Integrating Electrical Impedance Spectroscopy into Clinical Decisions for Pigmented Skin Lesions Improves Diagnostic Accuracy: A Multitiered Study

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ABSTRACT

Introduction: The number-needed-to-biopsy (NNB) metric measures the efficiency of a clinician’s ability to accurately diagnose and recommend pigmented skin lesions (PSLs) for biopsy for suspected melanomas. Electrical impedance spectroscopy (EIS) is a non-invasive technique that measures differences in resistance between healthy and cancerous skin cells, intended as an aid to enhance diagnostic accuracy.

Methods: Dermatology clinicians of three distinct groups (residents, physician assistants/nurse practitioners, and practicing dermatologists) were evaluated on their ability to accurately recommend suspect PSLs for biopsy before and after the integration of EIS data.

Results: All three groups had a reduction in NNB after the inclusion of EIS. Instances of missed biopsies for malignant melanoma were significantly reduced with simultaneous significant reductions in unnecessary biopsies for benign lesions. There was a material improvement of biopsy selection for PSLs having clinically challenging features. EIS also greatly improved the diagnostic acumen of clinicians whose assessments were less accurate than their peers prior to EIS incorporation.

Conclusions: The integration of EIS technology into the PSL biopsy decision was demonstrated to be effective in significantly enhancing clinician NNB and more accurate PSL biopsy selection.

INTRODUCTION

Early recognition and treatment of melanoma positively impacts outcomes and healthcare costs.¹-⁴ Significant heterogeneity exists with clinicians’ ability to correctly assess the severity of pigmented lesions, leading to missed melanomas and unnecessary biopsies.⁵ The number-
needed-to-biopsy (NNB) metric, expressed as a ratio between the total number of recommended biopsies divided by the number of biopsies for histologically confirmed malignant lesions, is typically used to assess biopsy efficiency.\(^6\)\(^,\)\(^7\)

Recent studies have suggested that dermatology clinicians of all levels could benefit from technology that augments clinical recognition of this tumor.\(^1\)\(^-\)\(^4\) Electrical Impedance Spectroscopy (EIS) is an FDA-approved technique in which the impedance (electrical resistance) of a pigmented skin lesion (PSL) is measured by the application of an electric current is applied across it and the resistance spectrum is analyzed. This device returns a value on a 0 – 10 scale with a higher score associated with an increased risk of malignancy. PSLs scoring between 0 – 3 have a negative predictive value of 99% and those scoring 4-10 have a monotonically increasing risk of being malignant with a probability from 9-64%.

To have the highest potential value in the practice setting, the greatest impact of diagnostic technologies should occur on clinically diagnostically challenging PSLs. The purpose of this study was to determine whether the integration of EIS data into the biopsy decision led to a decrease in NNB, increased sensitivity, fewer unnecessary biopsies and fewer missed malignant biopsy decisions across all levels of training and whether the greatest impact occurred in the most clinically challenging PSLs.

**METHODS**

A data set of 43 randomly chosen clinically suspicious PSLs (27 benign, 16 malignant) from a previously published prospective blinded trial of 2,416 lesions where clinical images,\(^8\) clinical ABCD criteria, and EIS scores were evaluated. A survey using these lesions was provided to clinicians with three levels of training: practicing dermatologists (267 respondents; 11,481 decisions), residents (164 respondents; 7,052 decisions), and midlevels (physician assistants/nurse practitioners; 160 respondents; 6,880 decisions). Lesion diagnoses were histologically confirmed, with benign lesions ranging from ordinary melanocytic nevi to mild or moderately dysplastic nevi. Since EIS has been shown to have some overlap with digital dermoscopy in PSL evaluation, dermoscopic evaluation was specifically excluded to better measure the independent effect of EIS on PSL diagnosis.\(^9\)

Respondents were asked to provide a biopsy recommendation twice: based on clinical morphology alone, and then again after the EIS device (Nevisense; Scibase AB, Stockholm, Sweden) score was provided. Significance was calculated using McNemar’s and differences of proportions testing. Sensitivity and specificity for all clinician levels before and after EIS incorporation were also calculated.

