The diagnostic accuracy of dermoscopy for basal cell carcinoma: A systematic review and meta-analysis

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Background: Dermoscopy is a noninvasive technique for the diagnosis of skin lesions. Its accuracy for basal cell carcinoma (BCC) has not been systematically studied.

Objective: We sought to systematically investigate the accuracy of dermoscopy for the diagnosis of BCC compared with examination with the naked eye.

Methods: A systematic review of studies reporting the accuracy of naked eye examination and dermoscopy for the diagnosis of BCC was conducted. A meta-analysis for sensitivity and specificity was performed using a bivariate mixed-effects logistic regression modeling framework.

Results: Seventeen studies were identified. The pooled sensitivity and specificity of dermoscopy for the diagnosis of BCC were 91.2% and 95%, respectively. In studies comparing test performance, adding dermoscopy to naked eye examination improved sensitivity from 66.9% to 85% (P = .0001) and specificity from 97.2% to 98.2% (P = .006). The sensitivity and specificity of dermoscopy were higher for pigmented than nonpigmented BCC. Sensitivity increased when dermoscopy was performed by experts and when the diagnosis was based on in-person dermoscopy as opposed to dermoscopic photographs.

Limitations: Significant heterogeneity among studies with a medium-to-high risk of bias.

Conclusion: Dermoscopy is a sensitive and specific add-on tool for the diagnosis of BCC. It is especially valuable for pigmented BCC. (J Am Acad Dermatol 2019;80:1380-8.)

Key words: dermoscopy; dermatoscopy; basal cell carcinoma.

Dermoscopy is a noninvasive technique for the diagnosis of skin lesions. Dermoscopy enables visualizing cutaneous structures not visible to the naked eye, increasing the accuracy of the dermatologic examination.[1]

Several algorithms have been created for the dermoscopic diagnosis of basal cell carcinoma (BCC),[2-4] based mainly on the identification of vascular structures, such as arborizing vessels, pigmented structures, such as blue-gray ovoid nests, and ulceration, in addition to the absence of structures associated with melanocytic lesions, such as areas of network.[3] BCC is the most common malignancy worldwide, and its incidence continues to increase.[5] While the published literature contains 5 systematic reviews examining the accuracy of dermoscopy for the diagnosis of melanoma,[1,6-9] none examine the accuracy of dermoscopy for the diagnosis of BCC.

We aimed to systematically review the literature on the use of dermoscopy for the diagnosis of BCC.

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METHODS

A systematic review and meta-analysis was conducted and reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses statement.[10] Adjustments were made to comply with recommendations for reviewing diagnostic test accuracy reports.[11] This review was registered with the international Prospective Register of Systematic Reviews (CRD42018095234).

Eligibility criteria

The study population included patients with histologically proven BCC who underwent dermoscopic examination. All studies including >4 cases of BCC were included in this review, regardless of design.

CAPSULE SUMMARY

- The accuracy of dermoscopy for basal cell carcinoma has not been systematically studied.
- Dermoscopy is a sensitive and specific add-on tool for the diagnosis of basal cell carcinoma, especially for the pigmented variant.
- Dermoscopy training should be included in dermatology residency programs because the level of expertise significantly affects diagnostic accuracy.

Outcomes

Primary outcomes. Primary outcomes included the accuracy of dermoscopy for the diagnosis of BCC and a comparison of the accuracy of naked eye examination followed by dermoscopy with naked eye examination alone for the diagnosis of BCC.

Secondary outcome. The secondary outcome was a comparison of the diagnostic accuracy of naked eye examination followed by dermoscopy with dermoscopy alone for the diagnosis of BCC.

Literature search

Two reviewers (Drs Reiter and Mimouni) searched PubMed, EMBASE, the Cochrane Central Register of Controlled Trials, and the ongoing trials registry of the US National Institutes of Health from inception until December 2017. Search terms included "dermoscopy" or synonyms (eg, dermatoscopy, epiluminescence microscopy, and skin surface microscopy) and BCC or synonyms and included Medical Subject Headings terms. Reference lists of included trials were searched for relevant publications. Authors were contacted for missing data and clarifications.

