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HEAD & NECK: NON-MELANOMA SKIN CANCER OF THE HEAD AND NECK (J MOYER, SECTION EDITOR)

# Mohs Micrographic Surgery for Treatment of Non-melanoma Skin Cancer

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**Abstract**

**Purpose of Review** The aims of this report are to review literature supporting the use of Mohs micrographic surgery for treatment of non-melanoma skin cancer and to address indications and potential limitations of this form of therapy for non-melanoma skin cancer.

**Recent Findings** The first randomized controlled trial comparing standard excision to Mohs micrographic surgery for treatment of facial basal cell carcinoma has recently been published, demonstrating a lower recurrence rate after Mohs surgery compared to standard excision after a 5-year and 10-year follow-up period, supporting its use in the treatment of high-risk basal cell skin cancer.

**Summary** Mohs micrographic surgery is indicated for treatment of basal cell carcinomas and cutaneous squamous cell carcinomas at high risk of recurrence and for tumors located in areas where tissue conservation and/or functional preservation is desired.

**Keywords** Mohs micrographic surgery · Basal cell carcinoma · Cutaneous squamous cell carcinoma

## Introduction

Non-melanoma skin cancers (NMSCs) represent the most common malignancies in the United States. Basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (cSCC) account for the majority of NMSC. The incidence of NMSC has been steadily rising for years, with greater than 5.4 million cases annually according to recent estimates. Rogers et al. recently found that incidence rates of skin cancer in the United States (US) sustained a 100% increase from 1992 to 2012 in the Medicare fee-for-service population. They also reported a 35% increase in NMSC in the US population over a 6-year period from 2006 through 2012 [1]. The aging population and increasing use of immunosuppressive medications, often in the setting of organ transplantation, have been significant factors in this increasing incidence [2].

Mohs micrographic surgery (MMS) has become the treatment of choice for high-risk NMSC due to the fact that it produces the highest cure rates while sparing as much normal tissue as possible. The goal of this report is to review the use of MMS for NMSC, including indications and potential limitations of this technique.

## Background

BCC is the most common malignancy affecting humans. The incidence of BCC has risen globally by 5.5% each year for the past few decades, and it is expected to continue increasing over time [3]. Tumors are generally located in areas with high levels of sun exposure, most commonly on the head and neck. While BCC typically has a good prognosis, tumors can cause significant morbidity, particularly due to the common occurrence in functional areas of the head and neck.

cSCC, the second most common skin malignancy, can occur on any area of the skin. The lifetime risk of developing cSCC in the US is up to 14% for men and 9% for women [4]. The main risk factor for the development of cSCC is

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cumulative sun exposure. Immunosuppression, often related to organ transplantation, has become an increasingly common risk factor in recent years [2]. The most frequently affected areas include the chronically sun-exposed skin of the head, neck, and upper extremities. Tumors can also develop in areas of chronic inflammation or within longstanding scars [5].

The choice of treatment modality for NMSC should take into consideration multiple factors, including recurrence rate, conservation of function, patient expectations, and possible adverse effects [6]. Surgical treatment is the mainstay of therapy for NMSC. Surgical treatment options include curettage and electrodessication, standard surgical excision, or MMS. MMS is the treatment modality with the highest reported cure rate for primary tumors (99% cure rate) [7]. MMS is most often the treatment of choice for tumors on the head and neck due to their higher risk of recurrence and location in areas where functional preservation is of utmost importance.

## Mohs Micrographic Surgery

MMS as it is practiced today is a modification of the method first developed by Dr. Frederic E. Mohs in 1941. His chemosurgery technique was based on chemical fixation of the diseased tissue with zinc chloride in vivo, after which the tumor was shaved off allowing 100% of the margins, both deep and peripheral, to be examined microscopically through horizontal sectioning of the removed tissue. If cancer was found persisting in any of the margins, these areas were localized on maps, and re-excision was performed only in areas of residual cancer [8, 9].

