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Mohs Surgery
Is curettage and electrodessication a thing of the past?

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Cutaneous malignancies, especially basal cell carcinomas (BCCs), are common and important aspects of any dermatologic practice. Miller and Weinstock reported that in the United States, between 1977 and 1994, the incidence of BCCs increased from 58% to 194% in men and from 38% to 71% in women, depending on the method of analysis.[1] This clearly represents a significant public health burden and as a result, the general dermatologist must be fully aware of the current and most effective treatments for BCCs. Various modalities are routinely used in the treatment of cutaneous tumours, including local excision, cryotherapy, curettage and electrodessication (C&E), laser therapy, radiation therapy, as well as local and systemic chemotherapy.[2] Newer modalities include immunomodulators (eg, 5% topical imiquimod) and photodynamic therapy. Cure rates for epidermal tumours vary between procedures, with local recurrence always remaining an important concern. In the management of BCCs, C&E may be the most common treatment modality, especially among dermatologists. The low cost, ease of administration, and the ease of learning the technique are cited as being the main advantages.[3] However, in a significant number of cases, C&E fails to remove the entire tumour. Edens et al noted that after 3 cycles of C&E, a residual neoplasm was found in 37% of treated lesions.[4] Similarly, Suhge d'Aubermont and Bennett found persistent tumour in 33.3% of BCC cases treated with C&E.[5] BCCs excised with positive histologic margins may persist and recur in up to 43% of cases during a 5-year follow-up period; this rises to 82% in high-recurrence areas such as the H-zone of the face.[6,7]

Mohs micrographic surgery (MMS) is a microscopically-controlled method of cutaneous neoplasm removal with increased certainty of complete tumour eradication as compared with C&E and surgical excision. This technique has been shown to result in higher definitive cure rates, with maximal sparing of unaffected adjacent tissue. This issue of *Dermatology Rounds* will review MMS and compare its value in the treatment of various skin tumours, particularly BCCs, to other modalities such as C&E and surgical excision.

Historical perspective

In the early 1930s, Frederick E. Mohs, a medical student at the University of Wisconsin, was working in a cancer research laboratory, testing the effect of various irritants on transplantable rat cancers.[2,8,9] He noticed that tissues injected with 20% zinc chloride maintained their histologic features after fixation and could be subsequently examined under the microscope. Mohs then proposed the idea of excising these cancers under microscopic control. Thus, the concept of micrographic chemosurgery was born.

Several years later, after formal training as a general surgeon, Mohs went on to treat patients with cutaneous malignancies. He would apply an *in-situ* fixative paste (containing zinc chloride, a plant extract from *Sanguinaria canadensis* that served as a binder, as well as stibnite that acted as a granular matrix) to cutaneous neoplasms and allowed fixation to take place over 12 to 24 hours. Subsequently, the tissue was surgically excised in a saucer-like configuration and horizontal sections were microscopically examined.[7] A detailed map of the tumour was drawn and cross-compared with the corresponding sites in the surgical wound bed. After

