Chapter 15
Oral Mucosal Grafting in Ophthalmology

Parisa Abdi, Golshan Latifi, and Hamed Ghassemi

1 Introduction

There are many ocular surface syndromes that can cause sight-threatening conditions, including cicatricial diseases such as Stevens-Johnson syndrome (SJS) and ocular cicatricial pemphigoid (OCP) and chemical burns [1]. These conditions may lead to scarring complications in the lid margin, tarsus, and fornix while also causing keratinization, trichiasis, entropion, and symblepharon, which result in visual morbidity. Autologous oral mucosal graft (OMG) can be an approach to overcome such complications [1].

The oral mucosa consists of keratinized or nonkeratinized stratified squamous avascular epithelium with underlying lamina propria that is a vascular connective tissue. Its interface has many connective tissue projections into the epithelium, which leads to an increased surface area and ability to resist forces. The epithelium is also rich in elastin, which makes it resistant to shearing, stretching, and compression forces [2].

The lamina propria has extensive blood vessels and nerve fibers that allow for excellent grafting that facilitates angiogenesis. In contrast to gastrointestinal mucosa, there is no muscularis mucosal layer between the epithelium and lamina propria in the oral cavity [2]. The oral mucosa has many advantages that make it optimal as a graft for the ocular surface including:

1. Good flexibility and minimal contraction in the recipient bed [2].
2. Not containing hair follicles [3].
3. Tolerating wet environment [4].
4. High histocompatibility.

P. Abdi · G. Latifi · H. Ghassemi (✉)
Cornea Service, Farabi Eye Hospital, Tehran University of Medical Sciences, Tehran, Iran
e-mail: h_ghassemi@sina.tums.ac.ir

L. Tayebi (ed.), *Applications of Biomedical Engineering in Dentistry*,
https://doi.org/10.1007/978-3-030-21583-5_15

5. High resistance to microbial agents due to (a) secretion of antimicrobial peptides (defensing and cytokines) [5, 6], (b) the presence of mucosa-associated lymphoid tissue (MALT) [5, 6], (c) its function as a barrier to microbial invasion, and (d) the presence of lymphocytes, PMNs, macrophages, plasma cells, and mast cells [5, 6].
6. Capability of rapid healing and reepithelialization faster than a dermal wound, due to the presence of growth factors and tissue factors [7].

The presence of epithelial stem cells in the oral tissue has also been proven, which helps reepithelialization [8]. OMG has gained widespread popularity in ophthalmology and is commonly used during ocular reconstruction surgeries to replace the conjunctiva and corneal surface, along with reconstruction of the fornices [9], eyelid margin [1], and ophthalmic socket [10]. OMG is readily accessible and available in most patients. The surgical technique is fast, inexpensive, and not complex. The transplantation is safe with few recipient and donor site complications [11].

In this chapter, after introducing different types of oral mucosal grafts and describing the procedure and complications of OMG, we will discuss its applications in ophthalmology to show how biomedical engineers can play key roles in such applications.

2 Types of Oral Mucosal Grafts

OMGs are 1–5 mm in size and can be harvested from the buccal mucosa, labial mucosa, or lingual mucosa [11].

2.1 Buccal Mucosa-Based OMG

The buccal mucosa refers to the mucosa overlying the inner cheek of the oral cavity. It is bordered by the outer commissures of the lips in the anterior, anterior tonsillar pillar in the posterior, maxillary vestibular fold superiorly, and mandibular vestibular fold inferiorly [2, 11]. Vascular supply is derived mainly from branches of the maxillary artery—the buccal artery, middle and posterior superior alveolar arteries, and the anterior superior alveolar branch of the infraorbital artery [2, 11]. The buccal mucosa is innervated by the long buccal nerve, a branch of the third division of the trigeminal nerve (CNV3), and the anterior, middle, and posterior superior alveolar branches of the second division of the trigeminal nerve (CNV2). The sensory innervation is through the facial nerve [2, 11].

The buccal mucosa should be dissected off the submucosal fat and minor salivary glands (MSGs) covering the buccinator muscle. The buccinator muscle is a muscle of facial expression, and trauma to it may lead to limitation of mouth opening [2, 11]. During the harvesting, the surgeon must pay attention to anatomical structures, including the buccal fat pad, Stensen's duct of the parotid gland, the facial artery and nerve anteriorly, the buccal artery posteriorly, and lymphatic vessels and buccal branches of the facial and trigeminal nerves [2, 11]. The buccal mucosa is tough, flexible, easy to harvest, easily recoverable, and simple to handle and leaves no visible scar after OMG [2].

