Diagnostic Efficacy Of Electrical Impedance Spectroscopy Versus Dermoscopy For Pigmented Skin Lesions: A Pilot Study

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It is critical for dermatology providers to accurately identify concerning pigmented skin lesions (PSLs) for biopsy, while avoiding biopsies for benign PSLs. Evidence shows that early recognition and removal of melanocytic neoplasms remains the most impactful prognostic factor for favorable melanoma outcomes.¹²³ Currently, dermatologists largely rely on visual inspection and dermoscopic examination to guide clinical decision-making for PSLs. However, this approach is not infallible: false positive diagnoses lead to unnecessary excisions, complications, and increases in health care costs; of even greater clinical concern, false negative diagnoses can leave malignant lesions undiagnosed, increasing patient mortality.⁴⁵

ABSTRACT

Introduction: Electrical impedance spectroscopy (EIS) is a non-invasive diagnostic device that measures the electrical impedance of skin lesions to assist in the detection of melanoma. While this tool has been shown to have a high sensitivity for melanoma diagnosis, data on its impact on clinical decision-making for pigmented skin lesions (PSLs) compared to other diagnostic tools is lacking. To gain further insight into its clinical utility, we conducted a pilot study to evaluate how this technology – specifically, the effect it has on clinical decisions for PSLs – compares to traditional dermoscopy.

Methods: Dermatologists, dermatology residents, and medical students completed an online survey eliciting their biopsy decisions for 24 PSLs of varying histopathological diagnoses. Half of the lesions from each diagnosis group were presented as a clinical image with associated dermoscopic image and the other half as a clinical image with the corresponding EIS score.

Results: Decisions made with EIS demonstrated a mean sensitivity of 75% for melanomas/severely dysplastic nevi vs. 66% for decisions made with dermoscopy (p=.008). While dermatologists biopsied with similar sensitivities when using EIS or dermoscopy (81% vs. 81%), residents and medical students biopsied with significantly greater sensitivity when using EIS. Respondents who reported rarely using dermoscopy showed the greatest improvement in sensitivity and specificity when using EIS compared to dermoscopy.

Conclusion: Given that not all providers are trained in dermoscopy, and our finding that EIS particularly benefits those who infrequently use dermoscopy, EIS may complement dermoscopy by helping a broader range of providers make improved PSL diagnostic decisions.

INTRODUCTION

It is critical for dermatology providers to accurately identify concerning pigmented skin lesions (PSLs) for biopsy, while avoiding biopsies for benign PSLs. Evidence shows that early recognition and removal of melanocytic neoplasms remains the most impactful prognostic factor for favorable melanoma outcomes.¹²³ Currently, dermatologists largely rely on visual inspection and dermoscopic examination to guide clinical decision-making for PSLs. However, this approach is not infallible: false positive diagnoses lead to unnecessary excisions, complications, and increases in health care costs; of even greater clinical concern, false negative diagnoses can leave malignant lesions undiagnosed, increasing patient mortality.⁴⁵
Electrical impedance spectroscopy (EIS) technology is a noninvasive, point-of-care diagnostic tool designed to aid clinicians in the decision to biopsy PSLs. Approved by the US Food and Drug Administration to assist in the detection of melanoma, the EIS device (Nevisense, Scibase, Stockholm, Sweden) utilizes a small, low voltage electrode to apply a painless electrical current to the skin. As benign and malignant tissues vary in cell shape, size, and molecular composition, EIS can measure the resulting differences in electrical impedance of different PSLs and generate scores correlating to the risk of malignancy. The device produces a score ranging from 0 to 10, which is associated with the likelihood that the tested lesion is a melanoma. EIS scores of 0 to 3 carry a negative predictive value of 99%, while those from 4 to 10 represent progressively increasing positive predictive values ranging from 7% to 61%.

Past studies evaluating the clinical utility of EIS have gathered some promising preliminary data, suggesting that it increases the sensitivity and specificity of dermatologists’ biopsy decisions for melanoma compared with visual inspection alone. The number needed to biopsy (NNB), a biopsy efficiency metric denoting the ratio of total biopsies to melanomas detected, also decreased when EIS use supplemented clinical decision-making on the basis of clinical morphology alone. While these studies have demonstrated that incorporating EIS into clinical decision-making for PSLs is superior to just visual clinical inspection alone, the diagnostic efficacy of EIS has yet to be compared head-to-head with that of dermoscopy, currently used as standard practice by dermatologists in evaluation of PSLs. To better understand the clinical utility of EIS, we investigated how this relatively new technology – specifically, the effect it has on clinical decisions for PSLs – compares to traditional dermoscopy.

