A New Composite Hemiface/Mandible/Tongue Transplantation Model in Rats

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Abstract: Extensive head and neck deformities, including bone and soft tissue defects, are always challenging for reconstructive surgeons. The purpose of this study was to extend the application of the face/scalp transplantation model in rats by the incorporation of vascularized mandible, masseter and tongue (based on the same vascular pedicle), and to use this as a model to test new reconstructive options for extensive head and neck deformities with involving large soft and bone tissue defects.

A total of 10 composite hemiface/mandible/tongue transplantations were performed in Lewis rats (RT1[1]). Hemimandibular bone, masseter muscle, tongue and hemifacial skin flaps were dissected based on the same vascular pedicle of common carotid artery and external jugular vein. The flaps were then transplanted to the recipient inguinal region. Evaluation methods included flap angiography, plain x-ray, computed tomographic scan, and histology.

All transplants survived indefinitely and no graft loss was noted. Flap angiography demonstrated intact vascular supply to the bone. Computed tomography scan and bone histology confirmed the viability of the bone components for the composite grafts. Hematoxylin and eosin staining determined the presence of viable bone marrow cells within the transplanted mandible. Viability of the tongue was confirmed by the presence of pink color and bleeding after puncture, as well as by histology.

We have introduced a new composite hemiface/mandible/tongue transplant model. The main advantage of this model is the presence of vascularized bone marrow within the mandibular component, which may facilitate future studies on chimerism and tolerance induction. Although this mandible composite allograft is placed heterotopically to the recipient inguinal region, we believe that it may serve as a new reconstructive option for the coverage of combined bone and soft tissue defects within the head and neck region.

Key Words: composite tissue transplantation model, hemiface transplantation, hemimandible transplantation, tongue transplantation, vascularized bone marrow transplantation

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The reconstruction of composite tissue defects within the head and neck regions is always challenging for the reconstructive surgeon. These large composite tissue defects, which frequently involve the bone, muscle or tongue, are often the results of high velocity gun-shot injuries, cancer ablative surgeries, burns, or trauma. Today, composite tissue transplants are being considered as an alternative option for treating these challenging defects.[1–6]

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Presently, 1 scalp transplantation[7] and 4 partial face transplantations have been reported.[8–11]

In the case of the first partial face transplant, Dubernard et al reported that the transplantation of donor bone marrows was a form of supportive therapy to the standard immunosuppressive protocols.[8]

During past 20 years of research in the field of composite tissue allotransplantation (CTA), we have designed, developed and tested different CTA models under different immunosuppressive protocols. This research was performed to extend allograft survival by inducing tolerance across the major histocompatibility barrier and to prevent chronic rejection and graft failure.[3–6] Our experience in this field revealed that rejection can be prevented by maintaining immunosuppressive therapy, as well as by inducing donor-specific tolerance to ameliorate the harmful effects of chronic immunosuppression.[12,13] Thus, induction of donor-specific tolerance without the need for chronic immunosuppression is the final goal for CTA transplantation. It has been shown that clinical tolerance can be achieved by the induction of mixed chimerism following donor bone marrow transplantation under different types of conditioning protocols.[14] To induce donor-specific chimerism, different cellular and vascularized bone marrow transplantation (VBMT) models were tested in experimental studies. These studies confirmed the superiority of VBMT for the hematopoietic reconstitution of donor bone marrow cells when compared with cellular bone marrow transplantations (BMT).[3–6,15–23]

In their recent comprehensive review on VBMT, Gordon et al examined the newly found benefits, the unique characteristics and the applicability of VBMT as an alternative to BMT. They emphasized the importance of VBMT to potentially reduce the risk of engraftment failure, provide a more rapid engraftment, enhance cellular function, reduce graft-versus-host disease, and aid in inducing immunologic tolerance.[16]

Different VBMT models were introduced in the literature, including marrow sources from the limb, sternum, femoral bone, and bilateral vascularized femoral bones.[3–6,16–23] In addition, we have introduced different models of face allotransplantation in rats including a full-face, hemi-face and hemiface/calvaria model.[24–28]

Herein, we introduce a new composite hemiface/mandible/tongue transplantation model based on the common carotid artery and the external jugular vein. In this composite isograft, we demonstrated that the hemimandible, which is a vascularized bone marrow component, has an independent vascular supply based on the inferior alveolar artery. This is also a new model of vascularized skin and bone marrow transplantation. To our knowledge, this is the first model of face transplantation that includes composites of vascularized mandible, masseter and tongue, and is also the first model to be tested as a new treatment option for the reconstruction of extensive head and neck deformities involving large soft and bone tissue defects.[29–33]

MATERIALS AND METHODS

All animals received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" as published by the National Institutes of Health. The animals were caged individually, their environment was maintained with a 12-hour

light/dark cycle, and animals were given free access to standard laboratory food and water. Five Lewis (RT^1) fresh cadaver rats were used to study the anatomy and vascular territories of the composite flaps.

