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Mohs micrographic surgery for keratinocyte carcinomas: clinicopathological predictors of the number of stages

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ABSTRACT

Background: The number of Mohs stages needed to remove a keratinocyte carcinoma affects resource use, expenses, and repair complexity. This study aimed to identify clinicopathological predictors associated with increased or decreased stages and areas for further research.

Methods: A retrospective review was conducted from a single private practice with two Mohs surgeons of 2788 consecutive Mohs cases between January 2017 and December 2021, analyzing the average number of stages taken versus national norms ($P = 0.21$) and subgroups using unpaired t tests ($^*<0.05$).

Results: Several tumor features were significantly associated with fewer stages: squamous cell carcinomas, Mohs appropriate use criteria score of 7 or 8, preoperative size <0.25 cm^2, tumors on the lips and extremities (including hands/fingers), and smoking. Clinicopathological features significantly associated with more stages included Mohs appropriate use criteria score of 9, recurrent skin cancers, basal cell carcinomas, tumor size of 2.25–3.99 cm^2, cancers on ears, solid organ transplant patients, treatment delays >180 days, and patients ≥ 90 years old.

Conclusions: Significant predictors exist for both increased and decreased numbers of Mohs micrographic surgery stages required to eradicate a tumor, which may help Mohs surgeons facilitate, plan, and allocate resources more effectively. Areas for further research in Mohs micrographic surgery are identified.

KEYWORDS Basal cell carcinoma; clinicopathological predictors; keratinocyte carcinoma; Mohs micrographic surgery; Mohs stages; nonmelanoma skin cancer; squamous cell carcinoma

Keratinocyte carcinomas (KCs) include basal cell carcinomas (BCCs) and squamous cell carcinomas (SCCs).[1] Multiple treatment options exist for these tumors, but Mohs micrographic surgery (MMS) is considered the "gold standard" to remove difficult-to-treat KCs.[2–5] MMS is performed in a stepwise method typically referred to as stages. Predicting the number of stages needed for MMS removal of KCs can be helpful in preoperative planning, including estimating the time and resources needed and the type of repair that will be necessary, and can give patients more accurate expectations for their surgery.[6–9] The purpose of this review was to identify clinicopathological predictors associated with an increased or decreased number of stages required to completely eradicate a KC utilizing MMS as well as identify areas where further research is needed.

METHODS

Data on tumor features and patient characteristics were searched and retrieved from a proprietary electronic health record system as well as a Mohs surgical note generating database from January 1, 2017, through December 31, 2021, for tumors treated with MMS. A total of 11,264 consecutive KCs were diagnosed on 5878 patients, with MMS performed on 2788 (24.8%) tumors during this timeframe. Every tumor treated with MMS was included in the review. Each tumor had a preoperative biopsy, either in house or via

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outside referral. MMS was performed in the typical fashion by two private-practice board-certified dermatologists (dermatology and micrographic dermatological surgery) with curettage[10] or scalpel debulking, as indicated, before the first stage, and taking 1 to 3 mm margins for each stage based on the surgeon's judgment.[4,5,11,12] BCCs were stratified into nodular, micronodular, infiltrative, sclerosing, superficial, other, or unspecified, as well as mixed aggressive and mixed nonaggressive. SCCs were stratified into moderately differentiated, well-differentiated including keratoacanthoma type, poorly differentiated, acantholytic, superficial, basosquamous, in situ, and other or unspecified.

Unpaired *t* tests were performed via Excel comparing the average number of stages for all nonmelanoma skin cancer Mohs cases in our data set (X = 1.77, N = 2788, SD = 0.95) versus subgroups. Our data set was statistically insignificant when compared to national norms ($P = 0.21$) previously established by Krishnan et al regarding average number of stages taken from 17,311 cases by 1845 Mohs surgeons between 2012 and 2014 (X = 1.74, SD = 0.44).[13,14]

RESULTS

For the 2788 MMS cases, the average number of stages required for tumor removal was 1.77. All subgroups were compared to the average rather than to one another to establish significance, as shown in *Table 1*. Overall, BCC required significantly more stages than SCC (1.84 vs. 1.57). A Mohs appropriate use criteria (AUC) score of 9 was significantly associated with more stages required for tumor removal at 1.92 stages ($P < 0.001$) compared to the average. An AUC score of 7 or 8 was associated with fewer stages at 1.51 and 1.68, respectively ($P < 0.001$, $P = 0.004$) compared to the average. Recurrent skin cancers required more stages than nonrecurrent skin cancers (1.98 vs. 1.75, $P = 0.003$).

Although not significant, for BCC, aggressive subtypes were associated with more stages, as compared to the average, with micronodular, infiltrating, and sclerosing requiring 1.84, 1.84, and 1.91 stages, respectively. Also, other/unspecified subtypes required significantly more stages at 2.00 ($P = 0.02$) compared to the average. The mixed types were divided into nonaggressive, which included both superficial and nodular subtypes, and aggressive, which included any other combination of subtypes. Although not significant, the mixed aggressive group required fewer stages than the mixed nonaggressive group at 1.82 and 1.89, respectively ($P = 0.32$, $P = 0.19$).

