Use of an elastic-scattering spectroscopy and artificial intelligence device in the assessment of lesions suggestive of skin cancer: A comparative effectiveness study

Danielle Manolakos, DO, MPH,[a] Genevieve Patrick, BS,[b] John K. Geisse, MD,[c] Harold Rabinovitz, MD,[d,e,f] Kendall Buchanan, MD,[f] Preston Hoang, MS,[g] Eladio Rodriguez-Diaz, PhD,[h] Irving J. Bigio, PhD,[i] and Armand B. Cognetta, MD[b,j]

Background: Skin cancer is the most common form of cancer worldwide. As artificial intelligence (AI) expands its scope within dermatology, leveraging technology may aid skin cancer detection.

Objective: To assess the safety and effectiveness of an elastic-scattering spectroscopy (ESS) device in evaluating lesions suggestive of skin cancer.

Methods: This prospective, multicenter clinical validation study was conducted at 4 US investigational sites. Patients with skin lesions suggestive of melanoma and nonmelanoma skin cancers were clinically assessed by expert dermatologists and evaluated by a device using AI algorithms comparing current ESS lesion readings with training data sets. Statistical analyses included sensitivity, specificity, AUROC, negative predictive value (NPV), and positive predictive value (PPV).

Results: Overall device sensitivity was 97.04%, with subgroup sensitivity of 96.67% for melanoma, 97.22% for basal cell carcinoma, and 97.01% for squamous cell carcinoma. No statistically significant difference was found between the device and dermatologist performance (P = .8203). Overall specificity of the device was 26.22%. Overall NPV of the device was 89.58% and PPV was 57.54%.

Conclusion: The ESS device demonstrated high sensitivity in detecting skin cancer. Use of this device may assist primary care clinicians in assessing suspicious lesions, potentially reducing skin cancer morbidity and mortality through expedited and enhanced detection and intervention. (JAAD Int 2024;14:52-8.)

Key words: artificial intelligence; devices; dermatology; elastic-scattering spectroscopy; skin cancer; skin lesions; spectroscopy.

INTRODUCTION

Nonmelanoma skin cancers (NMSCs), including basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), are the leading cause of cancer in the United States presently.[1] Although melanoma is less prevalent, it has a generally poorer prognosis with a higher likelihood of metastasis associated with delayed diagnosis.[2] Thus, early detection and intervention is a mainstay for melanoma management. The increasing frequency of NMSCs among the general population and the morbidity and mortality associated with melanoma present an opportunity to enhance current screening protocols.

A cross-sectional study found that less than 25% of individuals considered at high-risk for developing skin cancer reported undergoing a total body skin examination (TBSE) in their lifetime.[3] Although TBSE is currently not advocated for the general, asymptomatic population by the United States Preventive Task Force, regularly performed TBSEs in the primary care setting may alleviate the referral burden on dermatologists and improve skin cancer prognoses.[4]

Diagnostic tools used to aid skin cancer detection have evolved over time, but there are still limitations to their practical use. For example, dermatoscopy is a diagnostic modality of choice for many dermatologists, but proper lesion evaluation requires specialized training, thus restricting its use in the primary care setting.[5] Similarly, reflectance confocal microscopy is an effective noninvasive imaging technology that uses a diode laser to evaluate skin lesions of concern; however, its use also requires specialized training, and the technology is neither widely available nor cost effective.[6,7] Multispectral digital skin lesion analysis involves the use of a handheld device, visible light emissions, and computer algorithms to stratify skin lesions based on whether they should be biopsied.[8,9] However, this device is only Food and Drug Administration-approved for use by dermatologists and is primarily targeted toward pigmented lesions.[8,9]

An alternative, noninvasive, handheld device using elastic-scattering spectroscopy (ESS) and artificial intelligence (AI) may augment lesion risk stratification in the primary care setting and increase health care accessibility in resource-constrained settings. This device assesses the degree of variance among the cellular and subcellular components of a lesion based on photon backscatter reflections when using over 40 different wavelengths of light.[10] The ESS data were processed with an AI algorithm based on an expansive databank of spectral scans of various benign and malignant lesions from multiple health care settings, which are then used to categorize the lesion under evaluation as high or low risk for malignancy as it relates to biopsy-proven sample sets.