A total of 20 adult male inbred Lewis rats (LEW, $RT1^1$) weighing 200 to 250 g were used as donors (n = 10) and recipients (n = 10) of the composite hemiface/mandible/tongue transplantations. Ten donor and 10 recipient animals were used in this study. Anesthesia was induced with sodium pentobarbital (50 mg/kg), which was administered intraperitoneal. Further doses of 10 mg/kg per hour were administered to maintain anesthesia. Dissections and microvascular anastomoses were performed under operating microscope magnification (Zeiss OP-MI 6 SD; Carl Zeiss, Goettingen, Germany).

Anatomic Dissection Study in Fresh Rat Cadavers

Dissections were performed on 5 Lewis rat fresh cadavers to determine the vascular territories and the anatomy of the inferior alveolar artery, which is the first branch of internal maxillary artery. The entire composite flap was based on the common carotid artery and jugular vein, and we subsequently investigated the feasibility of isolating the composite hemiface/mandible/tongue flap with preservation of the vascular territories.

Experimental Groups

Ten Lewis rats were used as donors and 10 were used as recipients. Thus, 10 composite osseomusculocutaneous hemiface/mandible/tongue transplantations were performed among the genetically identical Lewis rats.

Surgical Procedure

Preparation of the Donor (Harvesting of the Composite Hemiface/Mandible/Tongue Flap)

In all surgical procedure aseptic technique was used. The head, neck and scalp were shaved and painted with iodine solution. Upper and lower eyelids were included in the flap.

Following the vertical midline skin incision in the anterior neck, the submandibular gland was excised after ligation of the glandular branches of the facial artery and vein. External jugular vein and its 2 main branches, the anterior and posterior facial veins, were dissected and preserved. The sternocleidomastoid muscle was detached from its sternoclavicular and mastoid insertion and excised to expose the common carotid artery and its main branches, the external and internal carotid arteries. The posterior belly of the digastric muscle was excised, the omohyoid muscle was transected and the greater horn of the hyoid bone was excised for better visualization of the external carotid artery and its branches. Tracheostomy was performed, and an angiocat was inserted as a tracheostomy tube. Mandible was divided at the symphysis and dissection was carried out at the mouth floor to the root of the tongue. Right pedicles were ligated and transected. The left side of the root of the tongue was left intact.

Internal carotid artery, superior thyroid artery, ascending pharyngeal artery, and ascending palatine artery were ligated and transected. Facial artery, superficial temporal artery, posterior auricular artery, lingual artery, and internal maxillary artery were preserved and included in the flap.

In the perioral region the levator labii superior and dilator naris muscles were transected and the facial artery and vein were identified. These vessels were included in the flap after ligation of the superior and inferior labial branches.

The dissection was carried out above the nose toward the occipital area. Periosteum was incised and dissected at the midline level of the temporoparietal area. Next the dissection was carried out under the temporal muscle plane toward the zygomatic arch. When the zygomatic arch was reached, the zygomatic arch was excised and orbital exenteration was performed.

The external ear canal was detached at the osteocartilaginous junction and the external ear was preserved within the flap. In front of the bulla, side branches of the internal maxillary vein were ligated and the internal maxillary vein was spared. The capsule of the temporomandibular joint was opened and dissection was continued bluntly toward the skull base. To preserve the vascular supply of the mandible, the inferior alveolar artery, which is the first branch of the internal maxillary artery, was preserved (Figs. 1, 2). Oral mucosa was incised and dissected from the maxilla at the level of the upper gingivobuccal sulcus. Finally, the common carotid artery and external jugular vein were divided to create a vascular pedicle of the

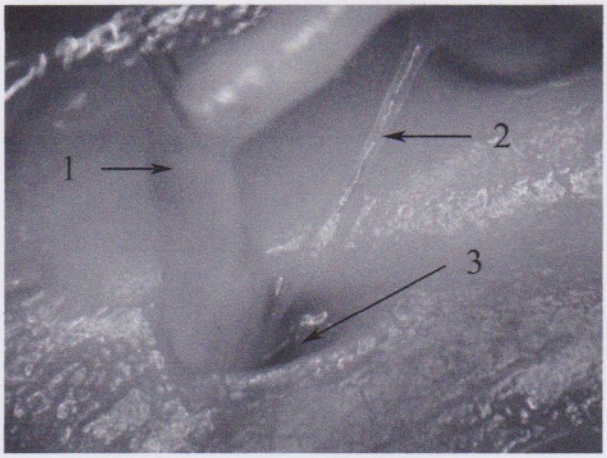

FIGURE 1. Anatomic dissection in fresh Lewis (LEW, RT^1) cadaver rat showing vascular integrity of mandibular bone component of composite hemiface/mandible/tongue isograft 1, inferior alveolar nerve; 2, inferior alveolar artery; 3, mandibular foramen.

