Recent advances in diagnosing cutaneous melanomas
Elisabeth MT Wurm, Claudia ES Curchin and H Peter Soyer*

Address: Dermatology Research Centre, The University of Queensland, School of Medicine, Princess Alexandra Hospital, 199 Ipswich Road, Brisbane, QLD 4102, Australia
* Corresponding author: H Peter Soyer (p.soyer@uq.edu.au)

Abstract
Early detection of lesions while minimising the unnecessary removal of benign lesions is the clinical aim in melanoma diagnosis. In this context, several non-invasive diagnostic modalities, such as dermoscopy, total body photography, and reflectance confocal microscopy have emerged in recent years aiming at increasing diagnostic accuracy. The main developments in this field are the integration of dermoscopy and digital photography into clinical practice.

Introduction and context
Successful treatment of melanoma, by surgical removal, is reliant on the early detection of the lesion. The challenge is to diagnose and remove all malignant lesions at an early stage while minimising the unnecessary removal of benign lesions. Visual inspection with the naked eye has a relatively low sensitivity in detecting early melanoma [1-3]. In this context, several non-invasive diagnostic modalities, such as dermoscopy, total body photography, and reflectance confocal microscopy (RCM), have emerged in recent years that are aimed at increasing diagnostic accuracy and raising the threshold for surgical procedures.

Recent advances
Dermoscopy
Dermoscopy (also known as dermatoscopy or epiluminescence microscopy) allows for the visualization of anatomical structures within the epidermis and papillary dermis that would otherwise not be able to be visualised by the naked eye [4]. This is achieved with the use of a hand held dermatoscope to magnify the skin surface and reduce the refraction of light by the corneal layer. Various diagnostic algorithms (pattern analysis, ABCD rule, Menzies method, seven-point checklist, and three-point check list) have been proposed to help assess the structures and patterns seen in dermoscopy. Recently, criteria for amelanotic/hypomelanotic melanoma have been described (Table 1).

There are two different types of dermatoscopes: the original, non-polarised version requires an immersion medium (oil, alcohol) and is superior in visualising blue-white areas (often associated with regression), milia-like cysts, and comedo-like openings (features of seborrheic keratosis). The alternative dermatoscope uses polarised light and has been found to be better for assessing vascular structures and shiny white streaks that could be a sign of fibrosis [5]. It has been proposed that using the two different dermatoscopes in conjunction with each other may help to increase the sensitivity and specificity of detecting melanoma [6].

Various studies and three meta-analyses of the literature have validated the ability of dermoscopy to increase diagnostic accuracy. Dermoscopy was shown to be superior to naked-eye examination performed by specialists in two meta-analyses [1,3]. Recently, a meta-analysis by Vestergaard et al. [2], which focused exclusively on trials that were performed in a clinical setting, found that the relative diagnostic odds ratio was 15.6 for the use of dermoscopy to diagnose melanoma compared with naked-eye examination.

Furthermore, it has been reported that dermoscopic training for primary care physicians can improve their ability to correctly refer individuals with suspicious lesions and decrease the rate of excision or referral in
benign skin lesions [7-9]. A complete skin examination with the aid of dermoscopy requires less than 3 minutes [10]. Haenssle and colleagues [11] performed a prospective long-term study with patients at high risk for melanoma in a real-life clinical setting using the seven-point checklist to dermoscopically score melanocytic lesions. A sensitivity of 62% for lesions scoring more than 3 points and specificity of 97% was found. Of the melanomas that were false negatives on dermoscopic evaluation, 25% were detected by dermoscopic follow-up and 13% by complementary patient history and the ‘ugly duckling’ sign. Regression pattern, radial streaming, and atypical vascular pattern were found to be the criteria associated with the highest relative risk for melanoma. Overall, there is strong scientific evidence that clinical examination, including detailed anamnesis for identifying melanoma risk factors (family and personal history of melanoma, total number of nevi, including number of atypical nevi, skin type, presence of ephelides, hair and eye colour, non-melanoma skin cancer history, history of intermittent sun exposure) [12], and full body clinical inspection with detection of any lesions that are dissimilar to the rest (‘ugly ducklings’ [13]) aided by dermoscopy, is the gold-standard in non-invasive diagnosis of melanoma.

**Total body photography and sequential dermoscopic follow-up**

Photography enables documentation of lesions and has the ability to track and compare any changes over time. Macroscopic digital pictures of standardised body positions and digital dermoscopic images of lesions of concern enable nearly the entire body surface to be recorded and referred to in follow-up examinations. This technique is particularly helpful in the surveillance of individuals with numerous nevi with a family history of melanoma (so-called dysplastic nevus syndrome). Photographic monitoring aids in identifying stable lesions and early detection of any concerning changes [14]. Theoretically, any photographic equipment can be used for total body photography but there are now specific digital skin photography systems available.