The purpose of this study was to assess the safety and effectiveness of the ESS device, as measured by device-related adverse events, and to assess the sensitivity and specificity of the device for identifying highly atypical or malignant melanocytic and nonmelanocytic lesions compared with histopathologic evaluation.

CAPSULE SUMMARY

- Artificial intelligence is rapidly evolving and expanding its scope within dermatology.

- This safe and effective device may improve clinicians' management and detection of clinically suspicious lesions, leading to reduced morbidity and mortality associated with skin cancer.

MATERIALS AND METHODS

Study design

This prospective, investigator-blinded clinical validation study was conducted at 4 sites located in the United States by board-certified dermatologists. This study received IRB approval from the Western Institution Review Board.

Study device

The device used in this study is handheld, wireless, and battery powered. It operates by emitting pulses of light at various wavelengths, ranging from 360 to 810 nm, via a compact integrated system illuminating tissue and recording the backscattered optical reflectance of the tissue. The wide wavelength range aids in the removal of regions with low signal-to-noise ratio. Similarly, the spectral waveform is preprocessed to minimize high-frequency noise.

The device uses an AI algorithm to compare ESS readings from the current lesion to a training data set of over 10,000 readings from over 2000 lesions. The algorithm version used at the time of study was version 1.0, which was revised to algorithm version 3.0, and study results were reanalyzed with the new device output. The training set comprises lesions from various company-sponsored and independent investigator clinical studies. Three different types of

Abbreviations used:

AI:	artificial intelligence
AUROC:	area under the receiver operating characteristic
BCC:	basal cell carcinoma
ESS:	elastic-scattering spectroscopy
NPV:	negative predictive value
PPV:	positive predictive value
SCC:	squamous cell carcinoma

training models were used based on different architectures and different versions of the training sets to represent various high-risk melanocytic lesions (eg, melanoma), high-risk nonmelanocytic lesions (eg, SCC), and low-risk lesions (eg, benign nevus). One network is a feedforward neural network that was trained based on segments of the training data set. The 2 other networks are deep neural networks based on ResNet-18 architecture that has been remodified with inputs based on ESS spectral data instead of imaging data. The final architecture has 10 neural networks that are trained based on different architectures and training set variations. The raw output was then adjusted based on the class distribution of the training set (ie, adjusting for priors).

Based on the characteristics of the lesion being evaluated, the device generates one of 2 outputs: "Monitor" (negative result) or "Investigate Further" (positive result). For "Investigate Further"–classified lesions, a spectral similarity score between 1 and 10 is assigned. The generated score is based on the degree of resemblance a lesion has to confirmed malignant lesions present in device training studies, with a score of 10 representing the greatest degree of similarity. This device is intended for use to differentiate between high- and low-risk lesions to inform referral decisions; it does not differentiate among malignant pathologies.

Study participants

Study enrollment was conducted from August 2018 to October 2020. Eligible patients were recruited during routine dermatology office visits. Eligibility criteria included adults aged 22 years or older with a maximum of 5 clinically suspicious lesion(s) measuring between 2.5 and 15 mm. Exclusion criteria included patients with more than 5 lesions requiring biopsy; lesions less than 2.5 mm or greater than 15 mm in diameter; lesions in areas inaccessible to the device probe, such as mucosal, nail, and acral lesions; or samples belonging to any participants who withdrew from the study. Written

informed consent was obtained from each participant prior to study enrollment.

Study enrollment

Baseline assessment. On determination of eligibility for this study, participants underwent baseline and lesion assessments. The baseline assessment gathered pertinent patient demographic information and identified any risk factors for the development of skin cancer. The device was then used on an area of unaffected skin for device algorithm development purposes. Five optional scans from uninvolved areas of skin in easily accessible locations (eg, dorsum of hand, forearm, neck, upper torso, and leg) were recorded.

Lesion assessment. Subsequently, the patient entered the lesion assessment phase in which the investigator provided subjective lesion findings, including its categorization as benign or malignant appearing, their level of confidence in the categorization (high/low), preprocedural diagnosis, and suspected malignancy level (high, medium, or low). Additional objective measurements recorded during this time included lesion(s)' anatomic location, size, and surface characteristics and clinical and dermatoscopic images. The device recorded 2 sets of ESS spectra from each enrolled lesion, with the second set used for additional data collection. After device evaluation, lesions with a high clinical index of malignancy were biopsied.