Since its inception, the technique has been refined and now is performed under local anesthesia using frozen sections, without in vivo tissue fixation. The procedure begins with debulking of the clinical lesion with either a scalpel or curette. The clinically affected tissue is then excised with a small margin of normal-appearing skin in a thin layer with the scalpel angled at 45° to the skin (producing a beveled edge). Importantly, anatomical orientation is maintained and a map is drawn. Subsequently, the technician compresses and mounts the tissue and serially cuts horizontal frozen sections across the bottom of the specimen. This allows for microscopic visualization of the entire deep margin as well as the peripheral epidermal margins. The slides are then reviewed by the surgeon, who marks any residual neoplasm on the map. Any areas of positivity are re-excised and processed as above until complete tumor clearance is achieved. The technique is named "micrographic" due to the combination of microscopic control of cancer excision and graphic mapping to aid in the re-excision of residual tumor [9, 10].

MMS differs from standard surgical excision in several ways. Most importantly, processing of the excisional specimen in MMS allows for histopathologic assessment of 100% of the excisional margin, compared to approximately 2% of the margin which is evaluated via the "breadloaf" technique used in standard histologic processing of excisional specimens. MMS allows for removal of the tumor with narrow margins and thus maximizes the rate of complete tumor removal while minimizing loss of normal tissue. Of all treatment modalities, MMS was demonstrated to have the highest cure rate for NMSC, with clearance rates of 99% for primary BCC and 95% for recurrent BCC after 5 years [7, 11].

Based on retrospective studies, MMS has long been considered the treatment of choice for high-risk NMSC based on tumor location, histology, recurrent nature, or patient factors such as immunosuppression. However, there has been a paucity of randomized controlled trials (RCTs) comparing outcomes between different treatment modalities, leading to a lack of consensus regarding the best treatment modality for all tumors.

Due to this lack of consensus, in 2012, a task force of the American Academy of Dermatology, the American College of Mohs Surgery, the American Society for Dermatologic Surgery Association, and the American Society for Mohs surgery published a set of appropriate use criteria for MMS. At the time these criteria were developed, evidence for the use of MMS for BCC and cSCC was limited to retrospective case series and meta-analyses [12].

Results from a RCT from the Netherlands evaluating recurrence rates of primary and recurrent facial BCCs after randomization to standard excision (SE) or MMS are now available. Interestingly, after the first follow-up period of 30 months, recurrence rates were slightly lower for both primary and recurrent BCCs treated with MMS versus SE, but no statistically significant differences were found for either group. After 5 years of follow-up, significantly fewer recurrences were reported of recurrent BCC after MMS compared to SE, but this difference was not found in primary BCC. After 10 years of follow-up, Van Loo et al. reported a recurrence rate of 4.4% for primary facial BCC treated with MMS versus 12.2% after standard excision ($p = 0.100$). Their findings for recurrent facial BCC also favored MMS, with a 10-year recurrence rate of 3.9% after MMS and 13.5% after SE ($p = 0.023$). Importantly, it was found that a significant number of recurrences of primary BCC (56%) developed after 5 years of treatment, underscoring the slow growth of these tumors and the importance of long-term follow-up for these patients. An aggressive histologic subtype was a significant risk factor for recurrence. These data provide the best available evidence at the current time to support the use of MMS for BCC at increased risk of recurrence [13•].

In addition to the high cure rate, another important benefit of MMS in the treatment of NMSC lies in the smaller surgical defects that result from this tissue-sparing technique. This becomes particularly important when the tumor is located in functional areas of the head and neck, as is often the case in

NMSC. A small RCT found that the median area of the defect after MMS for BCC was significantly smaller than that resulting from SE (116.6 versus 187.7 mm, $p < 0.001$) [14]. Another study found that for BCCs requiring more than one SE, or at least two stages of MMS, the defect size was significantly larger after excision compared to MMS for primary and recurrent BCCs [15]. In areas where functional preservation is critical, the use of a tissue-sparing modality such as MMS should be considered the treatment of choice.

There are currently no RCT data or prospective studies evaluating MMS compared to other treatment modalities for treatment of cSCC. However, considering the recent RCT data showing the superiority of MMS for primary and recurrent facial BCCs, one may reasonably deduce a similar benefit for cSCC. Cutaneous SCC is often characterized by asymmetric subclinical extension histologically and can present with perineural invasion. Because of these factors, MMS is often the treatment of choice to allow for complete margin evaluation and improved tumor clearance.