Technologic advances have led to the development of devices for sequential digital dermoscopy. Digital dermoscopic (and clinical) images are taken and linked to the body site via a computer. At follow-up visits the same lesion is re-photographed for comparison. This method has helped to detect a subgroup of slow-growing melanomas that lack suspicious features at baseline examination but exhibit detectable changes on follow-up [15].

However, due to the increased time expenditure and cost of follow-up for every melanocytic lesion in a given patient, there is a need to correctly identify those that benefit most from digital dermoscopic follow-up. Haenssle et al. [16] performed a prospective long-term study including patients at risk for development of melanoma to identify those who benefit most from sequential dermoscopy follow-up. According to the results, the authors suggested a follow-up plan as follows: (a) short-term follow-up of 3 months for patients with familial atypical mole and melanoma syndrome and (b) long-term follow-up of 6-12 months for those with atypical mole syndrome. Patients with multiple common nevi and no additional risk factors were found to have low benefit from sequential digital dermoscopy.

---

**Table 1. Melanoma features in dermoscopy**

| Positive features | Major criteria | Positive features | Negative features |
|-------------------|----------------|-------------------|-------------------|
| 1. Blue-white veil| Score: +2      | 1. Irregularly sized or distributed brown dots/globules    | 1. Symmetry of pattern |
| 2. Multiple brown dots | 2. Blue-whitish veil | 2. Multiple blue/grey dots            | 2. Presence of a single color |
| 3. Pseudopods      | 3. Atypical pigment network | 3. Irregularly shaped depigmentation   | 6. Predominant central vessels |
| 4. Radial streaming | 4. Blue-white veil | 5. More than one shade of pink         | 7. Dotted and linear irregular vessels |
| 5. Scar-like depigmentation | 5. More than one shade of pink | | |
| 6. Peripheral black dots/globules | 6. Predominant central vessels | | |
| 7. Multiple colors  | 7. Atypical vascular pattern | | |
| 8. Multiple blue/grey dots | | | |
| 9. Broadened network| | | |

**Negative features**

- Absence of negative features and presence of ≥1 positive feature is diagnostic of melanoma
- Score ≥3 is diagnostic of melanoma
- Absence of negative features and presence of ≥1 positive feature is diagnostic of melanoma

For more details on dermoscopic diagnosis, including ABCD rule and pattern analysis, see [41].
Some of the drawbacks of sequential dermoscopy include the potential for loss to follow-up [17]. Only preselected lesions are dermoscopically monitored and changes in a previously unsuspicious lesion or a de novo lesion might therefore be missed. Of note, suspicious nodular lesions should be excised immediately rather than observed over time as they are at higher risk of rapid change and spread if malignant.

The use of digital imaging has the added benefit of enabling teledermatologic applications. Teledermoscopy is defined as the transmission of digital dermoscopic images over a distance for specialist consultation, allowing primary care physicians to forward dermoscopic images to dermatologists for second opinion [18]. Good interobserver agreement between face-to-face diagnosis and diagnosis based on digital images has been demonstrated in several studies [19]. Furthermore, digital dermoscopic and clinical still images with complementary clinical data have been shown to increase confidence and interobserver agreement [20].

The feasibility of teledermoscopy using mobile devices has been recently demonstrated, highlighting the potential of mobile teledermoscopy as a screening and triage tool [21]. Teledermoscopy is particularly useful in remote areas where referral to a specialist is financially demanding and time consuming for the patient.

**Reflectance confocal microscopy**

RCM is a non-invasive imaging technique that uses a near infrared laser beam to create black and white images in a horizontal plane. The images are able to define cellular structures and morphology and can obtain images, with good resolution, of the epidermis, dermo-epidermal junction, and the superficial dermis. RCM images are created from the difference in reflectivity of different tissue structures. Melanin and melanosomes are strongly reflective, making RCM a suitable modality for examining melanocytic lesions [22].