The subtype of SCC associated with the most stages compared to the average was basosquamous cell carcinoma at 1.94 stages, although this did not reach statistical significance ($P = 0.16$). The subtypes of SCC significantly associated with fewer stages, as compared to the average, included superficial, moderate, and well differentiated at 1.44, 1.63, and 1.56 stages, respectively ($P < 0.001$, $P = 0.01$, $P = 0.002$). The acantholytic subtype displayed the fewest number of stages at 1.14 stages ($P = 0.08$), as compared to the average, but did not reach statistical significance. A preoperative size of $<0.25\ cm^2$ was significantly associated with a lower number of stages at 1.61 stages ($P = 0.01$) as compared to the average. Sizes of 2.25 to $3.99\ cm^2$ were significantly associated with an increased number of stages, at 1.94 ($P = 0.002$), as compared to the average.

The anatomical sites and their association with the number of stages is also noted in *Table 1*. The ears and the nose, as compared to the average, required an increased number of stages at 1.84 and 1.91, respectively, although only the ears reached statistical significance ($P = 0.002$). When compared to the average, the upper extremities, lower extremities, hands/fingers, and lips significantly required the least number of stages at 1.34, 1.45, 1.46, and 1.58 stages, respectively ($P = 0.01$, $P = 0.002$, $P = 0.01$, $P = 0.02$). The trunk was also associated with fewer stages at 1.57 as compared to the average.

Delays in treatment are shown in *Table 1*. Compared to the average number of stages required, an increased number of stages was seen with a delay of 60 to 89 days and >180 days at 1.91 and 2.13, respectively, with the latter reaching statistical significance ($P = 0.009$). Only one patient <20 years old was treated and required three stages. Otherwise, patients >90 years old had a significantly increased number of stages required at 1.91 ($P = 0.03$) as compared to the other age ranges.

As shown in *Table 1*, solid organ transplant patients required significantly more stages than nontransplant patients at 2.06 and 1.77, respectively ($P = 0.04$). No statistically significant differences were seen in the number of stages required for the insured versus the uninsured population. Finally, *Table 1* shows no difference in the number of stages required between men and women or between urban and rural patients. However, positive smoking status was associated with a decrease in the number of stages, at 1.64 ($P = 0.04$).

DISCUSSION

Predictors of the number of stages for MMS to completely eradicate a tumor have been described.[6–10,15–22] In our data set, BCC represented 73.7% of KC tumors and it took more stages to remove a BCC at 1.84 versus an SCC at 1.57 stages, a difference also shown by Diel et al.[23] Compared to the BCC mean number of stages, the aggressive subtype of BCC sclerosing (morpheaform) required an increased number of stages for complete removal, as expected.[6,23,24] Traditionally, micronodular and infiltrative BCCs have been considered more aggressive[9,17]; however, in our data set, the number of stages required for these BCCs was the same as the mean for all BCCs. The traditionally considered less aggressive BCCs of nodular and superficial[7] required just under the mean number of stages for all BCCs. Of interest, 90 (4.4%) diagnosed BCCs had no subtype on the original pathology report, or one of the less common subtypes, and were not further categorized. The mean was

Table 1. Mohs stages based on clinical and demographic variables*

Variable	*N*	%	Stages (*n*)	SD	*P* value
MMS KC overall					
Total Mohs cases	2788		1.77	0.95	
Basal cell carcinoma	2056	73.7	1.84	0.99	0.013*
Squamous cell carcinoma	732	26.3	1.57	0.79	<0.001*
Mohs appropriate use criteria					
7, 8, or 9	2775	99.5	1.77	0.95	
7	255	9.2	1.51	0.77	<0.001*
8	1295	46.7	1.68	0.90	0.004*
9	1225	44.1	1.92	1.00	<0.001*
Nature of KC					
Recurrent	205	7.4	1.98	1.11	0.003*
Nonrecurrent	2583	92.6	1.75	0.93	0.436
Basal cell carcinoma					
Nodular	899	43.7	1.82	1.01	0.177
Micronodular	160	7.8	1.84	0.90	0.364
Infiltrative	638	31.0	1.84	0.93	0.092
Sclerosing	57	2.8	1.91	1.01	0.271
Superficial	152	7.4	1.81	1.00	0.614
Other/unspecified	85	4.1	2.02	1.15	0.018*
Mixed	513	25.0	1.84	0.95	
Aggressive	401	19.5	1.82	0.91	0.322
Nonaggressive	112	5.4	1.89	1.08	0.193
Squamous cell carcinoma					
Moderate	331	45.2	1.63	0.82	0.010*
Well-differentiated/KA	198	27.0	1.56	0.64	0.002*
Poorly differentiated	6	0.8	1.67	0.75	0.797
Acantholytic	7	1.0	1.14	0.35	0.079
Superficial	113	15.4	1.44	0.85	<0.001*
Basosquamous	65	3.2	1.94	1.21	0.157
In situ	9	1.2	1.67	0.94	0.753
Other/unspecified	68	9.3	1.62	0.91	0.198
Preoperative sizes (cm^2)					
<0.25	243	8.7	1.61	0.86	0.011*
0.25–0.49	23.6	1.72	0.97	0.227	
0.50–0.99	625	22.4	1.78	0.99	0.814
1.00–1.49	469	16.8	1.73	0.85	0.392
1.50–2.24	283	10.2	1.86	0.94	0.130
2.25–3.99	321	11.5	1.94	0.96	0.002*
4.00–8.99	146	5.2	1.81	0.94	0.620
≥9.00	44	1.6	1.84	1.11	0.630
Site-specific locations					
Nose	827	29.7	1.84	1.02	0.067
Ears	510	18.3	1.91	0.94	0.002*
Eyelids	105	3.8	1.68	0.77	0.338
Lips	146	5.2	1.58	0.71	0.017*

