ORIGINAL RESEARCH

Electrical Impedance Spectroscopy Versus Clinical Inspection Approaches: Melanoma Efficacy Detection Comparison

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ABSTRACT

Early detection of melanoma continues to provide a diagnostic challenge for Dermatologists and other healthcare providers. Recently, there has been increased interest in the use of novel technology to aid in the detection of melanoma. We performed a post-hoc analysis of a subset of data from the Nevisense pivotal trial to retrospectively compare the results of one such technology—electrical impedance spectroscopy (EIS)—to existing melanoma detection tools in 265 cases of malignant melanoma. Lesions were analyzed using EIS, the clinical ABCD rule, the ABCD dermoscopy rule, and the standard and weighted melanoma 7-point checklists. The proportion of false negative cases was calculated for each method and correlation between EIS score and melanoma stage was calculated. Overall, EIS produced an acceptable false negative rate (3.4%) for the detection of melanoma. Additionally, there was a statistically significant, moderate correlation between EIS score and tumor staging (Spearman rho=0.32, p<0.001). In this sample, EIS was very sensitive for the detection of melanoma and may prove to be a useful clinical adjunct for ruling out malignant melanoma in challenging cases.

INTRODUCTION

Early detection and excision remain the most important prognostic factors in the treatment of melanoma.[1] Detection remains challenging and, resultantly, melanoma-related mortality is high. In 2017, an estimated 9,730 people will die from melanoma in the United States.[2] Accordingly, there has been significant interest in novel technologies aimed at augmenting the detection rate achieved with clinical diagnosis of melanoma.[3] Electrical impedance spectroscopy (EIS) (Nevisense, SciBase AB, Stockholm, Sweden) has been shown to have potential as a diagnostic aid for the detection of melanoma.[4,5] In the current study, we examined a subset of data from an international, multicenter, trial[4] in order to compare the sensitivity of EIS to

existing melanoma detection tools and to measure the enhancement in sensitivity of melanoma detection achieved by combining EIS with other methods. Additionally, we determined the correlation between EIS score and pathologic staging in biopsy-proven melanoma lesions.

METHODS

Of the 1,943 pigmented lesions evaluated in a prior series[4], the 265 biopsy-proven melanoma lesions (112 *in* situ, 153 invasive melanoma) were selected for inclusion in this sub-analysis. Prior to excisional biopsy, using the EIS device, lesions had been measured on a 0-10 scale, with a score of 4 or greater representing a positive score. Prior to biopsy, dermoscopic images were saved and these were analyzed in a post-excisional performance study of those lesions with sufficient image quality to allow classification using the clinical ABCD rule, the ABCD rule of dermoscopy (cutoff >4.75 for positive score), and both the melanoma 7-point checklist and the weighted 7-point checklist (cutoff ≥3 for positive score). Twenty-seven of the biopsy-proven melanoma lesions did not have sufficient image quality to allow classification by each of these methods and were thus excluded, leaving a total of 238 melanoma lesions (101 *in situ*, 137 invasive). False negative rate was calculated for each method.

Additionally, correlation between EIS score and pathologic stage (taking into account all 265 biopsy-proven melanoma lesions assessed with EIS) was measured using Spearman's rho.

RESULTS

The false negative rate for the detection of melanoma by visual inspection has been estimated to be approximately 20-30%.[6-8] In the present study, there were 9 false negative results by EIS (false negative rate 3.4%, sensitivity 96.6%). All false negative EIS results occurred in early lesions (7 *in situ*, 2 T1a). In this sample, there was also a trend towards lower false negative rate with EIS versus that of the clinical ABCD rule, although the result was not statistically significant (3.4% vs. 12.8%, p=0.294). The false negative rate for the detection of melanoma by EIS was statistically significantly lower compared to the ABCD rule of dermoscopy (3.4% vs. 45.8%, p=0.003), the 7-point checklist (3.4% vs. 50.8%, p=0.008), and the weighted 7-point checklist (3.4% vs. 39.3%, p=0.001) (Figure 1). The clinical ABCD rule was the only method that detected melanoma lesions that were missed by EIS (6 lesions). However, EIS detected more lesions that were missed by the clinical ABCD rule (31 lesions). There was a statistically significant, moderate correlation between EIS score and tumor staging (Rho=0.32, p<0.001, Figure 2).

