INTRODUCTION

Non-melanoma skin cancers are the most common malignancies in the United States, with over 3 million diagnoses made annually.1 The annual incidence of non-melanoma skin cancer has increased over the past several decades, with a 35% increase observed from 2006 to 2012 alone.1,2 This trend is expected to continue secondary to the global rise in life expectancy, improved screening protocols, and the ever-increasing popularity of tanning.3 The 2 major groups of non-melanoma skin cancer include squamous cell carcinomas and basal cell carcinomas, with the latter being 2–4 times more common than the prior.3,4 Compared with other malignancies, non-melanoma skin cancers exhibit low metastatic potential and are typically associated with a favorable prognosis.5 While their metastatic potential is limited, these malignancies can be highly destructive to local tissue, necessitating that some patients undergo complex excisional and reconstructive procedures. Because of this, it is imperative that plastic surgeons be familiar with the management of non-melanoma skin cancers to provide optimal care for their patients.

Mohs micrographic surgery is the gold-standard treatment for high-risk non-melanoma skin cancers in patients who are appropriate surgical candidates.6–8 Unfortunately, this procedure may not be available due to medical, financial, or geographic constraints. This article will serve as an overview for the management of non-melanoma skin cancers in settings where Mohs micrographic surgery may not be available.

DIAGNOSIS AND STAGING

Before performing a biopsy of a suspected lesion, the surgeon should take a thorough medical history and perform a physical examination. When collecting a medical history, the surgeon should assess a patient’s risk factors for tumor development and potential for metastatic spread. On examination, it is important to assess the size of the lesion and to palpate draining lymph nodes for any signs of nodal metastases.8 After collecting a thorough history and physical, the surgeon should then perform a punch biopsy of the lesion. Punch biopsy techniques are the gold standard for diagnosing non-melanoma skin cancers, though negative pathology reports do not necessarily rule out malignancy. This is because punch biopsy techniques are associated with false-negative rates, ranging from 6% to 19%.9–11 To minimize the risk of a false negative result, providers should ensure that the biopsy is 3 mm in width and deep enough to include the reticular dermis.6,7,9,12 If the sample comes back positive for non-melanoma skin cancer, the surgeon must differentiate whether it is a high-risk tumor or a low-risk tumor.

The National Comprehensive Cancer Network has developed guidelines for determining the level of risk of a non-melanoma skin cancer (Table 1).6,7 These guidelines

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take into account both the physical properties of the tumor and the patient’s medical history. The face is an anatomic region of high clinical importance for plastic surgeons in particular (Fig. 1). Tumors of the face are deemed high-risk due to their high rates of recurrence and their tendency to extensively invade local tissue. While both squamous cell carcinomas and basal cell carcinomas have multiple histologic subtypes of varying risks, squamous cell carcinomas, in general, are associated with higher rates of recurrence, metastasis, and mortality than their basal cell counterparts. Compared with the negligible metastasis and mortality rates demonstrated by basal cell carcinomas, squamous cell carcinomas have a metastasis rate of 2%–6% and a mortality rate of 1.5%. Once a tumor is diagnosed and its risk is classified, the provider may begin to develop a treatment plan that best suits the patient (Table 2).

**SURGICAL EXCISION**

In the absence of Mohs micrographic surgery, standard surgical excision with complete margin assessment is the gold-standard treatment for both low and high-risk non-melanoma skin cancers. When planning tumor resection, the surgeon must balance tissue conservation and tumor elimination. For low-risk malignancies, tumors should be resected along with their subcutaneous fat using 4-mm lateral margins. In lower-risk areas of the face such as the cheek and forehead, 3-mm lateral margins may be used to improve cosmesis; however, the use of smaller margins increases the risk for incomplete excision and recurrence. For high risk malignancies, it is recommended that surgeons utilize lateral margins > 10 mm and excise down to the first underlying anatomic plane. During resection, the surgical specimen should be handled with care as to avoid damaging the tissue. After removal, the specimen should be lightly irrigated with normal saline to remove excess blood and labeled for the purposes of orientation using markings or suture (Fig. 2). Should fixation be indicated, the specimen is then placed in a tube containing a solution of 10% formalin. It is imperative that the volume of the solution is 10 times greater than that of the specimen to ensure that it is adequately fixed. The specimen tube must always be labeled with a detailed description of the specimen, the location from which it was resected, and patient identifiers to minimize the risk of handoff-associated errors between the surgeon and pathologist. When performed properly, standard surgical excision and margin assessment results in 5-year cure rates, ranging from 90% to 99%.