2.2 Labial Mucosa-Based OMG

The labial mucosa refers to the mucosa overlying the inner lower lip. The mandibular labial alveolar mucosa is delineated by the vermilion border superiorly, the vestibular fold inferiorly, and the outer commissures of the lower lip laterally [2, 11]. Vascular supply is derived from the buccal and mental branches of the maxillary artery and the inferior labial branch of the facial artery [2, 11].

Sensory innervation is by the mental nerve, a terminal branch of the inferior alveolar nerve which is rising from the mandibular branch of CNV3. The mental nerve arises from the mental foramen, which is located between the first and the second premolar teeth. Thus, in harvesting the mucosa, the initial incision should be medial to the center of the canines to avoid mental nerve injury. Additionally, the incision should maintain at least a 1.0–1.5 cm margin from the lip vermilion to prevent lip contracture [12]. On the other hand, injury to the orbicularis oris muscle can cause limitation in lip motility and smiling. MSGs are easily accessible in the labial mucosa and form a continuous layer of tightly packed lobules between the quadratus labii and the labial mucosa [13]. MSG secretions are predominantly seromucinous [14].

2.3 Lingual Mucosa-Based OMG

The lingual mucosa refers to the mucosa overlying the tongue. The mucosa covering the undersurface and lateral surface of the tongue is indistinguishable from and the same in structure as the mucosa lining the rest of the oral cavity. It has no particular functional feature and is easily accessible and easy to harvest [15]. It is mostly used in complications of urethroplasty, which requires a large supply of graft tissue in patients with a small mouth or difficult mouth opening.

3 Procedure and Complications of Oral Mucosal Grafting

3.1 Graft Harvesting and Surgical Procedures

In the preoperative period, any inflammation should be controlled. To estimate the graft size, the conjunctival defect is measured. The shape and size of the graft is marked on the mucosa (Fig. 15.1a). The graft size should be larger than the defect,

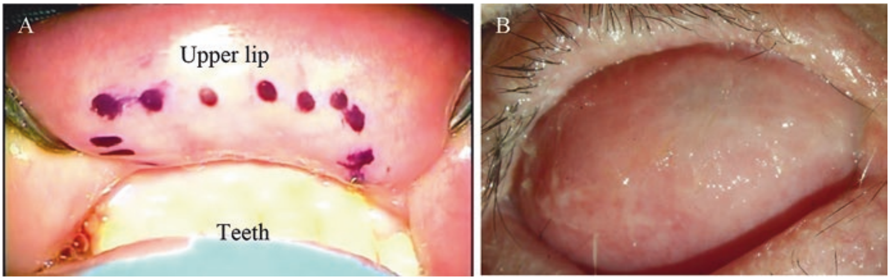

Fig. 15.1 (**a**) Marking the shape and size of the graft on the mucosa to be used for the OMG procedure. Due to the possible 20% contracture, the size of the graft is larger than the actual defect size. (**b**) OMG in an eye after the surgery (courtesy of Dr. Mehran Zarei-Ghanavati, MD)

taking into account an average of 20% contracture. For the buccal mucosa, the parotid duct must be avoided (which is usually located opposite the second upper molar). For the lip, the incisions should not extend too close to the vermilion or attached gingiva [16]. Injection of saline or local anesthetic solution with adrenaline (bupivacaine 0.25% mixed with 1/200,000 epinephrine) helps to elevate the graft from the submucosal tissue and reduce hemorrhage [17].

The graft should be excised as thinly as possible by a blade and scissors. Submucosal dissection should be above the adipose layer, superficial to the buccinator muscle. The graft is trimmed and the edges secured under the conjunctival margins with Vicryl sutures. The subconjunctival fibrovascular cicatrix should be dissected at the recipient bed [2, 11]. The graft bed can be left to granulate, or it can be sutured if the edges of the wound can be approximated without deforming the lip or the tissue [16]. The graft is then spread over a surface, and the excess fat is cleared from the undersurface of the graft. The graft is then spread on the defect at the recipient site and secured with suturing or fibrin glue (Fig. 15.1b).

