Review

Mohs surgery: Commentaries and controversies

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Introduction

There is an enormous amount of literature pertaining to the subject of Mohs surgery, ranging from its various indications to therapeutic results. One constant limiting factor in this body of knowledge, however, is the scarcity of randomized, controlled studies comparing Mohs surgery with other effective therapeutic modalities. Obviously, it is hard to gather solid scientific evidence in favor or against this technique without comprehensive controlled studies, but evidence in its favor abounds in the form of the personal experience of practitioners, several excellent comparative retrospective evaluations, and the outcomes of thousands of patients treated over the years.

In our opinion, there is sufficient evidence to support the use of Mohs surgery for treatment of selected skin cancers, and yet the medical community in general and dermatologists in particular are divided in their opinions concerning this therapeutic modality. As a matter of fact, Mohs surgery is frankly controversial among many of our colleagues, both in the academic and private sectors. It is not rare for a Mohs surgeon to be constantly antagonized by other specialists in different forums including tumor boards or scientific presentations, always with the complaint of using Mohs surgery without solid evidence of its effectiveness. Herein, we present our views on the available literature on Mohs micrographic surgery as regards its indications, advantages, disadvantages, and therapeutic results. Also, we explore the reasons for controversy and present some of our therapeutic failures to reflect on the nature and limitations of this fascinating technique.

Indications for Mohs Surgery

Indications for Mohs surgery are multiple and growing by the day. Most authors recognize those listed in Tables 1 and 2. Complete assessment of surgical margins made possible with the Mohs technique is relevant in the treatment of tumors with unifocal origin. Nevertheless, for multifocal tumors and neoplasms with a high incidence of satellite lesions the importance of surgical margins is diminished, and Mohs surgery is probably not the treatment of choice, as it is only as effective as other techniques. The available literature supports the use of Mohs surgery as first-line therapy only for the tumors listed in Table 3. The role of Mohs surgery for treatment of other cancers including melanoma and Merkel cell carcinoma is more controversial.

Patient selection for Mohs surgery

The recommendation for Mohs micrographic surgical treatment should be made after careful evaluation not only of

Table 1 Tumors treatable with Mohs micrographic surgery

Basal cell carcinoma	Squamous cell carcinoma
Malignant melanoma	Keratoacanthoma
Dermatofibrosarcoma protuberans	Atypical fibroxanthoma
Malignant fibrous histiocytoma	Microcystic adnexal carcinoma
Sebaceous carcinoma	Extramammary Paget's disease
Leiomyosarcoma	Adenoid cystic carcinoma
Merkel cell carcinoma	Other tumors

Table 2 Indications for Mohs surgery

Recurrent tumors
Large tumors (> 2 cm in diameter)
Tumors that are incompletely excised
Tumors located in areas where the risk of local recurrence is high (i.e. the central face and periorbital and periauricular areas)
Tumors located in areas where tissue conservation and a high cure rate are important
Tumors with indistinct clinical margins
Tumors with aggressive histologic subtypes (micronodular, infiltrative, and morpheaform BCCs, basosquamous carcinomas, and poorly differentiated SCCs)
Tumors with evidence of perineural invasion
Tumors arising in irradiated skin or in chronic scars

Table 3 Mohs surgery as first-line therapy

Basal cell carcinoma and squamous cell carcinoma
Recurrent in any location
Size > 1 cm in the nose and 2 cm elsewhere
Aggressive histology
Location on the "H zone" of the head and neck
Tumors on previously irradiated skin
Tumors with perineural invasion
Tumors in organ transplant recipients
Dermatofibrosarcoma protuberans
Atypical fibroxanthoma
Microcystic adnexal carcinoma
Leiomyosarcoma

the histology and location of the tumor, but of the patient's characteristics. Mohs surgery is a long and tedious procedure and many patients will have a hard time coping with it. Most frequently, we encounter difficulties in patients with dementia, spinal arthritis, or poor sphincter control. In these cases, faster alternatives (cryosurgery, curettage and excision, radiation therapy) should be considered. Questions regarding chronic arthritis and back or neck problems should be asked to ensure that the patient can tolerate sitting through a potentially lengthy procedure under local/regional anesthesia.

Informed consent

Informed consent is the right of the patient to be fully informed about the risks, complications, and alternatives to a medical treatment or surgical procedure before deciding whether or not to submit to it. Studies indicate that informed patients experience less anxiety, are more compliant with instructions, and express greater satisfaction with the results of surgery. To satisfy the law and to fulfil the moral obligations of the doctor related to consent, several conditions should be met:

- The patient should be capable of consenting (legally competent).
- The patient must be appropriately informed.
- The consent must be given voluntarily without constraint or coercion.

In regards to Mohs surgery, a recent study by this author showed that retention and recall of information given to patients before surgery in written and verbal format is less than 30% at 20 min and 1 week.[1] Obviously, patients forget most of the information almost immediately and we can only speculate about the reasons behind this fact: anxiety, memory problems, and unfamiliar surroundings may all play a role. Thus, as usual, patients trust their physicians to make the best recommendation possible and doctors have a significant moral responsibility to provide honest and complete information. In my opinion, Mohs surgery is never the only option available. It might be the best or most desirable alternative, but there are other therapeutic modalities that can be employed and should be explained by the Mohs surgeon, including radiation therapy, cryosurgery, and traditional surgical excision. For example, newer radiotherapy techniques result in excellent cure rates and cosmetic outcomes and there are recent studies suggesting that curettage of lesions followed by either cryosurgery or surgical excision is an effective modality for nonmelanoma skin cancers in various locations, as will be discussed later. For many patients, the difference in cure rates between Mohs surgery and other treatments may not be significant, and some may prefer a nonsurgical alternative such as radiation, which provides a lower cure rate but avoids potential mutilation. Unless the patient's tumor is potentially metastatic (melanoma, aggressive SCC), he/she should be given the option of choosing suboptimal treatment if it better suits his/her personality and needs.

