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Frozen Section Mohs

A Hybrid Technique and One Plastic Surgeon's Experience With 1714 Consecutive Skin Cancer Removals

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Abstract: While US nonmelanoma skin cancer (NMSC) mortality rate has decreased in the past decade, its incidence is rising. Traditional surgical treatments include wide local excision, intraoperative frozen section analysis (IFSA), and Mohs micrographic surgery (MMS). IFSA and MMS are techniques that provide intraoperative analysis allowing the surgeon to confirm margins clear of malignancy and minimize tissue damage, especially in cosmetically sensitive subunits. MMS, with cure rates up to 99%–100%, is considered the gold standard but is limited geographically and financially because of specialized training. We report a hybrid surgical technique that effectively excises cutaneous malignancy but can be utilized by plastic surgeons. This hybrid technique is called frozen section Mohs (FSM), which combines both techniques utilized in IFSA and MMS. FSM is similar to IFSA in that the middle breadloaf visualizes the central deep margin but is similar to MMS in that the entire periphery is also analyzed. This paper is a retrospective review of all patients who have undergone the FSM procedure by one plastic surgeon from September 2017 to June 2023. The primary outcomes were 1) recurrence, determined by excision of skin cancer demonstrated to be arising from postexcision scar tissue, and 2) concordance between intraoperative and final pathology. There were 1714 FSM procedures performed with a cohort averaging 73.8 years old and 57% male. Zero recurrences were identified (100% cure rate). Two cases (0.11%) were false negatives and the patients returned for re-excision. About 48.2% of cases were basal cell carcinoma while 40.7% were squamous cell carcinoma. The average number of stages per FSM procedure was 1.17. The mean defect size was 1.83 cm.^{2} Complication rate was 2.28% (n = 39), with the most common issue being bleeding that required suturing or cautery. Our proposed FSM technique's results demonstrate effective carcinoma removal comparable to MMS. Plastic surgeons may therefore utilize this technique to meet the growing demands of skin cancer surgery in the United States with equally effective outcomes.

Key Words: frozen section Mohs, non melanoma skin cancer, frozen section, skin cancer surgery, histopathology, intraoperative frozen section analysis, Mohs micrographic surgery

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Skin cancer continues to be the most frequently diagnosed cancer in the United States.[1] Since 1990, the prevalence of nonmelanoma skin cancer (NMSC) has been steadily increasing, with more than 1 million patients diagnosed every year.[2] While there have been described genetic risk factors for the development of skin cancer, most cases are attributed to external factors such as increased exposure to ultraviolet (UV) light, increased life expectancy, and ozone depletion.[3] Without intervention, medical or surgical treatment becomes necessary to avoid local tissue destruction, metastasis, disfigurement, or even death.[4]

The 2023 National Comprehensive Care Network guidelines most often suggest complete excision for the treatment of NMSC to preserve function and aesthetics.[5,6] These guidelines also suggest a 4-mm-wide local excision for basal cell carcinoma (BCC) and 4- to 6-mm excision for squamous cell carcinoma (SCC) followed by postoperative pathology analysis.

Mohs micrographic surgery (MMS) was developed by Frederick Mohs in the 1930s.[7] In contrast to wide local excision, MMS is an intraoperative technique commonly used by dermatologists and can utilize a narrower 1- to 2-mm excision margin.[8] Intraoperative coordination between the dermatologist and pathologist therefore enables complete removal if subsequent excisions are necessary. MMS cure rates are approximately 98%–99% and is currently the predominant treatment modality for NMSC.[9–13] Its success is attributed to the ability to visualize 100% of the peripheral margin upon histopathologic processing and hence minimizing false negatives (Fig. 1, bottom).[14,15]

Surgeons may alternatively use traditional intraoperative frozen section analysis (IFSA). This technique precedes MMS with its origins tracing back to the late 19th century and continues to be used today in neurosurgery, otolaryngology, gastrointestinal surgery, and urologic surgery. Histopathologic processing involves making thin vertical "bread loafs" that intend to represent a slice of the tissue (Fig. 1, top). In contrast to MMS, IFSA does not examine 100% of the peripheral margin. However, lack of a vertical "bread loaf" section may cause the pathologist to lose orientation of the deep margin. When facing the deep margin to attain full representation of the periphery, the Mohs surgeon may overcall a positive deep margin, requiring an unindicated second stage. Furthermore, Figure 2 demonstrates the difficulty of distinguishing between an infiltrating BCC and a benign hair follicle in MMS cut in cross section.

