Mohs Micrographic Surgery: Past, Present, and Future

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BACKGROUND Mohs micrographic surgery (MMS) is a frequently used technique that provides total margin visualization for treatment of skin neoplasms.

OBJECTIVE To provide a comprehensive review of MMS literature, focusing on its origins, evidence behind present-day uses of MMS, and future directions.

METHODS A literature search was conducted using PubMed to identify articles pertaining to MMS.

RESULTS The fresh frozen technique led to widespread use of MMS in the 1970s. One randomized controlled trial and several large prospective studies have demonstrated low recurrence rates for treatment of non-melanoma skin cancer (NMSC). MMS, when compared with surgical excision, also achieved a statistically significant higher cure rate for treatment of recurrent NMSC. Studies have demonstrated low recurrence for the treatment of melanoma and melanoma in situ with MMS. MMS has also been shown to effectively treat several rare cutaneous neoplasms. The future of MMS is likely to include the adoption of noninvasive imaging, immunostaining, and digital technology.

CONCLUSION Mohs micrographic surgery is an effective treatment modality for numerous cutaneous neoplasms. It has achieved statistically significant superiority to surgical excision for the treatment of recurrent and high-risk NMSC. The future is likely to see increased use of noninvasive imaging, immunostaining, and digital technology.

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Past

While performing research as a medical student at the University of Wisconsin-Madison, Dr. Frederic Edward Mohs conceived the surgical technique that now bears his name. Mohs worked in the laboratory of Professor Michael F. Guyer, head of Zoology at the University of Wisconsin. The 2 collaborated on research to examine leukocyte infiltration in cancerous and normal tissue.[1] During his experiments, he observed that fixation with 20% zinc chloride solution allowed the skin to retain its normal architecture, and thus the Mohs-fixed tissue technique was born. In 1936, after patenting a 20% zinc chloride paste formulation (to produce more controlled fixation), Mohs began to use the paste to treat patients with skin cancer.[2] He performed a layer-by-layer removal to efficiently and effectively examine the entire tumor margin.[1]

Although Mohs technique was effective at removing skin cancers, the fixation of tissue had many drawbacks. Most notably, the process was painful; it was once described as worse than the pain of renal colic.[3] Tissue fixation resulted in sloughing for days, followed by slow granulation of wounds. Any post-Mohs repairs needed to be delayed until sloughing of dead tissue was complete. People who were self-proclaimed "healers" were touting similar fixatives as quick cancer cures, but did not perform microscopic examination of tissue, which led to many recurrences. Not surprisingly, the "healers" generated skepticism around the use of fixatives for treatment of skin cancers.[2]

It was not until 1953 that Mohs first ceased using in vivo tissue fixation and used fresh frozen tissue in an attempt to speed-up his technique. The process was faster, local anesthesia reduced the pain, and there was

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less irritation to nearby structures. Histologic margins were adequately examined, and the tumor was confirmed to be removed. Another dermatologist, Dr. Theodore A. Tromovitch, was frustrated with complaints of pain from his patients in California and took note of the improvements with use of fresh frozen tissue. In 1970, at the American College of Chemosurgery meeting, Tromovitch presented successful use of fresh frozen tissue for removing skin cancers with the modified Mohs technique. Dermatologists realized the benefits of using fresh frozen tissue in the coming years, and this transition subsequently led to a more widespread adoption of Mohs surgery.[3] Over the years, the name for the procedure has undergone several iterations, eventually landing on the commonly used Mohs micrographic surgery (MMS).

Present

Nonmelanoma Skin Cancer

Moving forward into the 21st century brought an uptick in the incidence of cutaneous nonmelanoma skin cancers (NMSCs). From 1992 to 2012, there was a 100% increase in NMSC incidence in the Medicare population. In 2012, an estimated 5,434,193 NMSCs were treated.[4] Not surprisingly, the utilization of MMS has similarly trended upward.[5] MMS is now used for 1 of every 4 NMSCs, and has increased 400% between 1995 and 2009.[6] Several studies have investigated the utility of MMS. The preeminent studies, conducted within the past 30 years and involving large prospective cohorts of patients, will herein be reviewed.

One of the only prospective, randomized trials comparing recurrence rates of MMS to standard excision, conducted by Smeets and colleagues,[7] focused on basal cell carcinoma (BCC) of the face. Both primary and recurrent BCCs were included in the study. The authors did not find a statistically significant difference in recurrence rates when comparing treatments, although the absolute numbers favored MMS. During 30 months of follow-up, 5 primary tumors (3%) recurred after surgical excision, compared to 3 tumors (2%) treated with MMS (95% confidence interval [CI], 2.5%–3.7%, $p = .724$). Of the treated recurrent BCCs, 3 (3%) re-recurred after surgical excision and none re-recurred after MMS after 18 months of follow-up (95% CI, 2.0%–5.0%, $p = .119$). The authors concluded that the study might not have been powered well enough to detect a significant difference in treatments.

