Literature review

https://doi.org/10.31288/oftalmolzh202564853

Current approach to the treatment of periorbital basal cell carcinoma

Petrenko O. V. [1], **Tselishcheva M. O.** [5, 6], **Vasylenko S. S.** [2, 3], **Kalmykova A. V.** [4], **Buhryk V. V.** [3]

[1] Bogomolets National Medical University

[2] Central Polyclinic, Ministry of Internal Affairs of Ukraine

[3] Euroderm Personalized Medicine Clinic, Euroderm LLC

[4] Expert Laboratory for Pathomorphology

[5] Volodymyr Dahl East Ukrainian National University

Kyiv (Ukraine)

[6] University of Malaga

Malaga (Spain)

Key words:

basal cell carcinoma, eyelids, periorbital area, Mohs surgery, reconstruction, plastic surgery, inflammation, meibomian gland dysfunction, conservative treatment

Basal cell carcinoma (BCC) is the most common cancer worldwide, accounts for 75% of all skin cancers, and is considered the most common malignancy in Caucasians. Major risk factors include chronic exposure to ultraviolet radiation, Fitzpatrick skin type I or II, light eyes, genetic predisposition and immunosuppressive conditions. The purpose of this study was to perform a review of the current approaches to the treatment of periorbital BCC. Over 75% of BCCs occur in the head and neck region. Furthermore, 20% of all BCCs arise in the periorbital area. BCC accounts for more than 90% of all periorbital skin cancers, grows slowly and rarely metastasizes (< 0.1%). In spite of a generally favorable prognosis and effective treatment options, BCC with aggressive local growth and deep tumor invasion can result in significant functional and cosmetic defects. According to the literature, BCC is mostly treated surgically by excising the tumor using Mohs micrographic surgery. This technique is believed to be more efficacious than conventional wide excision of the tumor or other methods of tumor excision in this anatomically difficult area of resection. The review demonstrates periorbital reconstruction after Mohs surgery for BCC is a complex task which success largely depends on collaboration of a multidisciplinary team including a dermatology oncologist, a pathomorphologist and an ophthalmic plastic surgeon. The choice of the reconstruction method depends on the size, depth and location of the defect, the status of the periorbital tissue and the surgeon's experience. An individualized approach enables not only radical oncological treatment, but also the restoration of eyelid function and optimal esthetic outcome.

Introduction

Basal cell carcinoma (BCC) is the most common skin cancer worldwide, with its incidence steadily increasing [1, 2, 3]. The highest incidence is reported in Australia (up to 1,000/100,000 inhabitants per year, followed by the USA (212–407/100,000 female and male inhabitants respectively/year) and Europe (mean range from 76.21 /100,000 person-years in the UK to 157 per 100,000 person-years in 2009 in the Netherlands) [1, 2, 3].

BCC is most frequently seen in light-skin individuals older than 50 years. However, some patients (especially those with genetic predisposition syndromes, such as xeroderma pigmentosum (XP) or basal cell naevus syndrome (BCNS)) develop BCC at an earlier age [4]. The most significant risk factor for the development of BCC appears to be exposure to ultraviolet (UV) radiation. Short-wavelength UVB radiation (290-320 nm) has a more severe mutagenic effect than long-wavelength UVA radiation (320-400 nm) and can induce not only damage to the DNA and its repair system, but also the disruption of the local immune response. UV-induced mutations in the TP53 tumor-suppressor gene have been found in about 50% of BCC cases. BCC has been linked to disruption in the Hedgehog (Hh) signaling cascade; mutations in the hedgehog signaling pathway (particularly, Ptch1) have been frequently associated with periorbital BCC [5].

Over 75% of BCCs occur in the head and neck region. Furthermore, 20% of all BCCs arise in the periorbital area. BCC accounts for more than 90% of all periorbital skin cancers, grows slowly and rarely metastasizes (< 0.1%). In spite of a generally favorable prognosis and effective treatment options, BCC with aggressive local growth and deep tumor invasion can result in significant functional and cosmetic defects [1, 2, 5].

