor of the mouth, the left part of the mandible, and all dentition (Figures 1 and 2). The soft palate and pharynx were intact; the tongue was severely disintegrated but three-quarters was present and vascularized. The defects were temporarily approximated after debridement; the facial fractures were stabilized and kept in place with reconstruction titanium plates. Five days post trauma, a plicated left free anterolateral thigh (ALT) flap provided coverage of the external skin defect, separation of the oral and nasal cavity, reconstruction of the nasal canal, and obliteration of the dead space in a one-stage procedure. A

tracheostomy was required for breathing and a percutaneous gastrostomy tube for feeding. Swallowing was compromised due to oral incompetence with the risk of aspiration pneumonia; speech was very poor despite intensive orthophonic treatment.

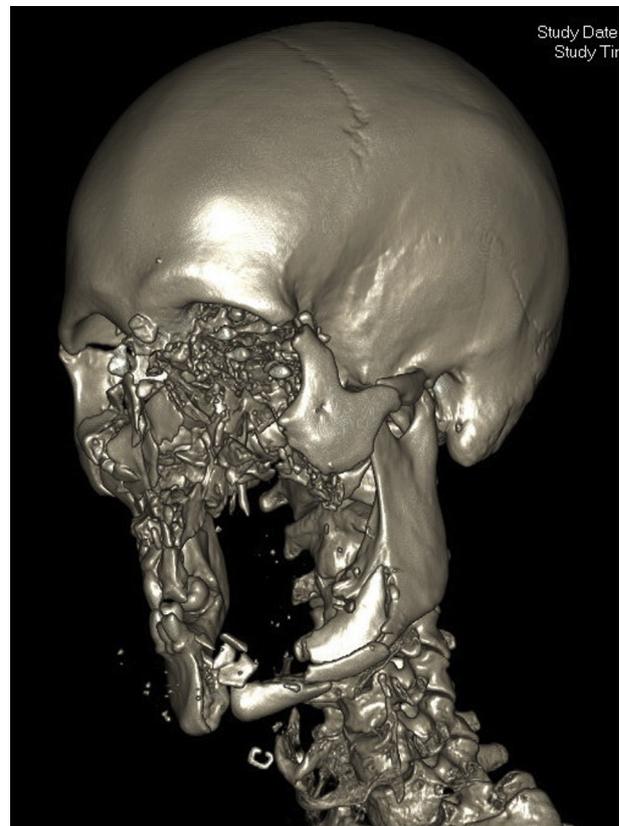


Figure 1 Left three-quarter view of the preoperative 3D CT scan of the patient, showing the missing facial bony structures: the bilateral medial orbital wall and floor, the nasal bones, the bilateral maxillary complex, the hard palate including dentition, and the horizontal part of the left mandible.

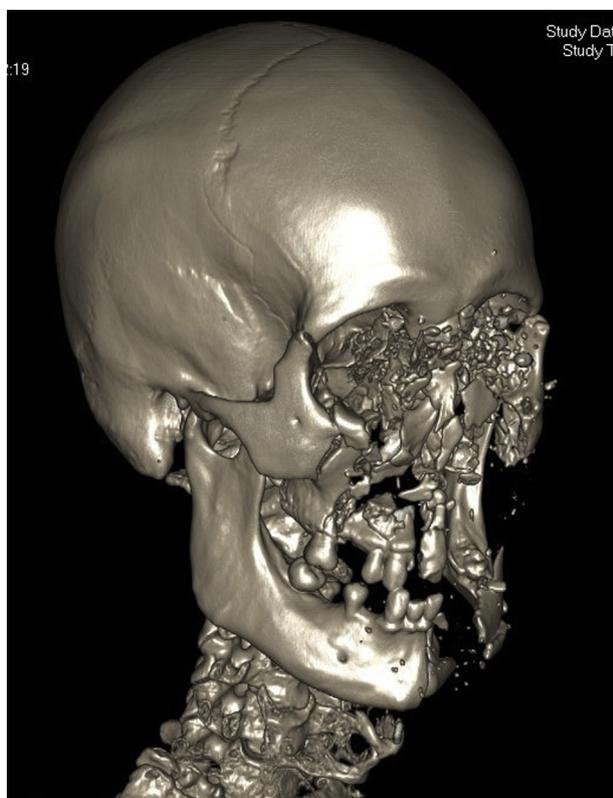


Figure 2 Right three-quarter view of the preoperative 3D CT scan of the patient.