In anatomic locations where tissue conservation is of the greatest concern, such as the face, the surgeon may utilize frozen section or staged surgical excision techniques. Frozen section techniques are beneficial as they conserve tissue and allow for immediate reconstruction once the
margins are clear. Although staged surgical excision is a more precise technique with lower recurrence rates, it is more expensive and requires patients to undergo multiple operations over the course of several days.

**ELECTRODESSICATION AND CURETTAGE**

Electrodessication and curettage (EDC) is an ablative procedure that serves as an alternative to surgical excision for the treatment of low-risk non-melanoma skin cancers. EDC involves the use of a curette to mechanically debride malignant tissue followed by electrocoagulation for the purposes of hemostasis. The curette preferentially removes malignant tissue during the debridement process because of the poor intercellular adhesion exhibited by cancerous cells. The process of curettage and electrocoagulation is repeated multiple times until the provider feels that they have sufficiently removed the malignancy. The resulting wound is then allowed to heal secondarily. While less invasive than surgical excision, EDC produces an unsightly hypopigmented scar and often results in

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**Table 2. Comparing Treatment Modalities for Low-risk and High-risk Non-melanoma Skin Cancers**

| Treatment Modality                  | 5-Year Recurrence Rate | Benefits                                                                 | Limitations                                                                                     |
|-------------------------------------|------------------------|--------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|
| **Low-risk lesions**                |                        |                                                                          |                                                                                                |
| Standard surgical excision          | 2–5% BCC/SCC           | Provides lowest rates of recurrence                                      | Invasive procedure; outcomes highly dependent on surgeon                                       |
| Electrodesiccation and curettage    | 1–9% BCC/SCC           | Less invasive when compared with surgical excision                       | Does not permit histologic margin assessment; secondary intention wound healing results in hypopigmented scar; produces post-procedural alopecia in hair-bearing areas |
| Brachytherapy radiation therapy     | 1–8% BCC/SCC           | Produces high-dose radiation with minimal impact to surrounding structures |                                                                                                |
| External beam radiation therapy     | 5–15% BCC/SCC          | Useful for nonsurgical candidates older than 60 years                    | Increases risk for future malignancy; complicates future excisions and reconstruction          |
| Cryotherapy                         | 1–5% BCC/SCC           | Quick, cost-effective, no local anesthesia required                       | Potential for posttreatment prolonged edema, neuropathic pain, scarring, hypopigmentation       |
| Photodynamic therapy                | 5–50% BCC/SCC          | Superior cosmetic outcomes compared to surgical excision                 | Painful treatments; potential for posttreatment chronic open wounds and hyperpigmentation       |
| Topical 5-FU and Imiquimod         | 10–15% BCC/SCC         | Superior cosmetic outcomes compared to surgical excision                 | Prolonged treatment time; end result heavily dependent on patient’s adherence to treatment       |
| **High-risk lesions**               |                        |                                                                          |                                                                                                |
| Standard surgical excision          | 4–10% BCC; 8% SCC      | Provides lowest rates of recurrence when MMS is not available             | Invasive procedure; outcomes highly dependent on surgeon                                        |
| Brachytherapy radiation therapy     | 6–13% BCC/SCC          | Produces high-dose radiation with minimal impact to surrounding structures| Not readily available in many regions                                                           |
| External beam radiation therapy     | 14%                    | Useful for nonsurgical candidates older than 60 years                    | Increases risk for future malignancy; complicates future excisions and reconstruction          |

BCC, basal cell carcinoma; 5-FU, 5-fluorouracil; MMS, Mohs micrographic surgery; SCC, squamous cell carcinoma.

‡Data for photodynamic therapy outcomes of BCC/SCC provides recurrence rates at 1–3 years, no data available for 5-year recurrence.
post-procedural alopecia. Because of this, patients with non-melanoma skin cancers of the face and scalp may elect to undergo another form of treatment. Despite the 91%–99% 5-year cure rates seen in patients treated with EDC, histologic margin assessment is not possible in these patients, given the destructive nature of the procedure. Because of this, patients and providers should pay close attention to the treatment area for signs of recurrence.

