Can a Handheld Elastic Scattering Spectroscopy Device Aid Primary Care Physicians In Their Detection and Management of Skin Cancer?

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Background and Objective

The incidence of skin cancer continues to grow world-wide [1], therefore early detection and treatment is crucial to prevent associated morbidity. However, primary care physicians (PCPs) have demonstrable difficulty in identifying skin lesions in need of further evaluation [2]. Additionally, access to dermatology specialty care is limited in much of the US, with 40% of the US population living in areas with a documented shortage in dermatologists [3]. As the most commonly diagnosed malignancy [1], skin cancer is a major public health concern. Leveraging technology may aid physicians in improving early detection

Elastic scattering spectroscopy (ESS) technology utilizes visual light and detects the backscatter of the light by subcellular structures to differentiate between benign and malignant cells [4]. A handheld ESS device has been developed to aid PCPs in their clinical assessment of concerning skin lesions and better inform referrals to dermatologists. The technology has been shown to have skin cancer sensitivity over 90% in various prospective, multi-center studies when compared to dermatopathology [4-6].

This two-part study aimed: 1. To validate the performance of a handheld ESS device compared to the gold standard of dermatopathology and 2. Evaluate whether device availability improved PCP detection and management of skin cancer.

Materials & Methods

The handheld ESS device measures spectra of skin lesions and uses an algorithm to classify the lesion's scanned properties against those of known malignant and benign lesions, providing an output of "Investigate Further" or "Monitor", respectively (Figure 1A and 1B). Additionally, for "Investigate Further" classified lesions, a score from 1 to 10 is provided which corresponds to the amount of spectral similarity a lesion has to malignant lesions in studies, with 10 representing the highest amount. The algorithm has been trained and validated with over 20,000 spectral scans from over 4,500 skin lesions, including histologically confirmed melanoma, BCC, SCC and benign lesions as well as unbiopsied benign lesions diagnosed by board-certified dermatologists.

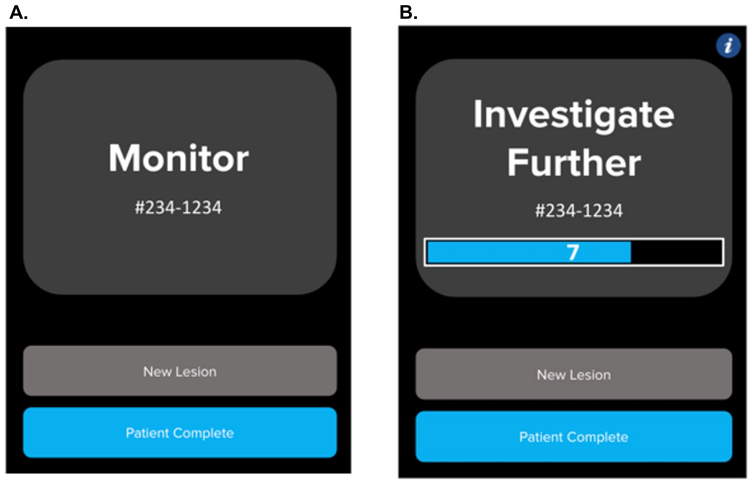

Figure 1. ESS device outputs for an example patient, with A. a negative "Monitor" or B. a positive "Investigate Further" result.

A blinded, prospective, multi-center study clinical validation study was performed at 22 primary care study sites across the US (18) and Australia (4). Lesions were first clinically assessed by PCP investigators and then scanned with the ESS device. Clinical care was provided according to standard of care for suspicious skin lesions. All lesions enrolled were biopsied. Standard of care dermatopathology results were used as the reference standard for assessing device performance Each lesion's diagnosis involved 2-5 dermatopathologists, dependent on pathology and discordance.

In an accompanying utility study, PCP readers evaluated 50 skin lesions (25 malignant, 25 benign), with and without ESS device output. For each case, high resolution digital clinical images, the patient's clinical information, including prior skin cancer history, risk factors, and physical examination results were provided. The PCP readers completed a questionnaire about their diagnosis of the lesion, their recommended management decision and their confidence level on their management decision for each case.

