ORIGINAL RESEARCH

Impact of Electrical Impedance Spectroscopy on Clinician Confidence and Diagnostic Accuracy in Evaluating Melanocytic Skin Lesions Suspicious for Melanoma: A Pilot Study

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ABSTRACT

Introduction: Nevisense is a non-invasive device that measures electrical impedance spectroscopy (EIS) of individual skin lesions to aid in the diagnosis of melanoma. While EIS has demonstrated high sensitivity in diagnosing melanoma, its impact on a clinician's diagnostic confidence remains unknown.
Objective: To conduct a pilot study to evaluate whether clinician diagnostic confidence, sensitivity, specificity and accuracy can be increased by adding EIS measurement scores to clinical and dermoscopic images of lesions clinically suspicious for melanoma.
Methods: Three pigmented lesions specialists and three 4th year medical students completed an online survey to evaluate 34 melanocytic lesions suspicious for melanoma. For each lesion, participants provided their diagnosis, biopsy recommendation, and confidence in diagnosing a lesion as benign or malignant based on history and clinical and dermoscopic images, and again after receiving an EIS score.
Results: Addition of EIS scores increased mean biopsy sensitivity for melanoma/severely dysplastic nevi from 70% to 84% (p = .014) and mean diagnostic accuracy from 74% to 86% (p = .005). Mean diagnostic confidence increased for all histopathologic categories for both students and dermatologists (all p < .05).
Conclusions: In this pilot study, EIS increased novice and expert diagnosticians' confidence regarding dermoscopically equivocal melanocytic lesions. Further studies are needed to explore how EIS can help clinicians reassure patients regarding the management of clinically dysplastic melanocytic nevi.

INTRODUCTION

There has been growing interest in the development of non-invasive modalities such as dermoscopy, Nevisense (Scibase), and the Pigmented Lesion Assay (DermTech) to facilitate the evaluation of lesions concerning for skin cancer, particularly melanoma [1-7]. The primary goal of these devices has been high levels of diagnostic accuracy in the identification of early stage melanomas, while maintaining low biopsy rates of benign lesions.

To date, few studies have examined how these modalities impact diagnostic confidence [8]. The impact on clinician

confidence is important. Confidence is defined as having trust and belief in oneself [9]. It plays a crucial role in decision-making, and may even impact the duration of the decision-making process, especially when the accuracy of the decision is important [10]. Confidence is also thought to influence the closely related concept of self-efficacy, or the belief in one's ability to perform a specific behavior or skill [9]. In the healthcare field, providers who have higher self-efficacy regarding their clinical reasoning and communication skills may be more likely to engage in discussions regarding patients' concerns [9,11]. Moreover, uncertainty and lower levels of clinician confidence may increase patients' anxieties while higher levels of confidence may facilitate, trust, comfort, and overall rapport [8,12]. Thus, confidence has the potential to have profound impacts on the patient-physician relationship [8,9,11].

Nevisense (SciBase, Sweden) is an FDA-cleared and CE-marked device that measures electrical impedance spectroscopy (EIS) in skin lesions to aid in biopsy decision-making for lesions suspicious for melanoma. The device reports a score of 0-10, with low scores (≤3) having a 99% negative predictive value for melanoma, and scores >3 having a sensitivity of 96.6% to diagnose melanoma in appropriately selected lesions [13]. The addition of EIS scores to clinical images resulted in more accurate biopsy decision-making by clinicians in survey studies.[14-16]. To date, however, the impact of EIS scores on clinician confidence in diagnosing lesions as benign or malignant remains unknown. In addition, there have not been studies examining the change in diagnostic accuracy among clinicians first presented with dermoscopic images in addition to clinical images, prior to learning the EIS score.

We conducted a pilot study to evaluate whether the addition of an EIS score to clinical and dermoscopic images increases diagnostic confidence, sensitivity, specificity and accuracy for the diagnosis of melanoma and severely dysplastic nevi using a set of images with corresponding EIS scores and histopathology results. We also compared the differential impact of EIS scores on the performance of novice diagnosticians (i.e., medical students) and pigmented lesion specialist dermatologists.

