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## **Dermoscopic Features of Basal Cell Carcinoma and its Subtypes: A systematic Review**

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white structures; rosettes; shiny white-red structureless background; blue-white veil; ulceration; multiple small erosions.

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### **Capsule Summary**

- The prevalence of dermoscopic features in basal cell carcinoma (BCC) and its subtypes has not been systematically studied.
- Even though not as well-known as arborizing vessels, shiny white structures are an important feature of BCC and its subtypes. Different constellations of dermoscopic features aid in the differentiation between BCC subtypes.

## Abstract

**Background:** Multiple studies have reported on dermoscopic structures in basal cell carcinoma (BCC) and its subtypes, with varying results.

**Objective:** To systematically review the prevalence of dermoscopic structures in BCC and its subtypes.

**Methods:** Databases and reference lists were searched for relevant trials according to PRISMA guidelines. Studies were assessed for the relative proportion of BCC dermoscopic features. Random effects models were used to estimate summary effect sizes.

**Results:** 31 studies, consisting of 5,950 BCCs, were included. The most common dermoscopic feature seen in BCC were arborizing vessels (59%), shiny white structures (49%) and large blue-grey ovoid nests (34%). Arborizing vessels, ulceration and blue-grey ovoid nests and globules were most common in nodular BCC; short-fine telangiectasia, multiple small erosions and leaf-like, spoke wheel and concentric structures in superficial BCC; porcelain white areas and arborizing vessels in morpheaform BCC; and arborizing vessels and ulceration in infiltrative BCC.

**Limitation:** Studies had significant heterogeneity; studies reporting on BCC histopathologic subtypes did not provide clinical data on pigmentation of lesions.

**Conclusion:** In addition to arborizing vessels, shiny white structures are a common feature of BCC. A constellation of dermoscopic feature may aid in differentiating between BCC histopathologic subtypes.

## Introduction

Basal cell carcinoma (BCC) is the most common human cancer worldwide, and even though it rarely metastasizes, it may cause significant morbidity if left untreated(1). BCC can be either clinically pigmented or non-pigmented, mainly dependent on the patient's skin type(1). In addition, it has several histopathologic subtypes, with the most common being nodular (nBCC), superficial (sBCC) and morpheaform (mBCC)(2).

Dermoscopy enables the visualization of skin structures that are not visible to the naked eye, through the use of a magnifying lens and polarized and/or non-polarized light. Adoption and use of dermoscopy is increasing with over 90% of dermatologists reporting using this tool in their day-to-day practice in certain countries(3, 4).

Dermoscopy increases sensitivity and specificity for the diagnosis of BCC (5). Multiple studies have previously reported on different structures that are observed under dermoscopy in BCC and its subtypes, with varying results. Based on these studies, dermoscopic structures have been incorporated into several algorithms that assist in the diagnosis of BCC(6, 7).

We present a systematic review summarizing the prevalence of dermoscopic structures observed in BCC and their relative distributions in BCC subtypes.

## Methods

A systematic review of the literature was conducted and reported in concordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement(8).

### Eligibility criteria

--Population: Patients with histopathologically proven BCC who underwent dermoscopic examination.

--Lesion type: Studies that reported on: (1) BCC in general; (2) clinically pigmented and/or non-pigmented BCC; (3) any of the four histopathologic subtypes: nBCC, sBCC, mBCC and infiltrative BCC (iBCC).

--Study design: All studies including more than four cases of BCC, regardless of design.

#### Exclusion criteria

--Studies that limited inclusion of lesions by either a specific anatomic locations (e.g. legs), above a certain diameter, or recurrent /post-biopsy tumors. These studies were excluded because they limit the generalizability of this review.

#### Outcomes

##### *Primary outcome*

Prevalence of dermoscopic structures in BCC

##### *Secondary outcomes*

1. Prevalence of dermoscopic structures in clinically pigmented and non-pigmented BCC
2. Prevalence of dermoscopic structures in 4 BCC histopathologic subtypes: nBCC, sBCC, mBCC and iBCC.

#### Literature search

Two reviewers (O.R. and I.M.) searched PubMed, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), and the ongoing trials registry of the US National Institutes of Health ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)) from inception until November 2018. Search terms included "Dermoscopy" or synonyms and basal cell carcinoma or synonyms and known basal cell carcinoma dermoscopic features (e.g. arborizing vessels, shiny white, ovoid nests etc.). MeSH terms were also included, and reference lists were searched. Authors were contacted for missing data and clarifications.

#### Study selection and data extraction

Two reviewers (O.R. and I.M.) screened the titles and abstracts of all retrieved records. Subsequently, when the title and/or abstract suggested eligibility for the review, the full text article was screened, and relevant data was extracted into an electronic form. Disagreement were resolved by discussion with a third reviewer (Y.A.L).

### Risk of bias assessment

Included articles were assessed for risk of bias using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) criteria, with a score range of 0-14(9). As performed by us in our previous review(5) and by others(10), we defined a score of 0-6 (<50%) as high risk of bias, 7-10 (50%-75%) as medium risk and 11-14 (>75%) as low risk of bias.

### Measures and statistics

Individual studies will be assessed for the outcome the relative proportion of the identified feature within each study. Estimates of relative proportion were made if not explicitly stated within the manuscript if enough information was available to infer the proportion. When the data were unattainable, we attempted to impute the missing responses in accordance with the recommendations put forth in the Cochrane Handbook for Systematic Reviews for Interventions.

