Simultaneous Intraoperative Mohs Clearance and Reconstruction for Advanced Cutaneous Malignancies

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Background: Improved control of cutaneous malignancies using Mohs micrographic pathologic clearance has been well established. However, surgical margin control of advanced and complex cutaneous tumors of the head and neck is commonly performed by far less reliable frozen section margin analysis.

Objective: To describe a routine and ideal collaboration between dermatologic surgery and facial plastic surgery/head and neck surgery in which the Mohs micrographic method is used intraoperatively to achieve marginal clearance during resection and reconstruction.

Methods: A single-institution retrospective analysis was performed of patients who underwent intraoperative Mohs micrographic surgery. Intraoperative margins (peripheral and deep) of tissue specimens were analyzed by the Mohs surgeon.

Results: Twenty-six patients underwent large cutaneous tumor resection using intraoperative Mohs micrographic surgery. Most lesions were basal (48%) or squamous (34%) cell carcinoma. A mean (SD) of 2.1 (0.98) resection layers were required before negative margins were achieved.

Conclusions: We demonstrate the intraoperative technique and utility of Mohs micrographic analysis via an efficient collaborative effort. Well established for accuracy greater than intraoperative frozen section margin analysis, intraoperative Mohs micrographic surgery provides an optimal method of intraoperative margin assessment of cutaneous malignancies.

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Skin cancer is the most common malignancy in the United States. Most of these are nonmelanoma skin cancer, with basal cell carcinoma (BCC) accounting for 75% and squamous cell carcinoma composing 20%.1 After appropriate diagnosis, treatment of these lesions is typically performed by surgical excision. Mohs micrographic surgery (MMS) and conventional excision with margin assessment by postoperative permanent or intraoperative frozen section histopathologic analysis are the most commonly performed excision techniques.2 Mohs micrographic surgery has demonstrated advantages over other methods of resection by providing improved margin control. Typically, MMS is used in the outpatient setting for small- and medium-sized tumors of the head and neck (<5 cm).3,4 Large or so-called giant tumors (>5 cm), aggressive pathologic features, and involvement of multiple aesthetic units or critical structures may warrant excision in the operating suite using general anesthesia along with extensive reconstructive measures. In these cases, conventional excision is typically performed using gross margin assessment and intraoperative frozen section analysis.3,6 In these situations, MMS is not commonly used despite established increased accuracy in margin assessment and superior tumor control.3,7 Given the limitations of conventional margin clearance, definitive reconstruction of defects is often withheld to observe for recurrence, resulting in additional patient morbidity and psychosocial detriment.

Compared with permanent pathologic analysis, frozen section analysis of the same tissue sample has an accuracy of 72% for assessing BCC.7 Accuracy is further limited by surgeon and pathologist selection error if a complete circumferential resection margin cannot be assessed. An estimated less than 1% of the specimen’s sections are typically assessed by a pathologist.3,4 The MMS technique, in contrast, allows for assessment of 100% of the ex-
cised tumor margin. Thus, MMS leads to more complete tumor clearance and improved cure rates. Established 5-year cure rates are shown to be up to 98.9% for primary and recurrent BCC and squamous cell carcinoma.8-11 As a result, MMS has been established as the criterion standard for excision of higher-risk cutaneous malignancies.12-14 These malignancies include tumors that are recurrent, are located in areas typically at high risk for recurrence (midface, ears, lips, and embryonic fusion planes), are larger than 2 cm, have ill-defined boundaries, or have aggressive pathologic findings.2

To achieve margin clearance greater than that provided by conventional resection techniques in the management of large, complex cutaneous malignancies, we used a novel collaborative approach of intraoperative MMS (IMMS) involving multiple subspecialties at Cleveland Clinic, Cleveland, Ohio (Figure 1). This method allows for optimal oncologic resection and immediate aesthetic and functional reconstruction of complex defects.

**METHODS**

A retrospective analysis was performed of patients between September 1, 2007, and June 1, 2010, who underwent resection of cutaneous head and neck malignancy using IMMS by the collaborative effort of Mohs dermatologic, head and neck, and facial plastic surgeons. The Cleveland Clinic institutional review board approved this study. Demographic details, tumor abnormalities and characteristics, surgical procedures, adjuvant therapies, recurrence, survival, and follow-up data were collected and assessed. Continuous variables are presented as mean (SD).