Several recent studies have identified RCM features of melanoma and nevi and have found key differences between the two. In short, features most suggestive of melanoma as found by Pellacani et al. [23,24] are displayed in Table 2. Other diagnostic algorithms for melanoma diagnosis have been proposed [25-27]. Gerger and colleagues [26] developed a decision tree analysis based on three RCM features (monomorphic melanocytic cells, keratinocyte borders, and polymorphic melanocytic cells). Segura and colleagues [27] recently presented a two-step algorithm for differentiation between melanocytic lesions and non-melanocytic lesions in the first step and between nevi and melanoma in the second step. A recent focus of interest is the value of RCM in diagnosis and pre-operative mapping of surgical margins in lentigo maligna (melanoma in situ in severely sun-damaged skin) [28,29]. A recently developed algorithm for diagnosis of lentigo maligna of the face is displayed in Table 2. Furthermore, a glossary of commonly used RCM terms has been published [30]. RCM is a promising potential clinical tool; however, large-scale clinical studies are required to be able to determine the entirety of its benefit.

**Other non-invasive diagnostic tools**

Other non-invasive diagnostic techniques currently in the process of being developed include multispectral image analysis, multiphoton laser scanning microscopy (MPM), optical coherence tomography, high frequency ultrasound, computer-assisted diagnosis, and molecular profiling.

### Table 2. Features of melanoma in reflectance confocal microscopy (RCM)

| Features of melanoma in RCM | Features of facial lentigo maligna in RCM |
|-----------------------------|------------------------------------------|
| **2 major criteria**        | **2 major criteria**                     |
| Score: +2                   | Score: +2                                |
| 1. Cell atypia at the DEJ   | 1. Round large pagetoid cells >20 µm     |
| 2. Non-edged papillae       | 2. Non-edged papillae                    |
| **4 minor criteria**        | **4 minor criteria**                     |
| Score: +1                   | Positive features, Score: +1             |
| 1. Roundish pagetoid cells  | 1. Three or more atypical cells at the DEJ in five fields of 500 × 500 µm |
| 2. Widespread pagetoid infiltration | 2. Follicular localization of atypical cells |
| 3. Cerebriform nests        | 3. Nucleated cells within dermal papillae |
| 4. Nucleated cells within dermal papillae | Negative feature, Score: -1 |
| Score ≥3 diagnostic for melanoma (sensitivity 97%; specificity 72%) | Score ≥2 diagnostic for lentigo maligna (sensitivity 85%; specificity 76%) |

The algorithm for melanoma diagnosis displayed above has been described by Pellacani et al. [42] and features of facial lentigo maligna have been described by Guitera et al. [29]. DEJ, dermal-epidermal junction.
Multispectral image analysis relies on the principle that different wavelengths of light penetrate the skin to different depths, enabling computer-aided visualization of criteria invisible to macroscopic and dermoscopic techniques.

High frequency ultrasound provides limited resolution images of the skin in the vertical plane. When used alone it is not reliable for diagnostic purposes. It can be used, however, as a tool for assessing tumour thickness and vascularity, which can assist in planning management preoperatively [31].

Optical coherence tomography is comparable to ultrasound but uses light instead of sound waves; it reaches a lower depth, providing a better resolution than ultrasound, but does not reach the resolution capabilities of RCM. Although there are studies regarding the various features of skin cancer, reports of diagnostic accuracy are lacking [32].

MPM utilizes non-linear excitation by a near-infrared laser source. Like RCM, the MPM allows imaging of horizontal sections of the skin, allowing visualization of cellular and subcellular structures. To date it is mainly used as a research tool [33].

Computer-assisted diagnosis uses automated diagnostic systems that extract and analyse criteria of skin lesions to provide a diagnosis without subjective human interpretation bias. It has been shown to reach levels of diagnostic accuracy similar to that of expert dermatologists [34,35]. However, in order not to miss a melanoma, there is a tendency for these tools to overdiagnose melanoma. A recent meta-analysis showed a slightly higher sensitivity for computer-aided dermoscopic diagnosis compared to expert diagnosis, but significantly lower specificity [36]. To date, a few fully automated systems are available, some of which are integrated in the software of videodermoscopy devices. MelaFind® uses multispectral imaging and the DB-MIPS system extracts information from dermoscopic images. The MelaFind system is currently in the final stages of being granted US Food and Drug Administration approval.

Molecular profiling for the diagnosis of melanoma is an emerging development. A method that uses RNA acquired from the cornified layer of a lesion gathered by tape stripping [37] is currently being investigated.

Implications for clinical practice
To date, the current standard method for melanoma diagnosis is naked-eye inspection with closer dermoscopic examination of suspicious lesions to determine which should be excised and sent for histopathological confirmation. The use of digital photography to track changes has been shown to be effective and is now integrated into practice. It is difficult to predict how clinical practice will be affected and if the new emerging imaging modalities, such as RCM, MPM, and computer-assisted diagnosis, will prevail, or if molecular analysis will substitute morphology. Further large-scale studies will determine their importance. Despite emerging technologies, it remains crucial to evaluate lesions in the context of the examination of the individual patient. Only those lesions that are considered suspicious can be further evaluated due to time expenditure, and, therefore, careful clinical examination and pre-selection is still irreplaceable.