Results of a 5-year follow-up on the study by Smeets and colleagues showed a statistically significant advantage for MMS compared to surgical excision for treatment of recurrent BCCs, with 2 (2.4%) tumors recurrent after MMS and 10 (12.1%) recurrent after surgical excision ($p = .015$). Outcomes from treatment of primary BCC did not achieve statistical significance. There were 4 (2.5%) and 7 (4.1%) recurrences for MMS and surgical excision, respectively, in the primary BCC group ($p = .40$).[8] Long-term data from the same cohort of patients were collected, and the 10-year cumulative probability of recurrence was found to be 4.4% for MMS and 12.2% for surgical excision for primary BCC ($p = .10$). For recurrent BCC, the 10-year cumulative probability of recurrence was found to be 3.9% after MMS and 13.5% after surgical excision ($p = .023$). Results emphasized the need for long-term follow-up because over half of all recurrences in the poststandard excision primary BCC group occurred more than 5 years after treatment.[9]

A large prospective study on MMS outcomes for BCC was conducted in Australia using the Australian Mohs Database. The database prospectively collected data from patients who underwent MMS from 1993 to 1999 with an Australian fellowship-trained Mohs surgeon. Three thousand three hundred seventy patients completed the 5-year follow-up; 56% of tumors were primary and 44% were recurrent. Recurrence rates for BCC treated with MMS were 1.4% for primary tumors and 4.0% for recurrent tumors. Nearly all (98.4%) tumors were located on the head and neck, and several tumors had high-risk features. The authors concluded that the low recurrence rates for both primary and recurrent BCCs treated with MMS confirmed the value in removing tumors with margin control.[10]

The same Australian Mohs Database was used to evaluate the treatment of squamous cell carcinoma

(SCC) with MMS. There were 1,263 patients who underwent MMS; 772 (61.1%) patients had primary tumors and 491 (38.9%) had recurrent tumors. 96.5% of tumors were located on the head and neck. Of the 381 patients who completed the 5-year follow-up, the overall recurrence rate of 3.9% (15 of 381 patients) was low. The recurrence rate was 2.6% for primary tumors and 5.9% for patients with recurrent SCC ($p < .001$). The tumors in this study were higher risk, with a high percentage of poorly differentiated large tumors located on the head and neck, and many were recurrent cases. The study reaffirmed that MMS offers the highest cure rate for high-risk primary and recurrent SCC.[11]

Another large, prospective study conducted in the United States by Chren and colleagues included 1,585 primary NMSCs in 1,253 patients treated in 1999 or 2000. The NMSCs were treated with either MMS or other common treatments, such as excision or destruction. Both BCCs and SCCs were included. Recurrence rates after MMS, surgical excision, and electrodessication and curettage were compared. The overall median follow-up time after treatment was 7.4 years (3.0–8.8). Follow-up was available for 1,174 patients. The overall 5-year recurrence rate (95% CI) was 3.3% (2.3–4.4), with a rate of 4.9% (2.3–7.4) for destruction, 3.5% (1.8–5.2) for excision, and 2.1% (0.6–3.5) for MMS. There was no significant difference between treatments after adjusting for risk factors. Other than the effectiveness of all treatments (at least 95%), no conclusions could be drawn regarding specific choice of therapeutic intervention.[12] A follow-up to the above study looked at recurrence rates of tumors judged appropriate for MMS under the Appropriate Use Criteria.[5,13] Although an improvement was observed in recurrence rates for tumors meeting Appropriate Use Criteria that were treated with MMS, the absolute difference in recurrence when compared to excision, destruction, and other modalities was less than expected.[13]

Several studies have demonstrated that histologic margin control with MMS for treatment of both BCC and SCC has a beneficial impact on recurrence rates.[7–13] The most significant reduction in recurrence rates occurs in scenarios where tumors are recurrent or display other high-risk features.[8,9] If MMS is not an option, primary BCCs or SCCs can be treated with surgical excision in most cases while still achieving a reasonably low recurrence rate. Further studies that are randomized and adequately powered to detect differences among treatments are needed (Figures 1–4).

