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Mohs Micrographic Surgery – what the gold standard in dermatologic surgery offers us
A Literature Review

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ABSTRACT

Introduction andobjective:

Micrographic Mohs surgery, a highly precise surgical technique, has long been regarded as a cornerstone in dermatology for the treatment of various skin cancers. This review aims to comprehensively summarize the current understanding of the principles and clinical applications of Mohs surgery, with a specific focus on providing insights to clinicians and researchers.

State of Knowledge:
Mohs surgery is particularly renowned for its unparalleled efficacy in treating basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and other skin malignancies, especially in anatomically challenging areas. The technique involves meticulous removal of cancerous tissue layers while sparing healthy surrounding tissue, facilitated by microscopic examination of surgical margins. Recent advancements in Mohs surgery have led to improved outcomes, with techniques such as immunostaining enhancing the accuracy of tumor detection and minimizing the need for additional surgeries.

Materials and methods:
This review of studies is based on scientific articles avaible in PubMed, Google Scholar databases and Elsevier.

Summary:
Micrographic Mohs surgery remains a cornerstone of dermatologic oncology, offering unparalleled precision and cure rates for various skin cancers. Its success lies in its ability to achieve complete tumor removal while preserving maximal tissue integrity and cosmesis. Future research endeavors should focus on refining surgical techniques, optimizing patient selection criteria, and exploring adjunctive therapies to further improve outcomes and patient satisfaction. By advancing our understanding and application of Mohs surgery, we can continue to provide optimal care for patients with skin cancer, ultimately improving their quality of life and prognosis.

Keywords: mohs micrographic surgery; basal cell carcinoma; dermatosurgery; cancer

Introduction

Dermatosurgery is an interdisciplinary field of dermatology focused on the surgical treatment of various skin diseases. Over the past few decades, it has significantly advanced both technologically and procedurally. Modern dermatosurgery encompasses a wide range of procedures, from simple removal of skin lesions to advanced reconstructive techniques. In this review, we will examine the role of dermatosurgery in treating different skin conditions, highlighting the latest techniques, their applications, and future development prospects. This analysis will provide a better understanding of the role of dermatosurgery in modern medicine and its impact on improving patients' quality of life. In the following work, I will present the most important technique in dermatosurgery – Mohs micrographic surgery. [1]

History

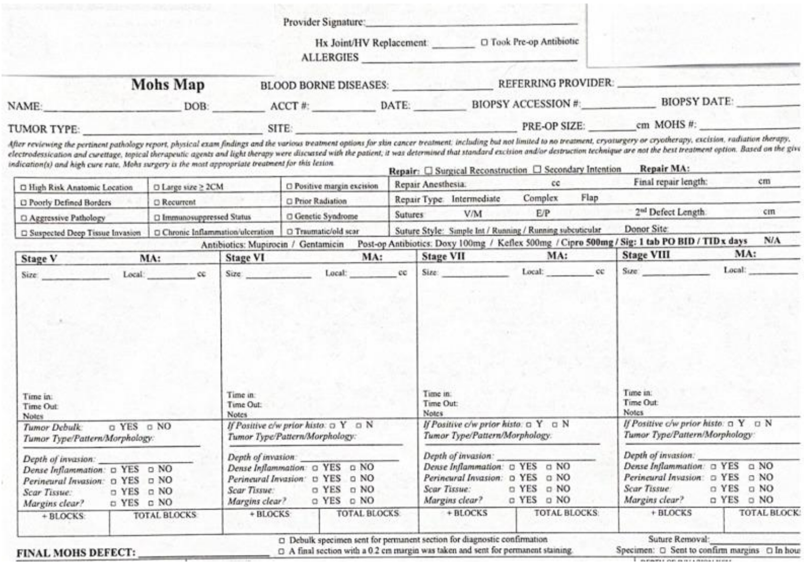
The excision technique is named after its pioneer, Dr. Frederic E. Mohs, who lived from 1910 to 2002. As a medical student, Mohs studied the effects of lymphocyte infiltration on tumor development. During these studies, he accidentally applied zinc chloride therapy and discovered that injecting it into tissue led to its histological fixation, allowing for detailed

cytological examination under a microscope [2]. In 1932, he used this substance to coagulate basal cell carcinoma and squamous cell carcinoma tissue.
He then removed the necrotic tissue. This process was repeated in horizontal layers until a layer without malignant tissue was obtained in the histopathological image.
Each layer took one day because the paste needed time to bind the tissue before removal. Patients with large tumors, requiring the removal of multiple layers, had to return for treatment daily, often for several days. The applied paste caused pain, local inflammation, as well as fever and lymph node enlargement [3,4].