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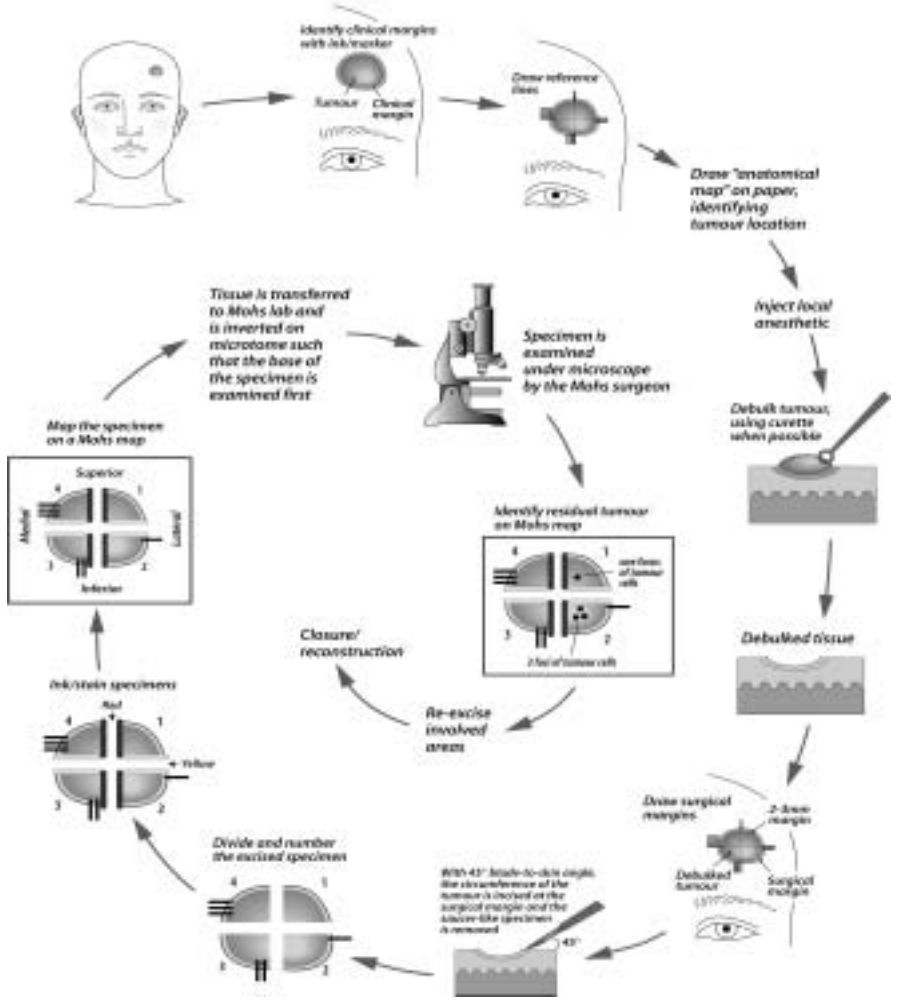
Figure 1: Fresh tissue MMS technique



re-application of the fixative, further serial removal of residual malignant tissue would ensue in accordance to the colour-coded map. The process was repeated until the margins were clear and the entire tumour was removed. Excising the tissue at a 45° blade-to-skin angle and horizontal sectioning allowed for complete histologic examination of the surgical margins.

Initially, Mohs' pioneering concept was not well-accepted by the medical community. The process was extremely labour-intensive and patients complained of pain secondary to the caustic effects of the zinc chloride. As well, local tissue inflammation from the fixation often made it difficult to interpret tumour histopathology and delayed surgical reconstruction and closure of the wound bed. Furthermore, the view that cutting through cancers would promote their metastatic spread via transplantation was largely prevalent and surgeons at the time preferred to use wide surgical margins.

In 1953, Mohs began using the "fresh-tissue technique," simply using local anesthetic and omitting fixation with zinc chloride. Equally high cure rates were reported with this new technique and served to prove that the real reason for the success of the "fresh-tissue" Mohs surgery was not the chemical fixation of the tissue, but the microscopic control. Because of the absence of tissue inflammation and sloughing that were previously observed secondary to zinc chloride application, the reconstruction of the wound bed could now take place on the same day as the excision. Another advantage of fresh-tissue MMS was that patients experienced less pain. Soon, the procedure gained wide acceptance, eventually leading to the establishment of the American Society for Mohs Surgery (ASMS) and fellowships in Mohs Micrographic Surgery through the American College of Mohs Micrographic Surgery and Cutaneous Oncology (ACMMSCO).

Outline of Mohs micrographic surgery

The fresh-tissue technique of MMS is outlined in Figure 1. MMS allows for examination of 100% of the surgical margin, as compared to less than 0.1% examined with standard vertical sections.[9,10] Occasionally, inflammation makes it difficult to visualize cancer cells and immunostaining techniques have been used with success to improve reliability.[11]

Table 1: Indications for Mohs Micrographic Surgery

I. **Basal cell carcinoma (BCC)**
1. High risk for local recurrence (ill-defined clinical borders, anatomic sites in which other types of treatment result in a higher potential risk of recurrence (ie, "H-zone" of the face, Figure 2)
2. History of incomplete removal
3. History of previous irradiation therapy
4. History of recurrence
5. Large size
6. Aggressive histologic pattern, ie, morpheaform or infiltrating, multicentric etc.
7. Areas of important tissue preservation (nasa ali, nasal tip, lips, eyelids, genitalia, ears)
8. Other (rapid growth or aggressive behavior, tumours in immunosuppressed patients)