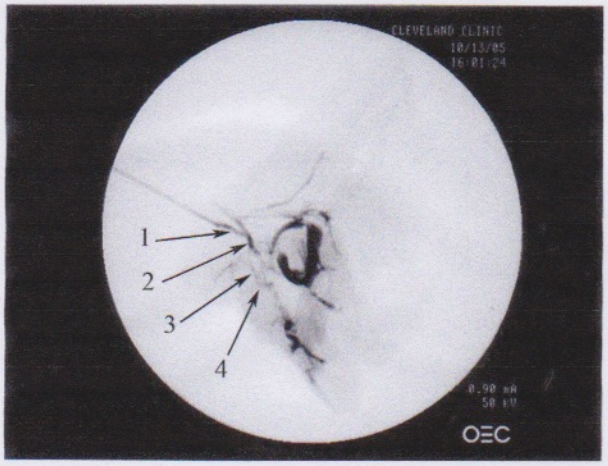

FIGURE 2. Barium sulfate was injected to the pedicle of harvested composite hemiface/mandible/tongue isograft, and plain x-rays were taken to assess the vascular territories. 1, common carotid artery; 2, external carotid artery; 3, internal maxillary artery; 4, inferior alveolar artery.

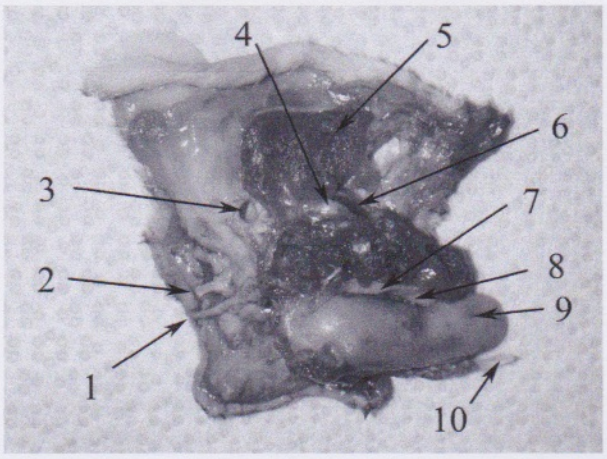

FIGURE 3. The inner aspect of the harvested composite hemiface/mandible/tongue isograft. 1, common carotid artey; 2, external jugular vein; 3, external auricular meatus; 4, mandibular condyle; 5, split temporalis muscle; 6, split masseter muscle; 7, oral mucosa; 8, hemimandible and teeth; 9, tongue; 10, mandibular tooth.

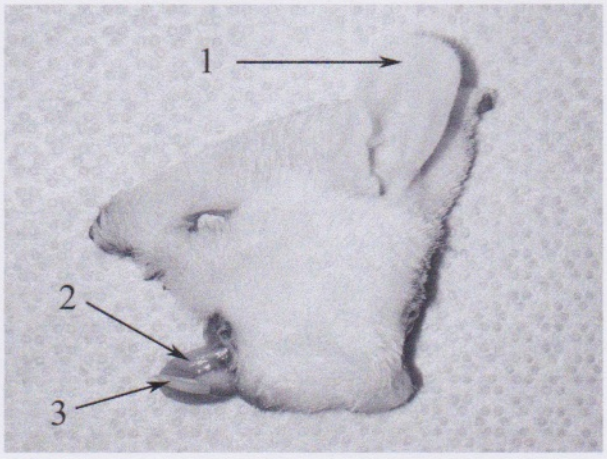

FIGURE 4. The outer aspect of the harvested composite hemiface/mandible/tongue isograft. 1, external ear; 2, tongue; 3, mandibular tooth.

composite flap. The harvested composite flap was perfused with heparinized lactated Ringer's solution until the venous outflow was clear (Figs. 3, 4).

Preparation of the Recipient

Under anesthesia, the right inguinal region of the recipient rats was shaved, and a skin incision was made 1 cm medial to the inguinal crease. Under an operating microscope, the femoral vessels were exposed and dissected from the inguinal ligament for microsurgical anastomosis. The donor flap was transferred into the recipients' inguinal region and was fixed with few stay sutures before the anastomosis was performed. Next, arterial anastomosis was performed using standard end-to-end microsurgical techniques between the common carotid artery of the donor and femoral artery of the recipient. Then, end-to-end anastomosis between the external jugular vein of the donor and the femoral vein of the recipient was performed under an operating microscope using 10/0 nylon sutures. The clamps were released and ischemia time was kept under 120 minutes. The skin was closed using 5/0 catgut. The wound was closed with great care so that there was no kinking or stretching of the anastomosed vessels. After transplantation, the recipients received 10 mL of subcutaneous lactated Ringer's solution to compensate for the perioperative fluid loss.