Radiological examination, based on computed tomographic (CT) scans with three-dimensional (3D) reconstruction, provided an inventory of missing bony structures (Figure 3). Clinical evaluation demonstrated multiple soft tissues defects including the left side of the nose, the left lower eyelid, part of the left upper eyelid, the left cheek, the left upper lip, and the oral commissure. The cheeks and chin were insensitive due to the avulsion of the lower branches of the trigeminal nerve. Destroyed muscles included the lower left orbicularis oculi, all levators and depressors of the mouth, and almost all of the orbicularis oris (see Figures 4 and 5 and Video 1).

Supplementary data related to this article can be found online at <http://dx.doi.org/10.1016/j.bjps.2014.11.005>.

Preparation

After thorough multidisciplinary team screening and extensive psychological and psychiatric assessment, the patient was considered to be a possible candidate for facial transplantation; blindness was not considered as a contraindication. Advice and feedback of other more experienced centers (Paris, France, and Cleveland, USA) were sought.

The patient and his family were well informed about and fully understood the risks and complications of this potentially life-threatening procedure as well as the side effects of the immunosuppressive therapy. In April 2011, written and video-recorded informed consent was obtained and he was registered on the Eurotransplant waiting list.¹⁵

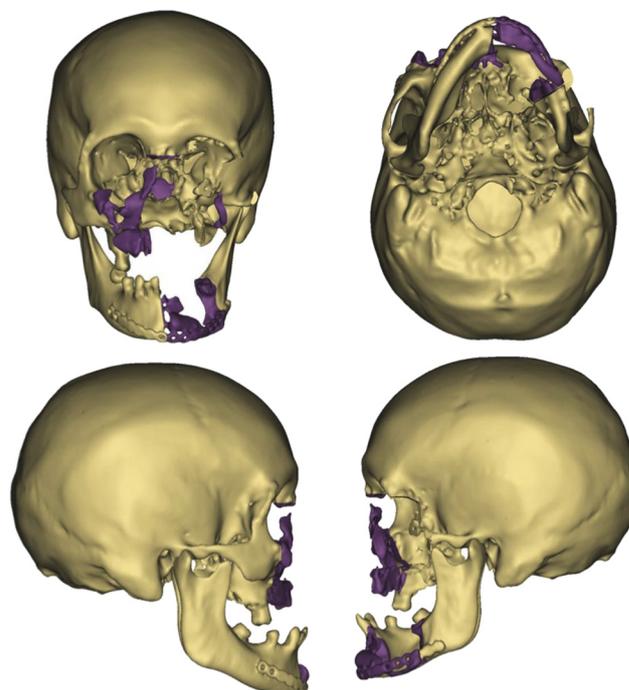


Figure 3 3D CT scan of preoperative situation in recipient. Purple indicates the bony parts of the maxilla and mandible to be resected before placing the allograft.

