Update on patterns of use of a genetic expression profiling adhesive test to detect melanoma: a cross-sectional survey of academic pigmented lesion experts and private practice clinicians

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Keywords: clinician, detection, DermTech, diagnostic, doctor, gene expression profiling, GEP, lesion assay, LINC, melanoma, physician, pigmented, PLA, PRAME, provider, survey, test

To the Editor:

Gene expression profiling (GEP) technology can assist both management and detection of melanoma. For example, GEP testing can guide management of melanoma by predicting recurrence or metastatic risk based on primary tumor expression patterns [1]. Alternatively, GEP technology such as the pigmented lesion assay (PLA), (DermTech, La Jolla, CA) can aid in the detection of melanoma [2]. The PLA is a non-invasive tape strip screening test for melanoma based on aberrant expression of long intergenic non-coding RNA 518 (LINC) and preferentially expressed antigen in melanoma (PRAME), [2]. Although the positive predictive value (PPV) of the PLA for melanoma is reportedly 93%, 50%, and 7% for LINC+/PRAME+, LINC-/PRAME+, and LINC+/PRAME- results respectively, the negative predictive value for LINC-/PRAME- lesions is >99% [2]. The aim of this study was to characterize how private practice providers and academic melanoma specialists have incorporated PLA technology into practice and to investigate how PLA results guide clinical management of pigmented lesions.

From June to November 2021, an electronic survey was administered to Melanoma Prevention Working Group (MPWG) members, comprised of academic melanoma specialists, and private practice clinicians who had used PLA and were identified by DermTech, with their permission. DermTech was not involved in any aspects of study design, data analysis, or publication. These populations were selected to capture both content experts and regular PLA users. Survey topics included provider demographics and clinical scenarios surrounding PLA usage. Statistical analysis was performed using SPSS version 27.0 (SPSS Inc., Chicago, IL). The Mass General Brigham Institutional Review Board approved this study.

A total of 66 dermatologists completed this survey, of which 63.6% were associated with academic or health maintenance organizations (HMO) and 36.4% were in private practice (**Table 1**). Response rates were 62.7% and 55.8% amongst academic melanoma specialists and private practice users, respectively. Of academic melanoma specialists,

Table 1. *Demographics and clinical characteristics of the study sample[a].*

	Academic[a] N=42, N (%)	Private practice N=24, N (%)	P-value[b]
Provider type			**0.04**
Physician	42 (100.0)	21 (87.5)	
Nurse practitioner	0 (0.0)	2 (8.3)	
Physician assistant	0 (0.0)	1 (4.2)	
Length in practice			**0.07**
<5 years	3 (7.1)	3 (12.5)	
5-10 years	11 (26.2)	4 (16.7)	
10-20 years	11 (26.2)	13 (54.2)	
>20 years	17 (40.5)	4 (16.7)	
Percentage of patients seen for pigmented lesions			**0.01**
0-10%	0 (0.0)	2 (8.3)	
10-25%	4 (9.5)	5 (20.8)	
25-50%	12 (28.6)	11 (45.8)	
50-100%	26 (61.9)	6 (25.0)	
Used PLA test in practice			**<0.001**
Yes	18 (42.9)	24 (100.0)	
No	24 (57.1)	0 (0.0)	
Reasons never used PLA test[c,d] (N=24, N=0)			
Cost or concern regarding insurance coverage	12 (50.0)	-	-
Do not feel it is useful in practice	13 (54.2)	-	
Practice setting does not permit use	3 (12.5)	-	
Inconvenient or impractical for patients to come back for additional visit pending PLA results	15 (62.5)	-	
Insufficient data/evidence to support use	11 (45.8)	-	
Other[e]	2 (8.3)	-	

Abbreviations: PLA, pigmented lesion assay

**Bold values indicate statistically significant difference, defined as P<0.05.*

[a]Academic includes academic only (83.3%), academic + government (7.1%), academic + private (4.8%), and health maintenance organization (4.8%).

[b]Fisher's exact tests used to calculate P values.

[c]Participants were permitted to select multiple options; column percentages may be >100%.

[d]Percentages based off of "no" responses to "ordered DermTech melanoma test (PLA)".

[e]Free text responses include "not familiar enough with the data to have instituted it into practice" and "with current tools in clinic, accuracy is sufficient for biopsy. Favor use outside of routine clinic setting."

42.9% reported using PLA in clinical practice. Most frequently cited reasons for academic non-users (N=24) were inconvenient/impractical for patients to return after test results (62.5%), not useful (54.2%), cost or concern regarding insurance coverage (50.0%), and insufficient data/evidence (45.8%).