**RESULTS**

Reductions in NNB were observed across all three clinician levels (Table 1) after incorporating EIS technology into their biopsy decisions, with decreases of 14.8%, 16.8%, and 16.0% for residents, midlevels, and practicing dermatologists, respectively. The number of unnecessary biopsies for benign lesions significantly decreased, with a corresponding significant increase in the number of biopsies for malignant PSLs (Figure 1). When grouped into quartiles based on percentages of correct assessments, groups with the lowest pre-EIS correct evaluations experienced the
Table 1. Number-needed-to-biopsy values and PSL biopsy selection sensitivity and specificity before and after incorporation of EIS technology (ranges in parentheses represent 95% confidence intervals) for residents, midlevels, and practicing dermatologists before and after incorporation of EIS technology.

| Level of Training | % Sensitivity Pre-EIS (95% CI) | % Sensitivity Post-EIS (95% CI) | % Specificity Pre-EIS (95% CI) | % Specificity Post-EIS (95% CI) | NNB Pre-EIS | NNB Post-EIS | % Reduction in NNB Post-EIS | Number of decisions (n)* | Missed melanomas Pre-EIS (%)* | Missed melanomas Post-EIS (%)* |
|-------------------|---------------------------------|---------------------------------|-------------------------------|-------------------------------|-----------|-----------|----------------------------|---------------------------|---------------------------|-----------------------------|
| Resident          | 79.5 (77.9 – 81.1)              | 94.9 (94.0 – 95.7)              | 49.8 (48.3 – 51.3)            | 57.3 (55.9 – 58.8)            | 5.6       | 4.7       | 14.8                       | n = 1312                   | 93 (7.09%)                | 13 (0.99%)                  |
| Midlevel          | 84.1 (82.7 – 85.5)              | 97.8 (97.2 – 98.3)              | 34.8 (33.4 – 36.3)            | 46.7 (45.2 – 48.2)            | 6.2       | 5.2       | 16.8                       | n = 1280                   | 80 (6.25%)                | 7 (0.55%)                   |
| Practicing Dermatologist | 84.4 (83.2 – 85.4)              | 98.0 (97.5 – 98.4)              | 33.6 (32.5 – 34.7)            | 44.5 (43.3 – 45.6)            | 6.3       | 5.3       | 16.0                       | n = 2136                   | 153 (7.16%)               | 12 (0.56%)                  |

* Refers to melanomas with EIS score of 7+ (total of 8 lesions)

Figure 1. Changes in Number of Biopsy Decisions

Figure 2. % Correct Assessment at All Levels of Training
Table 2. Number of melanomas that would be missed and benign biopsies that would be performed both clinically and with the addition of electrical impedance spectroscopy results by a sample of 591 dermatology clinicians (164 residents, 160 nurse practitioners/physician assistants, and 267 practicing dermatologists) assessing 43 pigmented lesions. With the availability of EIS data for the biopsy decision, 1334 more melanomas were chosen for biopsy and 1630 benign PSLs had biopsies avoided.