Melanoma

Similar to NMSC, the incidence of melanoma is on the rise in the United States. Incidence rates doubled from 1982 to 2011.[14] Seventy-six thousand three hundred eighty new cases of invasive melanoma were estimated to occur in 2016, along with 68,480 new cases of in situ melanoma (MIS).[15] This review will concentrate primarily on MIS (Figure 5). Current recommendations for treatment of MIS are for wide local excision (WLE) with a margin between 0.5 and 1.0 cm.[16] Several studies demonstrate that successful removal of MIS often requires margins greater than anticipated (especially on sun-damaged skin). This has resulted in further exploration of removal with complete margin examination using MMS and similar techniques.[17–19]

Although still infrequently used for the treatment of melanoma, use of MMS for melanoma is on the rise. Use of MMS for invasive melanoma and MIS in the United States increased by 60% from 2003 to 2008.[20] One reason for the lag in adoption of MMS for treatment of melanoma is the recognized difficulty in the identification of melanoma on frozen sections.[21] However, a recent study by Bene and colleagues examined the accuracy of melanoma detection on

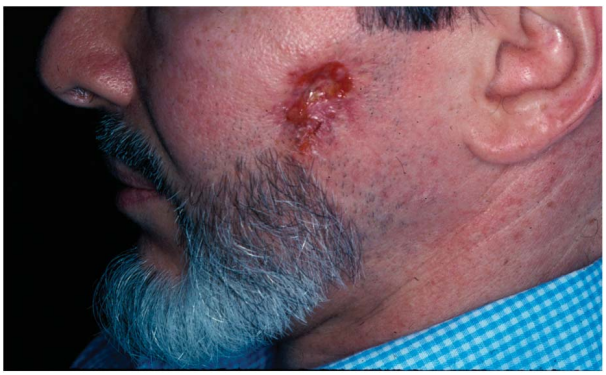

Figure 1. Multiple recurrent basal cell carcinoma before treatment with Mohs micrographic surgery.

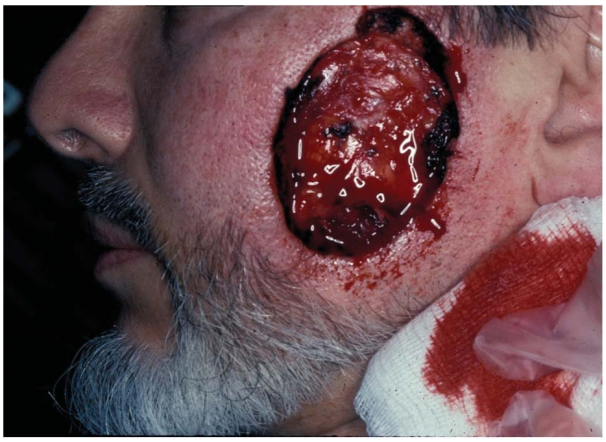

Figure 2. Patient in Figure 1 after 4 stages of Mohs micrographic surgery.

frozen sections with hematoxylin and eosin staining and showed promising results. After treatment with MMS, the final margin was evaluated using paraffin-embedded sections. Results showed a 95.1% accuracy in the prospective cohort of 167 patients who were treated with MMS for MIS.[22] Use of rapid immunostaining of frozen sections during MMS has also enhanced the identification of MIS.[23] Studies of various immunostains to better detect melanoma have thus far corroborated that melanoma antigen recognized by T cells 1 (MART-1) is superior to other immunostains.[24]

There have been no randomized clinical trials to assess the use of MMS for treatment of MIS. A recent retrospective study of a prospective database compared

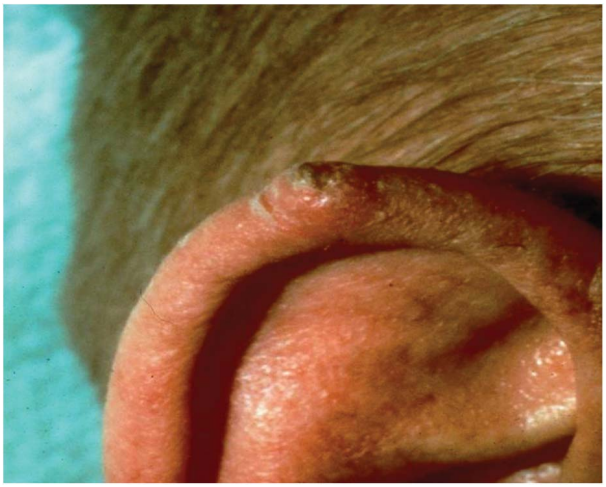

Figure 3. Squamous cell carcinoma on the helix before Mohs micrographic surgery.