METHODS

In November 2020, three pigmented lesions specialists and three 4th year medical students with 4-12 months of dermoscopy experience from NYU Grossman School of Medicine were invited to complete an online survey to evaluate 34 melanocytic lesions suspicious for melanoma. The study and waiver of consent were approved by the NYU Langone Health Institutional Review Board.

Cases were provided by SciBase for training for a separate skin cancer diagnostic clinical trial. The selection of cases by SciBase was intended for training purposes, and was based on the following two parameters: 1) adequate image quality for both clinical and dermoscopic images; and 2) atypical lesions that could be of concern to a clinician and benefit from additional information when making the decision to biopsy or not (**Figure 1**).

For each lesion, participants were provided the clinical history, and clinical and dermoscopic images. They were asked for their diagnosis, recommendation to biopsy or not, and level of confidence in classifying

a lesion as benign or malignant using a five-point scale (1 = not very confident, 2 = somewhat not confident, 3 = neutral, 4 = somewhat confident and 5 = very confident). Next, participants were provided with the EIS score and a clinical reference guide with positive and negative predictive values (**Figure 2**) [13]. They were again asked the same set of questions regarding diagnosis, recommendation to biopsy (or not), and confidence level. Participants learned the histopathology result of each lesion after completing all the evaluation steps. Lesions were presented in a random order.

Accuracy was defined as correctly diagnosing a lesion as "nevus" or "melanoma/severe dysplastic nevus" per histopathology. Mean levels of confidence were calculated for all evaluations as well as for evaluations with accurate diagnoses only. Medians, quartiles, and ranges of levels of confidence were calculated for each histopathologic category (common melanocytic nevi, dysplastic nevi, and melanoma). Diagnostic confidence, sensitivity, specificity, and accuracy [17,18] between the evaluations with and without EIS score were compared using paired *t*-tests. All statistical analyses were performed for all evaluators combined as well as students only and dermatologists only. Statistical analysis was performed using SPSS software (IBM Inc. Armonk, NY).

RESULTS

All 34 lesions were evaluated by the six evaluators for a total of 204 evaluations. Of the 6 common melanocytic nevi, 5 had an EIS score ≤3 while 1 had an EIS score of 4. For the 17 dysplastic nevi, the EIS score was ≤3 for 8 lesions and ≥4 for the remaining 9. The EIS scores for all 11 melanomas were ≥4 (**Table 1**).

Mean confidence increased for 29/34 (85%) lesions, did not change for 3/34 (9%) lesions, and decreased for 2/34 (6%) lesions. Of the lesions with increases in mean confidence, 26/29 (90%) were diagnosed correctly by ≥4 evaluators, and 2/29 (7%) by 2-3 evaluators. In addition, one mild to moderately dysplastic nevus with an EIS score of 6 (lesion number 11) was inaccurately diagnosed as a melanoma by all evaluators, with or without the EIS score. Of the two lesions for which confidence decreased, one was a mild-moderate dysplastic nevus with an EIS score of 4 (lesion number 15). It was diagnosed correctly by 2 students after viewing the EIS score, and by one student with or without the EIS score. It was incorrectly diagnosed as a melanoma with or without the EIS score by all 3 pigmented lesions specialists. The second lesion for which confidence decreased was a severely dysplastic nevus with an EIS score of 4 (lesion number 17). Without EIS it was accurately diagnosed by one student and one pigmented lesions specialist; with EIS it was accurately diagnosed by two of three students, and all three pigmented lesions specialists albeit with less confidence (**Table 1**).