Percentage of Biopsy-Proven Melanoma Lesions Detected by Various Clinical Diagnostic Algorithms vs. EIS
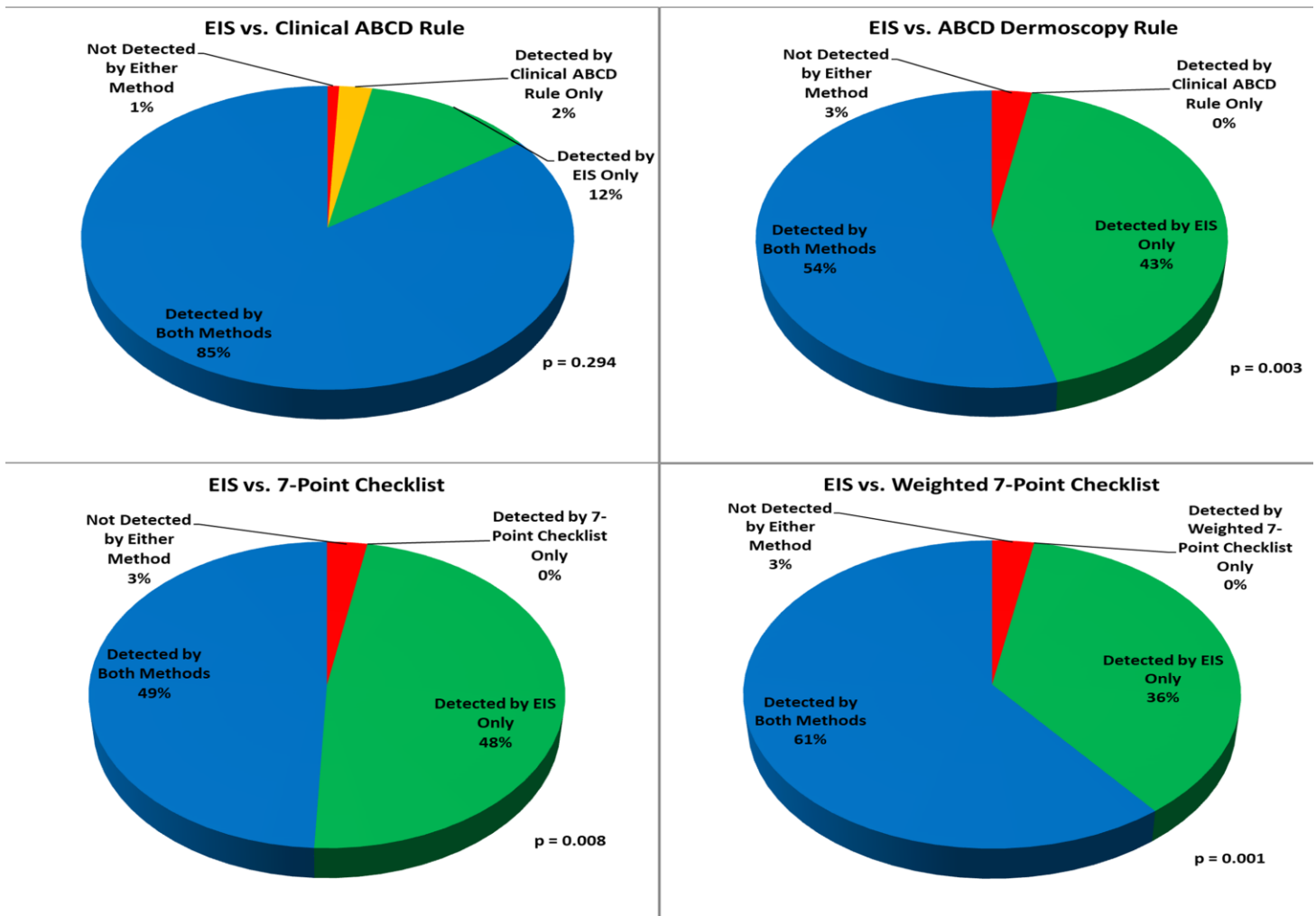