Given the drawbacks of both IFSA and MMS, a hybrid technique called frozen section Mohs (FSM) aims to combine the benefits of both and reduce false negatives and false positives.

The goals for patients with skin cancer are complete removal and tissue preservation. Plastic surgeons have the unique ability to remove carcinoma in cosmetically sensitive subunits such as the eyelids, lips, nose, and ears using various reconstructive techniques to restore form and function (ie, skin grafts and adjacent tissue transfers). We hypothesize that plastic surgeons' use of this hybrid technique is an effective method for NMSC removal. This paper reports a single institution,

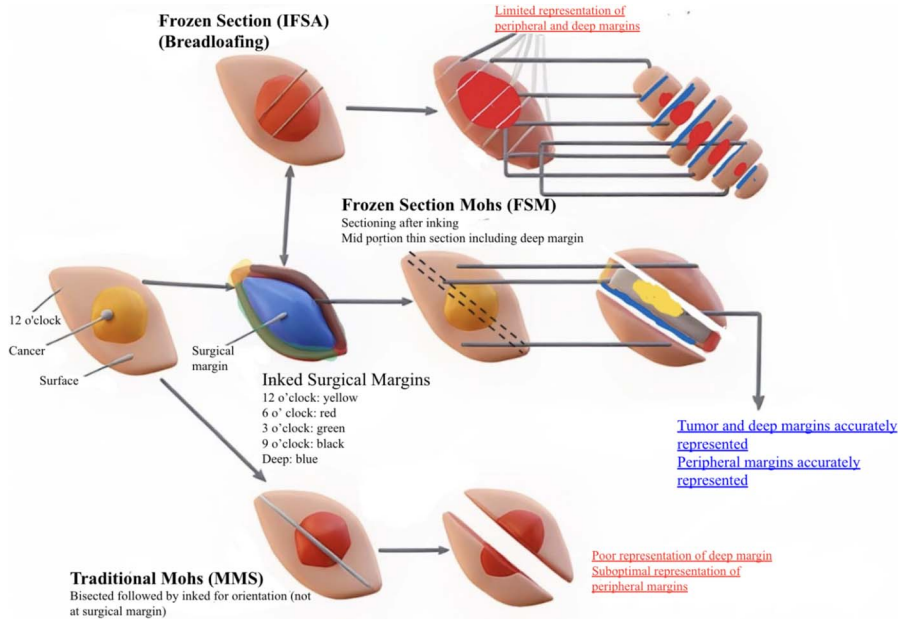

FIGURE 1. Diagram of histopathologic techniques for a skin cancer specimen. The top shows frozen section (breadloafing), the bottom demonstrates traditional Mohs micrographic surgery, and the middle depicts the hybrid technique frozen section Mohs.

single plastic surgeon's experience, and outcomes of this hybrid FSM technique.

MATERIALS AND METHODS

Study Design

After obtaining institutional review board approval through Christiana Care Hospital, a retrospective chart review was conducted of all patients undergoing skin cancer treatment at our skin cancer center by means of surgical excision and intraoperative analysis via FSM by an on-site pathologist performed by a single surgeon from January 2016 to July 2023. This retrospective review was removed of patient identifiers and conducted in compliance with all institutional guidelines and in accordance with guidelines for human subjects research.

Selection of Patients

Inclusion criteria were 1) patients who underwent skin cancer removal via excision with FSM between January 2016 and July 2023 and 2) over 18 years of age. Exclusion criteria included 1) incomplete records and 2) unclear or missing final diagnosis.

