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REFERENCES

1. Yu J, Atwater AR, Brod B, et al. Pediatric baseline patch test series: pediatric contact dermatitis workgroup. *Dermatitis*. 2018; 29:206-212.
2. Package Insert - TRUE TEST. Food and Drug Administration. Available at: https://www.fda.gov/media/83084/download. Accessed May 7, 2020.
3. Zug KA, Pham AK, Belsito DV, et al. Patch testing in children from 2005 to 2012: results from the North American contact dermatitis group. *Dermatitis*. 2014;25:345-355.
4. Moustafa D, Yu J. Contact allergy to hydroperoxides of limonene and linalool in a pediatric population. *J Am Acad Dermatol*. 2020;2:2-3.
5. Goldenberg A, Mousdicas N, Silverberg N, et al. Pediatric contact dermatitis registry inaugural case data. *Dermatitis*. 2016;27:293-302.

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Noncompliance with surgical margin guidelines is associated with histologic margin positivity: A retrospective case-control study

To the Editor: Variable recurrence and metastasis rates are noted following standard surgical excision (SSE) with postoperative margin assessment for cutaneous squamous cell carcinoma (cSCC).[1-4] The National Comprehensive Cancer Network (NCCN) cSCC guidelines postulate that this variability could be due to differences in margin sizes and whether clear histologic margins are achieved. The NCCN recommends 4-6-mm surgical margins for low-risk cSCC.[3] This study aims first to determine whether NCCN guideline–compliant surgical margin (GCM) selection and margin documentation are associated with improved tumor clearance and second to examine the factors associated with GCM.

Using an single-institution cSCC registry approved by an institutional review board, a retrospective Brigham and Women's Hospital (BWH) T stage–matched cohort of 462 patients with cSCC BWH stage of T2b or less and undergoing SSE with curative intent by dermatologists or nondermatologists was generated. The primary study endpoint was a negative histologic margin after SSE. Patient data, including demographic, tumor, treatment, and outcome data, were collected. Surgical margins were defined as the margin of normal-appearing skin incorporated into the excision design. Pathologic or histologic margins were defined as the microscopic presence or absence of malignant cells at the specimen margin. Margin compliance was graded according to NCCN guidelines[3] and stratified into 3 groups: (1) NCCN GCM, (2) NCCN guideline noncompliant margins, and (3) no documentation of surgical margins. Factors associated with GCM and positive histologic margins after excision were studied. Factors associated with positive histologic margins on excision were determined using stepwise logistic regression matched for surgical specialty and BWH stage. Data were managed using REDCap electronic data capture and analyzed using JMP Pro 14 (SAS Institute, Cary, NC). ANOVA and χ^2 testing were used to determine statistical significance; $P < .05$ was considered statistically significant.

Dermatology and nondermatology cohorts (n = 231 each) were well matched by mean patient age of 71.3 versus 72.6 years old ($P = .269$), gender being 39% versus 47% female ($P = .074$), mean tumor diameter of 1.4 cm (±SD 0.7 cm) versus 1.5 cm (±SD 1.3 cm; $P = .242$), and BWH stage, which was identical for dermatologists and nondermatologists with each cohort consisting of 78% T1 (n = 180), 22% T2a (n = 5), and 0.4% T2b (n = 1). Table I shows factors associated with margin documentation status and factors associated with positive pathologic margins after excision, matched for specialty and BWH T stage. Table II shows multivariate logistic regression modeling of factors associated with positive pathologic margins on excision after matching for specialty and BWH T stage. Positive histologic margins (incomplete tumor excision) occurred in 6.4% of all cases, including 2% of SSEs performed by dermatologists and 11% of SSEs performed by nondermatologists. Regardless of surgical specialty,

Table I. Factors associated with margin documentation status and factors associated with positive pathologic margins after excision, matched for specialty and Brigham and Women's tumor staging system