Procedure description

Tumor removal layer by layer and meticulous examination of the undersurface of each layer under the microscope through systematic use of frozen sections ensures complete elimination of the tumor, including its "hidden" extensions, while simultaneously maximizing preservation of healthy tissue. Mohs micrographic surgery on fresh tissue is typically employed for most tumors, but for melanomas, a safer technique using fixed tissue is preferable, as all incisions are made in fixed (dead) tissue. This avoids the risk of dissemination of highly transplantable melanoma cells that could be cut through due to clinically invisible extensions [5].

1. First, the area containing the tumor is accurately marked, followed by local anesthesia administration—usually buffered lidocaine with epinephrine. After anesthesia, visible portions of the tumor are removed using selected surgical tools such as a scalpel or a curette.
2. Subsequently, margins of the first stage are removed, with the blade set at a 45-degree angle to the skin. This allows for proper alignment of the outer edges of the tissue sample during preparation for histopathological examination. During the excision of the first layer, markings are made at the 12, 3, and 6 o'clock positions to facilitate further orientation and locating any remaining tumor (if observed during microscopic examination). After removal, the tissue is divided into smaller fragments and marked to precisely determine the tumor's location.



Provider Signature: ________
Hx Joint/HV Replacement: ____ ☐ Took Pre-op Antibiotic
ALLERGIES ________

Mohs Map BLOOD BORNE DISEASES: ____ REFERRING PROVIDER: ____

NAME: ____ DOB: ____ ACCT #: ____ DATE: ____ BIOPSY ACCESSION #: ____ BIOPSY DATE: ____

TUMOR TYPE: ____ SITE: ____ PRE-OP SIZE: ____ cm MOHS #: ____

After reviewing the pertinent pathology report, physical exam findings and the various treatment options for skin cancer treatment: including but not limited to no treatment, cryosurgery or cryotherapy, excision, radiation therapy, electrodessication and curettage, topical therapeutic agents and light therapy were discussed with the patient; it was determined that standard excision and/or destruction technique are not the best treatment option. Based on the give indication(s) and high cure rate, Mohs surgery is the most appropriate treatment for this lesion.

Repair: ☐ Surgical Reconstruction ☐ Secondary Intention **Repair MA:**

☐ High Risk Anatomic Location	☐ Large size ≥ 2CM	☐ Positive margin excision	Repair Anesthesia: cc Final repair length: cm
☐ Poorly Defined Borders	☐ Recurrent	☐ Prior Radiation	Repair Type: Intermediate Complex Flap
☐ Aggressive Pathology	☐ Immunosuppressed Status	☐ Genetic Syndrome	Sutures: V/M E/P 2nd Defect Length: cm
☐ Suspected Deep Tissue Invasion	☐ Chronic Inflammation/ulceration	☐ Traumatic/old scar	Suture Style: Simple Int / Running / Running subcuticular Donor Site:

Antibiotics: Mupirocin / Gentamicin Post-op Antibiotics: Doxy 100mg / Keflex 500mg / Cipro **500mg / Sig: 1 tab PO BID / TID x days** N/A