Data Collection

The records of Green Clinics Laboratory were searched for FSM examinations between calendar years 2016 through 2023. To assess for skin cancer recurrence, the included specimens were screened for subsequent excisions at the same site designated for FSM cases. The resulting list was then reviewed for histologic similarities between the index and second excision cases and whether the recurring cancer emerged from cicatrix. The cases identified as potential recurrences were then corroborated with the patient's clinical chart for precise

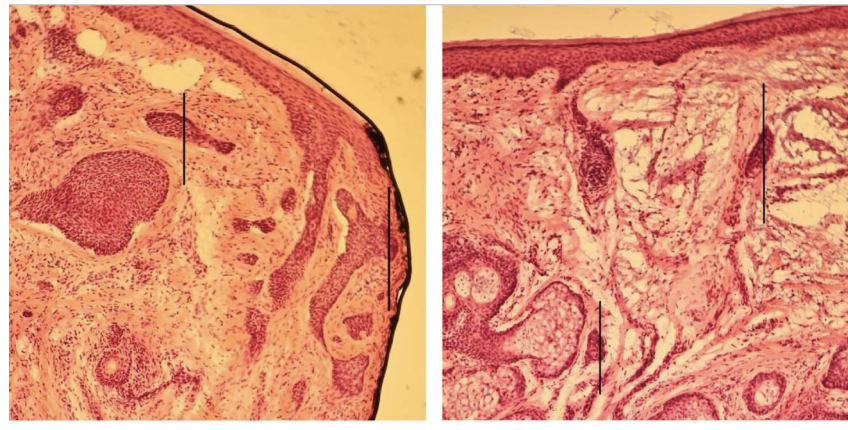

FIGURE 2. Histological specimens demonstrating a drawback of MMS. An infiltrating BCC (left) and a benign hair follicle (right) look very similar. This may mistakenly lead the pathologist to overcall a positive deep margin and an unnecessary subsequent excision.

localization. The rest of the data were collected via electronic medical record. The following variables were collected: age at time of surgery, sex, anatomical location of the lesion, closure method (adjacent tissue transfer or skin graft), surgery time, number of stages, type of biopsy, final diagnosis, specimen area, and complications. Additionally, patients' check in to check out time were recorded.

Statistical Methods

Statistical analysis was done in Stata Version 17.0 and Microsoft Excel program. Simple means and frequency calculations were performed on the data.

Surgery Technique

Patients are instructed to stop taking any nonsteroidal or aspirin-based medications a week prior to the planned procedure date. Furthermore, if medically cleared, patients are instructed to hold other anticoagulants 3 days prior to procedure. The skin cancer is visually identified on the patient's body, and the exact location is verified by previous photos at time of biopsy. The visible border of the skin cancer is carefully marked with a red marking pen, and a vertical black hash is placed at the 12 o'clock margin for pathologic orientation. The surgical site is cleaned with 70% isopropyl alcohol and locally anesthetized with 0.5% lidocaine with sodium bicarbonate buffer (1 cc NaHCO3 and 9 cc 0.5% lidocaine with 1:200,000 epinephrine). Depending on tumor size and expected reconstructive needs, 5–10 cc of lidocaine is injected with a #25 gauge needle. The surgical site is prepped with topical chlorhexidine and a sterile paper drape placed. With a #15 scalpel blade, a cut perpendicular to the skin is made along the outer edge of the marked visible border, which approximates a 1- to 2-mm visible margin and is carried into the deep dermis. At the level of the deep dermis, the scalpel blade is beveled at a 45 degree angle outward until the entire dermis has been transected. The scalpel blade is then directed under the specimen in an avascular plane at the interface of the deep dermis and superficial subcutaneous fat. In cases of a more extensive skin cancer, the depth of the incision may be carried deeper into the subcutis to achieve a clear deep margin. The resected tumor is then placed onto a Petri dish that is oriented at the 12 o'clock marked margin and taken to the lab for immediate histologic analysis. If it is intraoperatively determined that all of the skin cancer has been removed, the surgeon will repair the defect through various types of adjacent tissue transfer or skin grafting. However, if a positive margin is histologically identified, the surgeon will resect the positive margin(s) until the margins are clear.

