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Abstract
Mohs micrographic surgery (MMS) is used to obtain clear margins in skin cancer treatment. MMS involves staged excisions and complete margin assessment of the specimen from fresh tissue frozen sectioning. It has been shown to achieve higher cure rates with malignancies, including basal cell carcinoma (BCC), squamous cell carcinoma (SCC), lentigo maligna, melanoma in situ and dermatofibrosarcoma protuberans. This technique is especially useful in face, feet and hand regions to avoid cosmetic deformities.

Keywords: basal cell carcinoma, squamous cell carcinoma, Mohs, skin cancer, Mohs surgery

1. Introduction
Mohs micrographic surgery (MMS) is a method used by physicians to obtain clear margins in the treatment of skin tumors. It was first described by a general surgeon, Frederick Edwards Mohs [1, 2]. Originally, this technique involved the application of zinc chloride paste to the excised tissue for overnight. The technique was later modified with the introduction of fresh tissue-frozen technique and the elimination of zinc chloride fixation [3].

MMS is characterized by complete evaluation of all tumor margins. It has been proven beneficial for various types of skin malignancies including basal cell carcinoma (BCC), squamous cell carcinoma (SCC), lentigo maligna (LM) and melanoma in situ (MIS). This technique is especially useful in face, feet and hand regions to avoid wide excision, which may not be required for tumor control [4].

2. Indications
Recurrent tumors, tumors in the “h-zone” (central face, eyelids, eyebrows, nose, lips, chin, ear, hand, genitalia, feet, nail units, ankles and nipples/areola), tumors with more than 2 cm diameter
and tumors with aggressive histopathologic findings are candidates for MMS. In 2012, appropriate use criteria have been established by American Academy of Dermatology (AAD) and other collaborating organizations [5]. According to these criteria, all BCC, SCC, LM and MIS located in the “h-zone” and the “m-zone” (cheeks, forehead, scalp, neck, jawline and pretibial surface) are appropriate for MMS except focal in situ SCCs with actinic keratosis and superficial BCC with less than 0.5 cm diameter located in the “m-zone.” In the “L-zone” (trunk and extremities), only aggressive, recurrent or large tumors meeting certain criteria are considered suitable for MMS.

2.1. Basal cell carcinomas (BCC)

Recurrent BCC have been shown to have subclinical extension which might not be possible to identify during conventional excision. MMS has been reported to achieve better cure rates with these cases. It has been reported by Hoorens et al. that tumor with an area more than 1 cm², aggressive histology and patient age more than 80 are strong indications of MMS for BCC [6]. This aggressive biological behavior is characterized by sclerodermiform, infiltrative, micronodular or basosquamous histology. MMS technique for these tumors can achieve higher cure rates when compared to standard excision [7].

2.2. Squamous cell carcinoma (SCC)

MMS can achieve better cure rates for SCC when compared to conventional surgery. Lower recurrence rates have been reported in SCC cases over 5-year follow-up periods with MMS. MMS has been shown to provide better margin control in cases with larger than 2 cm diameter, poor differentiation and perineural invasion in which tumors are frequently known to extend beyond their macroscopic margins. [8].

2.3. Melanoma in situ and lentigo maligna

The role MMS in the management of invasive melanoma is controversial since it is difficult to identify the atypical melanocytes in frozen section. On the other hand, successful treatment of melanoma in situ (MIS) has been reported with MMS. The current standard in the MIS is wide local excision (WLE) with 0.5–1 cm margin. In a recent study by Nosrati et al., 277 patients treated with MMS and 385 patients treated with WLE were compared. No significant difference between the recurrence rate and melanoma-specific survival of the patients was found. This study is especially valuable since prior studies did not involve any direct comparison of these techniques [9]. The comparison of cosmetic and functional results of MMS compared to WLE is still not clearly understood. Further studies are needed in this regard.

Lentigo maligna (LM) is considered as a type of melanoma in situ. MMS that has been reported achieves similar cure rates compared to WLE in LM cases [10].

2.4. Other tumors

Dermatofibrosarcoma protuberosans (DFSP): The very high risk of recurrence associated with wide local excision has encouraged the use of MMS with DFSP. In spite of the absence of randomized controlled studies to compare MMS with WLE in DFSP, low recurrence rates associated with
MMS have been reported [11]. MMS can identify the subclinical extension of the tumor much better than the conventional WLE. It has been reported in a study that DFSP requires the highest number of Mohs stages when compared to other rare cutaneous tumors treated with MMS [12].

