group and indicated a poor prognosis. The low-pigmentation group was more likely to have a positive SLNB and to have the lymph node, skin, or lung as a first metastasis site. A first metastasis to distant organs was also associated with melanoma pigmentation. Interestingly, the multivariate analysis showed that a first lung metastasis was strongly associated with low- pigmentation. Patients with low-pigmentation acral melanoma may have a greater tendency to develop metastasis through the vascular system, but further studies are warranted to explain why lung involvement was more frequent than liver and brain involvement in these patients. In conclusion, low-pigmentation acral melanomas were significantly associated with advanced T stage, the presence of ulceration, a higher mitotic rate, SLNB positivity, and a higher risk of metastasis. Furthermore, low-pigmentation was independently associated with a first lung metastasis.

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The scalp is a high-risk site for cutaneous squamous cell carcinoma metastasis

To the Editor: The ear and lip have historically been considered anatomic sites at high risk for metastasis of cutaneous squamous cell carcinoma (cSCC). Although the Eighth Edition of the American Joint Committee on Cancer Staging (AJCC) for cSCC does not segregate risk by anatomic location,[1] current National Comprehensive Cancer Network (NCCN) guidelines include the lip and ear among "high-risk regions" and the scalp among "moderate-risk regions,"[2] implying a lower metastatic risk for cSCC on the scalp vs on the lip or ear. This retrospective cohort study compared rates of metastasis for cSCC ≥2 cm located on the scalp vs the ear or lip.

A prospectively updated database was searched to identify patients with invasive cSCCs that were ≥2 cm in diameter, located on the lip, ear, scalp, or pretibial leg, and treated with Mohs micrographic surgery between September 1, 2005, and September 1, 2019, at the Hospital of the University of Pennsylvania. The pretibial leg was included as a low-risk reference anatomic site, similar to the methods of Brougham et al.[3] Documented follow-up at the Hospital of the University of Pennsylvania was required for inclusion.

Because of the small lip sample size, lip and ear cSCC were pooled into a "high-risk" group. We used linear and Poisson regression, performed with R 3.5.2 software (https://CRAN.R-project.org/doc/FAQ/R-FAQ.html) and the miceadds 3.8-9 package (Robitzsch and Grund, 2020) package, to determine univariate and multivariate associations of risk factors with metastasis, respectively. Models were corrected for intrapatient correlation using clustered SEs. We did not examine T3 tumors separately.

We analyzed 432 cSCC, including 15 (3.5%) located on the lip, 73 (16.9%) on the ear, 198 (45.8%) on the scalp, and 146 (33.8%) on the pretibial

Table I. Unadjusted rate of metastasis for ear and lip, scalp, and pretibial leg and adjusted risk ratio for metastasis of ear and lip, scalp, and pretibial leg, controlling for sex, age at surgery, immunocompromised status, and anatomic depth of invasion

Variable	Ear + lip (n = 83)	Scalp (n = 166)	Difference	*P* value	Risk ratio	*P* value
Metastasis						
No. (%)	6 (7.2)	11 (6.6)				
Risk, %	9.09	9.09	<.001	>.99	1.01	.99
	Pretibial leg (n = 99)	**Scalp (n = 166)**	**Difference**	***P* value**	**Risk ratio***	***P* value***
Metastasis						
No. (%)	0 (0)	11 (6.6)				
Risk, %	0	9.09	9.09	.002	…	…
	Pretibial leg (n = 99)	**Ear + lip (n = 83)**	**Difference**	***P* value**	**Risk ratio***	***P* value***
Metastasis						
No. (%)	0 (0)	6 (7.2)				
Risk, %	0	9.09	9.09	.003	…	…

No., Number.
*The Poisson models did not converge, and risk ratios could not be determined.

Table II. Multivariate Poisson regression for risk factors for metastasis in ≥2 cm cutaneous squamous cell carcinoma tumors on the ear and lip vs scalp

	Ear + lip		Scalp*	
Factor	**Risk ratio (95% CI)**	***P* value**	**Risk ratio (95% CI)**	***P* value**
Immunocompromised status				
No	1 [Reference]		1 [Reference]	
Yes	6.02 (1.3-28.6)	.024	0.78 (0.4-1.4)	.387
Differentiation				
Well or moderate	1 [Reference]		1 [Reference]	
Poor	3.51 (0.8-15.1)	.093	0.58 (0.2-1.9)	.363
Tumor depth				
Dermis or subcutaneous fat	1 [Reference]		…	…
Beyond subcutaneous fat	0.93 (0.2-4.6)	.927		
Diameter				
2-3.99 cm	1 [Reference]		1 [Reference]	
≥4 cm	0.997 (0.2-4.3)	.996	0.93 (0.5-1.7)	.809

CI, Confidence interval.
*As a result of the insufficient sample size, anatomic depth of invasion could not be evaluated as a risk factor for the scalp.

leg. The scalp, ear, and lip populations had no statistical difference in tumor diameter, median follow-up time, depth of invasion, or degree of differentiation. The pretibial leg had significantly longer follow-up time compared with the ear ($P = .03$) and scalp ($P = .005$), a lower incidence of perineural invasion compared with the ear ($P = .005$), and shallower depth of invasion compared with all 3 anatomic sites (ear: $P < .001$; scalp: $P < .001$; lip: $P = .04$).

