MOHS MICROGRAPHIC SURGERY

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HISTORY AND DESCRIPTION

Mohs Micrographic Surgery (MMS), also known simply as Mohs, is a surgical technique utilized by dermatologic surgeons for the excision of skin cancers. Mohs allows for optimized control and evaluation of the tumor margins while minimizing the quantity of tissue being resected (1). This technique was named after Dr. Frederick Mohs, who in the 1930's pioneered the original concept while performing research as a medical student at the University of Wisconsin. During this time, Dr. Mohs was conducting cancer research projects with his mentor and zoology professor, Michael Guyer. Dr. Guyer was familiar with the preparation of frozen tissue for producing microscopic slides, as they were conducting experiments utilizing injectable irritants in rats to evaluate the effect on cancers as well as normal tissue. The pair inadvertently discovered that injection of 20% zinc chloride solution into the tumor and surrounding skin resulted in local tissue

necrosis, while preserving the microscopic tissue structure and cellular histology, similar to the results if the tissue had been excised and prepared with a fixative solution (2). This observation led Dr. Mohs to the idea that tumors could be excised in conjunction with precise microscopic control. These microscopic techniques were used by Dr. Mohs to map out cancer around nerves, blood vessels, muscle and bone. The cancers he examined were removed by shave, or saucerization excision, a technique that removes cancer as a thin disc of tissue so that the tumor and the inflammatory infiltrate surrounding the cancer can be examined microscopically (3).

While considering the potential for his new idea, it was quickly discovered that injections into the bloodstream of zinc chloride solution resulted in erratic absorption occasionally causing sudden death in rats. Therefore, Dr. Mohs began testing alternatives that would be safe for use in humans (4). After testing several different topical alternatives, he discovered, with the help of a pharmacist, that mixing zinc chloride with stibnite (as a matrix) and blood root powder Sanguinaria Canadensis (as a binder) resulted in a paste which allowed for excellent tissue penetration and fixation, cessation of fixation after a relatively brief amount of time, safety to the human host and surrounding tissue; and this concentration had the consistency and lack of odor enabling it to be applied to the skin for several hours (2). Dr. Mohs also realized that evaluation of this fixed tissue in vertically cut sections would not be practical or result in a superior cure rate and thus finally conceived of the idea to evaluate the fixed tissue with horizontal sections in order to allow full margin control and thus a theoretically superior cure rate (5).

In 1936, after experimenting with this new technique in humans, Dr. Mohs coined the term chemosurgery since the tissues were being chemically fixed prior to excision. Publishing of his research and innovative technique began by 1941 (5). Dr. Mohs initially directed his studies towards physician practicing general surgery, but it soon became apparent that dermatologists, given their background and experience in dermatopathology, were the specialists most suited to adopt this technique. Based on Gross et al. (3) acceptance of this novel technique was slow to gain momentum though. In 1953, while filming a fixed tissue technique for a BCC on the eyelid, due to timing constraints Dr. Mohs performed the last layers of excision without the

fixative as frozen sections. This idea worked so well and seemed equally efficacious to the fixed tissue technique that he began using the “fresh tissue technique” on all eyelid carcinomas (4). Later this technique was used as part of MMS.

By 1969 Dr. Mohs reported a treatment study of 66 patients with eyelid basal cell carcinomas or squamous cell carcinomas with 5-year cure rate of 100% utilizing the newer technique (4). Soon after, several dermatologic surgeons began studying this fresh tissue technique on cutaneous tumors on other areas of the body; their findings resulted in similarly exceptional cure rates (6). With the publication of these findings in the 1970’s, wide acceptance of the “Mohs” technique began to take root.

Now, with decades of accumulated experience and consistent evidence, the Mohs technique has become a major treatment modality for most skin cancers and is the treatment of choice for most high-risk skin cancers (7). It provides complete elimination of the tumor with the highest cure rate, while preserving as much healthy tissue as possible. Thanks to this elegant surgical procedure, tumors can now be excised with complete evaluation of all the excised margins and can be removed in successive stages until the margins are completely clear of tumor (8).