Meta-analytic techniques were performed using Stata v14.2 software (StataCorp, College Station, TX, USA) to provide summary prevalence estimates. Random effects models were used to estimate summary effect sizes along with 95% confidence intervals. Separate analyses were performed by BCC subtype. The degree of heterogeneity between studies was assessed by calculating the  $I^2$  statistic. Potential reporting bias was assessed by creating funnel plots to visually evaluate any systematic differences between smaller and larger studies and the observed effect sizes.

## **Results**

Our search yielded a total of 1,412 records (Figure I). Thirty-one studies, consisting of 5,950 BCCs, fulfilled the eligibility criteria and were included in the review. Some lesions were reported solely as BCCs without further details and others had additional information, including the histopathological subtype or pigmentation status. Only one study (11) provided data on both the histopathological subtype and the pigmentation status of the lesions, prohibiting analysis of



both parameters combined.. Individual studies included different BCC subtypes in their analysis and some included several subtypes of BCC. Out of the 31 studies, 17(11-27) included 1,590 sBCCs, 13(11, 12, 15-25) included 1,503 nBCCs, 7(12, 15, 17-20, 22) included 288 iBCCs and 6(12, 15, 18, 19, 21, 24) included 53 mBCCs. In terms of pigmentation status, 11 studies included 1,253 pigmented BCCs(11, 17, 21, 23, 25, 28-33) and 5 studies included 904 non-pigmented BCCs (11, 23, 28, 30, 34). Characteristics of included studies are detailed in Table I.

Studies described different dermoscopic structures among BCC lesions. These structures can be divided into 3 groups:

1. Pigmented structures – large blue-grey ovoid nests; multiple blue-grey dots and globules; multiple in-focus dots; leaf-like areas; spoke wheel areas; concentric structures.
2. Vascular structures – arborizing vessels; short-fine telangiectasia; dotted vessels; hairpin vessels; corkscrew vessels; glomerular vessels; polymorphous vessels.
3. Non-vascular and non-pigmented structures - shiny white structures. As each study used different terms in this category, we combined the terms shiny white lines, streaks, strands and blotches, crystalline structures and shiny white areas into ‘shiny white structure’; rosettes; shiny white-red structureless background; blue-white veil; ulceration; multiple small erosions.

Most studies used dermoscopic photographs and only 7 studies(13, 15, 18, 24, 29, 31, 35) used in-person dermoscopy. One study(22) used only nonpolarized dermoscopy, 7(14, 15, 21, 24, 26, 35, 36) used polarized dermoscopy and 5(16, 19, 28, 34, 37) used both. The remaining 18 studies did not report on polarization.

### Quality assessment

Studies varied in their risk of bias and their QUADAS scores ranged between 0-12. Only one (18) study had a low risk of bias, 9 had a medium risk and 21 of 31 studies had a high risk of bias, mainly due to failure to report whether pathologists, which provided the ‘gold criterion’ diagnosis, were blinded to suspected diagnosis or the dermoscopic description. The QUADAS assessment of participating studies is detailed in Table II.

### Primary outcome - Prevalence of dermoscopic structures in BCC

The prevalence of different dermoscopic features among BCC and its subtypes is detailed in Table III. Looking at BCCs in general, the most common dermoscopic feature was arborizing vessels, with a pooled prevalence of 59% (95% CI 53%-65%). However, it was not the only vascular structure that was reported. Other vascular structures included: short-fine telangiectasia, dotted vessels, polymorphous vessels, hairpin vessels, corkscrew vessels and glomerular vessels with varying prevalence (see Table III).

The second most common feature was shiny white structures (49%; 95% CI 40%-58%) followed by shiny white-red structureless areas (40%, 95% CI 28%-54%).

The third most common category was pigmented structures, including large blue-grey ovoid nests (34%, 95% CI 27%-42%) and multiple blue-grey dots and globules (34%, 95% CI 28%-41%).

#### *1. Clinically pigmented and non-pigmented BCC*

Both pigmented and non-pigmented BCC commonly presented with arborizing vessels (63%, 95% CI 43%-81% and 55%, 95% CI 45%-65%, respectively). However, while pigmented BCC presented pigmented structures with frequencies of up to 48%, non-pigmented BCC presented these structures in only 0-2% of lesions. On the other hand, non-pigmented BCC more commonly presented with vascular structures other than arborizing vessels.

### *BCC histopathologic subtypes*

#### *Nodular BCC*

nBCC most commonly presented with arborizing vessels (75%, 95% CI 69%-82%), shiny white structures (43%, CI 26%-61%) and ulceration (31%, 95% CI 20%-44%). When pigmentation was present, the most common structure was large blue-grey ovoid nests (36%, 95% CI 25%-47%). nBCC very seldomly presented with leaf-like areas (6%, 95% CI 2%-10%), spoke wheel structures (3%, 95% CI 1%-5%) or concentric structures (5%, 95% CI 3%-7%).

#### *Superficial BCC*

The most common dermoscopic structures described in sBCC were short-fine telangiectasia (60%, 95% CI 51%-69%), multiple small erosions (43%, 95% CI 31%-54%) and shiny white structures (43%, 95% CI 22%-66%). In addition, 79% of lesions presented with shiny white-red structureless background (95% CI 64%-94%). When pigmentation was present, it most commonly presented as multiple blue-grey dots and globules (27%, 95% CI 21%-34%) and leaf-like areas (25% 95% CI 18%-33%).