II. **Squamous cell carcinoma (SCC)**
1. High risk of local recurrence
   - Ill defined clinical borders
   - High risk anatomic sites
   - Large size
   - Ionizing irradiation induced lesions
   - Incomplete removal
   - Perineural and perivascular tumours
   - Anaplastic differentiation
   - Deep tissue and bone involvement
2. Areas of important tissue preservation (face, genitalia)
3. Tumours associated with high risk of metastasis including those arising in the following: Bowen's disease (SCC-in-situ), discoid lupus erythematosus, chronic osteomyelitis, lichen sclerosus et atrophicus, thermal or radiation injury, chronic sinuses and ulcers, adenoid type
4. Other (rapid growth or aggressive behavior, tumours in immunosuppressed patients, long-standing duration, certain genodermatoses)

III. **Melanoma** – useful for certain types and locations of melanoma

IV. **Other cutaneous tumours and lesions**
- Verrucous carcinoma
- Keratoacanthoma (aggressive, recurrent, or mutilating)
- Dermatofibrosarcoma protuberans
- Atypical fibroxanthoma and malignant fibrous histiocytoma
- Leiomyosarcoma
- Adenocystic carcinoma of the skin
- Sebaceous carcinoma
- Extramammary Paget's disease
- Erythroplasia of Queyrat
- Oral and central facial paranasal sinus neoplasms
- Microcystic adnexal carcinoma
- Apocrine carcinoma of the skin
- Merkel cell carcinoma

Indications for Mohs surgery and its use in clinical practice

A great variety of neoplasms are amenable to Mohs surgery and numerous case reports, as well as case series, have reported high cure rates in various conditions. In 1995, the American Academy of Dermatology proposed guidelines for MMS;[12] this adapted information is presented in Table 1. MMS is generally indicated in the treatment of recurrent or locally aggressive tumours that are difficult to eradicate by other routine modalities. The technique is particularly effective in treating tumours located in anatomical areas associated with a high risk of recurrence (those overlying embryonic fusion plates such as the "H-Zone" of the face depicted in Figure 2), large and aggressive tumours, tumours with poorly defined clinical margins, tumours arising in irradiated skin, and those with perineural involvement.[2] Incompletely excised tumours are also best treated with MMS.[13] The patients' immunologic status is another important variable to consider when deciding on a treatment modality since local tumour metastasis, although rare, is more prevalent in immunosuppressed patients.[14]

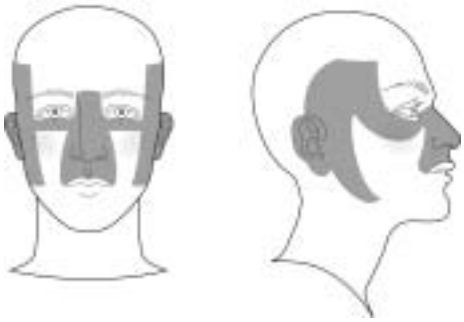
I. Basal cell carcinoma

Basal cell carcinomas (BCCs) account for the majority of non-melanoma skin cancers. Highly curable when diagnosed and treated promptly, they can lead to extensive local tissue destruction and even death if incorrectly or incompletely treated.[15] One of the main reasons for recurrence is that a clinically visible BCC tumour may represent a mere one-fifth of the actual histologic involvement.[16] Identifying aggressive primary BCCs with high statistical risk of recurrence is important in determining the therapeutic modality, which often makes MMS the treatment of choice.[17,18] In their review of 1131 cases of non-melanoma skin tumours treated by Mohs surgery, Batra and Kelly recently reported the most important predictors of extensive subclinical spread (Table 2).[19]

Overall 5-year cure rates documented in the treatment of primary and recurrent BCCs are:
- >99% and 96%, respectively, with MMS[20,21]
- 89.9% and 82.6%, respectively, with surgical excision
- 92.3% and 60%, respectively, with C&E
- 91.3% and 90.2%, respectively, with radiotherapy.[14]

