BJD
British Journal of Dermatology

Advances in the diagnosis of pigmented skin lesions

DOI: 10.1111/bjd.16109

Early detection of skin cancer allows timely treatment and improves clinical outcome. The armamentarium for diagnosing skin cancer has been growing notably over the last decades. New tools have led to earlier recognition and a more specific and sensitive diagnosis. In this editorial, we discuss several recent studies published in the *BJD* on the diagnosis of pigmented skin lesions.

The majority of studies published on the detection of skin cancer have investigated methods that are already widely accepted and increasingly used in dermatology, such as dermatoscopy, reflectance confocal microscopy (RCM) and teledermatology. Other investigators have walked off the beaten paths and reported unconventional findings, for example Willis *et al.* investigated a dog's olfactory ability to discriminate melanoma from control skin lesions.[1] In this study, a Labrador, named Ronnie, performed 20 double-blind tests, each requiring the selection of one melanoma from nine controls, consisting of three each of basal cell carcinomas, naevi and healthy skin. Ronnie correctly identified the melanoma on nine occasions (45%), vs. two expected by chance alone. This creative work demonstrates that invasive melanoma emits volatile organic compounds that differ from those of control lesions. The volatile compounds might be utilized as new biomarkers for a noninvasive diagnosis of melanoma using standardized biochemical assays.

In recent decades, dermatoscopy has developed to a state-of-the-art method for evaluating pigmented skin lesions. Devices have become more affordable, and their use has not only been implemented into the clinical routine of dermatologists, but has also expanded to other areas of medicine such as general practice. Australian general practitioners (GPs) were at the forefront, because of the medical need to establish a nationwide screening programme in a country with a very high incidence of melanocytic and keratinocytic cancers. It was shown that if subspecialized in recognizing skin cancer, not only dermatologists, but also GPs, increase their diagnostic accuracy using dermatoscopy.[2]

Comparable data regarding the implementation of dermatoscopy into primary care have been lacking in Europe, but a study from Chappuis *et al.* provided first insights.[3] Primary care physicians in France, who are trained in dermatoscopy, refer fewer patients to skin cancer specialists and need fewer invasive interventions (i.e. biopsies) to find a melanoma. These findings highlight that dermatoscopy should no longer be an instrument for dermatologists, but – similarly to the stethoscope – should be taught to every medical student. Such studies have a considerable socioeconomic impact, as widespread use of dermatoscopy by primary care physicians may lower the burden of unnecessary biopsies and referrals to specialists.

Site-specific architectural characteristics of the skin determine the dermatoscopic criteria for assessing skin lesions. For example, the evaluation of pigmented lesions on acral skin is dominated by the dogma that pigment in the fissures is associated with benign lesions (parallel furrow pattern), whereas pigment on the ridges is predictive of melanoma (parallel ridge pattern). However, up to one-third of acral melanomas do not adhere to the parallel ridge pattern and additional criteria are necessary. To improve the diagnostic criteria for pigmented lesions on acral skin, Lallas *et al.*[4] presented the 'BRAAFF' score, which is calculated according to Table 1. Lesions with a total BRAAFF score ≥ 1 are suspicious for melanoma. The BRAAFF score is intentionally kept simple and memorable, and is expected to improve significantly the diagnostic accuracy for pigmented lesions on acral skin.

Just as the evaluation of skin lesions at special anatomical sites can be demanding, some melanoma subtypes are particularly challenging to diagnose. Naevoid melanoma is a rare histopathological subtype that can be difficult to diagnose, as its morphology often resembles that of a naevus. To increase the diagnostic accuracy of these lesions, Longo *et al.*[5] collected 27 naevoid melanomas with the corresponding clinical, dermatoscopic and histopathological data. The authors were able to distinguish three subtypes of naevoid melanomas: (i) lesions with multiple-component patterns that can be diagnosed using well-established dermatoscopic criteria; (ii) naevus-like tumours with a papillomatous surface, irregular dots/globules and atypical vessels; and (iii) amelanotic tumours characterized mainly by atypical vessels. The authors concluded that although only the first subgroup of naevoid melanoma meets the standard melanoma criteria in dermatoscopy (multiple-component pattern), many naevoid melanomas show atypical vessels. Lesions with atypical vascular structures and irregular dots/globules should prompt consideration for a naevoid melanoma.

Table 1 BRAAFF scoring system for pigmented lesions

Irregular blotch	+1
Parallel ridge pattern	+3
Asymmetry of structures	+1
Asymmetry of colours	+1
Parallel furrow pattern	−1
Fibrillar pattern	−1

Lesions scoring ≥ 1 are suspicious for melanoma.