(*Continued on next page*)

Table 1. Continued

Variable	*N*	%	Stages (*n*)	SD	*P* value
Face, other	751	26.9	1.74	0.93	0.440
Scalp/neck	257	9.2	1.77	1.08	1.000
Upper extremities	32	1.1	1.34	0.47	0.011*
Hands/fingers	59	2.1	1.46	0.62	0.013*
Lower extremities/foot	87	3.1	1.45	0.64	0.002*
Trunk/chest	14	0.5	1.57	0.90	0.432
Delay from diagnosis to treatment (days)					
0–29	2246	80.6	1.77	0.94	1.000
30–59	367	13.2	1.71	0.88	0.252
60–89	66	2.4	1.91	1.04	0.238
90–119	14	0.5	1.50	0.50	0.288
120–179	18	0.6	1.67	0.94	0.656
≥180	48	1.7	2.13	1.33	0.009*
Unknown	29	1.0	2.10	1.03	0.063
Age at diagnosis (years)					
<20	1	0.0	3.00	0.00	
20–39	18	0.6	1.94	1.13	0.449
40–59	281	10.1	1.73	1.04	0.505
60–6	513	18.4	1.72	0.89	0.269
70–79	972	34.9	1.76	0.93	0.776
80–89	813	29.2	1.79	0.94	0.597
≥90	190	6.8	1.93	1.01	0.025*
Transplant status					
Solid organ transplant	49	1.8	2.06	1.30	0.036*
Nontransplant	2739	98.2	1.77	0.94	1.000
Insurance type					
Medicare	1886	67.6	1.79	0.96	0.482
Medicaid	10	0.4	1.70	0.90	0.816
Commercial	672	24.1	1.71	0.93	0.140
Uninsured	220	7.9	1.79	0.89	0.763
Other patient characteristics					
Male	1966	70.6	1.78	0.93	0.720
Female	822	29.4	1.74	0.99	0.431
Smoker	252	9.0	1.64	0.80	0.035*
Nonsmoker	2536	91.0	1.78	0.96	0.703
Urban ZIP code	2015	72.4	1.78	0.96	0.720
Rural ZIP code	768	27.6	1.75	0.91	0.602

*Total number of nonmelanoma skin cancers in the data set is 11,264 between January 1, 2017, and December 31, 2021. Significance (*) defined as <0.05.
KA indicates keratoacanthoma; KC: keratinocyte carcinoma.

2.0 stages, indicating these tumors were likely one of the more aggressive subtypes and/or on patients with more concerning clinical characteristics. Although one would expect the mixed aggressive subtypes to take more stages, the mixed subsets required about the same number of stages as the mean of all BCCs.

SCCs accounted for 26.3% of the tumors in our data set. The number of stages required for moderately and well-differentiated SCCs was similar to the mean for all SCCs. Although not statistically significant, SCC in situ[25–27] and poorly differentiated SCC required slightly more stages than the mean for all SCCs. Superficial SCC required the least

number of stages, except for acantholytic SCC. Acantholytic SCC has been previously considered an aggressive SCC, but this has been refuted.[28,29] Our data, although not statistically significant, showed it required fewer stages to remove this subtype of SCC compared to other subtypes of SCCs. The subtype basosquamous cell carcinoma was included under SCC because the biological behavior can be similar to SCC. Basosquamous cell carcinoma accounted for 3.2% of SCCs and required more than the average number of stages for SCC removal; however, this did not reach statistical significance. Finally, the number of stages for other subtypes of SCC and unspecified subtypes of SCC was similar to the mean for all SCCs.

