Computer-aided classification of melanocytic lesions using dermoscopic images

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Background: Computer-assisted diagnosis of dermoscopic images of skin lesions has the potential to improve melanoma early detection.

Objective: We sought to evaluate the performance of a novel classifier that uses decision forest classification of dermoscopic images to generate a lesion severity score.

Methods: Severity scores were calculated for 173 dermoscopic images of skin lesions with known histologic diagnosis (39 melanomas, 14 nonmelanoma skin cancers, and 120 benign lesions). A threshold score was used to measure classifier sensitivity and specificity. A reader study was conducted to compare the sensitivity and specificity of the classifier with those of 30 dermatology clinicians.

Results: The classifier sensitivity for melanoma was 97.4%; specificity was 44.2% in a test set of images. In the reader study, the classifier's sensitivity to melanoma was higher ($P < .001$) and specificity was lower ($P < .001$) than that of clinicians.

Limitations: This is a retrospective study using existing images primarily chosen for biopsy by a dermatologist. The size of the test set is small.

Conclusions: Our classifier may aid clinicians in deciding if a skin lesion should be biopsied and can easily be incorporated into a portable tool (that uses no proprietary equipment) that could aid clinicians in noninvasively evaluating cutaneous lesions. (J Am Acad Dermatol 2015;73:769-76.)

Key words: basal cell carcinoma; computer-assisted diagnosis; dermoscopy; information technology; machine learning; melanoma; skin cancer.

In the United States, nearly 10,000 people die of melanoma annually.[1] Early detection of melanoma is vital for reducing melanoma mortality and treatment costs. Dermoscopy can improve accuracy in melanoma detection, although this tool

Abbreviations used:

BCC: basal cell carcinoma
CI: confidence interval
LCB: lower confidence bound

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is used almost exclusively by dermatologists.[2] The rich images obtained through dermoscopy provide an opportunity to apply principles of machine learning and computer vision to the challenge of interpreting dermoscopic images, potentially making dermoscopy a more useful tool for nondermatologists.

We trained a software classifier on dermoscopic images of benign and malignant skin lesions that uses decision forest classification[3] to generate a severity score for each lesion. We tested the performance of the classifier on a collection of dermoscopic images of biopsy-proven benign and malignant skin lesions. We also asked a cross-section of dermatology providers to participate in a reader study in which they were asked to evaluate a set of dermoscopic images and indicate whether they would biopsy each lesion. The sensitivity and specificity of the classifier on the same set of images were compared with that of the clinicians in the reader study.

CAPSULE SUMMARY

- Choosing which skin lesions are suspicious for melanoma can be challenging for dermatologists and primary care providers.
- We describe a novel classifier that accurately identified 38 of 39 melanomas with a specificity of 44.2%.
- Computer-assisted diagnosis using conventional dermoscopic images may help to improve clinicians' sensitivity to melanoma with an acceptable specificity.

METHODS

Ethics approval

This protocol was reviewed and approved by the University of Pittsburgh Institutional Review Board.

Images

Dermoscopic images of skin lesions were collected before biopsy using contact dermoscopy with either isopropyl alcohol or a clear alcohol-based hand sanitizer as an immersion medium using a variety of dermoscopic devices and cameras. All lesions were biopsied based on clinical suspicion of malignancy and images were at least 640 × 640 pixels. Some dermoscopic images were collected prospectively and some were obtained from our collection of existing images. Inclusion criteria included patient 18 years of age or older, biopsy indicated clinically based on suspicion for malignancy, and histologic diagnosis was available in the medical record. All histologic diagnoses were rendered by at least 1 board-certified dermatopathologist and were used as the reference standard for diagnosis. Some dermoscopic images used to train the classifier were obtained from publicly available or purchased image libraries; such images were not included in the reader study or used to test the performance of the classifier.