Previously the gold standard for SCC, BCC and other neoplasms was amputation of the nail unit amputation; nowadays MMS is the treatment of choice (9). The use of MMS has shown to preserve to the maximum surrounding healthy tissue in the subungual and peringual carcinomas without osseous involvement.

INDICATIONS AND USE

Mohs Micrographic Surgery is most commonly used for the extirpation of skin tumors that are large, classified as aggressive or high-risk, are in difficult to access areas, or are cosmetically sensitive areas where maximum tissue preservation is essential (i.e. eye, nose, ears, lips, etc). Mohs is also utilized in functionally important areas such as the genital, perianal, anal, hand, foot and nail areas (10)

An absolute prerequisite for MMS is that the tumor be contiguous with no skip regions, otherwise the results can lead to false-negative histologic margins (11). Although many different types of tumors can effectively be treated with MMS, the most common indications are Basal Cell Carcinomas (BCC) and Squamous Cell Carcinomas (SCC) of the skin (12,13). Also indicated for MMS are recurrent cutaneous tumors in areas previously treated with radiation therapy as well as cutaneous tumors that have arisen in immunosupressed individuals. It is also an efficacious approach to certain melanomas.

SCC of the nail unit most commonly arises distally and laterally on the digits and slowly invades the nail by extension as previously described by Dr. Weiss and Dr. Zaiac (10). MMS is an excellent choice of treatment if no osseous involvement has been determined. Different considerations should be taken depending on the actual location of the tumor but the procedure itself has a standardized program and that should continue the same even on periungal and subungual locations.

The MMS procedure is typically performed in an outpatient setting. The surgeon excises the tumor in a tangential fashion with horizontal frozen sectioning of the excised margin (Fig. 1); the same surgeon then evaluates these sections microscopically. By creating this type of peripheral margin control, 100% of the tumor margin is evaluated enabling complete margin excision (14). The standard wide local excision with permanent fixation and vertical sectioning only allows for evaluation of a 90-95% of the true margins (15). For consistency the frozen section histology should then be correlated with the original biopsy pathology and with the clinical presentation of the patient. A Mohs anatomical map is then created to allow orientation of tumor margins. This map contains a drawing of the tissue excised with reference marks (Fig. 2). If a subsequent positive margin is discovered, the exact location should be marked on the Mohs map and another margin of tissue is removed on that specific location. The process is repeated until all margins are negative and the area clear of cancer cells. The resultant defect is then typically repaired utilizing a flap or a graft in order to maintain functional integrity and cosmesis. In the last few years, the trend has been to continue all medically necessary anti-coagulant and anti-platelet medications during the procedure as the risk of thromboembolic event outweighs the benefit

of minimizing bleeding risk (16). Typically hemeostasis is successfully obtained utilizing electrocautery or electrodessication and pressure bandages.

MMS is the gold standard treatment for most skin cancers (2). Although this is the case, it is important to understand that Mohs may not always be indicated for small or low-grade skin cancers. For some tumors in low-risk areas, lower cost and less time-consuming treatment modalities should be consider as they can potentially allow for results which are nearly as efficacious, while producing less morbidity and decreasing the consumption of medical resources (17).

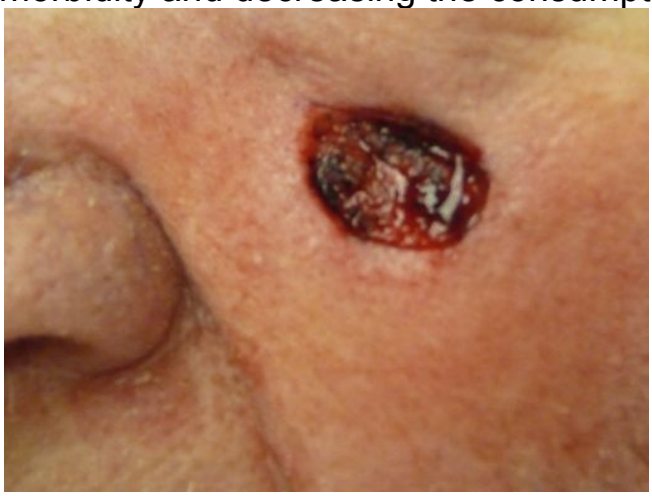

Fig. 1-Stage 1, first incision made on the site of lesion. This case was a BCC of the L cheek.