**OPERATIVE PROCEDURE AND TISSUE ANALYSIS**

General anesthesia was used in all cases, and initial tumor resection margins were jointly planned by the surgical teams. Unlike the traditional MMS technique, resection was performed with the intent of aggressive peripheral and deep margin clearance (ie, “wide-margin Mohs” that is not tissue sparing). This method ideally provides margin clearance in the first 1 or 2 resection layers. Tumor mapping was performed by the Mohs micrographic surgeon, while the ablative surgeon performed the initial resection. Once complete, the specimen was taken to the Mohs histology laboratory, where complete margin analysis was performed using the Mohs technique by a dedicated Mohs team consisting of several technicians and Mohs surgeons. Because the Cleveland Clinic Mohs team has made resource and time accommodations to enable rapid readings, large specimen reads were performed within 1 to 3 hours. Margins of particular concern were identified and read as a high priority to expedite final clearance. Tissues that were assessed by the Mohs technique included skin and deep tissues, muscle, fat, mucosa, cartilage, and periosteum. Major nerve margins (eg, facial nerve) were assessed using frozen section by the surgical pathologist. During margin analysis, additional required extirpative procedures, such as maxillectomy, neck dissection, and parotidectomy, were performed by the head and neck surgeon. Reconstructive efforts, including the raising of local, regional, or free tissue flaps and acquisition of cartilage or bone grafts, were also

**Figure 1.** The Mohs technique compared with frozen section method. A, Margin assessment by permanent and frozen section analysis assesses a small fraction of the tumor margins, leading to significant sampling error, resulting in potentially incomplete tumor resection and a lack of confidence when assessed margins are deemed to be negative. B, Frozen Mohs section analysis can assess the entire peripheral and deep surgical margin, leading to greater certainty of complete tumor resection. IMMS indicates intraoperative Mohs micrographic surgery.
commenced during this period if they were not dependent on the final margins.

Specific areas of positive margins were marked on the micrographic map, and the Mohs surgeon returned to the operating suite to discuss directly these areas needing further resection. Additional serial resection layers with immediate Mohs interpretation were performed in a similar manner until negative margins were achieved. Same-setting complete reconstruction was performed immediately after verifying tumor clearance. The following 3 cases illustrate the method of IMMS.

REPORT OF CASES

Case 1

A 59-year-old woman presented with a multiply recurrent BCC that initially involved the left nasofacial sulcus. The patient was previously treated and had recurrence after multiple excisions and radiotherapy. The extensive recurrence involved the left nasofacial sulcus, nasal ala, dorsum, cheek, and lateral nasal wall mucosal surface (Figure 2). She underwent IMMS necessitating a subtotal rhinectomy, left medial maxillectomy, and left infraorbital nerve excision. One layer was required to obtain negative margins. During margin assessment, a free anterolateral thigh fat/facial flap was harvested, and a cervicofacial flap was elevated. Once margins were confirmed, reconstruction was performed.

Figure 2. Case 1. Wide resection margins are demarcated by the ablative surgeons (A), with intraoperative tumor mapping performed by the Mohs surgeon (B). C, Subtotal rhinectomy, left medial maxillectomy, and left infraorbital nerve excision were performed. D, The harvested anterolateral thigh fascia was used to re-create the nasal lining, and the fat component was used to reconstitute the cheek contour. E, Cervicofacial, paramedian, and nasolabial flaps were used to provide defect skin coverage. F, The patient is without recurrence 2 years after surgery and maintains an optimized cosmetic and functional reconstruction. Adapted from Dermatol Clin. 2011;29(2):319-324.

Case 2

A 53-year-old woman presented with a large recurrent BCC involving the right side of the midface, nasal sidewall, and mucosal surface of the lateral nasal wall (Figure 3). Intraoperative MMS was performed requiring a subtotal rhinectomy, medial maxillectomy, and infraorbital nerve resection for perineural invasion. Four layers were required to clear the tumor from soft tissues. During margin assessment, a cervicofacial flap was elevated, cartilage grafts were harvested, and eyelid reconstruction was performed. After negative margins were obtained from all the resection surfaces, paramedian forehead and septal flaps were used to reconstruct the nose.

