

Clinical Performance of Novel Elastic Scattering Spectroscopy (ESS) in Detection of Skin Cancer: A Blinded, Prospective, Multi-Center Clinical Trial

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Background and Objective

Skin cancer is by far the most common type of cancer in the United States [1]. The most common types of skin cancer are basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) followed by melanoma [1,2]. In the United States, it is estimated that there will be 5.4 million new cases of nonmelanoma skin cancer (NMSC), 100,000 new cases of invasive melanoma and another 100,000 cases of melanoma in situ diagnosed annually [1].

Primary care providers (PCPs) have demonstrable difficulty in identifying skin lesions in need of further evaluation [3]. Access to a dermatologist for diagnosis and management of skin cancer is challenging, as around 40% of the United States population live in areas that have limited access to a dermatologist [4]. Leveraging technology may aid PCPs in improving skin cancer detection and corresponding referrals, thereby reducing associated mortality and morbidity and the burden on the healthcare system.

Elastic Scattering Spectroscopy (ESS), an optical tissue sampling technique, distinguishes between normal and abnormal tissue in vivo without the need to remove tissue. Measuring the ESS spectra of skin lesions, a novel handheld device classifies lesions as either high risk or low risk for malignancy with an output of “Investigate Further” or “Monitor”. The technology has been shown to have skin cancer sensitivity over 90% in various prospective, multi-center studies when compared to gold-standard dermatopathology results [5,6,7].

This study investigated the sensitivity and specificity of a non-invasive, hand-held ESS device in evaluating skin lesions compared to the in-person clinical evaluation by PCPs.

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. 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.

This blinded, prospective, multi-center study was conducted at 22 primary care study sites across the United States (18 sites) and Australia (4 sites). Patients with lesions suggestive of skin cancer were clinically assessed by PCPs and then evaluated by the ESS device. Patients and PCPs were blinded to device output. All lesions enrolled were biopsied per physician assessments and standard of care. Each lesion’s diagnosis involved 2-5 dermatopathologists, dependent on pathology and discordance. Statistical analyses after study unblinding included standard diagnostic test parameters of the device for detecting skin cancer as well as the influence of lesion and patient factors on device performance.

Patient Enrollment

Patients were enrolled from 22 sites, with 18 sites in the US and 4 in Australia by primary care providers. During 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 (Figure 2).

There were no adverse events related to device use.

A total of 1,005 patients with 1,579 lesions suggestive of skin cancer were enrolled. Among the patients enrolled, 51.4% were female with a mean age of 59 years, and 72.5% of patients were Fitzpatrick Skin Type I-III. (Table 1)



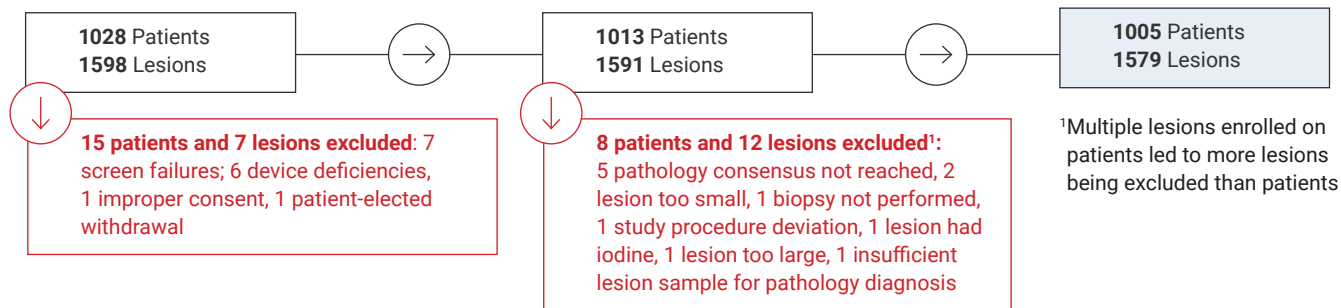
Figure 1. Handheld ESS Device

Materials & Methods

The handheld ESS device (Figure 1) measures spectra of skin lesions



Figure 2. Consort diagram of the study participant flow



Patient Demographics

Table 1: Description of Patient Characteristics Based on Investigators Assessment (N=1005)