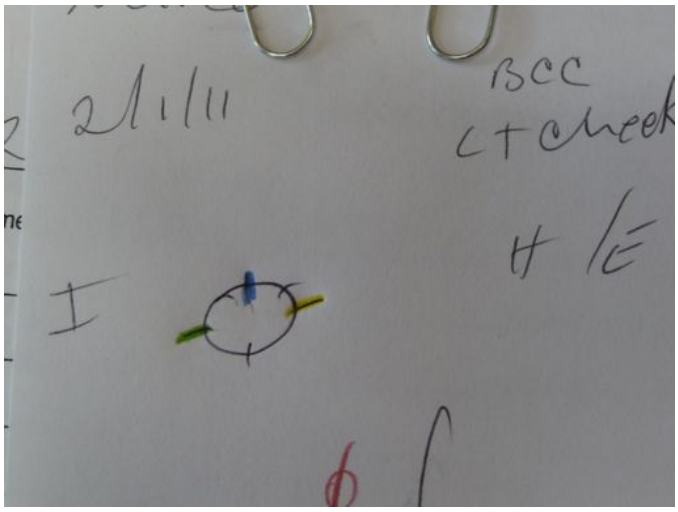

Fig. 2-This is the color-coding mapping done before the specimen is labeled using the same coding technique

PROCEDURE

Sometimes weeks or months may elapse between the time of the original biopsy and the MMS procedure, as such, the site of the original tumor with landmarks or a detailed picture should be used as a record at the time of first biopsy. This is done to ensure the accurate determination of the tumor location. After the patient is positioned and the surgical site is prepared, the clinical margins of the tumor are outlined utilizing a skin marker. A surgical margin is then outlined around the tumor clinical margin. Surgical margins range 1mm or more depending on tumor histologic subtype, anatomic location and surgeon preference. Larger margins are utilized for more aggressive or recurrent tumor types. Marker reference marks should be placed before starting the procedure and, at a minimum; one reference mark should be incorporated and designated as the12 o'clock mark.

After infiltrating the area with local anesthesia (0.5-2% lidocaine with epinephrine 1:100,000 or 1:200,000), the tumor is lightly curetted to better delineate the lesion margins. Typically a #15 blade scalpel is utilized and the initial incision is made at a 45-degree beveled angle to a depth at which the tumor is to be undercut. The incision is continued in a beveled fashion around the entire outlined surgical margin. The reference marks should be incised superficially on the peripheral tissue overlapping onto the specimen to preserve orientation. The tissue is then grasped with forceps and the remaining deep central portion of the specimen is then undercut in a horizontal fashion. The entire surgical procedure usually takes less than 10 minutes. The tissue is removed maintaining orientation and taken to the lab with the use of a transfer device for further analysis. Usually square gauze or a flashcard with a dot of ink on one corner is utilized. The marked corner is usually arranged to indicate the 12 o'clock position. Establishing a standard of operation within an office is essential, the landmarks used by the surgeon should be consistent and standardized in order to avoid tissue orientation errors.

At this point a Mohs map should be constructed indicating the actual size and shape of the tissue, the precise location of reference markings anatomically, and each subsequent section performed on the tissue as well as the size and shape of any residual tumor foci.

The tissue is sliced into sections and inked with different colored dyes for microscopic orientation (Fig. 3). The map should indicate these different orienting colors in order to be able to localize any areas of residual cancer cells.

In cases where the surgery is done on the nail and digits, if tumor extends below the nail, an avulsion of the nail plate may be necessary (10). The most important concept is that the first stage should have a tangential layer. Also the diagram should be done accurately for the nail unit, in order to orient the specimen if second stages are needed.