**METHODS**

Our survey for dermatologists, dermatology residents, and medical students compared clinical decision-making with EIS vs. dermoscopy. Participants were recruited via email over a period of 2 months. Images of twenty-four randomly selected, histologically-confirmed and EIS-evaluated PSLs, comprising 8 melanomas, 8 dysplastic nevi (6 mild-moderate dysplastic, 2 severe dysplastic), and 8 melanocytic nevi, from a previously published prospective blinded trial of 2416 lesions were included in this study. Twelve PSLs (half of the lesions from each diagnosis group) were randomly selected to be presented as a clinical image with associated dermoscopic image (dermoscopy group), while the other twelve lesions were presented as a clinical image with the corresponding EIS score (EIS group). After evaluating each lesion, respondents rated the necessity of a biopsy on a scale from 1-5 (1: ‘not necessary’, 5: ‘extremely necessary’).

A selection of 4 or 5 was considered to be a decision to biopsy, with 1-3 considered a decision not to biopsy. The sensitivity and specificity of biopsy decisions for melanomas and severely dysplastic nevi were determined. These metrics were further compared between different subsets of the respondent population by stratifying the population into groups based on their level of training and the frequency with which they use dermoscopy in clinical practice.
Differences in biopsy decision proportions, sensitivities, and specificities were compared using Pearson’s chi-squared test. Significance between the area under the curves (AUCs) of the receiver operating characteristic (ROC) curves was calculated using the bootstrap method computed with 2,000 replicates.

**RESULTS**

Eighty-nine participants (38 dermatologists, 25 dermatology residents, and 26 medical students) provided responses, making a total of 1740 clinical decisions (862 in the dermoscopy group, 878 in the EIS group). With dermoscopy, the decision to biopsy was made for 541 of 862 lesions vs. 422 of 878 lesions with EIS (62.8% vs. 48.1%, respectively; \(p<0.001\); Table 1).

Biopsy decisions made with dermoscopy demonstrated an overall sensitivity of 66% compared with a sensitivity of 75% with EIS (\(p=0.008\); Table 2). Similarly, biopsy decisions made with EIS yielded a greater specificity (70%) than dermoscopy (40%; \(p<0.001\)). Biopsy decisions were impacted by training level, with dermatologists exhibiting similar sensitivities with both EIS and dermoscopy (81% vs. 81%). However, dermatologists also saw the greatest increase (68% vs. 35%, \(p<0.001\)) in the specificity of biopsy decisions made with EIS when compared to dermoscopy. Residents and medical students biopsied with significantly greater sensitivity and specificity when using EIS compared to dermoscopy.

Conducting a receiver operating characteristic (ROC) analysis using different biopsy ratings (1-5) as varying thresholds demonstrated that with clinical photography, EIS produced an area under the curve (AUC) of 0.78, which was significantly greater than the AUC produced with dermoscopy (0.527; \(p<0.001\); Figure 1).

In each of the four strata representing varying frequencies of respondents’ dermoscopy usage, greater sensitivities and specificities were noted in biopsy decisions made using EIS than those made using dermoscopy (Table 3). The greatest difference was among those who rarely or never use dermoscopy, who made biopsy decisions with 13% greater sensitivity and 35% greater specificity using EIS compared to dermoscopy (\(p=0.067\) and \(p<0.001\), respectively).

![Figure 1](image)

Melanoma detection often poses a challenge to dermatologists, especially in patients with multiple nevi. The clinical evaluation of PSLs involves consideration of lesion-specific information as well as patient-derived melanoma risk factors.\(^9\) Even when utilizing all available clinical information, clinicians still occasionally find themselves...