When grouping lesions by histopathologic category (common melanocytic nevi, dysplastic nevi, and melanomas), there were significant increases in mean confidence in the correct diagnosis across all three categories for both students and pigmented lesions specialists (**Figure 3**). Specifically, the mean diagnostic confidence for the diagnosis of common melanocytic nevi rose from 2.86 to 4.06 ($p<.001$) for students, and 3.07 to 4.20 ($p=.005$) for pigmented lesions specialists. Similarly, the mean diagnostic

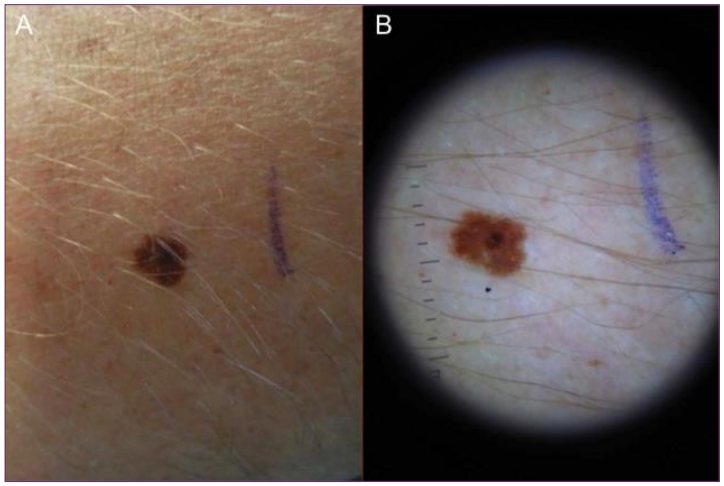

Figure 1. A) Clinical and B) dermoscopic images of a mildly dysplastic nevus with an electrical impedance spectroscopy score of 2 from the training set used for this study (lesion number 9)

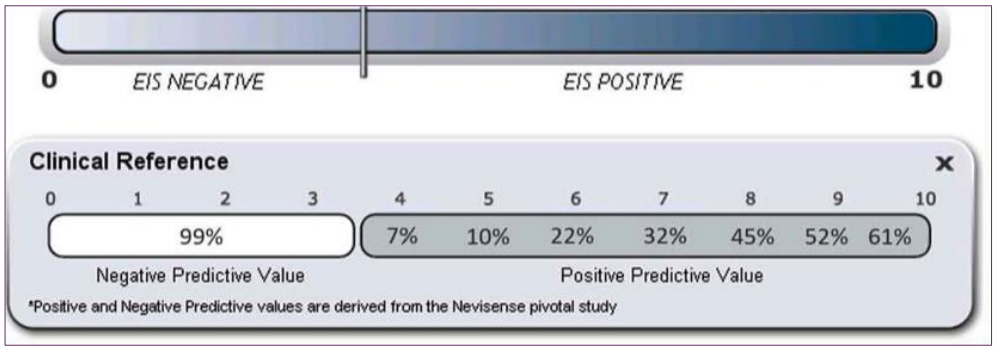

Figure 2. Clinical reference guide indicating positive and negative predictive values of electrical impedance spectroscopy scores