Table I summarizes the univariate linear regression and multivariate Poisson regression results for risk of metastasis. Scalp, ear, and lip cSCCs had significantly higher rates of metastasis compared with pretibial leg cSCCs (scalp: 9.1% vs 0%, $P = .002$; ear and lip: 9.1% vs 0%, $P = .003$). When controlling for depth of invasion, patient sex, age, and immunocompromised status, the rate of metastasis was not significantly different between the scalp and the ear or lip (9.09% vs 9.09%; $P = .99$). Location on the scalp, ear, or lip was an independent risk factor for metastasis when accounting for other risk factors (depth of invasion, patient sex, age, and immunocompromised status). Immunocompromised status was associated with an increased metastatic risk for cSCC on the ear or lip (risk ratio, 6.02; 90% confidence interval, 1.3-28.6) but not the scalp (Table II).

Our results demonstrate that the scalp is a "high-risk region" for metastasis of cSCC, similar to the lip and ear.

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Melanoma in situ and invasive melanoma of the vulva: An analysis of the National Cancer Database

To the Editor: Vulvar melanoma (VM) accounts for 6% to 10% of vulvar malignancies.[1] Current knowledge comes from smaller retrospective studies.[1,2] This study investigated the demographics and survival of VM in situ (MIS) and invasive VM (IVM) using the National Cancer Database (NCDB).

International Classification of Diseases for Oncology third edition histology codes for melanoma 8720 to 8774, combined with primary site codes for the vulva (C510-519), were used to identify patients with VM in NCDB between 2004 and 2016. The analysis included 394 patients with vulvar MIS and 1688 patients with IVM, with a median age at diagnosis of 63 and 66 years, respectively. The median Breslow thickness for IVM was 2.00 mm, and 56.8% of patients presented with ulceration. Regional lymph node metastasis was found in 22.8% of patients (Table I). The 5-year overall survival (OS) was 74.4% for vulvar MIS and 42.7% for IVM (Figs 1 and 2).

When adjusting for confounders, independent predictors of worse OS in IVM were age (hazard ratio [HR], 1.02; 95% confidence interval [CI], 1.01-1.03), Charlson-Deyo Comorbidity Index score of 1 (HR, 1.31; 95% CI, 1.06-1.63), and Charlson-Deyo Comorbidity Index score of ≥2 (HR, 2.181; 95% CI, 1.58-3.02), nodular melanoma histology (HR, 1.23; 95% CI, 1.00-1.52), Breslow thickness >4 mm (HR, 1.37; 95% CI, 1.07-1.74), stage II (HR, 1.94; 95% CI, 1.42-2.66), stage III (HR, 2.21; 95% CI, 1.45-3.38), stage IV (HR, 5.81; 95% CI, 3.77-8.93), positive regional lymph nodes (HR, 1.92; 95% CI, 1.33-2.79), and regional lymph nodes not examined (HR, 1.64; 95% CI, 1.31-2.04). Private insurance (HR, 0.49; 95% CI, 0.29-0.84) and government insurance (HR, 0.47; 95% CI, 0.33-0.98) were also independently associated with improved OS in IVM (Table II).

The 5-year OS for IVM (42.7%) is consistent with previous studies showing worse OS in IVM compared with cutaneous melanoma (52%-88% depending on the cutaneous melanoma subtype), even when accounting for stage.[1-3] These results underscore the importance of vulvar screening as part of full-body skin examinations and educating patients in self-examination in anatomically sensitive areas.

A survey of dermatologists showed that only 4% of dermatologists included the vulva as part of their full-body skin examinations.[4] Only 66% of dermatologists felt diagnosing VM was their role compared with 81% of gynecologists.[4] However, dermatologists play a key role in educating patients on features of VM and in bridging the gap with other specialties to ensure adequate screening.

Insurance coverage in our study for patients with IVM was independently associated with improved OS. Similarly, in patients with vulvar MIS, annual income >$63,000 was independently associated with improved OS. Low socioeconomic status has been previously linked with advanced disease at presentation and poor prognosis of melanoma, particularly in the elderly, which is especially relevant in VM given the median age of diagnosis.[5]