The development of the Mohs AUC and implementation into clinical practice is to help define tumors that will benefit from MMS.[30–32] This score considers many clinicopathological factors, including tumor size and location, aggressiveness, and immunosuppression in patients, among other criteria.[6,30,31,33] A score of 7, 8, or 9 indicates appropriateness for MMS, and all were significant in our data set, with a score of 9 taking the most number of stages for complete tumor removal. Recurrent tumors required more stages for removal. This is likely because they often have more aggressive features than primary tumors.[23,24,34] In general, the larger preoperative lesion size of the tumor, the more stages required[19–22,35,36] for eradication; however, the relationship was not completely linear.[23] Larger tumors tend to have more concerning histopathologic features.[19–22] Location of a KC on certain body parts demonstrated a relationship to the number of stages required, as has been previously reported.[4,5,7,37–41] The most common location for KC that received MMS was the nose, at 29.7% of tumors; however, the ears, which accounted for 18.3% of tumors, required the greatest number of stages. Mulvany et al showed that BCCs of the ear were often more aggressive than on other head and neck locations.[39] Delay in treatment after diagnosis has been associated with larger defects but not necessarily with more difficult repairs.[21,35,42] In our data set, the mean number of days from diagnosis until treatment was 28. Delays >180 days required more stages for tumor removal, but there was not a linear relationship.

Patient age had a relationship with the number of stages required for tumor removal, with younger as well as older patients taking more stages.[3,30,43] Older patients typically have more concerning clinicopathological features, and a priority of making smaller scars in younger patients may have contributed to increased stages in these age groups. Likely because of immunosuppression, solid organ transplant patients[44] required significantly more stages to completely eradicate tumor compared to nontransplant patients. It is noted that the calcineurin inhibitors, cyclosporine A and tacrolimus, greatly increase the risk of KC, particularly SCC.[45,46] Tacrolimus, because of its side effect profile, has recently been utilized more than cyclosporine A for immunosuppression in transplant patients.[37,41,45,46] However, the mTOR inhibitors, sirolimus and everolimus, which are also effective immunosuppressants, may actually be protective against KC and other cancers.[30,45–47] Insurance status seemed to have very little influence on the number of stages required for tumor removal.[48,49] The number of stages required for tumor removal was insignificant between men and women. Only 9.0% of our population indicated they smoked; however, smokers required fewer stages than nonsmokers.[50] SCC has been noted to be more common in smokers, especially of the lips and oral cavity.[51] Whether the patient, at the time of surgery, lived in urban versus rural zip codes (adjusted proportionally for our database) had no significant influence on the number of stages required for tumor removal.[52–54]

A separate study based on anatomic location and diagnosis with different margin sizes on the initial and subsequent stages would be required to see if the actual number of stages for complete tumor removed would be influenced by these factors. In our data set, and that of others, one could consider that the first stage on the ears and nose are potentially smaller to preserve tissue on sensitive anatomical areas as to minimize defects and facilitate a simpler repair; however, this may have resulted in more stages required to achieve tumor-free margins. Many reasons for fewer stages for SCC removal could be proposed, and this is also an area where further research is warranted. The difference is likely multifactorial, but knowing the exact margins on each stage, as mentioned above, and using that in the analysis may have changed the number of stages for tumor removal for various locations and SCC subtypes. The lips, hands/fingers, upper extremities, lower extremities, and trunk required fewer stages to clear tumor compared to other sites. Certainly, this is understandable for the extremities and the trunk, as larger initial margins can be taken on the first stage without compromising closure, except for possibly the pretibial area. The surgeon's bias of knowing SCC can have dire consequences, especially on the lips and hand/fingers,[55–58] if not completely removed, may have encouraged larger margins on the initial and subsequent stages.[59–62] Alternatively, SCCs on the lips or hands/fingers may be detected and treated sooner and, therefore, may not have as many aggressive histopathological features as those on other body locations. Also, since there are more SCCs in smokers, and SCC overall required less stages to clear tumor in our data set, this may have resulted in fewer stages overall required for smokers than nonsmokers. Further study would be required to confirm this hypothesis.

Histological subtypes in MMS present unique difficulties. Many pathology reports of BCC listed more than one histological subtype. Bartos et al found that up to 35% of BCCs were of the "mixed" type.[63] Often, a different subtype of BCC may be found during MMS than what was reported on the original biopsy.[64–67] A recent report by Lim et al showed that many superficial BCCs required more stages because of this "histological drift."[64] In our data set, the mixed groups, even aggressive mixed, were not associated

with more stages than the mean for all BCCs. Further study of which anatomical sites and sizes have tumors with mixed subtypes and other aggressive subtypes could help in the anticipation of difficult tumors. SCC subtypes have not been well studied to see if there is "histological drift" during Mohs surgery and whether it affects the number of stages required for removal.

