ONLINE
EXCLUSIVE

ORIGINAL RESEARCH

A worthwhile tool in evaluating worrisome lesions

This study demonstrated the value of using electrical impedance spectroscopy in primary care to manage and diagnose pigmented skin lesions.

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ABSTRACT

▶ **Background:** We sought to examine whether electrical impedance spectroscopy (EIS), a diagnostic tool approved by the US Food and Drug Administration for the evaluation of pigmented skin lesions (PSLs), is beneficial to primary care providers (PCPs) by comparing the accuracy of PCPs' management decisions for PSLs based on visual examination alone with those based on concurrent visual and EIS evaluation.

▶ **Methods:** Physicians and nurse practitioners (NPs) participated in an anonymous online survey in which they viewed clinical images of PSLs and were asked to make 2 clinical decisions before and after being provided an EIS score that indicated the likelihood that the lesion was a melanoma. They were asked (1) if they would biopsy the lesion/refer the patient out and (2) what they expected the pathology results would show.

▶ **Results:** Forty-four physicians and 17 NPs participated, making clinical decisions for 1354 presented lesions. Overall, with the addition of EIS to visual inspection of clinical images, the sensitivity of biopsy/referral decisions for melanomas and severely dysplastic nevi (SDN) increased from 69.2% to 90.0% (*P* < .001), while specificity increased from 44.0% to 72.6% (*P* < .001). Physicians and NPs, regardless of years of experience, each saw significant improvements in sensitivity, specificity, and diagnostic accuracy with the addition of EIS scores.

▶ **Conclusions:** The incorporation of EIS data into clinical decision-making by PCPs significantly increased the sensitivity and specificity of biopsy/referral decisions for melanomas and SDN and overall diagnostic accuracy compared with visual inspection alone. The results of this study suggest that diagnostic accuracy for PSLs by PCPs may be improved with adjunctive use of EIS with visual inspection.

Primary care providers (PCPs) are often the first line of defense in detecting skin cancers. For patients with concerning skin lesions, PCPs may choose to perform a biopsy or facilitate access to specialty services (eg, Dermatology). Consequently, PCPs play a critical role in the timely detection of skin cancers, and it is paramount to employ continually improving detection methods, such as the application of technologic advances.[1]

Differentiating benign nevi from melanoma and severely dysplastic nevi (SDN), both of which warrant excision, poses a unique challenge to clinicians examining pigmented skin lesions (PSLs). PCPs often rely on visual inspection to differentiate benign skin lesions from malignant skin cancers. In some primary care practices, dermoscopy, which involves using a handheld device to evaluate lesions with polarized light and magnification, is used to improve melanoma detection. However, while visual inspection and dermoscopy are valid, effective techniques for

> **Findings suggest that the use of electrical impedance spectroscopy is particularly advantageous to clinicians who are less proficient in assessing melanocytic lesions.**

the diagnosis of melanocytic lesions, in many instances they still can lead to missed cancers or unnecessary biopsies and specialty referrals. Adjunctive use of dermoscopy with visual inspection has been shown to increase the probability of skin cancer detection, but it fails to achieve a near-100% success rate.[2] Furthermore, dermoscopy is heavily user-dependent, requiring significant training and experience for appropriate use.[3]

❚ **Another option** is an electrical impedance spectroscopy (EIS) device (Nevisense, Scibase, Stockholm, Sweden), which has been approved by the US Food and Drug Administration (FDA) to assist in the detection of melanoma and differentiation from benign PSLs.[4] EIS is a noninvasive, rapidly applied technology designed to accompany the visual examination of melanocytic lesions in office, with or without dermoscopy. Still relatively new, the technology is employed today by many dermatologists, increasing diagnostic accuracy for PSLs.[5] The lightweight and portable instrument features a handheld probe, which is held against a lesion to obtain a reading. EIS uses a low-voltage electrode to apply a harmless electrical current to the skin at various frequencies.[6] As benign and malignant tissues vary in cell shape, size, and composition, EIS distinguishes differential electrical resistance of the tissue to aid in diagnosis.[7]

EIS provides high-sensitivity melanoma diagnosis vs histopathologic confirmation from biopsies, with 1 study showing a 96.6% sensitivity rating, detecting 256 of 265 melanomas.[4] The EIS device, by measuring differences in electrical resistance between benign and cancerous cells, outputs a simple integer score ranging from 0 to 10 associated with the likelihood of the lesion being a melanoma.[8] Based on data from the Nevisense pivotal trial,[4] Nevisense reports that scores of 0 to 3 carry a negative predictive value of 99% for melanoma, whereas scores of 4 to 10 signify increasingly greater positive predictive values from 7% to 61%.

We aimed to assess whether EIS may be beneficial to PCPs by comparing the accuracy of clinical decision-making for PSLs based on visual examination alone with that based on concurrent visual and EIS evaluation.

METHODS

A questionnaire was distributed via email to 142 clinicians at clinics affiliated with either of 2 organizations delivering care to the New York City area through a network of community health centers: the Institute for Family Health (IFH) and the Community Healthcare Network (CHN). Of these recipients, 72 were affiliated with IFH across 27 community health centers and 70 were affiliated with CHN across 14 community health centers. Recipients were physicians and nurse practitioners (NPs) practicing at primary health care facilities.

❚ **Survey instrument.** The first section of the survey instrument (**APPENDIX**) solicited demographic information and explained how to apply the EIS scores for diagnostic decision-making. The second featured images of 12 randomly selected, histologically confirmed, and EIS-evaluated PSLs from a previously published prospective blinded trial of 2416 lesions.[4] The Institutional Review Board of the Icahn School of Medicine at Mount Sinai reviewed and approved the study and survey instrument.

Clinical images of these lesions, comprising 4 melanocytic nevi, 4 dysplastic nevi (including 3 mild-moderately dysplastic and 1 severely dysplastic nevus), and 4 melanomas, were first presented to respondents with 2 tasks: (1) rate on a scale of 1 to 5 their likelihood to biopsy or refer this lesion to a dermatologist (1: not likely; 5: extremely likely); and (2) select what they expect the pathology results to be: melanocytic nevus, dysplastic nevus, or malignant melanoma. Subsequently, respondents repeated the assessments after being presented with the EIS score for the same lesion in conjunction with the clinical image.

