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Tongue Transplantation

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Abstract The tongue is a vital organ that is integral to many basic human functions, such as speech and deglutition. The primary challenges in tongue reconstruction lie in its unique form and function, and complete functional rehabilitation is equally dependent on restoring sensory and motor functions. This review article discusses the background, history, and future of tongue reconstruction in the era of human tissue allotransplantation.

Keywords Tongue reconstruction · Tongue transplantation · Face transplantation · Microvascular reconstruction · Head and neck reconstruction · Free tissue transfer · Head and neck cancer · Head and neck trauma

Introduction

The tongue is a vital organ that is integral to many basic human functions, such as speech and deglutition. Many complex human social interactions require the proper form and function of this highly specialized and unique organ. The multiplicity of human languages that exist today requires numerous and varied articulations and voice patterns—of which the tongue plays a major role. The very basic function of eating is not possible without a properly working tongue. But the tongue is not capable of these intricate activities without the coordinated muscle activity of other key aerodigestive tract structures—the floor of mouth muscles, larynx, and pharynx.

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Anatomy and Physiology

The tongue plays an important role in oral hygiene, mastication, deglutition, and speech. The tongue's mobility and acute sensory perception allow it to select food and debris for mastication, expulsion, or deglutition. The tongue's anterior–posterior mobility and obliteration of the oral cavity by contacting the hard and soft palate are critical to the oral phase of swallowing [1, 2]. Essential to the coordinated activity of the tongue's function is its sensory capabilities. Functional MRI has demonstrated a hierarchical overlap of the tongue, lips, and teeth in the primary somatosensory cortex [3]. Loss of this peripheral afferent input from the tongue has consequences in the central cortical control of mastication, deglutition, and speech [4]. Additionally, the tongue provides the special visceral afferent sensation for taste. From the evolutionary standpoint, this capability extends quantity of life by identifying poisonous or spoiled foods. In today's reality, this sense is an essential component of quality of life.

Although closely coordinated and structurally connected, for reconstructive purposes, the oral tongue and base of tongue are functionally distinct [5]. The oral tongue's function relies heavily upon its flexibility and mobility. It is critical to oral hygiene, speech, and the oral phase of swallowing. The oral tongue helps circulate saliva within the oral cavity and incorporates it into fragments of food. It positions food fragments between the teeth for mastication and creates the food bolus [6•]. The base of tongue's function depends more on its volume and shape, although its mobility is also important. It plays a vital role in initiating pharyngeal swallowing by propelling the food bolus into the posterior pharyngeal wall. Its bulk promotes passage of the food bolus over and around the larynx for airway protection [5, 7, 8]. The tongue's multi-purpose nature and almost whimsical mobility create difficult challenges for the head and neck reconstructive surgeon.

Conventional Methods of Tongue Reconstruction

Traditionally, tongue reconstruction has been defined by the quantity and location of the tongue defect. The amount of tissue missing defined by the ablative procedure that has led to the defect (i.e., partial glossectomy, hemi-glossectomy, subtotal glossectomy, total glossectomy, and total glossectomy with resection of adjacent tissues). The location of the defect is generally described as oral tongue or base of tongue.

Very small partial glossectomy defects may not require complex reconstruction. These defects require an epithelial reconstruction rather than the volumetric reconstruction that is needed for larger tongue defects. Healing by secondary intention, primary closure, split thickness skin grafts, or acellular dermis grafts may be utilized. In these cases, tongue reconstruction is performed to prevent post-operative restriction of the tongue's mobility—an issue which is most concerning for ventral tongue and floor of mouth defects. Even small defects in this area may require an epithelial reconstruction to prevent contracture and tethering.

Other larger partial glossectomy defects are usually reconstructed with a split thickness skin graft, acellular dermis graft, or local tissue flap. The buccinator muscle flap has been described for these types of tongue defects [9]. The limitation of this flap is the need for a secondary procedure to divide the pedicle and complete the flap inset. Additionally, patients with good dentition are at risk for biting and injuring the flap pedicle. There is also the possibility of post-operative trismus, especially in patients who may require post-operative radiation [9]. The submental island flap has also been used for tongue reconstruction [10]. The primary limitation of this flap is the concern for oncologic safety in oral cancer patients, given the theoretical risk of nodal disease within the flap. One notable limitation in all local flaps in the head and neck utilized for tongue reconstruction is the risk for compromised blood supply in the setting of a concurrent neck dissection. Primary closure is traditionally not recommended for larger partial glossectomy defects, however, McConnel has demonstrated comparable speech and swallowing outcomes with both primary closure and complex flap reconstruction [11].