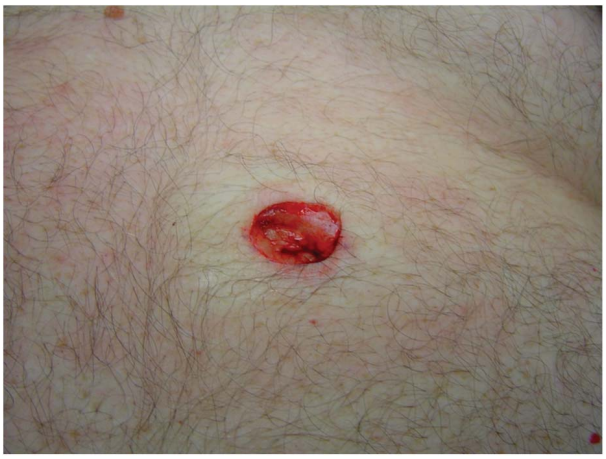

Figure 4. Defect after 2 stages of Mohs micrographic surgery.

WLE to MMS for treatment of MIS. All anatomical sites were represented, but sites on the face/neck/scalp were predominant (88.5%). There were no significant differences found in overall survival, melanoma-specific survival, or recurrence rates between the 2 treatments.[25] A 2007 review of MMS for treatment of MIS recommended the use of MMS for treatment of ill-defined lesions. The authors emphasized evaluation of the entire specimen, including margins, to rule out invasive disease, which was found as frequently as 1 in every 4 cases.[26] Etzkorn and colleagues used a specific tissue-processing methodology, combined with MART-1 immunostaining, with excellent results in the treatment of in situ and invasive melanomas with MMS. There was an overall 0.34% (2/597) recurrence rate with a mean follow-up of 2.8 years. The technique examined the peripheral and deep margins en face, and used bread loafing to examine the debulking excision for possible upstaging of the tumor. 5.5% (34/614) of tumors were upstaged, of which 97% (33/34) were detected by the Mohs surgeon, thereby allowing sentinel lymph node biopsy (if necessary) before reconstruction.[27] Further studies are needed to compare recurrence rates, survival outcomes, and functional/cosmetic outcomes of MMS to WLE before there is more widespread adoption of MMS for treatment of melanoma.

Rare Nonmelanoma Skin Cancer

In 1982, Dr. Neil Swanson accurately predicted the expansion of MMS for treatment of numerous types of cutaneous neoplasms beyond NMSC and melanoma.[3]

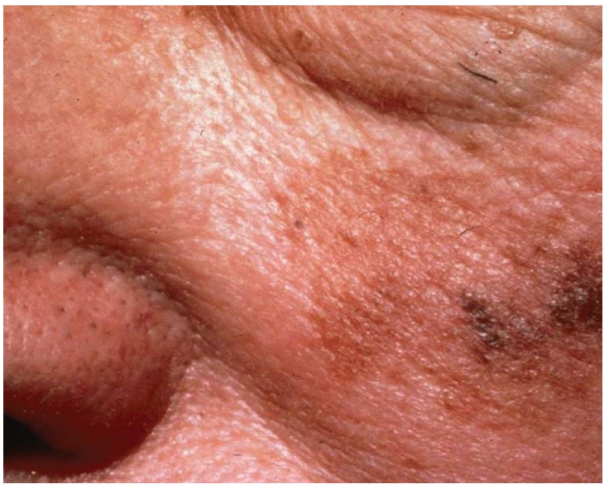

Figure 5. Melanoma in situ before Mohs micrographic surgery.

There are ever increasing reports of MMS for treatment of less common cutaneous neoplasms. Because of their rarity, most reports are case series at single institutions. Ghareeb and colleagues[28] identified that MMS is currently underutilized for the subset of rare skin cancers and can lead to improved clearance of tumors and lessen the likelihood of receiving radiotherapy. The following sections will highlight reports of MMS used for treatment of select rare tumors.

Dermatofibrosarcoma Protuberans

Dermatofibrosarcoma protuberans (DFSP) is a rare tumor with low metastatic potential but high reported recurrence rates after WLE. Reports of recurrence rates range from 11% to 60%.[29] A retrospective review by Lowe and colleagues compared DFSP treated with MMS to those treated with WLE at the Mayo Clinic. Results showed a significant reduction in recurrence with MMS treatment, as 2 (3.0%) recurrences were found, compared to 28 (30.8%) recurrences observed with WLE. Follow-up periods and preoperative lesion sizes were similar between the 2 groups.[30] A systematic review comprising 23 nonrandomized trials was published in 2012; the synthesis of data showed moderate-quality evidence (Level B) for comparative studies and low-quality evidence (Level C) for noncomparative studies. For comparative studies, recurrence rates were lower for MMS (1.11%; 95% CI, 0.02%–6.03%) compared to WLE (6.32%; 95% CI, 3.19%–11.02%). The recurrence rate after MMS for noncomparative studies was 1.03% (95% CI, 0.37%–2.22%). The authors concluded that the data supported the use of MMS as treatment for DFSP owing to the lower recurrence rates, but emphasized that high-quality trials comparing 5-year recurrence rates of MMS to WLE were lacking.[29]

