BACKGROUND

Skin malignancies are the most common type of cancer diagnosed in the United States and, in recent decades, incidence has been increasing across many parts of the world [1][2].

Fortunately, it remains highly curable if detected early. Visual inspection with diagnostic aids, such as the ABCDEs of melanoma, remains the standard of care yet accuracy of assessment is dependent upon the clinician's training and experience [3].

Other methods of skin cancer detection include:

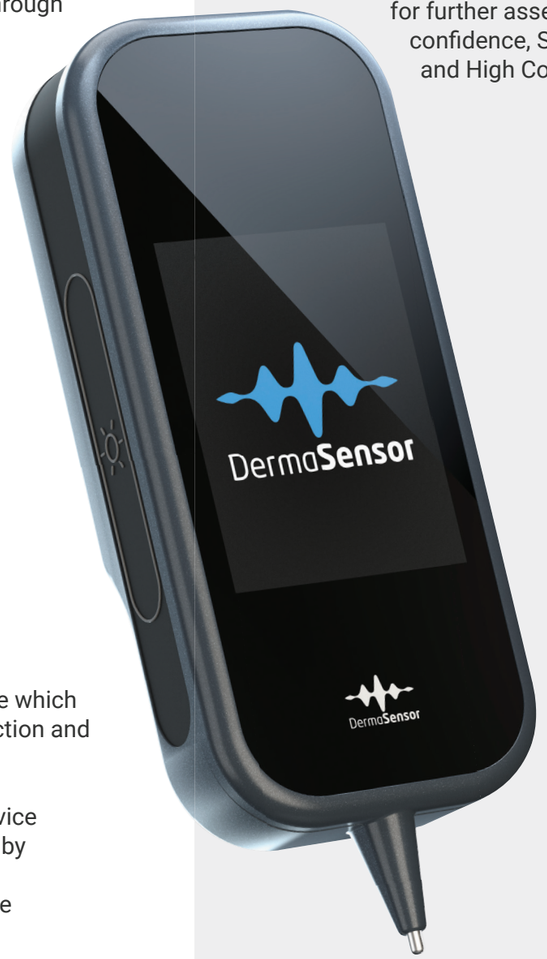
- Non-invasive optical technologies but most are expensive and require extensive training and ongoing skill maintenance [4].
- Non-invasive specialized form of spectroscopy known as Elastic-Scattering Spectroscopy (ESS) which measures reflected light spectra of a lesion's substructural components[5].

A portable hand-held ESS device, approved for use in Australia, New Zealand and Europe, uses an algorithm developed through convolutional neural networks CNN (a type of machine learning model) to compare the scan of a lesion under investigation with scans of known benign and malignant lesions [6][7].

It provides an output of "investigate further" or "monitor"' based upon a lesion's spectral similarities to scans of lesions in the training set.[8] The algorithm has been trained and validated with 6000 spectral recordings from ~1600 lesions including histologically confirmed melanoma and NMSC; as well as biopsied and unbiopsied benign lesions diagnosed by board-certified dermatologists.[9] This non-invasive technology has undergone rigorous clinical trials and is easy to use and cost effective for early detection of skin cancer.

OBJECTIVES

1. To test the potential of using a Handheld ESS device which incorporates machine learning to assist in the detection and appropriate management of skin cancer.
2. To establish whether the use of a Handheld ESS device improves clinicians' detection of skin malignancies by evaluating their clinical performance on cases with suspicious lesions as assessed with and without the output of a Handheld ESS device.



METHODS

A total of 57 U.S. board-certified PCP (33 IM (58%), 24 FM (42%) readers with different levels of primary care and dermatology experience participated in this study. 50 cases of skin lesions from different areas of the body were randomly selected from the DERM-ASSESS II Trial[10]

High resolution digital images of lesions as well as the patient's skin cancer history, risk factors and the results of their physical examinations were presented for each case.

The study was conducted in two phases:

Phase 1: Readers evaluated items listed above for each case without the Handheld ESS device output.

Phase 2: Phase 1 was repeated inclusive of the Handheld ESS device output.

Readers were educated on the Handheld ESS device before evaluating the 50 skin lesion cases in one of five randomly sorted orders during each phase. After evaluation in each phase, readers completed a questionnaire about their diagnosis (Benign or Malignant), management decision (Lesion's need for further assessment), and confidence level (No confidence, Slight confidence, Moderate confident and High Confidence).