❚ **Analysis.** A biopsy or referral rating of 4 or 5 was considered a decision to biopsy or refer (ie, a diagnostic decision consistent with melanoma or SDN warranting excision), whereas a selection of 1 to 3 was considered a decision not to biopsy or refer (ie, a diagnostic decision consistent with a benign PSL). The sensitivity and specificity of biopsy/referral decisions for melanomas and SDN, the proportion of missed melanomas and SDN, and the proportion of biopsy/referral decisions for

TABLE 1

Respondent demographics

Demographic	No. (%)
Occupation	
Physician	44 (72.1)
Nurse practitioner	17 (27.9)
Years in practice	
0-5	22 (36.1)
6-14	27 (44.3)
15+	12 (19.7)

benign lesions were separately determined for visual inspection alone and visual inspection with EIS score. Similarly, diagnostic accuracy was calculated for these clinical scenarios. These metrics were further stratified among different subsets of the respondent population. Differences in sensitivity, specificity, biopsy/ referral decision proportions, and diagnostic accuracy were calculated using McNemar's test for paired proportions.

RESULTS

Sixty-one respondents, comprising 44 physicians and 17 NPs, completed the survey, yielding a response rate of 43% (**TABLE 1**). In total, 1354 clinical decisions (677 based on visual inspection alone and 677 based on visual inspection plus EIS) were made. A biopsy/referral decision was made after assessing 416 of 677 cases (61%) with visual inspection alone and 360 of 677 cases (53%) when relying on visual inspection plus EIS. None of the respondents reported any prior experience with EIS.

When incorporating EIS scores, respondents' mean sensitivity for melanomas and SDN increased from 69.2% to 90.0% ($P < .001$) and specificity from 44.0% to 72.6% ($P < .001$; **TABLE 2**). At baseline, physicians demonstrated a sensitivity and specificity of 74.6% and 46.5%, respectively, while NPs demonstrated a sensitivity and specificity of 56.1% and 37.9%, respectively.

All respondent subgroups stratified by occupation and years of experience saw significant increases in both sensitivity and specificity upon the incorporation of EIS scores, with NPs seeing a greater increase

in sensitivity (56.1% vs 85.4%; $P < .001$) and specificity (37.9% vs 69.0%; $P < .001$) than physicians (sensitivity: 74.6% vs 91.9%; $P < .001$; specificity: 46.5% vs 74.1%; $P < .001$). The only difference in diagnostic performance based on years of experience was a greater pre-EIS sensitivity by clinicians who had been in practice for ≥ 15 years, compared with those in practice for shorter periods (**TABLE 2**).

Diagnostic accuracy increased significantly from 48% when based on visual inspection alone to 73% with the addition of EIS scores ($P < .001$; **TABLE 3**). Physicians and NPs each significantly increased their diagnostic accuracy upon the incorporation of EIS, with NPs exhibiting the greatest increase (from 36.9% to 65.7%; $P < .001$). PCPs with 6 to 14 years of experience saw the greatest increase in diagnostic accuracy when adding EIS (45.9% vs 76.4%; $P < .001$). Overall, the addition of EIS scores resulted in 58 fewer missed melanomas and SDN and 114 fewer benign referrals or biopsies (**TABLE 4**).

DISCUSSION

Primary care evaluation plays a significant role in the diagnosis and management of PSLs, ultimately shaping outcomes for patients with melanoma. Improved accuracy of PSL classification could yield greater sensitivity for the diagnosis of melanomas and high-risk melanocytic lesions at earlier stages, while also reducing the number of unnecessary biopsies and referrals—leading to decreased patient morbidity and mortality and reduced health care spending.[9]

Diagnostic tools are valuable insofar as

> ❯
> **The improvements, seen in clinicians of varying training and experience, suggest that the learning curve of EIS may not be as steep as that of dermoscopy.**

TABLE 2

Sensitivity and specificity of biopsy/referral decisions for melanomas and SDN based on visual inspection alone vs with EIS scores

Demographic	Visual inspection						Visual inspection and EIS						P value	
	TP, no.	FN, no.	Sensitivity, %[a]	TN, no.	FP, no.	Specificity, %[b]	TP, no.	FN, no.	Sensitivity, %[a]	TN, no.	FP, no.	Specificity, %[b]	Sensitivity[c]	Specificity[c]
Occupation														
Physician	147	50	74.6	131	151	46.5	181	16	91.9	209	73	74.1	< .001	< .001
Nurse practitioner	46	36	56.1	44	72	37.9	70	12	85.4	80	36	69.0	< .001	< .001
Years in practice														
0-5	64	33	66.0	63	77	45.0	89	8	91.8	102	38	72.9	< .001	< .001
6-14	82	40	67.2	74	100	42.5	106	16	86.9	123	51	70.7	< .001	< .001
15+	48	12	80.0	38	46	45.2	56	4	93.3	64	20	76.2	.011	< .001
Overall	193	86	69.2	175	223	44.0	251	28	90.0	289	109	72.6	< .001	< .001

EIS, electrical impedance spectroscopy; FN, false-negatives; FP, false-positives; SDN, severely dysplastic nevi; TN, true negatives; TP, true positives.

[a] Sensitivity calculated as TP/(TP + FN).

[b] Specificity calculated as TN/(TN + FP).

[c] Calculated using McNemar's test.

TABLE 3

Correct diagnoses based on visual inspection alone vs with EIS scores

Demographic	No. of lesions with correct diagnoses/no. of total lesions evaluated (%)		P value[a]
	Visual inspection alone	With EIS scores	
Occupation			
Physician	252/479 (52.6)	364/479 (76.0)	< .001
Nurse practitioner	73/198 (36.9)	130/198 (65.7)	< .001
Years in practice			
0-5	109/237 (46.0)	167/237 (70.5)	< .001
6-14	136/296 (45.9)	226/296 (76.4)	< .001
15+	80/144 (55.6)	101/144 (70.1)	.003
Total	325/677 (48.0)	494/677 (73.0)	< .001

EIS, electrical impedance spectroscopy.

[a] Calculated using McNemar's test.

they can improve accuracy and positively impact clinical management and patient outcomes.[10] In this case, increased sensitivity reduced missed melanoma diagnoses, while increased specificity avoided the additional costs and patient toll associated with a biopsy or referral for a benign lesion.