Stage V MA:	**Stage VI** MA:	**Stage VII** MA:	**Stage VIII** MA:
Size: ____ Local: ____ cc	Size: ____ Local: ____ cc	Size: ____ Local: ____ cc	Size: ____ Local: ____
Time in: Time Out: Notes	Time in: Time Out: Notes	Time in: Time Out: Notes	Time in: Time Out: Notes
Tumor Debulk: ☐ YES ☐ NO	*If Positive c/w prior histo:* ☐ Y ☐ N	*If Positive c/w prior histo:* ☐ Y ☐ N	*If Positive c/w prior histo:* ☐ Y ☐ N
Tumor Type/Pattern/Morphology:	*Tumor Type/Pattern/Morphology:*	*Tumor Type/Pattern/Morphology:*	*Tumor Type/Pattern/Morphology:*
Depth of invasion:	*Depth of invasion:*	*Depth of invasion:*	*Depth of invasion:*
Dense Inflammation: ☐ YES ☐ NO	*Dense Inflammation:* ☐ YES ☐ NO	*Dense Inflammation:* ☐ YES ☐ NO	*Dense Inflammation:* ☐ YES ☐ NO
Perineural Invasion: ☐ YES ☐ NO	*Perineural Invasion:* ☐ YES ☐ NO	*Perineural Invasion:* ☐ YES ☐ NO	*Perineural Invasion:* ☐ YES ☐ NO
Scar Tissue: ☐ YES ☐ NO	*Scar Tissue:* ☐ YES ☐ NO	*Scar Tissue:* ☐ YES ☐ NO	*Scar Tissue:* ☐ YES ☐ NO
Margins clear? ☐ YES ☐ NO	*Margins clear?* ☐ YES ☐ NO	*Margins clear?* ☐ YES ☐ NO	*Margins clear?* ☐ YES ☐ NO
+ BLOCKS: TOTAL BLOCKS:	+ BLOCKS: TOTAL BLOCKS:	+ BLOCKS TOTAL BLOCKS:	+ BLOCKS TOTAL BLOCK:

FINAL MOHS DEFECT: ____
☐ Debulk specimen sent for permanent section for diagnostic confirmation
☐ A final section with a 0.2 cm margin was taken and sent for permanent staining.
Suture Removal: ____
Specimen: ☐ Sent to confirm margins ☐ In hou

Figure 1. Blank Mohs Map [6]

3. The initial step in processing the tissue involves flattening the surgical specimen so that the beveled peripheral edges are aligned in the same plane as the deep margin.
4. The tissue is flattened, facilitating its examination under the microscope, where staining is used to assess the presence of tumor cells.
5. If residual tumor cells are noticed under the microscope, indicating that the surgeon did not remove the entire tumor, the Mohs micrographic surgery process continues. Another tissue sample is taken from the area where these tumor cells were found. A new tissue margin, usually 1–2 mm wide, is excised around this area and meticulously marked for microscopic purposes. If the tumor is found only in deeper tissue layers, the surgeon may proceed with another stage only in that area, without enlarging the width of the surgical defect.
6. After completely removing the tumor, the Mohs surgeon prepares to reconstruct the surgical defect. Various methods are employed to close both simple and more intricate skin defects, including complex linear closures, skin flap techniques, and skin grafts. Factors such as the location of the anatomical defect, the depth of the wound, the availability of nearby skin, and neighboring anatomical structures are considered when planning how to repair the defect, as these factors influence both function and appearance. In some cases, treatment may require more than one stage for more complex cases [7].

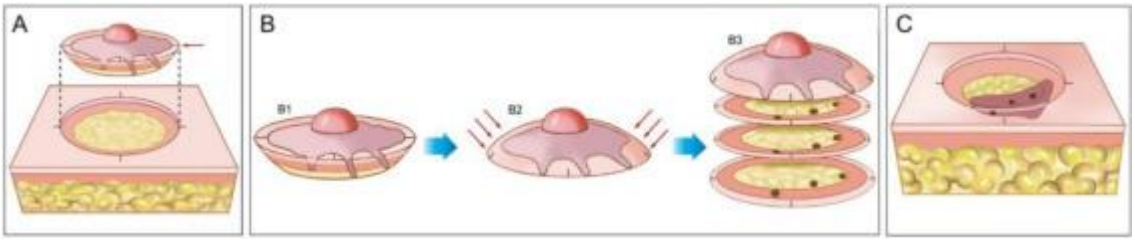


Figure 2. Mohs micrographic surgery. A Demarcation of the visible tumor and excision with a 1–2 mm margin. The incision is made with the scalpel angled at 45 degrees, allowing for the flattening of surgical margins on the same plane. (B), (1) Surgical specimen. The surgical margins to be examined correspond to all lateral and deep external areas of the fragment. (2) The red arrows indicate the "flattening" of the margins to the same plane. (3) After the fragment is frozen in the cryostat, "horizontal" histological sections are performed, allowing for the analysis of 100% of the lateral and deep margins. The three dark spots correspond to the "roots" of the tumor seen on microscopic examination. (C), The remaining tumor "roots" are excised for further analysis under the microscope. [5]