The main limitation of this study is its reliance on data from a single private practice with only two Mohs surgeons, which raises concerns about the generalizability of the findings beyond this specific setting. However, to address this limitation and enhance the validity of our conclusions, we compared our data to a larger dataset from Krishnan et al.[13] This dataset consisted of a substantial sample size of 17,311 Mohs surgeries performed by 1845 surgeons between 2012 and 2014, providing a broader perspective. Notably, our dataset was statistically insignificant ($P = 0.21$) when compared to Krishnan et al, allowing us to utilize our mean number of stages taken ($X = 1.77$, $N = 2788$, $SD = 0.95$) for subgroup comparisons. Despite our efforts to improve the generalizability of our conclusions through this comparison, it should be acknowledged that the benchmark dataset used for comparison is almost a decade old. While it is unlikely that significant changes in surgeons' practices have occurred during that time, it still raises questions about the current relevance and applicability of our findings.

In conclusion, this review shows that significant predictors exist for both increased and decreased numbers of MMS stages required to eradicate a tumor, which may help Mohs surgeons facilitate, plan, and allocate resources more effectively. Also, areas for further research in MMS are identified.

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1. Nehal KS, Bichakjian CK. Update on keratinocyte carcinomas. *N Engl J Med*. 2018;379(4):363–374. doi:10.1056/NEJMra1708701.
2. Alsaif A, Hayre A, Karam M, Rahman S, Abdul Z, Matteucci P. Mohs micrographic surgery versus standard excision for basal cell carcinoma in the head and neck: systematic review and meta-analysis. *Cureus*. 2021;13(11):e19981. doi:10.7759/cureus.19981.
3. Dinehart SM, Pollack SV. Mohs micrographic surgery for skin cancer. *Cancer Treat Rev*. 1989;16(4):257–265. doi:10.1016/0305-7372(89)90045-5.
4. Drake LA, Dinehart SM, Goltz RW, et al. Guidelines of care for Mohs micrographic surgery. American Academy of Dermatology. *J Am Acad Dermatol*. 1995;33(2 Pt 1):271–278. doi:10.1016/0190-9622(95)90261-9.
5. Mohs FE. Chemosurgical treatment of external cancer: a microscopically controlled method of excision. *SD J Med Pharm*. 1950;3(6):161–166.
6. Calvão J, Pinho A, Brinca A, Vieira R. Clinicopathological factors influencing the number of stages of Mohs surgery for basal cell carcinoma. *An Bras Dermatol*. 2022;97(3):291–297. doi:10.1016/j.abd.2021.08.007.
7. Alam M, Berg D, Bhatia A, et al. Association between number of stages in Mohs micrographic surgery and surgeon-, patient-, and tumor-specific features: a cross-sectional study of practice patterns of 20 early- and mid-career Mohs surgeons. *Dermatol Surg*. 2010;36(12):1915–1920. doi:10.1111/j.1524-4725.2010.01758.x.
8. Thomas CL, Lam A, Lam J, Paver R, Storey L, Fernandez-Peñas P. Factors affecting choice of repair in Mohs micrographic surgery for non-melanoma skin cancer of the head. *Australas J Dermatol*. 2017;58(3):189–193. doi:10.1111/ajd.12453.
9. Greywal T, Goldenberg A, Eimpunth S, Jiang SB. Key characteristics of basal cell carcinoma with large subclinical extension. *J Eur Acad Dermatol Venereol*. 2020;34(3):485–490. doi:10.1111/jdv.15884.
10. Ratner D, Bagiella E. The efficacy of curettage in delineating margins of basal cell carcinoma before Mohs micrographic surgery. *Dermatol Surg*. 2003;29(9):899–903. doi:10.1046/j.1524-4725.2003.29272.x.
11. Bittner GC, Cerci FB, Kubo EM, Tolkachjov SN. Mohs micrographic surgery: a review of indications, technique, outcomes, and considerations. *An Bras Dermatol*. 2021;96(3):263–277. doi:10.1016/j.abd.2020.10.004.
12. Dinehart SM, Dodge R, Stanley WE, Franks HH, Pollack SV. Basal cell carcinoma treated with Mohs surgery. A comparison of 54 younger patients with 1050 older patients. *J Dermatol Surg Oncol*. 1992;18(7):560–566. doi:10.1111/j.1524-4725.1992.tb03509.x.
13. Krishnan A, Xu T, Hutfless S, et al. Outlier practice patterns in Mohs micrographic surgery. *JAMA Dermatol*. 2017;153(6):565–570. doi:10.1001/jamadermatol.2017.1450.
14. Cochrane Handbook 7.7.3.3. Obtaining standard deviations from standard errors. https://handbook-5-1.cochrane.org/chapter_7/7_7_3_3_obtaining_standard_deviations_from_standard_errors.htm. Accessed January 31, 2023.
15. Batra RS, Kelley LC. Predictors of extensive subclinical spread in nonmelanoma skin cancer treated with Mohs micrographic surgery. *Arch Dermatol*. 2002;138(8):1043–1051. doi:10.1001/archderm.138.8.1043.
16. Orengo IF, Salasche SJ, Fewkes J, Khan J, Thornby J, Rubin F. Correlation of histologic subtypes of primary basal cell carcinoma and number of Mohs stages required to achieve a tumor-free plane. *J Am Acad Dermatol*. 1997;37(3):395–397. doi:10.1016/S0190-9622(97)70138-5.
17. van Kester MS, Goeman JJ, Genders RE. Tissue-sparing properties of Mohs micrographic surgery for infiltrative basal cell carcinoma. *J Am Acad Dermatol*. 2019;80(6):1700–1703. doi:10.1016/j.jaad.2019.01.057.
18. Clements S, Khachemoune A. Upstaging of basal cell and squamous cell carcinomas during definitive surgery: a review of predictive preoperative clinical and histologic features. *Arch Dermatol Res*. 2021;313(5):319–325. doi:10.1007/s00403-020-02151-5.
19. Scofield-Kaplan SM, Jackson C, Gurney T, McDonnell E, Mancini R. Predictive value of preoperative periocular skin cancer measurements for final Mohs defect size. *Ophthalmic Plast Reconstr Surg*. 2019;35(6):604–608. doi:10.1097/IOP.0000000000001421.
20. Beatson M, Misitzis A, Landow S, et al. Predictors of basal cell carcinoma and implications for follow-up in high-risk patients in the Veterans affairs keratinocyte carcinoma chemoprevention (VAKCC) trial. *J Cutan Med Surg*. 2021;25(1):102–103. doi:10.1177/1203475420945230.
21. Shoham G, Berl A, Shir-Az O, Shabo S, Shalom A. Predicting Mohs surgery complexity by applying machine learning to patient demographics and tumor characteristics. *Exp Dermatol*. 2022;31(7):1029–1035. doi:10.1111/exd.14550.
22. Sahai S, Walling HW. Factors predictive of complex Mohs surgery cases. *J Dermatolog Treat*. 2012;23(6):421–427. doi:10.3109/09546634.2011.579083.
23. Santos MF, Magro ACD, Marques TF, Cafrune FE. Fatores preditores de maior número de estágios na cirurgia de Mohs: estudo de 256 casos. *Surg Cosmet Dermatol*. 2020;12(4):332–338. doi:10.5935/scd1984-8773.20201243705.