Special circumstances and problems during Mohs surgery

Patients with dementia pose a definitive challenge for the Mohs surgeon. Although most of them have mild to moderate reduction of cognitive abilities and are able to consent to Mohs surgery, the intrinsic nature of the procedure can elicit problems. Some individuals with dementia are fully cooperative at the beginning of the procedure but become agitated and combative after 1–2 h of surgery. In some cases, I have been unable to complete the Mohs surgical procedure and had to perform cryosurgical treatment of the remaining positive margins. Patients referred from nursing homes or chronic

Table 4 Five-year recurrence rates for basal cell carcinoma

Method of treatment	5-year recurrence rates (%)
Surgical excision	10.10
Radiation therapy	8.70
Curettage/electrodessication	7.70
Cryosurgery	7.50
Mohs surgery	1

care facilities may be wheelchair bound and have difficulty moving or adopting a sitting or decubitus position. Mohs surgery under local anesthesia is difficult to perform in these individuals and other therapies may be advisable. Also, some patients with neurologic disorders have significant problems with sphincter control and are unable to undergo a lengthy surgical procedure without multiple interruptions which are frustrating to both the patient and the doctor alike.

Why recommend Mohs surgery?

I believe there are at least two undeniable facts that make Mohs surgery the optimal option for certain tumors. One is the higher cure rates achieved for neoplasms with unifocal origin and minimal potential for satellitosis. The other is the ability to preserve normal tissue in cosmetically sensitive areas.

In their review, Rowe *et al.*[2] concluded that 5-year recurrence rates for primary basal cell carcinomas (BCCs) were 8.7% for non-Mohs modalities and 1% for Mohs micrographic surgery. The figures for recurrent tumors were 19.9% and 5.6%, respectively. Recurrence rates for specific therapeutic techniques are shown in Table 4.

Although most of the studies were retrospective, common sense indicates that the evaluation of 100% of surgical margins leads to improved cure rates. The importance of surgical margins for nonmelanoma skin cancers was established many years ago. In 1965, Gooding showed a 34.8% recurrence rate for untreated positive-margin BCCs.[3] In 1968, Pascal reported a 33% recurrence rate for incompletely excised BCCs vs. 1.2% for "complete" excision.[4]

As regards tissue preservation, Bumsted *et al.* demonstrated that there was 180% excess tissue taken when BCCs smaller than 3 cm are excised with 8-mm margins using a standard surgical excision as compared with Mohs surgery.[5] Downes showed that Mohs surgery preserved 41% more tissue than a traditional excision for periocular BCCs. Additionally he showed a 64% rate of incomplete excisions when using traditional 4-mm margins.[6]

The difference between Mohs surgery and other surgical approaches is the method of assessment of surgical margins. It is worth remembering that surgical margins after traditional excision do not equate pathology margins. The excisional specimen shrinks owing to elastic dermal recoil, and tissue processing and embedding produce an additional 15–25% shrinkage. The sectioning method is of significance as well, with most pathologists using vertical sectioning techniques.

- So-called "cross method" is excellent for examination of the central portion of the specimen but the larger the specimen, the greater the ratio between unexamined and examined sections.
- "Bread-loaf method" allows for thorough examination of tissue, but intervening nonexamined areas depend on the size of the specimen. Overall, studies have shown that only 1% of the total volume of the sample is examined using this approach. Irregular extensions of a tumor may be undetected and a margin can be equivocally reported as tumor-free, leading to subsequent recurrence.
- Some pathologists combine the cross and bread-loaf methods in order to provide a more accurate assessment of the margins. This approach leads to examination of the margins in four quadrants but with the advantages and limitations of both methods.
- "Peripheral method" is rarely used alone. It leads to complete examination of the peripheral margins but with a total neglect of the deep margin. Most frequently, it is used to complement other methods.
- In comparison, the Mohs assessment of margins using horizontal sectioning allows the visualization of almost 100% of epidermal and deep margins.

If it makes sense, why is Mohs surgery controversial?

Several reasons explain the controversies surrounding Mohs surgery, including: The questionable need to remove all cancerous cells to achieve a cure, a lack of prospective randomized trials, over-estimation of cure rates, and the fact that the alternative therapies are extremely effective.

Questionable need to remove all cancerous cells to achieve cure

The rationale behind Mohs surgery is that assessment of 100% of surgical margins leads to removal of all tumor cells and consequently to higher cure rates. Nevertheless, experience has shown that complete removal of a tumor is not necessary in all cases. For example, only 40% of incompletely excised BCCs will have clinical recurrence.[4] Also, several authors have shown the persistence of BCC cells after curettage electrodessication, but the cure rates with this procedure are significantly greater than 90%.

Lack of prospective randomized trials

There are no prospective randomized trials to evaluate the Mohs technique and most studies are retrospective with an assessment of results against historical controls. It is practically impossible to compare results from various trials because of the marked variability in techniques; histology of tumors, or locations of lesions and conclusions must be drawn

using powerful statistical methods. The main limitations of available data, however, involve the reporting of recurrence rates and follow-up periods.