**CRYOSURGERY**

Cryosurgery is a non-invasive procedure frequently employed to treat superficial, low risk non-melanoma skin cancers. Cryosurgery uses a cryogen, usually in the form of liquid nitrogen, to eradicate malignant tissue by exposing the tumor to multiple cycles of freezing and thawing. Compared with standard surgical excision and EDC, cryosurgery is associated with minimal post-procedural morbidity and typically has excellent aesthetic outcomes. Although rare, patients have reported neuropathic pain, hypertrophic scarring, and depigmentation after undergoing cryosurgery. When treating superficial, low-risk non-melanoma skin cancers, cryosurgery has a 5-year recurrence rate, ranging from 1% to 5%. While effective at treating superficial, low-risk malignancies, cryosurgery is more often used to treat actinic keratoses—a premalignant lesion associated with squamous cell carcinoma. Cryosurgery is highly effective for the treatment of actinic keratoses, with clearance rates reaching 99%.

**PHOTODYNAMIC AND TOPICAL THERAPIES**

Photodynamic therapy and topical pharmacotherapy are other non-invasive interventions that may be utilized to treat superficial, low-risk non-melanoma skin cancers. Photodynamic therapy begins with topical application of a solution containing photosensitive porphyrins, such as aminolaevulinic acid and methyl-aminolaevulinic acid, to the affected tissue. After a latency period of 4–20 hours, the photosensitive porphyrins are illuminated with visible light and produce radical oxidative species that are cytotoxic to the malignancy. Most regimens include 2 or more treatments and can produce clearance rates ranging from 50% to 95%. This treatment is generally well-tolerated, though patients may suffer from pain, chronic open wounds, and hyperpigmentation.

Topical pharmacotherapy usually comes in the form of 5-fluorouracil and imiquimod creams. 5-fluorouracil and imiquimod disrupt the proliferation of neoplastic cells by inhibiting nucleic acid synthesis and activating the immune system to remove the malignancy, respectively. These medications are applied by the patient multiple times a day over a period of 2–3 months. The outcomes of topical pharmacotherapy are heavily dependent on patient compliance but exhibit cure rates ranging from 85%–90%. Common side effects of pain, erythema, and severe pruritis, along with the high associated cost of both medications, may result in poor patient compliance or premature cessation of treatment.

While surgical excision has superior clearance rates, PDT and topical pharmacotherapy have demonstrated superior cosmetic outcomes than surgical excision, making them attractive alternatives for malignancies of the head and neck. Additionally, these interventions may be used to treat the skin adjacent to the malignancy to prevent the development of future malignancies.

**RADIATION THERAPY**

Radiation therapy is a less commonly employed treatment modality for non-melanoma skin cancers. External beam radiation techniques are highly effective at treating non-melanoma skin cancers of the head and neck. In external beam radiation therapy, high energy beams are generated by an external device and are transmitted into the malignancy with the goal of disrupting cellular replication. While effective, external beam radiation therapy is primarily used to treat malignancies in patients over the age of 60 under special circumstances. In short, this form of radiation therapy is most often indicated in patients who are poor surgical candidates or have perineural or large nerve involvement. This is because external beam radiation therapy promotes tumorigenesis and can alter the structure of normal surrounding tissue, thereby complicating future excisions and reconstructions.

The reported 5-year recurrence rates of non-melanoma skin cancers treated with external beam radiation therapy range from 5% to 15%; however, squamous cell carcinomas tend to develop resistance with each treatment.

Brachytherapy has become an increasingly popular alternative to external beam radiation for the treatment of non-melanoma skin cancers. Brachytherapy is a form of radiation therapy where high doses of radiation are directly applied to the malignancy. The direct application of radiation maximizes the therapeutic effects of radiotherapy while minimizing the exposure of surrounding tissue to radiation. Brachytherapy is particularly useful for treating well-circumscribed malignancies in facial regions where surgical excision may result in a less-favorable cosmetic outcome. The reported 5-year recurrence rates of non-melanoma skin cancers following brachytherapy range from 1% to 13%. It should be noted, however, that there are limited data describing the long-term effects of brachytherapy for the treatment of non-melanoma skin cancer. Lastly, forms of brachytherapy specifically designed for the treatment of non-melanoma skin cancers are not as readily available as external beam radiation and standard surgical excision in many geographic regions.