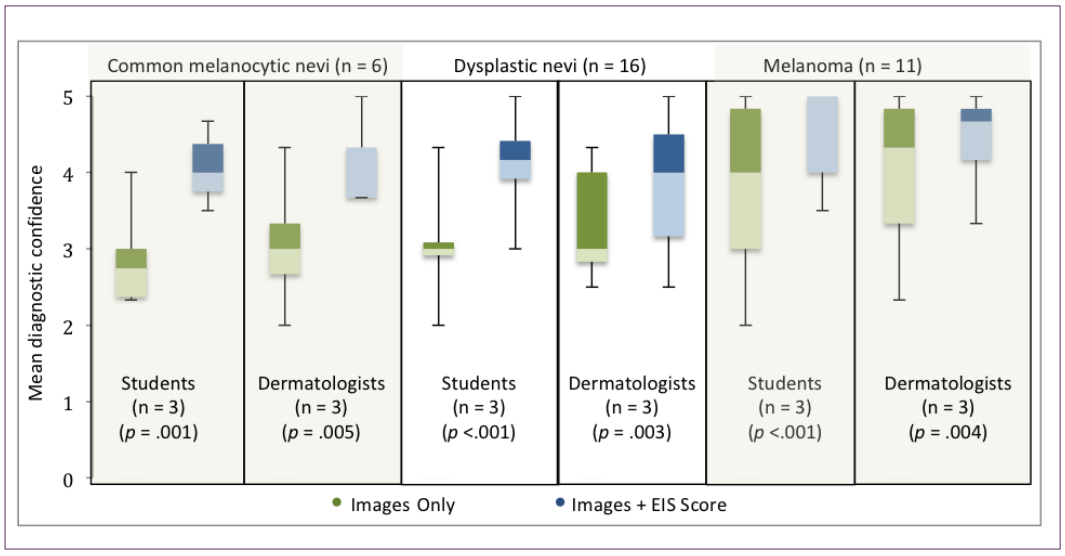

Figure 3. Box plot of mean diagnostic confidence for accurately diagnosed lesions in evaluations with images alone (green) and images plus electrical impedance spectroscopy (EIS) score (blue) by histopathologic category. Shading of boxes corresponds to quartiles. Boxes with a single color indicate that the median did not differ from either the first or third quartile

confidence for the diagnosis of dysplastic nevi increased from 3.00 to 4.17 (p<.001) for students, and 3.32 to 3.81 (p = .003) for pigmented lesions specialists. Finally, regarding melanoma, the mean diagnostic confidence rose from 3.83 to 4.59 (p<.001) for students, and 3.94 to 4.46 (p= .004) for pigmented lesions specialists. There were no statistically significant increases in confidence among lesion that were incorrectly diagnosed.

Mean diagnostic accuracy increased from 74% to 86% (*p* = .005) for all participants combined, and from 75% to 86% (p = .03) for students. The increase for dermatologists trended towards significance, increasing from 73% to 85% (p = .13). Across all 6 evaluators, the addition of EIS scores increased mean biopsy sensitivity for melanoma/severe dysplastic nevi from 70% to 84% (*p* = .014). There was a trend towards increased specificity, from 62% to 69% (p=0.06). For students, the biopsy sensitivity increased from 59% to 80% (p = .03); and there was a trend towards increased specificity from 67% to 75% (p=0.06). For the pigmented lesion specialists, the increases in sensitivity and specificity did not reach statistical significance (**Table 2**).

Though it was not the primary objective when developing the training material, the sensitivity of EIS for diagnosis of melanoma in the selected cases (100%) did not differ greatly from the sensitivity reported in the pivotal validation study for Nevisense (97%). However, the specificity of EIS for the cases in the training set (69%) was considerably higher than that of the pivotal study (34.4%) [13]. Study participants were unaware of these statistics prior to the study.

DISCUSSION

Although the performance of EIS scores as a diagnostic aid in the management of skin lesions suspicious for melanoma has been previously demonstrated, its impact on clinician confidence in their biopsy decisions has not been described. In this pilot study, we found that the addition of EIS scores to clinical and dermoscopic images significantly increased mean confidence in the correct diagnosis of common, dysplastic, and malignant melanocytic neoplasms for both students and pigmented lesions specialists. Also, the addition of EIS scores to clinical and dermoscopic images significantly increased diagnostic accuracy and biopsy sensitivity of suspicious melanocytic lesions among medical students. EIS scores elevated the biopsy sensitivity of students close to that of dermatologists with images alone, suggesting particular value of EIS for novice diagnosticians. Moreover, this improvement in diagnostic accuracy among medical students is consistent with recent studies where the addition of EIS scores to clinical images alone increased diagnostic accuracy for novice diagnosticians, including trainees and midlevel practitioners [14-16]. Among the pigmented lesions specialists, the addition of an EIS score resulted in a trend toward improved accuracy of diagnosis, but it did not reach statistical significance. There are several possible explanations for this observation including pigmented lesions specialists depending more heavily on dermoscopy compared to the EIS score since they had no prior experience integrating these scores into their decision-making

Table 1. Mean Diagnostic Confidence in Evaluations with Images Only and Images plus EIS score

