

Review Article

Dermoscopy of non-pigmented skin lesions: a literature review

文獻綜述：非色素性皮膚病變的皮膚鏡檢查

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In this article, we will review benchmark dermoscopic features of non-pigmented skin lesions used in the diagnosis of amelanotic melanoma, basal cell carcinoma and other non-pigmented lesions, described in previous literature. We will also evaluate the six common vascular patterns observed via dermoscopy, while discussing the relevant associations.

在本文中，我們將回顧以往文獻所描述的非色素性皮膚病變的皮膚鏡基準特徵，用於診斷無黑色素性黑素瘤、基底細胞癌和其他非色素性的皮膚病變。我們還將評估皮膚鏡下觀察到的六種常見血管模式，並討論其相關聯繫。

Keywords: Amelanotic melanoma, basal cell carcinoma, dermatoscopy, dermoscopy, non-pigmented skin lesion

關鍵詞：無黑色素性黑素瘤、基底細胞癌、皮膚鏡檢查、皮膚鏡檢查、非色素性皮膚病變

Introduction

Dermoscopy is a non-invasive technique combining digital photography and light microscopy for *in vivo* observation and diagnosis

of pigmented and non-pigmented skin lesions.^{1,2} Dermoscopy is being used increasingly in general dermatology as an adjunct to clinical examination, as it allows recognition of vascular structures and other subtle features that are usually not visible to the unaided eye.³

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There are four main types of dermoscopy: classical dermoscopy (for pigmented and non-pigmented skin tumours), entomodermoscopy (for skin infections and infestations), inflamoscopy (for inflammatory skin disorders), and trichoscopy (for hair and scalp disorders).⁴ The improved visualisation of surface and sub-surface structures obtained with classical dermoscopy allows the recognition of morphological structures within lesions, improving the accuracy of diagnosis without requiring lesion biopsy for histological

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confirmation.⁵ Trichoscopy, also performed with a handheld dermoscope, is a simple and efficient method to visualise hair shafts, hair follicular openings and perifollicular epidermis, in diagnosing patients with hair loss or scalp diseases.⁶

Pigmented lesions are traditionally considered less difficult to diagnose for various reasons. Soyer et al (2004) presented a 3-point checklist of dermoscopic criteria for pigmented lesions, including asymmetry, atypical network, and blue-white structures.⁷ Non-pigmented lesions, however, present a new set of challenges for the treating physician.

Amelanotic melanoma and basal cell carcinoma are non-pigmented lesions that often have delayed clinical diagnoses, because their clinical appearance can mimic other benign hypopigmented skin conditions, including dermal naevi, seborrheic keratoses and dermatofibromas.

In this review article we present a pertinent overview on dermoscopy of non-pigmented benign and malignant neoplastic skin lesions.

Materials and methods

A comprehensive literature search was carried out, following the PRISMA 27 point checklist, and taking into consideration the guidance offered by the Cochrane Collaboration. We completed a review of PubMed, Embase, MEDLINE and the Cochrane Library, from 1995 to July 2016. We used the search terms "dermoscopy" and "non-pigmented". This returned 312 articles. Screening of the title and abstract was carried out by one of the authors (ST), which helped identify the relevant articles. From these, an additional search was performed through reference lists of the retrieved articles. Our search yielded thirty-three articles for our review of dermoscopy of non-pigmented skin lesions.

Results

Thirty-six studies matched the search criteria and were included in our review. Nine studies looked at general dermoscopy of non-pigmented skin lesions. Four studies focused on dermoscopy of basal cell carcinoma, and five studies assessed dermoscopy of amelanotic melanoma. Two studies assessed vascular structures associated with certain skin tumours, and two papers looked at dermoscopy of actinic keratosis, intraepidermal carcinoma, or squamous cell carcinoma. Two papers assessed dermoscopy of dermatofibromas, and the final paper looked at dermoscopy of seborrheic keratosis.