3.2 Complications

Donor harvest site morbidities include persistent pain and wound contracture, which result in limitation of mouth opening and oral tightness. Moreover, other morbidities—such as buccal hematoma, inclusion cysts, numbness in the cheek and lip, parotid duct injury, lip contracture and inversion of the lip vermilion, and poor cosmesis—should be considered as well [18]. Common complications affecting OMG after implantation include as follows:

A. *Graft shrinkage or contracture*: It has been reported about 20–45% shrinkage in size for the buccal mucosa and about 10% for the hard palate. This contracture commonly appears within 6 months after implantation [11].

B. *Mucosal necrosis*: It has been reported 8–50% of eyes after osteo-odonto-keratoprosthesis undergo mucosal necrosis, which can lead to exposure of the underlying ocular surface or implant [19].
C. *Mucosal overgrowth*: In Basu's study, the rate of overgrowth was 13%, and all of them were managed by debulking and trimming [19].
D. *Excessive MSG secretions*: Excessive MSG secretions can be treated by graft excision, cryotherapy, or botulinum toxin injection [11].

4 Applications of Oral Mucosal Grafting in Ophthalmology

OMGs have been used for different purposes in ophthalmology, including ocular surface reconstruction, socket reconstruction, correction of eyelid abnormalities, glaucoma surgery, and lacrimal drainage surgery.

4.1 Ocular Surface Reconstruction

OMGs can be used in different scenarios for ocular surface reconstructions as described below:

A. Symblepharon (adhesion of the palpebral conjunctiva to the bulbar conjunctiva) can be a sight-threatening condition and may cause other ocular abnormalities, such as reduction of goblet cells, tear film and tear meniscus abnormalities, lid disorder like entropion and trichiasis, limitation in ocular motility, and failure of ocular surface reconstruction and corneal transplantation [16]. Many different materials have been employed to reconstruct the fornices, like conformers and rings; however, their effect is often temporary. To maintain the fornices, it is required to include epithelial tissue or basement membrane that can be populated by normal host epithelial cells [16]. Available graft materials include conjunctival autograft, OMG, and amniotic membrane graft (AMG) [16].

   The ideal material for fornix reconstruction is conjunctival or tarsal autograft, but there are limitations in their availability, especially in bilateral diseases. In such cases, a full-thickness oral mucosal membrane is the simplest available graft to use. Split-thickness mucosal grafts are less suitable for fornix reconstruction, as they contract more; but since they are less bulky and pink, they are used on the globe. Among OMGs, hard palate grafts are the thickest and the most difficult to harvest, but contract the least for ocular surface reconstruction [16]. OMG can also be employed for fornix reconstruction in the eyes with low-grade symblepharon. However, in severe cases, cases with difficulty in controlling inflammation, poor lacrimal function, or near-total lack of healthy conjunctiva, an oral mucosal graft may be more appropriate than an AMG [16]. In a study by Kheirkhah et al., 84.4% of eyes with severe (grade 3 or 4) symblepharon had a deep fornix with no scar or motility restriction after 16.4 ± 7.6 months of follow-up. In this study, a combined approach was employed: symblepharon lysis, intraoperative mitomycin C application, OMG in tarsal conjunctival defect, and amniotic membrane transplantation (AMT) in bulbar conjunctival defect [20].

B. Pterygium (a triangular tissue growth of thickened conjunctiva that grows over portion of the cornea) recurrence rate after simple excision is 24–67%, but with adjuvant therapy like conjunctival autograft, the rate is 0–47% [21]. OMG has been employed to cover the defects in pterygium surgery. It is especially useful in recurrent pterygium with conjunctival scarring, fornix shortening, inadequate conjunctiva, and limitation of ocular motility [21].
C. Osteo-odonto-keratoprosthesis is a procedure to restore vision in the most severe cases of corneal and ocular surface patients. In this procedure, a tooth is removed, a lamina of it is cut and drilled, and then the hole is fitted with optics. The lamina is grown in the patient's cheek for a period of months, and then prosthesis is implanted in the eye. In osteo-odonto-keratoprosthesis, OMGs have been used for ocular resurfacing and to provide a stable epithelium instead of a dry keratinized one [19]. However, complications have been reported, such as mucosal overgrowth over the optical cylinder, which decreases vision and causes necrosis [19]. On the other hand, melting of the cornea may occur, causing keratoprosthesis extrusion, particularly in patients with chronic conjunctival inflammation. In these patients with conjunctival deficiency, OMG is helpful to repair the defect [22].
D. OMGs have been employed to protect delicate corneas in cases of fitting cosmetic scleral shells. Traditionally, a Gunderson flap (a type of conjunctival flap that covers the total corneal surface) is used in such conditions. However, in some cases with conjunctival scarring or a large corneal diameter, OMGs are superior to flaps with a lesser risk of retraction [23].
E. OMGs combined with tenoplasty have been used to repair sclerocorneal melts in patients with chemical burns [24].