	Students (n = 3)			Dermatologists (n = 3)			Combined (n = 6)			
Histopathologic Diagnosis - EIS Score [a]	**Images Only**	**With EIS Score**	**p-Value**	**Images Only**	**With EIS Score**	**p-Value**	**Images Only**	**With EIS Score**	**p-Value**	**n with Correct Diagnosis**
Common melanocytic nevi (all)	2.72	3.78	**.001**	3.00	4.06	**.002**	2.86	3.92	**<.001**	
1. Common melanocytic nevus - 3	2.67	3.67	.23	2.67	3.67	.23	2.67	3.67	**0.04**	5
2. Common melanocytic nevus - 2	3.00	4.67	.13	3.33	4.33	.23	3.17	4.50	**0.03**	6
3. Common melanocytic nevus - 4	2.00	2.67	.18	2.67	3.33	.18	2.33	3.00	**0.03**	2
4. Common melanocytic nevus - 3	2.33	4.00	**.04**	3.00	4.33	.27	2.67	4.17	**0.02**	6
5. Common melanocytic nevus - 1	4.00	3.67	.74	4.33	5.00	.18	4.17	4.33	0.74	6
6. Common melanocytic nevus - 1	2.33	4.00	**.04**	2.00	3.67	.37	2.17	3.83	0.05	6
Dysplastic/Atypical Nevi (all)	3.16	4.20	**<.00**	3.39	3.80	**.005**	3.27	4.00	**<.001**	
7. DN - mild - 1	4.33	5	0.42	4.33	4.67	0.42	4.33	4.83	0.2	6
8. DN - mild - 3	3	4.33	0.27	2.67	4	0.06	2.83	4.17	**0.03**	6
9. DN - mild - 2	2.33	4	0.13	3	4.33	0.06	2.67	4.17	**0.007**	6
10. DN - mild/moderate - 3	2.67	4.33	0.13	3.67	4.33	0.18	3.17	4.33	**0.03**	6
11. DN - mild/moderate - 6	4	4.67	0.18	4	4.67	0.18	4	4.67	**0.03**	0
12. DN - mild/moderate - 6	2.67	4	0.42	2.67	3.33	0.18	2.67	3.67	0.18	4
13. DN - mild/moderate - 1	3.33	4.33	0.23	4	4.67	0.42	3.67	4.5	0.09	6
14. DN - mild/moderate - 5	3.67	3.67	>.99	2.67	2.67	>.99	3.17	3.17	>.99	4
15. DN - mild/moderate - 4	3.67	3.33	0.42	3.67	3.67	>.99	3.67	3.5	0.61	3
16. DN - mild/moderate - 3	3	4.33	0.06	3.33	3	0.84	3.17	3.67	0.54	5
17. DN - severe - 4	3.33	3.67	0.74	4	2.67	0.06	3.67	3.17	0.42	5
18. DN - severe - 3	3.33	4.67	0.27	4	4.67	0.18	3.67	4.67	0.08	3
19. DN - severe - 5	3	4.67	0.13	3	3.67	0.42	3	4.17	0.06	6
20. DN - severe - 4	3	3.67	0.53	2.67	3.33	0.18	2.83	3.5	0.18	6
21. DN - severe - 3	3	3.67	0.53	2.67	2.67	>.99	2.83	3.17	0.53	6
22. DN - severe - 7	2.23	4	**0.04**	3	3.67	0.18	2.67	3.83	**0.01**	6
23. DN - severe - 9	3	5	0.07	4.33	4.67	0.42	3.67	4.83	0.06	6
Melanoma (all)	3.86	4.67	**<.00**	3.92	4.47	**.001**	3.89	4.57	**<.001**	
24. Melanoma – in situ - 6	3	4	0.23	2.33	4.33	0.07	2.67	4.17	**0.02**	4
25. Melanoma – in situ - 6	3.33	4.33	0.23	2.33	3.67	0.06	2.83	4	**0.01**	5
26. Melanoma – in situ - 6	4.33	4.67	0.42	3.33	3.33	>.99	3.83	4	0.61	4
27. Melanoma – in situ - 7	4.67	5	0.42	4.67	4.67	>.99	4.67	4.83	0.61	6
28. Melanoma – in situ - 8	5	5	-	5	5	-	5	5	-	6
29. Melanoma – in situ - 8	3.67	4	0.42	4.67	4.33	0.42	4	4.33	0.18	6
30. Melanoma – in situ - 10	3	5	0.07	4.33	4.67	0.42	3.67	4.83	0.06	6
31. Melanoma – in situ - 8	2	4	0.07	3.33	4	0.18	2.67	4	**0.03**	5
32. Melanoma – T1 - 9	4.33	5	0.18	3.67	4.67	0.42	4	4.83	0.14	6
33. Melanoma – T1 - 10	5	5	-	5	5	-	5	5	-	6
34. Melanoma – T1B - 7	5	5	-	5	5	-	5	5	-	6