24. Chagas FSC, Santana Silva B de. Mohs micrographic surgery: a study of 83 cases. *An Bras Dermatol*. 2012;87(2):228–234. doi:10.1590/s0365-05962012000200006.
25. Chuang GS, Lu LK, Cummins DL, et al. Incidence of invasive squamous cell carcinomas in biopsy-proven squamous cell carcinomas in situ sent for Mohs micrographic surgery. *Dermatol Surg*. 2012;38(9):1456–1460. doi:10.1111/j.1524-4725.2012.02507.x.
26. Carley SK, Dixon A, Zachary CB, Steinman HK. Revised Mohs surgery care guidelines for squamous cell carcinoma *in-situ* are overdue. *Dermatol Online J*. 2019;25(3):1–3.
27. Knackstedt TJ, Brennick JB, Perry AE, Li Z, Quatrano NA, Samie FH. Frequency of squamous cell carcinoma (SCC) invasion in transected SCC *in situ* referred for Mohs surgery: the Dartmouth-Hitchcock experience. *Int J Dermatol*. 2015;54(7):830–833. doi:10.1111/ijd.12867.
28. Pyne J, Sapkota D, Wong JC. Aggressive basal cell carcinoma: dermatoscopy vascular features as clues to the diagnosis. *Dermatol Pract Concept*. 2012;2(3):0203a02. doi:10.5826/dpc.0203a02.
29. Garcia C, Crowson AN. Acantholytic squamous cell carcinoma: is it really a more-aggressive tumor? *Dermatol Surg*. 2011;37(3):353–356. doi:10.1111/j.1524-4725.2011.01886.x.
30. American Academy of Dermatology, American College of Mohs Surgery, American Society for Dermatologic Surgery Association, et al. AAD/ACMS/ASDSA/ASMS 2012 appropriate use criteria for Mohs micrographic surgery: a report of the American Academy of Dermatology, American College of Mohs Surgery, American Society for Dermatologic Surgery Association, and the American Society for Mohs Surgery. *Dermatol Surg*. 2012;38(10):1582–1603. doi:10.1111/j.1524-4725.2012.02574.x.
31. Blechman AB, Patterson JW, Russell MA. Application of Mohs micrographic surgery appropriate-use criteria to skin cancers at a university health system. *J Am Acad Dermatol*. 2014;71(1):29–35. doi:10.1016/j.jaad.2014.02.025.
32. Chong T, Tristani-Firouzi P, Bowen GM, Hadley ML, Duffy KL. Mohs appropriate use criteria: retrospectively applied to nonmelanoma skin cancers at a single academic center. *Dermatol Surg*. 2015;41(8):889–895. doi:10.1097/DSS.0000000000000412.
33. Amthor Croley JA. Current controversies in Mohs micrographic surgery. *Cutis*. 2019;104(4):E29–E31.
34. Paoli J, Daryoni S, Wennberg AM, et al. 5-year recurrence rates of Mohs micrographic surgery for aggressive and recurrent facial basal cell carcinoma. *Acta Derm Venereol*. 2011;91(6):689–693. doi:10.2340/00015555-1134.
35. Salman R, Daly C, Dani A, Eseonu A, Bibee K, Scott JF. Time to treatment and complexity of Mohs micrographic surgery. *Arch Dermatol Res*. 2022:1–2. doi:10.1007/s00403-022-02519-9.
36. Eide MJ, Weinstock MA, Dufresne RG, et al. Relationship of treatment delay with surgical defect size from keratinocyte carcinoma (basal cell carcinoma and squamous cell carcinoma of the skin). *J Invest Dermatol*. 2005;124(2):308–314. doi:10.1111/j.0022-202X.2004.23546.x.
37. Mohs FE. Chemosurgical treatment of cancer of the ear; a microscopically controlled method of excision. *Surgery*. 1947;21(5):605–622.
38. Pereira CT, Kruger EA, Sayer G, et al. Mohs versus surgical excision in nonmelanoma skin cancers: does location matter? *Ann Plast Surg*. 2013;70(4):432–434. doi:10.1097/SAP.0b013e3182834b47.
39. Mulvaney PM, Higgins HW, Dufresne RG, Cruz AP, Lee KC. Basal cell carcinomas of the ear are more aggressive than on other head and neck locations. *J Am Acad Dermatol*. 2014;70(5):924–926. doi:10.1016/j.jaad.2013.12.021.
40. Kuiper EM, van den Berge BA, Spoo JR, Kuiper J, Terra JB. Low recurrence rate of head and neck basal cell carcinoma treated with Mohs micrographic surgery: a retrospective study of 1021 cases. *Clin Otolaryngol*. 2018;43(5):1321–1327. doi:10.1111/coa.13176.