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**DISCUSSION**

Melanoma detection often poses a challenge to dermatologists, especially in patients with multiple nevi. The clinical evaluation of PSLs involves consideration of lesion-specific information as well as patient-derived melanoma risk factors.\(^9\) Even when utilizing all available clinical information, clinicians still occasionally find themselves...
misdiagnosing melanomas as benign lesions. Given the impact of early detection and treatment of melanoma on patient outcomes, improved evaluation tools may help clinicians to both reduce patient morbidity associated with unnecessary excision of benign lesions, as well as potentially reduce mortality by enhancing detection of malignant lesions. The value of a diagnostic tool lies in its ability to increase accuracy and positively impact clinical management: increased sensitivity reduces the false negatives of missed melanomas, while increased specificity avoids unnecessary biopsies of benign lesions.

In this study, which aimed to compare the individual influences of EIS and dermoscopy on clinical decision-making, EIS-assisted decisions demonstrated greater accuracy than those made using dermoscopy. Training level had a noticeable impact on the results observed. Of the three different levels of training included, all but

<table>
<thead>
<tr>
<th>Training level</th>
<th>Dermoscopy</th>
<th>EIS</th>
<th>P valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Decisions to biopsy, n (%)</strong></td>
<td><strong>Total clinical decisions made (n)</strong></td>
<td><strong>Decisions to biopsy, n (%)</strong></td>
<td><strong>Total clinical decisions made (n)</strong></td>
</tr>
<tr>
<td>Dermatologists (n=38)</td>
<td>256 (71.9)</td>
<td>356</td>
<td>188 (51.6)</td>
</tr>
<tr>
<td>Dermatology residents (n=25)</td>
<td>152 (60.6)</td>
<td>251</td>
<td>132 (51.8)</td>
</tr>
<tr>
<td>Medical students (n=26)</td>
<td>133 (52.2)</td>
<td>255</td>
<td>102 (39.4)</td>
</tr>
<tr>
<td>Total (n=89)</td>
<td>541 (62.8)</td>
<td>862</td>
<td>422 (48.1)</td>
</tr>
</tbody>
</table>

EIS, electrical impedance spectroscopy  

Table 1. Number of decisions to biopsy out of total clinical decisions made both based on visual plus dermoscopic examination and visual plus EIS evaluation across different training levels of the respondent population.

<table>
<thead>
<tr>
<th>Training level</th>
<th>Dermoscopy</th>
<th>EIS</th>
<th>P value, Sens., Spec.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TP (n)</strong></td>
<td><strong>FN (n)</strong></td>
<td><strong>Sens. (%) (95% CI)</strong></td>
<td><strong>TN (n)</strong></td>
</tr>
<tr>
<td>Dermatologists (n=38)</td>
<td>120</td>
<td>28</td>
<td>81 (75.8–86.4)</td>
</tr>
<tr>
<td>Dermatology residents (n=25)</td>
<td>64</td>
<td>40</td>
<td>62 (53.7–69.4)</td>
</tr>
<tr>
<td>Medical students (n=26)</td>
<td>52</td>
<td>53</td>
<td>50 (41.5–57.5)</td>
</tr>
<tr>
<td>Total (n=89)</td>
<td>236</td>
<td>121</td>
<td>66 (62–70.2)</td>
</tr>
</tbody>
</table>
Table 3. Sensitivity and specificity of biopsy decisions for melanomas and severely dysplastic nevi both based on visual plus dermoscopic examination and visual plus EIS evaluation across varying dermoscopy use frequencies of the respondent population.

<table>
<thead>
<tr>
<th>Dermoscopy usage frequency</th>
<th>Dermoscopy</th>
<th>EIS</th>
<th>P value, Sens.</th>
<th>P value, Spec.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TP (n)</td>
<td>FN (n)</td>
<td>Sens.(^a) % (95% CI)</td>
<td>Spec.(^b) % (95% CI)</td>
</tr>
<tr>
<td>Very frequently (multiple times/day)</td>
<td>133</td>
<td>47</td>
<td>74 (68.5–79.3)</td>
<td>34 (27.4–41.3)</td>
</tr>
<tr>
<td>Frequently (multiple times/week)</td>
<td>32</td>
<td>14</td>
<td>70 (58.3–80.8)</td>
<td>44 (29.4–58.1)</td>
</tr>
<tr>
<td>Less frequently (multiple times/month)</td>
<td>23</td>
<td>12</td>
<td>66 (52.4–79)</td>
<td>45 (28.4–61.3)</td>
</tr>
<tr>
<td>Rarely or never</td>
<td>48</td>
<td>48</td>
<td>50 (41.7–58.3)</td>
<td>45 (35.4–55.3)</td>
</tr>
</tbody>
</table>