#### *Morpheaform BCC*

Only 53 cases of mBCC were included in this review. One study found that 75% of mBCC showed structureless hypopigmentation (porcelain white areas)(38). Another common dermoscopic feature among mBCC was arborizing vessels (51%, 95% CI 26%-77%) and many of these tumors were ulcerated (58%, 95% CI 9%-99%). When pigmentation was present, it was most commonly large blue-grey ovoid nests (13%, 95% CI 0%-36%), however, in general mBCC rarely presented with pigmentation dermoscopically (average of 0-13% of lesions).

#### *Infiltrative BCC*

The majority of iBCC presented with arborizing vessels (76%, 95% CI 59%-77%), followed by ulceration (44%, 95% CI 26%-62%) and short-fine telangiectasia (40%, 95% CI 27%-53%). iBCC rarely presented with leaf-like areas (4% 95% CI 0-10%).

#### *Dermoscopic structures distribution between different BCC histopathologic subtypes*

No single dermoscopic structure was found to be unique for a specific histopathologic subtype. Nevertheless, some structures had different prevalence among different subtypes.

Pigmented structures - Leaf-like and spoke wheel areas were more common in sBCC compared to all other subtypes Large blue-grey ovoid nests were more common in nBCC compared to sBCC.

Vascular structures - Arborizing vessels were more common in nBCC and iBCC compared to sBCC. Short-fine telangiectasia were more common in sBCC compared to nBCC.

Non-vascular and non-pigmented structures - Shiny white structures were common among all BCC subtypes (41%-100%) but were not found to have different prevalence among different subtypes. Multiple small erosions were more common among sBCC compared to nBCC. The prevalence of ulcers, however, was not different among different subtypes.

## Discussion

The aims of this paper were to systematically review the evidence for the prevalence of dermoscopic structures among BCC and its clinical (pigmented vs non-pigmented) and histopathologic subtypes and to investigate whether these structures can differentiate between the subtypes.

There was not a single dermoscopic structure that appeared in all BCC lesions, nor was there a structure exclusive for a specific BCC subtype. It seems that the most prominent features for the diagnosis of BCC are blood vessels, specifically arborizing vessels or short fine telangiectasia, identified in 51%-75% of the tumors, depending on BCC subtype. The second important clue for the diagnosis of BCC is shiny white structures, that appeared in 41%-49% of tumors. Pigmented structures were only reported in up to 36% of cases of BCCs and its histopathological subtypes.

Pigmented structures appeared almost exclusively in pigmented lesions. Pigmented structures may be more easily identifiable than other BCC features (e.g. shiny white structures), which could explain why dermoscopy has a higher diagnostic accuracy for pigmented BCC versus non-pigmented BCC(5). The frequency of non-pigmented structures such as vascular structures was lower in pigmented versus non-pigmented BCC, probably due to obscuration of these structures by pigment in the former. As data on the histopathologic subtypes of pigmented vs non-pigmented BCC was not provided, we could not correlate the dermoscopic findings with the histopathological ones for these subgroups.

In analyzing histopathologic BCC subtypes, we found that even though they had different frequencies of dermoscopic structures, most could not clearly differentiate between the subtypes. For example, 43% of nBCCs presented shiny white structures, but the same frequency was observed in sBCCs. The only two dermoscopic structures that were relatively unique for one subtype were leaf-like areas and shiny white-red structureless background in sBCC.

Interestingly, “classic” nBCC features, such as large blue-grey ovoid nests that correlate with large tumor nests in the dermis(39), were also present in sBCCs and “classic” sBCC features, such as leaf-like areas that correlate with small basaloid cells nests in the dermo-epidermal junction(39), were present in nBCCs. This may at least partly be explained by variations in

histopathologic analysis. Depending on the different sectioning and readers, the same lesion can be classified as superficial, nodular or mixed type BCC.

The two most commonly observed vascular structures were arborizing vessels, more typical for nBCC and iBCC, and short-fine telangiectasia that were more characteristic of sBCC.

Nonetheless, all BCC subtypes displayed a variety of vessel morphologies, including ones not usually associated with BCC. The significance of this finding is that vessels should be interpreted in the context of the clinical and dermoscopic findings. For example, if a lesion displays glomerular vessels but also other findings consistent with BCC, expand your differential beyond Bowen's disease, as 6% of BCCs in this review displayed glomerular vessels. Another example of a feature that is classically associated with lesions other than BCCs is the blue-white veil, which was reported in 10% of BCCs lesions included in this review.

The main limitation of this review is the significant heterogeneity among the studies, which also prevented conducting a meta-analysis. One of the reasons for the heterogeneity is that dermoscopic criteria for BCC are still evolving and studies from different time points reported on different criteria and used different terms. Another reason can be attributed to the fact that studies used different light polarization mode, which is critical in evaluating the prevalence of dermoscopic features. Some dermoscopic features, such as shiny white structures, are only seen under polarized light, and some are seen better under non-polarized light. In addition, non-polarized dermoscopy is most-likely done with direct contact between the dermoscope and the skin, which may hamper the visualization of blood vessels as they are blanched due to the pressure of the lens(40).

Additional limitations include the medium to high risk of bias of most studies and that, except for one study(11), all studies that reported on histopathologic subtypes did not provide clinical data on pigmentation of lesions. It is to be expected that the prevalence of pigmented structures was directly impacted by the frequency of clinically pigmented lesions in these studies. Lacking this data, we cannot reach conclusions on the relative significance of pigmented structures in diagnosing the different BCC histopathologic subtypes.