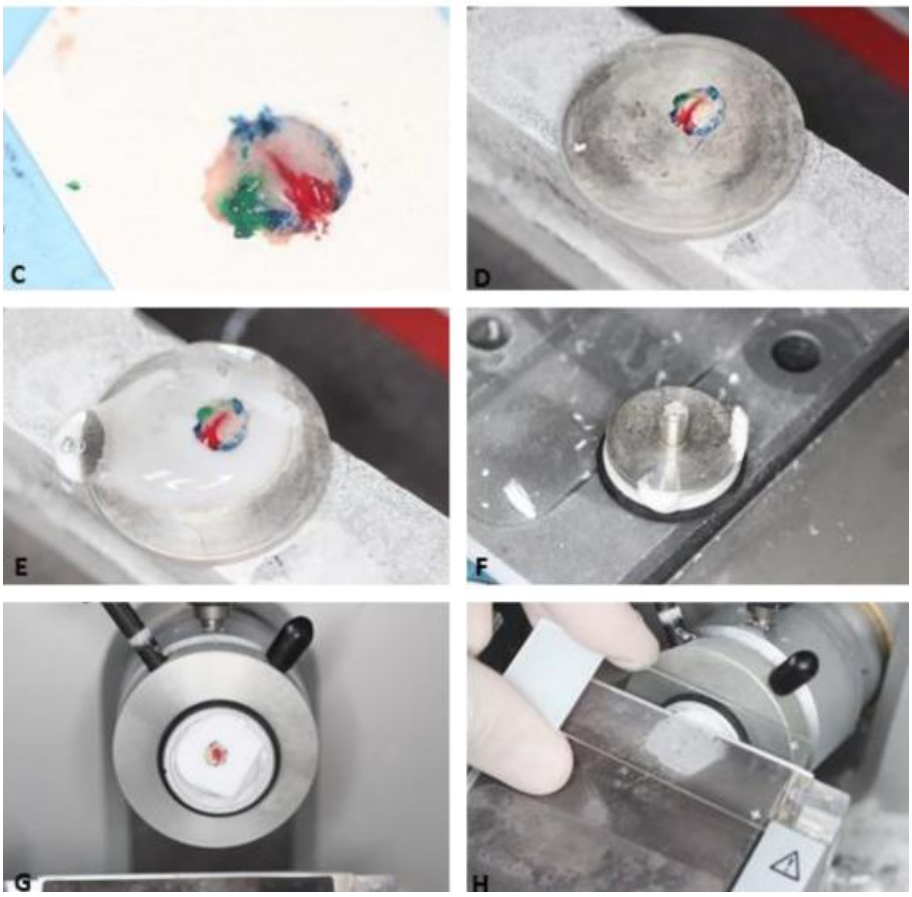


Figure 3: Flattening, Staining, and Sectioning Before Histopathological Evaluation of the Excised Layer. [5]

The most commonly used tissue stains in Mohs surgery are hematoxylin and eosin (H&E) and toluidine blue. Although most Mohs surgeons routinely use H&E, a significant number of specialists prefer toluidine blue for processing basal cell carcinoma (BCC) because the mucopolysaccharides and hyaluronic acid associated with BCC stain metachromatically to a magenta color. [8,9,10].

INDICATIONS FOR MOHS SURGERY

Mohs micrographic surgery (MMS) is employed in cases of skin tumors with a high risk where standard excision does not provide a complete determination of tumor margins and does not guarantee the total removal of the tumor lesion [2]. Increasing evidence suggests its efficacy in treating both primary and recurrent basal cell carcinoma and squamous cell carcinoma, especially in cases with nerve involvement [5]. Additionally, it allows for the treatment of Bowen's disease, melanoma, verrucous carcinoma, cuniculatum carcinoma, and benign tumors like onychomatricoma and glomus tumor [11,12,13]. This method is also particularly effective in the therapy of fibrosarcomatous dermatofibrosarcoma protuberans, especially in high-risk areas such as the head and neck, where wide local excision may be difficult to perform [4]. The Mohs technique is especially suitable for high-risk skin tumors prone to recurrence and in cases where preserving the maximum amount of healthy tissue is essential.