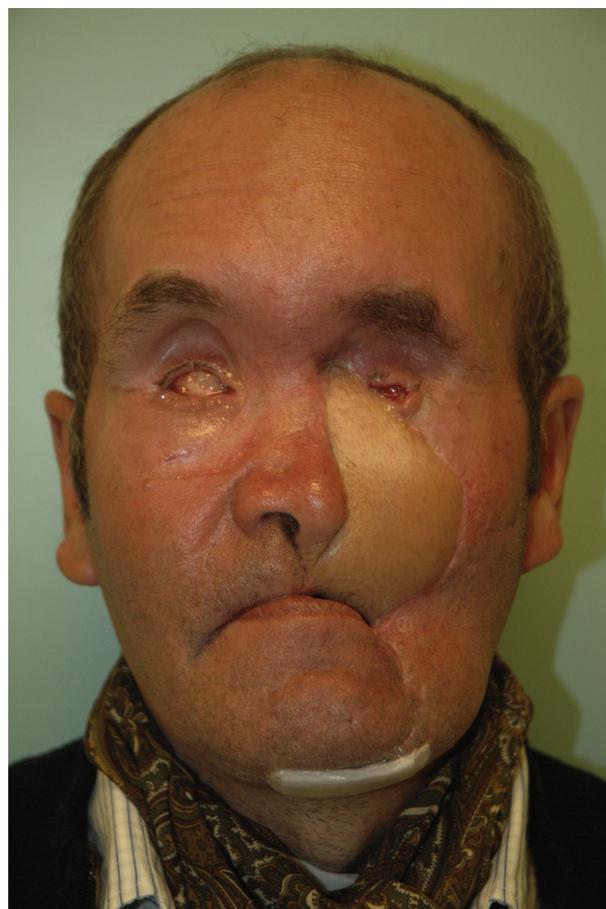


Figure 4 Frontal view of the patient before transplantation after temporary reconstruction with a plicated free ALT flap.



Figure 5 Lateral view of the patient; note the loss of mid-face projection, incapacity to close the mouth, and submandibular fistula needing continuous wound dressings.

The lack of radiographic records of our patient before the trauma made it impossible to measure and calculate the dimensions of the missing bones. As experienced during the cadaver dissections, intraoperative adjustments of the transplanted bone would take an excessive amount of time. To approach the ideal skeletal dimensions, we identified a person (his son) that morphologically resembled our patient the most. Digital subtraction of the cranial 3D CT images of both subjects showed the appropriate amount and shape of the missing facial bones. In several online meetings between the surgical team and the engineers of Materialise (Synthes ProPlan CMF/SurgiCase Connect, Materialise, Leuven, Belgium), the technical details of the osteotomies in both the donor and recipient and the repositioning of displaced bony fragments were calculated. Subsequently, specific models of the missing facial bones of the patient were created by 3D printing as well as jigs in order to guide the osteotomies in the donor and recipient face (Figures 6–8). The procedure was practiced with the full surgical team at the anatomy laboratory in multiple cadaver dissections.

The donor

A 22-year-old male donor, matching our patient in race, skin complexion, facial morphology, weight, and length with irreversible traumatic brain injury but otherwise healthy was found 8 months later. The blood group of the donor was O-positive and that of the recipient A-negative; the human leukocyte antigen status of the donor was A1 A3 B8 B16 B39 Bw6 DR2 DR16 DR3 DR17 DR51 DR52 and that of the recipient A2 A9 A24 B7 B27 DR2 DR15 DR4. Specific written permission for facial procurement was obtained from the family in accordance with the Belgian transplant laws and the requirements of the ethical committee.

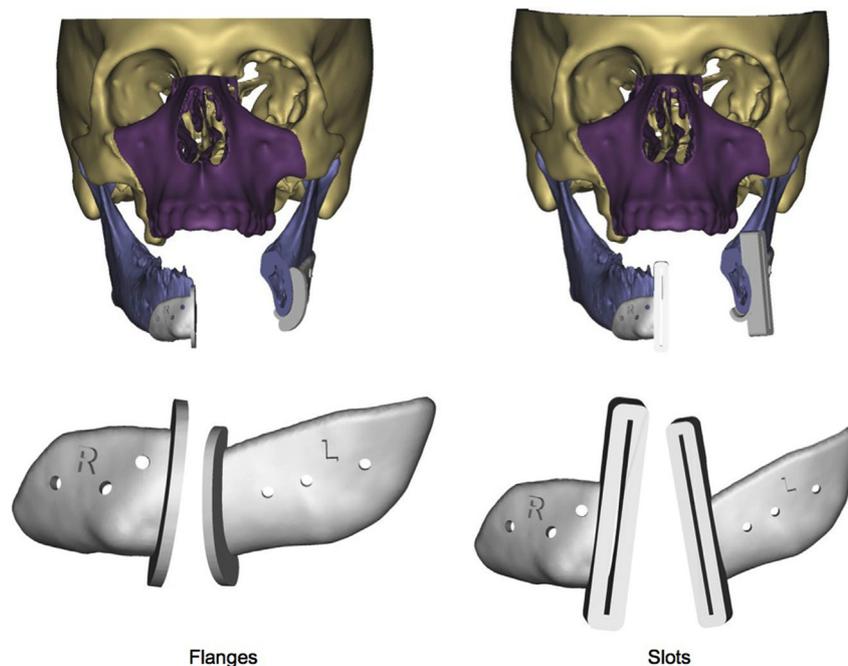


Figure 6 3D models of the recipient with maxilla graft in place (top) and mandible resection guides (bottom) used in recipient.