Once the tissue is transferred to the lab and the Mohs map constructed, each layer of cuts performed on the tissue should be placed on slides to be viewed and analyzed under the microscope. For this reason, the Mohs surgeon should be well trained in dermatopathology and the reading of frozen section slides (Fig. 4). It is important to ensure that all superficial and deep margins have been processed and that 100% of the margin is intact during microscopic evaluation. Of equal importance is maintenance of proper tissue orientation. After full examination of all tissue sections, any areas positive for tumor should then be marked on the Mohs map. If all sections are devoid of tumor, and it is determined that the sectioned slides are of appropriate quality, the area can be considered tumor-free and marked as negative.
In patients with any residual cancer the whole process is repeated again, with the subsequent stage excised where a surgical margin is drawn around the residual tumor foci. This stepwise process is repeated until the tumor is removed in its entirety, upon microscopic evaluation. After the procedure is completed, the defect should be closed by the Mohs surgeon or, if necessary, by a plastic surgeon. The procedure takes about 2-3 hours in total, depending on the number of stages required.

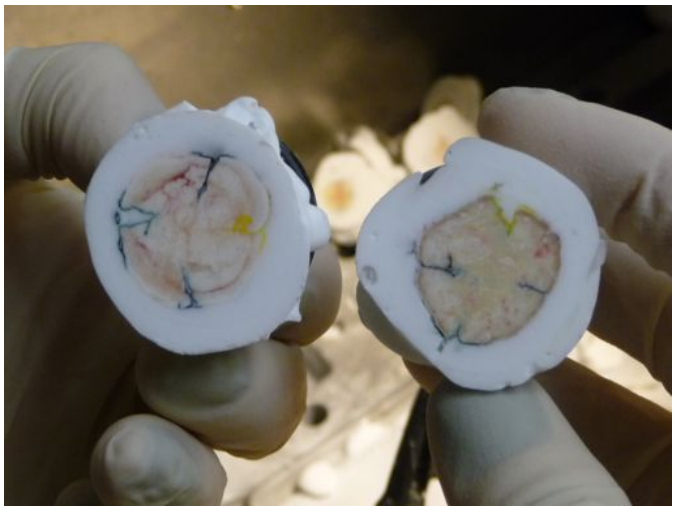

Fig. 3- Specimen cut and after cryostat technique

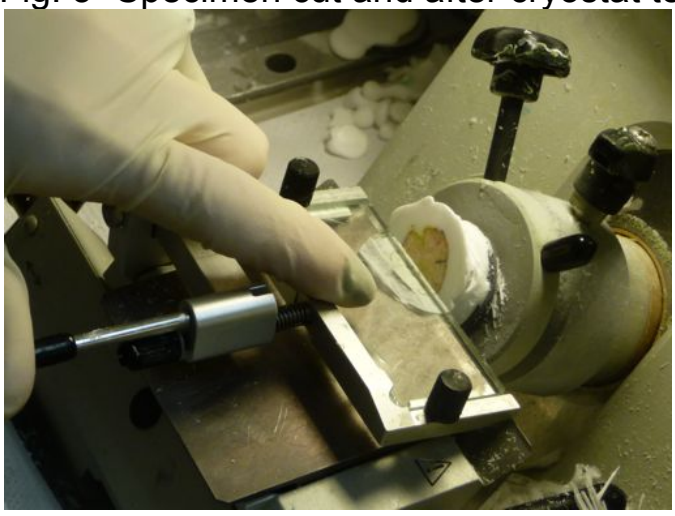

Fig. 4- Mounting of the slide, then staining occurs

EQUIPMENT

There are several instruments required for MMS all of which should be available when performing the procedure. A well-trained Mohs histotechnician will be able to produce high quality frozen section slides, which are critical to the process. The key elements of a Mohs laboratory are a grossing and inking station, a Cryostat with microtome, and a tissue staining area with adequate ventilation. A microscope reading area for the slides should be conveniently located between the lab and the operating area. Finally the operating room should contain all necessary instrumentation for the surgical procedure including a curette, scalpel blade holder with blade, tissue forceps, hemostats and skin hooks (2).