Post lesion assessment. For biopsied lesions, histopathology reports were acquired within 1 to 2 weeks of the procedure. Pathology overreads were performed by an independent dermatopathologist for high-risk melanocytic lesions requiring re-excision.

There were 2 distinct groups of lesions assessed in the final analysis, the testing group and the cross-validation group. The testing group compared the device's performance to the clinical and dermatoscopic evaluation of expert dermatologists. The cross-validation group evaluated the device's ability to use machine learning to determine whether previously unseen lesions were benign or malignant.

Statistical procedures

Descriptive statistics. Continuous outcomes were calculated with sample size, mean, median, SD, quartiles, minimum and maximum, and 2-sided 95% CIs of the mean. Categorical outcomes were reported using number and percentage of patients and 2-sided 95% CIs of the percentage. The Wilson score method for binary correlated data was used to calculate the CIs for sensitivity and specificity.[11] Statistical analyses were conducted through SAS

Table I. Participant and lesion dispositions—qualified lesions

Disposition	Testing group, *n* (%)	Cross-validation group, *n* (%)	Total, *n* (%)
Participants			
Completed	208	175	383
Lesions			
Evaluated	333	281	614
Biopsied	284 (85.3)	228 (81.1)	512 (83.4)
Pathology Overread*			
No	242 (72.7)	203 (72.2)	445 (72.5)
Yes	42 (12.6)	25 (8.9)	67 (10.9)
Missing	49 (14.7)	53 (18.9)	102 (16.6)

*Equivocal lesions requiring a second opinion were sent for independent dermatopathologist review (overread).

version 9.4 or later. *P* values are 2-sided and set at a 0.05 level of significance. Diagnostic performance, as measured by area under the receiver operating characteristic (AUROC) curve, was calculated for the device and investigators (dermatologists). For all lesions, the positive predictive value (PPV) and negative predictive value (NPV) were determined and then were evaluated independently.

Sample size calculation. Assuming that at least 90% of the enrolled lesions would be evaluable for analysis, it was anticipated that enrollment requirements would include at least 55 patients and 110 lesions to achieve 100 evaluable lesions, expecting 40 high-risk and 60 low-risk lesions. Assuming that the sensitivity of ESS device would be 90%, a 2-sided 95% CI would produce a width of approximately 20% with a sample size of 40 high-risk lesions. Assuming that the specificity is 30%, a 2-sided 95% CI for specificity would produce a width of 24% with a sample size of 60 benign lesions.

RESULTS

A total of 614 lesions from 394 participants were enrolled among the 4 study sites. One participant was unable to complete study because of an uncharged device battery at the time of enrollment. The testing group was comprised of 333 randomly selected lesions from 208 participants, and the cross-validation group was comprised of 281 lesions from 175 participants (Table I).

Thirty-two lesion samples from 21 subjects failed screening because of technical device error (device calibration errors wherein no device results were provided) or failure to meet inclusion criteria. All exclusions were made during study enrollment without unblinding the device results. No participants withdrew from the study or were lost to follow up. There were no adverse events reported at the completion of this study.

Approximately half of the patients in the testing set were male (54.33%), and most patients were over the age of 60 years (77.40% aged over 60 years, with 25.48% aged over 80 years). A majority of participants identified as White, not Hispanic or Latino, with Fitzpatrick skin types predominantly between I and III (Table II). Randomization in patient selection allowed similar distributions among the testing and cross-validations sets.

No statistically significant difference in overall sensitivity existed between the performance of the ESS device and the dermatologists (97.04% vs 96.45%, respectively; *P* = .8203). The overall specificity of the dermatologists was higher than that of the ESS device, at 56.10% compared with 26.22% (*P* < .0001), although this assumes that all unbiopsied lesions enrolled by the dermatologists were benign (Table III). The AUROC was calculated as 0.785 for dermatologists and 0.773 for the device.