Dermoscopy has been shown to improve the sensitivity and specificity of PSL diagnosis compared with visual inspection alone; however, without substantial training and experience, accuracy with dermoscopy can be no better than examination with the naked eye.[3,11,12] The dropout rates are high for training PCPs in its use, given that several months of training may be needed for competent use.[13,14] To improve the clinical management of PSLs broadly in primary care, a need exists

TABLE 4

Missed diagnoses and benign referrals/biopsies performed based on visual inspection alone and with the addition of EIS scores

Demographic	No. of melanomas and SDN missed/total no. of melanomas and SDN evaluated (%)		Net change in melanomas and SDN missed, no. (%)	P value[a]
	With visual inspection alone	With EIS scores		
Occupation				
Physician	50/197 (25.4)	16/197 (8.1)	–34 (–17.3)	< .001
Nurse practitioner	36/82 (43.9)	12/82 (14.6)	–24 (–29.3)	< .001
Years in practice				
0-5	33/97 (34.0)	8/97 (8.2)	–25 (–25.8)	< .001
6-14	40/122 (32.8)	16/122 (13.1)	–24 (–19.7)	< .001
15+	12/60 (20.0)	4/60 (6.7)	–8 (–13.3)	.011
Total	86/279 (30.8)	28/279 (10.0)	–58 (–20.8)	< .001
Demographic	No. of benign lesions biopsied or referred/total no. of benign lesions evaluated (%)		Net change in benign referrals and biopsies performed, no. (%)	P value[a]
	With visual inspection alone	With EIS scores		
Occupation				
Physician	151/282 (53.5)	73/282 (25.9)	–78 (–27.6)	< .001
Nurse practitioner	72/116 (62.1)	36/116 (31.0)	–36 (–31.1)	< .001
Years in practice				
0-5	77/140 (55.0)	38/140 (27.1)	–39 (–27.9)	< .001
6-14	100/174 (57.5)	51/174 (29.3)	–49 (–28.2)	< .001
15+	46/84 (54.8)	20/84 (23.8)	–26 (–31.0)	< .001
Total	223/398 (56.0)	109/398 (27.4)	–114 (–28.6)	< .001

EIS, electrical impedance spectroscopy; SDN, severely dysplastic nevi.

[a] Calculated using McNemar's test.

for easy-to-use adjunctive tools that increase diagnostic accuracy.[15]

In this study, with only a brief explanation of how to interpret EIS scores, clinicians without any prior experience using EIS demonstrated significantly improved accuracy in deciding appropriate management and classifying melanocytic lesions with the addition of EIS to visual inspection. These improvements, seen in clinicians of varying training and experience, suggest that the learning curve of EIS may not be as steep as that of dermoscopy.

The greater baseline sensitivity, specificity, and diagnostic accuracy of physicians' clinical decision-making compared with NPs before the incorporation of EIS in the study may be a product of comparatively more extensive medical training. In addition, EIS yielded a greater benefit to NPs than to physicians, with greater increases in sensitivity and specificity noted. This suggests that the use of EIS is particularly advantageous to clinicians who are less proficient in assessing melanocytic lesions. Using visual inspection alone, more experienced respondents made biopsy/referral decisions with greater sensitivity but similar specificity to those with less experience. With the incorporation of EIS scores, the sensitivity and specificity of respondents' clinical decision-making rose to comparable levels across all experience groups, providing further indication of EIS's particular value to clinicians who are less proficient in PSL evaluation.

This technology holds the potential to be seamlessly implemented into primary care practice, given that dermatology expertise training is not required to use the EIS de-

vice; this could allow for EIS measurement of lesions to be delegated to office staff (eg, nurses, medical assistants).[16] Future studies are needed to assess EIS use among PCPs in a real-world setting, where factors such as its application on nonmelanocytic lesions (eg, seborrheic keratoses) and its pairing with patient historical data could produce varying results.

❚ **Limitations.** While revealing, this study had its limitations. Respondents did not have access to additional pertinent clinical information, such as patients' histories and risk factors. Clinical decisions in this survey were made based on digital images rather than in vivo examination. This may not represent a real-life evaluation; there is the potential for minimization of the true consequences of a missed melanoma or unnecessary biopsy in the minds of participants, and this does not factor in the operation of the actual EIS device. The Hawthorne effect may also have influenced PCPs' diagnostic selections. Also, the limited sample size constitutes another limitation.

Of note, in this survey format, respondents rated their inclination to biopsy or refer each lesion from 1 to 5. For statistical analyses, lesions rated 1 to 3 were considered as not biopsied/referred and those rated 4 to 5 as biopsied/referred. The sensitivity and specificity values observed, for both visual examination and concurrent visual and EIS evaluation, are therefore based on this classification system of participants' provided ratings. It is conceivable that differing sensitivity and specificity values might have been detected if clinicians were instead given a binary choice for referral/biopsy decisions.

CONCLUSIONS

Among PCPs tasked with evaluating melanocytic lesions, the incorporation of EIS data into clinical decision-making in this study significantly increased the sensitivity, specificity, and overall diagnostic accuracy of biopsy or referral decisions for melanomas and SDN compared with visual inspection alone. Overall, the results of this preliminary study suggest that diagnostic accuracy for PSLs by PCPs may be improved with the adjunctive use of EIS with visual inspection. This would ultimately improve patient care and reduce the morbidity and mortality of a melanoma diagnosis. **JFP**

> **The results of this preliminary study suggest that diagnostic accuracy for pigmented skin lesions by PCPs may be improved with the adjunctive use of electrical impedance spectroscopy with visual inspection.**

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Appendix

Demographic Information

What is your position?
    A.   Physician
    B.   Nurse Practitioner

How many years have you been in practice?