Clinical Evaluation of Flap Viability

Following transplantation, the hemiface/mandible/tongue flaps were evaluated for the presence of any clinical signs of vascular failure on a daily basis during the first 3 months and on a weekly basis thereafter. In the early posttransplant period, skin flaps were observed for color and temperature changes, hematoma formation, progressive edema, and later for hair loss, desquamation, epidermolysis, exudation, and stiffness.

Histologic Evaluation

Two selected hemiface/mandible/tongue recipients were euthanized at day 100 posttransplant for histologic evaluation. Tissue biopsies were taken throughout the full-composit graft and included the skin, muscle, tongue and bone of the hemiface/mandible/tongue flap. The samples of the composite tissue component of the flap were harvested and fixed in 10% formalin solution and then decalcified in 5% formic acid solution for 3 days. Next the fixed specimens were embedded in paraffin, and 3-μm sections were stained with the hematoxylin-eosin dye. Histologic sections were evaluated for the integrity of skin, muscle, tongue and tooth, and for the viability of the bone marrow compartment.

Barium Angiography

Barium sulfate (3 mL, Biotrace, Bryan Corp., Woburn, MA) was injected to the pedicle of harvested flaps, and plain x-rays were taken to assess the integrity of the vascular territories. The anatomic terminology was used according to Greene's *Anatomy of the Rat*.[34]

Plain X-ray and Computed Tomografi

To confirm normal mandibular bone structure and a lack of bone absorption over time, 2 rats were evaluated at posttransplant days 100 by plain x-ray and spiral computed tomography.

RESULTS

Anatomic Study Results

Anatomic dissection revealed that vascular supply of the mandible was coming directly from the inferior alveolar artery, which is a direct branch of the internal maxillary artery (Figs. 1, 2). The internal maxillary artery, one of the terminal branches of the external carotid, begins just in front of the temporomandibular joint. It takes a deep course beneath the masseter muscle.

The inferior alveolar artery leaves the internal maxillary artery as the latter crosses the lateral surface of the neck of the mandible. The artery also runs medial to the mandible entering the mandibular canal through the mandibular foramen and is accompanied by the corresponding nerve. Within the mandibular canal it gives off an incisor branch, which curves posteriorly and enters the root of the lower incisor tooth. It continues as the mental branch through the canal, and connects with the mental branch of the inferior labial artery, which enters the mandibular canal through the mental foramen (Fig. 1).

The inferior alveolar vein begins in the mandibular canal where it continues with the mental branch of the inferior labial vein. In its course through the canal it receives a branch from the lower incisor tooth, and then emerges on the medial surface of the

mandible through the mandibular foramen. It then receives a large communicating vein from the internal maxillary vein.

The internal maxillary vein receives tributaries corresponding very closely to the branches of the internal maxillary artery. It is running under the cover of the temporalis and masseter muscles, and it then appears more superficially in the space between the neck of the mandible and the tymphanic bulla where it communicates with the inferior alveolar vein and continues posteriorly to unite with the superficial temporal vein to form the posterior facial vein.

Clinical Evaluation and Animal Survival

All transplanted flaps survived indefinitely. We did not observe vascular problems in any of the flaps. Successful flap transplantation was accomplished in all 10 animals, with 100% flap survival up to 350 days during the follow-up period. One complication was encountered, with one rat failing to recover from anesthesia and subsequently dying. The transplantation procedure was repeated on a different rat, which survived without any complications. Except for this case, all animals tolerated the operation well and returned to their normal activities on the day after the transplantation. After this posttransplantation recovery period we did not encounter any other complications related to flap survival. The mean surgical duration for the hemiface/mandible/tongue transplantation was 5 hours, and the mean time of warm ischemia was 80 minutes. The body weights were stable, and we did not observe any sign of infection. Clinically, all flaps were pink and pliable during the entire observation period. All flaps also showed tooth growth (Figs. 5, 6). New hair growth was observed within 20 to 25 days posttransplant. No auto-cannibalization was observed. The mandibular component of this flap was not reconstructed using rigid fixation, and thus this transplanted mandible lacked the ability to perform clinically relevant functions such as mastication. Although it has been known that bone atrophies could be expected when muscle forces become absent, as in this heterotopic and nonfunctional model, mandibular component of the flap could be easily palpated in animals at all time points after the transplantation.

