

Findings from a large US registry study to assess the real-world utility of a non-invasive gene expression test designed to rule out primary cutaneous melanoma

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SYNOPSIS

The Pigmented Lesion Assay (PLA) analyzes gene expression to objectively rule out melanoma. The test uses a non-invasive adhesive patch-based sample collection platform that enables guidance on biopsy decisions and elevates pigmented lesion management beyond what can be visually ascertained. The test's negative predictive value of >99%, and rapid, painless application make it an attractive pre-biopsy solution. It reduces biopsies by 90% while improving care and reducing cost. This registry study (53 US dermatology offices, 90 providers, median patient age 48 years, 60.80% female patients) assesses real-world utility to determine if the PLA changes clinical practice. The PLA assessed 3,418 concerning pigmented skin lesions. Three hundred and twenty-four lesions (9.48%) were PLA(+) and 3,094 (90.52%) were negative. A PLA test result is positive if LINC, PRAME, or both target genes are detected. These molecular pathology findings are known to correspond with histopathology findings of in situ or invasive primary melanoma in 7%, 50%, and 93%, respectively. The 9.48% PLA(+) cases consisted of 5.15% LINC-only, 1.93% PRAME-only, and 2.40% LINC and PRAME double positive cases. Notably, PLA(+) lesions were almost universally surgically biopsied (97.53%), while PLA(-) cases were nearly always monitored and not biopsied (99.94%). These studies demonstrate that the PLA has true clinical value in community-based practices where providers make important decisions based on the test's results. Pigmented lesions with PLA(+) test results are subjected to surgical biopsies, whereas PLA(-) lesions are followed clinically and not biopsied.

OBJECTIVES

- To assess the real-world use and utility of the PLA [1-4] and determine, if clinicians follow the guidance of the test

METHODS

We here expand on PLA follow-up and utility findings previously reported that also included long-term follow-up and US registry data; approval was obtained from the Western-Copernicus Group's independent review board [2, 4]. We report on a one-year PLA registry study initiated in June of 2018 with data acquisition between July of 2018 and June of 2019. Fifty-three US dermatology practices (and 90 providers within these practices including board certified dermatologists, primary care physicians, physician assistants, and nurse practitioners) participated in the registry and reported on 3,418 pigmented lesions clinically suspicious for melanoma that were evaluated by PLA. The PLA results and management decisions (clinical monitoring of a given lesion or biopsy) were correlated.

All lesion samples were obtained using a non-invasive adhesive skin collection kit (DermTech, La Jolla, CA) according to package insert instructions. In brief, a selected pigmented lesion suspicious for melanoma is cleansed with an ethanol swab and dried, and four adhesive patches from the sample collection kit are applied sequentially to collect one sample. Gentle pressure from about 5 circular thumb motions ensures contact between the adhesive and skin; no wait time is required. To enable separation of lesional from non-lesional surrounding skin tissue, the lesion is demarcated with a marker pen on each one of the applied adhesive patches. Patches are placed in a pre-addressed courier envelope and shipped to a central processing laboratory without need for refrigeration or special handling. The sample collection process takes about 1-2 minutes. A molecular pathology report is generally available within 48-72 hours.

RESULTS

Findings from a large US Pigmented Lesion Assay registry study (53 US dermatology offices, 90 providers) of 3,418 patients and their pigmented skin lesions clinically suspicious for melanoma and evaluated by PLA are presented. The median patient age was 48 years; 60.80% of patients were female and 39.20% were male. Overall, most lesions (55.18%) evaluated by PLA were located on the trunk, followed by locations on extremities (27.27%) and locations in face / head / neck areas (17.55%). Figure 1 provides details on lesion locations in male and female patients demonstrating similar lesion locations in face / head / neck areas (19.00% and 17.35%, respectively) while female patients' pigmented lesions evaluated by PLA were more often located on extremities (32.44% versus 18.70% in male patients).