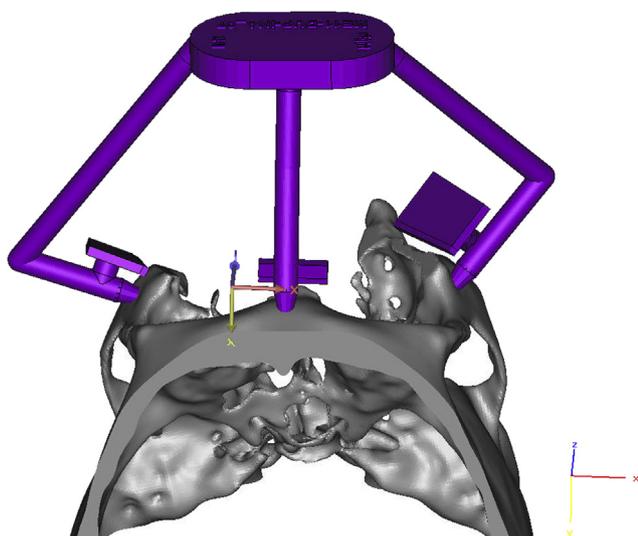


Figure 7 Cranial view of the 3D model of the maxilla resection guide, used to determine the correct plane and position of the osteotomies in recipient.

The surgical procedure

Both operations were performed simultaneously starting with a tracheotomy in the donor and recipient. Skin incisions in both subjects were performed preauricularly, through the lateral and medial canthi, nasion, and supra-laryngeal crease.

One surgical team performed the procurement of the allograft. Tissue perfusion was based on the main vascular (facial artery and vein) pedicles, isolated at the inferior margin of the mandible. The entire extracranial facial nerve and sensory (buccal, infraorbital and mental) nerves were isolated and preserved for reattachment in the



Figure 8 3D models of the maxilla and mandible graft (top left) and 3D models of the mandible-harvesting guides used in donor (top right: caudal view; bottom: lateral views).

recipient. Bilateral superficial parotidectomies were performed. The prefabricated models and jigs were used to exactly harvest the missing part of the maxillae and mandible. A standard radial forearm flap was dissected as a sentinel flap in the recipient.

The second surgical team prepared the recipient. Bilaterally, all branches of the facial nerve (except the intact frontal branch) were identified after superficial parotidectomy, followed by isolation of the facial vessels. All sensory nerves (infraorbital, mental, and buccal) were retrieved. The flap from the previous reconstruction and all old hardware were removed. Osteotomies were performed at the borders of the remaining bony structures, using the jigs and the skull models. Despite nearly intact soft tissues in the right periorbital and cheek area, the decision was made to transplant the entire midface from ear to ear as an esthetic unit including both lower eyelids (Figure 9).

At the end of the procurement, both vascular pedicles were clamped and the allograft was placed on a custom-made support structure (Figure 10). The defect in the donor face was covered with a manually fabricated silicon death mask, allowing the family to greet the deceased in a respectful and serene atmosphere.

The allograft was flushed for 30 min with a standard histidine–tryptophan–ketoglutarate solution. Following primary inset, the left facial vessels were anastomosed resulting in complete revascularization. The total duration of ischemia was 2 h and 27 min. After osteosynthesis, the contralateral vessels were anastomosed and all individual branches of the facial nerve as well as the sensory buccal nerves were coapted bilaterally. We performed shared nerve grafting of the right infraorbital nerve and mental nerves to the greater auricular nerves by interposition of the donor's radial nerve as primary suturing was impossible.¹⁶ Unfortunately, the left infraorbital nerve could not be retrieved. The soft tissues were sutured in layers, the oral mucosa was approximated, and the hard palate was sutured to the soft palate. A lateral canthopexy with additional soft tissue fixation of the cheeks to the lateral



Figure 9 Resected lower two-thirds of the face in the recipient, including the ALT flap from the previous reconstruction and nearly intact soft tissues on the right side of the face.