Larger hemi-glossectomy, subtotal glossectomy, and total glossectomy defects require significant volumetric reconstruction. These defects have been addressed with distant pedicled flaps, such as the pectoralis major myocutaneous flap [12], but are now typically reconstructed with a free tissue transfer reconstruction. The radial forearm, anterolateral thigh, rectus abdominis, gracilis, and latissimus dorsi free flaps have all been used for tongue reconstruction [8, 12–14]. The radial forearm free flap provides a pliable skin paddle that is well suited for hemi-glossectomy defects of the oral tongue—specifically the ventral tongue and floor of mouth. This flap allows a static reconstruction of the multiform contour of the tongue but with limited utility for volumetric reconstruction. The anterolateral thigh and rectus abdominis free flaps provide significant soft tissue bulk that is well suited for near total and total glossectomy defects. These flaps allow a static volumetric reconstruction of the tongue's bulk but with limited ability to recreate the varied contour of the tongue and floor of mouth. The radial forearm, anterolateral thigh, and rectus abdominis free flaps do not allow for the possibility of active intrinsic flap movement mediated by hypoglossal nerve reinnervation. The gracilis and latissimus dorsi free flaps provide soft tissue bulk with the potential for a dynamic reconstruction of the tongue defect. Haughey described his technique for latissimus dorsi harvest and inset for tongue reconstruction that aimed to restore both bulk and active intrinsic movement mediated by the hypoglossal nerve. A minor consideration is that patient positioning issues make a simultaneous two-team approach difficult with the latissimus dorsi free flap. Additionally, latissimus dorsi free flaps may suffer from loss of tissue bulk due to muscle atrophy over time [8].

Larger tongue defects often co-exist with tissue loss in the floor of mouth, mandible, buccal mucosa, lips, skin, pharynx, and larynx. These concomitant tissue defects often require utilization of free flaps with multiple skin paddles, vascularized bone, or the use of multiple free flaps. The scapular free flap with its multiple skin paddles, freedom of rotation, and vascularized bone stock is often an ideal single flap solution to complex oral cavity, oropharynx, and skin defects. The primary disadvantage lies in the need for patient positioning in the lateral decubitus position [15].

A special consideration involving large tongue resections is resultant tissue ptosis following reconstruction. Restoration of the structural integrity of the floor of mouth and suspension of the reconstruction from the skull base are critical elements. Ptosis can be prevented by suspending the reconstructive tissue from the left to the right skull base by suturing to the pharyngeal constrictors or creating a supportive sling composed of polytetrafluoroethylene, fascia, or acellular dermis [8].

Challenges in Tongue Reconstruction

The primary challenges in tongue reconstruction lie in its unique form and function. While most skeletal muscles of the human body move in a single plane, or at most two dimensions, the tongue is able to move in three dimensions. Coupled with its ability to volumetrically change the dead space of the oral cavity, the tongue is able to manipulate sound waves, saliva, and food in a serpentine ballet of expansion and propulsion.

With traditional methods of tongue reconstruction, some aspects of the tongue's form and function cannot be adequately restored [16]. While neurovascular reconstruction can be performed, the tongue's refined sensation and taste cannot reliably be reconstructed at this time. Additionally, the tongue's complex movements cannot be replicated—only replaced by poorly coordinated gross muscle activity [16]. As previously discussed, the tongue's function relies heavily upon the cortical integration of sensory input from the oral cavity that is translated into coordinated muscle activity between the tongue, floor of mouth muscles, larynx, and pharynx. Thus, complete functional rehabilitation is equally dependent on restoring sensory and motor functions [6•].

Appropriately sizing the tongue reconstruction presents another challenge. The tongue's ability to obliterate the oral cavity is integral to its role in food bolus propulsion. More soft tissue bulk favors this ability in the reconstructed tongue. However, greater bulk also has the potential for oropharyngeal airway obstruction, tracheostomy dependence, or inability to achieve complete mouth closure.

Critical to the reconstruction of the tongue is the status of the larynx—not only its presence or absence, but also its function [17]. A non-functional larynx that is either prone to aspiration or tracheostomy dependence significantly alters the goals of the tongue reconstruction. A patient that is gastrostomy tube dependent due to aspiration has little need for a large, dynamic tongue reconstruction to aide in deglutition. While a patient that is tracheostomy tube dependent will better tolerate a larger, bulkier soft tissue reconstruction with the hope of restoring serviceable oral intake. In the tracheostomy and gastrostomy tube-dependent patient, tongue reconstruction promotes oral hygiene by obliterating a potential reservoir for saliva pooling and maintains the native configuration of the mandible, which may undergo atrophy without the neotongue [Alam DS, personal correspondence 2012].