Pathology Technique

FSM was performed in an on-site laboratory within the clinician's office suite. Similar to IFSA, the pathologist marks the deep,

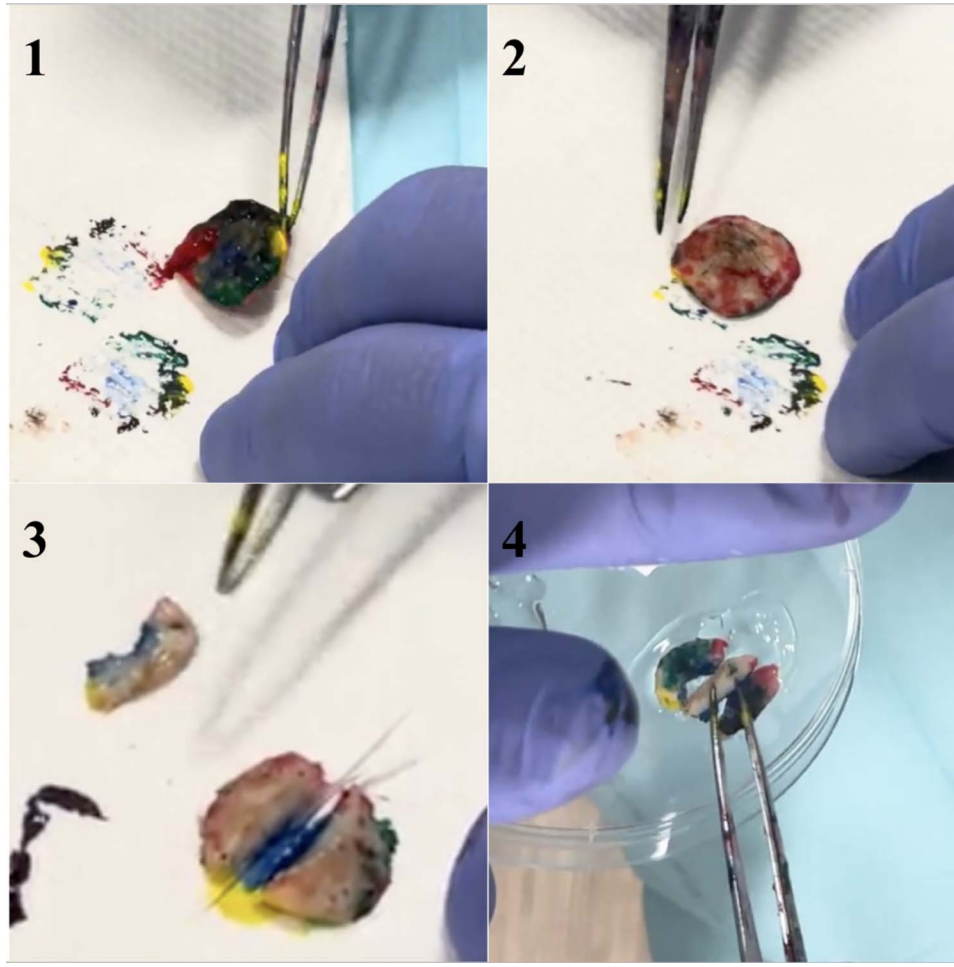

FIGURE 3. (1) The specimen margins are inked. (2) This orientation shows the tumor facing upward and the forceps indicating the 12 o'clock margin. (3) The specimen is sectioned such that a thin vertical slice is removed from the center. (4) The final orientation of the specimen, with the 2 side edges oriented en face while the middle vertical slice is rotated on its side.