[a] Negative predictive values (NPV) and positive predictive values (PPV) of being melanoma: 0-3 = 99% NPV, 4 = 7% PPV, 5 = 10% PPV, 6 = 22% PPV, 7 = 32% PPV, 8 = 45% PPV, 9 = 52% PPV, 10 = 61% PPV[13]
Abbreviations: DN, dysplatic nevus

Table 2. Sensitivity, specificity and accuracy for evaluations with images only and images plus electrical impedance spectroscopy score

	Fourth-Year Medical Students (n=3)			Pigmented Lesion Expert Dermatologists (n=3)			Combined (n=6)		
	Images Only	**With EIS Score**	**p-value**	**Images Only**	**With EIS Score**	**p-value**	**Images Only**	**With EIS Score**	**p-value**
Biopsy sensitivity	59.3	79.6	**.03**	81.5	88.9	.18	70.4	84.3	**.01**
Biopsy specificity [a]	66.7	75.0	.06	56.3	62.5	.42	61.5	68.8	.06
Accuracy	75.4	86.3	**.03**	72.5	85.3	.13	74.0	85.8	**.005**

[a] Biopsy specificities were positively skewed for students, resulting in greater mean specificities for students compared to dermatologists

These findings build on a previous report that found that dermoscopy increased diagnostic confidence for common nevi and melanomas, but not for dysplastic nevi when compared to clinical images alone [8]. Since dysplastic nevi are often equivocal on dermoscopy, EIS may be especially useful for the diagnosis of these lesions. The addition of EIS scores to trained clinical and dermoscopic evaluation may allow dermatologists to exhibit greater confidence regarding dermoscopically equivocal lesions and provide prompt explanations (i.e. affective and cognitive reassurance [19,20]) to alleviate patients' anxieties. This would be particularly helpful in clinically atypical, low scoring lesions where dermatologists can more confidently inform patients of the benign nature of these lesions. EIS scores may also foster confidence and learning among novice diagnosticians as they refine their diagnostic skills throughout their dermatologic training.

There are several limitations to this pilot study. Most importantly, we recognize the small sample size of participants in this study. The number of participants was intentionally kept small since the Nevisense device is not available in our center at this time for routine clinical use, and we did not want to inadvertently promote its use among trainees and other faculty members. Another important consideration is that in clinical settings many diagnostically equivocal pigmented lesions may be non-melanocytic (e.g. atypical solar lentigines). These lesions are known to have elevated EIS scores, so applying EIS measurement to a clinically suspicious, yet non-melanocytic lesion has a high chance of a false positive test result. Thus, clinicians have to make the additional decision of whether or not it would be appropriate to utilize EIS on a particular lesion, a step that was not included in this study. Moreover, the stakes of deciding whether or not to biopsy a lesion are higher in a clinical setting than in the context of a survey study. Additional limitations include the small number of lesions included and the potential for selection bias in the choice of lesions provided by SciBase. As noted above, the specificity of Nevisense for the diagnosis of melanoma/severely dysplastic nevus was higher than that reported in the pivotal clinical trial.

CONCLUSION

In this pilot study, we tested the concept that integrating EIS scores with clinical and dermoscopic images would significantly increase diagnostic confidence for both students and dermatologists in the

evaluation of melanocytic nevi and melanoma. Despite the small sample sizes, we did find statistically significant improvements in diagnostic confidence and accuracy among the students and pigmented lesions specialist dermatologists. Additional larger studies in real-world clinical settings are needed to more fully examine the role of EIS in providing patients with greater reassurance when their clinically atypical nevi are being evaluated, and facilitating clinical decision-making.

Conflict of Interest Disclosures: The authors have no financial conflicts of interest to declare. All authors except for LF are or were team members on a separate skin cancer diagnostic study utilizing Nevisense.

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