Based on our review of the literature, we will now summarise the relevant dermoscopic features of the following malignant and benign skin conditions: basal cell carcinoma, amelanotic melanoma, actinic keratosis, intraepidermal carcinoma, squamous cell carcinoma, keratoacanthoma, seborrheic keratosis and dermatofibroma.

Basal cell carcinoma (BCC)

Basal cell carcinoma is a locally aggressive but rarely metastatic form of skin cancer.⁸ It originates in the basal layer of the epidermis, and typically presents as a "pearly papule" to the unaided eye.

Argenziano et al (2003) reported arborising vessels, leaf-like structures, large blue-grey ovoid nests, multiple blue-grey globules, spoke wheel areas, and ulceration as features seen dermoscopically in basal cell carcinoma.⁹ Soyer et al (2001) in an algorithm for basal cell carcinoma, gave the dermoscopic criteria of leaf-like areas, arborising vessels, and irregular blue-grey globules.¹⁰ Altamura et al (2010) added further criteria in the diagnosis of superficial basal cell carcinoma: short fine superficial telangiectasia, and multiple small erosions (possibly signifying early stages of an erosion).¹¹

Dermoscopic diagnosis of BCC is more sensitive than macroscopic observation, and classically shows bright arborising telangiectasias, pink colour and focal ulcerations.¹² Dermoscopy can also be useful for observing pigmentation in clinically undetectable pigmented BCC, as shown in Figure 1.¹³

Pigmented BCCs typically have loosely arranged blue-grey globules. Leaf-like areas and spoke-wheel areas are increased in pigmented basal cell carcinomas compared with non-pigmented basal cell carcinomas. Menzies et al (2000) suggested that pigmented BCC should not have the negative feature of a pigment network, and should have one or more of the following six positive features: large grey-blue ovoid nests, multiple grey-blue globules, maple leaf-like areas, spoke-wheel areas, ulceration, and arborising 'treelike' telangiectasia (see Figure 2).⁹



Figure 1. Nodular BCC. This dermoscopy image of a clinically rather small nodular BCC displays a typical arborising vascular pattern. In addition, there are numerous blue-grey ovoid nests. Remarkably, despite the clear presence of small pigmented nests dermoscopically, this lesion was not pigmented clinically.

Heavily pigmented BCCs can show the most challenging combinations of dermoscopic features.¹⁴ Any of the clinical sub-types of basal cell carcinomas may present as a pigmented lesion, and this becomes more likely in individuals of darker Fitzpatrick skin types.

Based on these articles, the following dermoscopic criteria diagnostic for basal cell carcinoma are listed in Table 1.

Amelanotic melanoma

Amelanotic melanoma is a potentially lethal form of skin cancer, and represents 2-8% of all melanomas.¹⁵ Diagnosis of this lesion can pose a challenge even to the experienced physician. Menzies et al (2008) reported that non-pigmented melanomas had a dermoscopic sensitivity of 75%, compared to 90% for pigmented melanomas.¹⁶