Study selection and data extraction

Two reviewers (Drs Reiter and Mimouni) screened the titles and abstracts of all retrieved articles, proceeding to full-text screening if potentially eligible. Disagreements were resolved through discussion with a third reviewer (Dr Leshem). Studies thought to report results for overlapping populations were excluded. One reviewer (Dr Reiter) extracted the data from included studies into a predefined electronic form, validated by a second reviewer (Dr Mimouni). Table I shows the extracted parameters.

Risk of bias assessment

The risk of bias was assessed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) criteria, with a maximum score of 14 points.[12] As previously reported,[13] we defined a high risk of bias as a score of 1 to 6 (<50%), medium risk as a score of 7 to 10 (50-75%), and low risk as a score of 11 to 14 (>75%).

Measures and statistics

The tests for the diagnosis of BCC were evaluated using commonly accepted definitions, with histologic diagnosis of BCC serving as the criterion standard. Diagnostic accuracy was defined as a combination of sensitivity and specificity. Sensitivity was computed as true positive/(true positive plus false negative) and specificity was computed as true negative/(true negative plus false positive). All summary measures were calculated on a per-lesion basis. When results were reported for multiple evaluators, we used the average sensitivity and specificity.

The data were synthesized using a bivariate mixed-effects binary regression model.[14] Based on the model summary, operating sensitivity and specificity for each test were calculated, and a receiver operator characteristic curve space was estimated. This model accounts for the within- and between-study variability.

To appraise the heterogeneity of sensitivities and specificities reported in different studies, we used value ranges, forest plots, and tests and measures of heterogeneity. The graph assessments included 95% confidence intervals (CIs).

Exploratory subgroup analyses were planned for pigmented versus nonpigmented BCC, expert versus nonexpert dermoscopists, and in-person dermoscopy versus dermoscopy-based photographs. Sensitivity analysis based on the quality of studies was also planned.

Comparison between tests was performed using the "Describe" module of Winpepi software.[15] Other

Table I. Characteristics of included studies

Study/country	Study design	Dermoscope type	Dermoscopy protocol	Dermoscopist level	Included lesions	Sex (M, F)/age, y	Photo or in-person	Naked eye examination	Lesions, n	BCCs, n	Diagnostic accuracy			
											Naked eye examination		Dermoscopy	
											Sensitivity, %	Specificity, %	Sensitivity, %	Specificity, %
Comparison of naked eye examination to dermoscopy—full data														
Stanganelli et al,[17] 2000/Italy	P	Wild M650	N/A	Expert	Pigmented skin lesions	552, 1004 (1:1.8), median 30 (range 10-94)	Photo	Y	3372	43	48.8	99.8	79.1	100
Markowitz et al,[26] 2015*/USA	P	Dermlite HR (3Gen)	Two steps algorithm	N/A	Clinically challenging pink lesions (suspected BCC)	N/A	In-person	Y	115	70	62.9	48.9	78.6	55.6
Ulrich et al,[22] 2015*/Germany	P	Dermlite ProHr 3 (3Gen)	N/A	Expert	Clinically unclear pink lesions (suspected BCC)	N/A median: 70	In-person	Y	234	141	90.1	29	90.1	53.8
Comparison of naked eye examination to dermoscopy—partial data														
Steiner et al,[16] 1987/Austria	P	WILD M650	N/A	Expert	Diagnostically equivocal small pigmented lesions	N/A	In-person	Y	318	20	60		90	
Koelink et al,[18] 2014/Netherlands	RCT	Dermlite II PRO HR (3Gen)	7-point checklist	Novice	Suspected skin lesion	135, 246 (1:1.8), mean 54	In-person	Y	416†	57‡	83.9		90	
No comparison of dermoscopy to naked eye—full data														
Menzies et al,[3] 2000/Australia and the USA	HP	Dermaphot (Heine)	Menzies dermoscopic criteria	Expert	Pigmented skin lesions	N/A	Photo	N	426	142			93	90.5
Blum et al,[30] 2006/Germany and Italy	HP	Dermaphot (Heine)	Modified Dermoscopic Algorithm	N/A	Melanocytic and nonmelanocytic skin tumors	132, 117 (1.12:1)	Photo	N	249	25			80	99.6
Chan and Ho,[31] 2008/Hong Kong	HP	Delta 20 (Heine)	Menzies dermoscopic criteria	Novice	Pigmented skin lesions	N/A	Photo	Y	155	33			97	93.5
Lorentzen et al,[25] 2008§/Denmark	P	Dermaphot (Heine)	N/A	Expert	Lesions referred to nevus clinics	N/A	Photo	N	119	13			92.3	99.1