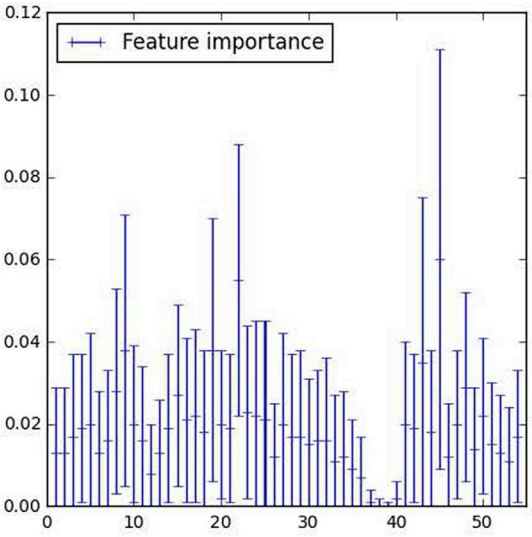
Images collected by the investigators were randomly divided into 2 sets by diagnosis, with half used as candidates for training and half used for testing, with the exception that all high-grade dysplastic nevi were exclusively assigned to the training set to increase the representation of dermoscopic features that could be present in melanoma. All images used in training were curated by 1 dermatologist experienced in dermoscopy (L. K. F.) both for image quality and for clinical representation of the spectrum of melanocytic lesions.

Image processing

The images were captured by different dermoscope/camera combinations that varied in resolution and lighting characteristics, but all were at least 640 × 640 pixels. Each image was segmented manually to delineate lesion from surrounding skin using a World Wide Web–based mark-up tool of our own creation that allows the user to shade the lesion in the image; nonshaded areas (ie, surrounding skin) were excluded from further analysis. Images were rescaled to 640 pixels on the longest axis and 54 features were computed for all segmented lesions. Extracted features included values related to lesion geometry, border gradient, color, and texture. Variations of some features described in Zortea et al[4] were included.

Classifier training

The 54 computed features for lesions in the training set were used to train a decision forest classifier consisting of 1000 decision trees. Lesions used for training were divided into 2 categories: benign and malignant. The malignant training set was composed of 105 melanomas (77 invasive melanomas, 28 melanoma in situ), 29 high-grade dysplastic nevi (included in training because these lesions contain dermoscopic features of melanoma although they are not actual malignancies), 23 basal cell carcinomas (BCC), and 3 squamous cell carcinomas. The benign training set was composed of 93 benign melanocytic lesions (42 benign nevi, 6 blue nevi, 9 lentigines, 33 low-grade dysplastic nevi, and 3 acral nevi) and 20 other benign lesions (4 dermatofibromas, 13 seborrheic keratoses, and 3 angiomas). Features extracted and their relative importance in the decision forest are reported (Fig 1). A decision forest approach was used for creation of the



1 Lesion Area	19 Border Scores std dev	37 Scharr 4
2 Lesion Area Filled	20 Shape Asymmetry Major Ratio	38 Scharr 5
3 Lesion Perimeter	21 Shape Asymmetry Minor Ratio	39 Scharr 6
4 Lesion Solidity	22 Color Asymmetry Major EMD	40 Scharr 7
5 Lesion Major Axis Length	23 Color Asymmetry Minor EMD	41 Color shape asymmetry mean
6 Lesion Minor Axis Length	24 Local Binary Pattern 0	42 Color shape asymmetry std dev
7 Lesion Eccentricity	25 Local Binary Pattern 1	43 Colors Histogram Average
8 Lesion Form Factor	26 Local Binary Pattern 2	44 Colors Histogram Variance
9 Lesion Intensity Minimum	27 Local Binary Pattern 3	45 Colors Histogram Nonzero
10 Lesion Intensity Mean	28 Local Binary Pattern 4	46 Colors PvsC mean difference L
11 Lesion Intensity Maximum	29 Local Binary Pattern 5	47 Colors PvsC mean difference a
12 Color Histogram black	30 Local Binary Pattern 6	48 Colors PvsC mean difference b
13 Color Histogram blue gray	31 Local Binary Pattern 7	49 Colors PvsC density Bayesian L
14 Color Histogram dark brown	32 Local Binary Pattern 8	50 Colors PvsC density Bayesian a
15 Color Histogram light brown tan	33 Scharr 0	51 Colors PvsC density Bayesian b
16 Color Histogram red	34 Scharr 1	52 Geometric p25
17 Color Histogram white pink	35 Scharr 2	53 Geometric p50
18 Border Scores Average	36 Scharr 3	54 Geometric p75