Histologic Evaluation

Histologic results confirmed the integrity and viability of flap components including the skin, muscle, tongue, and mandibular bone. Within the mandibular bone, active hematopoiesis was noted and no necrosis or fibrosis was identified. Skin biopsy showed normal epidermis and dermis (Figs. 7–10).

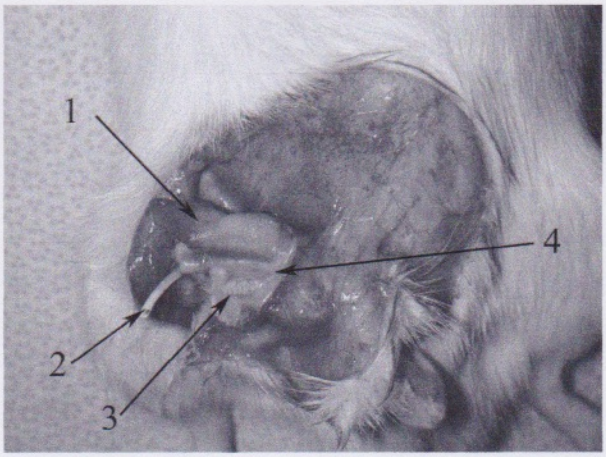

FIGURE 5. Viable tissue component of composite hemiface/mandible/tongue isograft (LEW to LEW) at 45th day posttransplantion. 1, tongue; 2, mandibular tooth; 3, hemimandible and teeth; 4, oral mucosa.

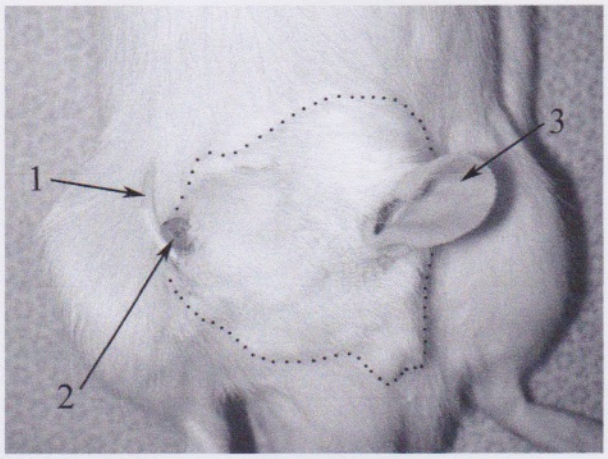

FIGURE 6. Composite hemiface/mandible/tongue isograft (LEW to LEW) at 100th day posttransplantation (boundaries of composite flap are encircled). 1, mandibular tooth; 2, tongue; 3, external ear.

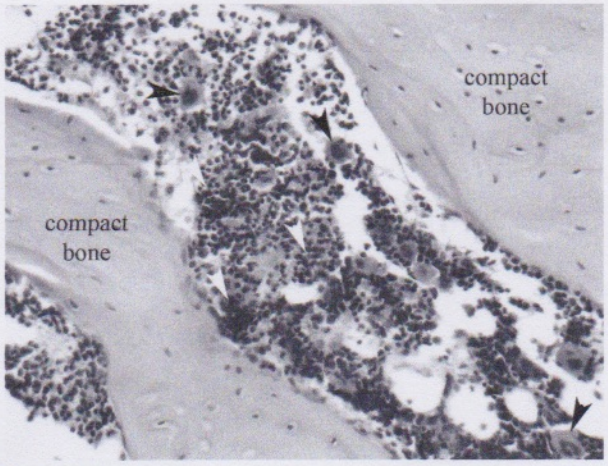

FIGURE 7. The presence of viable bone marrow cells within the transplanted mandible component of the composite hemiface/mandible/tongue isograft (LEW to LEW) (black arrowhead indicates megakaryocyte and white arrowheads indicates active hematopoiesis) at 100th day posttransplantion (H&E, ×300).

Barium Angiography

Radiologic evaluation with barium sulfate showed that the inferior alveolar artery, the main arterial branch that supplies the mandible, was well-preserved within the flap (Fig. 2).

Plain X-ray and Computed Tomografi

Plain x-ray and computed tomography of hemiface/mandible/tongue flap showed persistence of the mandibular bone (Figs. 11, 12).