In conclusion, it comes as no surprise that arborizing blood vessels, which are the most well-known characteristic of BCC, are also its most common dermoscopic feature. However, shiny white structures, which are not as well-known, were found to be the second most common

feature of BCC. Frequencies of dermoscopic features differ between BCC histopathologic subtypes and the constellation of features may aid in the diagnosis: nBCC is associated with arborizing vessels, ulceration and blue-grey ovoid nests and globules; sBCC is associated with short-fine telangiectasia, multiple small erosions and leaf-like, spoke wheel and concentric structures; mBCC is associated with porcelain white areas and arborizing vessels; and iBCC is associated with arborizing vessels and ulceration. The paucity of dermoscopic findings in the latter subtypes may contribute to difficulty in making these diagnoses. Further studies are required to differentiate dermoscopic findings in pigmented and in non-pigmented BCC histopathologic subtypes.

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Figure I. Systematic literature search according to the PRISMA guidelines

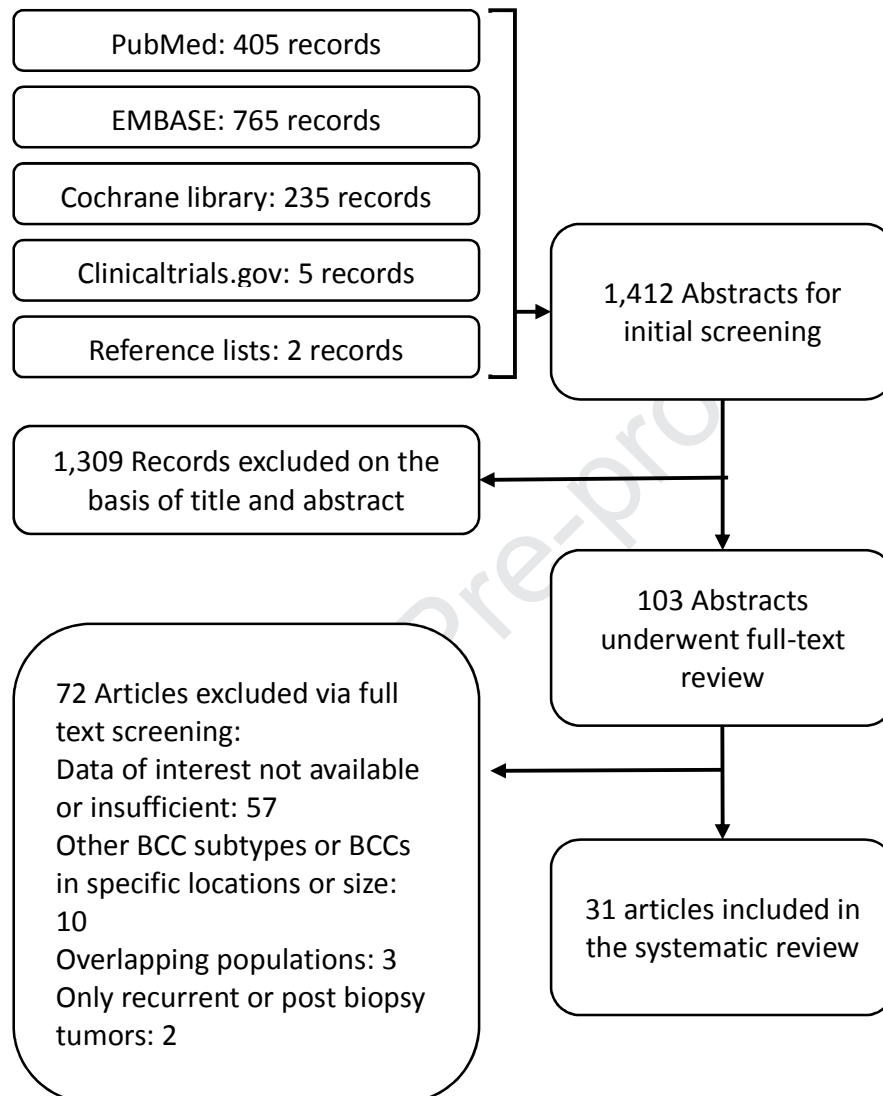


Table I. Characteristics of included studies

Study	Country	Study design	Dermoscope type	Polarized/ nonpolarized	Total number of patients	Age (mean or median)	Photo or in-person dermoscopy	Tumor type	Total number of lesions	Large blue grey ovoid nests	Multiple blue grey dots/globules	Multiple in focus blue grey dots/globules	Leaf-like areas	Spoke Wheel areas	Concentric structures	Shiny white structures	Rosettes	Shiny white-red structureless background	Ulceration	Multiple small erosions	Arborizing vessels	Short fine telangiectasia	Dotted vessels	Polymorphous vessels	Hairpin vessels	Corkscrew vessels	Glomerular vessels	Blue-white veil
Kreusch 1996	Germany	R	Ot				P	BCC	86											77		1	2	9				
Argenziano 2004	Italy	R	Hn				P	BCC	117											96			6	3		0		
Giacometl 2005	Australia		Hn		18	65md	IP	sBCC	24							24		24	17	2	22			1				
Demirtasoglu 2006	Turkey	Pr	MM		30	68md	IP	pBCC	32	27	20		16	0					20		26						3	
Scalvenzi 2008	Italy	Pr	DL	P	42	60md	P	sBCC	42	2	6		7	0				42	0	33	0	28						
Chan 2008	Hong Kong	HP	Hn		32	77md	P	pBCC	33	19	22		2	2					25		16							
Tabanlıoglu Onan 2010	Turkey	Pr	Hn		29	62mn	IP	pBCC	40	14	2		11	15					11		11						23	
Altamura 2010	Italy & Australia	R	Ot		609	63md	P	BCC	609	289	159	31	97	55	46				239	52	348	61			16		86	
								npBCC	92	0	0	0	0	0	0				45	7	77	13					0	
								pBCC	517	289	159	31	97	55	46				194	45	271	48					86	
Sakakibara 2010	Japan	R	Hn			49md	P	pBCC	119											86			4	0		0		
Liebman 2011	USA	Pr	DL	P&NP			P	BCC	149	22	76		20			103	17		42		57	23						
Balagula 2011	USA & Switzerland	Pr	DL	P			IP	BCC	82							39												
Micantonio 2011	Italy	R	Ot		417	64md	P	BCC	504											306	167			52		41		
								nBCC	171											152	18			19		15		

							sBCC	333												154	149			33		26	
							pBCC	138												63	28			4			
							npBCC	323												172	139			48			