Figure 1. Comparison of electrical impedance technology to other adjuncts to clinical diagnosis in the detection of malignant melanoma lesions. EIS = electrical impedance spectroscopy.
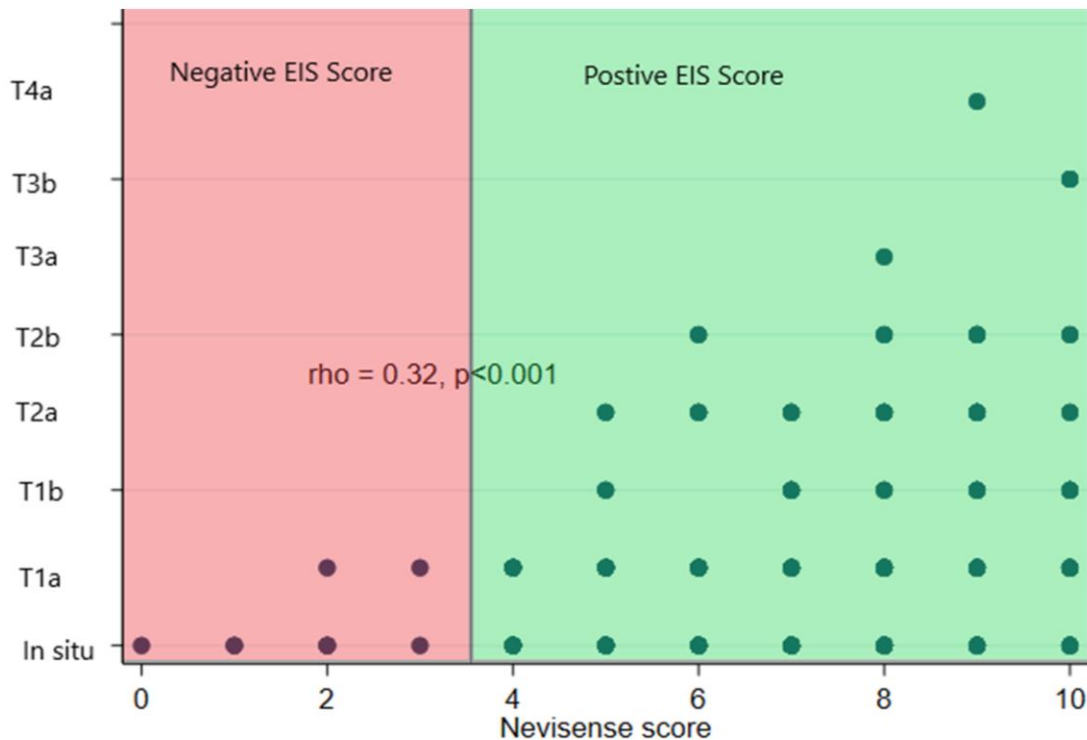
Figure 2. Correlation between pathologic tumor stage and electrical impedance spectroscopy score in a sample of 265 biopsy-proven melanoma lesions. EIS = electrical impedance spectroscopy.

DISCUSSION

This subgroup analysis of biopsy-proven melanoma lesions from the pivotal study examining the clinical performance a novel EIS system demonstrates that the false negative rate of EIS for the detection of melanoma is quite low, making this tool potentially useful as a method of ruling out malignancy in equivocal pigmented skin lesions.[4] Additionally, when combined with other adjunctive methods (as would be done in a real-world setting), EIS has the potential to increase sensitivity for detection of melanoma. However, it is important to remember that when combining two techniques such as EIS and dermoscopy, sensitivity for detection will increase relative to each individual technique at the cost of a

lower combined specificity compared to each individual technique (because the number of false positive lesions will increase). Thus, the benefit of increased sensitivity (lower likelihood of missing a melanoma lesion) must be considered in the context of the detriment of decreased specificity (higher likelihood of performing additional, unnecessary biopsies). This is particularly important given the relatively lower overall specificity of EIS (35.8%) versus the adjunctive methods (94.0% for ABCD dermoscopy and 94.2% for the seven-point checklist) in the pivotal trial.[4] Thus, it is important that EIS be used as an adjunct to aid in ruling out melanoma in equivocal lesions rather than a sole means of diagnosis. It must be considered in the

context of the entire clinical picture. However, given the higher costs to an individual and society of a missed melanoma compared to a negative biopsy, EIS should be considered when the benefits are felt to outweigh the risks by the seasoned clinician (e.g. high-risk patients with equivocal lesions).

Additionally, the moderate correlation between EIS score and stage in this study provides useful information. Lesions with lower EIS scores still in the range of positive are more likely to represent in situ and T1 lesions, although a high score does not necessarily mean an advanced lesion. Further, in this sample, all melanomas that were false negatives by EIS were early stage lesions.

There are several limitations to this study in addition to the considerations surrounding specificity mentioned above. First, although all included lesions were suspicious and underwent clinical evaluation (which may have included use of adjunctive tools such as dermoscopy) to guide the decision to biopsy, the data from the adjunctive methods in this study comes from post-excisional analysis of the dermoscopic images. The clinicians interpreting the dermoscopic images were not privy to a full skin examination of the patient. Thus, the decision-making did not completely simulate a real-life clinical scenario, in which a provider would perform a clinical and dermoscopic exam while considering the context of the remainder of the patient history and clinical exam. Second, all lesions included were deemed clinically suspicious and scheduled for excisional biopsy (an inclusion criteria for the original study). Thus, the lesions examined by dermoscopy may not be reflective of the larger population of lesions for which this technique would be employed in standard practice. However,

EIS technology is meant to be utilized by trained dermatologists to examine clinically equivocal lesions, so the comparison in this study is likely akin to that of a real-world setting. Additionally, the dataset utilized in this post-hoc analysis included only the biopsy-proven melanomas from the original pivotal trial; thus, specificity could not be calculated directly in this sub-analytic study.

CONCLUSION

EIS may produce a lower incidence of false negative results than common diagnostic adjuncts for the detection of melanoma. Further, there appears to be a moderate correlation between EIS score and pathologic stage. Combining EIS with clinical evaluation and other adjunctive tools may improve the sensitivity for the detection of melanoma, but this should be done when deemed clinically appropriate (e.g. high-risk patients) due to the resultant reduction in specificity.

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