Patient Enrollment

During the clinical validation study enrollment, five lesions (0.3%) were excluded due to device data capture issues and five lesions (0.3%) due to lack of dermatopathology consensus. All exclusions were documented prior to unblinding of the study database and device results. A total of 1,005 patients with 1,579 lesions suggestive of skin cancer were enrolled. There were no adverse events related to device use.

PCP Reader Recruitment

PCPs were recruited from around the US for participation in the clinical utility study. One hundred and eighteen (118) board-certified PCPs completed at least one lesion case in the study, and 108 PCPs completed all 100 lesion case assessments and were included in the study effectiveness analysis,. There were 48.1% (n=52) Internal Medicine physicians and 51.9% (n=56) Family Medicine physicians, with 65.7% (n=71) male and 34.3% (n=37) female physicians included. Years in practice varied with most physicians reporting 21+ years in practice (31.5%).

Patient Demographics

Table 1: Description of patient characteristics based on investigators assessment

Characteristics	Clinical Study, N=1005 (%)	Reader Study, N=50 (%)
Gender		
Male	487 (48.5%)	28 (56.0%)
Female	518 (51.5%)	22 (44.0%)
Age (years)		
Mean (SD)	59 (15)	60 (15)
min, max	22, 95	23, 87
Ethnicity		
Hispanic or Latino	79 (7.9%)	3 (6.0%)
Not Hispanic or Latino	913 (90.8%)	47 (94.0%)
Unknown	13 (1.3%)	0 (0%)
Race		
White	976 (97.1%)	50 (100%)
Native Hawaiian or Other Pacific Islander	3 (0.3%)	0 (0%)
Asian	9 (0.9%)	0 (0%)
Black or African American	7 (0.7%)	0 (0%)
Other/Multiracial	10 (1.0%)	0 (0%)
Fitzpatrick skin type		
I - Always burns, never tans	99 (9.9%)	6 (12.0%)
II - Always burns, tans minimally	278 (27.7%)	18 (36.0%)
III - Sometimes mild burn, tans uniformly	352 (35.0%)	16 (32.0%)
IV - Burns minimally, always tans well	148 (14.7%)	5 (10%)
V - Very rarely burns, tans very easily	110 (10.9%)	4 (8%)
VI - Never burns	18 (1.8%)	1 (2%)

Enrolled Lesions

In the clinical validation study, dermatopathology evaluation confirmed 224 malignant lesions: 48 melanomas (including highly atypical nevi), 90 basal cell carcinomas and 86 squamous cell carcinomas. There were 1355 benign lesions, with the majority being benign nevi and seborrheic keratosis. A subset of 50 lesions were randomly selected for the reader study with a similar breakdown of pathologies.

Table 2: Dermatopathology Diagnoses

Diagnosis	Clinical Study, n=1579 (%)	Reader Study, n=50 (%)
Malignant lesions	224 (14.2%)	25 (50.0%)
Basal cell carcinoma	90 (5.7%)	10 (20.0%)
Squamous cell carcinoma	86 (5.4%)	9 (18.0%)
Melanoma	48 (3.0%)	6 (12.0%)
Benign lesions	1355 (85.8%)	25 (50.0%)
Benign nevus	500 (31.7%)	9 (18.0%)
Seborrheic keratosis	490 (31.0%)	9 (18.0%)
Benign Other	365 (23.1%)	7 (14.0%)

Clinical Validation Results

PCPs had an overall clinical assessment sensitivity of 83.0%, while the ESS device had an overall sensitivity of 95.5% ($p<0.0001$). The overall specificity of the device was 20.7% for ruling out benign biopsied lesions. The NPV of the device for a 'Monitor' result was 96.6% and the PPV for an 'Investigate Further' result was 16.6% (NNB of 6:1). The sensitivity + specificity logistic regression model of the device demonstrated statistical significance (OR: 4.93, $p<0.0001$). Device AUROC was 0.7796.