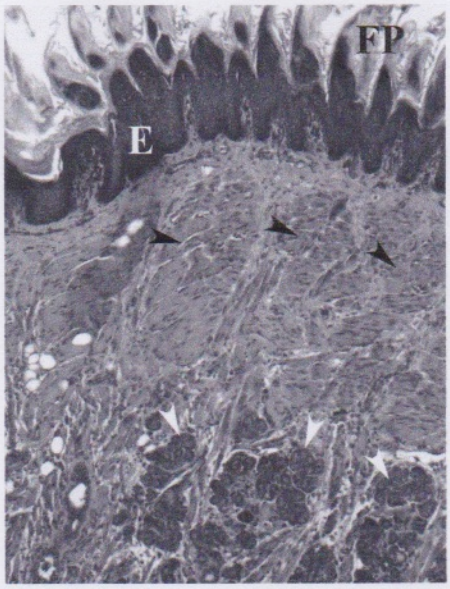

FIGURE 8. Histology of the tongue demonstrated integrity of the tongue component of the composite hemiface/mandible/tongue isograft (LEW to LEW) at day 100th posttransplantation. Black arrowhead indicates muscle layer and white arrowhead indicates lingual salivary glands. FP, Filiform papilla; E, epithelium (H&E, ×300).

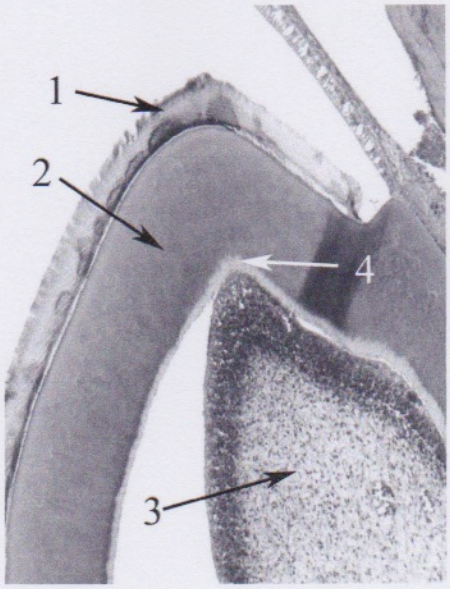

FIGURE 9. Histology of the tooth demonstrated integrity of the tooth component of the composite hemiface/mandible/tongue isograft (LEW to LEW) at day 100th posttransplantation. 1, enamel; 2, dentin; 3, dental pulp; 4, odontoblasts (H&E, ×300).

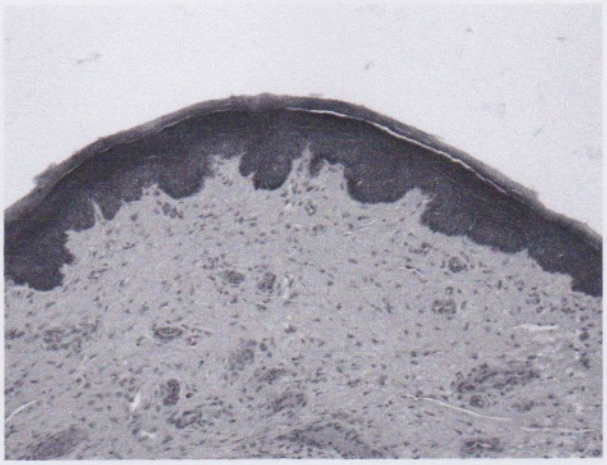

FIGURE 10. Skin biopsy from composite hemiface/mandible/tongue isograft (LEW to LEW) at day 100th posttransplantation shows normal epidermis and dermis (H&E, ×300).

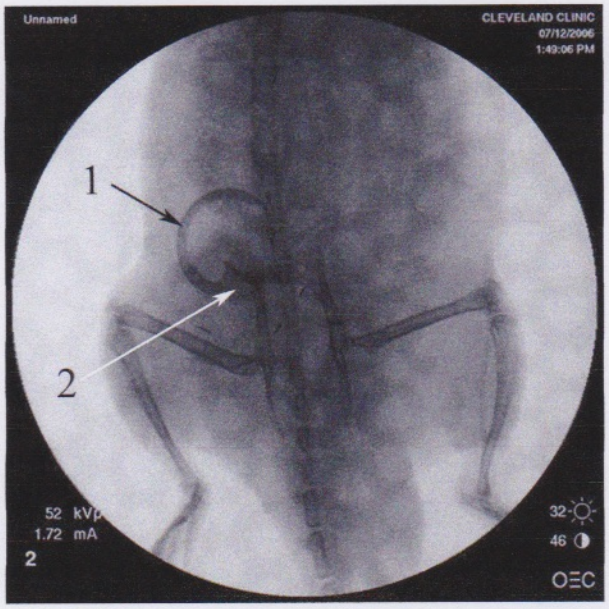

FIGURE 11. Plain x-ray of composite hemiface/mandible/tongue isograft (LEW to LEW) at day 100th posttransplantation. 1, mandibular tooth; 2, hemimandible.