There are many ways to report recurrences and the methods significantly affect the results. Most studies have used either raw recurrence (RR) or strict recurrence rates.

- Raw RRs are obtained by counting all recurrences from all treated tumors. This approach falsely lowers the RR because patients lost to follow up are free of recurrence.
- Strict RRs account for recurrences vs. recurrence-free cases at 5 years. This method falsely elevates the RR because patients with less than 5 years' follow up but without recurrence are ignored.
- Recurrence rates using 5-year modified life-tables are most accurate. In this method, all available data are used and credit is given to recurrence-free cases with less than 5 years' follow up. Very few trials have used this approach.

In terms of follow up, the traditional period in cutaneous oncology has been 5 years but this is clearly inadequate. There are several studies demonstrating that at least 20% of recurrences occur after 5 years, and some authors have suggested that the ideal follow up after treatment of skin cancer should be 10 years.

Over-estimation of cure rates

Another factor contributing to the controversy over Mohs surgery is the overestimation of cure rates. In one of his original articles, Dr Mohs reported 99.3% cure rates for BCC, but this figure drops slightly to 98.3% after taking into account 99 recurrences that were retreated with Mohs surgery and finally cured. Also the 94% cure rate reported for squamous cell carcinoma (SCC) drops to 92.9% if 70 local recurrences are taken into account. In another landmark paper, Robins reported 5-year cure rates of 97.4% for BCC and 96.6% for SCC but metastatic and unresectable disease was not included in the statistical analysis.[7] More significant is the fact that in almost every series the cure rates drop to 50–90% when treating nonmelanoma skin cancers larger than 3 cm in diameter.

Alternative therapies are extremely effective

Some physicians have problems accepting Mohs surgery because their preferred modalities (cryosurgery, curettage/electrosurgery, excision, radiation) achieve 90% or higher cure rates.[4] Mohs surgery may be tedious and time consuming, and some tumors show multifocality or a high incidence of satellite lesions, making the control of margins less significant (melanoma, Merkel cell carcinoma, extramammary Paget's disease, sebaceous carcinoma).

What Is the Scientific Evidence Supporting the Use of Mohs Surgery?

Basal cell carcinoma

Silverman *et al.* published data from the oncology section of the skin cancer unit at NYU from 1955 to 1982. They treated 5755 BCCs with curettage/electrosurgery (CE), surgical excision (SE), or radiation. Primary tumors had a 5-year recurrence rate of 10.6% while the figure for recurrent tumors was 15.4%. The greatest risk for recurrence occurred 1–4 years after therapy. The authors concluded that the method of reporting the RRs greatly affected the results.[8,9] The group also published the results of each individual therapeutic technique, as shown in Table 5. It should be noted that only 60% of the patients treated with radiation therapy had good or excellent cosmetic outcomes at 15 years.[8–11]

Recently, Thissen *et al.* published a systematic review of treatment modalities for primary BCCs.[12] They included articles in English, French, German, Dutch, Spanish, and Italian between 1970 and 1977. The authors selected papers with a prospective evaluation of RRs in at least 50 patients and with minimal a follow up of 5 years. Only 18 of 298 studies found in the literature fulfilled these criteria and RRs were lowest for Mohs surgery as compared with excision, cryosurgery, curettage/electrofulguration, and radiation therapy (Table 6).

Sexton *et al.* correlated the histologic subtype of BCCs with therapeutic results after surgical excision.[13] The percentage of tumors with positive margins after excision are shown in Table 7.

Table 5 Recurrence rates

Method	Number of tumors treated	5-year RR for primary tumors	5-year RR for recurrent tumors	RR based on location	RR based on size
Curettage/ electrosurgery	2314 primary 666 recurrent	13.20%	18.10%	9.5% low-risk vs. 16.3% high-risk (central face)	10.5% (lesion < 1 cm) vs. 26.1% (lesion > 2 cm)
Surgical excision	588 primary 135 recurrent	4.80%	11.60%	0.7% for low-risk	3.2% (lesion < 6 mm) vs. 9.0% (lesion > 1 cm)
Radiation therapy	863 primary 211 recurrent				4.4% smaller than 1 cm

RR = recurrence rate.

Table 6 Recurrence rates

Method	Recurrence rate (%)
Mohs surgery	1–2
Surgical excision	3–8
Cryosurgery	3–16.5
Curettage/Electrodessication	5–18
Radiation (only one study)	7.40

Table 7 Positive margins after surgical excision

Type and number of BCC	Positive margins (%)
Nodular (218)	6.40
Superficial (181)	5.60
Micronodular (151)	18.60
Infiltrative (77)	26.50
Morpheaform (11)	33.30

BCC = basal cell carcinoma.

Micronodular BCC

In a recent publication[14] Hendrix *et al.* reported their findings on 69 micronodular and 69 nodular BCCs after Mohs surgical treatment. The overall subclinical extension was 5.4 mm for micronodular and 1.6 mm for nodular tumors. The figures for primary lesions were 5 mm vs. 2.4 mm, respectively; and for recurrent tumors, 5.9 mm vs. 3.9 mm, respectively. The authors recommended 5–8-mm surgical margins for micronodular BCC.