<b>Liebman 2012</b>	USA	R	DL	P			P	BCC	191							91	27										
<b>Trigoni 2012</b>	Greece	R	DL		96			BCC	132	24	27		6	6				98	39		87	51			43		
								nBCC	93	3	12		0	0				67	6		72	30			13		
								sBCC	39	21	15		6	6				31	33		15	21			30		
								pBCC	96	18	21		6	6				62	27		76	15			36		
								npBCC	36	6	6		0	0				36	12		11	36			7		
<b>Verduzco-Martinez 2013</b>	Mexico	R	DL		48	70mn	P	BCC	56	29	20		3	4				4		26							1
								nBCC	38	22	15		0	0				2		20							1
								pBCC	7	3	2		3	2				0		0							0
								sBCC	4	1	0		0	2				0		0							0
								iBCC	6	3	2		0	0				2		6							0
<b>Lallas 2013 (1)</b>	Italy	R	DL	P&NP	313	67mn	P	BCC	313	110	100	33	50	32	45			68	148	49	171	81					
								nBCC	154	77	46	13	13	9	11			17	82	10	114	22					
								sBCC	77	4	25	10	29	14	21			36	21	31	12	40					
								mBCC	8	0	0	0	0	0	0			2	7	0	3	3					
								iBCC	32	8	7	3	1	2	3			7	17	4	19	8					
<b>Lallas 2013 (2)</b>	Italy	R	DL		507	66.8mn	P	BCC	507	184	147	38	70	39	49												
								nBCC	274	138	75	14	16	11	13												
								sBCC	113	5	32	13	39	17	22												
								iBCC	45	10	9	3	1	2	3												
								mBCC	15	2	2	0	0	0	0												
<b>Longo 2014</b>	Italy, Spain, USA & Australia	R	DL		88	61mn	P	BCC	88	17	31	21	17	8	7			49	13	21	35	45					
								nBCC	22	12	9	5	2	2	2			3	6	1	19	4					
								sBCC	44	4	16	13	14	5	3			30	5	17	5	31					

								iBCC	22	1	6	3	1	1	2			16	2	3	11	10						
Seidenari 2014	Italy	R	FF	NP	335	62mn	P	BCC	400	119	150		74	30	28			167	119	122	263	198						
								iBCC	54	19	22		9	2	4			22	33	13	42	24						
								sBCC	119	11	32		26	13	10			74	13	55	50	86						
								nBCC	208	87	88		35	12	11			71	66	47	158	75						
Zivkovic 2014	Serbia				190	67md	P	sBCC	87	8	6		7					76	21	28	36	44						
								nBCC	87	9	9		1					13	55	2	78	8						
								pBCC	42	28	8		21					7	15	6	25	10						
Popadic 2015 (1)	Serbia		DL		7	69mn	IP	mBCC	4	0	1	1	0	1		3			0	2	1	3						
								iBCC	3	1	2	1	0	1		3			1	3	2	0						
Popadic 2015 (2)	Serbia	Pr	DL	P	116	68md	P	BCC	151	43	54	35	29	22		78			35	59	53	30						0
								nBCC	60	17	20	15	6	8		35			12	19	31	2						
								sBCC	57	16	24	16	20	12		24			1	35	7	22						
Suppa 2015	Italy	R	Hn	P&NP	400	64md	P	sBCC	335	129	103	60	131	44	42	102	8		109	58	124	129		32	26	6	10	39
								nBCC	166	64	39	28	22	1	4	52	2		62	5	130	6		11	10	3	6	34
Emiroglu 2015	Turkey	Pr	DL	P	98	64mn	P	BCC	98	42	7		9	6		38		42	29		42	15						
								sBCC	19	0	2		0	0		3		19			0	6						
								nBCC	37	12	0		1	0		15		9			22	3						
								pBCC	3	0	3		2	3		0		0			1	0						
								mBCC	15	9	2		0	0		5		6			6	0						
Kim 2015	Korea		DL		141	69mn		BCC	145	106	86		28	12	23				90	16	77	42						53
Elwan 2015	Egypt		DL	P	12		IP	BCC	12	7	9		4	1				1	9		8							2
								nBCC	6	5	5		2	1				0	4		3							1
								sBCC	3	1	3		2	0				0	2		2							1
								mBCC	1	0	0		0	0				1	1		1							0
Ahnlide 2016	Sweden	Pr					IP	BCC	393	94								125	160	72	282	211						
								sBCC	70	15								39	14	33	20	54						
								nBCC	187	54								47	66	20	149	91						

