

Supplementary Online Content

Massey PR, Wang DM, Murad F, et al. Extensive perineural invasion vs nerve caliber to assess cutaneous squamous cell carcinoma prognosis. *JAMA Dermatol*. Published online October 18, 2023. doi:10.1001/jamadermatol.2023.3703

eTable 1. Association Between Assessed Perineural Invasion (PNI) Factors of Interest and Brigham and Women’s Hospital (BWH) Risk Factors

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Association Between Assessed Perineural Invasion (PNI) Factors of Interest and Brigham and Women’s Hospital (BWH) Risk Factors

	Tumor diameter <2cm	Tumor diameter ≥2cm	P value	Tumor depth dermis or fat	Tumor depth beyond fat	P value	Tumor differentiation well/moderate	Tumor differentiation poor	P value	PNI <0.1mm	PNI ≥0.1mm	P value
N=	69	59		99	38		90	47		66	74	
PNI extent												
Focal	44 (62%)	27 (38%)	.21	60 (79%)	16 (21%)	.04	53 (70%)	23 (30%)	.16	47 (61%)	30 (39%)	<.001
Moderate	13 (35%)	24 (65%)		27 (66%)	14 (34%)		26 (63%)	15 (37%)		15 (35%)	28 (65%)	
Extensive	11 (58%)	8 (42%)		11 (58%)	8 (42%)		10 (53%)	9 (47%)		3 (16%)	16 (84%)	
PNI location												
Intratumoral	7 (29%)	17 (71%)	.41	19 (70%)	8 (30%)	.69	16 (59%)	11 (41%)	.55	10 (37%)	17 (63%)	.17
Advancing edge	28 (74%)	10 (26%)		31 (84%)	6 (16%)		27 (73%)	10 (27%)		31 (79%)	8 (21%)	
Extratumoral	23 (48%)	25 (52%)		39 (70%)	17 (30%)		38 (68%)	18 (32%)		18 (32%)	38 (68%)	
Nerve caliber												
<0.1mm	43 (69%)	19 (31%)	.001	50 (78%)	14 (22%)	.15	41 (64%)	23 (36%)	.71			
≥0.1mm	26 (39%)	40 (61%)		49 (67%)	24 (33%)		49 (67%)	24 (33%)				
PNI depth												
Dermis	36 (60%)	24 (40%)	.20	52 (83%)	11 (17%)	.01	43 (68%)	20 (32%)	.56	43 (66%)	22 (34%)	<.001
Beyond dermis	33 (49%)	35 (51%)		47 (64%)	27 (36%)		47 (64%)	27 (36%)		23 (31%)	52 (69%)	

P values based on nonparametric test for trend.

PNI, perineural invasion. BWH, Brigham and Women’s Hospital.

eTable 2. Poor Outcomes by Assessed Perineural Invasion (PNI) Characteristic

	Local recurrence		P value	Any metastasis (NM/DM)		P value	Disease specific death		P value	Any poor outcomes (LR/NM/DM/DSD)		P value
	No	Yes		No	Yes		No	Yes		No	Yes	
N=	128	12		130	10		129	11		123	17	
PNI extent												
Focal	74 (96%)	3 (4%)	.003	73 (95%)	4 (5%)	.32	73 (95%)	4 (5%)	.05	72 (94%)	5 (6%)	.001
Moderate	39 (91%)	4 (9%)		39 (91%)	4 (9%)		40 (93%)	3 (7%)		38 (88%)	5 (12%)	
Extensive	14 (74%)	5 (26%)		17 (89%)	2 (11%)		15 (79%)	4 (21%)		12 (63%)	7 (37%)	
PNI location												
Intratumoral	25 (93%)	2 (7%)	.81	26 (96%)	1 (4%)	.71	26 (96%)	1 (4%)	.80	25 (93%)	2 (7%)	.95
Advancing edge	34 (87%)	5 (13%)		35 (90%)	4 (10%)		34 (87%)	5 (13%)		31 (79%)	8 (21%)	
Extratumoral	52 (93%)	4 (7%)		52 (93%)	4 (7%)		52 (93%)	4 (7%)		50 (89%)	6 (11%)	
Nerve caliber												
<0.1mm	61 (92%)	5 (8%)	.69	62 (94%)	4 (6%)	.64	63 (95%)	3 (5%)	.17	60 (91%)	6 (9%)	.30
≥0.1mm	67 (91%)	7 (9%)		68 (92%)	6 (8%)		66 (89%)	8 (11%)		63 (85%)	11 (15%)	
PNI depth												
Dermis	59 (91%)	6 (9%)	.80	59 (91%)	6 (9%)	.37	60 (92%)	5 (8%)	.95	56 (86%)	9 (14%)	.57
Beyond dermis	69 (92%)	6 (8%)		71 (95%)	4 (5%)		69 (92%)	6 (8%)		67 (89%)	8 (11%)	

P values based on nonparametric test for trend.

PNI, perineural invasion; NM, nodal metastasis; DM, distant metastasis; LR, local recurrence; DSD, disease specific death.