Given an increasing prevalence of BCC and its clinical course and complications, there is a need in performing a systematic review of available data on the methods of diagnosis and treatment of BCC. Performing such a review will assist with determining current approaches to the

treatment of periorbital BCC and objectively evaluating their efficacy.

The purpose of this study was to perform a comprehensive review of the current literature on the treatment of periorbital BCC, with a special emphasis on current approaches.

Major part

BCC develops from the basal cells of the interfollicular epidermis and/or the hair follicle. This tumor type is morphologically variable. Despite this variation, all BCC subtypes share key features, including small islets or nests of basaloid tumor cells with hyperchromatic nuclei and scant cytoplasm and peripheral palisading.

The variation among histopathological patterns of BCC resides in clinical manifestations and response to treatment. Histopathologically, BCC is diverse, encompassing several recognized patterns, including superficial, nodular, infiltrating, micronodular, basosquamous, etc. and sclerosing or morphoeic types. Infiltrating, micronodular and basosquamous BCC are believed to be the most aggressive and dangerous [6]. BCC tumors can be classified as low or high risk based on the histopathological pattern, tumor size and location, etc (Table 1 [7]).

TNM classification of primary skin cancer. Staging for cancers (including BCC and other malignant skin cancers) typically involves the use of the 8th edition of the Union for International Cancer Control (UICC)/ American Joint Committee on Cancer (AJCC) tumor, node, and metastasis (TNM) classification. “H” area of the face includes eyelids, eyebrows, periorbital area, nose, lips, chin, mandible, periauricular and postauricular area, and temple; this area is associated with the highest risk of tumor recurrence [8, 9].

Periorbital area

The two most common subtypes of periorbital BCC are nodular and infiltrating BCC. Infiltrating BCC has the most aggressive local course and has been associated with the highest risk of orbital invasion and tumor recurrence [9]. BCC represents up to 90% of all eyelid malignancies. More than 50% of the BCCs appear on the lower eyelid, 30% on the medial canthus, 15% on the upper lid and 5% on the lateral canthus. BCC with orbital invasion occur more frequently in the medial canthus (average 60%) compared to the lower eyelid (average 30%), upper eyelid (average 6%) or lateral canthus (average 14%) [10]. Risk factors of orbital invasion include male gender, multiple recurrences, large lesion size, aggressive histologic subtype, perineural invasion, medial canthal location and advanced patient age (about 70 років).

Clinical and dermoscopic signs

BCC subtypes have certain clinical and dermoscopic features. Superficial BCC typically presents as a pink, scaly papule or plaque that may exhibit multiple superficial ulcerations and signs of marked inflammation. Nodular BCC typically presents as a pearly or pink dome-shaped nodule with central ulcerations and superficial arborizing telangiectasias. Infiltrative BCC typically presents as a scar-like plaque with ill-defined edges, arborizing telangiectasias, and superficial ulcerations. Meibomian gland dysfunction and chronic blepharitis are common in patients with infiltrative BCC.

Dermoscopy is an important noninvasive skin imaging technique that allows identifying the specific features of different BCC subtypes which are too small to be seen with the naked eye [11]. In studies comparing test performance, adding dermoscopy to naked eye examination im-

Table 1. Stratification for determining the variants of treatment for local BCC based on the risk factors for recurrence

Risk group	Low-Risk Factors	High-Risk Factors
Clinical data and anamnesis		
Location/size	Trunk or extremities with <2.0 cm diameter	Trunk or extremities with ≥2.0 cm diameter Tumors of any size located on the head, neck, hands, feet, pretibial, and anogenital area
Borders	Well defined	Poorly defined
Tumor occurrence	Primary	Recurrent
Immunosuppression	No	Yes
Prior radiation therapy	No	Yes
Pathomorphology		
Histologic subtypes	Superficial and nodular (including keratotic and pigmented variants), infundibulocystic, fibroepithelioma of Pinkus	Aggressive forms (basosquamous, infiltrative, sclerosing/morpheaform, micronodular, carcinosarcomatous)
Perineural Invasion (PNI) *	No	Yes