Fig 1. Relative weight of feature in the random forest classifier in the same order as described in the "Methods" section and detailed in the following chart. The tallest 5 peaks are: number of distinct color histogram values (45), Earth Mover's Distance (*EMD*) color symmetry along major axis (22), minimal lesion intensity value (9), SD of border gradient scores (19), and average color histogram value (43). *PvsC*, Periphery of lesion vs center of lesion.

classifier. Through incremental exploratory analysis on labeled images of lesions, 54 features were deemed relevant. These include features such as border irregularity, eccentricity, length of major and minor axes, and color histogram properties. Discovering how these features should be weighted and combined is the problem addressed by the decision forest approach. One thousand binary trees were generated using a randomized procedure in which each interior node of a tree corresponded to a predicate on a feature. The 2 links out of each node corresponded to that predicate being true or false, respectively. A subset of the images in the training set was chosen randomly, and the feature that best divided the subset into malignant and benign groupings was identified. This feature was assigned to the root of a new decision tree. This process was then repeated, generating a new interior node of the tree each time, until we had only images in a single category. The result was 1 decision tree. This process was repeated to construct a forest of 1000 decision trees, with each tree based on a different random subset of the training data. When the classifier was applied to a new image, its features were passed from root to leaf of every tree, thus generating 1000 individual malignant or benign results. The fraction of trees in which the path ends in "malignant" was then used to generate the severity score. A threshold

value for this score could be set to measure sensitivity and specificity. The threshold was set to 0.4 in our classifier; a lesion was classified as malignant if its image traced a path to a malignant node in at least 40% of the trees.

Classifier testing

The performance of the classifier was evaluated using a set of images with known histologic diagnoses that were distinct from those images used in training. Lesions used in classifier testing consisted of 39 melanomas (25 invasive and 14 in situ; Breslow depth for invasive melanomas ranged from 0.2-2.98 mm with mean depth of 0.76 mm, median depth of 0.5 mm), 11 BCC, 3 squamous cell carcinomas, and 120 benign lesions (42 benign nevi, 47 low-grade dysplastic nevi, 10 lentigines, 5 blue nevi, 2 Spitz nevi, 11 seborrheic keratoses, 2 angiomas, and 1 dermatofibroma). Because these lesions had all been selected for biopsy on clinical grounds and thus would be expected to represent the more dermoscopically atypical end of the spectrum of lesions encountered in clinical practice, a separate unbiopsied benign test set was also evaluated. This set consisted of 27 images of lesions that were chosen as not appropriate for biopsy by 2 dermatologists, and thus did not have available histology. The classifier specificity on the unbiopsied benign set was calculated and reported solely to provide additional information, but not used to calculate overall specificity.

Each lesion in the test set was given a severity score of 0 to 1, corresponding to the fraction of decision trees that classify a lesion as malignant. The sensitivity and specificity of the classifier was calculated using a threshold severity score of 0.4 (ie, at least 40% of decision trees classifying a lesion as malignant).

Reader study

A reader study was performed that included a subset of a total of 65 lesions: 25 melanomas (15 invasive and 10 in situ) and 40 benign lesions (16 low-grade dysplastic nevi, 14 benign nevi, 2 blue nevi, 4 lentigines, and 4 seborrheic keratoses). The Breslow depths for invasive melanomas in the reader study set ranged from 0.2 to 2.98 mm (mean depth 0.93 mm, median depth 0.74 mm). All images used for the reader study were first evaluated for image quality by 1 investigator who was blinded to their diagnosis. Although the 1 melanoma that was misclassified as benign by the classifier was intentionally included in the reader study, the remaining images were randomly selected among those determined to be of suitable image quality for display on a computer screen.