| EIS Score | Clinical ABCD Features Present | Practicing Dermatologists | Residents | Midlevels | Combined | Net Change in Number of Melanomas Biopsied with Addition of EIS (n) | p-value* |
|-----------|--------------------------------|---------------------------|-----------|-----------|----------|---------------------------------------------------------------|----------|
| 9         | ABCD                           | 237 (88.8)                | 265 (99.3) | 142 (85.6) | 163 (99.4) | 141 (88.1)                                     | 160 (100) | 520 (88.0) | 588 (99.5) | 68       | < 0.001 |
| 8         | ABCD                           | 267 (100)                 | 267 (100)  | 163 (99.4) | 163 (99.4) | 156 (97.5)                                     | 159 (99.4) | 586 (99.2) | 589 (99.7) | 3        | 0.180   |
| 7         | ABCD                           | 259 (97.0)                | 266 (99.6) | 153 (93.3) | 162 (98.8) | 154 (96.3)                                     | 159 (99.4) | 566 (95.8) | 587 (99.3) | 21       | < 0.001 |
| 9         | ABCD                           | 266 (99.6)                | 267 (100)  | 163 (99.4) | 162 (98.8) | 160 (100)                                      | 160 (100)  | 589 (99.7) | 589 (99.7) | 0        | 1       |
| 8         | ABCD                           | 263 (98.5)                | 267 (100)  | 162 (98.8) | 164 (100)  | 160 (100)                                      | 160 (100)  | 589 (99.0) | 591 (100)  | 6        | 0.014   |
| 8         | ABC                            | 237 (88.8)                | 265 (99.3) | 145 (88.4) | 161 (98.2) | 141 (88.1)                                     | 160 (100)  | 523 (88.5) | 586 (99.2) | 63       | < 0.001 |
| 7         | ABC                            | 266 (99.6)                | 264 (98.9) | 161 (98.2) | 158 (96.3) | 159 (99.4)                                     | 156 (97.5) | 586 (99.2) | 578 (97.8) | -8       | 0.033   |
| 7         | ABC                            | 214 (80.1)                | 258 (96.6) | 127 (74.7) | 148 (90.2) | 133 (83.1)                                     | 158 (98.8) | 474 (80.2) | 564 (95.4) | 90       | < 0.001 |
| 10        | ABC                             | 252 (94.4)               | 264 (98.9) | 155 (94.5) | 162 (98.8) | 153 (95.6)                                     | 157 (98.1) | 560 (94.8) | 583 (98.6) | 23       | < 0.001 |
| 8         | BCD                            | 202 (75.7)                | 263 (98.5) | 136 (82.9) | 162 (98.8) | 135 (84.4)                                     | 158 (98.8) | 473 (80.0) | 583 (98.6) | 110      | < 0.001 |
| 6         | AB                              | 163 (61.0)                | 263 (98.5) | 93 (56.7)  | 156 (95.1) | 93 (58.1)                                      | 158 (98.8) | 349 (59.0) | 577 (97.6) | 228      | < 0.001 |
| 6         | AB                              | 209 (78.3)                | 238 (89.1) | 111 (67.7) | 131 (79.9) | 118 (73.8)                                     | 138 (86.3) | 438 (74.1) | 507 (85.8) | 69       | < 0.001 |
| 6         | AC                              | 113 (42.3)                | 254 (95.1) | 55 (33.5)  | 141 (86.0) | 71 (44.4)                                      | 152 (95.0) | 239 (40.4) | 547 (92.6) | 308      | < 0.001 |
| 6         | CD                              | 214 (80.1)                | 262 (98.1) | 116 (70.7) | 155 (94.5) | 118 (73.8)                                     | 155 (96.9) | 448 (75.8) | 572 (96.8) | 124      | < 0.001 |
| 6         | CD                              | 193 (72.3)                | 263 (98.5) | 89 (54.3)  | 149 (90.9) | 116 (72.5)                                     | 158 (98.8) | 398 (67.3) | 570 (96.4) | 172      | < 0.001 |
| 6         | C                               | 249 (93.3)                | 259 (97.0) | 116 (70.7) | 153 (93.3) | 146 (91.3)                                     | 156 (97.5) | 511 (86.5) | 568 (96.1) | 57       | < 0.001 |
| Total     |                                  | 3604                      | 4185       | 2087       | 2490      | 2154                                             | 2504       | 7845       | 9179      | 1334     | < 0.001 |

*Net Changes in Decision to Biopsy

**The values in the table are based on the number of melanomas and benign biopsies identified with and without the addition of EIS data. The table shows the number of melanomas and benign biopsies that were chosen for biopsy with the addition of EIS data for the biopsy decision. The p-values indicate the statistical significance of the differences observed with and without EIS data.**
### EIS Score 2

