Despite advancements in diagnostic imaging technologies, mostly based on optical coherence tomography, an easy-to-use, practical system for diagnosis of melanoma in the clinical practice setting has remained elusive. As such, dermatologists continue to rely on visualization to identify suspicious lesions, followed by biopsy to confirm or rule out the skin cancer diagnosis. The AAD’s current Guidelines of Care for Melanoma continue to state that histopathologic diagnosis of a biopsy sample remains the cornerstone of skin cancer diagnosis.

Though biopsy is essential to achieving a confirmed diagnosis of melanoma, it does present certain risks, including scarring and infection. These risks tend to be minimal and readily managed, but dermatologists and their patients would generally prefer to minimize unnecessary biopsies and thereby eliminate risks. Furthermore, if a reliable alternative to biopsy existed, it would likely be adopted for use in cosmetically sensitive areas, such as on the face, or for areas under tension where wound closure and healing may be challenging.

In light of these considerations, a non-invasive diagnostic tool remains desirable, especially for those lesions that fall just beneath our individual thresholds to biopsy. A non-invasive pigmented lesion assay (PLA) for detecting LINC00518/PRAME has been shown to have a sensitivity of 91 percent and specificity of 69 percent for the classification of pigmented lesions clinically suspicious of melanoma. The authors say these figures “compare favorably to the 85%–87% level from histopathologic assessments after surgical biopsies.”

The two-gene PLA developed by DermTech to detect expression of LINC00518 and PRAME has been shown to have a sensitivity of 91 percent and specificity of 69 percent for the classification of pigmented lesions clinically suspicious of melanoma. The authors say these figures “compare favorably to the 85%–87% level from histopathologic assessments after surgical biopsies.”

The non-invasive, two-gene assay detects RNA transcripts of LINC and PRAME in skin samples collected through an adhesive patch-based Class I biopsy device (See Image).

A “real-world” performance and utility study was undertaken to assess how the PLA changes physician behavior via an observational cohort analysis of 381 patients assessed with the PLA. Surgical biopsy was performed for all of 51 PLA(+) test results. Nineteen of these (37 percent) were melanomas in situ or stage 1, corresponding to a number needed to biopsy of 2.7 and a biopsy ratio of 1.7. This equates to a near 10-fold reduction in surgical biopsy procedures. Of the 330 PLA(-) test results, 99 percent were clinically managed with surveillance. None of the three follow-up biopsies performed in the following three months were diagnosed as melanoma histopathologically. In this trial, the estimated sensitivity of the PLA was 95 percent, and the specificity was 91 percent.

Whereas 50 percent of PRAME-only lesions and seven percent of LINC00518-only lesions were histopathologically confirmed as melanomas, 93 percent of PLA results positive for both LINC00518 and PRAME were diagnosed histopathologically as melanoma.

Another publication assessing the potential application of the two-gene PLA notes that visual inspection plus histopathology has a relatively low negative predictive value (NPV) of approximately 83 percent for melanoma, meaning that
17 percent of melanomas are interpreted as benign. These may not be appropriately treated. In contrast, the PLA has a very high NPV, which is greater than 99 percent. “By adding the PLA to the current care pathway, the number of surgical biopsies needed to find a melanoma (number needed to biopsy) is markedly reduced from 20-25 biopsies for dermatologists and 39 biopsies for physician assistants, to an average of 2.7,” the authors conclude.

Efficacy trumps all, but it is heartening to see evidence that the PLA may be cost-efficient, as well. An assessment published in JAMA Dermatology found that the non-invasive PLA reduced costs by $400-600 per assessed pigmented lesion vs. the current histopathologic standard of care, based on typical reimbursement rates for the PLA. These savings were primarily attributed to reduction in initial surgical biopsies and excisions and reduced stage-related treatment costs from missing fewer melanomas.

So far, a non-invasive PLA is available only for identifying melanomas, but DermTech has announced completion of enrollment of more than 600 subjects in its Carcinome clinical study, aimed at developing a non-invasive genomic test to differentiate basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) from non-cancerous lesions like actinic keratosis.

WHAT’S NEXT?

A non-invasive patch for use in the clinical setting to support decision-making is a welcome advancement. Unlike other technologies, including imaging systems, there is no hardware to purchase, maintain, or dedicate space for. Not only does the evidence suggest that non-invasive gene testing is reliable, it is also cost effective. It may reduce unnecessary biopsies as well as the attendant risks for scarring and other adverse events.

There are some limitations to the PLA. It does not work on the mucous membranes, the palms of hands, the soles or feet, or nails. Unfortunately, these are areas where patients and dermatologists are highly motivated to avoid unnecessary cuts for functional or aesthetic reasons. The PLA also is not for use on ulcerated or bleeding lesions. From a clinical standpoint, ulceration or bleeding are strong clinical indicators of a need to biopsy, so this limitation is not significant.

The DermTech PLA is currently available for use in clinical practice.

Jonathan Wolfe, MD is an Associate Professor of Dermatology at the University of Pennsylvania.

5. Hamburgen J, Siegel DM. Economic Analysis of a Noninvasive Molecular Pathologic Assay for Pigmented Skin Lesions. JAMA Dermatol. 2018 Sep 1;154(9):1025-1031.