							iBCC	126	23								37	74	19	109	64						
							mBCC	10	2								2	6	0	8	2						
<b>Navarrete-Dechent 2016</b>	USA	R	DL	P&NP	287	62mn	P	npBCC	287						110	20											
<b>Romano 2016</b>	Argentina	R	DL	P	30	56mn	P	sBCC	30	4	11		17		5	16		25	6	11	7	22			13		5
<b>Wolner 2018</b>	USA	R	DL	P&NP	348	65mn	P	BCC	392	96	135	179	79			155			117		262	212		149			
							pBCC	226	96	135	179	79				76			63		134	129		86			
							npBCC	166	0	0	0	0				79			54		128	83		63			
<b>Papageorgiou 2018</b>	Greece	R	DL		194		P	sBCC	194	32	61		58 (leaf-like+spoke wheel+concentric)		24			56	69	37	146	35		49		19	

BCC – Basal cell carcinoma; DL – DermLite; Hn – Heine; FF – Fotofinder; HP – Historical prospective; iBCC – Infiltrative BCC; IP – In person; mBCC – Morpheaform BCC; MM – Molemax; nBCC – Nodular BCC; npBCC – Non-pigmented BCC; Ot – Other; P – Photo; pBCC – Pigmented BCC; Pr – Prospective; R - Retrospective

Table II. QUADAS criteria(9) for included studies\*

Study	1	2	3	4	5	6	7	8	9	10	11	12	12	14	Total
Kreusch 1996	UC	UC	UC	UC	UC	UC	UC	UC	UC	N	UC	UC	N	N	0
Argenziano 2004	N	Y	Y	UC	Y	Y	UC	Y	N	UC	UC	N	N	N	5
Giacomel 2005	UC	N	Y	UC	Y	Y	UC	Y	N	UC	UC	Y	N	N	5
Demirtasoglu 2006	UC	N	Y	UC	Y	Y	UC	Y	N	UC	UC	Y	N	N	5
Scalvenzi 2008	Y	Y	Y	UC	Y	Y	UC	Y	N	UC	UC	Y	N	N	7
Chan 2008	UC	Y	Y	UC	N	N	UC	Y	N	Y	UC	UC	Y	Y	6
Tabanlıoglu Onan 2010	Y	Y	Y	UC	Y	Y	UC	Y	N	UC	UC	Y	N	Y	8
Altamura 2010	UC	N	Y	UC	Y	Y	UC	UC	N	UC	UC	N	N	N	3
Sakakibara 2010	UC	N	Y	UC	Y	Y	UC	N	N	UC	UC	UC	N	N	3
Liebman 2011	Y	N	Y	UC	Y	Y	UC	Y	N	UC	UC	UC	N	Y	6
Balagula 2011	Y	N	Y	UC	Y	Y	UC	N	N	Y	UC	Y	N	N	6
Micantonio 2011	Y	Y	Y	UC	Y	Y	UC	N	N	UC	UC	UC	N	N	5
Liebman 2012	UC	UC	Y	UC	Y	Y	UC	Y	N	UC	UC	N	N	Y	5
Trigoni 2012	UC	N	Y	UC	UC	UC	UC	Y	N	UC	UC	UC	N	N	2
Verduzco-Martinez 2013	UC	Y	Y	UC	Y	Y	Y	Y	Y	Y	Y	N	N	N	9
Lallas 2013 (1)	UC	Y	Y	UC	Y	Y	UC	Y	Y	UC	UC	UC	Y	Y	8
Lallas 2013 (2)	UC	Y	Y	UC	Y	Y	UC	Y	N	N	UC	N	Y	N	6
Longo 2014	UC	Y	Y	UC	Y	Y	UC	Y	N	UC	UC	N	N	N	5
Seidenari 2014	UC	N	Y	Y	Y	Y	UC	Y	N	Y	UC	N	N	N	6
Zivkovic 2014	UC	UC	Y	UC	Y	Y	UC	Y	N	UC	UC	UC	N	N	4
Popadic 2015 (1)	UC	UC	Y	UC	Y	Y	UC	Y	N	N	UC	Y	N	N	5
Popadic 2015 (2)	Y	Y	Y	UC	Y	Y	UC	Y	Y	UC	UC	Y	N	N	8
Suppa 2015	Y	UC	Y	UC	Y	Y	UC	Y	N	UC	UC	UC	N	N	5
Emiroglu 2015	UC	N	Y	UC	Y	Y	UC	Y	N	UC	UC	UC	N	N	4
Kim 2015	UC	Y	Y	UC	Y	Y	UC	Y	Y	UC	UC	UC	Y	Y	8
Elwan 2015	UC	Y	Y	Y	Y	Y	UC	Y	N	Y	UC	Y	Y	N	9
Ahnlide 2016	Y	Y	Y	Y	Y	Y	UC	Y	Y	Y	UC	Y	Y	Y	12