Nodular melanomas represent approximately 20% of all melanomas and play a significant role in global skin cancer mortality. Pigmented nodular melanomas are usually easy to diagnose, but when they appear nonpigmented and symmetrical, they are sometimes mistaken for benign melanocytic lesions or nonmelanocytic skin neoplasms. Delay in diagnosis and treatment may have serious consequences. Pizzichetta and colleagues[6] set out to redefine their dermatoscopic features, which are often different from those of other melanoma subtypes such as superficial spreading melanoma, acral melanoma and lentigo maligna melanoma. In Pizzichetta's study,[6] nodular melanoma frequently showed (i) ulceration, (ii) asymmetric pigmentation, (iii) blue-black pigmented areas, (iv) reddish homogeneous or structureless asymmetry and (v) abnormal vascular structures. This work refined the dermatoscopic features that are associated with nodular melanoma compared with other melanoma subtypes and nonmelanocytic lesions. Although these new dermatoscopic characteristics will help to diagnose nodular melanoma more accurately, it should be emphasized that all growing nodular lesions with an uncertain clinical diagnosis should always be immediately biopsied.

Despite remarkable progress in increasing the diagnostic accuracy of pigmented and nonpigmented skin lesion using dermatoscopy, a minority of lesions still remain ambiguous. One option to increase diagnostic accuracy is to monitor ambiguous lesions with digital dermatoscopy.[6] In digital dermatoscopy, ambiguous lesions are photographed at the initial visit and compared side by side at the follow-up visits. While the majority of naevi are stable, malignant lesions usually change over time. However, digital dermatoscopy has the disadvantage that excision is delayed and potentially malignant lesions may progress – or even metastasize – until the follow-up visit. In particular, pigmented skin lesions in adults with a pattern of clods have the risk of be faster-growing melanomas, and therefore a decision regarding their malignancy should be made at the initial visit rather than at follow-up.[7]

To improve further the diagnostic accuracy of dermatoscopically ambiguous lesions, several groups have started to use RCM. The analysis of globular patterns by RCM was initially described by Ahlgrimm-Siess *et al.*,[8] and has more recently been applied to distinguish melanomas from naevi. Benati *et al.*[9] found that dense nests in RCM, together with a regular globular pattern in dermatoscopy, are suggestive for a naevus. In contrast, loosely arranged nests in RCM, together with irregular distribution of globules in dermatoscopy, favours the diagnosis of a melanoma and should prompt excision.

Another group of lesions that frequently cause diagnostic problems is spitzoid pigmented skin lesions. Guida *et al.*[10] used RCM to differentiate Spitz naevi from melanomas. Spindled cells and peripheral clefting were found exclusively in Spitz naevi, whereas melanoma exhibited striking atypical cells or nests within the epidermis or the dermoepidermal junction. As a caveat, Spitz and Reed naevi were grouped together in this study, but according to other groups they should be investigated as separate categories.[11]

In summary, these studies indicate that combined approaches of dermatoscopy and RCM might increase diagnostic accuracy for melanocytic lesions. To avoid missing a melanoma, clinicians should carefully analyse melanocytic lesions with complementary approaches such as clinical evaluation, dermatoscopy and RCM.

Dermatology is a discipline that is based mainly on visual inspection of the skin and is therefore well suited for telemedicine. With the advancements in telecommunication and smartphone technologies, telemedicine has several advantages for physicians and patients, such as reduced travel and waiting time, broader access to care and efficient referral to specialists. However, there are also disadvantages, most importantly the lack of direct interaction between patients and doctors.

Horsham *et al.*[12] studied patients' acceptance rate of mobile teledermatology to detect melanoma early. In this study, patients at high risk for melanoma photographed their pigmented skin lesions at their homes. Approximately 90% of the participants agreed that this teledermatology approach was easy to use and that it improved their self-examination performance. However, nearly half of the patients did not completely trust the diagnosis, and approximately 20% had difficulties in taking pictures in areas difficult to reach. The authors concluded that teledermatology is easy to use and that its acceptance rate is high, but also that many patients do not entirely trust this new technology.

In recent years, a large number of smartphone applications ('apps') have become available that aim to prevent or detect melanoma. These apps are intended to be used either by patients or by healthcare professionals (dermatologists, GPs, specialized nurses), but experts are concerned regarding their safety and diagnostic utility. Kassianos and colleagues[13] identified close to 40 apps focusing on pigmented skin lesions for nonspecialist users (previously unaffected individuals, patients with previously diagnosed with skin cancer and GPs). The majority of these apps educate about melanoma, prevention of ultraviolet radiation exposure and skin self-examination strategies. Half of the apps enabled patients to capture and store images of their skin lesions, either for self-monitoring to identify morphological changes over time or for review by a dermatologist. Only four apps provided a risk assessment about a skin lesion. The authors concluded that although education and training to detect skin cancer are desirable, there is little evidence of clinical or research-based input into the design of these apps. Clinicians should be cautious about supporting the use of such apps.