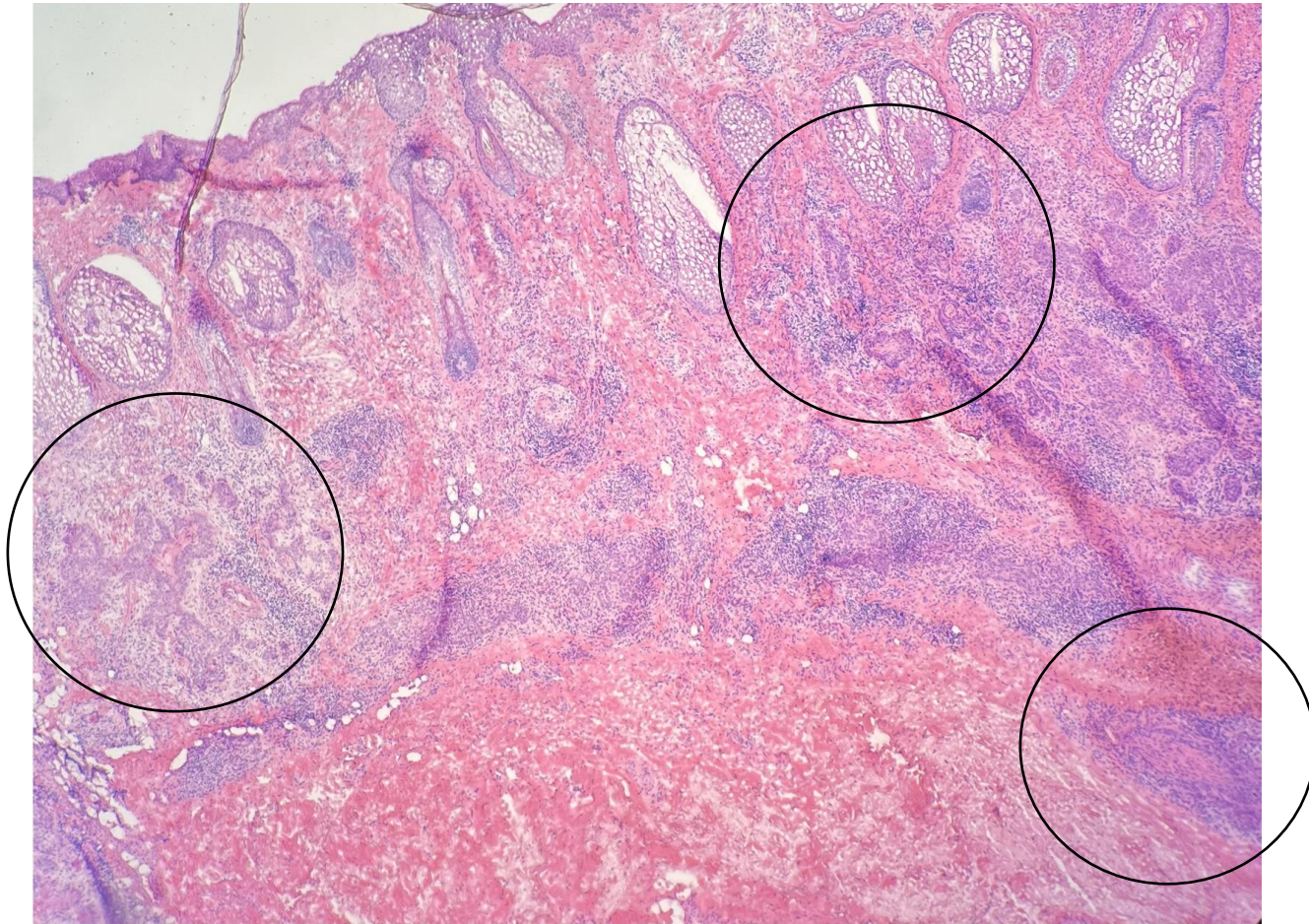
eTable 3. Test Characteristics of Models Under Study to Detect Any Poor Outcome

	Current BWH	BWH with ePNI in lieu of lcPNI	BWH with ePNI or lcPNI
Sensitivity (95% CI)	0.706 (0.627, 0.785)	0.692 (0.611, 0.774)	0.769 (0.695, 0.844)
Specificity (95% CI)	0.455 (0.369, 0.541)	0.682 (0.600, 0.764)	0.491 (0.403, 0.579)
PPV (95% CI)	0.164 (0.100, 0.228)	0.204 (0.133, 0.276)	0.152 (0.088, 0.215)
NPV (95% CI)	0.911 (0.862, 0.960)	0.949 (0.911, 0.988)	0.947 (0.908, 0.987)
AUC (95% CI)	0.585 (0.468, 0.702)	0.690 (0.562, 0.817)	0.644 (0.532, 0.757)

Bolded cells highlight best model for each characteristic. Sensitivity, specificity, PPV and NPV calculations performed by stratification of tumors into high (T2b/T3) and low (T2a/T1) BWH T stage.

BWH, Brigham and Women's Hospital; ePNI, extensive perineural invasion; lcPNI, large caliber perineural invasion; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value; AUC, area under the curve.

eFigure. Example of Perineural Invasion in at Least 3 Distinct Nerves of a Hematoxylin and Eosin–Stained Mohs Section



Circles represent distinct nerve foci. Note differences in nerve caliber and spatial orientation among foci (original magnification x40).