Morpheaform BCC

Salasche and Amonnette[15] studied 51 patients with morpheaform BCC with 55% of lesions clustered around the nose and naso-labial folds. They found subclinical extension of 7.2 ± 3.8 mm vs. only 2.1 mm for nodular lesions, and recommended Mohs surgery as the treatment of choice.

High-risk BCC

Randle[16] reviewed published studies on RRs, size, and metastases of BCCs. He identified the so-called "high-risk" tumors as those with the following characteristics: Size larger than 5 cm, recurrent after treatment, long duration/neglect, located on the mid-face or ear, aggressive histology, and arising on previously irradiated skin. The author found that at least 18% of recurrences happened after 5 years and patients with a BCC have 46.9% chance of developing a second lesion within 3.5 years.

Perineural involvement

Ratner *et al.*[17] prospectively evaluated 434 BCCs treated with Mohs surgery and found perineural involvement in 6.7%. The Mohs defects were 105–605% larger for tumors with perineural spread.

Cost effectiveness

Cook and Zitelli[18] described the cost of treating a series of skin cancers with Mohs surgery compared with calculated estimates of the cost to treat the same tumors with traditional surgical excision. A total of 400 consecutive cases were selected. The cost of treatment in the reference group included diagnosis, Mohs surgery, reconstruction if needed, follow up, and the cost to treat the recurrences. These costs were compared with traditional excision, excision with permanent section margin control, excision with frozen section control, and excision with frozen section control in an ambulatory surgical facility. For the study's purposes, it was assumed that all tumors in the comparison groups would be excised with standard surgical margins and the defects would be reconstructed with the simplest margins possible. The cost of diagnosis, excision, pathology, reconstruction, and treatment of disease recurrence were then calculated and compared with those of Mohs surgery. Results showed that the cost of Mohs surgery is similar to office-based traditional surgical excision and less expensive than ambulatory surgical facility-based surgical excision. The average cost of Mohs surgery was $1243 vs. $1167 for excision with permanent section control, $1400 for excision in the office with frozen section control, and $1973 for excision with frozen section control in the ambulatory setting. Analysis based on anatomic location yielded similar results. The authors concluded that Mohs surgery is a method of surgical excision with high intrinsic value which is cost-effective in comparison with traditional excision.

Squamous Cell Carcinoma

Dzubow *et al.*[19] identified risk factors for local recurrence of primary cutaneous SCC by reviewing 414 tumors treated with Mohs surgery. Local recurrences occurred in 3.4% of cases (14 of 414), metastases were noted in 0.7% of cases (three of 414), and total recurrence rate was 4.1% (17 of 414). Rowe *et al.*[20] studied prognostic factors for local recurrence, metastasis, and survival rate in SCC of the skin, ear, and lip by reviewing studies conducted between 1940 and 1992. Overall there were lower RRs with Mohs surgery as compared with non-Mohs modalities (Table 8).

In 1989, Dinehart *et al.*[21] looked at metastases from SCC of the skin and lip in 365 cases treated with Mohs surgery. A metastasis rate of 7.4% (27 of 365) was reported after a mean follow up of 1.7 years, and 90% of the reported metastases appeared within the first 2 years. High-risk areas for metastasis were noted as the temple, dorsum of the hand, and lip. There was no association between the occurrence of metastasis and perineural invasion. The study did note that there was a 50% metastasis occurrence in cases with parotid involvement.

Table 8 Recurrence rates

	MMS (%)	Non-MMS (%)
SCC of skin/lip	3.10	16.90
SCC of ear	5.30	18.70
Recurrent SCC	10	23.30
Perineural SCC	0	47
SCC > 2 cm	25	41
Poorly differentiated tumors	32.60	53.60

MMS = Mohs micrographic surgery; SCC = squamous cell carcinoma.

Holmkvist and Roenigk[22] retrospectively reviewed 50 cases of SCC of the lip treated with Mohs surgery to assess 5-year outcomes. They reported that 92% of cases (46 of 50) remained tumor-free at 5 years. Eight percent showed local superficial recurrence (four of 50) with the average time of diagnosis being 2.5 years. There were no recurrences in cases where the lesion was less than 1 cm or if actinic chelitis was treated concomitantly with a CO_2 laser. Feasel *et al.*[23] looked specifically at cutaneous malignancies with perineural invasion and noted an increase in morbidity and mortality. Five-year survival rates ranged from 20 to 64%, with increased mortality for tumors larger than 2.5 cm. Sixty to 70% of patients with perineural invasion had no symptoms. Interestingly, the use of adjuvant radiation therapy for SCC with perineural involvement is completely anecdotal, as there are no studies to prove its value.

Carcinoma of the External Ear

Mohs *et al.*[24] reported his results using Mohs surgery for excision of carcinoma of the external ear. He noted that in determinate cases, 5-year cure rates were 97.1% for BCC (902 of 929) and 92.3% for SCC (515 of 558). When indeterminate cases, or cases where surgical margins were unclear, were added to the case totals the cure rates were 92% for BCC (902 of 973) and 89% for SCC (515 of 578). Also published were the RRs according to therapeutic modality (Table 9).

Carcinoma of the Eyelid

Mohs *et al.*[25] reported their results using Mohs surgery for excision of eyelid cancers and it was shown to have a cure rate of 98% at 5-year follow up (1385/1414), including 359 indeterminate cases. Size of the lesion was considered to be a determining factor with a cure rate of 99.6% for tumors less than 1 cm and a cure rate of only 80% in cases where the BCC was greater than 3 cm. In cases of BCC occurring on the lateral canthus, a cure rate of 91% was reported. The same study looked at SCC of the eyelid and reported a 98.1% cure rate at 5 years in cases treated with Mohs surgery (158 of 161) with 52 indeterminate cases included. Again, size was a significant determinant of treatment success with a cure rate of only 50% for lesions greater than 3 cm. Squamous cell carcinoma of the lateral canthus treated with Mohs surgery had a reported cure rate of 87.5%.