Eccrine porocarcinoma (EPC): There are no large studies comparing WLE with MMS in EPC. Although it has been suggested by some authors that MMS outcomes could be better than WLE, many surgeons prefer to treat EPC with WLE [13–15].

Microcystic adnexal carcinoma (MAC): Recurrence rates of up to 50% have been reported with WLE. Recurrence rates with MMS have been reported from 0 to 22% [16]. One important aspect of MAC is that paraffin embedding with horizontal sectioning is usually preferred instead of frozen sectioning since it is easier to interpret. This process is also called “slow Mohs.”

Merkel cell carcinoma: Kline and Coldiron have reported in a recent study that the MMS results are at least comparable to WLE. They have reported 5% recurrence rate as opposed to 32–50% recurrence rate with WLE [17].

Sebaceous carcinoma: Brady and Hurst have shown that MMS has been shown to be associated with lower recurrence and metastatic rates when compared to WLE [18].

Angiomyxoma: Despite its benign pathological features, high recurrence rates up to 40% have been reported with conventional surgery. MMS has been reported to decrease the recurrence rate significantly. But it has been argued in a paper that the pathological features of angiomyxoma might be hard to detect with a frozen section [19].

Lymphoepithelioma, trichilemmal carcinoma, spiradenocarcinoma, nerve sheath myxoma, cutaneous angiosarcoma, granular cell tumor, atypical fibroxanthoma and extramammary Paget’s disease are among other skin tumors which have been treated with MMS.

3. Technique and principles

Conventional MMS begins with the removal of the tumor with a small free margin usually between 1 and 2 mm depending on the tumor location as opposed to standard excision of skin cancers, in which at least 5 mm of margin is preferred. The lateral borders are excised at a 45° angle to allow for flattening of the lateral borders of the specimen. Complete circumferential peripheral and deep margin assessment (CCPDM) is performed following the excision. This technique provides the complete evaluation of all tumor margins as opposed to traditional margin assessment. Following mapping of the excised tissue lateral borders are delineated with a “mashing the pie pan” technique and are positioned at the same horizontal level as the deep margin (Figures 1 and 2). The purpose of this technique is to flatten the lateral margins at the same horizontal plane as the deep margin. Afterwards, tissue is embedded in OCT compound in cryostat to obtain horizontal–tangential sections from the deep margin, which also contains the lateral borders after the flattening, instead of conventional vertical sections. Following the staining with hematoxylin and eosin (H&E) or toluidine blue, slides are interpreted under microscopy. Consecutive re-excisions are performed until a clear surgical margin is achieved (Figure 3). The final step of MMS involves the reconstruction of the final defect which most frequently involves primary closure, local flaps and skin grafts [4].
4. Outcomes and complications

There is a considerable amount of variations in the reported cure rates for MMS among different surgeons. Misinterpretation of the pathological slides, misoriented tissue margins, freezing
artifacts, poor staining, difficulty of defining atypical cells in the presence of inflammation and scar tissues, inadequate amount of sectioning and problems with flattening the resected tissues are among the reasons for less than ideal outcomes of MMS. All of these can be related to poor training of the physicians and the technicians. Certain pitfalls can be encountered during interpretation of frozen sections. These include adnexal structures which are mistaken for BCC, sun-damaged skin resembling lentigo maligna and pseudocarcinomatous hyperplasia mistaken for SCC [20, 21].

Complications such as tumor recurrence, hematoma, infection, cosmetic and functional deformities can be seen following MMS. Lips, nasal region and eyelids are among the most common sites for cosmetically poor results after MMS. Plastic surgeons should be consulted for reconstruction in cases where the primary closure of the defect with simple methods is not possible.

5. Conclusion

Mohs surgery is an important technique for the treatment of certain types of skin cancer. It is the modality of choice for high-risk basal cell carcinomas (BCC) and squamous cell carcinomas, particularly for the ones located in the facial region. This method achieves very high cure rates for both primary and recurrent BCC. Surgeons can usually avoid large deformities of the face region with application of this technique. This is an important tool that requires special training in the surgery and the pathology of the skin.
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References