Note: *, perineural invasion (if involving nerve below dermis or if largest nerve involved is ≥0.1 mm in caliber, or if tumor cells are found intraneurally)

Table 2. Tumor staging [7]

Stage	Tis	N0	M0
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
Stage III	T1, T2, T3	N1	M0
Stage IVA	T1, T2, T3	N2, N3	M0
Stage IVA	T4	Any N	M0
Stage IVB	Any T	Any N	M1

proved sensitivity from 66.9% to 85% (P = 0.0001) and specificity from 97.2% to 98.2% (P = 0.006) [12]. Table 3 presents major dermoscopic signs of BCC.

Methods of treatment for periorbital BCC

Current guidelines advocate for surgical excision as a first-line treatment for periorbital BCC. There are two methods of surgical treatment for periorbital BCC, wide surgical excision and Mohs micrographic surgery (MMS).

MMS is the primary surgical technique of choice for periorbital BCC [8] because it allows intraoperative histological analysis of 100% of the excision margin in a three-dimensional fashion. MMS has several advantages over wide local excision which include (1) minimization of the amount of surgical procedure, (2) preservation of maximum amount of normal tissue, (3) reduction in the risk of tumor recurrence, (4) enabling performing reconstructive surgery with histologically clear resection margins (R0), and (5) promoting better esthetic outcomes.

Two meta-analyses published in 1989 associated Mohs with 5-year recurrence rates of 1.0% for primary BCC, and 5.6% for recurrent BCC. In these studies, the recurrence rates for Mohs were lower than those for standard excision (10.1% and 17.4% for primary and recurrent BCC, respectively) [13].

Closure of the postoperative defect is an essential part of the comprehensive treatment for periorbital BCC. Eyelid reconstruction requires a highly technological approach and is aimed at restoring both the anatomical and functional integrity of the eyelid [14]. A multidisciplinary team (including a dermatology oncologist, a pathomorphologist and an ophthalmic plastic surgeon) must collaborate in planning management of periorbital BCC. The dermatology oncologist performs radical tumor excision, the pathomorphologist performs intraoperative resection margin control, and the ophthalmic plastic surgeon performs eyelid reconstruction immediately after confirmation of clear resection margins [13, 15]. This collaboration provides an optimal balance between radicality and minimum loss of healthy tissue, with the preservation of function and cosmesis.

The defects left after the excision of periorbital BCC [10, 16] can be categorized by the percentage of lid length affected into small (< 30%), medium (25–50%), large (50–75%), or subtotal (>75%) defect. Additionally, they can be categorized by the depth into superficial (involving the anterior lamella consisting of the skin and the orbicularis oculi muscle) and full-thickness (with loss of both the anterior and posterior lamellae, the latter consisting of the tarsal plate and conjunctiva) defects.

Small-to-medium defects are more common than large-to-subtotal defects (about 70-80% versus 20-30% respectively, of all cases) [17, 18]. Defect type depends on how early the tumor is detected and histological subtype and location of the tumor. Retrospective studies have reported that, in most periocular tumor resection surgeries, the size of the excised tumor did not exceed 30-40% of the lid length [19], and in 20-30% of periocular tumor resection surgeries, the size exceeded 50% of the lid length.

The choice of the reconstruction method depends on the size of the defect, the need for restoration of the tarsal plate, and the status of the periorbital tissue [20].

Primary closure is used to close small defects (<30%). This type of reconstruction provides the best esthetic result without the use of grafts. A lateral canthotomy or subcutaneous peeling can be used to reduce tension [19, 21, 22, 23].

Free skin grafts: partial-thickness grafts (entire epidermis and part of dermis) are rarely used because they tend to heal with significant contraction and may appear lighter in color than the surrounding skin [24]. Full-thickness grafts (both epidermis and dermis along with some subcutaneous fat) are used for moderate defects of the anterior lamella, with the donor sites including upper eyelid skin, retroauricular skin, preauricular skin, supraclavicular skin, and upper arm skin [24, 25].