Table 9 Carcinoma of the external ear

Treatment modality	< 5-year RRs (%)	> 5-year RRs (%)
Non-Mohs modalities	16.10	18.70
MMS	NA	5.30

MMS = Mohs micrographic surgery; RR = recurrence rate.

Leshin, Anscher, and Sutton compared the efficacy of Mohs surgery to radiotherapy for the management of periocular BCC.[26] Mohs surgery had a cure rate of 98.1% in 268 patients with a follow up of 1–5 years. Five to 10 percent of patients reported some complication related to treatment. Radiation therapy cure rate at 3 years was 94% in a multicenter, overall controlled trial. Thirteen percent of radiotherapy patients experienced complications. The authors recommended surgery for small primary lesions, Mohs surgery for recurrent tumors, and radiation therapy for medium to large primary lesions.

Malignant Melanoma

Zitelli *et al.*[27] evaluated the depth and diameter of malignant melanoma in 533 lesions treated with Mohs surgery. Eighty-three percent of the lesions were excised with 6-mm margins and 95% with 9-mm margins. A surgical margin of 1.2 cm was needed to remove 97% of cases. Melanomas larger than 2–3 cm required wider margins than their smaller counterparts. Margins were also wider for lesions occurring on the head, neck, hands and feet as compared with the margins required for lesions occurring on the trunk and proximal extremities. The minimal acceptable margin for melanoma of the head, neck, hands, and feet was 1.5 cm. Malignant melanoma larger than 3 cm needs 2.5-cm surgical margins.

Snow *et al.*[28] studied 113 cases of cutaneous melanoma treated with Mohs surgery. Thirty-three cases examined as fresh tissue had a mean thickness of 1.59 mm, a median thickness of 0.7 mm, and a 5-year survival rate of 84.7%. Eighty-five cases examined as fixed tissue had a mean thickness of 1.16 mm, 0.75-mm median thickness, and a 5-year survival rate of 87.1%.

Mohs surgery has also been used for treatment of nail apparatus melanoma. Brodland *et al.*[29] reviewed 14 of these cases consisting of nine females and five males and ranging in depth from 0 to 3.3 mm (average 1.38 mm). Tumor-free margins were achieved in all cases. With a mean follow up of 7.7 years there were nine of 14 patients who remained disease

free, three had local recurrences, and one was alive with positive nodes. Two patients died with metastases and two died of unrelated conditions but without melanoma. Overall survival was 78.5%.

Diagnosis of melanoma by frozen section, as is used in Mohs surgery, was shown to have 100% sensitivity and 90% specificity (n = 221 specimens from 59 patients) as reported by Zitelli in 1997.[27] A more recent study conducted by Barlow in 2002[30] showed a 59% sensitivity and 81% specificity in 50 of 154 difficulty-to-interpret frozen sections. Specific immunostatins can aid in the diagnosis of melanoma. S-100, an acidic calcium and zinc binding cytoplasmic protein, is sensitive for the dermal but weak for the epidermal component of melanoma.[31] It also identifies benign melanocytes, dendritic cells, histiocytes, and Schwann cells.[32] Mel-5 is an immunostain which recognizes gp75 and is useful in the diagnosis of lichen planus, keratosis, and pigmented BD.[33] HMB-45 recognizes the 30–35-kDa protein in stage II–III melanosomes of neoplastic melanocytes.[34,35] It has a 97% sensitivity but is negative in spindle-cell, desmoplastic, and neurotropic melanoma. Melan-A recognizes 22-kDa cytoplasmic melanosome-associated differentiation antigen. This antigen is present in 80–100% of melanomas and is probably the most consistently crisp stain.[36,37]

Appropriate surgical margins for the treatment of lentigo maligna have also been studied. Robinson[38] reported that margins less than 6 mm removed only 23% of 16 LM. Margins up to 1.3 cm were required to remove all tumors. Zalla *et al*.[39] described an average surgical margin of 8.3 mm required for clearance for *in situ* and a margin of 11.1 mm for invasive melanoma. In contrast to Zitelli, only 50% were clear with 6-mm margins. In Cohen's 1998 study,[40] 26 patients with lentigo maligna and 19 patients with lentigo maligna melanoma had their lesions excised and examined with frozen sections followed by rush permanent sections. Mean subclinical extension was 13 mm. There was a 97% cure rate with only one recurrence at a mean follow up of 58 months.

The vertical dimension in the surgical treatment of cutaneous malignant melanoma was discussed in the *European Journal of Plastic Surgery* in 2001.[41] Forty-eight cases were examined and found to have a mean Breslow of 1.6 mm. After a 10-year follow up 21% of cases had local or distant recurrence (10 of 48). Survival was better for cases with a deep margin greater than 3 mm.