Case 3

A 71-year-old woman presented with a large neglected BCC involving the right hemiface (Figure 4). She required an extensive soft-tissue resection, orbital exenteration, subtotal rhinectomy, and partial maxillectomy. The tumor was cleared in 2 layers using IMMS. Although grossly appearing clear of tumor, the first layer was approximately 75% positive, and a further 1-cm circumferential excision was required to obtain clear margins on all edges. Reconstruction was initiated during margin assessment and included a free latissimus dorsi flap with split-thickness skin graft and cervicofacial advancement flap.
RESULTS

Intraoperative MMS was used in 26 patients during the study (Table 1). The mean (SD) patient age was 68.7 (12.2) years. Lesions were most commonly BCC (48%) or squamous cell carcinoma (34%). Intraoperative MMS was used for similar pathologic conditions for which MMS would be indicated. One patient had Gorlin basal cell nevus syndrome, and 4 (15%) had a history of solid organ transplantation. Four patients (15%) had undergone previous radiotherapy. The mean resection area of tumors was large at 60.9 cm². Most malignancies were recurrent (73%), and many displayed perineural invasion (38%). The nose and central face was the most frequently involved anatomical area (41%), followed by the parotid and temple (28%).

Owing to aggressive initial resection, the mean (SD) number of layers required to achieve negative margins was 2.1 (0.98) (Table 2). Tumor clearance was achieved in the first resected layer in 7 cases. A maximum of 5 layers was required in 5 cases. The mean time required for Mohs micrographic margin assessment was 93.9 minutes (range, 25-190 minutes) for the first layer, 54.5 minutes (range, 25-130 minutes) for the second layer, and 41.1 minutes (range, 25-59 minutes) for the third layer. If a fourth or fifth layer was needed, these required a mean of 29.7 and 38.5 minutes, respectively.

In 3 cases (12%), the deep layer of the resection was bone, allowing IMMS assessment of only the peripheral margins. These cases required analysis of bony deep margins by the surgical pathologist.

Immediate reconstruction was performed on all defects, with 8 of 29 lesions (28%) undergoing free flap reconstruction. Three patients (12%) required postoperative radiation therapy. Indications for radiation therapy in these patients were recurrence, regional nodal metastasis, and extensive infraorbital nerve involvement. Mean follow-up was 17.1 months (range, 2.8-40.9 months). Twenty-one patients (81%) remain alive, and 4 (15%) have experienced recurrence. Of the 5 patient deaths, 3 were of unrelated causes and due to other medical comorbidities and 2 were due to recurrent disease. Two recurrences occurred at the orbital apex and cavernous sinus, 1 at the resection margin, and 1 patient developed nodal metastasis.

COMMENT

Mohs micrographic surgery is a well-established and preferred technique for excising cutaneous lesions, particularly BCC and squamous cell carcinoma, and is associated with high cure rates. Recent literature has shown the absolute accuracy of frozen section analysis in recurrent or facial cutaneous BCC to be as low as 72%. This
difference highlights the important role that MMS may play in the operating room. Typically, MMS is performed on small- and medium-sized tumors in the outpatient setting under local anesthetic. The Mohs micrographic surgeon serially removes and assesses margin layers until a completely negative margin is reached. Because the entire peripheral and deep margin is histopathologically assessed, the potential for complete tumor removal is higher than with traditional excision methods, where only a small fraction of the margin may be examined. Transferring MMS to the operating suite for resection of large cutaneous tumors provides for more reliable margin clearance and, thus, may improve oncologic outcomes. In addition, increased confidence in margin control allows for simultaneous reconstruction without the need for long-term defect monitoring for local recurrence.