Thirty of 35 invited participants, all of whom self-reported some training and experience with the use of dermoscopy, completed the reader study. Participants were assigned to 1 of 3 subgroups based on their self-reported level of training in dermatology: board-certified dermatologist, dermatology resident, or dermatology physician assistant. Participants were asked how often they use dermoscopy when examining pigmented skin lesions and also to evaluate the 65 dermoscopic images detailed above and to indicate if they would biopsy the lesion.

Statistical analysis

Receiver operating characteristic curves were generated and areas under the curve calculated to evaluate the performance of the classifier on both the reader study and extended test sets. The sensitivity and specificity of the classifier, with 95% confidence intervals (CI) and 95% lower confidence bounds (LCB), were computed. The average sensitivity and specificity of the readers were calculated based on biopsy decisions on the reader study test set and compared with the sensitivity and specificity of the classifier on the same set of images using a 2-sided, 1-sample *t* test. The Fleiss kappa statistic was calculated to quantify degree of agreement between readers.

RESULTS

Performance of classifier

To determine the optimal threshold severity score to use to maximize classifier sensitivity and specificity, a receiver operating characteristic curve was generated showing the performance of the classifier on the 39 melanomas and 120 benign lesions in our test set (area under the curve 0.818) (Fig 2). Based on these findings a threshold severity score of 0.4 was established and used to calculate classifier sensitivity and specificity (Table I). Among lesions with known histologic diagnosis and for which greater than 5 examples were present in our data sets, the median severity score of lesions was highest for invasive melanomas (0.772) and lowest for benign nevi (0.337). Median severity scores by diagnosis are shown (Fig 3).

Of the 39 melanomas evaluated, 38 were correctly classified as malignant, yielding a sensitivity to melanoma of 97.4% (95% CI 86.5%-99.9%, and 95% LCB 88.4%). Eight of the 11 BCC and all of the 3 squamous cell carcinomas were correctly classified as malignant, yielding a sensitivity to nonmelanoma skin cancer of 78.6%. Among the 120 benign lesions

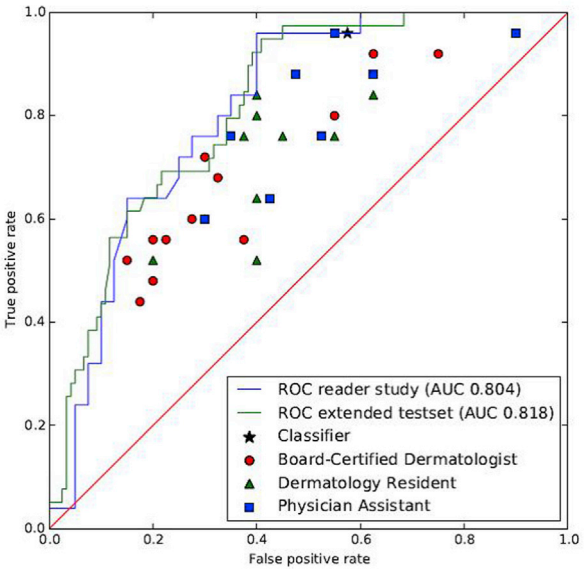


Fig 2. Receiver operating characteristic (*ROC*) curves demonstrating sensitivity and specificity for melanoma of classifier and readers on lesions. The test set includes all 39 melanomas and 120 benign lesions in the test set. Reader study test set includes only those lesions used in the reader study. *AUC*, Area under the curve.