Other Cutaneous Tumors

Microcystic adnexal carcinoma

Snow *et al*. followed seven cases of microcystic adnexal carcinoma treated with Mohs surgery at the University of Wisconsin and reviewed an additional six cases previously reported. All tumors were located on facial skin (nine in upper lip) and three cases had perineural extension. There were no recurrences after follow up ranging from 1 to 8 years. Since 1972 there have been 73 reported cases of microcystic adnexal carcinoma treated with Mohs surgery, 39 of which had a follow up of greater than 2 years. Success rate was 89%, as four of the 39 cases had local recurrence. Seventy-five cases of microcystic adnexal carcinoma treated with non-Mohs modalities reported a local recurrence rate of 47%.[42]

Table 10 Recurrence rates

Tumor	MMS RR, Huether *et al.*[43]	MMS RR in the literature	Non-MMS RR in the literature
DFSP	1/33 (3%)	4/169 (2.4%)	100/489 (20%)
AFX	2/29 (6.9%)	0/19 (0%)	4/25 (16%)
MFH	3/7 (43%)	2/25 (8%)	86/196 (44%)
LMS	1/7 (14%)	NA	3/21 (14%)
SCT-NOS	0/12 (0%)	NA	NA

AFX = atypical fibroxanthoma; DFSP = dermatofibrosarcoma protuberans; LMS = leiomyosarcoma; MFH = malignant fibrous histiocytoma; MMS = Mohs micrographic surgery; RR = recurrence rate; SCT-NOS = spindle cell tumor not otherwise specified.

Spindle cell tumors

In 2001, Huether *et al*.[43] reported his experience treating spindle cell tumors and compared it with the literature, as reported in Table 10.

Leiomyosarcoma

Leiomyosarcoma, a relatively rare tumor, comprises 7% of soft tissue sarcomas and arises from the arrector pili muscle of sweat glands or subcutaneous blood vessels. Cutaneous leiomyosarcomas occur most commonly on the extremities and there is a tendency to involve proximal extensor surfaces. In a few instances, leiomyosarcoma has developed at the site of previous trauma or at areas exposed to radiotherapy.[44,45] Subcutaneous leiomyosarcoma is situated in the subcutaneous fat but may also extend into the overlying dermis. This type is most often vascular in origin, with aggregates of atypical smooth muscle cells that intertwine without the fascicular pattern observed in dermal leiomyosarcoma. The subcutaneous type may also demonstrate, in contrast to the cutaneous type, a pseudocapsular formation of compressed tumor cells with connective tissue fibrous stroma at its borders.[46] Median age of 40–70 years and there is no difference in sex or race distribution. They are usually solitary lesions with slow growth and occur most frequently on the extremities followed by the trunk and face. Clinically they appear as a red, blue, or tan nodule or ulceration and are painful in 30% of cases. Immunohistochemistry shows leiomyosarcomas to be actin positive, desmin positive or negative, and vimentin positive. Treatment with wide local excision has a historical recurrence rate of 40–60%. Bernstein *et al*.[47] reported a recurrence rate of 14%

Table 11 Recurrence rates for atypical fibroxanthoma (AFX) treated with a wide excision[48]

Study	Recurrence rate
Fretzin and Helwig	9%
Kempson and McGravan	9.50%
Kroe and Pitcock	10%
Dahl	1/43 MR at 5 years
Hausner	21%
Davis *et al.*	12%

MR = metastasis rate.

Table 12 Recurrence rates for atypical fibroxanthoma (AFX) treated with Mohs surgery[48]

Study	Recurrence rate	Mean follow up
Brown/Swanson	*n* = 17 MFH, AFX	
Dzubow	*n* = 3.0% RR	11 months
Davis	*n* = 19.0% RR	29 months

MFH = malignant fibrous histiocytoma; RR = recurrence rate.

(three of 21) in their 1996 study. Metastases are rare but subcutaneous lesions metastasize to the lung and bone 30–60% of the time. Mohs surgery for the treatment of leiomyosarcoma in a small series and case reports demonstrates a recurrence rate of 14%.[43]

Atypical fibroxanthoma

Atypical fibroxanthoma is a tumor arising most commonly in sun-exposed areas of elderly people, where it presents as a rapidly growing nodule. The lesion is a pink to translucent asymptomatic nodule, generally 1–2 cm in diameter, and is often accompanied by ulceration. They are often mistaken for BCCs because of the ulceration, translucent appearance, and location on sun-exposed skin. Histologically, these lesions have large epitheliod and spindle cells and multinucleated giant cells are often present. The course of atypical fibroxanthoma is usually benign and local excision is the treatment of choice.[48] Recurrence rates range from 9% to 21% for traditional surgery and 3% to 19% for Mohs surgery, as shown in Tables 11 and 12.

Merkel cell carcinoma

Merkel cell carcinoma, originally described by Toker,[49] is an uncommon malignant neuroendocrine carcinoma of the skin which clinically resembles a small cell carcinoma of the lung in its malignant potential. Immunohistochemistry for Merkel cell carcinoma is shown in Table 13. Recommended therapy for Merkel cell carcinoma is surgical excision with 1–3-cm margins with intraoperative frozen sections or Mohs surgery. There is a 20–100% recurrence rate with surgery alone and a 10–40% recurrence rate with adjuvant radiation.[50] Sentinel node biopsy is also recommended. The Merkel cell carcinoma database includes 66 cases from 1945 to 1995. Fifty-five cases were men and 11 were women. A 2001 analysis[51] of 18 of these cases containing adequate data showed that survival rates and loco-regional control was similar for 1, 2, and > 2-cm margins. Post-operative radiation improved both local and regional RRs. Regardless of therapy, distant disease developed in 36% of patients. A study conducted at the University of Alabama from 1986 to 2000[52] included 16 patients (12 men, four women), three of which were immunosuppressed. Five of the 16 patients also had a history of SCC. Adjuvant radiation was used in seven of 16 cases. Local recurrence occurred in 30%, and seven of the 16 cases had metastases. The mean survival was 97 months for stage I disease and 15 months for stage II disease.