4.2 Socket Reconstruction

After enucleation, the conjunctival contraction is common in the anophthalmic socket, leading to cosmetic deformity and difficulty in filling the prosthesis. This condition is more common after irradiation of the ophthalmic socket, for instance, in patients with uveal melanoma. An OMG can be used in these patients, as it is thin and easily accessible and maintains moisture of the prosthesis [25]. OMGs can augment the conjunctival surface, especially in fornices, to have sufficient depth for the prosthesis [26]. OMGs have been used in combination with hard palate grafts to make a stable fornix and provide rigidity and support in the palpebral surface [26].

Another post-enucleation complication is orbital volume loss. It can be corrected with orbital floor wedge implant, but it may shorten the fornix, which can be managed by OMG simultaneously. Another approach is using a buccal mucous membrane-fat graft to correct the volume and the surface simultaneously [27]. OMGs have also been used to manage hydroxyapatite orbital implant exposures [28].

4.3 Correction of Eyelid Abnormalities

Eyelid abnormalities are commonly seen in cicatricial disorders, such as mucous membrane pemphigoid (MMP), Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), trachoma, and chemical burns. These abnormalities are lid margin scarring, trichiasis, distichiasis and entropion [26]. OMGs are commonly used to reconstruct these eyelid abnormalities, particularly before other procedures, such as limbal stem cell grafts and penetrating or lamellar keratoplasties [29]. OMG also has been used in correcting congenital distichiasis by resecting a strip of tarsus in the eyelid margin with the roots of lashes and replacing it with an OMG [30]. OMGs with more stromal fat have been used to increase the tarsal height and correct the cicatricial lagophthalmos [1]. A complex skin-muscle-mucosa graft from the lower lip can be employed as a one-stage procedure to repair lid margin defects after tumor resection [31]. OMGs have been used to repair congenital eyelid defects like cryptophthalmos [32]. In ichthyosis, the oral mucosa is not affected by the disease and is used to lengthen the anterior lamella and correct the ectropion. After transplantation, this tissue undergoes metaplasia into keratinized skin [26].

4.4 Glaucoma Surgery

One of the complications of glaucoma drainage devices is erosion and exposure of the plate or the tube through the conjunctiva. It is usually repaired with conjunctival flaps or autologous conjunctival grafts. OMGs are used in cases with scarred or insufficient conjunctiva to cover the eroded tube or plate [33].

4.5 Retinal Surgery

Scleral buckles are used in retinal detachment surgery. One of the complications is the explant exposure through the overlying tissue or conjunctiva. In these cases, the explant is usually covered with a scleral patch graft. OMGs have been used to cover this scleral graft, especially in patients with scarred conjunctiva due to multiple retinal procedures [34].

4.6 Lacrimal Drainage Surgery

Conjunctivodacryocystorhinostomy (CDCR) is a procedure that is performed in patients with total canalicular block. In this procedure, a Jones tube is placed in the canalicule. However, if the tube becomes dislodged or lost, the channel will be closed. OMGs have been used to line the CDCR tract to epithelize the channel and obviate closure in these cases. OMGs also have been used to reconstruct the medial canthal area and canalicules secondary to chemical burn. On the other hand, OMGs have been used in challenging cases of rE-DCR (dacryocystorhinostomy) with extensive scarring and mucosal shortage, to maintain the patency of the DCR tract [35, 36].

5 Summary

OMG can be used to promote ocular surface barrier function when it is defective. It is one of the finest substitutes for the conjunctiva in different ocular reconstruction procedures when autologous conjunctiva is unavailable. It can be harvested from the mucosa overlying the inner cheek of the oral cavity (buccal mucosa-based OMG), mucosa overlying the inner lower lip (labial mucosa-based OMG), or, less frequently, mucosa overlying the tongue (lingual mucosa-based OMG). Some of the most popular indications of OMG in ophthalmology are fornix reconstruction, fixing contracted anophthalmic socket, ocular resurfacing in osteo-odonto-keratoprosthesis, and prevention of channel closure in CDCR.