Extramammary Paget Disease

Extramammary Paget disease (EMPD) is another rare neoplasm that is slow growing but has indistinct margins and, therefore, high recurrence rates are observed after WLE. Extramammary Paget disease is usually confined to the epidermis, but deeper invasion begets a poorer prognosis.[31,32] Analysis of a retrospective cohort of 207 patients with EMPD treated with WLE and MMS at the Mayo Clinic found no statistically significant differences in outcomes, but recurrence-free survival rates were better with MMS (91% for MMS vs 66% for WLE).[32] An older study, also using patients treated at the Mayo Clinic in both Minnesota and Arizona, showed favorable results for treatment of EMPD with MMS. One of 12 patients experienced a recurrence after MMS (8%), compared to 18 of 83 recurrences (22%) after WLE. However, follow-up time after MMS was 24 months, as compared to 65 months for WLE.[31]

Merkel Cell Carcinoma

Merkel cell carcinoma (MCC) is a rare, aggressive cutaneous malignancy. Current National Comprehensive Cancer Network (NCCN) guidelines recommend sentinel lymph node biopsy in combination with WLE for all tumors.[33] A recent publication compared outcomes of WLE and MMS for MCC derived from a nationally represented US population database. The study used the Surveillance, Epidemiology, and End Results program. Of 2,610 cases of MCC, 2,039 were treated with WLE and 174 were treated with MMS. The authors found no significant difference in overall and MCC-specific survival between WLE and MMS. However, there was strong evidence that MMS is a viable option for treatment of MCC, particularly for early-stage tumors on the head and neck. The authors also noted that Mohs surgeons should follow NCCN guidelines for sentinel lymph node biopsy because

findings showed that patients who had MMS were less likely to undergo nodal biopsy.[34] Another recent retrospective review of 22 patients with MCC treated with MMS at a single institution showed favorable outcomes, with an overall local recurrence rate of 5% (1/22).[35]

Sebaceous Carcinoma

Sebaceous carcinoma is derived from sebaceous glands occurring anywhere on the skin, but has a predilection for the periocular region. Sebaceous carcinoma can be aggressive and has a 5-year mortality rate of 18% to 30%. Retrospective reviews of treatment of sebaceous carcinoma with MMS have shown reduced recurrence rates as compared to the fairly high recurrence rates observed with WLE (as high as 36% within 5 years).[36] Of 18 patients treated for sebaceous carcinoma with MMS between 1988 and 1998, 2 had recurrences. One patient had a local recurrence and metastatic disease of the parotid lymph nodes 9 months after MMS. The other patient had a local recurrence 19 months after MMS without metastatic disease.[36] A retrospective review at a single institution found 37 patients with 45 sebaceous carcinomas over a 12-year period from 2001 to 2013. Five patients had Muir–Torre syndrome in this cohort. All patients were treated with MMS. There were no local recurrences, metastases, or disease-specific deaths noted after an average follow-up of 3.6 years.[37] A retrospective review conducted by the Mayo Clinic compared WLE to MMS for treatment of sebaceous carcinoma. There was 1 recurrence found after each treatment, resulting in recurrence rates of 1 per 35 for MMS at 5.95 years after diagnosis and 1 per 24 for WLE at 0.32 years after diagnosis. The authors concluded that both treatments were deemed effective, with no superiority of one treatment over the other[38] (Figure 6).

Other Adnexal Carcinomas

In addition to sebaceous carcinoma, there are reports of several other adnexal carcinomas treated with MMS. A 2017 review focused on 9 different malignancies in the category. Comparative studies were not found, likely because of the rarity of adnexal carcinomas.[39] Treatment of primary cutaneous mucinous carcinoma with MMS showed the highest recurrence rate, reported at 9.6%, and the highest metastasis rate, reported at 6.4%. Data were based on a systematic review/meta-analysis[40] and a large case series,[41] combining for a total of 31 patients. Other adnexal carcinomas, such as pilomatrix carcinoma and malignant eccrine spiradenoma, had very few reported cases treated with MMS.[42–44] Overall, there was not enough evidence to definitively conclude that MMS is superior to WLE, but current studies suggest a trend toward the superiority of MMS.[39]