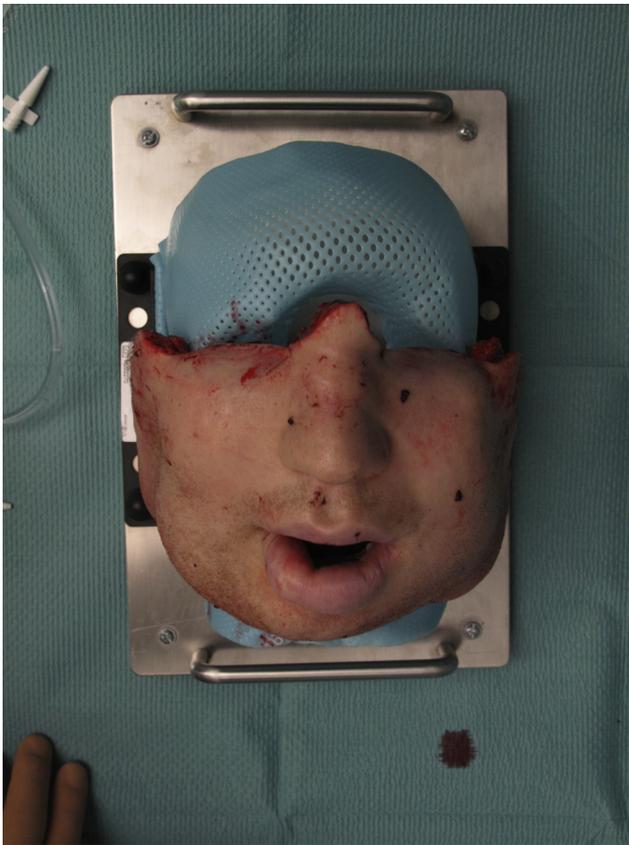


Figure 10 Custom-made support structure to transport the facial allograft and to facilitate preparations/surgical handling necessary before the actual transplantation.

orbital wall was performed using a Mitek Anchor System (Mitek Products Inc., Westwood, MA, USA) to avoid ectropion of the transplanted lower eyelids and sagging of the soft tissues. The donor radial forearm flap was anastomosed to the left femoral vessels of the recipient at the site of the previously harvested ALT flap. The patient required a total transfusion of six units of packed cells and four units of fresh frozen plasma; the entire surgical procedure lasted 20 h [Video 2](#) shows a computer animation of the preoperative 3D planning and the surgery.

Supplementary data related to this article can be found online at <http://dx.doi.org/10.1016/j.bjps.2014.11.005>.

Immunosuppression

The immunosuppression induction protocol consisted of intravenous anti-thymocyte globuline (ATG Fresenius 4 mg/kg/day for 7 days), tacrolimus, mycophenolate mofetil, and methylprednisolone 500 mg intravenously (IV) at incision. The maintenance immunosuppressive regimen included tacrolimus targeted at a concentration of 10–15 ng/ml in the first months with mycophenolate 1 g BID and tapered dosing of methylprednisolone to 8 mg at the end of month 3. Prophylactic treatment of *Pneumocystis jirovecii*, cytomegalovirus (CMV), and fungal infections was provided by co-trimoxazole 400/80 mg, valganciclovir 900 mg, and itraconazole 100 mg daily postoperatively (PO). For an

impaired glucose tolerance testing at month 1, metformin 500 mg BID was started. Vitamin D cholecalciferol 880 U with CaCO₃ 1 g daily was prescribed preventatively for osteoporosis.

Results

The immediate PO course was uneventful, and the patient was able to produce simple one-syllable words and swallow liquids 6 days after the transplantation. CT scans showed nearly optimal fit of the bony elements as in a successful Le Fort III fracture realignment (see [Video 3](#)).

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Logopedic rehabilitation therapy started 1 week PO, focused mainly on breathing, swallowing, oral motor functions, and an increase of overall speech intelligibility.^{17,18} Furthermore, tactile recognition of the facial structures, facial massage, and mime therapy were initiated together with continuation of low-vision training. Oronasopharyngeal endoscopy on day 26 showed no signs of infection, ischemia, or necrosis in the mucosa of the allograft.

Unfortunately, we were not able to perfectly align the hard palate of the donor with the soft palate of the recipient due to size discrepancy. A small fistula responsible for moderate hypernasality was treated with a custom-made obturator prosthesis. Oral inspection showed a class 2 malocclusion due to overjet of the transplanted maxilla without functional problems. The patient was discharged from the hospital in good clinical condition 4 weeks after transplantation. The oral intake was normal 2 months PO; the tracheostomy was eliminated 1 year after the transplantation and the maximal mouth opening was 4 cm interincisal. Two years after the transplant, correction of the tracheostomy scar was performed in combination with the placement of Brånemark implants in the left eye socket for epithetic reconstruction; eye prosthesis will be provided for the right side.