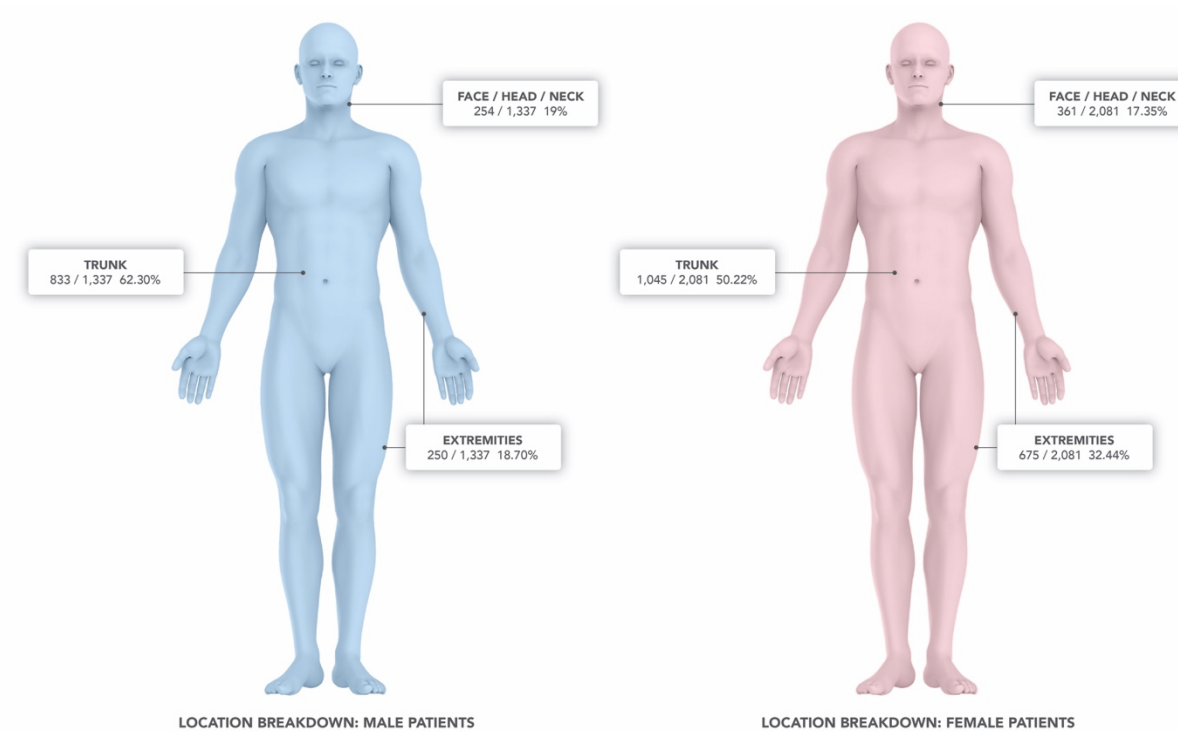


Figure 1. Anatomical locations of pigmented lesions evaluated by PLA in male and female patients.

Of 3,418 pigmented skin lesions clinically suspicious for melanoma and assessed by PLA, 324 lesions (9.48%) were PLA(+) and 3,094 (90.52%) were negative (Figure 2). PLA test results are positive if LINC, PRAME, or both target genes are detected; these molecular pathology findings are known to correspond with histopathology findings of in situ or invasive primary melanoma in 7%, 50%, and 93%, respectively [14]. The 9.48% PLA(+) cases consisted of 5.15% LINC only, 1.93% PRAME only, and 2.40% LINC and PRAME double positive cases (Figure 2). Notably, PLA(+) lesions were surgically biopsied in 97.53% while PLA(-) cases were clinically monitored and not biopsied in 99.94% of the cases. PLA(+) cases with detectable levels of both target genes or detectable levels of PRAME were surgically biopsied in all cases, while 95.45% of LINC-only cases were biopsied (Figure 2).