DISCUSSION

Reconstruction of head and neck deformities secondary to burn injury, trauma, or cancer resections is a challenging procedure for surgeons. For small head and neck defects, transfer of the adjacent tissues may give satisfactory results. However, for the coverage of more extensive deformities in bones and soft tissues, local flaps are usually inadequate and microsurgical free tissue transfer are generally required.[35]

There is a considerable demand for routine CTA transplantation. However, the need for life-long immunosuppression means that routine clinical application of CTA transplantation is undesir-

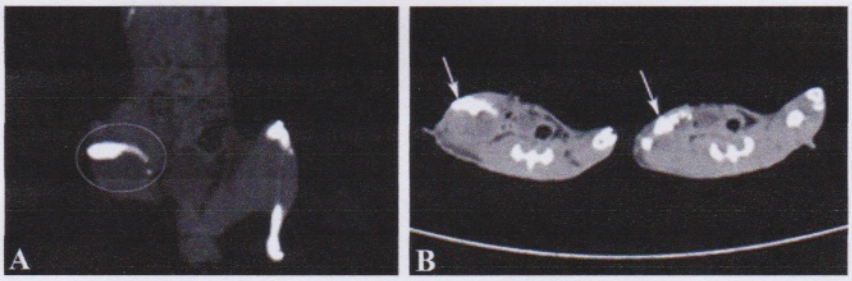

FIGURE 12. Computed tomographic scan demonstrated the viability of bone components of the composite hemiface/mandible/tongue isograft (LEW to LEW) at day 100th posttransplantation. A, hemimandibular bone is encircled by white elliptical circle. B, hemimandibular bones are indicated by white arrows.

able in many cases. After introducing composite full-face and hemiface allograft transplantation models in rat,[24–27] Siemionow et al reported detailed cadaveric studies confirming the technical feasibility and applicability of face/scalp transplantation in humans.[26,27,36–39] So far, 1 scalp[7] and 4 partial face transplantations have been performed in humans.[8–11] Unlike the face allotransplantation models in rats, in transplants using cadaver tissues, or in human scalp and partial face transplantations, the hemiface/mandible/tongue transplantation model includes vascularized bone, bone marrow, tongue, oral mucosa, teeth and muscle within the flap. The unique properties of this model allow not only for skin coverage of the face but also for extensive coverage of soft and bone tissue defects in a single reconstructive procedure.[29–33]

Yazici et al introduced the composite hemiface/calvaria transplantation model, which included vascularized calvarial bones, as a new treatment option for severe craniofacial defects.[28] This was the sole published study where vascularized bone with bone marrow compartment was incorporated into a hemi-face transplantation model in rats. In the hemiface/calvaria model, bone perfusion to the dura, the periosteum, the temporalis muscle and the underlying calvarial bone was provided via the middle temporal artery. In contrast to the calvaria model, the mandible has its own direct vascular supply from the inferior alveolar artery. Thus, we have incorporated the bone component of this flap based on the vascular supply of the inferior alveolar artery. Preserving direct vascular supply of the hemimandible is the unique property of this model.

In their partial face transplantation in humans, Guo et al included both the frontal maxillary sinus wall and the zygomatic bone. It was the first clinical face transplantation model that incorporated bone structure from the maxillary sinus wall and the zygomatic bone. However, neither the maxillary sinus wall nor the zygomatic bone in this clinical model received constant vascular supply. In our present study, the mandible has its own vascular supply from the inferior alveolar artery, thus our transplant procedure may be more similar to a real vascular bone transplantion model.[9]

Interruption of the inferior alveolar arterial flow and its effect on mandibular collateral circulation was investigated in rhesus monkey by Castelli et al.[40] They found that even if the blood flow through the inferior alveolar artery was interrupted, the mental artery and the mandibular branch of the sublingual artery promptly provided collateral circulation, maintained the viability of the bone, and accelerated the healing process. Thus, these findings confirmed that we could expect perfusion of the vascularized bone component in our model.

Our model is not technically challenging and produces low postoperation complication rates. This model will be applicable for the transfer of hemiface/mandible/tongue components to cover severe head and neck deformities. In CTA models, skin is considered one of the most antigenic tissues.[41] Thus, the inclusion of skin, cartilaginous ear, tongue, oral mucosa, teeth and hemimandible components makes this a more challenging transplant model.[29–33]

Similar to the limb allograft model, the hemiface/mandible/tongue transplantation model is permissive for tolerance induction because it contains bone as a vascularized source for the delivery of donor-specific stem and progenitor cells to the recipients. Unlike limb transplantation, in this model there is no need for osteotomy and/or intramedullary fixation that may alter the quantity of bone marrow compartment. Since rats are smaller than humans and the tissues are not suitable for fixating the composite flap into its native position, we fixed the composite flap to the inguinal region. Thus, we did not endanger the survival of a smaller animal. The clinical translation of this model mandated the rigid fixation of mandible, which may be considered a limit of this study. However, this model could be applied to bigger animal models. Indeed, the flap could be placed into its original position without endangering the survival of the subject and allowing sufficient vascularity to support bone healing, using rigid fixation and mastication. In addition we did not perform neurologic anastomoses, which might increase the utility of this flap. Briefly, this model is heterotopic and nonfunctional and only investigates vascular reliability of a composite hemiface/mandible/tongue flap in a rat.