Intensive psychological and psychiatric support was provided to the patient and his partner. During the 15-month postsurgical period, multiple psychiatric and psychological sessions took place. To date, the patient is psychologically doing well. He has no symptoms of depression, post-traumatic stress disorder, or any anxiety disorder. He reports good dyadic adjustment and healthy family functioning.¹⁹ Despite his blindness, he has successfully reintegrated into his community participating in several social and family activities and regained a good level of autonomy.

PO complications

No clinical or histological signs of graft rejection were encountered during the first 15 weeks. Subsequently, the patient developed swelling and pain in the left jaw due to an abscess on a screw of the mandibular osteosynthesis plate. Cultures grew *Aspergillus fumigatus* despite anti-fungal therapy. After surgical drainage of the abscess and removal of the screw, the therapy was switched to voriconazole. After 8 days, the patient developed syndrome of

inappropriate secretion of antidiuretic hormone (ADH) (SIADH) for which antifungal treatment had to be switched to caspofungin IV daily maintenance.

Thirteen days later, the patient developed grade 4 rejection of the graft, histologically proven by biopsies taken from the oral mucosa. Rejection was successfully treated with methylprednisolone IV and hyperimmune CMV intravenous immunoglobulins for 4 days. He developed sinusitis due to *Pseudomonas aeruginosa* successfully treated with oral ciprofloxacin.

Despite 40 days of IV antifungal treatment, small pulmonary nodules were discovered on CT scan suspect for aspergilloma. He redeveloped SIADH; antifungal drugs were re-switched and given orally for 52 days with decreasing pulmonary lesions on CT scan.

At month 7, the patient developed painful osteoporotic thoracic vertebral fractures; analgesia and diphosphonate zoledronic acid were started in combination with wearing an orthopedic corset.

At month 11, the pulmonary aspergilloma relapsed with clinical symptoms of fever and radiologic progression. The patient had to be hospitalized for IV treatment with amphotericin B lipid complex for 3 weeks. Unfortunately, nephrotoxicity developed, and the antifungal therapy was switched to liposomal amphotericin B for 2 weeks resulting in clinical and radiological remission; a superimposed *P. aeruginosa* pneumonia was successfully treated by IV tazobactam. Since then, the clinical situation remains remarkably stable and the patient is doing well. Minimal rest lesions on pulmonary CT scan and negative blood galactomannan are suggestive of cured *Aspergillus* infection.

Functional recovery of the facial allograft

The first fasciculations in the orbicularis oris muscle occurred at week 13. The first active and controlled smile without synkinesis was seen at 4 months. Six months PO, the patient could lift both oral commissures independently, and nonverbal communication and facial expressions were returning with nearly normal mouth closure due to improved tonicity of the soft tissues and disappearance of the initial swelling.

At the 24-month follow-up, the patient reported recovery of sensation in the transplanted face better on the right than on the left side; independent voluntary movements of both sides of the face were possible without mass movements or synkinesis (see [Figures 11 and 12](#) and [Video 4](#)).

Supplementary data related to this article can be found online at <http://dx.doi.org/10.1016/j.bjps.2014.11.005>.

Discussion

In this patient, 3D models and digital planning were used to perform a facial VCA. In previous osteomyocutaneous facial transplantations, no specific technique has been described to provide a solution for the problem of the measurements of the graft and the fitting in the recipient defect. Based on our experience with 3D CT modeling in facial surgery and anaplastology, we have implemented this concept to VCA of the face as well. It has already been used in the planning of craniofacial, orthopedic, and cardiac surgical procedures,



Figure 11 Frontal view of the patient 23 months postoperatively.

and it has proven its efficiency producing excellent functional and precise results.^{20–22} We believe that digital planning and 3D models in facial transplantation allow the surgeons not only to harvest the exact amount of bone but also to precisely prepare the recipient site. They can be valuable tools in cases where an extensive osteomyocutaneous graft has to be transplanted, thus simplifying and shortening a complex surgical procedure. We experienced a class 2 malocclusion without functional problems; perhaps, this could have been avoided by applying digital planning to the actual donor as shown by Rodriguez et al.²³ However, this is more time consuming, superimposing risks concerning the hemodynamic stability of the donor and interfering with the timing of the subsequent organ transplant surgeons. Moreover, no preoperative printed models and jigs can be generated. The 3D imaging has helped us considerably to save operating time, to determine the amount of bone needed in the upper and lower jaw, and to obtain a result as superior as possible taking all factors into consideration. The absence of a perfect occlusion is due to the discrepancy between the donor and recipient bony structures.