HISTOLOGY

Evaluation of the finalized slides (Fig 5.) under the microscope should be done by a well trained dermatologist who is knowledgeable in the most common histology of the skin (Fig. 6) For example, in the case of the BCC a “morpheiform patent and sclerosing, perineural infiltration, multicentric, metatypical, and deep invasion”(18) can be seen. However, one must take into account that there are many variants and simulants of BCC, which may cause clinical and histopathology confusion (3). These tumors may have certain features in common with BCC, with nodular or sclerosing islands, peripheral palisading, stromal retraction, glandular formation, and/or mucin.

BCCs consist of “basaloid cells with darkly staining nuclei and sparse cytoplasm” (19) They can be described as more immature cells in comparison to SCCs. As previously stated, Mucin can sometimes be present in the stroma which may be viewed easily with the tolueidine blue staining. It is essential to have an excellent grasp and understanding of the presentatations of many subtypes of BCC’s within a histopathological evaluation in Mohs.

Also, some surgeons believe that aggregates of inflammatory cells may indicate the tumor is nearby and is a sign that deeper cuts are needed (20). This belief has proven to be controversial though, as sometimes nodular aggregates of inflammatory cells are present at quite some distance and deeper excision is not needed (21). Also, it is important to take into account that most BCCs excisions extending into superficial adipose tissue are usually of adequate lengths.

Immunohistochemistry stains (IHS) are used to differentiate skin cancers, for Melanoma S-100 and MAR1 are some of the common markers used. Congo red stains can be used to differentiate from different skin cancers as well. In general IHS should be used in difficult cases for better pattern recognition.

The histology of SCC’s presents with a poorly differentiated pattern, “acantholytic, with perineural invasion, or deep perivascular involvement” (18). It is important to understand that SCCs presents

with higher risks when they have the following characteristics: large size >2cm, recurrent, pleomorphism or with poor differentiation, “Spindle cell” histology, deep involvement, in locations like the lips and ears, or when seen in immunosupressed patients (22).

There are also different imitators of cutaneous SCCs including: irritated Seborrheic Keratosis, irritated verrucae vulgaris, hypertrophic actinic keratosis, Keratoacanthoma, tangential section of the epidermis, pseudoepithelioid hyperplasia, other spindle cells tumors, and adnexal structures (3).

Well-differentiated SCCs exhibit keratinizing cells with eosinophilic cytoplasm, keratin pearls, and intracellular bridges. It is more difficult to make a distinction with poorly differentiated SCCs as they do not exhibit the same characteristics, and they develop atypia more often than not, which recent studies have found are a sign of malignant progression (23).

Another category of skin cancers are the basosquamous cell carcinomas, which present as a combination of BCC and SCC. They are also called metatypical BCC because of their histological presentation (3). Also when analyzing areas such as the nail unit, which can have a similar histopathology in terms of the tumors analyzed, also exhibit a very different histology than the surrounding skin. For example, the basal cells of the matrix are more basophilic than the ones of the normal basal cell layer, and are easily confused with BCC (10). The Mohs surgeon should pay close attention to this in order to avoid unnecessary stages of surgery.

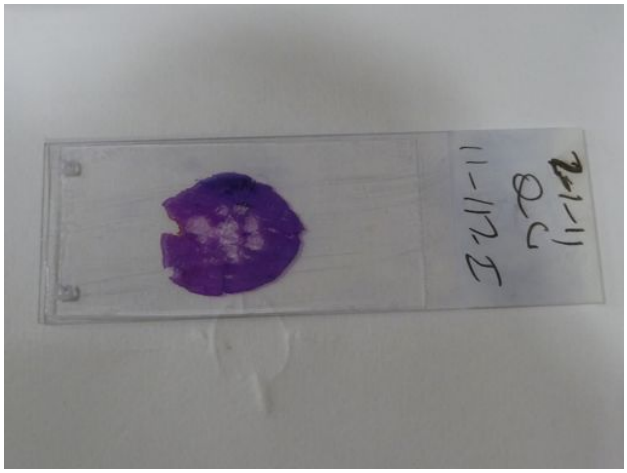

Fig. 5- Finalized slide

Fig. 6- Analyzing histology under the microscope

REPAIR SURGERY OPTIONS:

Spontaneous granulation - Skin tissues have a remarkable capacity to heal themselves, based on location and other clinical factors spontaneous granulation could be a good healing technique without major repairs. This is good option when recurrence is a possibility in difficult tumors. This technique is sometimes used to later plan for a reconstruction of the scar left by the healing process.