    _____

Have you used electrical impedance spectroscopy?
    A. Yes
    B. No

Brief Instructions

Nevisense (Scibase AB, Stockholm, Sweden) is a handheld device based on electrical impedance spectroscopy (EIS) technology designed to aid as a point-of-care diagnostic tool in the detection of melanoma. When held to a lesion, it transmits harmless electrical currents through the skin and measures tissue resistance to distinguish between normal and abnormal tissue, ultimately producing an EIS score of 0-10 which correlates to the risk of melanoma. Scores in the range of 0-3 have been shown to represent a negative predictive value (NPV; probability that the lesion is not malignant) of 99%, and scores of 4-10 represent progressively increasing positive predictive values (PPV; probability that the lesion is malignant). See below a sample Nevisense EIS reading producing a score of 3.
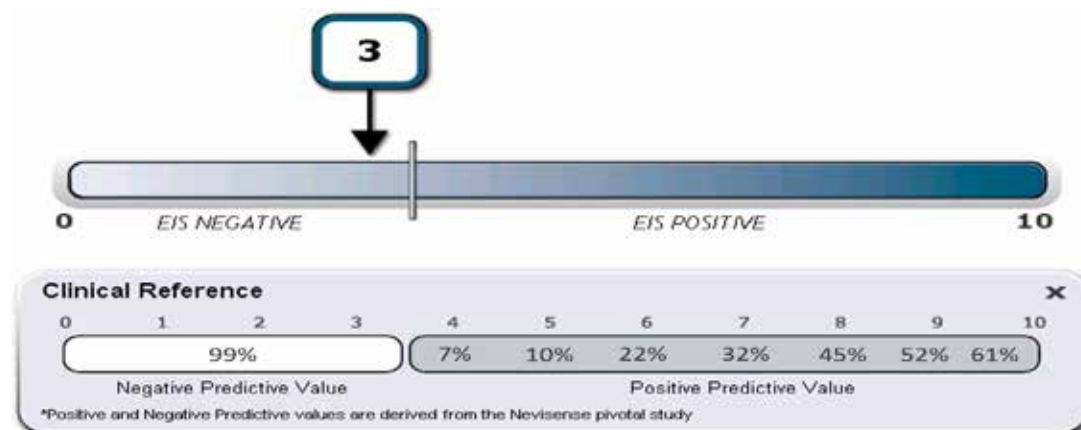
For 12 pigmented skin lesions, you will be presented a clinical photo and/or EIS score. Please click next to view the first lesion and corresponding questions.

Lesion 1
Below is a clinical photo for a 5x5 mm lesion on the upper back.

Clinical image of a
melanocytic nevus

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?

    A. 1   B. 2   C. 3   D. 4   E. 5
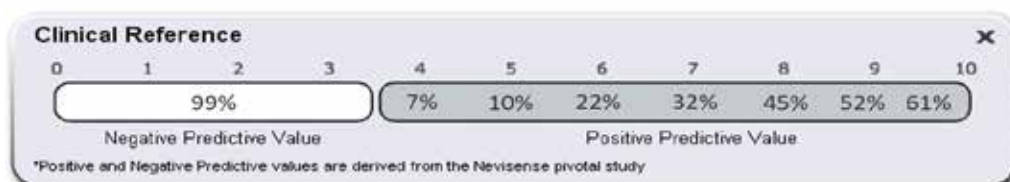
What do you expect the pathology results to be?

    A. Melanocytic nevus
    B. Dysplastic nevus
    C. Malignant melanoma

>Next Page

Below is a clinical photo and EIS result for the SAME 5x5 mm lesion on the upper back.

Clinical image of a
melanocytic nevus

With the additional information now taken into consideration, please provide your selections below.

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?

    A. 1   B. 2   C. 3   D. 4   E. 5

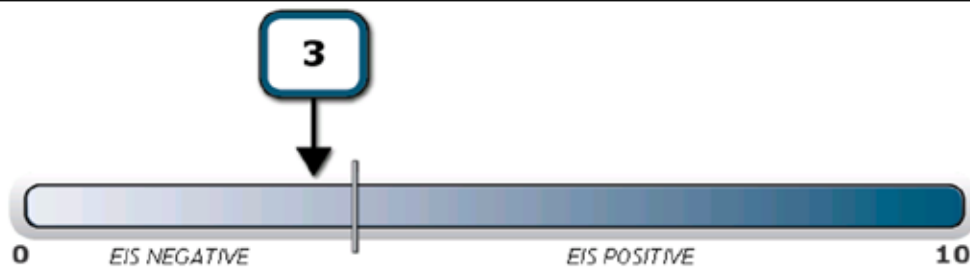What do you expect the pathology results to be?

    A. Melanocytic nevus
    B. Dysplastic nevus
    C. Malignant melanoma

Lesion 2

Below is a clinical photo for a 6x4 mm lesion on the upper leg.

Clinical image of a melanocytic nevus

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?

    A. 1   B. 2   C. 3   D. 4   E. 5

What do you expect the pathology results to be?

    A. Melanocytic nevus
    B. Dysplastic nevus
    C. Malignant melanoma

>Next Page

Below is a clinical photo and EIS result for the SAME 6x4 mm lesion on the upper leg.

Clinical image of a melanocytic nevus

3

0   EIS NEGATIVE   EIS POSITIVE   10

Clinical Reference   ✕

0	1	2	3	4	5	6	7	8	9	10
	99%			7%	10%	22%	32%	45%	52%	61%

Negative Predictive Value   Positive Predictive Value

*Positive and Negative Predictive values are derived from the Nevisense pivotal study

With the additional information now taken into consideration, please provide your selections below.

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?
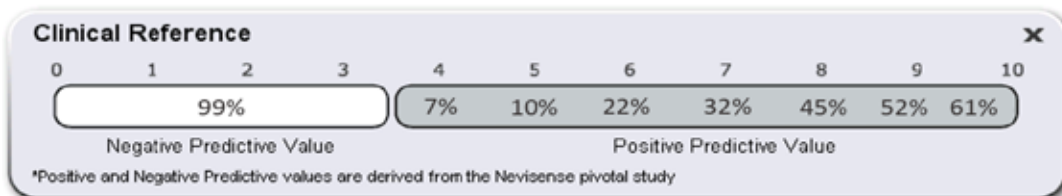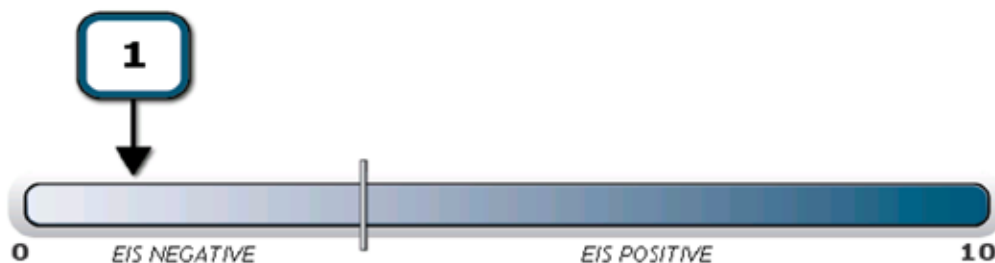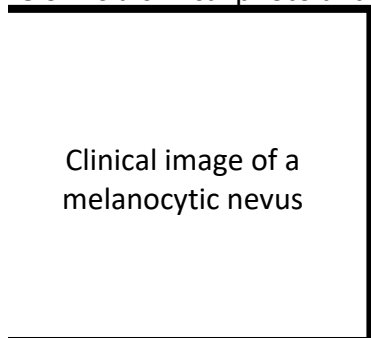
    A. 1   B. 2   C. 3   D. 4   E. 5

What do you expect the pathology results to be?