So far, 28 facial allotransplantations have been performed worldwide including our case.¹⁴ VCA has become a feasible and reproducible surgical procedure as many technical, logistic, social, and immunologic issues have been improved or resolved during the last decade. VCA should be taken into consideration as an early option in extreme cases not amenable to modern-day reconstructive surgery to spare the patient years of continued



Figure 12 Lateral view of the patient; note the good mid-face projection and skin color match.

disfigurement in both the face and donor areas, facial malfunctioning, and the cumulative financial and psychological burden of multiple reconstructions.^{24–30} The extensiveness and the complexity of the defect to the central most mobile area of the face of our patient and the expected poor PO clinical and functional outcome after reconstruction made it very likely that further conventional reconstructive surgery would be a long-lasting process requiring multiple procedures with inferior results.^{31,32} Therefore, allotransplantation of the face was considered in an early phase as the best option in the long-term to reestablish vital functions, aesthetics, and overall quality of life in a one-staged procedure.

We experienced one episode of a biopsy-proven grade 4 rejection. At the same time, the sentinel flap on the left leg showed minimal clinical and histological changes during this rejection. This contradictory phenomenon has been observed by some others^{14,33} but not all.^{7,26} The possible reasons may include the differences in tissue composition of the face (compound) and sentinel (skin) flap, the latter being less antigenic. The cellular and molecular basis for skin rejection in VCA, although partially delineated, remains largely unknown and there are only few reports on the pathology of face transplant.^{34,35} Rejection in VCA is a major challenge and the final decision upon diagnosis and treatment should be made based on both clinical signs and histological findings of skin/mucosa biopsies.

The main drawbacks of facial transplantation are not associated with the allograft itself but the need for lifelong

immunosuppressive therapy with associated long-term side effects (opportunistic infections, secondary malignancies, and cardiovascular morbidity) and potential mortality; until now, three therapy-related deaths have been reported.¹⁴ Our patient also suffered from many and severe medical complications mainly caused by the pharmacological treatment. As a result, he was frequently hospitalized, underwent different medical treatments, and experienced a decreased physical quality of life. These findings underscore the absolute need of a continuous multidisciplinary treatment of these patients as they turn chronically ill; the associated complications not only affects them but also poses a severe burden to the family.

There has been controversy if facial transplantation should be performed in blind patients, based on functional, social, rehabilitative, and ethical concerns.³⁶ Before transplantation, our patient was already well adapted to his handicap due to early rehabilitation. We experienced no issues with compliance to rehabilitation, surveillance of the graft, and identity transfer.^{17–19} He demonstrated good recovery of motor and sensory function and social reintegration with improved quality of life. Blindness is not a contraindication in well-selected and motivated face transplant candidates, and these patients might even have more psychological benefits of the knowledge of having a normal facial appearance and not being stared at in a crowd.

In early cases of facial transplantation, esthetic subunits were considered of less importance. Based on the advice and experience of other authors, we decided to transplant the soft tissues of the entire lower two-thirds of the face as esthetic units, thus simplifying facial allograft procurement and favoring a more aesthetically pleasing result without a patchy mutilated appearance.^{30,37–41}

Conclusion

In our experience, 3D CT modeling, preparatory cadaver dissections, and meticulous planning with a multidisciplinary team have proven to be valuable tools for a fluent intraoperative course, adequate bony alignment, and good functional and esthetic outcome in the first Belgian face transplant. These findings are in accordance with other reports and hopefully will contribute to further support and optimize facial transplantation and outcomes.

Ethical approval

Ethical approval was obtained by the ethical committee of the University Hospital of Ghent in accordance with the principles of the Declaration of Helsinki (file nr. 2001/022).

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Conflicts of interest

None declared.

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