Similarly, the effectiveness analysis for biopsied lesions for the device was validated against the dermatologist/dermatopathologist diagnosis with no statistical difference between the 2 groups for sensitivity (*P* = .8203), but the specificity of the device was 21.74% compared with 37.39% for study dermatologists (*P* = .0096) (Supplementary Tables I and II, available via Mendeley at https://data.mendeley.com/datasets/z4w5crbsm7/1). For biopsied lesions, device AUROC was 0.734, whereas dermatologist AUROC was 0.699. The specificity of the device for unbiopsied lesions (ie, lesions equivocal to a nondermatologist) was 36.73% (Supplementary Table III, available via Mendeley at https://data.mendeley.com/datasets/z4w5crbsm7/1).

Additional subgroup analyses demonstrated a device sensitivity for melanoma at 96.67% (melanoma includes other high-risk melanocytic pathologies such as severely atypical melanocytic nevi and abnormal melanocytic proliferations), for BCC at 97.22%, and for SCC at 97.01% (Supplementary

Table II. Demographic information of participants

Total No. of participants: 383	Testing group, *n* (%) Total No. of participants: 208	Cross-validation group, *n* (%) Total No. of participants: 175
Sex		
Male	113 (54.33)	90 (51.43)
Female	95 (45.67)	85 (48.57)
Age, y		
22-29	3 (1.44)	2 (1.14)
30-39	8 (3.85)	4 (2.29)
40-49	11 (5.29)	4 (2.29)
50-59	25 (12.02)	17 (9.71)
60-69	44 (21.15)	44 (24.14)
70-79	64 (30.77)	58 (33.14)
80-89	40 (19.23)	36 (20.57)
90+	13 (6.25)	10 (5.71)
Ethnicity		
Hispanic or Latino	8 (3.85)	5 (2.86)
Not Hispanic or Latino	198 (95.19)	163 (93.14)
Unknown	2 (0.96)	7 (4.00)
Race		
White	208 (100.00)	174 (99.43)
Asian	-	-
Black	-	1 (0.57)
American Indian or Native Alaskan	-	-
Native Hawaiian or Other Pacific Islander	-	-
Fitzpatrick skin type		
I: always burn, does not tan	43 (20.67)	16 (9.14)
II: burns easily, tans poorly	111 (53.37)	99 (56.57)
III: tans after initial burn	37 (17.79)	48 (27.43)
IV: burns minimally, tans easily	12 (5.77)	9 (5.14)
V: rarely burns, tans darkly easily	5 (2.40)	1 (0.57)
VI: never burns, always tans darkly	-	2 (1.14)
Risk factors for skin cancer		
Personal history of skin cancer	152 (73.08)	130 (74.29)
Family history of skin cancer	68 (32.69)	60 (34.29)
Fair skin, freckling, light hair	94 (45.19)	76 (43.43)
UV light exposure (natural or tanning bed)	83 (39.90)	71 (40.57)
New or changing lesions	75 (36.06)	70 (40.00)
Many moles or dysplastic nevi	55 (26.44)	34 (19.43)
Weakened immune system	6 (2.88)	4 (2.29)
Xeroderma pigmentosum	-	-
None of the above	2 (0.96)	5 (2.86)

Table IV, available via Mendeley at https://data.mendeley.com/datasets/z4w5crbsm7/1).

The overall NPV of the ESS device for all lesions was 89.58% (Table III). For biopsied lesions only, NPV was 83.33% compared with 87.76% for dermatologists (Supplementary Tables 1 and 2, available via Mendeley at https://data.mendeley.com/datasets/z4w5crbsm7/1). Overall PPV for the device was 57.54% for all lesions and 64.57% for biopsied lesions only at a prevalence of 60%. (Table III; Supplementary Table 1, available via Mendeley at https://data.mendeley.com/datasets/z4w5crbsm7/1).