    A. Melanocytic nevus
    B. Dysplastic nevus
    C. Malignant melanoma

Lesion 3

Below is a clinical photo for a 5x5 mm lesion on the upper back.

Clinical image of a melanocytic nevus

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?
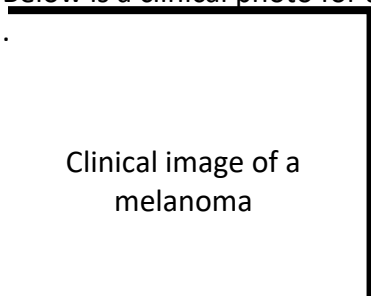
    A. 1   B. 2   C. 3   D. 4   E. 5

What do you expect the pathology results to be?

    A. Melanocytic nevus
    B. Dysplastic nevus
    C. Malignant melanoma

>Next Page
Below is a clinical photo and EIS result for the SAME 5x5 mm lesion on the upper back.

Clinical image of a
melanocytic nevus

1

0   EIS NEGATIVE   EIS POSITIVE   10

Clinical Reference   ✕

0	1	2	3	4	5	6	7	8	9	10
		99%		7%	10%	22%	32%	45%	52%	61%

Negative Predictive Value   Positive Predictive Value

*Positive and Negative Predictive values are derived from the Nevisense pivotal study

With the additional information now taken into consideration, please provide your selections below.

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?
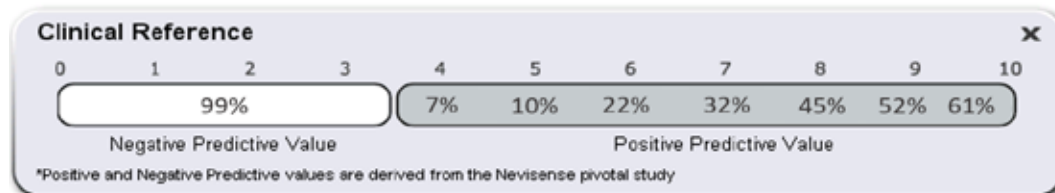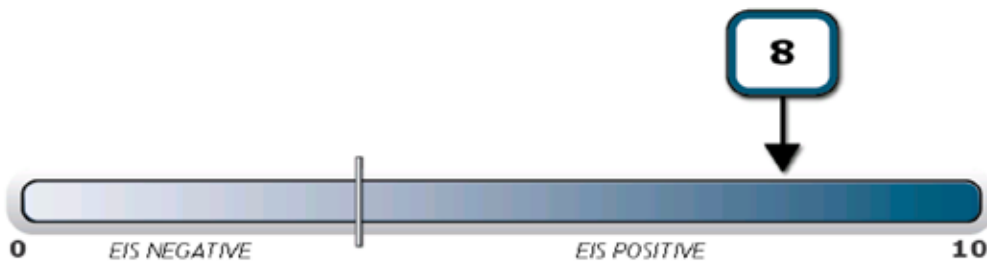   A. 1   B. 2   C. 3   D. 4   E. 5
What do you expect the pathology results to be?
   A. Melanocytic nevus
   B. Dysplastic nevus
   C. Malignant melanoma

Lesion 4
Below is a clinical photo for a 10x9 mm lesion on the upper back.
.

Clinical image of a
melanoma

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?

    A. 1   B. 2   C. 3   D. 4   E. 5

What do you expect the pathology results to be?

    A. Melanocytic nevus
    B. Dysplastic nevus
    C. Malignant melanoma

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Below is a clinical photo and EIS result for the SAME 10x9 mm lesion on the upper back.

With the additional information now taken into consideration, please provide your selections below.

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?
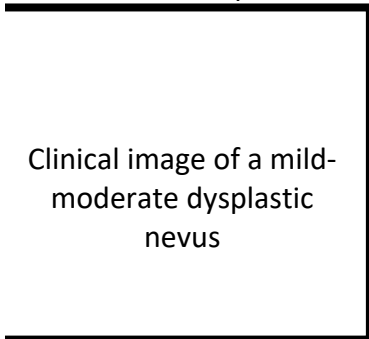
    A. 1   B. 2   C. 3   D. 4   E. 5
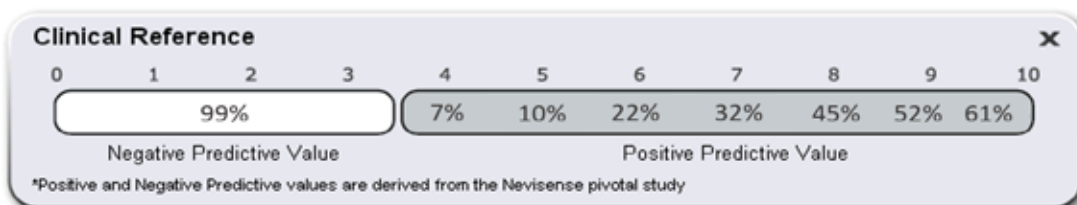
What do you expect the pathology results to be?

    A. Melanocytic nevus
    B. Dysplastic nevus
    C. Malignant melanoma

Lesion 5

Below is a clinical photo for a 6x5 mm lesion on the forearm.

Clinical image of a mild-moderate dysplastic nevus

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?

    A. 1   B. 2   C. 3   D. 4   E. 5
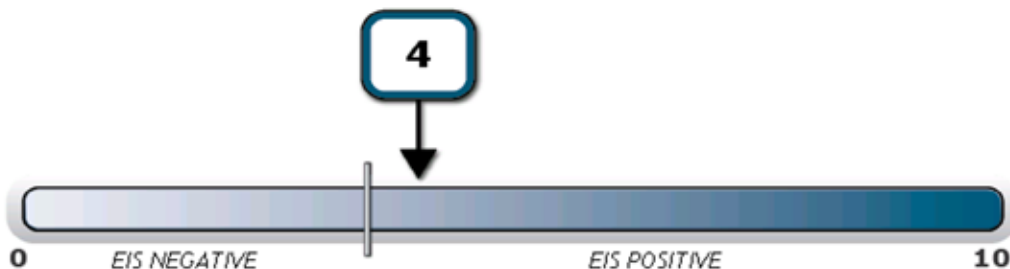
What do you expect the pathology results to be?

    A. Melanocytic nevus

    B. Dysplastic nevus

    C. Malignant melanoma

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Below is a clinical photo and EIS result for the SAME 6x5 mm lesion on the forearm.