	Margin documentation status				Histologic margin status		
Variables of interest	Documented, appropriate, N = 199 (43.1%)	Documented, inappropriate, N = 95 (20.5%)	Undocumented, N = 168 (36.4%)	*P* value	Positive histologic margins, N = 30 (6.5%)	Negative histologic margins, N = 432 (93.5%)	*P* value
Mean age at diagnosis, years (±SD)	71.3 (12.3)	71.1 (13.2)	73.1 (13.1)	.31	73.7 (15.2)	71.8 (12.6)	.43
Patient sex, n							
Male	115 (57.8%)	55 (57.9%)	95 (56.5%)	.96	16 (53.3%)	249 (57.6%)	.64
Female	84 (42.2%)	40 (42.1%)	73 (43.5%)		14 (46.7%)	183 (42.4%)	
Immunosuppression							
Yes	38 (19.1%)	15 (15.8%)	31 (18.5%)	.78	5 (16.7%)	79 (18.3%)	.82
No	161 (80.9%)	80 (84.2%)	137 (81.5%)		25 (83.3%)	353 (81.7%)	
Poor tumor differentiation							
Yes	1 (0.5%)	0 (0%)	5 (3.0%)	.08	1 (3.3%)	5 (1.2%)	.35
No	177 (88.9%)	82 (86.3%)	137 (81.5%)		27 (90.0%)	369 (85.4%)	
Unknown	21 (10.6%)	13 (13.7%)	26 (15.5%)		2 (6.7%)	58 (13.4%)	
Anatomic location, n							
High-risk head and neck	4 (2.0%)	8 (8.4%)	23 (13.7%)	<.0001	8 (26.7%)	27 (6.25%)	<.0001
Head and neck	11 (5.5%)	18 (19.0%)	34 (20.2%)		10 (33.3%)	53 (12.3%)	
Non–head and neck	184 (92.5%)	69 (72.6%)	111 (66.1%)		12 (40.0%)	352 (81.5%)	
Mean tumor size, cm (±SD)	1.3 (0.6)	1.6 (1.6)	1.4 (1.0)	.03	1.6 (1.2)	1.4 (1.0)	.23
Tumor size group, n							
<2 cm	164 (82.8%)	69 (72.6%)	123 (77.4%)	.02	21 (70.0%)	335 (79.4%)	.03
2-4 cm	34 (17.2%)	22 (23.2%)	28 (17.6%)		6 (20.0%)	78 (18.5%)	
≥4 cm	0 (0%)	4 (4.2%)	8 (5.0%)		3 (10.0%)	9 (2.1%)	
Perineural invasion							
Yes	3 (1.5%)	0 (0%)	4 (2.4%)	.32	2 (6.7%)	5 (1.2%)	.02
No	196 (98.5%)	95 (100%)	164 (97.6%)		28 (93.3%)	427 (98.8%)	
Treatment status							
Recurrent tumor	3 (1.5%)	8 (8.4%)	11 (6.6%)	.01	4 (13.3%)	18 (4.2%)	.02
Primary tumor	196 (98.5%)	87 (91.6%)	156 (93.4%)		26 (86.7%)	413 (95.8%)	
Brigham and Women's tumor stage, n							
T1	163 (81.9%)	69 (72.6%)	128 (76.2%)	.13	20 (66.7%)	340 (78.7%)	.02
T2a	36 (18.1%)	26 (27.4%)	38 (22.6%)		9 (30.0%)	91 (21.1%)	
T2b	0 (0%)	0 (0%)	2 (1.2%)		1 (3.3%)	1 (0.2%)	
AJCC8 stage, n							
T1	12 (80.0%)	21 (80.8%)	40 (75.5%)	.97	10 (55.5%)	63 (82.9%)	.009
T2	2 (13.3%)	3 (11.5%)	7 (13.2%)		3 (16.7%)	9 (11.8%)	
T3	1 (6.7%)	2 (7.7%)	6 (11.3%)		5 (27.8%)	4 (5.3%)	
Surgical specialty performing excision, n							
Dermatology	165 (82.9%)	30 (31.6%)	36 (21.4%)	<.0001	5 (16.7%)	226 (52.3%)	.0002
Other specialty	34 (17.1%)	65 (68.4%)	132 (78.6%)		25 (83.3%)	206 (47.7%)	
Histologic margin status of excision, n							
Positive	2 (1.0%)	5 (5.3%)	23 (13.7%)	<.0001	—	—	
Negative	197 (99.0%)	90 (94.7%)	145 (86.3%)		—	—	
Margin group, n							
Documented, appropriate	—	—	—		2 (6.7%)	197 (45.6%)	<.0001
Documented, inappropriate	—	—	—		5 (16.7%)	90 (20.8%)	
Undocumented	—	—	—		23 (76.6%)	145 (33.6%)	

Table II. Factors associated with positive pathologic margins on excision after matching for specialty and Brigham and Women's tumor staging system in multivariate logistic regression

Variable of interest	No. patients (%)	Odds ratio (95% confidence interval)	*P* value
Head and neck location			
Not head and neck	364 (78.8%)	1 [Reference]	.0005
Head and neck	98 (21.2%)	4.1 (1.8-9.2)	
Margin group			
Documented, appropriate	199 (43.1%)	1 [Reference]	.0005
Documented, inappropriate	95 (20.5%)	3.5 (0.6-19.2)	
Undocumented	168 (36.4%)	9.6 (2.1-42.7)	
Treatment status			
Primary	439 (95.2%)	1 [Reference]	.14
Recurrent	22 (4.8%)	2.5 (0.7-8.9)	

histologic margins were negative in 99.0% of cases reporting GCM. Most positive histologic margins (93.3%) were in cases in which surgical margins were not compliant with NCCN guidelines (n = 5) or not reported (n = 23).

Our data support the NCCN guidelines for surgical margins when treating cSCC with SSE. These findings emphasize the importance of following evidenced-based guidelines. When these guidelines are followed, there is a significantly lower rate of positive histologic margins (regardless of surgical specialty), and the need for re-excision is lowered.

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REFERENCES

1. Rogers HW, Weinstock MA, Feldman SR, Coldiron BM. Incidence estimate of nonmelanoma skin cancer (Keratinocyte Carcinomas) in the U.S. Population, 2012. *JAMA Dermatol.* 2015;151:1081-1086.
2. Rogers HW, Weinstock MA, Harris AR, et al. Incidence estimate of nonmelanoma skin cancer in the United States, 2006. *Arch Dermatol.* 2010;146:283-287.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines, Squamous Cell Skin Cancer, Version 1.2020. Accessed April 15, 2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/squamous.pdf
4. Xiong DD, Beal BT, Varra V, et al. Outcomes in intermediate-risk squamous cell carcinomas treated with Mohs micrographic surgery compared with wide local excision. *J Am Acad Dermatol.* 2020;82:1195-1204.

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Hypopigmented macules in neurofibromatosis type 1: A case control study

To the Editor: Neurofibromatosis type 1 (NF1) is an autosomal dominant, neurocutaneous disorder. In most cases, cutaneous pigmentary manifestations are the main diagnostic clue. NF1 is characterized by hyperpigmentation—café au lait macules (CALMs), skinfold freckling, and melanotic plexiform neurofibromas. However, hypopigmented lesions have received little attention in patients with NF1. Riccardi[1] described the presence of hypopigmented macules (HMs) in approximately 2% to 3% of patients with NF1 in 1987. Studies regarding the physiopathology of HM in NF1 are lacking. This study aimed to characterize the prevalence of HMs in our pediatric patients diagnosed with NF1.