Cure rates by MMS vary depending on BCC subtype, size, and location, as well as whether the tumour is recur-

Figure 2: H-zones of the face



rent or primary. Table 3 presents 5-year recurrence rates following treatment of primary BCCs by various modalities, as reported by Rowe, who cumulatively reviewed all studies on the subject since 1947.[22] For all modalities, excluding MMS, the 10-year recurrence rate was 10.6%. More recently, Thissen et al, while falling short of developing evidence-based meta-analysis guidelines for care of primary BCCs, demonstrated that the lowest 5-year recurrence rates for treated BCCs occurred with MMS.[23]

Silverman et al reported a 13.2% 5-year recurrence rate following C&E of primary BCCs.[24]

- Low-risk sites (eg, neck, trunk, and extremities, irrespective of the size of the BCC) had an overall 5-year recurrence rate of 3.3%.
- Middle-risk sites (eg, scalp, forehead, pre- and post-auricular areas and malar regions with BCCs of ≤10 mm in diameter) had a 5-year recurrence rate of 5.3%. However, BCCs >10 mm had a recurrence rate of 22.7%.
- High-risk sites (eg, nose, paranasal region, nasal-labial groove, ear, chin, mandibular area, perioral and peri-ocular regions with lesions <6 mm in diameter) had a recurrence rate of 4.5%, whereas those with BCCs >6 mm in size in these high risk regions had a 5-year recurrence rate of 17.6%.

Table 2: Predictors of subclinical spread of BCC[19]

- Basosquamous subtype of the nose
- Morpheaform subtype of the nose
- Nodular subtype of the nose
- Recurrent BCC of the nose
- Morpheaform BCC on the cheek
- Any subtype on the eyelids, temple, or ear helix
- Any subtype on the neck in men
- Recurrent BCCs in men
- Tumours with preoperative size >10 mm

Table 3: 5-year recurrence rates for BCCs

Surgical excision	10.1%
Radiotherapy	8.7%
C & E	7.7%
Cryosurgery	7.5%
MMS	1.0%

These numbers are interesting given the fact that 85% of all BCCs are found on the head and neck.[25] In fact, one-quarter occur on the nose alone. Salasche reported that 25%-30% of lesions on the nose and in the nasolabial folds were found to have residual tumour as compared with 12% in lesions found elsewhere on the head and neck.[26]

An important phenomenon noted in the treatment of BCCs with C&E is that, although 21%-37% of tumours may remain behind after treatment,[4,5,26] recurrence rates range only from 3.3%-18.8%.[23,24] It has been hypothesized that an immunologic response removes the remainder of the tumour. If so, it is likely that the immunologic activity against the tumour occurs during the immediate inflammatory phase of wound healing. This was the premise of the study conducted by Spencer et al,[27] who examined primary BCCs <1 cm in diameter after 3 cycles of treatment with C&E, either immediately, or after 1 month. The clearance rate was 75.9% for BCCs examined immediately and 78.6% for specimens examined 1 month later. The authors concluded that for BCCs <1 cm in diameter, there was no evidence that inflammation occurring immediately after C&E clears BCC. In a subsequent study by Nouri et al, treated areas were examined immediately after C&E and 3 months later, it was concluded that the proliferative phase of wound healing had no effect on the clearing of BCC.[3] They suggested that nonspecific immune responses may play a role in disrupting the tumour or the supporting stroma.

II. Squamous cell carcinoma

Treatment of squamous cell carcinoma (SCC) poses a greater challenge than that of BCC, as the likelihood of local and distant metastasis is increased.[2] Mohs presented his series of 3299 patients with SCC treated with MMS, with a 5-year cure rate of 98%, which dropped to 16% in patients who had metastasis.[21] Perineural invasion provides a path of minimal resistance for tumour spread and it is much more frequently reported with SCC than with BCC. Sixty-four per cent of tumours measuring ≥2.5 cm have been shown to have associated perineural invasion.[28,29] Compared to other modalities, MMS results

in the highest cure rates for SCC in these cases.[20,31] Khanna et al confirmed this conclusion in an analysis of the literature in which numerous studies demonstrated a correlation between tumour thickness and depth of invasion with metastatic potential in cutaneous squamous cell carcinoma.[32]