The use of IMMS for large head and neck cutaneous neoplasms using general anesthesia was first described by Levine et al15 at Cleveland Clinic in 1979. Soon thereafter in the 1980s, Baker et al16,17 similarly reported a small case series using this advantageous combined-modality approach. These initial studies demonstrated the utility of IMMS. A recent publication by Ducic et al18 demonstrates use of a “ring of Mohs” to assess the circumferential (but not deep) tissues by MMS.

To our knowledge, no studies have demonstrated regular use of this technique for advanced cutaneous malignancies. Despite the established advantages of Mohs clearance, the potential for prolonged operative time due to large specimen reads and the requirement for additional personnel and resource coordination have likely hindered the development and acceptance of IMMS. We demonstrate that these limitations can be overcome with an organized and routine collaborative approach to IMMS.

With dedicated efforts and resources, the Mohs micrographic surgeon can quickly read margins and direct further margin resection as needed to optimize complete resection. In this study, the mean read times for the first and second resection layers were 93.9 and 54.5 minutes, respectively. During this time, the facial plastic/head and neck surgeon can perform additional required extirpation, such as neck dissection, parotidectomy, and maxillectomy, or initiate reconstructive efforts.

In the authors’ experience, there are minimal or no intraoperative delays or case time prolongation due to pending Mohs histopathologic assessment. This is mainly due to 2 factors. First, appropriate advanced tumors are selected for this method. These tumors are not amenable to resection under local anesthetic, and they often require complex reconstruction or ancillary extirpative procedures, which are performed during ongoing margin interpretation. Second, a dedicated and highly efficient Mohs dermatologic team is used. Typically, 2 technical teams are reserved to allow for rapid tissue processing and assessment.

Figure 4. Case 3. A and B, A large neglected basal cell carcinoma involving the right upper hemiface. C, The patient required an extensive soft-tissue resection, orbital exenteration, subtotal rhinectomy, and partial maxillectomy. D-F, Reconstruction was performed after intraoperative Mohs micrographic surgery revealed full soft-tissue tumor clearance. A free latissimus myogenous flap with a split-thickness skin graft and a cervicofacial advancement flap were used. Adapted from Dermatol Clin. 2011;29(2):319-324.
In this series, cutaneous malignancies that were treated using IMMS were large (mean, 60.9 cm²) and most often involved the central face/nose (41%) and temple/parotid (28%). These lesions were also often recurrent (73%) and involved nerve (38%). Reconstructive efforts were undertaken in 100% of patients in the same setting as resection, with 28% of patients undergoing free tissue transfer.

In many intraoperative instances, Mohs micrographic evaluation revealed positive margins in areas that were not clinically suspected to have residual disease. If frozen section assessment had been used instead of IMMS, these areas may not have been sampled or adequately assessed by either the surgeon or the pathologist, creating a false-negative sampling error.

Because follow-up in this study was relatively short, only limited conclusions can be made regarding recurrence and survival. However, the Mohs micrographic technique is the best possible method of nonmelanoma skin cancer tumor clearance, and a complete resection may decrease the high recurrence rates inherent to large nonmelanoma skin cancer. Of the 4 recurrences in this series, only 1 occurred locally at the resection margins; the remaining occurred regionally in the neck or at the orbital apex and cavernous sinus, presumably via perineural tracking.

Postoperative radiation therapy was used in only 3 patients (12%), which is considerably low given the extent of these large, aggressive lesions. In our experience, before initiating IMMS, many indications for postoperative irradiation in this patient population were for positive margins (reversed from frozen section assessment) or “close” margins on final pathologic analysis. Using IMMS, improved effectiveness of and confidence in margin clearance has led to less frequent requirements for adjunctive radiation therapy.

A limitation of this study is its short follow-up. However, preliminary findings are promising that this technique is beneficial. This method is feasible, may improve patient care and outcomes, and is easily adoptable into practice by collaborative efforts at most institutions.

In conclusion, in the management of cutaneous malignancies, Mohs margin assessment has clearly established advantages over traditional frozen or permanent section pathologic reads. We described a routine collaborative approach that allows for the use of this technique for tumor clearance of advanced malignancies that necessitate resection under general anesthesia. This method may provide improved tumor control and optimal coordination of cancer extirpation and reconstruction.

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REFERENCES