Since dermatoscopy was described for the first time a century ago, it has developed into a central technique to diagnose melanoma. To meet its full potential, dermatoscopy should not be regarded as an instrument for specialized dermatologists, but rather as a tool for all physicians – similar to the stethoscope. However, training and experience are always required to master a tool, and in dermatoscopy the knowledge

of the particular diagnostic criteria at special anatomical sites and for less common subtypes of skin cancer is crucial. Soon, RCM might also give additional diagnostic clues and will likely develop into an ancillary diagnostic tool at specialized centres. The data obtained by these various techniques will probably be stored digitally for telemedicine and might also be analysed with computational algorithms to improve diagnostic accuracy further. Winston Churchill once said that 'it is always wise to look ahead, but difficult to look further than you can see'. This quote is, of course, also correct for the new developments in dermatology – the future will tell us which techniques will live up to their expectations and change the way we diagnose skin cancer.

Conflicts of interest

None declared.

Department of Dermatology, Medical University of Vienna, Waehringer Guertel 18–20, 1090 Vienna, Austria
P. Tschandl
T. Wiesner
E-mails: philipp.tschandl@meduniwien.ac.at, thomas.wiesner@meduniwien.ac.at

References

1 Willis CM, Britton LE, Swindells MA *et al.* Invasive melanoma *in vivo* can be distinguished from basal cell carcinoma, benign naevi and healthy skin by canine olfaction: a proof-of-principle study of differential volatile organic compound emission. *Br J Dermatol* 2016; **175**:1020–9.
2 Rosendahl C, Williams G, Eley D *et al.* The impact of subspecialization and dermatoscopy use on accuracy of melanoma diagnosis among primary care doctors in Australia. *J Am Acad Dermatol* 2012; **67**:846–52.
3 Chappuis P, Duru G, Marchal O *et al.* Dermoscopy, a useful tool for general practitioners in melanoma screening: a nationwide survey. *Br J Dermatol* 2016; **175**:744–50.
4 Lallas A, Kyrgidis A, Koga H *et al.* The BRAAFF checklist: a new dermoscopic algorithm for diagnosing acral melanoma. *Br J Dermatol* 2015; **173**:1041–9.
5 Longo C, Piana S, Marghoob A *et al.* Morphological features of naevoid melanoma: results of a multicentre study of the International Dermoscopy Society. *Br J Dermatol* 2015; **172**:961–7.
6 Pizzichetta MA, Kittler H, Stanganelli I *et al.* Pigmented nodular melanoma: the predictive value of dermoscopic features using multivariate analysis. *Br J Dermatol* 2015; **173**:106–14.
7 Beer J, Xu L, Tschandl P, Kittler H. Growth rate of melanoma *in vivo* and correlation with dermatoscopic and dermatopathologic findings. *Dermatol Pract Concept* 2011; **1**:59–67.
8 Ahlgrimm-Siess V, Massone C, Koller S *et al.* *In vivo* confocal scanning laser microscopy of common naevi with globular, homogeneous and reticular pattern in dermoscopy. *Br J Dermatol* 2008; **158**:1000–7.
9 Benati E, Argenziano G, Kyrgidis A *et al.* Melanoma and naevi with a globular pattern: confocal microscopy as an aid for diagnostic differentiation. *Br J Dermatol* 2015; **173**:1232–8.
10 Guida S, Pellacani G, Cesinaro AM *et al.* Spitz naevi and melanomas with similar dermoscopic patterns: can confocal microscopy differentiate? *Br J Dermatol* 2015; **174**:610–6.
11 Bär M, Tschandl P, Kittler H. Differentiation of pigmented Spitz nevi and Reed nevi by integration of dermatopathologic and dermatoscopic findings. *Dermatol Pract Concept* 2012; **2**:1–12.
12 Horsham C, Loescher LJ, Whiteman DC *et al.* Consumer acceptance of patient-performed mobile teledermoscopy for the early detection of melanoma. *Br J Dermatol* 2016; **175**:1301–10.
13 Kassianos AP, Emery JD, Murchie P, Walter FM. Smartphone applications for melanoma detection by community, patient and generalist clinician users: a review. *Br J Dermatol* 2015; **172**:1507–18.