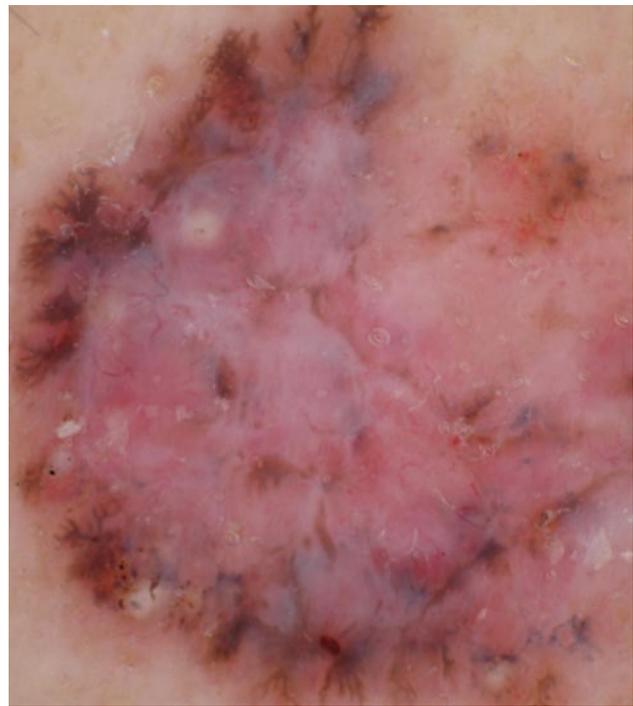


Figure 2. Pigmented BCC. This pigmented BCC reveals several rather classical leaf-like structures on the left margin. The typical arborising vessels cannot be observed, and the differential diagnosis of course includes a hypomelanotic melanoma.

A history of change within an "odd-looking" pink lesion should raise a level of concern. Focal, faint tan irregular pigmentation around the periphery of the lesion is common. Polymorphous or dotted vessels may be present, and milky pink to red areas may be noted (Figures 3 and 4).¹⁷ A pink to white veil or inverse network may also be seen. Steglich et al (2012) suggested vascular polymorphism, globules and

milky-red areas, chrysalis and multiple blue-grey dots indicate amelanotic malignant melanoma (Table 2).¹⁸

Any non-pigmented lesion, regardless of pattern analysis, which is raised and firm, for which a specific benign diagnosis cannot be made, should be excised to exclude the nodular variant of amelanotic melanoma.¹⁹

Table 1. Dermoscopic criteria, and their definition, observed in basal cell carcinoma (BCC)

Criteria	Definition	Sensitivity*
Arborising telangiectasias	Telangiectasias with tree and branch-like structures	57%
Blue-grey ovoid nests	Well circumscribed, near ovoid areas, not connected to pigment body	48%
Leaf-like structures	Brown, grey or blue extensions of pigment forming leaf-like structures	16%
Spoke-wheel areas	Tan, blue or grey, well circumscribed radial projections	9%
Ulcerations	Larger atraumatic loss of epidermis	39%
Short fine superficial telangiectasia**	Sharply focused, small calibre, irregularly dispersed vessels	10%
Focal ulcerations**	Atraumatic deprivation of epidermis in small area	9%

*The sensitivity values are cited from Altamura et al, 2010.

**These two criteria are characteristic of superficial BCC (Altamura et al, 2010).

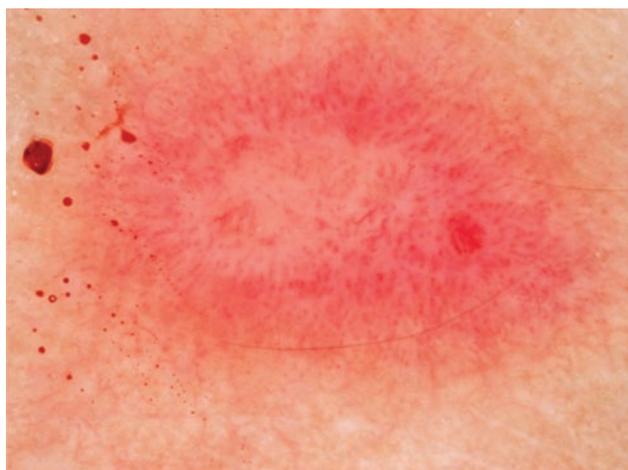


Figure 3. Amelanotic melanoma. This amelanotic superficial melanoma is characterised by numerous polymorphous vessels, some of which are dotted while others are linear irregular. Please note that in such cases a benign Spitz naevus is another differential diagnosis.