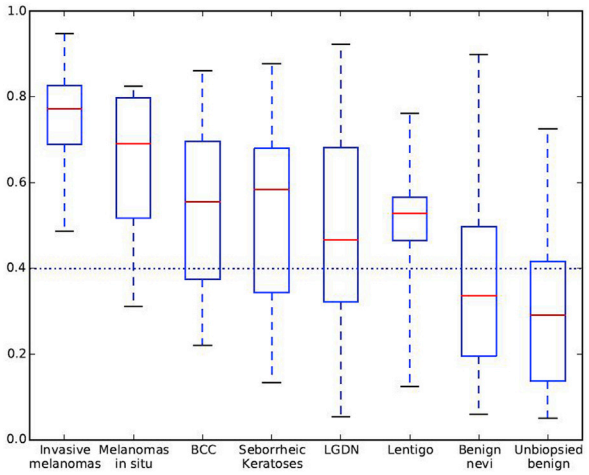


Fig 3. Median severity score by diagnosis for full and unbiopsied benign test set images. Score by diagnosis is shown. The *boxed area* is 25th to 75th percentile, the *center line* is median value, and *whiskers* indicate minimum and maximum values. Diagnoses with 5 or fewer images are not shown. *BCC*, Basal cell carcinoma; *LGDN*, low-grade dysplastic nevi.

Table I. Classifier performance on the test set

Lesion	Total	TP	Sensitivity
Melanoma	39	38	97.4%
Invasive	25	25	100%
In situ	14	13	92.9%
Nonmelanoma skin cancer	14	11	78.6%
BCC	11	8	72.7%
SCC	3	3	100%

Lesion	Total	TN	Specificity
All biopsied benign	120	53	44.2%
Benign nevi	42	22	52.4%
LGDN	47	20	42.6%
Lentigo	10	2	20.0%
SK	11	4	36.4%
Other*	10	5	50.0%
Unbiopsied benign	27	20	74.1%

BCC, Basal cell carcinoma; *LGDN*, low-grade dysplastic nevi; *SCC*, squamous cell carcinoma; *SK*, seborrheic keratoses; *TP*, true positive; *TN*, true negative.
*Includes blue nevi (5), typical Spitz nevus (2), angioma (2), dermatofibroma (1).

evaluated, 53 were correctly classified as benign, yielding a specificity of 44.2% (95% CI 35.1%-53.5%, and 95% LCB 36.5%). In addition, among the 27 unbiopsied but presumed benign lesions evaluated, 20 were classified as benign, yielding a specificity of 74.1% (95% CI 53.7%-88.9% and 95% LCB 58.8%) (Table I).

Performance of dermatology practitioners versus classifier

A total of 30 dermatology practitioners (12 board-certified dermatologists, 10 dermatology residents, and 8 physician assistants currently practicing dermatology) completed the reader study (response rate of 85.7%). Readers were asked how frequently they use dermoscopy when evaluating pigmented lesions in their clinical practice. All reported using dermoscopy at least some of the time. Among board-certified dermatologists, 67% reported using dermoscopy "always/almost always" or "very frequently." This degree of dermoscopy use was reported by 90% of the dermatology residents and 75% of the physician assistants who participated in the reader study. Performance of each individual reader is shown (Fig 2). Overall, clinician sensitivity to melanoma was 70.8%, and specificity was 58.7%. On the same set of images, the sensitivity of the classifier to melanoma was 96.0%, and the specificity of the classifier was 42.5% (Table II). There was a fair level of agreement[5] among readers in aggregate, with a kappa score of 0.346. In total, 2 melanomas (8.0%) were chosen to be biopsied by all readers. The melanoma in situ that was incorrectly classified as benign by the classifier was chosen for biopsy by 23.3% of the readers. Examples of lesions from the reader study test set and 1 lesion from the unbiopsied benign test set are shown (Fig 4).

Table II. Performance of classifier and dermatology practitioners who participated in the reader study on the reader study test set

	Sensitivity	*P* value*	Specificity	*P* value*
Classifier	96.0%		42.5%	
All readers (n = 30)	70.8%	<.001	58.7%	<.001
Board-certified dermatologists (n = 12)	64.7%	<.001	65.4%	.002
Dermatology residents (n = 10)	70.4%	<.001	59.0%	.002
Physician assistants (n = 8)	80.5%	.015	48.1%	.423

**P* values for comparison of classifier vs reader sensitivity or specificity.

DISCUSSION

We designed a classifier that uses decision tree analysis to score dermoscopic images. Using a fixed cutoff, the sensitivity of our classifier for melanoma was greater than that of the 30 clinicians who participated in our reader study, however overall clinicians' specificity was higher.