**CHEMOTHERAPEUTIC AGENTS**

Chemotherapeutic agents may be employed in cases of advanced local or metastatic disease. Hedgehog pathway inhibitors, such as vismodegib and sonidegib, may be used to treat advanced basal cell carcinoma. These medications selectively inhibit the smoothened protein receptor, which is frequently involved in the pathogenesis of this malignancy. These medications are primarily used to shrink large tumors before surgical excision due
to the severe side-effect profile associated with extended treatment.\textsuperscript{8,35} Advanced and metastatic squamous cell carcinomas may be treated with a wide variety of systemic chemotherapeutic agents, though these treatments are associated with inconsistent response rates and severe side effects.\textsuperscript{35}

**POSITIVE MARGINS AND RECURRENCE**

The presence of positive margins upon histologic examination of the surgical specimen warrants further treatment. The management of patients with positive margins is largely dependent on the patient’s ability to undergo surgical excision or radiation therapy.\textsuperscript{6,7} In the absence of Mohs micrographic surgery, patients with positive margins are treated with further excision regardless of their tumor’s pre-excision risk classification.\textsuperscript{6,7} Frozen section techniques are recommended in these cases to ensure that the margins are sufficiently clear before reconstruction.\textsuperscript{6,7} Patients who are unsuitable candidates for surgery should undergo radiation therapy.\textsuperscript{6,7} A multidisciplinary tumor board should be consulted in cases where negative margins cannot be achieved and surgical excision and radiation therapy can no longer be tolerated.\textsuperscript{5,7} The tumor board can then decide which form of chemotherapy would be able to best treat the patient’s malignancy.

All recurrent tumors are treated as high-risk malignancies regardless of their pre-interventional risk classification.\textsuperscript{6–8} Recurrent tumors that remain localized without signs of invasion are treated with surgical excision or radiation therapy. Tumors with nodal or systemic metastasis necessitate consultation of a multidisciplinary tumor board for further management.\textsuperscript{7,8}

**FOLLOW-UP**

The importance of patient education and proper tumor surveillance following the treatment of a non-melanoma skin cancer cannot be understated. This is because patients with a history of non-melanoma skin cancer have a 10-fold risk of developing a second malignancy with 30\%–50\% developing a new lesion within 5 years.\textsuperscript{6,7} Patients should be scheduled for follow-up appointments every 2–3 months for the first 2 years following treatment.\textsuperscript{6–8} After 2 years, patients may follow-up with their provider every 6 to 12 months.\textsuperscript{6–8} At each follow-up visit, the provider should conduct a full-body skin check, treat precancerous lesions, and biopsy lesions that are suspicious for malignancy. Patients must also be educated about the importance of sun protection and the cessation of tanning bed use, if applicable, as these behavioral modifications can lower the risk of developing novel malignancies.\textsuperscript{6–8} Avoidance of midday sun exposure along with the use of protective clothing and sunscreen are all modifiable risk factors that prevent the development of future malignancies.\textsuperscript{6–8}

**RECONSTRUCTION**

Oncologic reconstruction following surgical excision of non-melanoma skin cancer is highly dependent on the risk classification of the tumor and the size and location of the post-excisional defect.\textsuperscript{8} Delaying oncologic reconstruction until negative margins are confirmed on histology lowers the risk of tumor seeding and the need for multiple reconstructive procedures. While patients with high-risk malignancies should always have confirmed negative margins before reconstruction, patients with low-risk malignancies may elect to undergo immediate reconstruction.\textsuperscript{8} Reconstruction of post-excisional defects located on the face poses several challenges for the plastic surgeon. The surgeon must exhibit exceptional creativity when reconstructing a facial defect as minor irregularities of the face are highly distinguishable.\textsuperscript{50} Furthermore, the concave and convex nature of many facial structures requires a thorough understanding of wound healing and how it may affect surrounding structures.\textsuperscript{51} Herein, we will discuss several reconstructive modalities used for the treatment of facial defects following surgical resection of non-melanoma skin cancer.