III. Malignant melanoma

At present, excisional surgery remains the standard of care for local cutaneous stage I and stage II malignant melanoma, as well as for melanoma *in situ*.[33] However, in view of frequently asymmetric growth pattern of melanoma, MMS has been used as an alternative treatment modality. Mohs' data on 5-year cure rates is notable: 100% for Clark level II, 92% for Clark level III, 64% for level IV, and 33% for level V. A number of more recent studies have also demonstrated efficacy of MMS with long-term cure rates equaling or exceeding conventional wide local excision.[34-36]

Much discussion has surrounded the reliability of the Mohs technique if melanoma cells are visualized histopathologically on routine frozen sections, since it is often challenging to distinguish freeze-artifact and actinic keratoses from junctional melanocytic proliferations that are often present at the periphery.[37] Use of special immunohistological stains for melanocytes on permanent or frozen sections has improved the reliability of MMS in the management of melanoma. In a recent study by Albertini et al, the authors advocate the use of Melan–A/MART-1 stain to improve the diagnostic accuracy of melanoma staining, as it consistently demonstrated more melanocytes compared to other routinely used S-100 and HMB-45 immunostains.[34]

IV. Other cutaneous tumours

With the evolution of MMS, the list of neoplasms amenable to this technique is growing (Table 1). Higher cure rates have been demonstrated for MMS as compared with conventional therapy for numerous cutaneous malignancies including verrucous carcinoma, keratoacanthoma,[38] extramammary Paget's disease,[39] and dermatofibrosarcoma protuberans (DFSP).[40] For the latter, for example, in a review of patients' charts at the Mayo Clinic and literature review, Gloster et al concluded that MMS was the treatment of choice for locally aggressive DFSP, with 1.6% total recurrence of the tumour when treated with MMS, compared to 20% observed with local excision.

Limitations of Mohs surgery

The main limitation of MMS is that the process is labour-intensive, technically challenging, and requires the expertise of a qualified surgeon. It is important to note that a physician performing Mohs surgery should ideally fulfill a unifying role of a cutaneous oncologic surgeon, a pathologist, and a reconstructive surgeon. Personally handling the excised specimen and reviewing the histopathology of the sections avoids orientation errors and mislabeling of specimens, either of which results in a poor outcome.[7] Yet, at the same time, a multidisciplinary approach is important, as it is often beneficial to collaborate with specialized reconstructive surgeons for repairing large defects, including oculo-plastic surgeons, plastic surgeons, and otolaryngologists.

Interestingly, the apparently high initial financial burden of Mohs surgery is deceptive. The cost-effectiveness of MMS was demonstrated in a study by Cook and Zitelli, who performed true-cost analysis of MMS (including diagnosis, surgical procedure, reconstruction, follow-up, and cost to treat disease recurrence if necessary), comparing it to overall cost of traditional surgical excision methods. From a study group of 400 consecutive tumours, the authors reported that MMS was similar in cost to office-based traditional surgical excision and even less expensive than ambulatory facility-based surgical excision.[41] The cure rates obtained with Mohs were superior. When one considers that repeat excisions of BCCs on the face may be required, the savings achieved by surgical removal of the tumour over the course of a single day becomes evident.

Discussion

Mohs micrographic surgery allows for the accurate determination of the subclinical spread of skin cancer and results in generally higher cure rates when compared with other modalities of treatment for cutaneous neoplasms, including C&E. The concept of sequential, microscopically-controlled tumour removal, with precise margin control, results in a balance between cure rate and tissue-sparing. Since its development, superior cure rates have been demonstrated with Mohs surgery for various types of cutaneous tumours, especially BCCs. MMS has emerged as the treatment of choice for many of these neoplasms. With significant recurrence rates for all treatments (except MMS), combined with the satisfactory cosmetic results achieved by MMS, can we justify the use of C&E for the treatment of facial BCCs, excluding ongoing resource problems and limited access to Mohs surgeons? Is curettage and electrodessication for head and neck BCCs a thing of the past? From the current evidence, it definitely appears so. Knowing these statistics, as a physician, if you developed a BCC, which technique would you choose for yourself?

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