Other investigators have used computer vision to aid in diagnosing melanoma from dermoscopic images. Zortea et al[4] used features similar to some of those used in our classifier and reported that their classifier had a sensitivity of 86% and specificity of 52% in a small study. One imaging device, MelaFind (MELA Sciences, Irvington, NY), is Food and Drug Administration approved for the early detection of melanoma; it performs multispectral imaging and provides a lesion score and recommendation of whether or not a biopsy is indicated. The labeling for this device restricts its use to dermatologists.[6] Although the sensitivity of MelaFind is very high (98.3%), concerns have been raised about the low specificity (9.9%) of the device.[7] Another device that aids in noninvasively classifying a lesion as benign or malignant is Nevisense (Scibase, Stockholm, Sweden), which uses electrical impedance spectroscopy, with a sensitivity of 96.6%, and a specificity of 34.4%.[8] Both devices show superior sensitivity to melanoma than physicians in accompanying reader studies.

The trade-off of a higher sensitivity at the cost of specificity is, to some degree, inevitable and seen not just in devices and tests, but in clinicians as well. In our study, those practitioners who had the highest sensitivity to melanoma generally also had the lowest specificity. Although a high specificity is ideal, unnecessary biopsy of a benign lesion causes less harm than failing to biopsy a melanoma, and thus specificity that significantly sacrifices sensitivity is unacceptable. Because our classifier generates a severity score, the threshold at which a lesion is considered malignant is easily tunable. Our choice of score was chosen based on our receiver operating characteristic curves with a goal of maximizing sensitivity. However, the severity score itself could likely provide the clinician with guidance on making a more informed biopsy decision.

We are encouraged that in our study the magnitude of the increase in sensitivity to melanoma of our classifier compared with that of readers is greater than the magnitude of the loss of specificity. Further development and testing of our classifier is needed to fully determine its clinical use and our study has limitations. Although in this initial proof-of-concept study only 1 melanoma in situ among 39 melanomas was given a severity score that fell under our threshold, further validation on additional lesions is needed as our sample size is lower than those in the pivotal studies of devices that have received or are seeking regulatory approval (ie, Nevisense and MelaFind). Also, our reader study was relatively small, both in the number of readers and number of lesions included, and data should be interpreted with this in mind as the ratio of benign to malignant lesions in a reader study cannot mirror that seen in clinical practice. In addition, different groups of clinicians are likely to vary in the choices they make about how to manage pigmented skin lesions, even when using similar technologies.[9] Similarly to studies of other diagnostic aids, the lesions in our study were primarily selected for biopsy because they were determined to be suspicious by a dermatologist. Encouragingly, however, the specificity of our classifier was highest on our set of clinically benign unbiopsied lesions and these lesions had the lowest severity score of any group of images we tested, suggesting that our classifier will not recommend biopsy of benign lesions at an unacceptably high rate. Performance on a similar set of lesions has not been reported for Nevisense or MelaFind and we report these data as exploratory because we do not have histologic confirmation of the diagnosis of these lesions. Another limitation of our classifier is that although our sensitivity to melanoma is high, our sensitivity to BCC in this small series was lower at 72.7%. For comparison, Nevisense has a sensitivity of 100% for nonmelanoma skin cancer; sensitivity of MelaFind for nonmelanoma skin cancer has not been reported.[6,8] Although these tumors are rarely fatal and early detection is not associated with improved survival, we would like to optimize our classifier's performance on these common tumors. In our reader study, we only provided dermoscopic images