Myocutaneous pedicle flaps (Tenzel flap, Mustardé flaps, and nasal-based V-Y flap) are effective for defects involving 25-60% of the lid length, have high survival rates and provide good anatomical correspondence, but require a more complex technique [26].

A Hughes tarsoconjunctival flap reconstruction can offer a superior reconstructive result for full-thickness lower eyelid defects involving > 50% of the lower eyelid margin. However, the procedure is dual-stage and, following flap placement, the upper and lower eyelids are temporarily closed, rendering the patient unable to see from the affected eye [27].

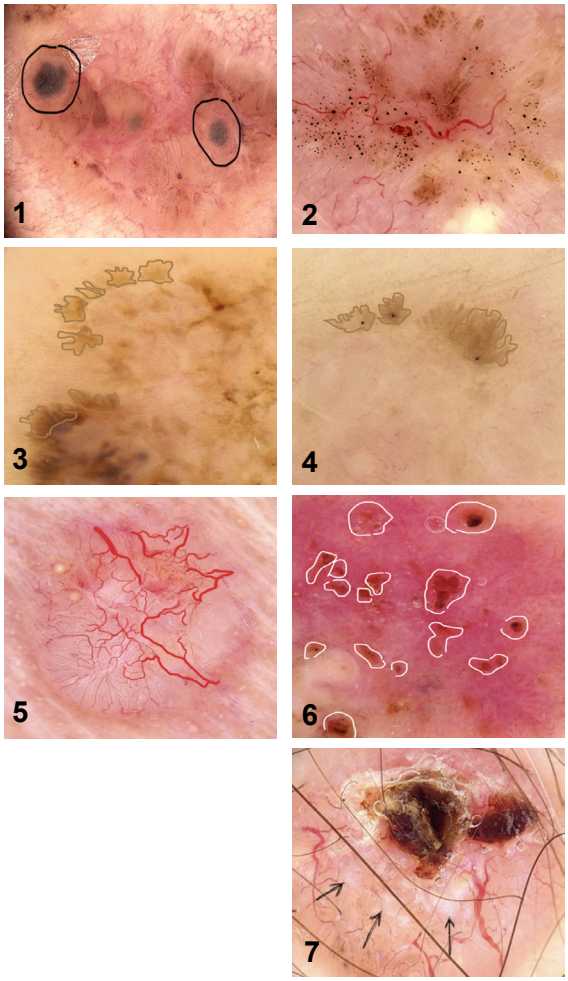
A lid-switch flap (the Cutler Beard flap) is used for defects larger than 50% of the upper eyelid, frequently in combination with a cartilage autograft. A patient operated by this technique requires a temporary tarsorrhaphy [17].

Reconstruction methods used depending on defect size

Clinicians generally select the procedure [26] on the basis of recommendations below and taking in to account the patient's age, tissue elasticity and skin quality.

Table 3. Major dermoscopic signs of basal-cell carcinoma (BCC) [3, 9, 10, 11, 13].

	Dermoscopic signs of BCC	Definition
1	Blue-gray ovoid nests	Well-circumscribed pigmented ovoid structures larger than 0.2 mm. Typical for nodular BCC.
2	Numerous blue-gray dots and globules	Pinpoint blue-gray dot structures that are often distributed in a buckshot scatter pattern. They will prove to be nodular BCC on histopathology.
3	Leaf structures	These areas are defined as discrete, linear to bulbous extensions connected at an off-center base area, forming a leaf-like pattern. They are usually brown or gray-blue in color.
4	Spoke-wheel-like structures	These are radial projections that surround a central darker point. The spoke-wheel-like structure is highly specific for superficial BCCs.
5	Arborizing telangiectasia	These consist of multiple branching blood vessels in a tree-like pattern. Arborizing vessels are associated with nodular BCC.
6	Ulceration	These structures consist of shallow erosions that may be covered with coagulated blood or serous crust.
7	Shiny white structures	These structures can only be seen with polarized dermatoscopy. They appear as white spots or lines.