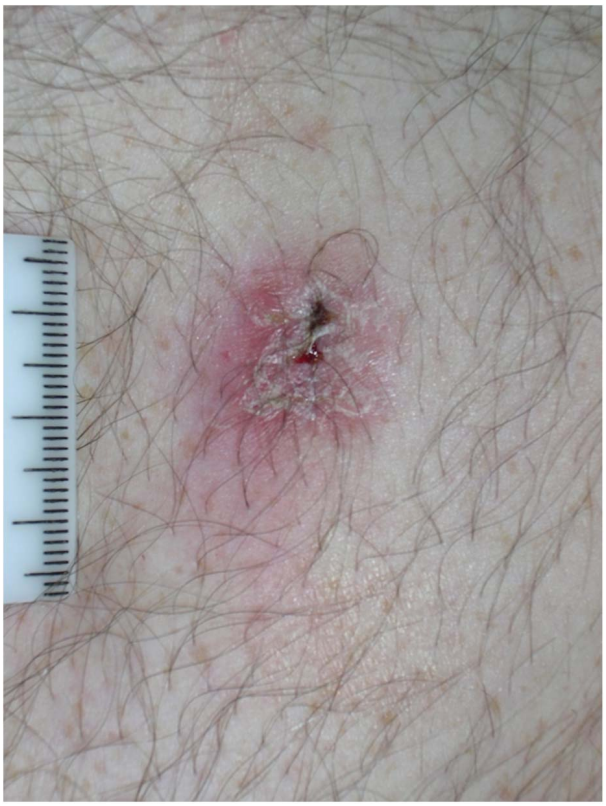

Figure 6. Sebaceous carcinoma before Mohs micrographic surgery.

Future

Noninvasive Imaging

Looking into the future of the field of MMS, the combination of MMS with noninvasive imaging of the skin holds promise to enhance the field. Visualization of subclinical tumor extension could lead to reduced number of Mohs stages and reduced procedure time, as well as improvement in the cure rate of Mohs surgery.

Two of these technologies, optical coherence tomography (OCT) and multispectral optoacoustic tomography (MSOT), will be discussed. These technologies currently exist, but are not in widespread use. An informal survey of Mohs surgeons revealed that current adoption is mostly limited to large academic institutions. Barriers to adoption include the high cost, lack of insurance reimbursement, and training that is needed to effectively use the devices. As of April 2018, there are category III *Current Procedural Terminology* codes assigned for use of OCT, but these investigational codes typically do not allow for reimbursement.[45] Further research is needed to provide a cost-benefit analysis for use of these devices in conjunction with MMS.

Optical Coherence Tomography

Optical coherence tomography is a noninvasive optical imaging technique used to characterize tissue microstructure. The technology can be thought of as similar to ultrasound with its real-time, cross-sectional views. However, OCT uses optics in contrast to the acoustics that are used with ultrasound. A new multi-beam OCT system offers broader lateral resolution than previous single-beam systems. In a pilot study, a multi-beam OCT system was used to predict the lateral margin of a BCC before MMS. After MMS proceeded per usual, the OCT-predicted margin was compared to the final defect after histologic confirmation of tumor removal. The MMS procedure required 2 stages for BCC removal, and there was good correlation between the OCT-predicted lateral margins and the final margins after completion of MMS.[46]

Another larger pilot study conducted by Wang and colleagues recruited 52 participants with biopsy-proven BCCs undergoing MMS. Optical coherence tomography was able to visualize to a depth of 2 mm into the skin. For 41 lesions that required only 1 stage to clear, the estimated clinical margin was found to be 0.4 mm larger than the OCT margin. This study demonstrated that OCT can also be useful in ensuring that the smallest margin possible is taken with MMS. Optical coherence tomography was also able to predict extension of the lesion boundary for all 11 tumors that required 2 stages to clear.[47] Carvalho and colleagues developed a marking technique with a permanent silver marker used on the skin surface that can be visualized on OCT by a strong signal shadow. With this technique, marking is extended until the tumor is contained within the signal shadow before the Mohs layer is excised[48] (Figure 7).