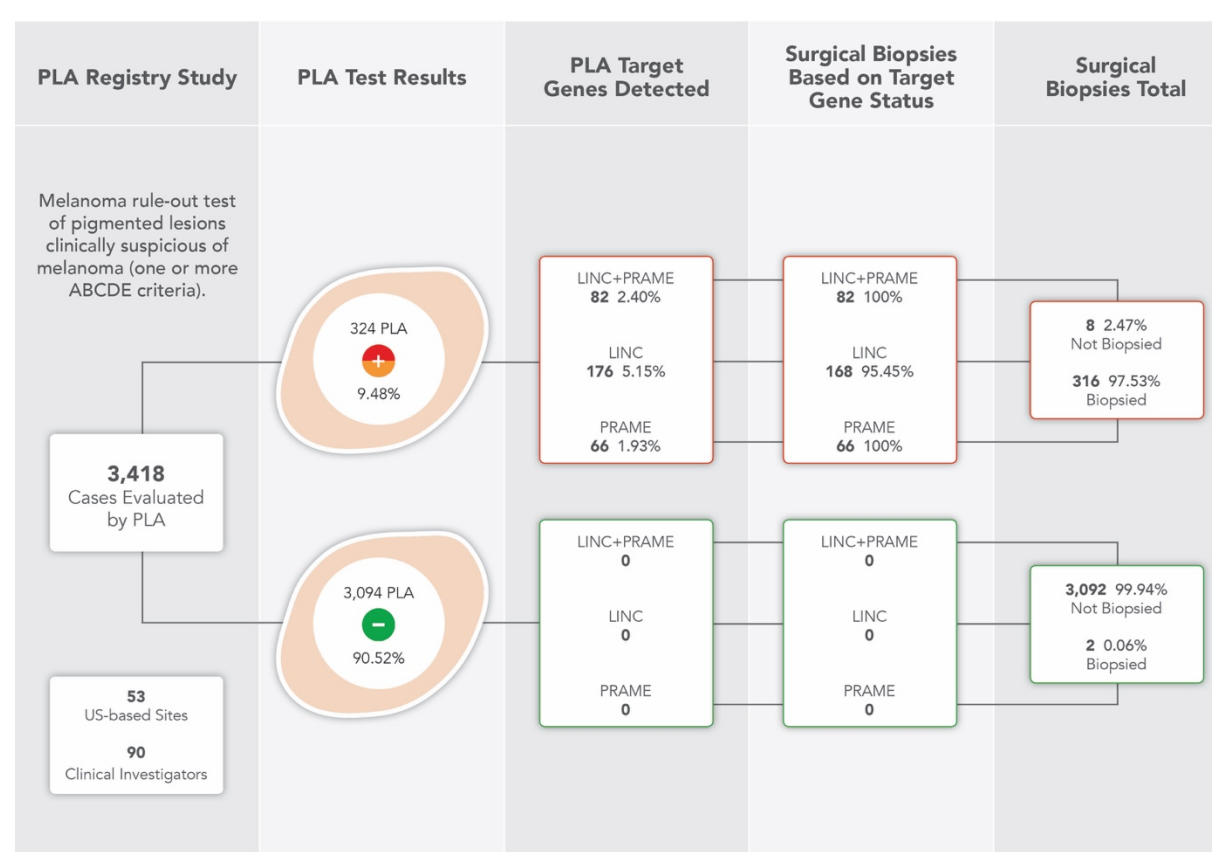


Figure 2. PLA registry study outline and a summary on how PLA test results guide biopsy decisions.

Of a total of 3,094 PLA(-) lesions, only two (0.06%) were subjected to surgical procedures. One was a melanocytic nevus subjected to a shave/scoop biopsy and the second was a squamous cell carcinoma in situ removed by MOHS surgery. The remaining 3,092 PLA(-) cases were monitored clinically and not biopsied or excised. Of these, 179 (5.79%) were scheduled for follow-up in three months, whereas 1,198 (38.75%) and 1,504 (48.64%) were scheduled for follow-up in 6 and 12 months, respectively. In addition, 211 patients (6.82%) were scheduled for follow-up at other time frames.

The vast majority (316 of 324 or 97.53%) of PLA(+) cases (9.48% of all pigmented lesions assessed by PLA in this study), were surgically biopsied as described. Of these biopsies, 51.58% were shave/scoop, 10.13% were punch, and 38.29% were excisional procedures. Table 1 summarizes the types of biopsy procedures employed and provides further details on how not only PLA results, but the detection of either one or both of the target genes affects the type of biopsy procedure selected. All 8 PLA positive cases not subjected to biopsies were LINC-only cases, which have a lower probability of being melanomas histopathologically [2].

Biopsy Type after PLA	BIOPSY TYPE AFTER PLA				
	Total PLA	Total PLA	Total LINC+PRAME	Total LINC	Total PRAME
Shave	1 (0.03%)	163 (51.58%)	23 (28.05%)	105 (59.66%)	24 (36.36%)
Punch	0	32 (10.13%)	19 (23.17%)	19 (10.80%)	4 (6.06%)
Excision	1 (0.03%)	121 (38.29%)	40 (48.78%)	44 (25.00%)	38 (57.58%)
No Biopsy	3092 (99.94%)	8 (2.47%)	0	8 (4.55%)	0

Table 1. Biopsy type after PLA. Gene expression test characteristics and selected biopsy types after PLA(-) and PLA(+) test results (n=3,418). The PLA is positive if either LINC or PRAME or both LINC and PRAME are detected. LINC positive, PRAME positive and LINC and PRAME double positive cases correlate with a histopathologic diagnosis of melanoma in 7%, 50%, and 93%, respectively [2].

CONCLUSIONS

- Findings from this large US Pigmented Lesion Assay (PLA) registry study of 3,418 cases of pigmented skin lesions clinically suspicious for melanoma and assessed by PLA confirm the test's high clinical utility and high negative predictive value.
- Clinicians follow the guidance of the test and rely on its performance.
- PLA negative lesions are monitored clinically and not biopsied in 99.94% of cases.
- PLA positive lesions are biopsied as intended in 97.53% of cases.
- The PLA helps clinicians avoid over 90% of unnecessary surgical procedures while missing fewer melanomas.

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