Fusiform closure - Excellent cosmetic results can often be obtained by simply approximating the skin edges of the defect together in a linear fashion with the appropriate suture. This approach usually requires additional tissue (Burrow's triangles) to be removed at the oblique margins in order for the final linear to lie flat. This technique is utilized with small defects or when the defect can be oriented within a wrinkle or a previous scar.

Skin flaps - Skins flaps involve the movement of nearby or adjacent healthy skin to cover the surgical wound. This form of closure provides excellent cosmetic results for larger defects, defects under tension, and when exact matching of the skin texture, consistency and color is a necessity.

Skin graft – Skin grafts are areas of skin that are harvested from a secondary, non-contiguous site and used to fill in the primary surgical defect. This is typically utilized when with large defects or when other

types of repair options are not practical as they can result in discrepancies in tissue color, contour, and consistency.
Split-thickness skin grafts are thin shavings of skin usually harvested using a dermatome blade. They can be used as permanent primary defect coverage or as temporary coverage prior to the final reconstructive cosmetic procedure.
Full-thickness skin grafts are full-thickness layers of skin that are harvested and placed within the defect and are usually used as permanent coverage.
Consultation with other reconstructive specialists - If surgical repairs may prove to be extensive, involve cartilage, muscle, bone, or critically functional areas such as the eyelid, consulting reconstructive surgeons may be considered. They would typically perform the reconstructive surgery either the same day as MMS or within several days following the MMS.

RESULTS

The most important benefits of this technique is the precision achieved for tumor margin control and resultant superior cure rates, real-time histological evaluation, and tissue sparing capability when compared to other surgical modalities. MMS enables an excellent efficacy with 5-yr. cure rates of approximately 99% for most primary BCCs, 95% for most recurrent BCCs, 97% for most primary SCCs, and 92% for most recurrent SCC (24, 25).

Technical factors affecting the recurrence rate are poor slide interpretation, orientation errors, poor tissue staining and sectioning, amongst others. Only the full attention to detail by everyone involved in the process, the surgeon, the histotechnician and staff will allow higher cure rates via MMS for cancer of the skin.

CONSIDERATIONS

All available treatment alternatives should be discussed with the patient prior to the intervention including their risks and benefits. As noted before, the primary benefit of MMS is the precision with which tumors can be excised, resulting in excellent long-term cure rates for high-risk skin tumors. Another major advantage is the ability of MMS to spare normal tissue, thus potentially allowing preservation of vital

structures, simplifying repair (and the cost of the repair) of the surgical wound, and improving the cosmetic results (26).

As discussed, a typical MMS procedure may take 2-3 hours, keeping in mind, more complicated cases will take longer. Reconstruction following MMS can add another hour to the procedure. A significant amount of the total time is spent with histological preparation and analysis; during this time, patients are temporarily bandaged and may await the final results in a waiting room. Elderly patients may find it difficult to tolerate a procedure of this length, thus preparing them adequately is essential.

Additionally, due to the complexities of MMS, it is somewhat more expensive than other surgical treatment options for skin cancer. Whether MMS is cost-effective or not is a controversial issue. One study concluded that MMS was in fact cost-effective because of the vast decrease in subsequent rates of local recurrence when compared to other modalities (27). In contrast, a subsequent analysis concluded that MMS was not cost effective, based upon the low rates of recurrence seen in the randomized trial. These results prove to be difficult to interpret since the study was limited to a follow-up period of 30 months for primary BCCs and 18 months for recurrent lesions. In addition, the study was carried out in the Netherlands where cost determination/accounting for surgery differs considerably from that in the United States (28).

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