Abbreviations
MPM, multiphoton microscopy; RCM, reflectance confocal microscopy.

Competing interests
HPS is co-founder and share holder of e-derm-consult GmbH, a spin-off company of the Medical University of Graz (Graz, Austria) with emphasis on holistic solutions for teledermatology. He is also share-holder and consultant for MoleMap Australia by Dermatologists Pty Ltd. EMTW and CESC declare that they have no competing interests.

References
1. Bafounta ML, Beuchet A, Aegerter P, Saig P: Is dermoscopy (epiluminescence microscopy) useful for the diagnosis of melanoma? Results of a meta-analysis using techniques adapted to the evaluation of diagnostic tests. Arch Dermatol 2001, 137:1343-50.
2. Vestergaard ME, Macaskill P, Holt PE, Menzies SW: Dermoscopy compared with naked eye examination for the diagnosis of primary melanoma: a meta-analysis of studies performed in a clinical setting. Br J Dermatol 2008, 159:669-76.
3. Kistler H, Pehamberger H, Wolff K, Binder M: Diagnostic accuracy of dermoscopy. Lancet Oncol 2002, 3:159-65.
4. Argenziano G, Soyer HP: Dermoscopy of pigmented skin lesions - a valuable tool for early diagnosis of melanoma. Lancet Oncol 2001, 2:443-9.
5. Benvenuto-Andrade C, Dusza SW, Agero AL, Scope A, Rajadhyaksha M, Halpern AC, Marghoob AA: Differences between polarized light dermoscopy and immersion contact dermoscopy for the evaluation of skin lesions. Arch Dermatol 2007, 143:259-38.
6. Esmaeili AC, Scope A, Halpern AC, Marghoob AA: Imaging techniques for the in vivo diagnosis of melanoma. Semin Cutan Med Surg 2008, 27:2-10.
7. Terushkin V, Warycha M, Levy M, Kopf AW, Cohen DE, Polsky D: Analysis of the benign to malignant ratio of lesions biopsied by a general dermatologist before and after the adoption of dermoscopy. Arch Dermatol 2007, 143:343-4.
8. Argenziano G, Puig S, Zalaudek I, Sera F, Corona R, Alsina M, Barbato F, Carrera C, Ferrara G, Guiltier A, Massi D, Moreno-Romero JA, Mullot-Santos C, Petrillo G, Segura S, Soyer HP, Zanchini R, Malvehy J: Dermoscopy improves accuracy of primary care physicians...
to triage lesions suggestive of skin cancer. J Clin Oncol 2006, 24:1877-82.

9. Menzies SW, Emery J, Staples M, Davies S, McAvoy B, Fletcher J, Shahid KR, Reid G, Avramidis M, Ward AM, Burton RC, Elwood JM: Effect of dermoscopy and short-term sequential digital dermoscopy imaging for the management of pigmented lesions in primary care: a sequential intervention trial. Br J Dermatol 2009, 161:1270-7.

F1000 Factor 3.0 Recommended
Evaluated by Giuseppe Argenziano 31 Mar 2010

10. Zalaudek I, Kittler H, Marghoob AA, Balato A, Blum A, Dalle S, Ferrara G, Fink-Puches R, Giorgio CM, Hofmann-Wellenhof R, Malvehy J, Moscariello E, Puig S, Scalvenzi M, Thomas L, Argenziano G: Time required for a complete skin examination with and without dermoscopy: a prospective, randomized multicenter study. Arch Dermatol 2008, 144:509-13.

11. Haenssle HA, Korpas B, Hansen-Hagge C, Buhl T, Kaune KM, Caini S, Gandini S, Sera F, Raimondi S, Fargnoli MC, Boniol M, Argenziano G, Kittler H, Ferrara G, Rubegni P, Malvehy J, Puig S, Rosenberger A, Krueger U, Schön MP, Emmert S: Seven-point checklist for dermoscopy: performance during 10 years of prospective surveillance of patients at increased melanoma risk. J Am Acad Dermatol 2012, 67:785-93.

12. Caili S, Gandini S, Sera F, Raimondi S, Fargnoli MC, Boniol M, Armstrong BK: Meta-analysis of risk factors for cutaneous melanoma according to anatomical site and clinico-pathological variant. Eur J Cancer 2009, 45:3054-63.

13. Scope A, Dusza SW, Halpern AC, Rabinovitz H, Braun RP, Zalaudek I, Argenziano G, Marghoob AA: The “ugly duckling” sign: agreement between observers. Arch Dermatol 2008, 144:558-64.