Durdu et al,[24] 2011‖/Turkey	p	Mini 2000 (Heine)	2-step algorithm	Expert/ novice	Pigmented skin lesions	64, 112 (1:1.75), mean 48 (range 4-85)	In-person	Y	200	34	94.1	98.2
Ahnlide and Bejellerup,[19] 2013/Sweden	P	N/A	N/A	Expert	Lesions sent for excision	1415, 1538 (1:1.1, lesions), median 65 (range 7-93)	In-person	Y	2953	1180	95.4	89.6
Amirnia et al,[20] 2016/Iran	P	N/A	3-point checklist	N/A	Lesions sent for excision or evaluation	25, 36 (1:1.4), mean 49.5 (range 24-81)	In-person	Y	61	27	100	97
Guitera et al,[29] 2016¶/Australia and Italy	HP	Dermlitel Fotofinder; Sentry, DELTA20	Pattern analysis	Expert	Lightly colored or amelanotic lesions	N/A, mean 54.8 (range 7-92)	Photo	Y	171	44	70.5	71.7
Nelson et al,[23] 2016¶/USA	P	Dermlite (3Gen)	Two steps algorithm	Expert/ Novice	Skin lesions clinically suspected of BCC	65, 22 (2.9:1), mean 73 (range 44-93)	Photo	Y	100	90	97.8	80
Witkowski et al,[28] 2016¶/USA	HP	Dermlite FOTO system	N/A	N/A	Clinically equivocal pink cutaneous lesions	N/A	Photo	N	260	114	85.1	92.5
No comparison of dermoscopy to naked eye—partial data												
Rosendahl et al,[27] 2011/Australia	HP	Dermlite fluid device (3 Gen)	N/A	N/A	Pigmented skin lesions	262, 127 (2.1:1), mean ± SD 57 ± 17	Photo	Y	463	72	98.6	
Di Carlo et al,[21] 2014#/Italy	P	Videocap 200	Menzies dermoscopic criteria	N/A	Skin lesions	24, 12 (2:1), median 72 (range 55-75)	In-person	Y	135	48	83.3	

BCC, Basal cell carcinoma; *F*, female; *HP*, historical prospective; *M*, male; *N*, no; *N/A*, not applicable; *P*, prospective; *RCT*, randomized controlled trial; *SD*, standard deviation; *Y*, yes.
*Dermoscopy was compared with optical coherence tomography.
†416 total (222 in the clinical group; 194 in the dermoscopy group).
‡57 total (31 in the clinical group; 26 in the dermoscopy group).
§Dermoscopy was compared with acrylic globe magnifier dermoscopy.
‖Dermoscopy was compared with Tzanck smear.
¶Dermoscopy was compared with reflectance confocal microscopy.
#Dermoscopy was compared with video thermography.

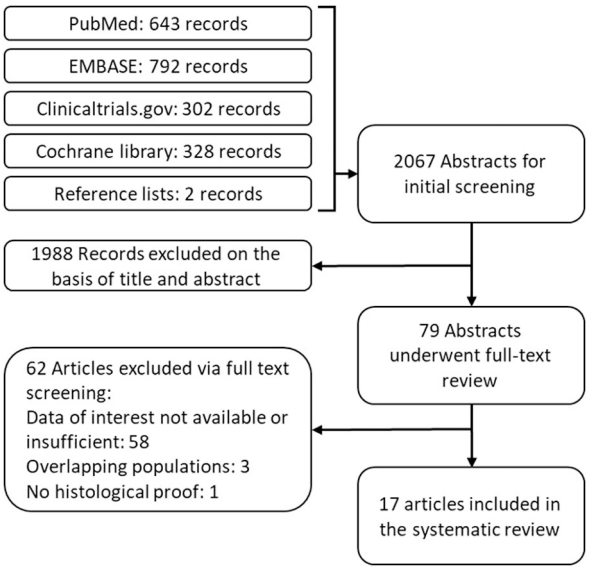

Fig 1. Selection of studies for this meta-analysis.

analyses were performed using Stata software (release 13; StataCorp LP, College Station, TX).