41. Duffy KL, McKenna JK, Hadley ML, Tristani-Firouzi P. Nonmelanoma skin cancers of the ear: correlation between subanatomic location and post-Mohs micrographic surgery defect size. *Dermatol Surg*. 2009;35(1):30–33. doi:10.1111/j.1524-4725.2008.34379.x.
42. Lee J, Forrester VJ, Novicoff WM, Guffey DJ, Russell MA. Surgical delays of less than 1 year in Mohs surgery associated with tumor growth in moderately- and poorly-differentiated squamous cell carcinomas but not lower-grade squamous cell carcinomas or basal cell carcinomas: a retrospective analysis. *J Am Acad Dermatol*. 2022;86(1):131–139. doi:10.1016/j.jaad.2021.08.059.
43. Camarero-Mulas C, Delgado Jiménez Y, Sanmartín-Jiménez O, et al. Mohs micrographic surgery in the elderly: comparison of tumours, surgery and first-year follow-up in patients younger and older than 80 years old in REGESMOHS. *J Eur Acad Dermatol Venereol*. 2018;32(1):108–112. doi:10.1111/jdv.14586.
44. Wheless L, Jacks S, Mooneyham Potter KA, Leach BC, Cook J. Skin cancer in organ transplant recipients: more than the immune system. *J Am Acad Dermatol*. 2014;71(2):359–365. doi:10.1016/j.jaad.2014.02.039.
45. Parlakpinar H, Gunata M. Transplantation and immunosuppression: a review of novel transplant-related immunosuppressant drugs. *Immunopharmacol Immunotoxicol*. 2021;43(6):651–665. doi:10.1080/08923973.2021.1966033.
46. Collins L, Quinn A, Stasko T. Skin cancer and immunosuppression. *Dermatol Clin*. 2019;37(1):83–94. doi:10.1016/j.det.2018.07.009.
47. Madeleine MM, Patel NS, Plasmeijer EI, et al. Epidemiology of keratinocyte carcinomas after organ transplantation. *Br J Dermatol*. 2017;177(5):1208–1216. doi:10.1111/bjd.15931.
48. Clarke EL, Willenbrink TJ, Shelton M, et al. Association of tumor characteristics with insurance type among patients undergoing Mohs micrographic surgery for nonmelanoma skin cancer. *JAMA Dermatol*. 2022;158(8):919–922. doi:10.1001/jamadermatol.2022.1802.
49. Wolfson J, Smith JL, Proper SA. Avoiding and managing Medicare fraud and abuse investigations of Mohs surgery: Mohs in the crosshairs. *JAMA Dermatol*. 2018;154(11):1249–1250. doi:10.1001/jamadermatol.2018.2402.
50. Leonardi-Bee J, Ellison T, Bath-Hextall F. Smoking and the risk of nonmelanoma skin cancer: systematic review and meta-analysis. *Arch Dermatol*. 2012;148(8):939–946. doi:10.1001/archdermatol.2012.1374.
51. Howard A, Agrawal N, Gooi Z. Lip and oral cavity squamous cell carcinoma. *Hematol Oncol Clin North Am*. 2021;35(5):895–911. doi:10.1016/j.hoc.2021.05.003.
52. ProximityOne. Resources to create & apply insights. http://proximityone.com/. Accessed February 4, 2023.
53. Jewett PI, Henning-Smith C, Lazovich D, Ahmed RL, Vogel RI. Incidental sun exposures as a source of sunburn among rural compared to urban residents in the United States. *J Rural Health*. 2023;39(2):402–407. doi:10.1111/jrh.12712.
54. Bowles TL, Sweeney C, Snyder J, et al. Impact of rurality on melanoma diagnosis in Utah. *Melanoma Manag*. 2021;8(2):MMT56. doi:10.2217/mmt-2020-0023.
55. Delgado Jiménez Y, Camarero-Mulas C, Sanmartín-Jiménez O, et al. Differences of Mohs micrographic surgery in basal cell carcinoma versus squamous cell carcinoma. *Int J Dermatol*. 2018;57(11):1375–1381. doi:10.1111/ijd.14223.
56. Lee KC, Higgins HW, Cruz AP, Dufresne RG. Characteristics of basal cell carcinoma of the lip treated using Mohs micrographic surgery. *Dermatol Surg*. 2012;38(12):1956–1961. doi:10.1111/j.1524-4725.2012.02580.x.
57. Que SKT, Zwald FO, Schmults CD. Cutaneous squamous cell carcinoma: incidence, risk factors, diagnosis, and staging. *J Am Acad Dermatol*. 2018;78(2):237–247. doi:10.1016/j.jaad.2017.08.059.
58. Waldman A, Schmults C. Cutaneous squamous cell carcinoma. *Hematol Oncol Clin North Am*. 2019;33(1):1–12. doi:10.1016/j.hoc.2018.08.001.

