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Patient and provider-directed adjunct diagnostic tools in the detection of skin cancer

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To the Editor:

Significant advances in non-invasive ancillary products to support skin cancer risk assessments and diagnostics include adhesive skin sampling, spectroscopy, electrical impedance dermography, artificial intelligence (AI)-driven mobile applications, and more. However, up-to-date data on the accuracy, accessibility, and applicability of these diagnostic aids are limited. Thus, we sought to critically appraise adjunctive skin cancer detection products.

MEDLINE was queried in September 2022 using the search terms: non-invasive, melanoma, squamous cell carcinoma, basal cell carcinoma, skin cancer, detection, screening, diagnostic aid, imaging, and artificial intelligence. Two independent reviewers (GW, CK) evaluated products for technological and scientific basis, validity, accessibility, and cost.

Eleven adjunct diagnostic aides for skin cancer detection were identified (Tables 1, 2). The DermTech Smart Sticker™ utilizes a pigmented lesion assay (PLA) to identify increased expression of long intergenic non–protein coding RNA 518 (LINC00518) and preferentially expressed antigen of melanoma (PRAME), and a telomerase reverse transcriptase (TERT) assay to assess for driver mutations in TERT. Real-world performance of the PLA demonstrated that a binary test result, including positivity in LINC, PRAME, or both LINC and PRAME,

provide 91-95% sensitivity and 69-91% specificity in detecting melanoma [1]. DermTech, however, is not appropriate for certain sites, including mucous membranes, palms, and soles. Alternatively, the SkinVision mobile application offers at-home spot checks using AI-based image processing [2]. SkinVision generates lesion risk levels (low risk, low risk with symptoms, and high risk) and offers a 93% sensitivity for melanoma and 97% sensitivity for non-melanoma skin cancers [2]. Home dermatoscope attachments are directly accessible for online purchase. However, they rely on the quality of patient-directed self-imaging, and images ultimately still require evaluation by a trained provider. The sensitivity of home dermoscopy imaging was 75% for cancerous and precancerous lesions, including melanoma, squamous cell carcinoma, basal cell carcinoma, Bowen disease, and actinic keratoses, which remain lower than in-office skin examinations [3].

Several devices for in-office provider use leverage pathophysiological differences between benign and cancerous lesions (Table 2). DermaSensor is a handheld, point-and-click device that uses elastic scattering spectroscopy to evaluate cellular and subcellular features with 100% sensitivity for detecting melanoma and 94% sensitivity for non-melanoma skin cancers [4]. Similarly, SpectraScope is

also a lightweight, handheld device that instead employs laser-induced plasma spectroscopy to detect biochemical variation between benign and malignant lesions with 93% sensitivity for melanoma [5]. Patients must be seen in person to be evaluated with these tools and device accuracy relies on user technique and machine learning programming for risk stratification.

Our review illustrates the diversity of products available to support skin cancer detection. Ongoing technological development continues to advance the diagnostic accuracy of current tools and supports the innovation of new products. Although these tools do not replace clinical evaluation or biopsy, they may guide decision-making and facilitate early disease detection.

Potential conflicts of interest

Dr. Feldman has received research, speaking and/or consulting support from Eli Lilly and Company, GlaxoSmithKline/Stiefel, AbbVie, Janssen, Alovtech, vTv Therapeutics, Bristol-Myers Squibb, Samsung, Pfizer, Boehringer Ingelheim, Amgen, Dermavant, Arcutis, Novartis, Novan, UCB, Helsinn, Sun Pharma, Almirall, Galderma, Leo Pharma, Mylan, Celgene, Ortho Dermatology, Menlo, Merck & Co, Qurient, Forte, Arena, Biocon, Accordant, Argenx, Sanofi, Regeneron, the National Biological Corporation, Caremark, Teladoc, BMS, Ono, Micreos, Eurofins, Informa, UpToDate and the National Psoriasis Foundation. He is founder and part owner of Causa Research and holds stock in Sensal Health. The remaining authors declare no relevant interests.