RESULTS

Our search yielded 2067 records (Fig 1). Seventeen studies consisting of 9747 skin lesions and 2153 BCCs fulfilled the eligibility criteria. The characteristics of the included studies are detailed in Table I. We designated studies examining prospective consecutive patients as prospective cohort studies[16-26] and studies retrospectively studying photographs as retrospective cohort studies.[3,27-31] Only 13 studies reported both sensitivity and specificity of dermoscopy for the diagnosis of BCC,[3,17-19,21-25,28-31] allowing for analysis of test accuracy. Five studies directly compared naked eye examination with to without dermoscopy for the diagnosis of BCC[16-18,22,26]; 3 of them provided both sensitivity and specificity.[17,22,26]

Data regarding polarization of dermoscopy were available from only 5 studies: 3 used polarized dermoscopy,[18,22,23] 1 used nonpolarized dermoscopy,[27] and 1 used both.[29] Studies also varied in the dermoscopic criteria and algorithms used (7 studies did not provide these data). We did not perform a statistical analysis of diagnostic accuracy based on dermoscopic polarization or diagnostic criteria because of the low number of studies in each group.

Quality assessment

The QUADAS scores[12] ranged from 5 of 14 to 10 of 14, corresponding to a medium-to-high risk of bias (data not shown), mostly attributed to a failure to clearly describe the dermoscopic process/algorithm and the histopathologic tests, including whether the pathologists were blinded.

Primary outcomes

Overall accuracy of dermoscopy. The 13 studies that reported both sensitivity and specificity[3,17-19,21-25,28-31] yielded a pooled sensitivity of 89% (95% CI 82-93%). The rate increased slightly to 91.2% (95% CI 90.0-92.4%) when we added the 4 studies that reported only sensitivity.[16,18,21,32] The pooled specificity was 95% (95% CI 85-99%).

The coupled forest plots for individual studies and the pooled estimates of the sensitivity and specificity of dermoscopy for the diagnosis of BCC are shown in Fig 2, and Fig 3 shows the summary receiver operating characteristic curve for dermoscopy in the diagnosis of BCC. Both reflect significant heterogeneity. All 4 outliers (studies 2, 3, 11, and 12)[22,23,26,29] compared dermoscopy with novel technologies, including reflectance confocal microscopy and optical coherence tomography, and all reported a lower accuracy of dermoscopy than the newer technologies. This may be attributable to the inclusion of more challenging lesions that required more advanced technologies or unintentional bias in favor of the novel technologies. The heterogeneity might also reflect some variability in the diagnostic threshold between studies because of differences in the implementation of dermoscopy, levels of skill, equipment, diagnostic algorithms, and study populations (Table I).

Diagnostic accuracy of dermoscopy following naked eye examination compared with naked eye examination alone. Five trials (4455 lesions) directly compared sensitivity between dermoscopy with naked eye examination and naked eye examination alone for the diagnosis of BCC[16-18,22,26] (Table I). In 4 trials, naked eye examination was followed by dermoscopic examination, and the probable diagnosis was recorded after each examination.[16,17,22,26] In the fifth trial, the diagnostic accuracy of 2 groups of primary care physicians was compared, 1 using dermoscopy following naked eye examination and the other using naked eye examination alone.[18]

The pooled sensitivity was 85.0% (95% CI 80.9-89.0%) for naked eye examination with subsequent dermoscopy and 66.9% (95% CI 60.9-72.4%) for naked eye examination alone (P = .0001). These results were sustained when excluding the study comparing 2 different groups of evaluators.[18] The pooled sensitivity in these 5 studies[17,21,25,26,32] was lower than the pooled sensitivity of all 17 studies (91.2%). A possible explanation is that 3 of 5 studies included only