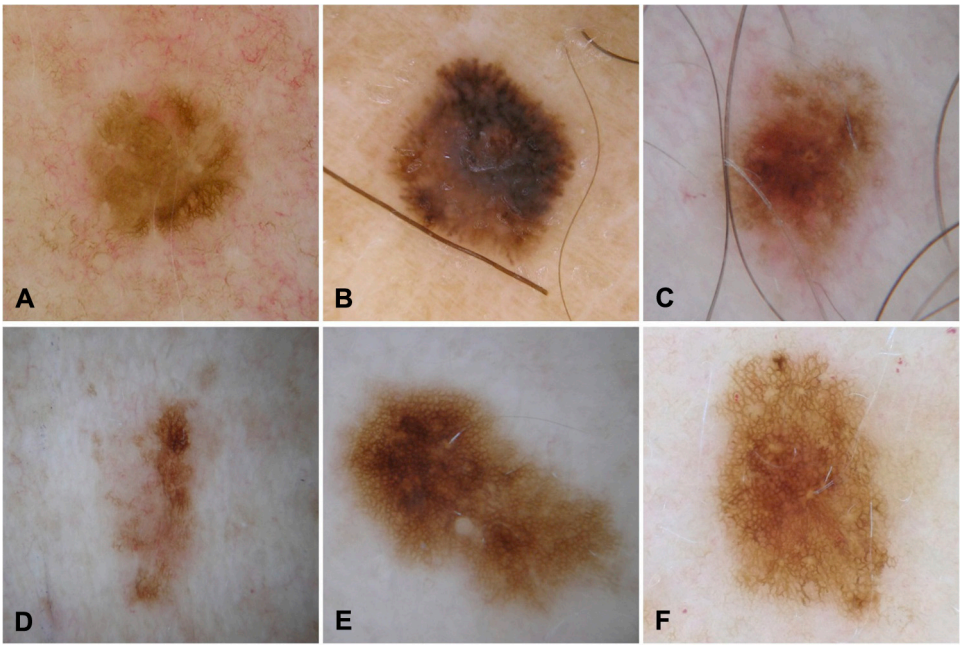


Fig 4. Examples of images used in image testing and reader study. **A**, Melanoma in situ given a severity score of 0.31 (classified as benign); this image was selected for biopsy by 23.3% of reader study participants. **B**, Invasive melanoma (Breslow depth 0.26 mm) given a severity score of 0.87 (classified as malignant) and selected for biopsy by 100% of reader study participants. **C**, Invasive melanoma (Breslow depth 0.45 mm) given a severity score of 0.772 (classified as malignant) and selected for biopsy by 26.7% of reader study participants. **D**, Low-grade dysplastic nevi (LGDN) given a severity score of 0.289 (classified as benign) and selected for biopsy by 53.3% of reader study participants. **E**, LGDN given a severity score of 0.719 (classified as malignant) and selected for biopsy by 10% of reader study participants. **F**, Lesion from the unbiopsied benign test set (chosen as clinically benign by 2 dermatologists, and not included in the reader study) given a severity score of 0.31 (classified as benign).

and not clinical images. This is not representative of the true patient encounter and may have decreased the accuracy of the biopsy decisions made by participants. However, our reader study results are similar to those reported by others[6,8] and suggest that the lesions used to test our classifier were not clinically obvious cases but represent the type of skin lesions that are diagnostically challenging even for dermatologists.

Many patients with a lesion suspicious for melanoma will not have easy access to a dermatologist.[10] In addition, population-based screening performed primarily by nondermatologists can lower melanoma mortality.[11] This provides an opportunity to aid clinicians, particularly nondermatologists, by providing them an accessible tool to improve early detection of melanoma by aiding them in choosing lesions that are appropriate for biopsy. In developing our classifier, we considered how it may ultimately and practically be incorporated into a tool that can be widely and inexpensively used by a variety of health care practitioners. The classifier was trained on images taken by several different camera and dermoscope combinations so that its use would not be restricted to a single piece of equipment. It can be run using modest computing resources, using a dermoscope attached to a smartphone or tablet computer, reducing its cost of operation. Because a tool that uses our classifier is likely to be of greater use to nondermatologists, who may select different lesions for biopsy than dermatologists, we also plan to validate the performance of our classifier on lesions that were referred to our teledermatology service by primary care providers. Providing useful information to aid in the evaluation and management of skin lesions has the potential to improve melanoma detection, particularly among nondermatologists and in patients with limited access to dermatologists.

We are indebted to the participants in the reader study.

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