59. Soleymani T, Brodland DG, Arzeno J, Sharon DJ, Zitelli JA. Clinical outcomes of high-risk cutaneous squamous cell carcinomas treated with Mohs surgery alone: an analysis of local recurrence, regional nodal metastases, progression-free survival, and disease-specific death. *J Am Acad Dermatol*. 2023;88(1):109–117. doi:10.1016/j.jaad.2022.06.1169.
60. Zakhem GA, Pulavarty AN, Carucci J, Stevenson ML. Association of patient risk factors, tumor characteristics, and treatment modality with poor outcomes in primary cutaneous squamous cell carcinoma: a systematic review and meta-analysis. *JAMA Dermatol*. 2022:5–8. doi:10.1001/jamadermatol.2022.5508.
61. Dinehart SM, Pollack SV. Metastases from squamous cell carcinoma of the skin and lip. An analysis of twenty-seven cases. *J Am Acad Dermatol*. 1989;21(2 Pt 1):241–248. doi:10.1016/s0190-9622(89)70168-7.
62. Phillips TJ, Harris BN, Moore MG, Farwell DG, Bewley AF. Pathological margins and advanced cutaneous squamous cell carcinoma of the head and neck. *J Otolaryngol Head Neck Surg*. 2019;48(1):55. doi:10.1186/s40463-019-0374-3.
63. Bartoš V, Kullová M. Basal cell carcinoma of the skin with mixed histomorphology: a comparative study. *Cesk Patol*. 2016;52(4):222–226.
64. Lim GFS, Perez OA, Zitelli JA, Brodland DG. Correlation of basal cell carcinoma subtype with histologically confirmed subclinical extension during Mohs micrographic surgery: a prospective multicenter study. *J Am Acad Dermatol*. 2022;86(6):1309–1317. doi:10.1016/j.jaad.2022.02.037.
65. Kyllo RL, Staser KW, Rosman I, Council ML, Hurst EA. Histopathologic upgrading of nonmelanoma skin cancer at the time of Mohs micrographic surgery: a prospective review. *J Am Acad Dermatol*. 2019;81(2):541–547. doi:10.1016/j.jaad.2019.02.058.
66. Sohn GK, Keniston K, Kannan S, Hinds B, Jiang SIB. Characteristics of superficial basal cell carcinomas containing more aggressive subtypes on final histopathologic diagnosis. *J Drugs Dermatol*. 2021;20(3):283–288. doi:10.36849/JDD.5383.
67. Cerci FB, Kubo EM, Werner B. Comparison of basal cell carcinoma subtypes observed in preoperative biopsy and Mohs micrographic surgery. *An Bras Dermatol*. 2020;95(5):594–601. doi:10.1016/j.abd.2020.04.005.