References

1. Fu, Y., Liu, J., & Tseng, S. C. (2011). Oral mucosal graft to correct lid margin pathologic features in cicatricial ocular surface diseases. *American Journal of Ophthalmology, 152*(4), 600–608.
2. Markiewicz, M. R., Margarone, J. E., III, Barbagli, G., & Scannapieco, F. A. (2007). Oral mucosa harvest: An overview of anatomic and biologic considerations. *EAU-EBU update series, 5*(5), 179–187.
3. Cohen, S. D., Armenakas, N. A., Light, D. M., Fracchia, J. A., & Glasberg, S. B. (2012). Single-surgeon experience of 87 buccal mucosal graft harvests. *Plastic and Reconstructive Surgery, 130*(1), 101–104.
4. Akyüz, M., Güneş, M., Koca, O., Sertkaya, Z., Kanberoğlu, H., & Karaman, M. İ. (2014). Evaluation of intraoral complications of buccal mucosa graft in augmentation urethroplasty. *Turkish Journal of Urology, 40*(3), 156.
5. Rudney, J. D., & Chen, R. (2006). The vital status of human buccal epithelial cells and the bacteria associated with them. *Archives of Oral Biology, 51*(4), 291–298.
6. Walker, D. M. (2004). Oral mucosal immunology: An overview. *Annals-academy of Medicine Singapore, 33*, 27–30.

7. Wong, E., Fernando, A., Alhasso, A., & Stewart, L. (2014). Does closure of the buccal mucosal graft bed matter? Results from a randomized controlled trial. *Urology, 84*(5), 1223–1227.
8. Sotozono, C., Inatomi, T., Nakamura, T., Koizumi, N., Yokoi, N., Ueta, M., Matsuyama, K., Kaneda, H., Fukushima, M., & Kinoshita, S. (2014). Cultivated oral mucosal epithelial transplantation for persistent epithelial defect in severe ocular surface diseases with acute inflammatory activity. *Acta Ophthalmologica, 92*(6), e447–e453.
9. Kheirkhah, A., Blanco, G., Casas, V., Hayashida, Y., Raju, V. K., & Tseng, S. C. (2008). Surgical strategies for fornix reconstruction based on symblepharon severity. *American Journal of Ophthalmology, 146*(2), 266–275.
10. Klein, M., Menneking, H., & Bier, J. (2000). Reconstruction of the contracted ocular socket with free full-thickness mucosa graft. *International Journal of Oral and Maxillofacial Surgery, 29*(2), 96–98.
11. Grixti, A., & Malhotra, R. (2018). Oral mucosa grafting in periorbital reconstruction. *Orbit, 37*(6), 411–428.
12. Muruganandam, K., Dubey, D., Gulia, A. K., Mandhani, A., Srivastava, A., Kapoor, R., & Kumar, A. (2009). Closure versus nonclosure of buccal mucosal graft harvest site: A prospective randomized study on post operative morbidity. *Indian journal of urology: IJU: journal of the Urological Society of India, 25*(1), 72.
13. Geerling, G., Raus, P., & Murube, J. (2008). Minor salivary gland transplantation. In *Surgery for the dry eye* (Vol. 41, pp. 243–254). Karger Publishers.
14. Holsinger, F. C., & Bui, D. T. (2007). Anatomy, function, and evaluation of the salivary glands. In *Salivary gland disorders* (pp. 1–16). Berlin, Heidelberg: Springer.
15. Song, L. J., Xu, Y. M., Lazzeri, M., & Barbagli, G. (2009). Lingual mucosal grafts for anterior urethroplasty: A review. *BJU International, 104*(8), 1052–1056.
16. Bertolin, M., Breda, C., Ferrari, S., Van Acker, S. I., Zakaria, N., Di Iorio, E., Migliorati, A., Ponzin, D., Ferrari, B., Lužnik, Z., & Barbaro, V. (2019). Optimized protocol for regeneration of the conjunctival epithelium using the cell suspension technique. *Cornea, 38*(4), 469–479.
17. Goel, A., Dalela, D., Sinha, R. J., & Sankhwar, S. N. (2008). Harvesting buccal mucosa graft under local infiltration analgesia—Mitigating need for general anesthesia. *Urology, 72*(3), 675–676.
18. Dublin, N., & Stewart, L. H. (2004). Oral complications after buccal mucosal graft harvest for urethroplasty. *BJU International, 94*(6), 867–869.
19. Basu, S., Pillai, V. S., & Sangwan, V. S. (2013). Mucosal complications of modified osteo-odonto keratoprosthesis in chronic Stevens-Johnson syndrome. *American Journal of Ophthalmology, 156*(5), 867–873.
20. Kheirkhah, A., Ghaffari, R., Kaghazkanani, R., Hashemi, H., Behrouz, M. J., & Raju, V. K. (2013). A combined approach of amniotic membrane and oral mucosa transplantation for fornix reconstruction in severe symblepharon. *Cornea, 32*(2), 155–160.
21. Forbes, J., Collin, R., & Dart, J. (1998). Split thickness buccal mucous membrane grafts and β irradiation in the treatment of recurrent pterygium. *British Journal of Ophthalmology, 82*(12), 1420–1423.
22. Ziai, S., Rootman, D. S., Slomovic, A. R., & Chan, C. C. (2013). Oral buccal mucous membrane allograft with a corneal lamellar graft for the repair of Boston type 1 keratoprosthesis stromal melts. *Cornea, 32*(11), 1516–1519.
23. Ma'luf, R. N., & Awwad, S. T. (2005). Mucous membrane graft versus Gunderson conjunctival flap for fitting a scleral shell over a sensitive cornea. *Ophthalmic Plastic & Reconstructive Surgery, 21*(5), 356–358.
24. Wang, S., Tian, Y., Zhu, H., Cheng, Y., Zheng, X., & Wu, J. (2015). Tenonplasty combined with free oral buccal mucosa autografts for repair of sclerocorneal melt caused by chemical burns. *Cornea, 34*(10), 1240–1244.
25. Nasser, Q. J., Gombos, D. S., Williams, M. D., Guadagnolo, B. A., Morrison, W. H., Garden, A. S., Beadle, B. M., Canseco, E., & Esmaeli, B. (2012). Management of radiation-induced