- Small defects (< 30% of lid length affected) are usually repaired with primary closure and subcutaneous dissection

- Moderate defects (25-50% of lid length affected) are usually repaired with primary defect closure + a lateral canthotomy, pedicle/ full-thickness skin graft

- Large (50–75%) lower eyelid defects are usually repaired with a Hughes flap + full-thickness skin graft, whereas large upper eyelid defects, with a Cutler Beard flap, either alone or in combination with a cartilage autograft

- Extensive (>75%) defects are usually repaired with a combination multi-stage approach involving a tarsoconjunctival flap, free skin graft and cartilage autograft.

Indications for and efficacy, advantages and disadvantages of, the major techniques used for eyelid reconstruction are presented in Table 4.

Eyelid reconstructive surgeries provide restoration of the anatomy and function in 90-95% of cases [16, 26, 27]. Major possible complications include ectropion, lagophthalmos, cicatricial deformities, and partial graft or flap necrosis, and the rate of these complications ranges from 5 to 10% [15, 21]. Meticulous graft/flap size planning, using the donor tissue that is well matched in texture, quality, and appearance to the affected eyelid, and maintenance of intraoperative homeostasis and adequate graft immobilization are essential for the success of surgery.

Good or excellent esthetic results, with mostly inconspicuous scars, well-contoured eyelid, and no defect present, are achieved in the majority of patients [24]. Reconstructions of eyelid defects exceeding 50% of the eyelid (especially, the upper eyelid) may result in the lack of eyelashes, asymmetrical eyelids or alterations in the eyelid folds. The final outcome, however, is functionally and

Table 4. Methods of eyelid reconstruction

Method	Indications	Success and survival rates	Advantages	Shortcomings
Direct closure	Defects smaller than 30% of the eyelid length	In the presence of clear margins, a success rate exceeds 90%, with an excellent cosmetic result [23]	A simple, one-stage procedure; an almost inconspicuous scar	Cannot be used for defects exceeding 30% of the eyelid length; risk of ectropion in the presence of excessive tension
Free skin graft	Defects between 25% and 50% of the eyelid length (anterior lamella defects)	Graft survival rates for full-thickness free-skin grafts are of 85–95% [24, 25]	Effective closure of extensive defects	Risk of color mismatch and shrinkage; no support for the eyelid; a well vascularized basis for the graft is required
Local pedicle flap	Defects between 30% and 60% of the eyelid length	A rate of successful healing of about 95% with a good eyelid function [26]	A flap has its own blood supply; good match for color; enables restoration of a large segment of the eyelid	A technically difficult procedure; additional incisions and scars; sometimes a two-stage procedure
Hughes flap	Lower eyelid defects between 50% and 100% of the eyelid length	High efficacy, with the restoration of full eyelid thickness and a low recurrence rate	Restores the anatomy and function of the eyelid; can be used even for subtotal defects	A two-stage procedure; the eye is closed for several weeks between the two stages; loss of a portion of the upper eyelid
Cutler –Beard procedure	Upper eyelid defects between 50% and 70% of the eyelid length	Almost the whole eyelid (including the palpebral conjunctiva) can be reconstructed [17]	Preserves blinking; can be used for subtotal defects of the upper eyelid	A two-stage procedure; the palpebral aperture is temporarily closed; loss of eyelashes due to the loss of the tarsal plate
Auricular cartilage autograft	Full-thickness defects with loss of the tarsal plate	A graft survival rate of about 100% for an autologous tissue graft [21]	Provides optimal rigidity; reduced risk of graft rejection	The need for mucosal lining and additional incision in the ear; possible stiffness sensation

cosmetically acceptable to the patient when the procedure is performed as prescribed, with further correction if necessary [25].