Another study conducted at the Mayo Clinic from 1975 to 1995 compared Merkel cell carcinoma treated with surgical excision with those treated with Mohs surgery.[53] At a 60-month follow up, 31.7% (13 of 41) of the cases treated with surgical excision experienced local recurrence and 48.8% (20 of 42) had regional metastases. With a mean follow up of 36 months, the cases treated with Mohs surgery had an 8.3% (one of 12) local RR and a 33.3% (four of 12) regional metastasis rate.

A retrospective review of 45 stage I Merkel cell carcinoma treated with Mohs surgery with or without adjuvant radiation was published in 2002.[54] There was no difference in overall survival or disease-free survival. Forty-eight percent of cases required margins greater than 1 cm, 25% would have been inadequately excised with 2-cm margins, and 12% would have been incompletely excised with 3-cm margins. Limitations of this study included the fact that this was a retrospective study of 45/54 cases which only included cases that

Table 13 Immunostains for Merkel cell carcinoma

Test	Sensitivity	Specificity	Excludes	Does not exclude
NSE	50–100%	Low	Most cancers	Carcinoid, lung small cell
CK	Up to 100%	Moderate	Lymph, MM	Carcinoid, lung small cell
Neurofilament	Up to 100%	Moderate	Lymph, MM	Carcinoid, lung small cell
EMA	90%	Low		Most epithelial CA
S-100	Low	Moderate	MM	

NSE = neuron specific enolase.

achieved tumor-free margins during Mohs surgery. There was also insufficient follow up ($n = 6$), unresectable primary lesions ($n = 2$), and synchronous metastases ($n = 1$). Radiation was performed within 4 months of surgery (surgical site with or without nodal basin) and three of the 20 patients in the radiation group also received chemotherapy. The mean follow-up time was relatively short at 28 months.

Brissett *et al.*[55] looked at 22 patients with Merkel cell carcinoma at the Mayo clinic between 1981 and 1998. At 2 years, patients treated with Mohs surgery ($n = 6$) had a survival rate of 33%, cases treated with surgical excision ($n = 8$) had a survival rate of 68%, and survival rate of those cases treated with surgical excision and lymph node dissection ($n = 8$) was 100%.

A 1999 study[56] looked specifically at Merkel cell carcinoma of the lip, which account for 9% of Merkel cell carcinomas. Twenty-six percent of cases experienced recurrences after surgery and radiation and 22% had nodal metastases. Mortality was reported as 67% in cases with positive nodes as compared with 27% for cases without nodes. The recommendation of this study for the treatment of Merkel cell carcinoma was surgery, sentinel lymph node mapping, and postoperative radiation.

Merkel cell carcinoma of the eyelid accounts for 10% of cases. After treatment 30% of cases had a local recurrence, 21–66% experienced nodal metastases, and 30% had distant metastases. Surgery with margins greater than 5 mm and frozen sections had no recurrences or metastases at a 45-month follow up.[57,58]

A 2001 study[59] identified prognostic and therapeutic implications of sentinel lymphnodectomy and S-staging in Merkel cell carcinoma by evaluating five patients with Merkel cell carcinoma of the head and neck, trunk or extremities. Four out of five patients had positive sentinel lymph nodes. The patient with negative sentinel node findings was alive and recurrence free at 21 months. It was noted that penetration of less than 1 mm into the node is less likely to result in further nodal involvement.

In summary, the 5-year survival rate for Merkel cell carcinoma is between 50 and 60%. Local control can be achieved in 60–90% of cases with surgery plus radiation and recurrent local disease can be eradicated in 50% of cases. Merkel cell carcinoma with lymph node involvement has a 5-year survival rate of 48%. Distant metastases occur in 30% of cases. The recommended management of Merkel cell carcinoma is surgery with sentinel lymph node examination and adjuvant radiation therapy.

Drawbacks and Limitations of Mohs Surgery

In theory, if unifocal tumors are treated with Mohs surgery and 100% of the margins examined, then there should be no recurrences. Rigel, Robins, and Friedman[60] reviewed data from 5020 patients and 7010 BCCs to identify factors that predict recurrence after Mohs surgery. Of the cases 2960 had a 5-year follow up and overall recurrence was 2.6%. They established a recurrence index score based on the following characteristics and grouped patients into the recurrence risk groups described in Fig. 1 and Table 14.