Starting at the bottom of the reconstructive ladder, healing by secondary intention is a viable option for reconstructing excisional defects. Secondary wound closure may be used for small, superficial defects located in
areas where the risk of structural distortion secondary to wound contraction is low. While this form of reconstruction is non-invasive, patients are often left with an unsightly hypopigmented scar that may be undesirable for some patients. The advent of biologic wound agents has permitted secondary closure to be applied broadly with significant improvements in aesthetic outcomes. For example, reconstruction of isolated vermillion defects using traditional methods, such as myomucosal tongue flaps, has largely been replaced by secondary closure with the use of biologic wound agents because of their superior aesthetic outcomes and absence of donor site morbidity (Fig. 3).

Linear closure with excision of dog ears is frequently used to treat a multitude of facial defects. This form of reconstruction is most effective in areas of greater laxity such as the cheek, lip, and forehead and is particularly useful in elderly patients. Compared with more complex reconstructive techniques, linear closure often produces equivalent or even superior cosmetic outcomes when used

Fig. 4. Patient with a large, circumferential defect of the infraorbital cheek following excision of her malignancy (A). The defect was reconstructed utilizing a cervicofacial flap (B). Patient 3 weeks postoperatively without signs of ectropion or lip retraction (C). Patient 1 year postoperatively with minimal scarring (D).
to treat large defects.\textsuperscript{54} Additionally, the complications associated with locoregional tissue transfer, such as flap loss, are non-existent in reconstruction by linear closure.\textsuperscript{54}

Skin grafting is frequently utilized for facial reconstruction following surgical excision. Full-thickness skin grafts are used to treat small, superficial facial defects and can produce excellent aesthetic results if the graft is color-matched to the tissue surrounding the defect.\textsuperscript{51,53,55,56} Split-thickness skin grafts are primarily used to cover large defects, particularly those of the scalp, because of the minimal donor site morbidity associated with harvest.\textsuperscript{8} Skin grafts require an underlying vascular bed to survive after placement over the defect. Should an adequate vascular bed not exist, acellular dermal matrices may be used to develop one before graft placement.\textsuperscript{8}

Locoregional tissue transfer is frequently employed to treat large, complex deformities of the face.\textsuperscript{57,58} Reconstruction of defects involving the cutaneous portion of the upper lip, also known as the ergotrid, is challenging due to the risk of distorting the philtral columns and adjacent structures.\textsuperscript{50,59} Small rotational flaps, such as the ergotrid flap, may be used to correct these defects while

\begin{figure}[h]
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\caption{Patient with a full-thickness defect of the nasal ala following excision of a nonmelanoma skin cancer (A). Inset of the paramedian forehead flap into the alar defect (B). Patient 3 weeks post-operatively following inset of the flap (C). Patient 3 months postoperatively following flap division and inset (D).}
\end{figure}
preserving the natural structure of surrounding anatomy should linear closure be contraindicated. 59 Similar to defects of the erognotid, reconstruction of large defects of the cheek is complicated by its proximity to the lip, nose, and eye. 59 Large rotational flaps, such as the cervicofacial flap, allow the surgeon to mimic the color and texture of tissue surrounding the defect while minimizing the risk of distorting said structures (Fig. 4). 53

Regional flaps, such as the paramedian forehead flap, are frequently employed to reconstruct the nose (Fig. 5). 56, 60 This interpolated flap, along with cartilage grafting, is used to provide coverage, lining, and support to the reconstructed nose in a 2-stage procedure. This procedure is considered to be the gold standard treatment for complex nasal reconstruction because it produces excellent aesthetic outcomes with minimal donor site morbidity. 60 In addition to its efficacy, this procedure has demonstrated complication rates as low as 4%, making it a reliable and safe reconstructive modality. 53

**CONCLUSIONS**

The annual rise in incident non-melanoma skin cancer necessitates that plastic surgeons become more familiar with the diagnosis, management, and prevention of these malignancies. In the absence of Mohs micrographic surgery, surgical excision is the gold-standard treatment for non-melanoma skin cancers. Despite this, there are a multitude of available treatment modalities that may be more desirable in certain circumstances. Reconstruction of the face is highly complex; however, techniques lower on the reconstructive ladder, such as linear closure, should not be overlooked because they can produce excellent aesthetic results with minimal morbidity. The prevention of malignancy is best done by educating patients about modifiable risk factors and treating precancerous lesions.

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