Clinical image of a mild-moderate dysplastic nevus

4

0   EIS NEGATIVE   EIS POSITIVE   10

Clinical Reference   ✕

0	1	2	3	4	5	6	7	8	9	10
	99%			7%	10%	22%	32%	45%	52%	61%

Negative Predictive Value   Positive Predictive Value

*Positive and Negative Predictive values are derived from the Nevisense pivotal study

With the additional information now taken into consideration, please provide your selections below.

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?
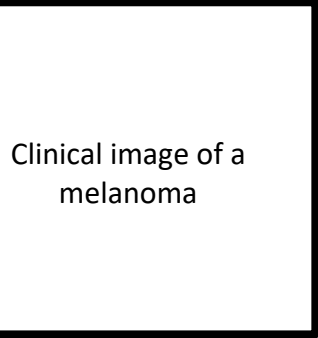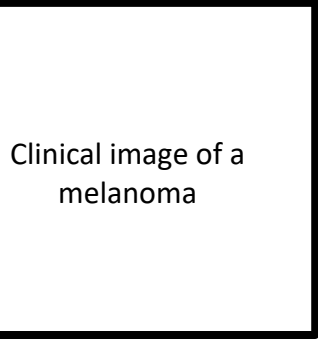
    A. 1   B. 2   C. 3   D. 4   E. 5

What do you expect the pathology results to be?

    A. Melanocytic nevus

    B. Dysplastic nevus

    C. Malignant melanoma

Lesion 6

Below is a clinical photo for a 5x6mm lesion on the upper leg.

Clinical image of a melanoma

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?

    A. 1   B. 2   C. 3   D. 4   E. 5
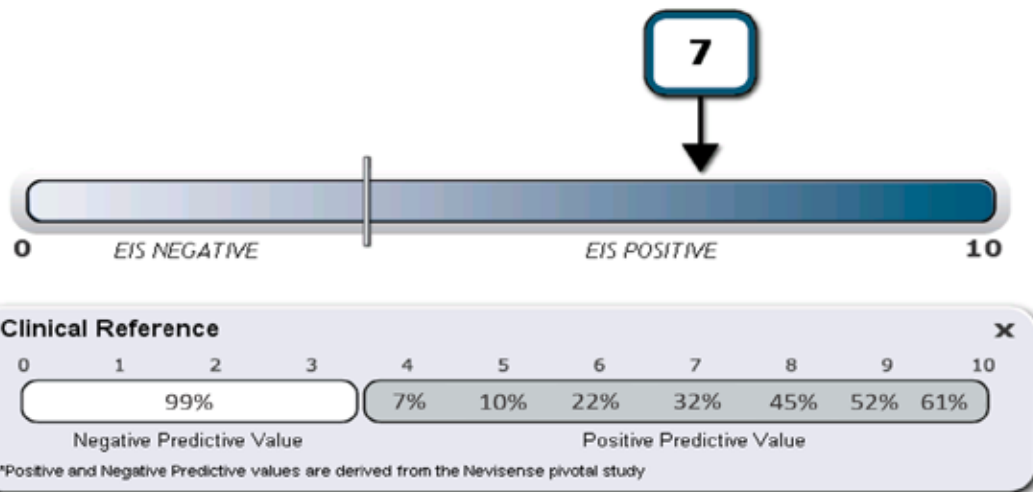
What do you expect the pathology results to be?

    A. Melanocytic nevus

    B. Dysplastic nevus

    C. Malignant melanoma

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Below is a clinical photo and EIS result for the SAME 5x6mm lesion on the upper leg.

Clinical image of a melanoma

7

0   EIS NEGATIVE   EIS POSITIVE   10

Clinical Reference

0	1	2	3	4	5	6	7	8	9	10
	99%			7%	10%	22%	32%	45%	52%	61%

Negative Predictive Value   Positive Predictive Value

*Positive and Negative Predictive values are derived from the Nevisense pivotal study

With the additional information now taken into consideration, please provide your selections below.

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?
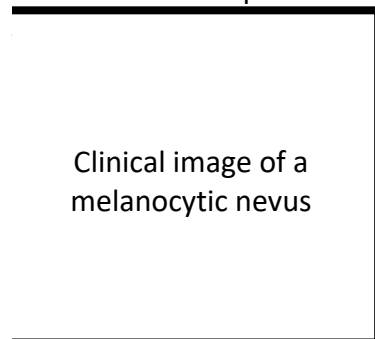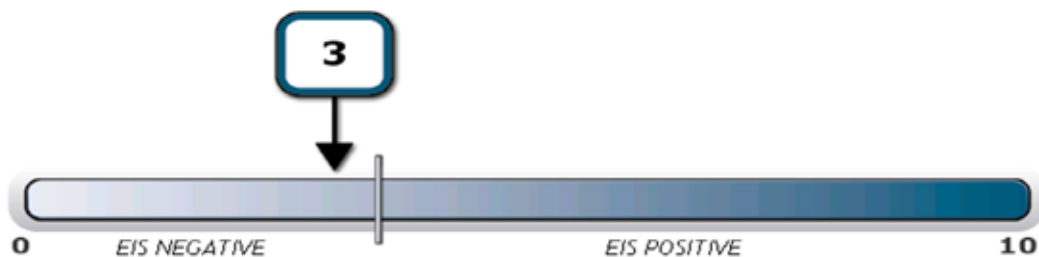
   A. 1   B. 2   C. 3   D. 4   E. 5

What do you expect the pathology results to be?

   A. Melanocytic nevus
   B. Dysplastic nevus
   C. Malignant melanoma

Lesion 7

Below is a clinical photo for a 5x5 mm lesion on the lower back.

Clinical image of a melanocytic nevus

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?

   A. 1   B. 2   C. 3   D. 4   E. 5

What do you expect the pathology results to be?

   A. Melanocytic nevus
   B. Dysplastic nevus
   C. Malignant melanoma

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Below is a clinical photo and EIS result for the SAME 5x5 mm lesion on the lower back.

Clinical image of a melanocytic nevus

3

| 0 | EIS NEGATIVE | EIS POSITIVE | 10 |

Clinical Reference ✕

0	1	2	3	4	5	6	7	8	9	10
		99%		7%	10%	22%	32%	45%	52%	61%

Negative Predictive Value   Positive Predictive Value

*Positive and Negative Predictive values are derived from the Nevisense pivotal study

With the additional information now taken into consideration, please provide your selections below.