The presence or absence of a graftable hypoglossal nerve also impacts the reconstructive goals. If there is no graftable hypoglossal nerve, then there is no potential for intrinsic voluntary neotongue mobility. Additionally, if there is no viable hypoglossal nerve at all, then there is also no potential for extrinsic voluntary neotongue mobility based on the residual tongue's mobility. Neotongue mobility will rely upon extrinsic movement from the floor of mouth muscles and pharyngeal constrictors.

Haughey described the ideal characteristics of the tissue used for subtotal and total glossectomy reconstruction [8]. The tongue reconstruction should not only have sufficient bulk to obliterate the oral cavity but also create a shelf superior to the laryngeal inlet to guide the food bolus into the hypopharynx during deglutition. The tissue should also be pliable enough to allow coordinated movement with residual tongue and muscles of deglutition. Ideally, this tissue should also be capable of intrinsic voluntary coordinated movement with an associated motor nerve that may be anastomosed to the hypoglossal nerve. It should also have an associated donor sensory nerve that may be anastomosed to the recipient glossopharyngeal or lingual nerves to allow for sensory innervation of the neotongue. Haughey believed that the latissimus dorsi free flap reasonably incorporated all of these ideal characteristics and that the only tissue that would be better suited was another human tongue.

Tongue Allotransplantation

The complexity of tissue defects of the head and neck has fueled the development of composite tissue allotransplantation as a potential solution to these challenging problems [18, 19, 20•]. While the development of allotransplantation remains a landmark event in head and neck reconstruction, the potential application is limited by the morbidity of immunosuppression. The ideal composite tissue allotransplant recipient is a young healthy patient with a tissue deficit following a traumatic injury, a benign tumor resection or who is already on a post-transplant immunosuppression regimen [19]. The indication for tongue allotransplantation would be significant functional deficit following total or subtotal loss of tongue tissue with graftable hypoglossal and lingual nerves in the absence of other contraindication to oral intake.

Animal Models

In 1999, Haughey first demonstrated that allotransplantation of the tongue was possible in a large mammal with long-term survival of tissue and recovery of sensory and motor function [16]. Haughey successfully developed a canine model of hemitongue allotransplantation between same-sex, littermates. The contralateral native hemitongue served as a control group. Microvascular anastomosis was performed between the donor and recipient lingual artery and vein, hypoglossal nerve, and lingual nerve. The dogs were maintained under cyclosporine immunosuppression.

Five of twenty dogs survived between six and thirteen months for long-term evaluation—the remaining succumbed to overwhelming infection or uncontrollable graft rejection. Haughey found that intrinsic transplanted tongue movement was achieved through ipsilateral reinnervation and not cross-neurotization from the native tongue. On average, the contractile force of the transplanted hemitongue was approximately 68 % of the native hemitongue. But, it was not the finely coordinated movements of the native tongue. As with the first human larynx transplant, the first canine tongue transplant did not yield physiologically useful movement [16, 19]. Additionally, Haughey demonstrated lingual nerve regeneration suggesting the potential for sensory recovery—a finding that is also seen in face transplant recipients who have regained facial sensation [16, 20•].

Sieminow's rat model of composite face transplantation further demonstrated the feasibility and potential for tongue allotransplantation [21]. It also identified the potential immunosuppressive challenge of a higher antigenic load with tongue allotransplantation.

Human Tongue Allotransplantation

To date, there has been one published case of allotransplantation of the human tongue alone without the face [22, 23]. A tongue was transplanted from an ABO-matched beating heart donor into a 42-year-old man with T4N2bM0 squamous cell carcinoma of the tongue with invasion of the floor of mouth and mandible. The tongue allotransplantation procedure was approved by the institution's ethics committee. The procedure was performed 6 weeks after chemo-radiation therapy in conjunction with bilateral level 1–3 neck dissection, total glossectomy, right resection of floor of mouth, and right hemi-mandibulectomy. Donor allograft procurement was performed simultaneously with the ablative procedure. The donor hypoglossal nerves, lingual nerve, and lingual vessels were dissected. Information regarding the donor patient was not disclosed. Anastomosis was performed to recipient bilateral hypoglossal nerves, left lingual nerve, and bilateral facial vessels. The recipient right lingual nerve was sacrificed at the time of tumor resection. The ischemic time for the allograft was 245 min, and it was flushed with a cold crystalloid organ preservative solution. The patient's immunosuppressive regimen included intra-operative methylprednisolone, post-operative anti-thymocyte globulin for 5 days, followed by daily doses of tacrolimus, mycophenolate mofetil, and prednisolone. The patient was started on speech therapy. At 10 months, the patient did not have clinically evident intrinsic tongue mobility and electromyographic evaluation demonstrated only pathologic spontaneous activity. Video fluoroscopy demonstrated poor mobility, poor bolus preparation, and incomplete tongue-to-palate contact. His speech was intelligible, and he was able to swallow saliva and small quantities of pulp consistency foods without evidence of aspiration. Sensory evaluation revealed superficial discrimination to sharp and blunt contact on the left side of the tongue only. Twelve months post-operatively, a recurrence was found in the right neck and the patient expired at home one month later. An autopsy was not performed.