TABLE 1. Anatomical Location of Skin Cancer and Cancer Subtype on Histology for 1714 Lesions

Anatomical Location	
Nose	189 (11.03%)
Cheek	183 (10.68%)
Scalp	165 (9.63%)
Ear	154 (8.98%)
Lower leg	139 (8.11%)
Forehead	112 (6.53%)
Temple	88 (5.13%)
Chest	82 (4.78%)
Forearm	81 (4.73%)
Back	71 (4.14%)
Lesion diagnosis	
BCC	827 (48.25%)
SCC	697 (40.67%)
Other	190 (11.1%)

12, 3, 6, and 9 o'clock margins. Then, the pathologist sections a thin ellipse along the long axis of the specimen, in which only this section is rotated 90 degrees as shown in Figures 2 and 3. The long axis is chosen because the surgeon most often orients the excised specimen with the tips of this axis further from the tumor compared to the shorter axis. Therefore, when this thin slice is rotated, the tips are more unlikely to contain tumor. Relaxing incisions are made to the two peripheral halves, which flank the rotated thin middle slice. The thin middle slice enhances visualization of the deep margin and allows the pathologist to maintain vertical orientation. The FSM technique retains the benefit from breadloafing by having the thin middle section rotated to better view the deep margin. FSM simultaneously retains the benefit of Mohs by allowing the total view of peripheral margin because the majority of the specimen is horizontally sectioned.

RESULTS

A total of 1714 FSM procedures that took place between January, 2016 and July, 2023. The range of follow-up was between 1.75 and 9 years. The average patient age was 73.8 years old and 57% were male and 43% were female. There were 827 (48.25%) BCC excisions and 697 (40.67%) squamous cell carcinoma excisions. The most common locations of excision were the nose (11%), cheek (10.7%), and scalp (9.6%) (Table 1). The pathology lab identified zero documented cases out of 1714 total cases who had re-excision of previously treated areas, representing a 0% recurrence rate. It required an average of 1.17 stages to achieve clear margins (Table 2). There were 2 false-negative cases (0.125%) corresponding to negative intraoperative margin but positive on the permanent section. The average defect size was 1.83 cm^2. There was a reported 2.28% complication rate, with 25 cases (1.45%) involving infection requiring oral antibiotics, 5 cases (0.29%) of bleeding requiring additional suture or cauterization, and 6 cases (0.35%) of poor wound healing. The check-in to check-out time, encompassing surgical removal, real-time analysis, and surgical repair, was recorded for 500 consecutive patients, with an average total duration of 44 minutes.

TABLE 2. FSM Excision Rates, Stages, and Recurrences for 1714 Lesions

No. Excisions for Clear Margins	
1	1473 (85.94%)
2	199 (11.61%)
3	36 (2.1%)
4	6 (0.35%)
Mean no. stages	1.168
False negative rate	2 (0.13%)
No. recurrences to date	0
Cure rate	100%

DISCUSSION

Conventional surgical excision for low risk NMSC remains the most widely available treatment, with cure rates potentially exceeding 95%.[16–19] However, without the access of intraoperative analysis, this method does not provide real-time feedback and may lead the surgeon to (1) incompletely excise the tumor or (2) create unnecessarily large defects. Additionally, standard final pathological processing using vertical sections allows assessment of less than 50% of the peripheral margin.[20]

MMS facilitates this intraoperative analysis and demonstrates consistently high cure rates of 98%–99%.[9–13] However, underserved and rural communities may lack access to Mohs-trained surgeons and histotechnicians.[21,22] Patient preference, cost, and availability are important considerations for these treatment modalities. The histologic preparation of IFSA and MMS each have their benefits and drawbacks. Indeed, MMS is predominantly used by Mohs surgeons due its high reported cure rates and its ability to examine the entire peripheral margin. However, because of the absence of vertical sectioning as performed in IFSA, assessing the deep margin may result in the pathologist overdiagnosing a positive margin, which could lead to unnecessary tissue excision. Furthermore, Krishnan et al reported outlier practice patterns in MMS suggesting the lower outliers could be due to overly aggressive first stages.[23]

The hybrid FSM technique used in this study has demonstrated high efficacy in excising skin cancer with a 0% recurrence rate (100% cure rate) and a 0.13% false-negative rate. We recorded a mean of 1.2 stages for the FSM technique, which is lower than the reported average of 1.77 stages for MMS.[24] To our knowledge, these collated data represent the largest published dataset (1714 cases) for the treatment of NMSC utilizing this hybrid FSM technique.