Navarrete-Dechent 2016	Y	Y	Y	UC	Y	Y	UC	Y	N	Y	UC	N	N	Y	8
Romano 2016	UC	UC	Y	UC	Y	Y	UC	UC	UC	UC	UC	UC	Y	Y	5
Wolner 2018	Y	Y	Y	UC	Y	Y	UC	Y	N	UC	UC	UC	Y	Y	8
Papageorgiou 2018	UC	Y	Y	UC	Y	Y	UC	Y	N	Y	UC	N	N	N	6

N – No; UC – unclear; Y – Yes

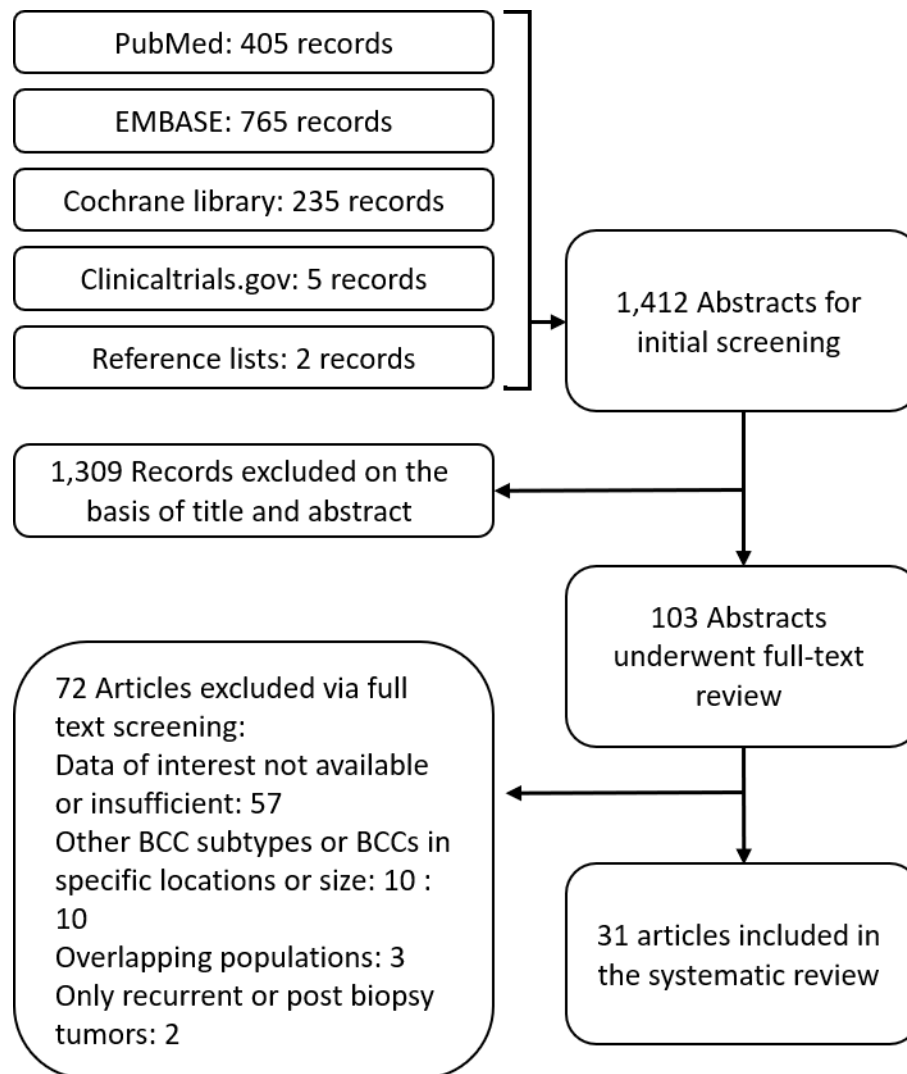
1. Was spectrum of patients representative of patients who will receive the test in practice?
2. Were selection criteria clearly described?
3. Is the reference standard likely to correctly classify the target condition?
4. Is the time period between the reference standard and index test short enough to be reasonably sure the target did not change between tests?
5. Did the whole sample or a random selection of the sample receive verification using a reference standard of diagnosis?
6. Did patients receive the same reference standard regardless of the index test result?
7. Was the reference standard independent of the index test?
8. Was the execution of the index test described in sufficient detail to permit replication?
9. Was the execution of the reference standard described in sufficient detail to permit replication?
10. Were the index test results interpreted without knowledge of the results of the reference standard?
11. Were the reference standard results interpreted without knowledge of the results of the index test?
12. Were the same clinical data available when the test results were interpreted as would be available in practice?
13. Were uninterpretable/intermediate test results reported?
14. Were withdrawals from the study explained?