Of PLA users that reported anatomic location influenced PLA use (71.4% of PLA users), the most commonly cited location was the face (70.0%, Table 2). Private practice PLA users reported more regular PLA use (≥2 times monthly) than academics (79.2% private practice versus 22.2% academic; P=0.001) and more had received inconclusive PLA results (100.0% versus 38.9%; P<0.001). Three academic PLA users (16.7%) had negative PLA results (LINC-/PRAME-) for lesions subsequently diagnosed as melanoma. These lesions had an average diameter of 1.33cm (range 1.0-1.5cm), were irregularly pigmented (N=1) or pink-brown (N=2), and were diagnosed on average two years later (range 1.5-2.25 years).

Most PLA users reported managing LINC-/PRAME- results with clinical follow-up (92.9%, **Table 3**). In contrast, LINC+/PRAME-, LINC-/PRAME+, and LINC+/PRAME+ results were typically managed with biopsy (92.9%, 100%, and 100%, respectively). For LINC+/PRAME+ results, management differed by practice setting. Most academic users recommended

Table 3. *Clinician management of DermTech Pigmented Lesion Assay (PLA) results among reported PLA users[a].*

	Academic N=18, N (%)	Private Practice N=24, N (%)	P value[b]
Management of LINC-/PRAME- PLA result			1.00
Follow clinically	17 (94.4)	22 (91.7)	
Incisional biopsy	0 (0.0)	0 (0.0)	
Narrow excisional biopsy	0 (0.0)	1 (4.2)	
Wide excisional biopsy[c]	0 (0.0)	0 (0.0)	
Other[d]	1 (5.6)	1 (4.2)	
Management of LINC+/PRAME- PLA result			0.35
Follow clinically	2 (11.1)	0 (0.0)	
Incisional biopsy	5 (27.8)	10 (41.7)	
Narrow excisional biopsy	8 (44.4)	11 (45.8)	
Wide excisional biopsy[c]	0 (0.0)	1 (4.2)	
Other[e]	3 (16.7)	2 (8.3)	
Management of LINC-/PRAME+ PLA result			0.78
Follow clinically	0 (0.0)	0 (0.0)	
Incisional biopsy	5 (27.8)	7 (29.2)	
Narrow excisional biopsy	11 (61.1)	13 (54.2)	
Wide excisional biopsy[c]	0 (0.0)	2 (8.3)	
Other[f]	2 (11.1)	2 (8.3)	
Management of LINC+/PRAME+ PLA result			**0.001**
Follow clinically	0 (0.0)	0 (0.0)	
Incisional biopsy	4 (22.2)	1 (4.2)	
Narrow excisional biopsy	13 (72.2)	10 (41.7)	
Wide excisional biopsy[c]	0 (0.0)	11 (45.8)	
Other[g]	1 (5.6)	2 (8.3)	

Abbreviations: f/u, follow-up; mgmt., management; mm, millimeter; PLA, Pigmented Lesion Assay

**__Bold__ values indicate statistically significant difference, defined as P<0.05.*

[a]Reported non-users of the DermTech PLA test included 24 academic providers and 0 private practice providers, not included in this table.

[b]Fisher's exact tests used to calculate P values.

[c]Wide excisional biopsy with 5mm or more clear clinical margins.

[d]Other free text responses include "It depends on the history, age, location, personal history, phenotype, dermoscopy" and "shave".

[e]Other free text responses include "Depends on clinical scenario and my pretest probability. But in general my concern for these is low", "Biopsy with two mm margins (can be deep scoop shave to get past the bottom, doesn't need to be excision", "if large, scouting biopsies", "shave/scrape biopsy", and "shave".

[f]Other free text responses include "Biopsy with two mm margins (can be deep scoop shave to get past the bottom, doesn't need to be excision), "if large, scouting biopsies", "shave/scrape biopsy", and "shave".

[g]Other free text responses include "Biopsy with two mm margins (can be deep scoop shave to get past the bottom, doesn't need to be excision), "shave/scrape biopsy", and "shave."

narrow excisional biopsy (72.2% academic versus 41.7% private practice), but more private practice users recommended wide excisional biopsy (45.8% private practice versus 0.0% academic), (P=0.001).

We observed increased PLA adoption among academic melanoma specialists (42.9% in our study versus 21% in a prior study), [3]. Although the PPV of PLA for melanoma for LINC+/PRAME- results is 7% [2], the majority of PLA users in our study opted for management with biopsy. Additionally, nearly half of private practice PLA users in our study recommended wide excisional biopsies for LINC+/PRAME+ results, which have a 93% PPV [2]. However, the American Academy of Dermatology recommends narrow excisional biopsies for melanoma detection when possible [4]. Frequently cited reasons for inconclusive PLA results (N=31) were lesions <5mm (58.1%), hair/blood on the adhesive (48.4%), and palm and sole locations (9.7%), despite PLA instructions cautioning against use in these scenarios [5].