Although no studies have reported using the FSM technique for NMSC surgery as outlined here, several studies on IFSA are summarized in Table 3. Bilden et al[25] is a single plastic surgery center retrospective review involving 3 plastic surgeons removing 204 NMSC lesions on 171 patients. There is one false-positive case representing a rate of 0.49% and 5 false-negative results (2.45%). There are 15 patients who had local recurrence (7.35%). This higher recurrence rate may be explained by

TABLE 3. Characteristics of Studies Involving IFSA in Skin Cancer Surgery

	No. IFSA Procedures	**False Negative Rate**	**Recurrence Rate**
Benedict et al, 2019*	204	2.45%	7.35%
Nizamoglu et al, 2016*	70	2%	0%
Stolle et al, 2013*	153	2.6%	0.4%
Loh et al, 2021*	86	1.33%	1.16%
Hutting et al, 2017*	160	1.2%	4.6%
Moncrieff et al, 2015*	253	28.7%	Not reported
Otsuka et al, 2022	542	2%	0.86%
Castley et al, 2013	150	<2.3%	Not reported
Ghauri et al, 1999	210	<8.8%	Not reported
Manstein et al, 2003	60	<15%	Not reported

*Studies performed by plastic surgeons.

IFSA's histopathologic processing in which breadloafing does not evaluate the entire peripheral margin and thus may lead to incomplete carcinoma excision. Loh et al reported a cohort of 86 patients and 86 NMSC lesions.[3] Using en face frozen sections for intraoperative analysis, results include 1 recurrence (1.1%) and 1 false-negative case (1.3%) requiring a second excision. Hutting et al describe a single center retrospective review of 152 patients with 160 cutaneous squamous cell carcinomas of the face.[26] There is a 4.6% recurrence rate, and 1.5% of the lesions metastasized. The concordance rate between IFSA and final pathologic analysis by paraffin section is 98.8%. The mean duration of treatment is 77 minutes, and the complication rate is 8.1%. Our study, in contrast, averages 44 minutes per complete treatment session. Nizamoglu et al reviewed 70 high-risk NMSC lesions of 69 patients at a single hospital system. Only 2% of excisions were false negatives, and there were no reported recurrences.[27] Stolle et al described a single center retrospective study in which 153 IFSA procedures are performed for the treatment of NMSC.[28] Complete excision is achieved in 90.4% patients. Three patients (0.4%) had a recurrent tumor and the false-negative rate calculated to be 2.6%. Moncrieff et al demonstrated in their review of 253 cases an incomplete excision margin rate (prevalence of tumor being within 1 mm of the excision margin) of 28.7% when using bread-loafing IFSA.[29] Because of the high incomplete excision margin rate, the plastic surgeons ultimately discontinued use of IFSA in their unit in favor of intraoperative MMS.

Other considerations for using this hybrid FSM technique versus MMS for NMSC treatment are operative timing and reconstructive results. Plastic surgeons have unique training to use a variety of reconstructive techniques to restore form and function of soft tissue defects. A few examples include skin grafts, locoregional flaps, and adjacent tissue transfer. Often, Mohs trained surgeons consult plastic surgeons for reconstructive assistance, requiring the patient to return for surgery several days after their initial carcinoma removal. This time delay has been shown to increase postoperative complications rates, particularly when the delay is longer than 2 days.[30] Our study demonstrates that surgical removal, real-time analysis, and surgical repair can take an average of just 44 minutes.

The primary limitation of this study is the retrospective nature of this analysis. We could not account for patients that either died or followed up with another skin cancer provider. However, it was standard protocol in our practice for all patients to regularly follow up every 6–12 months for routine skin checks. Future studies could provide statistical comparisons of outcomes between hybrid FSM to other skin cancer surgery techniques.

CONCLUSIONS

To date, this paper represents the largest single-institute study on this hybrid technique for the treatment of NMSC. Our results suggest that FSM is a safe means of treating NMSC and has comparable efficacy to MMS, based on the current available data. FSM may guide surgeons, particularly plastic surgeons, to perform efficient, office-based surgical treatment of NMSCs to deliver cosmetically acceptable and oncologically exceptional results.

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