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Table 1. *Patient-directed adjunct tools to aid skin cancer diagnostics.*

Product name	Mechanism	Statistical data	Accessibility	Cost	Limitations
DermTech Smart Sticker	Sampling of stratum corneum with adhesive tape Samples processed with RNA extraction, amplification, and gene expression Epidermal genomic biomarker information helps differentiate melanomas from benign nevi Two assays: Pigmented Lesion Assay (PLA) and Telomerase Reverse Transcriptase (TERT)	Sensitivity 95%, specificity 91% in detecting melanoma	Obtain via prescription or DermTech Connect (mobile app for telemedicine consultations)	DermTech Connect Telehealth Consult, $39, (includes evaluation by a board-certified dermatologist to determine eligibility) Most patients pay less than $75 per sticker Covered by Medicare and some commercial insurance Financial assistance available	Samples stratum corneum while melanocytes reside in the basal layer, making accurate sampling challenging Cannot be used on mucous membranes, palms, soles, previously biopsied sites, or areas where hair cannot be adequately removed Can only be used to detect genetic markers of melanoma, not other skin cancers Low specificity may result in high false positives leading to a potentially unnecessary test
SkinVision app	Use smart device to image lesions and upload to the SkinVision app Images are processed and triaged using Convolutional Neural Network (CNN) which provides a risk level: low, low with symptoms, and high risk	Sensitivity 93% for melanoma, sensitivity 97% for NMSC, specificity 78% for melanoma and NMSC overall	App Store	One spot check, $6.99 Three-month unlimited plan, $29.99 One-year unlimited plan, $49.99	Effectiveness depends on consumer ability to take quality images Risk stratification tool relies on the accuracy of AI technology
Miiskin app	Mobile app that uses AI-powered skin tracking for at-home mole mapping Use smart device to image lesions and upload to the Miiskin app Images are arranged side-by-side to detect changes/evolution over time Option for store-and-forward images to teledermatologists Premium offers face tracking over time	*Currently investigational*	App Store	Basic option, free Premium option, $5.99 per month or $29.99 per year	Not covered by insurance Dependent on consumer ability to take quality images May be difficult to image hard-to-reach areas

MoleScope by metaOptima	Smartphone-compatible dermatoscope to image lesions Images are reviewed via DermEngine, a teleconsultation platform	Clinical validation studies of home dermoscopy (not specific to dermatoscope products included here) demonstrated sensitivity 75%, specificity 87% at the lesion-level for skin cancer or cancerous precursor (melanoma, squamous cell carcinoma, basal cell carcinoma, Bowen disease or intraepidermal carcinoma, actinic keratoses)	App Store or Android Store (purchase dermatoscope attachment separately)	MoleScope Lite (smartphone compatible dermatoscope), $49 Cost for DermEngine to review images is not publicly available	Teleconsult not available in all regions (regional availability not publicly available) Dependent on consumer ability to take quality images May be difficult to image hard-to-reach areas
Modern Ritual	Smartphone-compatible rental dermatoscope to image lesions Images reviewed by a board-certified dermatopathologist or dermatologist within 2 days Dermatoscope is returned by mail		App store (dermatoscope attachment available to North Carolina residents only)	One spot check, $79 Three spot checks, $177 Annual membership (up to 12 spots per year), $600	Only in North Carolina Out-of-pocket not covered by insurance or HSA/FSA eligible Cannot review spots underneath fingernails
DermLite	Smartphone-compatible dermatoscope to image lesions Images sent to a provider for review		Direct purchase via product site	DermLite HÜD 2 Home Dermatoscope, $195	Dependent on consumer ability to take quality images May be difficult to image hard-to-reach areas
Sklip	Smartphone-compatible dermatoscope to image lesions Images sent to a provider for review		Direct purchase via product site	Oregon Health & Science University offers a free two-week period to borrow a Sklip® Dermatoscope	Dependent on consumer ability to take quality images May be difficult to image hard-to-reach areas

AI, artificial intelligence; App, application; CNN, convolutional neural network; FSA, flexible savings account; HSA, health savings account; NMSC, non-melanoma skin cancer; PLA, pigmented lesion assay; RNA, ribonucleic acid; TERT, telomerase reverse transcriptase.