## Selection Criteria for MMS for Basal Cell Carcinoma

Given the low metastatic rate of BCC, the risk for local tumor recurrence is felt to be the most clinically relevant factor driving the selection of treatment modality for BCC. The National Comprehensive Cancer Network (NCCN) has created a risk stratification based on clinical and pathological features, which is useful in guiding treatment selection for patients with BCC [16]. The NCCN stratification considers parameters such as location, size, ill-defined tumor borders, primary versus recurrent, immunosuppression, site of prior radiation therapy, histologic growth pattern, and perineural involvement to help distinguish low-risk from high-risk tumors. High-risk tumors as defined by these parameters constitute indications for treatment with MMS (Table 1).

Notably, location of a tumor in what has been named the "H"-zone of the face (see Table 1 for definition) confers a high risk of recurrence and thus represents an indication for treatment with MMS, regardless of the size of the lesion. Mora and Robins found in their case series of 848 treated BCCs that tumors located on the central face were more invasive, more destructive, and more frequently recurrent than tumors elsewhere [17].

Tumor clearance may be challenging in some areas in the "H-zone" due to the presence of embryonic fusion planes in which the spread of tumor can be very subtle; these include the ala-nasolabial junction, the postauricular sulcus, and the preauricular area (especially the tragus). Tumor clearance in other areas, such as the nasal ala, may be challenging due to the possibility of subclinical perichondrial spread. Use of MMS for treatment of tumors in these areas has the advantage of allowing evaluation of 100% of the peripheral and deep margins, leading to improved cure rates. MMS is also the treatment of choice for tumors in the "H"-zone as this zone includes anatomic units with critical functional and cosmetic importance [9].

**Table 1** National Comprehensive Cancer Network stratification of low- versus high-risk BCC (Version 1.2018)

| Parameters | Low risk | High risk |
|---|---|---|
| Clinical | | |
| Location[1]/size | Area L < 20 mm | Area L ≥ 20 mm |
| | Area M[2] < 10 mm | Area M ≥ 10 mm |
| | | Area H[3] |
| Borders | Well defined | Poorly defined |
| Primary vs recurrent | Primary | Recurrent |
| Immunosuppression | No | Yes |
| Site of prior radiation therapy | No | Yes |
| Pathological | | |
| Growth pattern subtype | Nodular, superficial[4] | Aggressive[5] |
| Perineural involvement | No | Yes |

[1] Area L = trunk and extremities (excluding hands, feet, nail units, pretibial area, and ankles). Area M = cheeks, forehead, scalp, neck, and pretibial area. Area H = central face, eyelids, eyebrows, periorbital skin, nose, lips, chin, mandible, pre- and postauricular skin/sulci, temple, ear, genitalia, hands, and feet

[2] Location independent of size may constitute high risk

[3] Area H constitutes high risk based on location, independent of size

[4] Low-risk growth patterns also include keratotic, infundibulocystic, and fibroepithelioma of Pinkus

[5] Having morpheaform, basosquamous (metatypical), sclerosing, mixed infiltrative, or micronodular features in any portion of the tumor

## Selection Criteria for MMS for Cutaneous Squamous Cell Carcinoma

While it is known that the majority of cSCCs can be treated successfully with surgical excision or electrodessication and curettage, it is recognized that certain tumors have a higher risk of local recurrence and therefore MMS should be considered as the treatment of choice. The NCCN Clinical Practice Guidelines for cSCC utilize clinical and pathological factors to provide a risk stratification system, similar to the one described for BCC, which serves to help guide treatment selection for SCC. This is based on available evidence in the literature as well as expert opinion [18]. MMS is generally recommended for treatment of high-risk cSCC, as per NCCN stratification (Table 2). Clinical factors that define high-risk cSCC include certain locations and tumor size, ill-defined borders, recurrent nature, development within a site of prior radiation therapy or

**Table 2** National Comprehensive Cancer Network stratification of low- versus high-risk cSCC (version 2.2018)

| Parameters | Low risk | High risk |
|---|---|---|
| Clinical | | |
| Location[1]/size[2] | Area L < 20 mm | Area L ≥ 20 mm |
| | Area M[3] < 10 mm | Area M ≥ 10 mm |
| | | Area H[4] |
| Borders | Well defined | Poorly defined |
| Primary vs recurrent | Primary | Recurrent |
| Immunosuppression | No | Yes |
| Site of prior radiation therapy or chronic inflammatory process | No | Yes |
| Rapidly growing tumor | No | Yes |
| Neurological symptoms | No | Yes |
| Pathological | | |
| Degree of differentiation | Well to moderately differentiated | Poorly differentiated |
| High-risk histopathological subtype[5] | No | Yes |
| Depth (thickness or Clark level)[6] | < 2 mm, or I, II, III | ≥ 2 mm or IV, V |
| Perineural, lymphatic, or vascular involvement | No | Yes |