Malignant Lesions	25
Squamous cell carcinoma	9
Basal cell carcinoma	9
Melanoma	4
Severely atypical melanocytic nevus	3

Benign Lesions*	25
Benign melanocytic nevus	3
Benign other	4
Blue nevus	1
Lentigo	2
Seborrheic keratosis	10
Mildly atypical melanocytic nevus	2
Actinic keratosis	3

*13 biopsied and assessed histologically
*12 diagnosed as benign by dermatologists

RESULTS

Table 1: Diagnostic and management performance for detection of skin cancer with and without the use of the Handheld ESS device

	Performance		95% Confidence Interval		P-value
	Without ESS	With ESS	Without ESS	With ESS	
Diagnosis					
Sensitivity %	67 (958/1425)	88 (1261/1425)	62-72	84-92	<.0001
Specificity %	53 (761/1425)	40 (577/1425)	49-57	37-44	0.0516
Management Decision					
Sensitivity %	81 (1160/1425)	94 (1342/1425)	77-85	91-96	0.0009
Specificity %	36 (516/1425)	31 (437/1425)	31-42	28-34	0.3558

Note. Data in parentheses are the number of cases correctly identified as malignant (for sensitivity analysis) and benign (for specificity analysis) over the total number of lesions evaluated (25 lesions x 57 readers = 1425).

Diagnostic sensitivity of the readers with and without the use of the ESS device was 88% —

(1261/1425; 95% CI, 84% - 92%) and 67% (958/1425; 95% CI, 62% - 72%), respectively (Table 1).

Management sensitivity of the readers with and without the use of the ESS device was 94% —

(1342/1425; 95% CI, 91% - 96%) and 81% (1160/1425; 95% CI, 77% - 85%), respectively (Table 1).

Table 2. Shifts in levels of confidence of PCPs in their management decision

Confidence without the device	Confidence Level with the device				
	None	Slight	Moderate	High	**Total**
None	3	12	20	18	**53**
Slight	9	91	297	252	**649**
Moderate	10	138	619	688	**1455**
High	7	36	118	532	**693**
Total	**29**	**277**	**1054**	**1490**	**2850**

Kappa statistic: 0.1490; OR (95% CI): 4.210 (3.764 to 4.708); p-value: <.0001

DISCUSSION

- Maximizing sensitivity in cancer detection is critical given the negative consequences of mismanagement of malignant skin lesions.
- Prior publications reviewing non-invasive tools for melanoma detection indicate that spectroscopy achieved best performance in terms of sensitivity (93%, 95% CI 92.8–93.2%) and specificity (85.2%, 95%CI 84.9–85.5%) while reflectance-confocal-microscopy demonstrated good diagnostic performance (sensitivity 88.2%, 80.3–93.1%; specificity 65.2%, 55–74.2%) with better robustness [11].
- Given the high requisite investment in equipment and training for reflectance-confocal-microscopy, it remains out of reach for most PCPs while ease of use and low cost suggest handheld spectroscopy may be a highly acceptable non-invasive tool for the detection of skin malignancies for PCPs.
- Use of the ESS device significantly increased the diagnostic sensitivity of readers by 21% ($P < 0.0001$) with no significant difference ($P = 0.0516$) in specificity with and without device use.
- Use of the ESS device significantly increased the management sensitivity by 13% ($P = 0.0009$) with no significant difference ($P = 0.3558$) in specificity with and without device use.

Additionally, there is an increase in levels of confidence in management decision with the use of the Handheld ESS device—

and a direct correlation between this improvement in level of confidence and the correct management of true malignancies.

CONCLUSIONS

The study met its primary endpoint of demonstrating that management sensitivity of the PCP with knowledge of the device output is superior to management sensitivity without knowledge of the device output.

The use of the Handheld ESS device in a primary care setting is further supported by a reduction in the subjectivity of the PCPs regarding their evaluations and the limited training required for its use.

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ABBREVIATIONS

AUC: Area under curve;
CNN: Convolutional neural networks;
ESS: Elastic-scattering spectroscopy;
FM: family medicine;
IM: internal medicine;
PCP: primary care physician;
ROC: receiver operating characteristic;
SROC: summary receiver operating characteristics

DISCLOSURES

This study was sponsored by DermaSensor Inc.
Author T Silva reports a non-financial advisory relationship with Dermasensor Inc.

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7. Data on file, Dermasensor Inc.
8. Device output labels have been revised to 'Monitor' and 'Investigate Further' by the time of this going to press.
9. Device algorithm has been trained on 11,000 scans from over 2,300 lesions by the time of this going to press.
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Clinical Utility of a Handheld Elastic Scattering Spectroscopy Tool and Machine Learning on the Diagnosis and Management of Skin Cancer by Primary Care Physicians

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