Conclusion

This review of available data on current approaches to the treatment of periorbital BCC demonstrates that a combination of current ophthalmic plastic surgical methods with precision Mohs surgery and expert histological analysis is an effective standard of treatment for periorbital BCC. Periorbital reconstruction after Mohs surgery for BCC is a complex task which success largely depends on collaboration of a multidisciplinary team including a dermatology oncologist, a pathomorphologist and an ophthalmic plastic surgeon. The choice of the reconstruction method depends on the size, depth and location of the defect, the status of the periorbital tissue and the surgeon's experience. Primary closure is effective for small defects (<30%). Moderate defects (25–50%) are usually closed with local flaps or full-thickness skin grafts. Patients with large and subtotal defects (>50–75%) require difficult to perform reconstructive techniques (the Hughes flap or Cutler Beard flap) or their combinations with other reconstruction types. An individualized approach enables not only radical oncological treatment, but also the restoration of eyelid function and optimal esthetic outcome.

References

1. Basset-Seguin N, Herms F. Update on the management of basal cell carcinoma. Acta Derm Venereol. 2020; 100(11): 5750. https://pmc.ncbi.nlm.nih.gov/articles/PMC9189749/
2. Celebi ARC, Kiratli H, Soylemezoglu F. Evaluation of the Hedgehog signaling pathways in squamous and basal cell carcinomas of the eyelids and conjunctiva. Oncol Lett. 2016; 12: 467–472. https://pubmed.ncbi.nlm.nih.gov/27347166/
3. Nasr I, McGrath EJ, Harwood CA, et al. British Association of Dermatologists guidelines for the management of adults with basal cell carcinoma 2021. Br J Dermatol. 2021; 185(5): 899–920.
4. Rogers HW, Weinstock MA, Feldman SR, Coldiron BM. Incidence estimate of nonmelanoma skin cancer in the United States, 2006. Arch Dermatol. 2010; 146(3): 283–287.
5. Yin VT, Merritt H, Esmaeli B. Targeting EGFR and sonic hedgehog pathways for locally advanced eyelid and periocular carcinomas. World J Clin Cases. 2014; 2(10): 432–438. https://pubmed.ncbi.nlm.nih.gov/25232546