| Clinical Features Present | Benign Biopsies without EIS, n (%) | Benign Biopsies with EIS, n (%) | Benign Biopsies without EIS, n (%) | Benign Biopsies with EIS, n (%) | Benign Biopsies without EIS, n (%) | Benign Biopsies with EIS, n (%) |
|---------------------------|-----------------------------------|---------------------------------|-----------------------------------|---------------------------------|-----------------------------------|---------------------------------|
| ABCD                      | 215 (80.5)                        | 77 (28.8)                       | 81 (49.4)                         | 14 (8.5)                        | 123 (76.9)                        | 45 (28.1)                       |
| ABCD                      | 259 (97.0)                        | 267 (100)                       | 150 (91.5)                        | 161 (98.2)                      | 160 (100)                        | 159 (99.4)                      |
| ABCD                      | 263 (98.5)                        | 177 (66.3)                      | 158 (96.3)                        | 102 (62.2)                      | 160 (100)                        | 100 (62.5)                      |
| ACD                       | 223 (83.5)                        | 91 (34.1)                       | 122 (74.4)                        | 40 (24.4)                       | 135 (84.4)                        | 0 (0)                           |
| ACD                       | 235 (88.0)                        | 131 (49.1)                      | 138 (84.1)                        | 61 (37.2)                       | 147 (91.9)                        | 78 (48.8)                       |
| ABD                       | 261 (97.8)                        | 264 (98.9)                      | 150 (91.5)                        | 151 (92.1)                      | 158 (98.8)                        | 156 (97.5)                      |
| ABC                       | 185 (69.3)                        | 261 (97.8)                      | 85 (51.8)                         | 149 (90.9)                      | 116 (72.5)                        | 159 (99.4)                      |
| ABC                       | 241 (90.3)                        | 249 (93.3)                      | 128 (78.0)                        | 131 (79.9)                      | 143 (89.4)                        | 148 (92.5)                      |
| ABC                       | 237 (88.8)                        | 110 (41.2)                      | 125 (76.2)                        | 46 (28.0)                       | 142 (88.8)                        | 63 (39.4)                       |
| ABD                       | 147 (55.1)                        | 40 (15.0)                       | 95 (57.9)                         | 17 (10.4)                       | 97 (60.6)                         | 22 (13.8)                       |
| BCD                       | 213 (79.8)                        | 234 (87.6)                      | 119 (72.6)                        | 124 (75.6)                      | 131 (81.9)                        | 147 (91.9)                      |

### EIS Score 4

| Clinical Features Present | Benign Biopsies without EIS, n (%) | Benign Biopsies with EIS, n (%) | Benign Biopsies without EIS, n (%) | Benign Biopsies with EIS, n (%) | Benign Biopsies without EIS, n (%) | Benign Biopsies with EIS, n (%) |
|---------------------------|-----------------------------------|---------------------------------|-----------------------------------|---------------------------------|-----------------------------------|---------------------------------|
| AB                        | 157 (58.8)                        | 220 (82.4)                      | 97 (59.1)                         | 116 (70.7)                      | 108 (67.5)                        | 130 (81.3)                      |
| AC                        | 194 (72.7)                        | 256 (95.9)                      | 46 (28.0)                         | 142 (86.6)                      | 109 (68.1)                        | 156 (97.5)                      |
| AC                        | 141 (52.8)                        | 45 (16.9)                       | 39 (23.8)                         | 6 (3.7)                         | 78 (48.8)                         | 23 (14.4)                       |
| AC                        | 161 (60.3)                        | 41 (15.4)                       | 55 (33.5)                         | 10 (6.1)                        | 90 (56.3)                         | 15 (9.4)                        |
| AC                        | 142 (53.2)                        | 29 (10.9)                       | 35 (21.3)                         | 2 (1.2)                         | 81 (50.6)                         | 19 (11.9)                       |
| AC                        | 161 (60.3)                        | 261 (97.8)                      | 83 (50.6)                         | 135 (82.3)                      | 91 (56.9)                         | 155 (96.9)                      |
| BC                        | 218 (81.6)                        | 245 (91.8)                      | 108 (65.9)                        | 120 (73.2)                      | 131 (81.9)                        | 142 (88.8)                      |
| BC                        | 155 (58.1)                        | 34 (12.7)                       | 51 (31.1)                         | 10 (6.1)                        | 0 (0)                             | 26 (16.3)                       |
| CD                        | 61 (22.8)                         | 210 (78.7)                      | 53 (32.3)                         | 102 (62.2)                      | 61 (38.1)                         | 128 (80.0)                      |
| CD                        | 174 (65.2)                        | 103 (38.6)                      | 67 (40.9)                         | 22 (13.4)                       | 102 (63.8)                        | 46 (28.9)                       |
| CD                        | 96 (36.0)                         | 204 (76.4)                      | 32 (19.5)                         | 75 (45.7)                       | 61 (38.1)                         | 129 (80.6)                      |
| A                         | 150 (56.2)                        | 43 (16.1)                       | 65 (39.6)                         | 10 (6.1)                        | 88 (55.0)                         | 20 (12.5)                       |
| C                         | 55 (20.6)                         | 24 (9.0)                        | 2 (1.2)                           | 1 (0.6)                         | 33 (20.6)                         | 3 (1.9)                         |
| C                         | 131 (49.1)                        | 238 (89.1)                      | 29 (17.7)                         | 111 (67.7)                      | 77 (48.1)                         | 143 (89.4)                      |
| C                         | 191 (71.5)                        | 74 (27.7)                       | 76 (46.3)                         | 22 (13.4)                       | 114 (71.3)                        | 50 (31.3)                       |
| C                         | 120 (44.9)                        | 76 (28.5)                       | 34 (20.7)                         | 9 (5.5)                         | 78 (48.8)                         | 38 (23.8)                       |