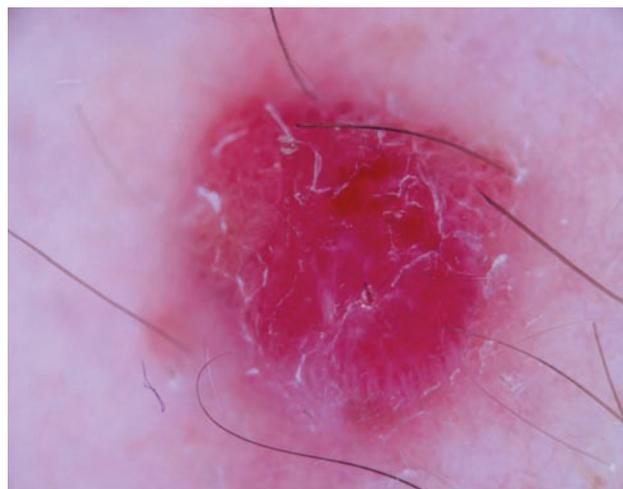


Figure 4. Amelanotic melanoma. This is another example of an amelanotic nodular melanoma located pretibial in a 26-year-old female, with no familial or personal history of melanoma (case reported by Curchin et al, 2012). The dermoscopy image reveals a subtle ulceration in the upper right quarter of the lesion. Otherwise just a few polymorphous vessels are noted in the lower part of the lesion.

Actinic keratosis / intra-epidermal carcinoma / squamous cell carcinoma / keratoacanthoma

In 2014, Zalaudek et al looked at dermoscopic differences between actinic keratosis, intraepidermal carcinoma, and squamous cell carcinoma.²⁰ Actinic keratoses, a common lesion in fair-skinned, sun exposed populations, presents dermoscopically as a strawberry pattern, red pseudo-network, surface scale, and surrounding erythema. Dotted or glomerular vessels, diffuse yellow opaque scales, and micro-erosions are found significantly more with intra-epidermal carcinoma. Facial non-pigmented actinic keratoses also show background erythema accentuated by a reddish pseudonetwork, and

prominent hair follicle openings surrounded by a white halo.²¹

Dermoscopic examination of non-pigmented intraepidermal carcinoma (Bowen disease) generally reveals numerous glomerular vessels distributed evenly throughout the lesion, and occasional scales.²² Hairpin vessels, linear-irregular vessels, targetoid hair follicles, white structureless areas, central keratin mass and ulceration were more associated with squamous cell carcinoma (which also had similar dermoscopic findings to keratoacanthomas).

Rosendahl et al (2012) compared dermoscopic findings between squamous cell carcinoma and

Table 2. Dermoscopic criteria for amelanotic melanoma

Criteria	Definition	Histopathologic substrate	Sensitivity*	Specificity*
Asymmetrical peripheral streaks of pigment	Focal faint tan pigmentation around periphery of lesion	Discrete nests of pigmented junctional nests of melanocytes	75%	46%
Polymorphous vessels (dotted and linear irregular)	Different vascular morphologies in the same lesion	Neovascularisation of tumour structure	30%	85%
Predominant central vessels	Main visible vessel structures are central in the lesion	Neovascularisation of tumour structure	16%	94%
Milky pink to red areas	Hazy, milky pink to red areas	Lack of melanin in tumour cells or scar related regression	51%	71%
Irregular dots/globules	Small dark dots or globules throughout lesion	Collections of melanocytes/melanin in epidermis (black) or dermis (brown)	24%	91%
Irregularly shaped depigmentation	Asymmetrical loss of pigment	Decreased melanin in epidermis or dermis	23%	94%
Blue/white veil	Irregular structureless area of blue pigment with a ground-glass haze	Acanthotic epidermis overlying melanin containing area of dermis	11%	99%
>3 milia-like cysts (negative predictor)	White or yellowish dots, more likely seen in seborrheic keratosis	Intraepidermal horn globules	1%	90%

*The sensitivity and specificity values of the criteria are cited from Menzies et al, 2008.

keratoacanthoma, finding that central keratin was more common in keratoacanthomas, but could be found in either lesion.²³

Seborrheic keratoses

Seborrheic keratoses are a common skin tumour among elderly populations, with milia-like cysts, comedo-like openings, fissures and ridges, brown circles, and sharp demarcation (see Figure 5).²⁴ Although seborrheic keratoses are often diagnosed clinically, flat pigmented lesions may mimic lentigo maligna clinically, making dermoscopy more useful in such situations.