[1] Area L = trunk and extremities (excluding hands, feet, nail units, pretibial area, and ankles). Area M = cheeks, forehead, scalp, neck, and pretibial area. Area H = central face, eyelids, eyebrows, periorbital skin, nose, lips, chin, mandible, pre- and postauricular skin/sulci, temple, ear, genitalia, hands, and feet

[2] Including peripheral rim of erythema

[3] Location independent of size may constitute high risk

[4] Area H constitutes high risk based on location, independent of size

[5] Acantholytic (adenoid), adenosquamous, desmoplastic, or metaplastic (carcinosarcomatous) subtypes

[6] A modified Breslow measurement should exclude parakeratosis or scale/crust and should be made from base of ulcer is present. If clinical evaluation of incisional biopsy suggests that microstaging is inadequate, consider narrow margin excisional biopsy

chronic inflammation, history of immunosuppression, or a history of rapid growth or neurological symptoms (which suggests perineural involvement). Histopathological features that define a high-risk cSCC include poor differentiation, depth of 2 mm or greater, or any perineural, lymphatic, or vascular involvement.

Similar to BCC, the choice of treatment modality for cSCC must take into account the degree of risk as well as other factors including preservation of function, possible adverse effects, and patient expectations [6].

## Limitations of Mohs Micrographic Surgery

MMS has limitations in certain situations. Aggressive histologic subtypes such as sarcomatoid/spindle cell or infiltrative cSCC are more challenging to identify on frozen sections and may lead to false-negative interpretations [19]. These histologic subtypes may be best treated with standard surgical excision and permanent paraffin sections for optimal histopathologic evaluation. Additionally, the fact that MMS layers are not further evaluated for high-risk features using paraffin sections presents another limitation. This can be surmounted by submitting the tumor debulking specimen for paraffin sections in order to assess for high-risk features and/or perform additional testing (e.g., molecular studies) if indicated.

## Conclusions

MMS represents a highly specialized surgical technique which allows for complete margin assessment and provides the highest cure rate for treatment of NMSC. MMS differs from standard surgical excision because the processing of the excisional specimen allows histopathologic assessment of 100% of the excisional margin, maximizing the rate of complete tumor removal. In addition to the benefit of total margin control, the advantage of tissue preservation is of particular importance in areas where these tumors tend to occur including most functional areas of the head and neck.

Until recently, recommendations for treatment of NMSC with MMS were based on retrospective data and consensus/expert opinion. There is now evidence from a RCT showing that after a 10-year follow-up period, primary and recurrent facial BCCs treated with MMS developed fewer recurrences

than those treated with standard excision (4.4 versus 12.2% for primary BCC; 3.9 versus 13.5% for recurrent BCC) [13•].

MMS is indicated to treat BCC and cSCC considered to be at high risk for recurrence. Factors that confer a higher risk include location in the H-zone of the face, recurrent nature, size, aggressive growth pattern, immunosuppression, prior radiation therapy, perineural involvement, and other factors (Tables 1 and 2).

It is important to note that MMS is not ideal to treat certain types of tumors, such as sarcomatoid/spindle cell or poorly differentiated cSCC, as these tumor cells may be more difficult to evaluate with frozen sections. Standard excision with permanent section histopathologic assessment of margins may be preferred for these specific histologic subtypes.

## Compliance With Ethical Standards

**Conflict of Interest** The authors declare that they have no competing interests.

**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.

## References

Papers of particular interest, published recently, have been highlighted as:
- Of importance