Table III. Dermoscopic features prevalence among BCC and its subtypes

	Feature	BCC		Nodular BCC		Superficial BCC		Infiltrative BCC		Morpheaform BCC		Non-pigmented BCC		Pigmented BCC	
		N	ES	N	ES	N	ES	N	ES	N	ES	N	ES	N	ES
Pigmented structures	Large blue-grey ovoid nests	14	0.34 (0.27, 0.42)	12	0.36 (0.25, 0.47)	15	0.14 (0.07, 0.23)	7	0.21 (0.13, 0.31)	6	0.13 (0.0, 0.39)	3	0.02 (0.0, 0.12)	9	0.48 (0.35, 0.61)
	Multiple blue-grey dots and globules	13	0.34 (0.28, 0.41)	11	0.26 (0.17, 0.35)	14	0.27 (0.21, 0.34)	6	0.28 (0.18, 0.39)	5	0.05 (0.0, 0.19)	3	0.02 (0.0, 0.12)	9	0.38 (0.23, 0.55)
	Multiple in focus blue-grey dots and globules	6	0.17 (0.06, 0.32)	5	0.13 (0.07, 0.22)	5	0.18 (0.13, 0.25)	4	0.07 (0.02, 0.14)	3	0.01 (0.0, 0.16)	2	0.0 (0.00, 0.01)	2	0.23 (0.20, 0.27)
	Leaf-like areas	13	0.15 (0.12, 0.18)	11	0.06 (0.02, 0.10)	14	0.25 (0.18, 0.33)	6	0.04 (0.0, 0.10)	5	0.0 (0.0, 0.01)	3	0.0 (0.0, 0.0)	9	0.27 (0.16, 0.39)
	Spoke wheel areas	11	0.08 (0.07, 0.09)	10	0.03 (0.01, 0.05)	11	0.10 (0.06, 0.15)	6	0.02 (0.0, 0.06)	5	0.0 (0.0, 0.03)	2	0.0 (0.0, 0.01)	7	0.13 (0.04, 0.25)
	Concentric structures	6	0.10 (0.07, 0.13)	5	0.05 (0.03, 0.07)	6	0.14 (0.09, 0.20)	4	0.08 (0.04, 0.13)	2	0.0 (0.0, 0.08)	1	0.0 (0.00, 0.04)	1	0.09 (0.07, 0.12)
Vascular structures	Arborizing vessels	16	0.59 (0.53, 0.65)	12	0.75 (0.69, 0.82)	16	0.21 (0.13, 0.30)	6	0.76 (0.59, 0.90)	5	0.51 (0.26, 0.77)	4	0.63 (0.43, 0.81)	11	0.55 (0.45, 0.65)
	Short fine telangiectasias	12	0.32 (0.22, 0.43)	10	0.17 (0.08, 0.28)	14	0.60 (0.51, 0.69)	5	0.40 (0.27, 0.53)	4	0.24 (0.0, 0.61)	4	0.55 (0.27, 0.81)	6	0.20 (0.05, 0.42)
	Dotted vessels	1	0.01 (0.00, 0.06)	0	--	1	0.18 (0.13, 0.34)	0	--	0	--	0	--	0	--
	Polymorphous vessels	3	0.12 (0.00, 0.42)	1	0.07 (0.03, 0.12)	1	0.10 (0.07, 0.13)	0	--	0	--	1	0.38 (0.31, 0.46)	2	0.23 (0.19, 0.28)
	Hairpin vessels	4	0.06 (0.02, 0.12)	2	0.08 (0.06, 0.12)	5	0.16 (0.07, 0.26)	0	--	0	--	1	0.15 (0.11, 0.19)	2	0.01 (0.0, 0.03)
	Corkscrew vessels	1	0.33 (0.25, 0.41)	2	0.05 (0.03, 0.08)	2	0.05 (0.03, 0.07)	0	--	0	--	1	0.19 (0.08, 0.36)	1	0.38 (0.28, 0.48)
	Glomerular vessels	2	0.06 (0.04, 0.08)	2	0.06 (0.04, 0.09)	4	0.07 (0.03, 0.13)	0	--	0	--	0	--	1	0.0 (0.0, 0.03)
Other	Shiny white structures	6	0.49 (0.40, 0.58)	3	0.43 (0.26, 0.61)	6	0.43 (0.22, 0.66)	1	1.0 (0.29, 1.00)	2	0.41 (0.18, 0.66)	2	0.42 (0.37, 0.46)	2	0.31 (0.24, 0.38)
	Rosettes	2	0.13 (0.10, 0.17)	1	0.01 (0.0, 0.04)	1	0.02 (0.01, 0.05)	0	--	0	--	1	0.07 (0.04, 0.11)	0	--
	Shiny white-red structureless areas	7	0.40 (0.28, 0.54)	8	0.24 (0.12, 0.39)	11	0.79 (0.64, 0.91)	4	0.39 (0.23, 0.57)	4	0.29 (0.12, 0.50)	1	1.00 (0.90, 1.00)	3	0.28 (0.0, 0.74)
	ulceration	11	0.08 (0.07, 0.09)	10	0.31 (0.20, 0.44)	14	0.23 (0.13, 0.35)	6	0.44 (0.26, 0.62)	4	0.58 (0.09, 0.99)	3	0.38 (0.27, 0.50)	8	0.37 (0.28, 0.48)
	multiple small erosions	7	0.20 (0.12, 0.29)	7	0.10 (0.04, 0.18)	10	0.43 (0.31, 0.54)	5	0.19 (0.08, 0.32)	3	0.06 (0.0, 0.38)	1	0.08 (0.03, 0.15)	2	0.09 (0.06, 0.11)
	Blue-white veil	5	0.10 (0.01, 0.26)	3	0.11 (0.0, 0.29)	3	0.06 (0.03, 0.10)	1	0.0 (0.0, 0.46)	1	0.0 (0.0, 0.98)	0	0.0 (0.0, 0.04)	4	0.19 (0.03, 0.42)

N – Number of studies; ES – Effect size;

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### **Capsule Summary**

- The prevalence of dermoscopic features in basal cell carcinoma (BCC) and its subtypes has not been systematically studied.
- Even though not as well-known as arborizing vessels, shiny white structures are an important feature of BCC and its subtypes. Different constellations of dermoscopic features aid in the differentiation between BCC subtypes.