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?
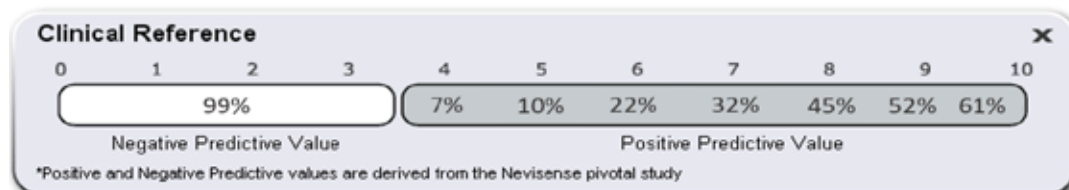   A. 1   B. 2   C. 3   D. 4   E. 5

What do you expect the pathology results to be?
   A. Melanocytic nevus
   B. Dysplastic nevus
   C. Malignant melanoma

Lesion 8
Below is a clinical photo for a 7x8 mm lesion on the abdomen.

Clinical image of a melanoma

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?
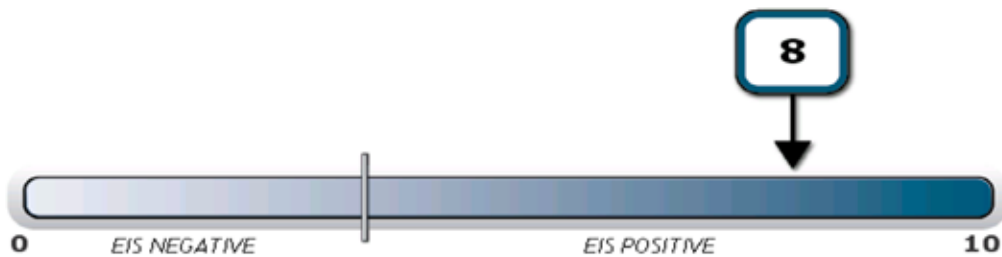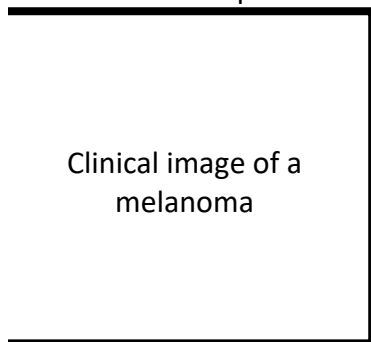
    A. 1   B. 2   C. 3   D. 4   E. 5

What do you expect the pathology results to be?

    A. Melanocytic nevus
    B. Dysplastic nevus
    C. Malignant melanoma

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Below is a clinical photo and EIS result for the SAME 7x8 mm lesion on the abdomen.

Clinical image of a melanoma

With the additional information now taken into consideration, please provide your selections below.

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?

    A. 1   B. 2   C. 3   D. 4   E. 5

What do you expect the pathology results to be?

    A. Melanocytic nevus
    B. Dysplastic nevus
    C. Malignant melanoma

Lesion 9

Below is a clinical photo for a 7x8 mm lesion on the abdomen.

Clinical image of a mild-
moderate dysplastic
nevus

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?

A. 1 B. 2 C. 3 D. 4 E. 5
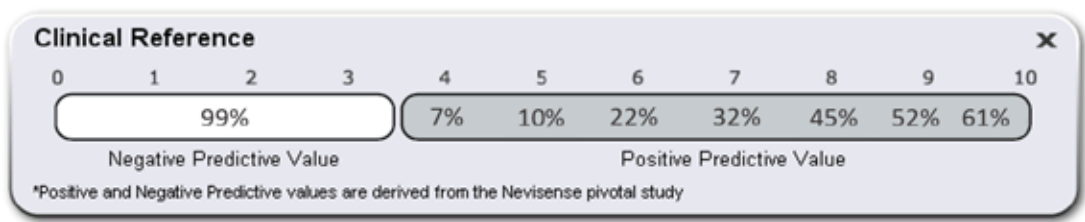
What do you expect the pathology results to be?

A. Melanocytic nevus
B. Dysplastic nevus
C. Malignant melanoma

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Below is a clinical photo and EIS result for the SAME 4x4 mm lesion on the abdomen.

Clinical image of a mild-
moderate dysplastic
nevus

3

0 EIS NEGATIVE EIS POSITIVE 10

Clinical Reference ✖

0	1	2	3	4	5	6	7	8	9	10
	99%			7%	10%	22%	32%	45%	52%	61%

Negative Predictive Value   Positive Predictive Value

*Positive and Negative Predictive values are derived from the Nevisense pivotal study

With the additional information now taken into consideration, please provide your selections below.

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?

    A. 1   B. 2   C. 3   D. 4   E. 5

What do you expect the pathology results to be?

    A. Melanocytic nevus
    B. Dysplastic nevus
    C. Malignant melanoma

Lesion 10

Below is a clinical photo for a 9x5 mm lesion on the lower leg.

Clinical image of a melanoma

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?

    A. 1   B. 2   C. 3   D. 4   E. 5
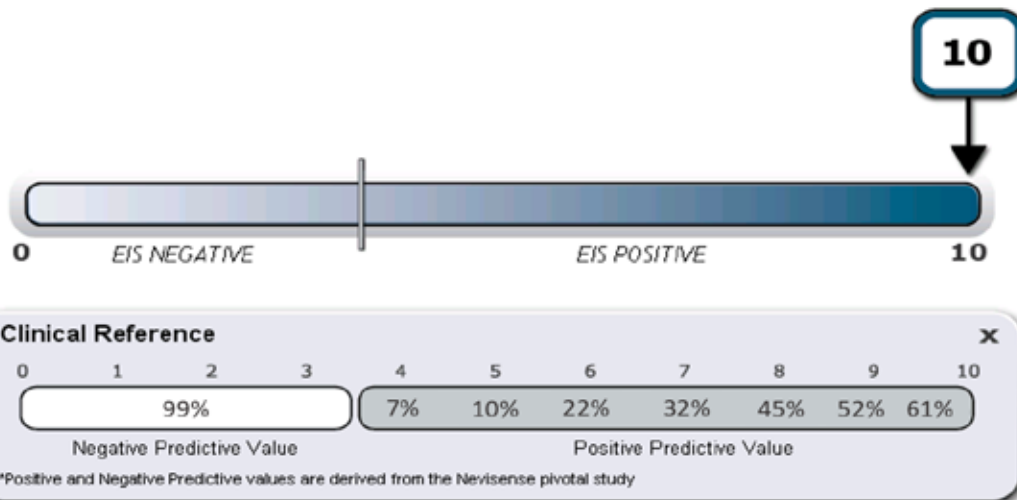
What do you expect the pathology results to be?