severe anophthalmic socket contracture in patients with uveal melanoma. *Ophthalmic Plastic and Reconstructive Surgery, 28*(3), 208.
26. Mai, C., & Bertelmann, E. (2013). Oral mucosal grafts: Old technique in new light. *Ophthalmic Research, 50*(2), 91–98.
27. Kim, H. E., Jang, S. Y., & Yoon, J. S. (2014). Combined orbital floor wedge implant and fornix reconstruction for postenucleation sunken socket syndrome. *Plastic and Reconstructive Surgery, 133*(6), 1469–1475.
28. Yoon, K. C., Yang, Y., Jeong, I. Y., & Kook, M. S. (2011). Buccal mucosal graft for hydroxyapatite orbital implant exposure. *Japanese Journal of Ophthalmology, 55*(3), 318–320.
29. Iyer, G., Pillai, V. S., Srinivasan, B., Guruswami, S., & Padmanabhan, P. (2010). Mucous membrane grafting for lid margin keratinization in Stevens–Johnson syndrome: Results. *Cornea, 29*(2), 146–151.
30. White, J. H. (1975). Correction of distichiasis by tarsal resection and mucous membrane grafting. *American Journal of Ophthalmology, 80*(3. Pt 2), 507.
31. Sakai, S. (1993). Marginal eyelid reconstruction with a composite skin-muscle-mucosa graft from the lower lip. *Annals of Plastic Surgery, 30*(5), 445–447.
32. Weng, C. J. (1998). Surgical reconstruction in cryptophthalmos. *British Journal of Plastic Surgery, 51*(1), 17–21.
33. Rootman, D. B., Trope, G. E., & Rootman, D. S. (2009). Glaucoma aqueous drainage device erosion repair with buccal mucous membrane grafts. *Journal of Glaucoma, 18*(8), 618–622.
34. Murdoch, J. R., Sampath, R., Lavin, M. J., & Leatherbarrow, B. (1997). Autogenous labial mucous membrane and banked scleral patch grafting for exposed retinal explants. *Eye, 11*(1), 43.
35. Tao, J. P., Luppens, D., & McCord, C. D. (2010). Buccal mucous membrane graft-assisted lacrimal drainage surgery. *Ophthalmic Plastic & Reconstructive Surgery, 26*(1), 39–41.
36. Benlier, E., Bozkurt, M., & Kulahci, Y. (2008). An alternative procedure for conjunctivodacryocystorhinostomy: Supratrochlear artery-based island flap combined with buccal mucosal graft. *Annals of Plastic Surgery, 60*(1), 55–57.