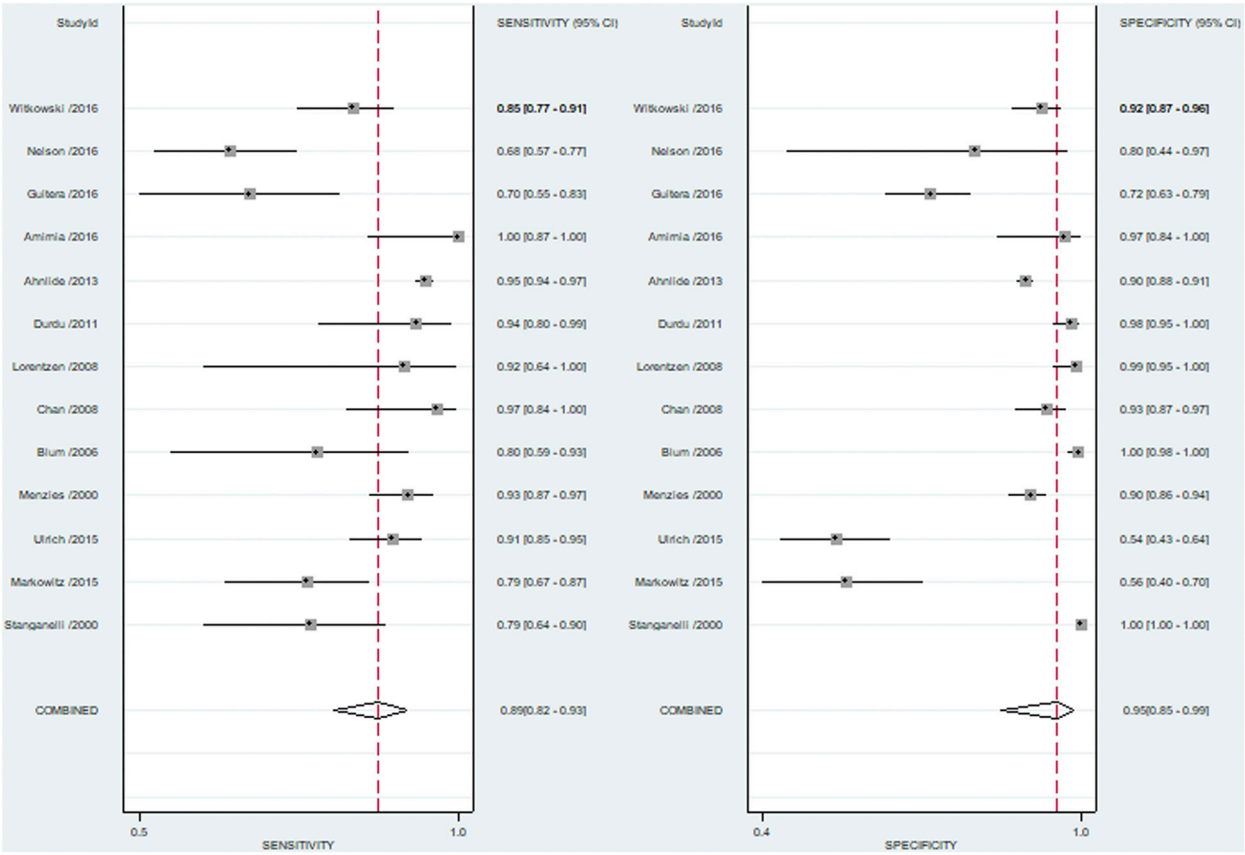

Fig 2. Coupled forest plots for individual studies and the pooled estimates of sensitivity and specificity of dermoscopy for the diagnosis of basal cell carcinoma.

clinically equivocal lesions, potentially lowering sensitivity relative to unselected lesions.

The pooled specificity of dermoscopy in the 3 studies that provided these data[17,22,26] was 98.2% (95% CI 97.7-98.6%), slightly superior to the pooled specificity of 97.2% (95% CI 96.6-97.7%) for the naked eye examination alone (P = .006).

Secondary outcome

Diagnostic accuracy of naked eye examination followed by dermoscopy compared with dermoscopy alone. This comparison aimed to assess the added benefit of a naked eye examination to dermoscopy. Nine studies provided data for analysis.[17,19,20,22-24,26,29,31] The addition of a naked eye examination increased the sensitivity of dermoscopy, although not significantly (91.8% [95% CI 90.4-93.0%] vs 88.8% [95% CI 84.7-91.%]; P = .132), with no difference in specificity (94.8% [95% CI 94.2-95.3%] vs 94.7% [95% CI 92.9-96.1%]; P = .908).

