Table II. Cox proportional hazards analysis for disease-specific survival (*DSS*) in patients with metastatic Merkel cell carcinoma

Variable	DSS hazard ratio (95% CI)	*P* value
Age at diagnosis	1.03 (1.02-1.05)	<.0001
Sex		
Female (Ref)	1.0	
Male	1.14 (0.83-1.56)	.417
Race		
White (Ref)	1.0	
African American	1.82 (0.78-3.73)	.155
Primary site		
Head and neck (Ref)	1.0	
Trunk	1.39 (0.86-2.27)	.181
Upper and lower extremities		
Other	1.05 (0.72-1.53)	.805
Other*	1.53 (1.01-2.32)	.044
Tumor size		
0-10 mm (Ref)	1.0	
11-20 mm	1.48 (0.79-2.78)	.222
21-30 mm	1.07 (0.60-1.92)	.818
31-40 mm	0.84 (0.42-1.68)	.627
41-50 mm	1.63 (0.82-3.25)	.166
>50 mm	1.61 (0.86-3.02)	.136
Bone metastasis		
No (Ref)	1.0	
Yes	1.18 (0.84-1.67)	.083
Brain metastasis		
No (Ref)	1.0	
Yes	3.85 (1.58-9.38)	.0030
Liver metastasis		
No (Ref)	1.0	
Yes	1.86 (1.37-2.52)	<.0001
Lung metastasis		
No (Ref)	1.0	
Yes	1.12 (0.77-1.64)	.555

CI, Confidence interval; *Ref*, reference.

*Owing to the nature of coding in the Surveillance, Epidemiology, and End Results database, the "other" category contains patients with overlapping primary skin sites and those with an unknown primary where Merkel cell carcinoma was first discovered in a lymph node or visceral location.

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A retrospective cohort study of comprehensive peripheral and deep margin assessment in Merkel cell carcinoma: Standard margins may be unreliable

To the Editor: The National Comprehensive Cancer Network (NCCN) guidelines recommend wide excision with 1- to 2-cm margins to investing muscular fascia or pericranium for Merkel cell carcinoma (MCC) treatment. The ideal method of excision and surgical margin assessment has not been established. The goal of this study was to assess the adequacy of currently recommended surgical margins using complete histopathologic margin evaluation methods: Mohs micrographic surgery (MMS) or wide local excision with complete circumferential peripheral and deep margin assessment with intraoperative en face frozen sections.

An Institutional Review Board-approved retrospective review was performed of patients with MCC treated by MMS or wide local excision with complete circumferential peripheral and deep margin assessment (MMS-assessment) from January 2012 through May 2018. The initial and subsequent surgical margin and stages required for complete tumor extirpation were recorded. If a variable depth or width was noted in operative notes, the narrowest or most superficial dimensions were recorded. The Clark level of residual tumor was noted. Any residual margin positivity was graded in quartiles as the percentage of a ×2 microscopic field filled by tumor, designated as mild, 0% to 25%; mild-moderate, 26% to 50%; moderate, 51 to 75%; and high, 76% to 100%. All patients and slides were independently reviewed by A.V., T.K., and E.W. Summary statistics pertaining to positive margins were calculated to evaluate the sufficiency of standard margins.

There were 22 patients with MCC, mean tumor size 1.8 cm (SD, 1.3 cm), treated during the 6-year period.

Table I. Demographics and tumor characteristics of Merkel cell carcinoma cohort

Variable*	Total (N = 22)
Age, y	70.5 (57-90)
Sex	
Male	14 (64)
Female	8 (36)
Immune status	
Immunocompetent	22 (100)
Immunocompromised	0
Site	
Head and neck	14 (64)
Trunk	0
Extremities	8 (36)
Tumor size	
Not reported	2 (9.5)
<1 cm	6 (28.6)
1.1-2 cm	7 (33.3)
>2 cm	6 (28.6)

*Data are reported as mean (range) or number (%).

Table II. Margin status of Merkel cell carcinoma treated with Mohs micrographic surgery or excision with complete peripheral and deep frozen section margin assessment

Variable*	Total (N = 22)
Initial peripheral margin	
<1 cm	1 (4.5)
1.0-2.0 cm	16 (72.7)
2.1-3 cm	4 (18.2)
>3 cm	1 (4.5)
Initial peripheral margin status	
Positive	3 (13.6)
Negative	19 (86.4)
Number of stages required for tumor clearance	1.59 (1-2)
Initial deep plane of resection	
Subcutis	1 (4.5)
Fascia	4 (18.2)
Intramuscular	10 (45.5)
Periosteum/perichondrium†	7 (31.8)
Initial deep margin status	
Positive	12 (54.5)
Negative	10 (45.5)
Degree of microscopic margin positivity	(n = 13)
Mild (0%-25%)	6 (46.2)
Mild-moderate (26%-50%)	1 (7.7)
Moderate (51%-75%)	2 (15.4)
High (>75%)	4 (30.8)

*Data are presented as number (%) or mean (range).
†Includes full-thickness eyelid tumors.