In 2012, the most extensive facial allotransplantation to date was performed that included all facial skin, mimetic muscles, the tongue, the midface via Le Fort III osteotomy, and the mandible via sagittal split osteotomies [24]. The patient was a 37-year-old male who suffered a shotgun wound to his midface. Pre-operatively, he was missing a portion of his tongue but tolerating an oral diet with intelligible speech. At one-year post-operatively, the patient is noted to have intelligible speech and re-learning to eat.

Challenges in Human Tongue Allotransplantation

Donor tissue procurement is one of the greatest challenges to human tissue allotransplantation. Like facial allotransplantation, consideration must be made for the donor's appearance after tissue procurement [25]. Given the tissue deficit is intra-oral, replacing the donor tissue deficit is not a priority. However, masking the cutaneous incisions is important. The most aesthetically sensitive approach incorporates bilateral peri-auricular incisions with a supraclavicular incision at the midline. The tongue allograft is then released with intra-oral mucosal incisions and delivered through the neck.

The timing of tongue reconstruction prior to the degeneration of the central and peripheral nervous pathways necessary for speech and deglutition is also a major consideration. Considering that the greatest need would be in head and neck cancer patients, full immunosuppression and tongue allotransplantation would have to wait several years pending oncologic outcome. Haughey suggested immediate tongue reconstruction with autogenous tissue with sensory and motor nerve anastomosis, followed by a waiting period—allowing for cancer surveillance and potential matched donor recruitment. If the patient remained free of cancer with persistent and severe functional deficits, then elective allotransplantation could be considered [16].

Immunosuppression for Composite Tissue Allotransplantation

The success of recent composite tissue allotransplantation is often attributed to improved microvascular techniques, but little consideration is given to the ongoing development of modern immunosuppressive techniques [26, 27]. Siemionow's rat model of composite face transplantation and subsequent human cadaveric studies continue the search for tolerance induction with composite tissue allotransplantation. Freedom from immunosuppression can only be achieved by inducing mixed chimerism and allograft tolerance. Her work suggests that the inclusion of donor allograft containing lymphoid and vascularized bone marrow may be the key to developing and maintaining donor-specific chimerism [21, 28, 29]. The previously described full face, double jaw, and tongue transplant included vascularized bone marrow within the mandible and may offer additional insight into the development of donor tolerance [24]. As demonstrated in the first tongue allotransplantation, the concern for co-incident or recurrent cancer, while on immunosuppression is a serious consideration [22, 23]. Ironically, immunosuppression is known to lead to cancers of the lip and tongue.

Conclusions

Complex head and neck defects continue to remain a problem for reconstructive surgeons. Composite tissue allotransplantation may offer a solution to certain defects in certain patients but consideration must be given to the morbidity of immunosuppression. Some would argue that composite tissue allotransplantation in the head and neck is for quality of life, not quantity of life [18]. While others suggest that although the tongue is not essential in sustaining life, it may be essential in sustaining the will to live [30]. Until new immunosuppressive methods are developed, conventional free tissue transfer reconstruction of glossectomy defects will remain the mainstay of treatment for head and neck cancer patients. Although the greatest need for tongue reconstruction exists in patients with head and neck cancer, the most recent cases of total face and tongue allotransplantation for trauma suggests a new application for tongue allotransplantation. The future of composite tissue allotransplantation—tongue, larynx, face, or hands—may depend upon the development of organ-specific immunosuppression strategies and improved techniques for reinnervation [19]. But, the reconstructive goal remains the same: restore form and function with minimal morbidity to the patient.

Compliance with Ethics Guidelines

Conflict of Interest John J. Chi and Bruce H. Haughey declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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