

Integrating the 31-gene expression profile test with clinical and pathologic features can provide personalized precision estimates for sentinel lymph node positivity

Chase Kriza, MD¹ and Joseph Bennett, MD¹

1.ChristianaCare Helen F. Graham Cancer Center & Research Institute, Newark, DE

Background

>The 31-gene expression profile (31-GEP) test for cutaneous melanoma (CM) is a validated prognostic test to predict risk of tumor recurrence and sentinel lymph node (SLN) positivity.¹⁻⁷

>A recent publication validated the incorporation of age, Breslow thickness, ulceration, and mitotic rate with the 31-GEP continuous score using a neural network algorithm for precise SLN biopsy (SLNB) positivity prediction (i31-GEP SLNB).⁸

Objective

>Evaluate the performance of the i31-GEP SLNB algorithm in patients from ChristianaCare Helen F. Graham Cancer Center clinically tested with the 31-GEP.

Methods

>Retrospective chart review was performed on de-identified data for patients at ChristianaCare Helen F. Graham Cancer Center who had known SLN status and the 31-GEP test ordered between 2015-2021 (n=156). The i31-GEP SLNB result was analyzed, and the area under the receiver operating characteristic curve (AUC) was used to determine accuracy. A 5% risk of SLNB positivity was used for consistency with NCCN guidelines (e.g., T1a with no high-risk features), which recommend that SLNB be discussed with patients who have >5% risk of SLNB positivity.

Results

Table 1. Participant demographics presented according to low risk (<5%) or high risk (>5%), as determined by i31-GEP SLNB test.

Demographics (n=156)	<5% Risk (n=30)	≥5% Risk (n=126)	p-value
Age, Median (Range)	69 (43-85)	63 (20-91)	0.046
T-category			<0.001
T1a	11	6	
T1b	13	15	
T2a	5	29	
T2b	1	11	
T3a	0	20	
T3b	0	20	
T4a	0	9	
T4b	0	16	
Breslow Thickness, mm			
Median (Range)	0.8 (0.2-1.9)	2.1 (0.3-16.0)	<0.001
Ulceration present			
Yes	3	51	0.002
Mitotic rate (1/mm ²), Median (Range)	1 (0-2)	2 (0-25)	<0.001
SLN positive			
Yes	0	32	0.002

Results

Table 2. SLNB positivity risk by i31-GEP SLNB or T-stage

Group	<5% Risk	SLN+	>5% Risk	SLN+
Overall Population (T1-T4)				
i31-GEP SLNB (n=156)	30	0 (0%)	126	32 (25.4%)
T1-T4 (n=156)	2 (both T1a w/o HRF)*	0 (0%)	154	32 (20.8%)
T1-T2 Population				
T1-T2 i31-GEP SLNB (n=91)	30 (33.0%)	0 (0%)	61 (67.0%)	11 (18.0%)
T1-T2; (n=91)	2 (both T1a w/o HRF)*	0 (0%)	89	11 (12.4%)
T3-T4 Population				
T3-T4 i31-GEP SLNB (n=65)	0 (0%)	0 (0%)	65	21 (32.3%)
T3-T4 (n=65)	0 (0%)	0 (0%)	65	21 (32.3%)

*T stage only identified two patients who were <5% risk of SLN positivity, and their tumors were both T1a and had no high-risk features (HRF). HRF included: age <40 years, mitotic rate ≥2/mm², presence of regression, lymphovascular invasion, transected base, and absence of tumor-infiltrating lymphocytes.

Table 3. Accuracy metrics

Population	Sensitivity	Specificity	PPV	NPV
i31-GEP SLNB, 5% threshold ^a				
T1-T2	100%	37.5%	18.0%	100%
T1-T2, ≥55 years	100%	43.5%	10.3%	100%
Tumor stage ^b				
T1-T2	100%	2.5%	12.4%	100%
T1-T2, ≥55 years	100%	1.6%	6.2%	100%

^a<5% risk was considered negative; >5% risk considered positive.

^bT1a with no HRF considered negative; T1a with HRF and T2 considered positive.