Table 3: Concordance between device assessment and biopsy

Device Reading	Biopsy diagnosis	
	Benign (n=1355)	Malignant (n=224)
Monitor	281 (20.7%)	10 (4.5%)
Investigate Further	1074 (79.3%)	214 (95.5%)

Clinical Utility Results

PCP readers performed 5400 lesion assessments for malignant lesions and 5400 lesion assessments for benign lesions. Both PCP management and diagnostic sensitivity increased significantly (from 82.0% to 91.4% [p=0.0027] and 71.1% to 81.7% [p=0.0085], respectively) with device results, with associated decreases in specificity for diagnosis (60.9% to 54.7%) and referrals (44.2% to 32.4%). Management performance, (i.e., AUROC) of the PCPs with device output increased to 0.762 from 0.708 without device output.

Table 4: Concordance between device assessment and biopsy

Management Decision	Without Device (95% CI)	With Device (95% CI)
Sensitivity	82.0% (76.4-87.6%)	91.4% (85.7-97.1%)
Specificity	44.2% (36-52.4%)	32.4% (20.7-44.1%)

High confidence in the physician management decision (defined as 8 or higher) was 43.2% for malignant lesions without the device result and 63.3% with the device result. For all lesion assessments combined (n=5,400), the level of high confidence in the physician management decision was 36.8% without the device result and 53.4% with the device result (Figure 2).

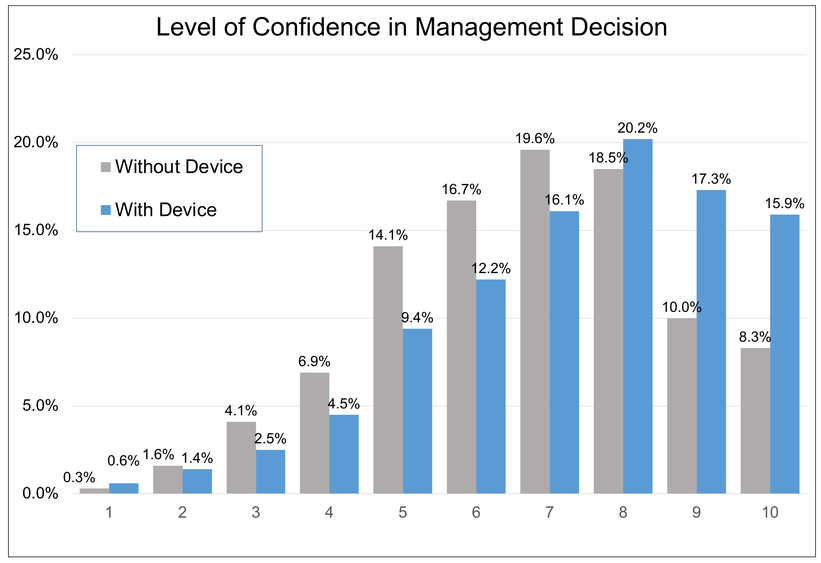

Figure 2. PCP Confidence in management decisions with and without device output

Conclusion

The novel hand-held ESS device demonstrated high sensitivity of 95.5% in detecting skin cancer when compared to histopathologic examination with a corresponding specificity of 20.7%. The high NPV of 96.6% provides physicians with confidence that a "Monitor" output is unlikely to miss a cancer.

Additionally, use of the ESS device by PCPs significantly improved both diagnostic and management sensitivity, with clinically acceptable decreases in associated specificities. With the availability of the device output, there was an improvement in overall PCP management capabilities, as demonstrated by AUROC. These findings suggest use of the ESS device has the potential to improve PCP skin cancer detection as well as their confidence in skin lesion evaluation and management.

This highly sensitive, non-invasive, hand-held ESS device has demonstrated capabilities to fill a well-recognized void in PCP dermatologic care by providing an objective, point-of-care test for clinical assessment.

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