Dermatofibroma

Dermatofibromas are a common, benign fibrohistiocytic mesenchymal growth of skin with an unclear aetiology.²⁵ They present dermoscopically with a white central patch (hypopigmentation), and delicate light brown network (brown circles), as shown in Figure 6.²⁶

The six vascular dermoscopic patterns

Soyer et al (2001) discussed the vascular structures seen via dermoscopy, along with their diagnostic significance.²⁷ Comma vessels were mainly seen in melanocytic naevi, especially dermal naevi, but rarely in melanoma. Arborising vessels were described as being commonly seen in basal cell carcinoma, but rarely in naevi, melanoma or seborrheic keratosis. Hairpin vessels were seen more commonly in melanomas and seborrheic keratosis, along with other various lesions. Dotted vessels were reported in all types of melanocytic tumours, but rarely in basal cell carcinomas. Linear irregular vessels were reported as common in melanomas, particularly with Breslow thickness greater than 0.75 mm. Vessels within regression structures may also indicate a white area of regressive melanoma.

Argenziano et al (2004) also described six different vascular structures seen by dermoscopy, and evaluated their association with various melanocytic and non-melanocytic skin tumours in

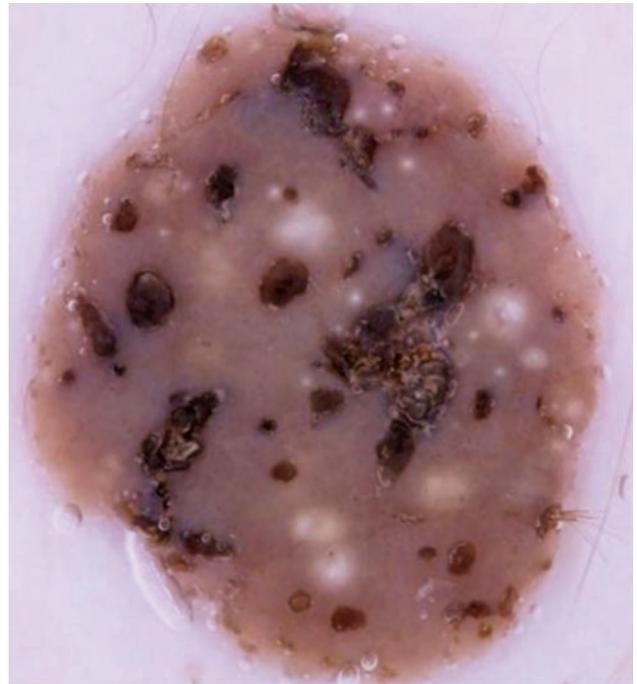


Figure 5. Seborrheic keratoses. This is a simple seborrheic keratosis of the acanthotic type, exhibiting several comedo-like openings and milia-like cysts. In a case like this, basically no other differential diagnosis needs to be considered.

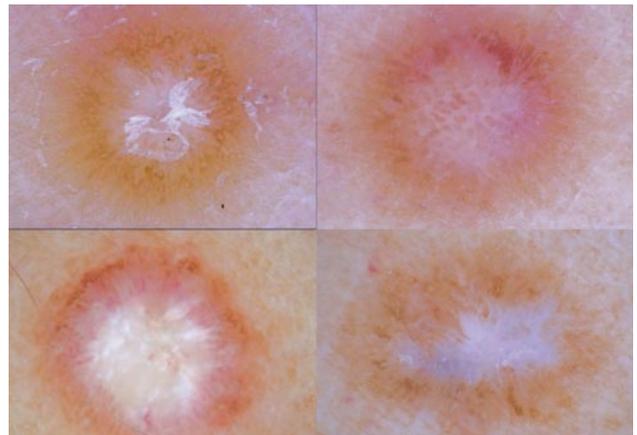


Figure 6. Variants of dermatofibroma. This composite figure well demonstrates the variation on the theme of central white scar-like patch, representing a classical dermoscopic clue for dermatofibroma (Ferrari et al, 2000).