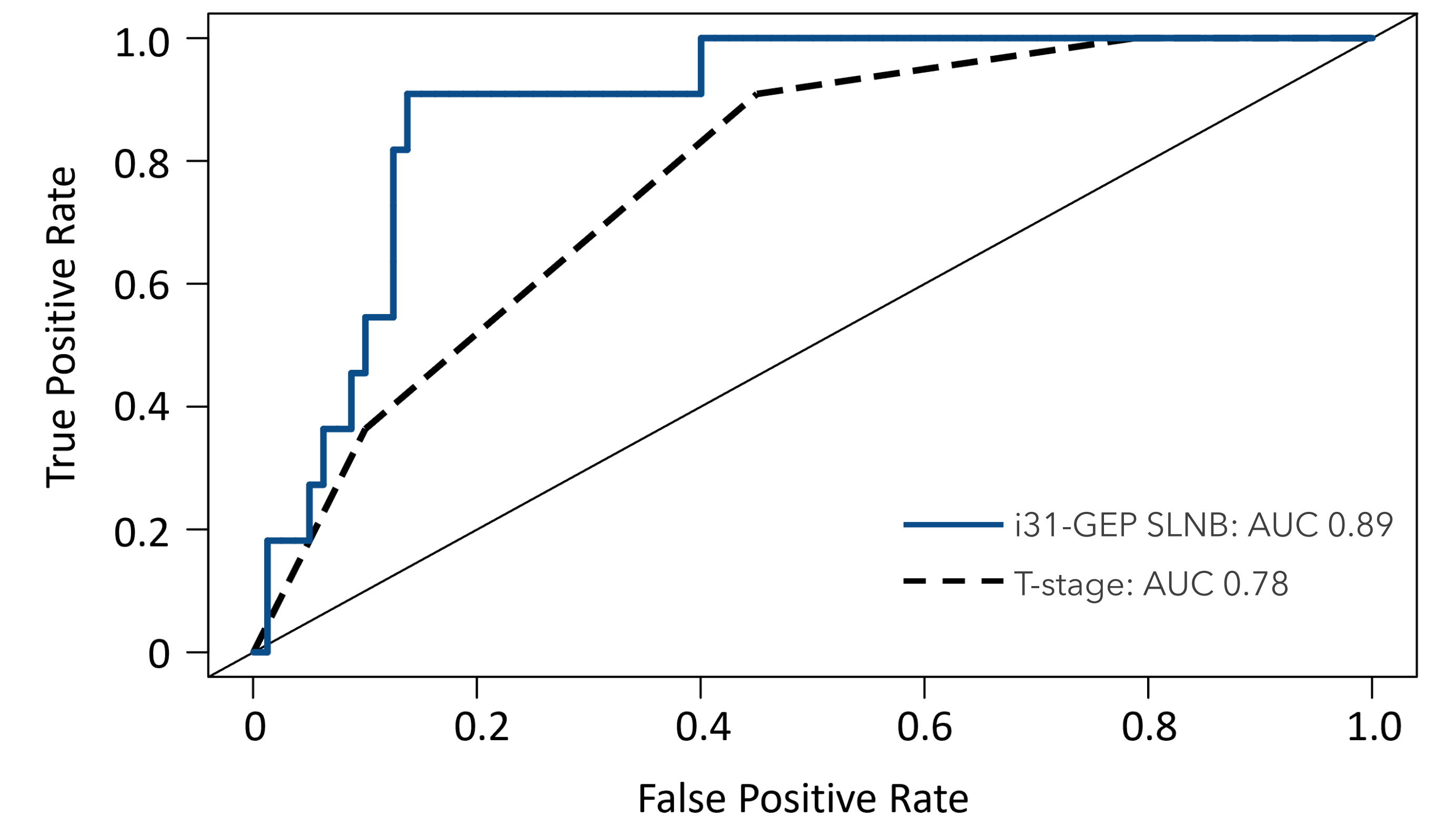
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Figure 1. ROC curves for T1-T2 i31-GEP SLNB versus T-stage



In patients with T1-T2 tumors, the i31-GEP SLNB outperformed T-stage alone for predicting SLNB positivity.

Conclusions

- > The i31-GEP SLNB identified 33.0% of patients with T1-T2 tumors as having a SLN positivity risk below 5% with an NPV = 100%, while increasing SLNB positivity from 12% with staging alone to 18% (PPV).
- > The i31-GEP SLNB outperformed T-stage at identifying patients with low-risk tumors who could forego SLNB.
- > The i31-GEP SLNB identified 30 out of 91 patients with T1-T2 tumors who had a <5% risk of SLN positivity, with zero positive biopsies. In contrast, using T-stage alone only identified 2 patients who had no other high-risk tumor features (HRF) with <5% risk of SLN positivity.
- > Removing patients from SLNB consideration with i31-GEP SLNB could have increased the SLNB positivity yield in the cohort from 12.4% to 18.0%, without missing a single positive node.