Patient demographics and tumor characteristics are summarized in Table I. Initial and subsequent peripheral and deep margin dimensions/planes and margin status are summarized in Table II. The initial peripheral surgical margin equaled NCCN guidelines in 72.7% of patients and exceeded guidelines in 22.7%. The initial deep surgical margin equaled NCCN guidelines in 18.2% of patients and exceeded guidelines in 77.3%. There were 13 patients (59.1%) with a positive initial margin (first stage), including 12 positive deep margins (92.3%) and 3 positive peripheral margins (23.1%). All 13 positive cases were initially excised with peripheral and deep margins that met or exceeded the NCCN recommendations. All cases had negative margins upon excision of a subsequent stage.

Residual tumor on surgical margins has been variably reported in 3.7% to 51% of patients with MCC.[1-3] An 8% local recurrence rate after excision with negative margins vs an 18% local recurrence rate with positive margins has been reported, and survival is worse in the setting of positive margins.[3,4] In our study, despite resection margins that met or exceeded NCCN recommendations, the surgical margin was positive in 57% of the patients, and 92% of those were positive at the deep margin. Past studies have evaluated various peripheral margin widths, but the deep margin is less frequently studied.[4,5] In our study, the deep margin remained positive after excision with the recommended margins more frequently than the peripheral. Especially when residual tumor is focal, it may not be recognized on routine permanent section pathology.

This study is not without limitations. In accordance with general MMS practice, the frozen section slides were not routinely sent for permanent section consultation, and immunohistochemistry was not performed. We suspect such practices would be more likely to result in additional margins being considered positive rather than reversing a positive margin frozen section interpretation. Our reported margin positivity is higher than in other published studies and may be partly due to reporting of margin status after a single Mohs stage (vs final margin status) and a selection bias of large tumors and complex anatomic sites at a tertiary academic medical center.

Given the importance of achieving negative margins and the demonstrated inadequacy of standard recommended margins in this study, a method of complete margin assessment is suggested. The role of expanded margins and adjuvant radiation therapy in this context require further study.

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Accuracy of commercial panels to evaluate myositis autoantibodies: A single-institution perspective

To the Editor: Laboratory panels for myositis-specific antibodies (MSA) and myositis-associated antibodies (MAA) are increasingly being used in the diagnosis and prognostication of dermatomyositis (DM).[1,2] However, many commercial panels used in clinical settings have limited validation compared to other methodologies.[3] To understand the accuracy of commercial myositis panels in the clinical setting, we performed a cross-sectional analysis of patients with DM, comparing commercially available myositis panels to panels performed in the research setting.

Eighty patients from a DM database at the University of Pennsylvania had sera that were assayed at Johns Hopkins University for MSA/MAA, including TIF1-γ, Mi-2α, Mi-2β, SRP, Ku, Ro-52, MDA-5, SAE-1, PM-75, PM-100, Jo-1, PL-7, PL-12, OJ, and EJ. Anti—TIF1-γ was detected using an enzyme-linked immunosorbent assay from MBL (Woburn, MA). All other antibodies were detected using the EUROIMMUN line blot assay (Autoimmune Inflammatory Myopathies 16 Ag panel, Lubeck, Germany).[4] Charts were reviewed for demographics and commercial myositis panel results. Commercial tests were *concordant* if their results matched that of the research panels and *discordant* if results differed. Panel results were categorized by the time difference between the commercial and research panels (the bleed date). Summary statistics were performed with the data (Table I).

Of 80 patients, 27 (33.8%) had commercial assays performed. The median age was 49.8 years. Most patients were female (92.6%) and white (88.9%). Commercial myositis panels were performed at ARUP Laboratories (Salt Lake City, UT; 13 panels, 48.1%), Quest Diagnostics (Secaucus, NJ; 7 panels, 25.9%), RDL Reference Laboratory (3 panels, 11.1%), Immco Diagnostics (Williamsville, NY; 3 panels, 11.1%), and Oklahoma Medical Research Foundation (Oklahoma City, OK; 1 panel, 3.7%). Of these 27 patients, 19 (70.4%) were positive for MSA/MAA using the research panels compared to 7 (25.9%) using the commercial panels (Table I). ARUP Laboratories had 5 panels (41.7%) showing discordant antibodies, and Immco Diagnostics had 1 discordant antibody (33.3%) (Table I). Although Quest and RDL had 100% concordance in our cohort, they did not test for anti-TIF1-γ, SAE1, NXP-2, or MDA-5, with the Quest panels also not testing for anti—Ro-52 or PM-Scl. We did not observe a relationship between antibody discordancy and bleed date differences.

The findings are limited by the sample size, bleed date differences, and the cross-sectional nature of the study. Furthermore, there is a possibility, although unlikely, that research panels yielded false positive results. Despite this, our findings show that commercial myositis panels will require improved precision and standardization to be a vital component of the DM workup. In our experience, a positive myositis autoantibody may help diagnose and treat DM in cases with uncertain clinical presentation or bring attention to antibody-specific DM phenotypes. However, a negative myositis panel result does not