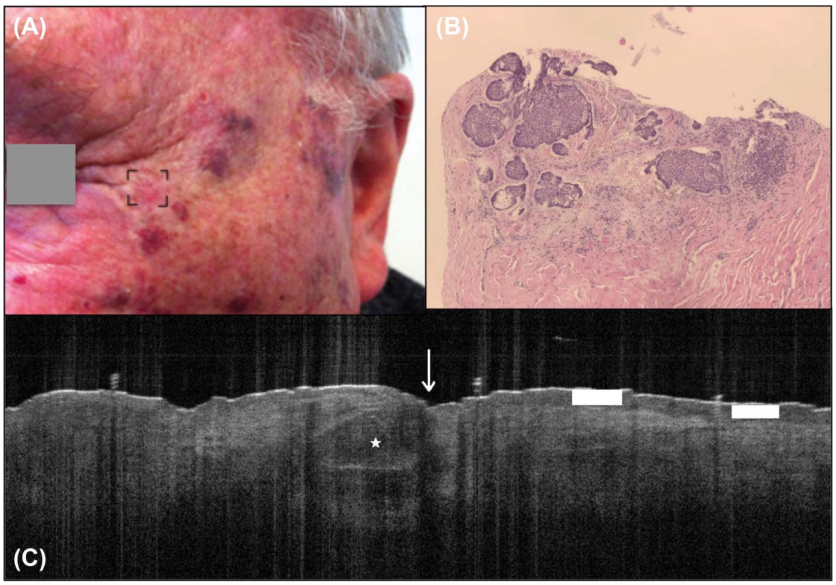

Figure 7. Example of an OCT system, courtesy of Hussain and colleagues.[60] (A) A 71-year-old male patient with infantile hemangioma located adjacent to the eye and concern for recurrent basal cell carcinoma at the site marked by brackets. (B) Histological image that confirmed the subclinical recurrent basal cell carcinoma found by OCT. (C) The OCT examination of the treated area revealed a subclinical recurrent basal cell carcinoma. OCT, optical coherence tomography.

Multispectral Optoacoustic Tomography

Multispectral optoacoustic tomography, another noninvasive imaging tool, shows optical contrast and ultrasonic spatial resolution to provide valuable functional information about the skin. Depth of penetration is higher than OCT, reaching as deep as 10 mm below the skin surface. The main chromophores of the skin—melanin, oxyhemoglobin, and deoxyhemoglobin—absorb most of the energy and can be spatially resolved with high sensitivity. Spherical tomographic imaging allows for 3D image acquisition.[49,50]

In one study, MSOT was performed on 3 suspicious skin tumors, including one tumor that was confirmed as a pigmented BCC and subsequently treated with MMS. The extent of tumor dimensions with MSOT corresponded well to the confirmed tumor dimensions observed with histology.[50] Another group looked at both 2D and 3D MSOT used on NMSCs in 21 Asian patients. Good correlation was again observed between tumor dimensions measured with MSOT and ex vivo histology of excised lesions. Information regarding tumor aggressiveness was also gleaned from MSOT analysis of tumor neovasculature[49] (Figure 8).