a large series of cases (see Table 3).²⁸ The authors found that arborising vessels were seen in 82.1% of basal cell carcinomas, while comma vessels were significantly associated with dermal/congenital naevi, glomerular vessels with Bowen disease, crown vessels with sebaceous hyperplasia, and hairpin vessels with seborrheic keratosis.

Zalaudek et al (2010) suggested that hairpin, glomerular and arborising vessels are generally indicative of keratinocytic tumours, while comma, dotted and linear irregular vessels are more associated with melanocytic tumours.²⁹

Discussion

Dermoscopy of non-pigmented lesions is a simple, time-efficient and inexpensive method to improve patient safety and diagnostic certainty, and avoid excessive biopsies.³⁰

Whilst being aware that dermoscopy has limitations, and is inferior to histopathological

diagnosis, adequately skilled clinicians can utilise simple checklists to: assess overall patterns cognitively, compare naevi for any ugly ducklings, and compare with former digital images for recent change.³¹

While the "ugly duckling" sign may be the principle method of diagnosing melanoma, Pizzichetta et al (2004) noted that irregular pigmentation, irregular dots or globules, regression structures, and a blue-whitish veil, as well as vascular patterns such as milky-red areas or linear irregular vessels, were useful in distinguishing amelanotic melanoma from other lesions.^{32,33}

In amelanotic melanoma, vascular patterns alone may be insufficient to diagnose melanoma because dotted, arborising, hairpin vessels and even milky-red areas have also been found in common naevi, BCC, and seborrheic keratosis.³³

Some feature-poor melanomas remain difficult to diagnose, even with the assistance of dermoscopy.³⁴ Erring towards caution and biopsy for histopathological confirmation, when unable

Table 3. Common vascular patterns observed in dermoscopy

Structure	Description	Diagnosis	Significance
Comma vessels	Single parentheses like structured vessel	Dermal naevi	Rarely seen in melanoma
Arborizing vessels	Telangiectasias with larger tree and connected finer branch like structures	Basal cell carcinoma (BCC)	Highly significant for BCC
Hairpin vessels	Horse-shoe like vessel structure	Squamous cell carcinoma, keratoacanthoma, seborrheic keratoses	In seborrheic keratoses are more uniformly distributed
Dotted vessels	Multiple pin-head like dots	Seen in melanoma, spitz naevus, dermatofibroma, clear cell acanthoma	Seen in melanoma but nonspecific
Linear irregular vessels	Long vessel structure with irregular kinking	Melanoma, squamous cell carcinoma, melanoma metastasis	Common to various neoplastic lesions, particularly melanoma
Glomerular vessels	Large reddish dots of curled up individual capillaries	Intraepidermal carcinoma	Significant for intraepidermal carcinoma

to dermoscopically exclude amelanotic melanoma, is a safe approach.

Conclusion

Dermoscopy is a key tool in the diagnosis of non-pigmented skin tumours, and requires recognition of simple structures and patterns assisting in the categorisation of neoplastic skin lesions. Using dermoscopy to distinguish basal cell carcinoma, amelanotic melanoma and other sinister non-pigmented lesions from more benign lesions is a pragmatic, simple method to reduce unnecessary biopsy, and improve clinician diagnostic certainty. Adequate training of clinicians in identifying these lesions via key structure recognition further improves patient satisfaction and outcomes.

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