6. World Health Organization (WHO). WHO Classification of Skin Tumours. International Agency for Research on Cancer (IARC), Lyon; 2018. Consensus and Editorial Meeting, 24–26 September 2017.
7. [The 2024 unified clinical protocol for the management of basal cell carcinoma in the primary and secondary care]. Ukrainian.
8. Colevas AD, et al. NCCN Guidelines® Insights: Basal Cell Skin Cancer, Version 2.2025: Featured Updates to the NCCN Guidelines. J Natl Compr Canc Netw. 2025.
9. Furdova A, Kapitanova K, Kollarova A, Sekac J. Periocular basal cell carcinoma – clinical perspectives. Onco Targets Ther. 2020; 13: 10479–10487.
10. Sun MT, Wu A, Figueira E, Huilgol S, Selva D. Management of Periorbital Basal Cell Carcinoma with Orbital Invasion. Future Oncol. 2015; 11(22): 2973–2980.
11. Navarrete-Dechent C, et al. Association of shiny white blotches and strands with nonpigmented basal cell carcinoma: Evaluation of an additional dermoscopic diagnostic criterion. JAMA Dermatol. 2016; 152(5): 546–552.
12. Reiter O, Mimouni I, Gdalevich M, et al. The diagnostic accuracy of dermoscopy for basal cell carcinoma: A systematic review and meta-analysis. J Am Acad Dermatol. 2019 May;80(5):1380–1388.
13. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Basal Cell Skin Cancer. Version 1.2026. Plymouth Meeting (PA): National Comprehensive Cancer Network; 2026.
14. Harvey DT, Taylor RS, Itani KM, Loewinger RJ. Mohs Micrographic Surgery of the Eyelid: An Overview of Anatomy, Pathophysiology, and Reconstruction Options. Dermatol Surg. 2013 May;39(5):673–697.
15. Nerad J, Carter KD. Reconstruction of the eyelids and ocular adnexa. Clin Plast Surg. 2016; 43(2): 253–263.
16. Nerad JA, editor. Techniques in Ophthalmic Plastic Surgery. 2nd ed. Elsevier; 2021.
17. Bowman PH, Fosko SW, Hartstein ME. Periocular Reconstruction. Semin Cutan Med Surg. 2003; 22(4): 263–272.
18. Esmaeli B, Nasser Q, Holden JT, et al. Surgical management of periocular basal cell carcinoma with orbital extension. Ophthalmic Plast Reconstr Surg. 2014; 30(1): 45–49.
19. Pierson JC, Ophof RA, Koornneef L. Subcutaneous dissection in eyelid reconstruction. Ophthalmic Plast Reconstr Surg. 2021; 37(3): 252–260.
20. Bartley GB, Garrity JA, Waller RR. Basal cell carcinoma of the eyelid: determination of factors predisposing to recurrence. Ophthalmic Surg. 2015; 23(9): 603–612.
21. Chandler DB, Gausas RE. Lower eyelid reconstruction. Otolaryngol Clin North Am. 2005; 38(5): 1033–1042.
22. Robinson JK. Closure of surgical defects of the eyelids and canthus. Dermatol Clin. 2016; 34(4): 439–447.
23. Levine MR, Elluru RG, Courtney RJ. Lateral canthotomy and cantholysis in reconstructive surgery of the eyelids. Ophthalmic Surg. 2019; 24(4): 278–284.
24. Mack WP, Belanger C. Split-thickness skin grafts in eyelid and periorbital reconstruction: Indications and outcomes. Facial Plast Surg Clin North Am. 2019; 27(3): 287–297.
25. Patel BC, Brown KE. Full-thickness skin graft. StatPearls Publishing. Updated 2023.
26. Hausheer JR, Hintschich CR. Lower eyelid reconstruction: The state of the art. Facial Plast Surg Clin North Am. 2020; 28(4): 511–523.
27. Hughes WL. A new method for rebuilding a lower lid and for restoring continuity to the lids when they have been divided. Am J Ophthalmol. 1937; 20: 948–953.

Disclosures

Received: 18.08.2025

Accepted: 26.10.2025

Corresponding author: *Tselishcheva M. O. – tselishchevamaryna@gmail.com*

Author contribution. *Conceptualization and Design of the Study: OVP, SSV and AVK; Data Collection: AVK, MOT, VVB; Literature Review: AVK, MOT, VVB; Writing – Original Draft: MOT, VVB; Writing – Review and Editing: OVP, SSV and AVK; Project Administration: OVP, SSV and AVK. The final manuscript was read and approved by all the authors.*

Funding: *The authors have no funding sources to declare.*

Conflicts of interest. *The authors declare that they have no conflicts of interest that could influence their opinions on the subject matter or materials described and discussed in this manuscript.*

Ethical Considerations: *This was a review study. No humans or animals were included in this study. Ethics committee approval and informed consent were not required.*

Data Availability Declaration*: All the data used in this study has been incorporated into this article and supplementary material.*

Abbreviations: *AJCC, American Joint Committee on Cancer; BCC, basal cell carcinoma; BCNS, basal cell nevus syndrome (Gorlin–Goltz syndrome); Hh, Hedgehog signaling pathway; H-zone, high-risk face areas (central face, eyelids/canthi, eyebrows, nose, lips, chin, ear, and periauricular area); MMS, Mohs Micrographic Surgery; Mohs, Mohs Micrographic Surgery; PTCH1, Patched 1 (a receptor of the Hedgehog signaling pathway); PNI, perineural invasion; R0, radical excision with histologically clear resection margins; TP53, tumor protein p53 (a tumor suppressor gene); TNM, Tumor/Node/Metastasis; UICC, Union for International Cancer Control; UV, ultraviolet; UVA, ultraviolet A (320–400 nm); UVB, ultraviolet B (290–320 nm); V-Y, V-Y advancement flap; XP, xeroderma pigmentosum*