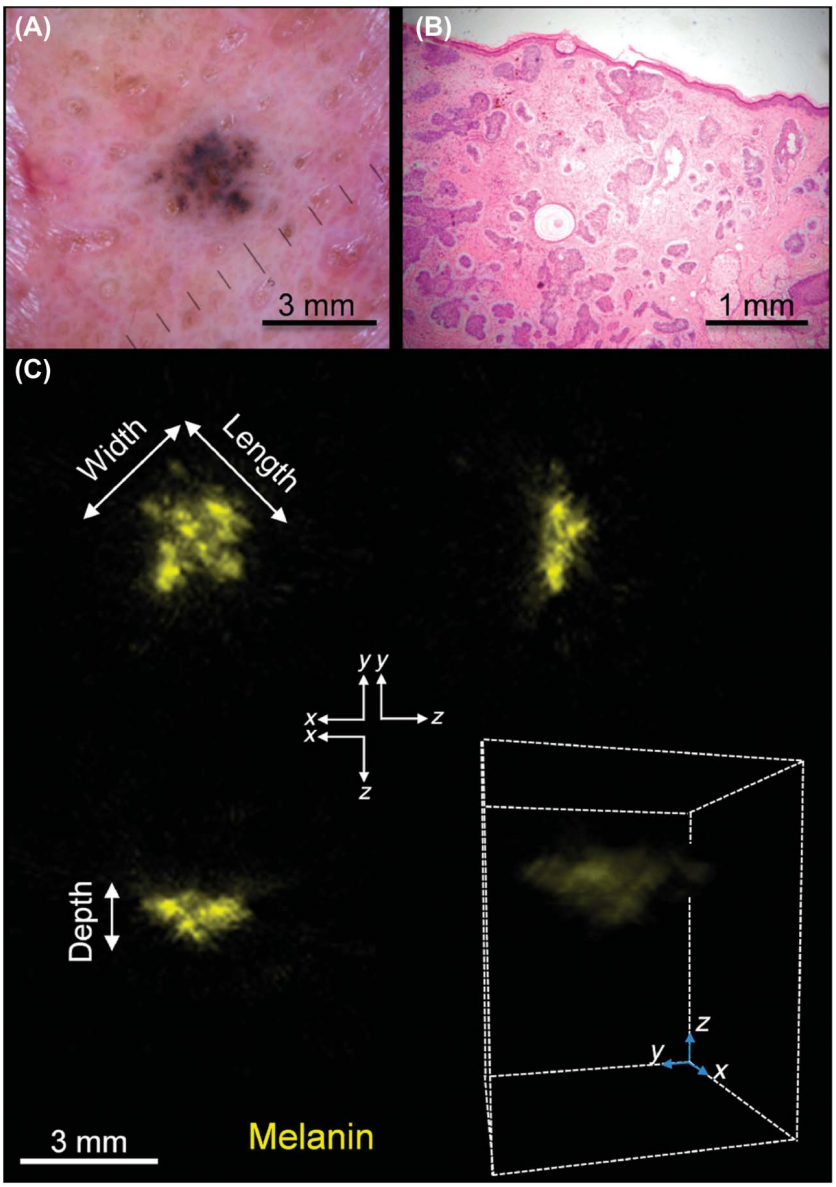

Figure 8. Example of MSOT, courtesy of Chuah and colleagues.[50] (A) Pigmented macule on the nose. (B) Histology confirmed the macule to be nodular basal cell carcinoma. (C) In vivo MSOT images in different orthogonal views and 3D map of tumor. MSOT, multispectral optoacoustic tomography.

Immunostains. Immunostains were first introduced into the practices of Mohs surgeons in the 1980s, initially for use with squamous carcinoma and basal carcinoma, but are now available for a variety of cutaneous malignancies.[51] Although there are a handful of Mohs surgeons who already use immunostains, widespread adoption has lagged due to factors such as high cost, significant time commitment, and lack of reliability.[52]

Results of a 2013 survey on the use of rapid immunostaining among Mohs surgeons showed that only 21.7% of the 378 respondents had adopted the use of immunohistochemical stains since fellowship. 20.4% of respondents were using immunostains in conjunction with Mohs for melanoma. However, most respondents (90%) felt that immunostains could be reliably used with Mohs.[52] In the future, the adoption of immunostains in MMS stands to expand, given development of rapid immunostaining protocols,[53–55] falling costs of immunostains, and improving reliability.

Digital Technology. Digital technologies in the form of videos, text messages, and smartphone apps have been implemented and studied in several medical specialties. A small body of literature exists around the use of digital technologies in the context of MMS. Studies have shown that video education is preferred to pamphlets, may reduce procedural anxiety,[56] and can improve time management during patient care. Text message–based wound care instructions are well received.[56] Dynamic telepathology systems used during MMS have proven to be accurate and effective.[57,58] Inexpensive telepathology systems have been devised as alternatives to cost-prohibitive telepathology services.[58] Smartglasses have been effectively used to communicate among specialties when coordinating reconstructive efforts after tumor removal.[59] It is expected that digital technologies will be increasingly used in Mohs surgery as they become more ubiquitous in health care.

Conclusion

The field of MMS began in the 1930s as a pioneering technique wrought with skepticism but has evolved to become a widely adopted and highly effective treatment for skin cancer. Refinement of the technique with the advent of fresh frozen tissue, thereby minimizing pain and allowing for immediate surgical reconstruction, was the driving factor that led to the successful implementation of MMS.[2] Mohs micrographic surgery is now used for 1 of every 4 NMSCs.[6]

Although there is a lack of randomized, prospective trials comparing MMS to surgical excision, several large prospective studies (and one randomized trial) favor MMS, especially for treatment of recurrent NMSCs.[7–9] Noncomparative trials show extremely low recurrence rates for the treatment of NMSC.[10,11] Mohs micrographic surgery has also demonstrated efficacy for several rare types of NMSC, including DFSP, EMPD, MCC, and sebaceous carcinoma.[29,30,32,34,37] Although use of the MART-1 immunostain allows for adequate detection of melanoma on frozen sections,[23,24,27] further studies are needed to demonstrate that MMS can improve recurrence rates and survival for the treatment of melanoma.

The future of MMS will likely involve introduction of noninvasive imaging, used to enhance the tissue sparing nature of the technique and to improve efficiency and cure rates.[47,48] Noninvasive imaging also has the potential to elucidate functional characteristics of tumors, and thereby predict tumor aggressiveness.[50] It remains to be seen exactly how this information will be used intraoperatively. It is likely there will be more widespread use of immunostains as they become less expensive and protocols become faster. Digital technology in the form of patient education and telemedicine also stands to become more commonplace. These changes ultimately seek to enhance cure rates and the patient experience during MMS.

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