EIS, electrical impedance spectroscopy; FN, false negatives; FP, false positives; TN, true negatives; TP, true positives
\(^a\) Sensitivity of biopsy/referral decisions for melanomas and severely DN, calculated as TP/(TP+FN)
\(^b\) Specificity of biopsy/referral decisions for melanomas and severely DN, calculated as TN/(TN+FP)
\(^c\) Chi-squared test

Dermatologists saw an increase in the sensitivity of their biopsy decisions with EIS compared to dermoscopy, and all three saw increases in their specificity with EIS compared to dermoscopy. While dermatologists’ biopsy decisions exhibited similar sensitivities with both EIS and dermoscopy, this group also saw the greatest improvement in the specificity of their biopsy decisions with EIS when compared to dermoscopy. This indicates that dermatologists in this study, while still biopsying with the greater sensitivity, were more likely than residents and medical students to biopsy benign lesions when using dermoscopy, leading to a lower specificity of their dermoscopy-assisted biopsy decisions. EIS served to reduce the number of benign biopsies made by this group, increasing their specificity considerably and maintaining sensitivity. Given EIS’ high observed NPV of 99%,\(^6\) it is conceivable that lesions receiving a “negative” EIS score (0 to 3), which would have otherwise been biopsied based on visual and dermoscopic criteria, are responsible for this rise in specificity. Those who rarely used dermoscopy appeared to benefit more from EIS than their counterparts with greater dermoscopy experience, with this group demonstrating the greatest improvement in both sensitivity and specificity when using EIS compared to
dermoscopy. This finding suggests EIS may be of particular benefit to clinicians less proficient in dermoscopy.

Of note, the EIS sensitivities (75% overall, 81% among attendings) detected in this study are less than that in the EIS pivotal trial (97%), while the specificities observed (70% overall, 68% among attendings) are higher than that in the pivotal trial (34%). This may be attributed to our survey format, in which respondents rated their inclination to biopsy each lesion from 1-5. For our analysis, lesions rated 1-3 were considered as unbiopsied and those rated 4-5 as biopsied. In comparison to the pivotal trial's binary biopsy choice, this approach may have yielded a greater number of lesions deemed unbiopsied, thus lowering the sensitivity, and fewer lesions biopsied, thus raising the specificity. This approach was applied equally to dermoscopy- and EIS-assisted biopsy decisions, however, so relative accuracy would not have been affected. In clinical practice, tools to assist in accurately identifying ambiguous lesions to biopsy would have the greatest yield in diagnosing melanomas without biopsyng benign lesions. The significantly greater AUC of EIS-assisted biopsy decisions demonstrates that EIS improved accuracy across all levels of biopsy confidence.

However, this study had limitations. One limitation is that respondents’ biopsy decisions were made on the basis of clinical images in an online survey rather than in vivo examination. As such, the true consequences of a missed melanoma or an unnecessary biopsy were likely diminished compared to lesions examined in a real clinical setting. This survey also did not include nonmelanocytic lesions such as seborrheic keratoses, which could alter the accuracy of EIS-based biopsy decisions. Lastly, inherent to survey-based studies is the potential for participation bias.

CONCLUSION

Implementing the use of diagnostic tools that improve accuracy in malignant PSL detection is crucial to improve patient outcomes and reduce unnecessary biopsies. In this pilot study, we found that dermatologists made biopsy decisions with similar sensitivity when utilizing either EIS or dermoscopy. However, those with comparably less dermoscopy experience (i.e. residents, medical students) demonstrated significantly improved sensitivity when using EIS compared to dermoscopy. Given that not all providers are trained in dermoscopy, and our finding that EIS particularly benefits those who infrequently use dermoscopy, EIS may complement dermoscopy by helping a broader range of providers make improved PSL diagnostic decisions. This will ultimately improve patient care and reduce the morbidity and mortality of a melanoma diagnosis.

Conflict of Interest Disclosures: None

Funding: None

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