Table 2. *Provider-directed adjunct tools to aid skin cancer diagnostics.*

Product name	Mechanism	Statistical data	Accessibility	Cost	Limitations
DermaSensor	Handheld, point-and-click device that uses light pulses and spectroscopy to assess cellular and subcellular features of lesions Light scatter is analyzed by a built-in computer using elastic scattering spectroscopy (ESS) Device categorizes scanned lesions into further investigate or monitor	Sensitivity 100% for melanoma, sensitivity 94% for NMSC, specificity 36% for melanoma and NMSC overall	Used in office by PCPs to support clinical decision-making (currently available in Australia and New Zealand, investigational in the United States)	Australia: Devices are leased and use a pay-as-you-go model (providers pay a one-time activation fee of $399 and then approximately $7/skin assessed)	Patients require an in-person visit to access this product Risk stratification tool relies on accuracy of AI technology
DecisionDx-Melanoma – Castle Biosciences, Inc	Gene expression profile (GEP) test for 31 genes in melanoma to identify the risk of recurrence or metastasis Guide intensity of follow-up, surveillance, and patient selection for sentinel lymph node biopsy (SLNB)	Sensitivity 76%, specificity 76%, PPV 46%, NPV 92% for recurrence-free survival (RFS) of melanoma Sensitivity 76%, specificity 69%, PPV 35%, NPV 93% for distant metastasis-free survival (DMFS) of melanoma	Must be ordered by provider Company collects sample and sends results to ordering provider	Covered by insurance, including Medicare, commercial insurers, **and Veteran's Health**. Financial assistance is also available	Used only as a prognostic tool for patients with proven melanoma and cannot be used for screening
SpectraScope (Speclipse)	Device uses laser-induced plasma spectroscopy (LIPS) to detect biochemical data in skin lesion Laser irradiation induces microplasma emissions that reveal biochemical differences between cancerous and benign lesions Device generates a LIPS score and a corresponding NPV and PPV	Sensitivity 93% for melanoma, sensitivity 95% for BCC, sensitivity 94% SCC, specificity 89% overall	Used in office by dermatologists or other providers to support clinical decision-making	Cost details are not available	Patients require an in-person visit to access this product Risk stratification tool relies on accuracy of AI technology
Veriskin	Handheld unit detects hemodynamic abnormalities between normal and malignant skin tissue via dynamic Epidermal Capillary Measurement (DECAM) technology Device uses a neural network-based AI algorithm to provide a score of 0 to 100, i.e. probability of a cancerous lesion	Sensitivity >99%, specificity 94% (based on 125 biopsy-verified lesions in screening for skin cancer, subtypes unspecified)	Used in office by dermatologists or other providers to support clinical decision-making	*Currently investigational*	Poor user technique may impact device accuracy **Potential for "noise" to interfere with** hemodynamic signals from blood flow
URSKIN	Device applies high-frequency, painless current through skin lesion	Significant electrical differences between BCC and adjacent normal skin	Used in office by dermatologists or other providers to	*Currently investigational*	Small pilot study in development phase

| | Measures opposition of electrical current, termed electrical impedance dermography (EID)
Basal cell carcinomas generate a different voltage captured by EID | Reproducible measurements (differences in longitudinal conductivity of 0.13 and transverse conductivity of 0.06) | support clinical decision-making | | No comparisons to standard diagnostics tools or measured sensitivity and specificity
Only evaluated for BCC |

AI, artificial intelligence; BCC, basal cell carcinoma; DECAM, dynamic epidermal capillary measurement; DMFS, distant metastasis-free survival; EID, electrical impedance dermography; ESS, elastic scattering spectroscopy; GEP, gene expression profile; LIPS, laser-induced plasma spectroscopy; NMSC, non-melanoma skin cancer; NPV, negative predictive value; NNT, number needed to treat; PCP, primary care provider; PPV, positive predictive value; RFS, recurrence-free survival; SNLB, sentinel lymph node biopsy; SCC, squamous cell carcinoma.