1. Rogers HW, Weinstock MA, Feldman SR, Coldiron BM. Incidence estimate of nonmelanoma skin cancer (keratinocyte carcinomas) in the U.S. population, 2012. JAMA Dermatol. 2015;151(10):1081–6. https://doi.org/10.1001/jamadermatol.2015.1187.
2. Kim C, Cheng J, Colegio OR. Cutaneous squamous cell carcinomas in solid organ transplant recipients: emerging strategies for surveillance, staging, and treatment. Semin Oncol. 2016;43(3):390–4. https://doi.org/10.1053/j.seminoncol.2016.02.019.
3. Lomas A, Leonardi-Bee J, Bath-Hextall F. A systematic review of worldwide incidence of nonmelanoma skin cancer. Br J Dermatol. 2012;166(5):1069–80. https://doi.org/10.1111/j.1365-2133.2012.10830.x.
4. Miller DL, Weinstock MA. Nonmelanoma skin cancer in the United States: incidence. J Am Acad Dermatol. 1994;30(5 Pt 1):774–8.
5. Alam M, Ratner D. Cutaneous squamous-cell carcinoma. N Engl J Med. 2001;344(13):975–83. https://doi.org/10.1056/NEJM200103293441306.
6. Chren MM, Sahay AP, Bertenthal DS, Sen S, Landefeld CS. Quality-of-life outcomes of treatments for cutaneous basal cell carcinoma and squamous cell carcinoma. J Investig Dermatol. 2007;127(6):1351–7. https://doi.org/10.1038/sj.jid.5700740.
7. Rowe DE, Carroll RJ, Day CL Jr. Long-term recurrence rates in previously untreated (primary) basal cell carcinoma: implications for patient follow-up. J Dermatol Surg Oncol. 1989;15(3):315–28.
8. Mohs FE. Microscopically guided excision of cancer of the skin by means of chemosurgery. J Ark Med Soc. 1968;65(6):203–9.
9. Swanson NA. Mohs surgery. Technique, indications, applications, and the future. Arch Dermatol. 1983;119(9):761–73.
10. Shriner DL, McCoy DK, Goldberg DJ, Wagner RF Jr. Mohs micrographic surgery. J Am Acad Dermatol. 1998;39(1):79–97.
11. Rowe DE, Carroll RJ, Day CL Jr. Mohs surgery is the treatment of choice for recurrent (previously treated) basal cell carcinoma. J Dermatol Surg Oncol. 1989;15(4):424–31.
12. Ad Hoc Task F, Connolly SM, Baker DR, Coldiron BM, Fazio MJ, Storrs PA, et al. AAD/ACMS/ASDSA/ASMS 2012 appropriate use criteria for Mohs micrographic surgery: a report of the American Academy of Dermatology, American College of Mohs Surgery, American Society for Dermatologic Surgery Association, and the American Society for Mohs Surgery. J Am Acad Dermatol. 2012;67(4):531–50. https://doi.org/10.1016/j.jaad.2012.06.009.
13.• van Loo E, Mosterd K, Krekels GA, Roozeboom MH, Ostertag JU, Dirksen CD, et al. Surgical excision versus Mohs' micrographic surgery for basal cell carcinoma of the face: a randomised clinical trial with 10 year follow-up. Eur J Cancer. 2014;50(17):3011–20. https://doi.org/10.1016/j.ejca.2014.08.018. **This was the first randomized controlled trial evaluating Mohs versus standard excision which demonstrated a significantly lower recurrence rate for high-risk facial basal cell carcinoma treated with Mohs micrographic surgery compared to standard excision after a 10-year follow-up period.**
14. Muller FM, Dawe RS, Moseley H, Fleming CJ. Randomized comparison of Mohs micrographic surgery and surgical excision for small nodular basal cell carcinoma: tissue-sparing outcome. Dermatol Surg. 2009;35(9):1349–54. https://doi.org/10.1111/j.1524-4725.2009.01240.x.
15. Smeets NW, Krekels GA, Ostertag JU, Essers BA, Dirksen CD, Nieman FH, et al. Surgical excision vs Mohs' micrographic surgery for basal-cell carcinoma of the face: randomised controlled trial. Lancet. 2004;364(9447):1766–72. https://doi.org/10.1016/S0140-6736(04)17399-6.
16. NCCN Clinical Practice Guidelines in Oncology: Basal Cell Skin Cancer. Version I.2018.
17. Mora RG, Robins P. Basal-cell carcinomas in the center of the face: special diagnostic, prognostic, and therapeutic considerations. J Dermatol Surg Oncol. 1978;4(4):315–21.
18. NCCN Clinical Practice Guidelines in Oncology: Squamous Cell Skin Cancer. Version 2. 2018.
19. Ebede TL, Lee EH, Dusza SW, Busam KJ, Nehal KS. Clinical value of paraffin sections in association with Mohs micrographic surgery for nonmelanoma skin cancers. Dermatol Surg. 2012;38(10):1631–8. https://doi.org/10.1111/j.1524-4725.2012.02570.x.