To assist clinicians in determining whether a particular tumor should be treated with this method, guidelines have been developed regarding the appropriate use criteria (AUC) for Mohs surgery. They are based on body location, patient characteristics, and tumor characteristics. [14,15,16].

Body areas within the "H" zone, such as:

- Central part of the face, eyelids, corners of the eyes, eyebrows, nose, lips, chin, ears, and perioral areas.
- Genitalia.
- Hands, feet, ankles, nail units.
- Breasts and areolae.

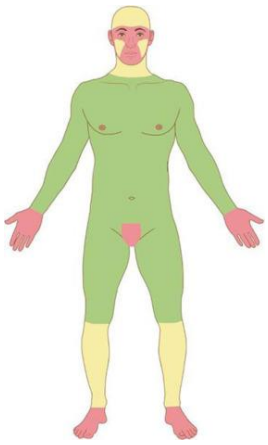


Figure 4. Illustrates anatomic risk areas. Red: High-risk areas. [3]

Characteristics of patients at increased risk include:

- Decreased immunity.
- Genetic syndromes (such as basal cell nevus syndrome and xeroderma pigmentosum).
- Skin previously exposed to radiation.
- Patients with a history of high-risk tumors.

Characteristics of tumors include:

- Positive margins after recent excision.

Aggressive features posing a high risk of basal cell carcinoma (BCC) recurrence:

- Aggressive histologic subtype (morpheaform, infiltrative, micronodular).
- Perineural involvement.
- Metatypical or keratotic.

Aggressive features of squamous cell carcinoma (SCC) include:

- Poorly or undifferentiated tumor (characterized by high nuclear pleomorphism, high mitotic rate, or low keratinization).
- Perineural or perivascular involvement.
- Presence of spindle cells.
- Breslow depth of 2 mm or more.
- Clark level IV or higher. [14,15,16]

Advantages of using mohs technique

Mohs micrographic surgery (MMS) stands out for its exceptionally high efficacy in treating skin cancers. Additionally, due to minimal removal of healthy tissue, it ensures excellent cosmetic outcomes. [17] The five-year recurrence rates following various treatment methods are as follows: Mohs micrographic surgery - 1.0%, surgical excision - 10.1%, curettage and electrodesiccation - 7.7%, radiation therapy - 8.7%, and cryosurgery - 7.5%. [18] This difference in local recurrence rates in favor of Mohs micrographic surgery applies to primary SCC of the skin and lips (3.1% compared to 10.9%), SCC of the ear (5.3% compared to 18.7%), locally recurrent (previously treated) SCC (10% vs 23.3%), SCC involving the perineum (0% vs 47%), SCC larger than 2 cm (25.2% vs 41.7%), and poorly differentiated SCC (32.6% vs 53.6%). [18]

The preservation of healthy tissue has always been a focus of skin cancer surgery. Numerous studies have demonstrated that Mohs micrographic surgery (MMS) conserves tissue compared to standard excision. A recent study on infiltrative basal cell carcinomas (BCCs) found that MMS preserved 46% more healthy tissue than standard surgery. [21] Another study showed significant preservation of healthy tissue (56–86%) for facial BCCs near free margins compared to recommended standard excision margins. [22] Similarly, Gniadecki et al. demonstrated that MMS resulted in 43% and 45% smaller defects compared to standard excision for primary BCCs (4 mm margins) and high-risk recurrent BCCs (6 mm margins), respectively. [23]

In a further study, a retrospective cohort study was conducted to assess the risk of local recurrence and progression in 614 patients with invasive or in situ melanoma who underwent Mohs micrographic surgery (MMS). Local recurrence was observed in 0.34% of cases (2 out of 597 lesions), with a mean observation time of 1026 days (2.8 years). An increase in the degree of advancement was also noted in 34 cases out of 614 lesions (5.5% of all cases), with 97% of these changes (33 out of 34) being detected by the Mohs surgeon before reconstruction. [24]