This study was limited to academic melanoma specialists and a specific population of frequent PLA

users provided by DermTech, so conclusions about nationwide PLA use cannot be drawn. Although three cases of negative PLA results were subsequently diagnosed as melanoma, we lacked knowledge of the total number of tests performed and thus, we could not estimate the incidence of this occurrence. Our study reinforces the role of clinician judgment when using the PLA to interpret results and recommend appropriate treatment and follow-up. Additionally, our results provide further insight into how the use and interpretation of PLA results may impact clinical management in different practice settings.

Acknowledgements

Dr. Hartman is supported by the Melanoma Research Foundation and a VISN-1 Career Development Award. Dr. Grossman is supported by the University of Utah Department of Dermatology and the Huntsman Cancer Foundation. Authors Trepanowski, Chang, Ziad, Kim, and Hartman have no conflicts of interest to declare.

Potential conflicts of interest

Dr. Grossman was an investigator for DermTech and serves on the advisory board of Orlucent, Inc.

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Table 2. *Clinician use patterns of the DermTech Pigmented Lesion Assay (PLA) among reported PLA users[a].*

	Academic	Private Practice	P value[b]
Frequency ordered			**0.001**
Less than once per month	6 (33.3)	1 (4.2)	
Once per month	8 (44.4)	4 (16.7)	
2-10 times per month	4 (22.2)	13 (54.2)	
>10 times per month	0 (0.0)	6 (25.0)	
Average number of PLA tests per patient			0.37
1 per patient	17 (94.4)	20 (83.3)	
2 per patient	1 (5.6)	4 (16.7)	
Performs the PLA test[c]			
Physician	17 (94.4)	13 (54.2)	**0.005**
Nurse or physician assistant	1 (5.6)	5 (20.8)	0.21
Medical assistant	1 (5.6)	10 (41.7)	**0.01**
Anatomic location influences PLA use			0.51
Yes	14 (77.8)	16 (66.7)	
No	4 (22.2)	8 (33.3)	
Anatomic location most likely consider using PLA[d] (N=14, N=16)			0.15
Face	11 (78.6)	10 (62.5)	
Chest	0 (0.0)	3 (18.8)	
Back	2 (14.3)	0 (0.0)	
Other	1 (7.1)	3 (18.8)	
Remotely ordered PLA during teledermatology			0.73
Yes	4 (22.2)	7 (29.2)	
No	14 (77.8)	17 (70.8)	
Had inconclusive result with PLA			**<0.001**
Yes	7 (38.9)	24 (100.0)	
No	11 (61.1)	0 (0.0)	
Circumstances possibly related to inconclusive result[c,e] (N=7, N=24)			
The person who collected the sample (insufficient training)	1 (14.3)	8 (33.3)	0.64
Small lesions (<5 mm)	4 (57.1)	14 (58.3)	1.00
Particular anatomic sites[f]	1 (14.3)	8 (33.3)	0.64
Presence of hair or blood on tape strip	3 (42.9)	12 (50.0)	1.00
Other[g]	1 (14.3)	3 (12.5)	1.00
Management after inconclusive PLA result[c,e] (N=7, N=24)			
Repeat test, if concerned about the lesion	4 (57.1)	15 (62.5)	1.00
Clinically monitor, if not concerned about the lesion	5 (71.4)	4 (16.7)	**0.01**
Biopsy of the lesion	2 (28.6)	10 (41.7)	0.68
Other[h]	0 (0.0)	1 (4.2)	1.00
Had negative PLA result (LINC-/ PRAME-) that was eventually biopsied and diagnosed as melanoma			0.07
Yes	3 (16.7)	0 (0.0)	
No	15 (83.3)	24 (100.0)	

Abbreviations: mm, millimeter; PLA, pigmented lesion assay

**__Bold__ values indicate statistically significant difference, defined as P<0.05.*

[a]Reported non-users of the DermTech PLA test included 24 academic providers and 0 private practice providers, not included in this table.

[b]Fisher's exact tests used to calculate P-values.

[c]Choices designated as "select all that apply", column percentages may be >100%.

[d]Percentages based off of "yes" responses to "anatomic location influences PLA use".

[e]Percentages based off of "yes" responses to "had inconclusive result with PLA".

[f]Anatomic sites mentioned in free text response include palm/sole (N=3), buttock (N=2), breast (N=1), flank (N=1), back (N=1), abdomen (N=1), legs (N=1), dorsal feet (N=1), hair-bearing areas (N=1), and feet (N=1).

[g]Other free text responses include "sample received too late at laboratory (>10 days)", "don't know why, lesions were large and I am well-trained and performed it myself", "not enough material to process", and "patient might have been sweating".

[h]Other free text responses include "retest if due to hair of blood, otherwise biopsy or very closely clinically monitor".