- Sex
  - Male = 15
  - Female = 0
- Age
  - Over 50 = 0
  - Under 50 = 22
- Size of lesion
  - < 1 cm = 10
  - 1–1.9 cm = 16
  - 2–2.9 cm = 19
  - 3–3.9 cm = 21
  - 4–4.9 cm = 50
  - ≥ 5 cm = 56
- Number of stages
  - ≤ 6 = 0
  - ≥ 7 = 44
- Previous Treatment
  - None = 0
  - Any = 12
- Location
  - Retroauricular = 134
  - Ear = 43
  - Chin = 43
  - Periorbital = 40
  - Scalp = 37
  - Nose = 30
  - Cheek = 24
  - Perioral = 19
- Curettage/Electrodessication
  - ≥ 3 times, add 18 points
- Excision
  - ≥ 2 times, add 24 points

Figure 1 Recurrence index

Table 14 Risk index

Group	Score	% of Cases	No recurrence	Recurrence	Recurrence (%)
No risk	10–34	4.10%	78	0	0
Low risk	35–54	22.50%	424	3	0.70
Average risk	55–99	60%	1107	29	2.60
High risk	≥ 100	13.30%	226	25	10

Hruza[61] reviewed 2414 cases treated with Mohs surgery and noted a 1.4% RR (33 of 2414). The recurrences were 83% BCC (25 of 33), 7% basosquamous (two of 33), 7% squamous (two of 33), and 3% microcystic adnexal carcinoma (one of 33). Thirty-even percent of the tumors were reported to be new primaries and 63% were recurrent. The mean time to recurrence was 38.5 months with a range from 5 to 104 months. Twenty percent of these recurrences occurred after 5 years. In 23 of the 30 local recurrences a cause was identified. Of the recurrences 20% still had the tumor when the slides were reviewed (six of 30), 7% with inflammation identified that was not excised (two of 30), 30% with missing epidermis on the slides (nine of 30), 10% with a large dermal defect (three of 30), and 10% with incorrect map/excision (three of 30). The cause of recurrence was not identified in 7 of 30 cases and this raises the possibility of noncontiguous lesions.

Katz *et al.*[62] reported that dense inflammation does not mask residual primary BCC during Mohs surgery. They reviewed

Table 15 Curettage electrofulguration

Author	Treatment	5-year cure rates
Knox *et al.*[65]	CE × 2	96.40%
Knox *et al.*[68]	CE × 2	97.50%
Kopf *et al.*[69]	Unsupervised trainees	81%
	Supervised trainees	90.40%
	Specialists	94.30%
Spiller and Spiller[70]	CE × 1–3	97%
Rowe *et al.*[2]	Review article	92.30%

25 cases of BCC with dense inflammation. Hemotoxylin and eosin and Ber-EP4 showed no cases of residual BCC. By cutting deeper into the block of tissue they were able to assure clearance rather than obtaining another Mohs layer.

Therapeutic Alternatives To Mohs Surgery

Lawrence[63] reported in 1993 that surgical excision is as effective as Mohs surgery for primary BCC (98% cure rate). However, he noted that surgical excision is much less effective than Mohs surgery for recurrent tumors (13% vs. 3.5% RR).

Curettage/Electrosurgery[64–71]

Reported 5-year cure rates for curettage/electrosurgery are shown in Table 15.

Curettage alone had a 90.3% cure rate for 310 BCCs, 91.5% cure rate for 328 BCCs less than 15 mm, and 81.1% cure rate for 345 BD. When curettage was followed with electrosurgery there was a 98% cure rate for low-risk BCCs less than 2.5 cm in size. A cure rate of 96.6% was reported for 236 BCCs and 100% cure rate for 26 SCCs. When curettage was followed by cryosurgery there was a 98% cure rate for BCCs < 2 cm and 90.6% cure rate for BCCs > 2 cm. Thirty-nine BCCs, three BD, and one basosquamous carcinoma of the ear were treated with only one recurrence. In 61 BCCs of the nose there was a 100% cure rate, making this treatment an available alternative to Mohs surgery.

Cryosurgery

Kuflik[72] reviewed 5-year cure rates for cutaneous malignancies treated with cryosurgery alone. He found that 98.4% (n = 3540) of lesions were satisfactorily treated with cryosurgery alone. Ninety-nine percent of primary lesions (n = 684) and 88.4% of recurrent BCCs were recurrence-free. Other reported cure rates for cryosurgery include:

Cryosurgery	5-year cure rates
Zacarian[73]	97.3% (n = 4228)
Graham[74]	98.2% (n = 3593)
Holt[75]	97% (n = 279)
Goncalves[76]	94.2% (n = 52)

Table 16 Radiation therapy

Institution	Eyelid CA	BCC (%)	Cure rates (%)
Royal Marsden Hospital, London	689	91	93
Princess Margaret Hospital, Toronto	1166	91	95
Institut Curie, Paris	850	82	96
Massachusetts General Hospital	300	100	97

Table 17 Radiation therapy

Institution	Nose CA	Cure rates (%)	Necrosis (%)
Group European Curietherapy	1612	94	2
NYU	237	91	NS
Princess Margaret Hospital, Toronto	110	94	2
Wadsworth Medical Center, LA	350	95	0
Henri Mondor Hospital, Creteuk	468	97	2

Nordin and Stenquist[77] reported 5-year results of 100 consecutive auricular nonmelanoma skin cancers treated with curettage and cryosurgery. Their study excluded recurrent BCC, SCC, and morpheaform BCC. There was only one reported recurrence and no metastases at 5-year follow up. Acceptable cosmetic results were achieved in all cases.

Curettage and surgical excision

Another alternative to Mohs surgery is combined curettage and excision, as reported by Johnson *et al.*[78] They reviewed 403 primary BCCs, 186 of which had inadequate follow up or incomplete excision (n = 12). Five of 205 patients experienced recurrence (2.4%) and there was a total failure rate of 7.8% (12 inadequate excisions, five recurrences).

Radiation Therapy

Radiation therapy is another treatment modality used in the treatment of nonmelanoma skin cancers. Morrison *et al.*[79] reviewed cases occurring on the eyelid and nose treated with radiation therapy. Their results are described in Tables 16 and 17.

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