Clinical data of patients diagnosed between September 2014 and March 2017 at the Dermatology Department of Policlinico Sant'Orsola-Malpighi University of Bologna were retrospectively evaluated. Among 285 patients treated with Mohs micrographic surgery (MMS), disease recurrence occurred in 9 cases (3.1%). In contrast, among 378 patients treated with traditional surgical methods, 53 experienced disease recurrence (14%). In 13 of these patients, residual tumor was found at the deep or lateral margins of the main surgical specimen. [25]

Complement to treatment

In today's era, we can perform lesion excision procedures with even greater precision thanks to advancements in technologies such as Reflectance Confocal Microscopy (RCM), Optical Coherence Tomography (OCT), High-Frequency and High-Resolution Ultrasound (HFHRUS), and Raman Spectroscopy (RS). These technologies promise to enhance diagnostic accuracy and provide real-time visualization of excised tissue, thereby improving tumor margin assessment. [26]. Additionally, we can utilize skin bioprinting, a transformative

technology used to fabricate biomimetic scaffold architectures mimicking human skin. This allows for achieving even better visual outcomes. [27]
In comparison to other surgical methods with postoperative repair, Mohs micrographic surgery costs about the same as simple excision done in the office, with permanent section postoperative margin control. It's also less costly than excisions with intraoperative margin control using frozen sections, whether performed in a private office or an outpatient surgical facility. [28] The potential synergy of artificial intelligence with these innovations could revolutionize the detection of skin cancers and improve the effectiveness of skin cancer treatment. [26]

Complications

Although Mohs micrographic surgery is considered the gold standard in dermatologic surgery, it has its drawbacks. Some of these complications stem directly from the method itself, while others are due to the medical procedures commonly used in such treatments. The first complication is contact dermatitis, which can be caused by disinfectants, latex gloves, adhesives in dressings, or sutures [29]. Another potential issue is the toxicity from anesthetic overdose, vasovagal syncope, and reactions to epinephrine [30]. Bleeding and hematoma formation are complications that can often be managed by discontinuing anticoagulant medications in the patient. If the patient is not on such medications and bleeding occurs, we use local hemostatic agents, electrosurgery, thermal cauterization, or manual pressure [31]. When blood flow to the tissue is impaired, necrosis may appear on the edges of the sutured skin. This is a possible consequence of using the MMS technique in wounds that are closed primarily, with skin flaps, or grafts [32]. There is no concrete evidence that postoperative antibiotics prevent infections [33]. However, non-primary wound closures may require antibiotic prophylaxis [34]. Additionally, there may be suture dehiscence and the separation of wound edges. If the edges are fresh and uninfected, re-suturing can be considered [35]. One of the most intriguing complications can be the interactions with implantable electronic devices (IEDs). These interactions arise from the use of electrosurgery and electrocautery to achieve hemostasis. Currently, modern implantable electronic devices generally pose a low risk of electromagnetic interference during electrosurgery. Nevertheless, it is advisable to minimize this risk. Instead of traditional electrosurgery, the use of electrocoagulation or bipolar electrosurgery is preferred to assist with hemostasis during MMS procedures.

Summary

Mohs micrographic surgery is the most advanced method in dermatologic surgery. It allows for achieving a smaller excision margin, more precise lesion margins, and reduces the risk of malignant lesion recurrence. It enables the removal of tumors from hard-to-reach areas. Recently, with access to reliable immunohistochemical staining, Mohs micrographic surgery has also proven to be highly effective in treating some forms of malignant melanoma, such as lentigo maligna melanoma, superficial spreading melanoma, and thin melanoma. The tissue-sparing properties of Mohs micrographic surgery make it particularly useful in areas of functional and aesthetic significance, such as the head and neck, perianal and genital areas, hands, and feet. With the increasing incidence of non-melanoma skin cancers, as well as

melanomas themselves, the need for innovation and improvements in Mohs technique will continue to grow. At this moment, it remains a pioneer among surgical methods for lesion removal [36].

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