Subgroup analyses

Subgroup analyses could only be performed for the 13 studies that reported both sensitivity and specificity.[3,17-19,21-25,28-31]

Pigmented versus nonpigmented BCC. Four studies (4153 lesions) included only pigmented lesions (melanocytic and nonmelanocytic),[3,17,24,31] and 4 (780 lesions) included only nonpigmented lesions.[22,26,28,29] Studies that included both pigmented and nonpigmented lesions[19,20,23,25,30] were excluded from this subanalysis. Both the sensitivity and specificity of dermoscopy were significantly higher for pigmented than nonpigmented BCC. The pooled sensitivity of dermoscopy was 91.3% (95% CI 87.1-94.2%) for pigmented BCC and 84.3% (95% CI 80.2-87.6%; P = .008) for nonpigmented BCC. The respective pooled specificity values were 99.0% (95% CI 98.7-99.3%) and 73.2% (95% CI 68.8-77.3%; $P < .001$).

The added benefit of dermoscopy to naked eye examination in cases of pigmented BCC is reflected in 2 studies wherein dermoscopy following naked eye examination had a sensitivity of 82.5% (95% CI 73.1-92%) compared with 52.3% (95% CI 39.9-64.8%) for naked eye examination alone (P = .001).[16,17] Only 1 study of pigmented BCC reported specificity[17]—100% for dermoscopy and 99.76% for naked eye examination alone. By contrast, for nonpigmented lesions, no added benefit in

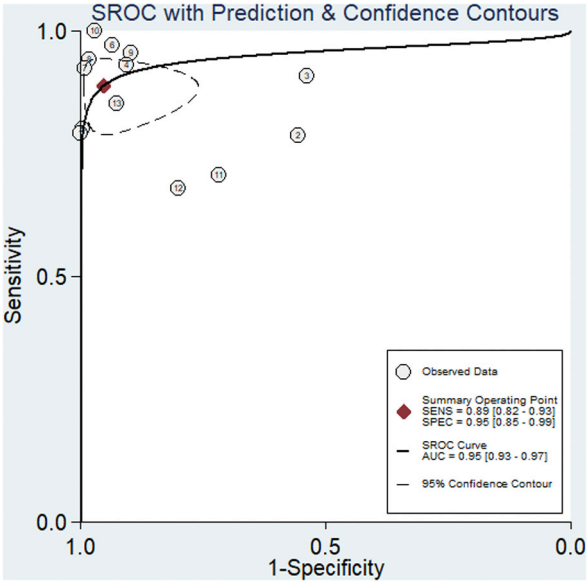

Fig 3. Summary receiver operator characteristic (SROC) curve for dermoscopy in the diagnosis of basal cell carcinoma. *AUC* = Area under the curve; *SENS* = sensitivity; *SPEC* = specificity.

sensitivity was found: 86.7% (95% CI 82.1-91.3%) for dermoscopy and 81% (95% CI 75.7-86.3%) for naked eye examination alone ($P = .114$).[22,26] Specificity was improved by dermoscopy (54.3% [95% CI 46-62.7%] compared with 35.5% [95% CI 27.5-43.5%] for naked eye examination alone; $P = .003$).[22,26]

Expert versus nonexpert dermoscopists. Investigator expertise in dermoscopy varied among studies. In 6 studies, the investigators were experienced dermoscopists[3,17,19,22,25,29]; in 2, the majority of investigators were either dermatology residents or "novice" dermoscopists (<2 years' experience).[23,31] Studies that did not report their investigators' experience level[20,24,26,28,30] were excluded from this subanalysis. Experience significantly increased the sensitivity but not the specificity of dermoscopy for BCC. The calculated pooled sensitivity of dermoscopy performed by experienced dermoscopists was 93.6% (95% CI 92.3-94.7%) compared with 75.6% (95% CI 67.3-82.3%) if at least 1 dermoscopist was not experienced ($P < .001$). Experienced dermoscopists achieved a pooled specificity of 94.9% (95% CI 94.3-95.4%) compared with 92.4% (95% CI 86.6-95.8%) for nonexperienced dermoscopists ($P = .571$). The addition of dermoscopy to the naked eye examination significantly improved both the sensitivity and the specificity of the diagnosis of BCC when the dermoscopic test was performed by experts (data not shown). None of the studies directly compared expert and nonexpert dermoscopy.