Vascularized sternum and vascularized femur transplantation models are other proposed models for bone marrow augmentation.[3–6,17–22] Tai et al developed a technically simple model of vascularized femur transplantation called extraperitoneal isolated vascularized bone marrow transplant (iVBMT).[23] In iVBMT, this transplant was placed subcutaneously and resulted in minimal morbidity in the recipient animals. The authors also demonstrated peripheral chimerism in the recipient via polymerase chain reaction.[23] However, these models did not include transplantation of the skin, which is an essential component in many CTA models.[3–6,17–23]

Since we preserved the structural integrity of the mandible, we can now expect bone marrow-derived cell engraftment. In addition, the large skin component in this model will enable the monitoring of flap viability in an isotransplant setting. Moreover, it will allow the monitoring of graft acceptance and rejection if it is used in the allotransplant setting.

Bone transplantation has considerable potential for reconstructing osseous defects. Bone allografts, either vascularized or nonvascularized, have been used with some success.[42] Weiland et al compared free vascularized bone grafts, matchstick autografts, and segmental autografts and allografts by mechanical testing and histology. They have demonstrated that free vascularized bone autografts were superior to nonvascularized bone in the reconstruction of musculoskeletal defects created in the laboratory.[43]

The vascularized bone graft, in the absence of an immune response, remains viable. In addition, vascularized donor bone receives a continuous supply of the hematogenous cells required for bone healing.[44]

To simplify the hemimandibular allograft transplantation procedure in young rabbits, Randzio et al excluded the internal maxillary trunk from the donor module and perfused using the collateral

connections between the facial artery system and the inferior alveolar artery system.[45] The mortality rate improved compared with previous model but survivors developed necrosis of the condylar head. Thus, the authors excluded the condyle and upper ramus from the donor module, and the complete hemimandible transplantation was replaced using a partial hemimandible transplantation. This partial hemimandibular transplantation proved to be a more dependable preparation.[45] In contrast to Randzio et al, we did not interrupt the internal maxillary artery and the inferior alveolar artery, and the vascular supply of the mandible was left intact. Thus, we did not observe condylar head necrosis of the hemimandible.

When compared with the models by Randzio et al,[45] Gold et al[46] and Höhnke et al,[47] all of which were not composite tissue transfer models but rather vascularized bone (mandible) transfer models, the hemiface/mandible/tongue transplantation model was shown to be a true composite tissue graft that included, skin, muscle, tongue, bone, cartilage and tooth. These components make this model a more challenging composite tissue transplantation.

In the model developed in canines by Hu et al, there was not a large skin component, which is the most important part in CTA transplantation.[48,49] Indeed, this model included only a small amount of skin with blocks of mandibular component. The aim of this prior model was to evaluate the feasibility of transplanting composite mandibular allografts to reconstruct large mandibular defects, and the authors showed that the composite mandibular allografts could be used for severe mandibular defects.[48,49] Conversely, our model included all hemiface components of the rat, including all hemiface skin and auricular cartilages. Furthermore, our model included the tongue, which is entirely distinct organ for transplantation. Thus, our model could serve to represent a higher antigenic load for future allotransplantation studies. In addition, our model is the first to be developed in rats, as well as the first experimental model of face transplantations including the hemimandible as a vascularized bone and large amounts of skin component (hemiface), including the cartilaginous ear, eyelids, tongue, oral mucosa and teeth makes it a more challenging transplant model.

Hirabayashi et al transplanted the whole head of an infant animal heterotopically to an isohistogeneic animal's inguinal region.[50] They then observed growth of the transplanted head. In the study presented here, all components of the composite graft showed positive growth, including the hemimandibular incisors. This finding was consistent with data reported in the literature.[50] To prevent any abdominal or thoracic injury, the projecting edges of the incisor were trimmed. The histologic specimens confirmed the viability of the bone and teeth components of the graft.

In conclusion, the hemiface/mandible/tongue transplantation model presented herein is less technically demanding and presents with lower morbidity and mortality rates when compared with the full face and hemiface transplantation models, because the flap is transplanted to the recipient inguinal region. This composite tissue transplantation model included a large amount of skin components, tongue, oral mucosa and a reliable component of vascularized bone with intact bone marrow compartment, teeth and incisors. For these reasons, it is an attractive and reliable model to be considered for tolerance induction studies in an allograft transplantation setting.

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