### Net Change in Decision to Biopsy

| p-value* | -1368* |

*McNemar’s test

**EIS** = electrical impedance spectroscopy, % = percent, A = asymmetry, B = border irregularity, C = color variegation, D = diameter ≥ 6mm

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greatest improvement (Figure 2), more closely approximating the correct percentage biopsy-decision levels of their diagnostically superior colleagues. Overall sensitivity and specificity for all clinicians improved by 14% and 10.2%, respectively. The sensitivities and specificities for each level of training also significantly improved (Table 1). When evaluating melanomas with EIS scores of 7 or higher, the probability of correctly identifying melanomas across all levels of training significantly increased from 93.1% with clinical evaluation alone to more than 99.3% when EIS was integrated into the biopsy decision (p<0.00001) (Table 1).

In the composite training level analysis, EIS technology contributed to 1,343 fewer missed melanomas, and 1,613 unnecessary benign biopsies were avoided. EIS score integration had the greatest impact noted on the more clinically challenging PSLs for all 3 groups (Table 2). There was a significantly greater increase in PSLs selected for biopsy post-integration of EIS data for the melanomas that had fewer (1-2) clinical ABCD criteria and a similar significantly greater decrease for those benign PSLs with the greatest number (3-4) ABCD criteria clinically noted.

DISCUSSION

Recent technological advances in PSL diagnosis have aimed at improving accuracy and efficiency. In order to have their greatest potential positive influence, the greatest impact should be on lesions that are clinically equivocal. These findings suggest that integrating EIS into the biopsy decision, beyond the overall improvement in PSL selection for biopsy, has a materially positive effect on the more clinically challenging lesions.

The smaller NNB noted in the study for all levels of training suggests that EIS data made the biopsy selection more efficient. The reductions in NNB led to a decrease in unnecessary biopsies of benign lesions, and a simultaneous increase in biopsies recommended for malignant PSLs (Figure 1). The percent reduction and values of NNB post-EIS data integration demonstrates the benefits that EIS provides beyond baseline diagnostic skill. This finding is further strengthened by the lowest-scoring study participants demonstrating the greatest improvements in percentage of correct assessments, narrowing the relative gaps in diagnostic acumen compared to their more diagnostically astute peers.

A malignant melanoma that is missed during initial consultation will also lead to an increase in downstream diagnosis and treatment costs, as well as less favourable patient outcomes. When evaluating the eight PSLs that were histologically proven to be malignant and had EIS scores of 7+, the fact that almost none of these melanomas (0.7%) escaped biopsy reinforces the inference that integration of EIS information into the biopsy decision could materially lower the economic and social costs associated with missed melanomas.

A limitation of this study is that decisions were made based on clinical images alone versus in vivo examination. Dermoscopic images were also not included to remove any possible confounding effects of dermoscopy, allowing for assessment of the independent impact of EIS technology. In addition, despite its growing use as a biopsy efficacy metric, NNB may not be ideal due to a lack of standardization and underreporting. For these reasons, a lower NNB may not necessarily lead to more efficient outcomes.
Our study demonstrated the benefits of incorporating EIS technology beyond clinical PSL diagnosis alone for biopsy selection across all levels of training, as measured by decreases in NNB, increased sensitivity and specificity, fewer unnecessary biopsies of benign lesions, and more importantly, almost the complete elimination of missed higher probability malignant melanomas in our study series. Greater homogeneity in diagnostic acumen was achieved, thus increasing the overall efficacy in correct PSL assessments. The fact that a material positive impact on PSL biopsy selection occurred in the most clinically-challenging lesions suggests that this technology may be particularly helpful in this spectrum of PSLs. In an era of healthcare economics and better evaluation of social costs, maximizing efficiency in melanoma detection is paramount in order to address the steadily rising rates of this cancer.

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