Characteristics	N (% of Patients)
Gender	
Male	48.5%
Female	51.5%
Age (years)	
Mean (SD)	59 (15)
min, max	22, 95
Ethnicity	
Hispanic or Latino	7.9%
Not Hispanic or Latino	90.8%
Unknown	1.3%
Race	
White	97.1%
Native Hawaiian or Other Pacific Islander	0.3%
Asian	0.9%
Black or African American	0.7%
Other/Multiracial	1.0%
Fitzpatrick Skin Type	
I - Always burns, never tans	9.9%
II - Always burns, tans minimally	27.7%
III - Sometimes mild burn, tans uniformly	35.0%
IV - Burns minimally, always tans well	14.7%
V - Very rarely burns, tans very easily	10.9%
VI - Never burns	1.8%

Lesion Characteristics

The majority of lesions were located on the trunk (52.3%). Average size of enrolled lesions was 7mm x 5mm. The majority were elevated, smooth and dark. Most lesions were identified by the patient (67.8%) and only 27.2% were identified by a healthcare provider. (Table 2).

The PCPs diagnosed 807 lesions as “malignant”, of which 322 were classified as “melanoma” (Table 3).

Table 2: PCP Assessment of Lesion Characteristics (n=1579)

Characteristics	% Total Lesions
Lesion Location	
Head	15.6%
Arm	18.9%
Leg	13.1%
Trunk	52.3%
Length (mm)	7
Width (mm)	5
Flat or Elevated	
Flat	39.4%
Elevated	60.6%
Smooth or Rough	
Smooth	54.7%
Rough	45.3%
Light or Dark	
Light	36.8%
Dark	63.2%
Lesion(s) discovery	
Patient	67.8%
Family Member/Partner	5.0%
Health Care Provider	27.2%

Table 3: PCP Clinical Assessment of Lesions (n=1579)

Characteristics	PCP Assessment, n (%)
Clinical diagnosis	
Malignant	807 (51.1%)
Benign	772 (48.9%)
Level of Confidence	
High	931 (59.0%)
Low	648 (41.0%)
Diagnoses	
Melanoma	322 (20.4%)
BCC	217 (13.7%)
SCC	268 (17.0%)
Benign	772 (48.9%)



Dermatopathology evaluation confirmed 224 high risk lesions: 48 melanomas (including highly atypical nevi), 90 basal cell carcinomas and 86 squamous cell carcinomas (Table 4).

Table 4: Dermatopathology Risk Classifications and Diagnosis (n=1579)

Risk Classification and Diagnosis	n (%)
High Risk Lesions	224 (14.2%)
Basal cell carcinoma	90 (5.7%)
Squamous cell carcinoma	86 (5.4%)
Melanoma	48 (3.0%)
Low Risk Lesions	1355 (85.8%)
Benign nevus	500 (31.7%)
Seborrheic keratosis	490 (31.0%)
Other	365 (23.1%)

Table 5: Concordance Between Device Assessment and Biopsy Results

Device Reading	Biopsy Diagnosis	
	Benign	Malignant
Benign	281 (20.7%)	10 (4.5%)
Malignant	1074 (79.3%)	214 (95.5%)
Total	1355	224

Table 6: Device PPV Across Spectral Scores

Device Spectral Score	PPV (95% CI)	NNB
1-3	5.9% (4.1-8.5%)	16.9
4-7	18.4% (14.8-22.7%)	5.4
8-10	39.6% (33.4-46.2%)	2.5

Device Effectiveness Results

PCPs had an overall 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 correctly classifying 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 was statistically significant with an odds ratio of 4.93 (95% CI: 2.84-8.5, $p < 0.0001$). For spectral scores of 1-3, the associated PPV was 5.9% (NNB 16.9) and this increased to 39.6% (NNB 2.5) for scores of 8-10.

Conclusion

The novel hand-held ESS device demonstrated high sensitivity in detecting skin cancer when compared to the gold standard of histopathologic examination. Use of this device has the potential to improve PCP sensitivity for skin cancer from 83.0% to 95.5% for high-risk lesions. Coupled with clinical exam findings, this device may aid PCPs to improve clinical decisions about suspicious skin lesions (i.e., to refer, or monitor), with this study suggesting device use could rule out 20.7% of suspicious lesions from needing further evaluation. This highly sensitive, non-invasive, hand-held ESS device may fill a well-recognized

void in PCP dermatologic care by providing an objective, point-of-care test for clinical assessment. This device may help increase quality of referrals to dermatology by providing PCPs with an additional instrument to assess lesions for skin cancer risk.

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Disclosures

This study was funded by DermaSensor, Inc. Dr. Leffell is a Scientific Advisory Board member for DermaSensor has a commercial interest in the company, and Drs. Nguyen and Chatha are employees of DermaSensor Inc.

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