    A. Melanocytic nevus
    B. Dysplastic nevus
    C. Malignant melanoma

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Below is a clinical photo and EIS result for the SAME 9x5 mm lesion on the lower leg.

Clinical image of a melanoma

Clinical Reference ✕

0	1	2	3	4	5	6	7	8	9	10
	99%			7%	10%	22%	32%	45%	52%	61%

Negative Predictive Value   Positive Predictive Value

*Positive and Negative Predictive values are derived from the Nevisense pivotal study

With the additional information now taken into consideration, please provide your selections below.

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?
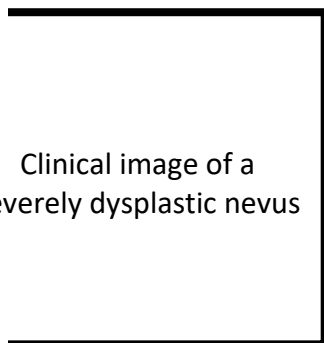　　A. 1　　　　　B. 2　　　　　C. 3　　　　　D. 4　　　　　E. 5
What do you expect the pathology results to be?
　　A. Melanocytic nevus
　　B. Dysplastic nevus
　　C. Malignant melanoma

Lesion 11
Below is a clinical photo for a 7x4 mm lesion on the upper back.

Clinical image of a severely dysplastic nevus

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?
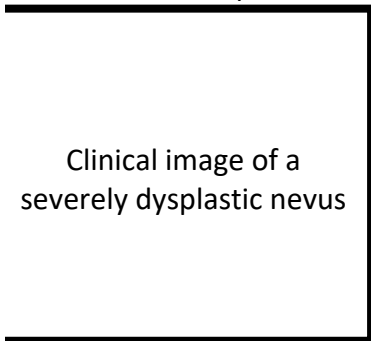　　A. 1　　　　　B. 2　　　　　C. 3　　　　　D. 4　　　　　E. 5
What do you expect the pathology results to be?
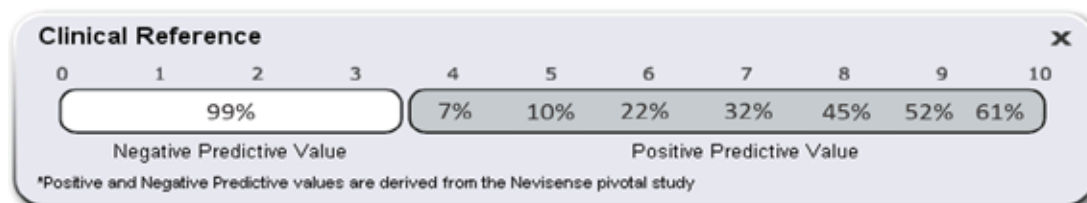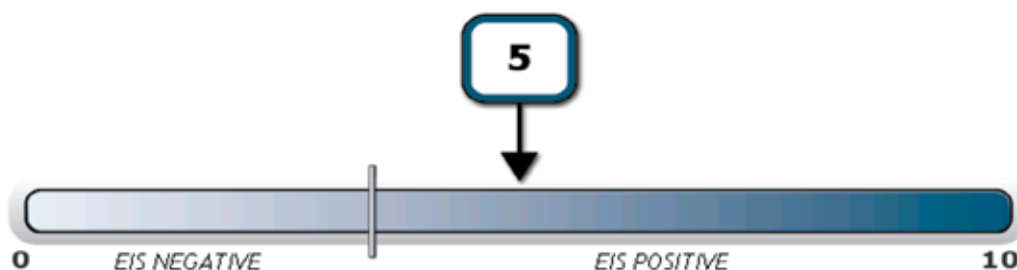　　A. Melanocytic nevus
　　B. Dysplastic nevus
　　C. Malignant melanoma

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Below is a clinical photo and EIS result for the SAME 7x4 mm lesion on the upper back.

Clinical image of a severely dysplastic nevus

5

0 EIS NEGATIVE   EIS POSITIVE   10

Clinical Reference   ✕

0	1	2	3	4	5	6	7	8	9	10
	99%			7%	10%	22%	32%	45%	52%	61%

Negative Predictive Value   Positive Predictive Value

*Positive and Negative Predictive values are derived from the Nevisense pivotal study

With the additional information now taken into consideration, please provide your selections below.

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?
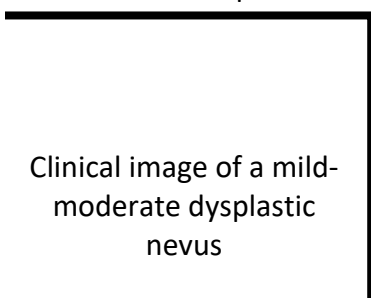   A. 1   B. 2   C. 3   D. 4   E. 5

What do you expect the pathology results to be?
    A. Melanocytic nevus
    B. Dysplastic nevus
    C. Malignant melanoma

Lesion 12
Below is a clinical photo for a 9x5 mm lesion on the upper back.

Clinical image of a mild-moderate dysplastic nevus

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?

    A. 1   B. 2   C. 3   D. 4   E. 5
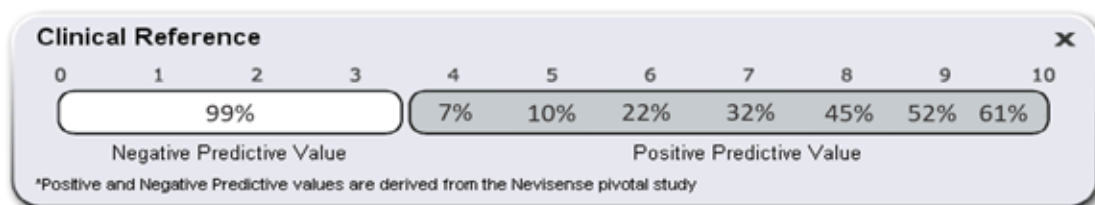
What do you expect the pathology results to be?

    A. Melanocytic nevus
    B. Dysplastic nevus
    C. Malignant melanoma

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Below is a clinical photo and EIS result for the SAME 9x5 mm lesion on the upper back.

Clinical image of a mild-moderate dysplastic nevus

With the additional information now taken into consideration, please provide your selections below.

On a scale of 1-5, with 1 being not likely and 5 being extremely likely, how likely are you to biopsy this lesion / refer to a dermatologist?

    A. 1   B. 2   C. 3   D. 4   E. 5

What do you expect the pathology results to be?

    A. Melanocytic nevus
    B. Dysplastic nevus
    C. Malignant melanoma