Clinical performance of a noninvasive melanoma rule-out test across Fitzpatrick skin types

To the Editor: Numerous studies suggest that melanoma in individuals with higher Fitzpatrick skin types (FST) is more likely to present at an advanced stage and result in higher mortality.[1] A noninvasive genomic rule-out test assessing gene expression of *LINC00518* and *PRAME* has been introduced to help augment detection of melanoma at an early stage while reducing the number of biopsies performed for benign pigmented lesions that simulate melanoma.[2,3] Clinical validation using histopathologic consensus diagnoses as a reference standard demonstrated the test has a ≥99% negative predictive value (NPV), indicating that a lesion that tests negative is unlikely to be a melanoma.[4,5] Although patients of all skin types were eligible for inclusion in the validation study, the cohorts consisted mostly of samples from individuals with FST I, II, or III. The purpose of the current study was to assess the performance of this noninvasive rule-out melanoma test across all FST, with a particular focus on NPV in FST IV-VI patients.

Test performance metrics for patients with FST I-III (n = 4152) and IV-VI (n = 130) across 73 US clinical practice sites were compared using biopsy results and follow-up information compiled through the DermTech Melanoma Test Registry Protocol (WCG IRB waiver obtained March 3, 2021). Performance metrics were also calculated for a cohort limited to lesions with at least 6 months of follow-up or biopsy results.

Full cohort characteristics and follow-up details are summarized in Table I, and performance of the test in all subjects is summarized in Table II. In the full cohort (N = 4282), sensitivity was 0.9429 (66/70), specificity was 0.9086 (3709/4082), positive predictive value (PPV) was 0.1503 (66/439), and NPV was 0.9989 (3709/3713) for FST I-III. For FST IV-VI, sensitivity was 1.0 (3/3), specificity was 0.9449 (120/127), PPV was 0.3 (3/10), and NPV was 1.0 (120/120). Three of 3 melanomas (0.55 mm, 0.40 mm, and melanoma *in situ* in non–sun-exposed areas on the trunk) in the IV-VI group diagnosed by histopathology were correctly identified as positive with the test. The 95% confidence intervals for the differences in sensitivity, specificity, NPV, and PPV between the 2 groups included 0, indicating no significant difference in any of the performance metrics.

Additional analyses limited to subjects with either a biopsy result or at least 6 months (≥182 days) of follow-up after testing (N = 2266) confirmed the results observed in the full cohort for sensitivity, specificity, PPV, and NPV, and no statistically significant differences between groups were observed (Table II).

Table I. Characteristics of subjects by Fitzpatrick skin type groups

	FST I-III (N = 4152)	FST IV-VI (N = 130)
Median age, y (range)	59 (18-99)	58 (18-93)
Female sex, *n* (%)	2564 (62%)	69 (53%)
Subjects with test-positive lesions, *n* (%)	439 (11%)	10 (8%)
Subjects with test-negative lesions, *n* (%)	3713 (89%)	120 (92%)
Subjects with follow-up, *n* (%)	2525 (61%)	75 (58%)
Subjects with ≥6 mo follow-up, *n* (%)	2197 (53%)	69 (53%)

FST, Fitzpatrick skin type.

The results of this study demonstrate that the performance of the noninvasive test in FST IV-VI patients does not differ from that in FST I-III patients. These findings support the test's utility of guiding biopsy decisions for ambiguous pigmented skin lesions of all skin types without a need to limit access for patients with FST IV-VI.

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Table II. Test performance in patients with all Fitzpatrick skin types

	Lesions with biopsy or any follow-up			Lesions with biopsy or ≥6 mo follow-up		
	FST I-III (*N* = 4152)	FST IV-VI (*N* = 130)	Significant difference?	FST I-III (*N* = 2197)	FST IV-VI (*N* = 69)	Significant difference?
Sensitivity	94.3%	100%	No	94.3%	100%	No
Specificity	90.9%	94%	No	82.5%	89.4%	No
PPV	15%	30%	No	15%	30%	No
NPV	99.9%	100%	No	99.8%	100%	No

The full data set ($N = 4282$) included all cases with Fitzpatrick skin type (FST) information (biopsied or not and any length of follow-up). The most stringent data set summarized ($N = 2266$) includes cases that were either biopsied or have ≥6 months (≥182 days) of follow-up. No statistically significant differences were observed between groups with either data set.
FST, Fitzpatrick skin type; *NPV*, negative predictive value.

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Patient consent: The need for patient consent does therefore not apply. No recognizable patient photographs or other identifiable materials were used.

IRB approval status: On March 3, 2021, the WCG IRB approved a request for a waiver of authorization for use and disclosure of protected health information (PHI) for this study via expedited review.

Key words: Fitzpatrick skin type; genomic test; medical dermatology; melanoma; noninvasive test; oncology; rule-out test; skin cancer.

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Conflicts of interest

Drs Skelsey, Loftis, Kaufmann, Siegel, Bhatia, Wangia, and Walker are investigators and/or consultants of DermTech; Drs Rigby, Whitaker, Stone, Moccia, O'Brien, Jansen, and Clarke are employees of DermTech.

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Impact of 8th edition American Joint Committee on Cancer staging changes on sentinel lymph node biopsy practices in melanoma

To the Editor: In 2018, the American Joint Commission on Cancer (AJCC) revised its melanoma staging system, redefining pathologic T1a versus T1b tumors. Presence of mitoses was replaced in the system by tumor thickness ≥0.8 mm.[1] Clinical guidelines for sentinel lymph node biopsy (SLNB) incorporated these changes, recommending against routine SLNB for patients with T1a tumors and careful consideration for those with T1b tumors.[2] Concerns have been raised that restaging might lead to over-application of SLNB in relatively low risk T1b patients.[3] Using the National Cancer Database, we explored whether staging changes have impacted patient selection for SLNB and the rate of SLN positivity in T1 melanoma by examining patients diagnosed with pathologic T1a or T1b melanoma in either 2017 or 2019. A total of 37,176 patients were identified: 18,583 in 2017 and 18,593 in 2019. The median age was 63 years (IQR 52-73), 55% of patients were male, and 98% were White. In 2017, 25% of all T1 patients underwent SLNB compared to 26% in 2019 ($P = .021$). Comparing patients who underwent SLNB in 2019 versus 2017, 54% versus 55% of patients