DISCUSSION

The results of this study validate the device sensitivities for biopsied lesions between the ESS device and dermatologists compared with histopathology results. Of particular importance, the device's sensitivity for detecting high-risk, pigmented lesions was 96.08% and 96.67% for detecting all stages of melanoma, including melanoma in situ (>50% of biopsy-proven cases), stage 1 (Breslow depth 0.2–0.8 mm, ~25% biopsy-proven cases), and stage 2 or greater (remaining biopsy-proven cases, *n* = 6). A limitation

Table III. Overall device vs dermatologist effectiveness analysis for the testing group—all lesions

Total No. of lesions: 333[*]	Statistical metric	Sensitivity (value [n/N])	Specificity (value [n/N])	PPV	NPV	AUROC
Device		97.04 (164/169)	26.22 (43/164)	57.54	89.58	0.773
Dermatologist		96.45 (163/169)	56.10 (92/164)	69.36	93.88	0.785
	Adjusted Wilson Score Method (95%)	91.82 to 98.50	47.68 to 64.18	-	-	-
	P value[†]	.8203	<.0001	-	-	-

NPV, Negative predictive value; PPV, positive predictive value; AUROC, Area under the receiver operating characteristic curve.
Note: All malignant lesions in the study were biopsied. Dermatologists' clinical assessment was the gold standard for the diagnosis of unbiopsied skin lesions. Therefore, the performance measures for the evaluation of unbiopsied lesions carry a biased specificity of 100%.
*Total number of biopsied and unbiopsied lesions.
[†]Device vs dermatologist two-sided P value.

of this study was that the sample size was for all cancer lesions and not specifically for melanoma. Therefore, the sample size for melanoma in this study (n = 30) must be considered in context of the results reported. A subsequent study examined 440 lesions from 328 enrolled patients to address the use of the device as an adjunctive tool for the evaluation of pigmented lesions suspicious for melanoma, and the device's sensitivity for melanoma was found to be 95.5% (n = 88).[12]

Beyond the application of skin cancer devices in dermatology practices, they may also be employed by primary care providers to support clinical management of suspicious lesions with ultimate goals of prioritizing referrals and avoiding unnecessary procedures.[13-17] Additional studies were conducted to evaluate the effectiveness of the device in primary care settings and found a device sensitivity of at least 90%, whereas the specificity was up to 61% (77% for pigmented lesions).[18,19]

Similarly, the device demonstrated significant sensitivities for the detection of NMSCs with various morphological subcharacteristics (including superficial, nodular, micronodular, infiltrative, and pigmented BCC subtypes and in situ, well-differentiated, adnexal-extended, and keratoacanthoma subtypes for SCC). The specificity of the ESS device ranges across the different pathologies from 14.29% to 35.00%, with the highest specificity for melanocytic nevi (35.00%) and lowest for actinic keratoses (14.29%). Clinically, actinic keratoses can have a varied presentation, and the actual progression to SCC is estimated to be 10% although this percent may vary depending on several individual factors.[10] Differentiating a hypertrophic actinic keratosis from an early SCC often requires a biopsy as their relative clinical presentations may be identical.[20] Understanding this principle may contribute to the low specificity of the device regarding actinic keratoses. Regardless, future studies will be required to further evaluate the specificity of the device for actinic keratoses

and the factors influencing their detection by the device.

The specificity of the device for the unbiopsied benign lesions, as may be routinely encountered in practice, was greater than that of biopsied lesions suspicious for skin cancer (36.73% vs 21.74%, respectively). Since histopathologic diagnoses were not obtained for unbiopsied lesions, dermatologists' specificity and AUROC results including unbiopsied lesions may be overrepresentative. The AUROC, NPV, and PPV for the device supports its potential benefit to primary care clinicians with patient populations that often present with benign skin lesions.[21,22] The data collected from this study further validate the effectiveness of the ESS device as an adjunctive tool for the clinical differentiation between benign and malignant lesions as compared with the current standards of care (eg, dermatologist dermatoscopic evaluation of lesions).[10,23-26]

Overall, study limitations include the blinding of investigators to the device output owing the comparative effectiveness study design and exclusion of the assessment of impact on clinical care pathways. Finally, not all lesions included in this study were biopsied for comparison with histopathologic evaluation.

CONCLUSION

The ESS device is an intuitive, noninvasive, safe, and effective handheld device that may assist primary care clinicians in the assessment of clinically suspicious lesions. Its rapid clinical analysis of lesions allows for its easy integration into clinical practice infrastructures. Proper use of this device may aid in the reduction of morbidity and mortality associated with skin cancer through expedited and enhanced detection and intervention.

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