In-person dermoscopy compared with dermoscopic photography. In 8 studies, dermoscopic photographs were used to evaluate the diagnostic accuracy of dermoscopy for BCC.[3,17,23,25,28-31] Five studies used in-person dermoscopy.[19,20,22,24,26] The calculated pooled sensitivity was 83.1% (95% CI 79.6-86.2%) for dermoscopic photography and 94.2% (95% CI 92.9-95.3%; $P < .001$) for in-person dermoscopy. The pooled specificity of dermoscopic photography was 98.0% (95% CI 97.6-98.4%) compared with 88.1% (95% CI 86.6-89.4%) for in-person dermoscopy ($P < .001$). The addition of dermoscopy, both in-person or from photographs, improved naked eye diagnosis (data not shown).

Medium versus high risk of bias (per QUADAS). No statistically significant difference in dermoscopy sensitivity or specificity was found between studies with a medium or a high risk of bias (data not shown).

DISCUSSION

In this systematic review and meta-analysis, we aimed to evaluate the accuracy of dermoscopy for the diagnosis of BCC. We found an overall pooled sensitivity of 91.2% and a pooled specificity of 94.8% for dermsocopy. The addition of dermoscopy to the naked eye examination improved the diagnostic accuracy, particularly sensitivity.[16-18,22,26] Even though dermoscopy is more accurate than naked eye examination alone, it should not serve as the sole basis of dermatologist decision-making. When dermoscopy followed a naked eye examination that provided clinical context, its sensitivity for the diagnosis of BCC improved, albeit not enough to achieve statistical significance.[3,17,19,20,22-26,28-31]

Adding dermoscopy to naked eye examination significantly improved the sensitivity for pigmented but not for nonpigmented BCC. This finding was not unexpected given the large proportion of the dermoscopic criteria for the diagnosis of BCC that involve pigmented structures.[3]

Our results emphasize that dermoscopy is an operator-dependent test. Sensitivity was greatly affected by the level of expertise, yet specificity was not. This finding may be explained by the differential diagnosis of BCC. For malignant lesions, the differential is often melanoma versus BCC (especially pigmented). The latter may be more likely be classified as melanoma by nonexperts, leading to decreased sensitivity. It is fairly easy for both experts and nonexperts alike to rule out malignancy in the common benign lesions included

in the differential (eg, intradermal nevi and sebaceous hyperplasia), which may account for the similar specificity in the 2 groups.

Studies that used dermoscopic photographs reported higher specificity but lower sensitivity[3,17,23,25,28-31] than studies using in-person dermoscopy.[19,20,22,24,26] This difference may be attributed to the different setting of these studies. Investigators that used in-person dermoscopy were treating patients before a definitive diagnosis and therefore may have erred on the side of caution to avoid missing a diagnosis of BCC, thereby decreasing specificity and inflating sensitivity. In contrast, investigators that assessed photographs might have felt that their diagnostic abilities were being tested, and knowing that this was a post hoc assessment, they were less pressured to avoid missing a BCC, leading to increased specificity. This finding emphasizes the importance of interpreting these studies in the context in which they were performed.

This review has several limitations. There was significant heterogeneity among the studies, which is expected in meta-analyses of diagnostic test accuracy.[33] Furthermore, only a small number of studies directly compared naked eye examination alone and with dermoscopy, restricting the comparison of the 2 tests. BCC subtypes (eg, nodular, superficial, and morpheaform) were often not provided, and all studies had a medium-to-high risk of bias, limiting the validity of our findings.

In conclusion, as previously reported for melanoma,[1,6-9] dermoscopy is a sensitive and specific tool for the diagnosis of BCC and should be used as an add-on test to the clinical examination of a suspected skin lesion. Its use is especially beneficial for pigmented lesions. We advocate including dermoscopy training as part of dermatology residency programs because the level of expertise significantly affects diagnostic accuracy.

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