14. Banky JP, Kelly JW, English DR, Dowling JP: Incidence of new and changed nevi and melanomas detected using baseline images and dermoscopy in patients at high risk for melanoma. Arch Dermatol 2005, 141:998-1006.

15. Argenziano G, Kittler H, Ferrara G, Rubegni P, Malvehy J, Puig S, Cowell L, Stanganeli I, De Giorgio CM, Thomas L, Bahadoran P, Menzies SW, Piccoli D, Marghoob AA, Zalaudek I: Slow-growing melanoma: a dermoscopy follow-up study. Br J Dermatol 162:267-73.

16. Haenssle HA, Korpas B, Hansen-Hagge C, Buhl T, Kaune KM, Johnsens S, Rosenberger A, Schön MP, Emmert S: Selection of patients for long-term surveillance with digital dermoscopy by assessment of melanoma risk factors. Arch Dermatol 146: 257-64.

17. Argenziano G, Mordente I, Ferrara G, Gambato A, Annese P, Zalaudek I: Dermoscopic monitoring of melanocytic skin lesions: clinical outcome and patient compliance varying according to follow-up protocols. Br J Dermatol 2008, 159:331-6.

18. Wurm EM, Campbell TM, Soyer HP: Teledermatology: how to start a new teaching and diagnostic era in medicine. Dermatol Clin 2008, 26:295-300, vii.

19. Whited JD: Teledermatology research review. Int J Dermatol 2006, 45:220-9.

20. Ferrara G, Argenzio Z, Argenziano G, Cerio R, Cerroni L, Di Blasi A, Feudale EA, Giorgio CM, Massone C, Nappi O, Tomassini C, Urcu L, Zalaudek I, Kittler H, Sover HP: The influence of clinical information in the histopathologic diagnosis of melanocytic skin neoplasms. PLoS One 2009, 4:e5375.

F1000 Factor 6.0 Must Read
Evaluated by Debora Cadore de Farias 24 Dec 2009

21. Massone C, Brunasso AM, Campbell TM, Soyer HP: Mobile teledermoscopy - melanoma diagnosis by one click? Semin Cutan Med Surg 2009, 28:203-5.

22. Hofmann-Wellenhof R, Wurm EM, Ahlgrimm-Siess V, Richteg G, Koller S, Smolle J, Gerger A: Reflectance confocal microscopy: state-of-art and research overview. Semin Cutan Med Surg 2009, 28:172-9.

23. Pellacani G, Vincenti M, Bassoli S, Braun R, Gonzalez S, Guitera P, Longo C, Marghoob AA, Menzies SW, Puig S, Scope A, Seidenari S, Malvehy J: Reflectance confocal microscopy and features of melanocytic lesions: an internet-based study of the reproducibility of terminology. Arch Dermatol 2009, 145:1137-43.

24. Pellacani G, Guiterra P, Longo C, Avramidis M, Seidenari S, Menzies S: The impact of in vivo reflectance confocal microscopy for the diagnostic accuracy of melanoma and equivocal melanocytic lesions. J Invest Dermatol 2007, 127:2759-65.

25. Langley RG, Walsh N, Sutherland AE, Propperova I, Delaney L, Morris SF, Gallant C: The diagnostic accuracy of in vivo confocal scanning laser microscopy compared to dermoscopy of benign and malignant melanocytic lesions: a prospective study. Dermatology 2007, 215:365-72.

26. Geger A, Hofmann-Wellenhof R, Langsenlehner U, Richteg G, Koller S, Weger W, Ahlgrimm-Siess V, Horn M, Samonigg H, Smolle J: In vivo confocal laser scanning microscopy of melanocytic skin tumours: diagnostic applicability using unscreened tumour images. Br J Dermatol 2008, 158:329-33.

27. Segura S, Puig S, Carrera C, Palou J, Malvehy J: Development of a two-step method for the diagnosis of melanoma by reflectance confocal microscopy. J Am Acad Dermatol 2009, 61:216-29.

F1000 Factor 3.0 Recommended
Evaluated by H Peter Soyer 02 Nov 2009

28. Ahlgrimm-Siess V, Massone C, Scope A, Fink-Puches R, Richteg G, Wolf IH, Soper S, Gerger A, Smolle J, Hofmann-Wellenhof R: Reflectance confocal microscopy of facial lentigo maligna and lentigo maligna melanoma: a preliminary study. Br J Dermatol 2009, 161:1307-16.

29. Guitera P, Pellacani G, Crotty KA, Scolyer RA, Li LX, Bassoli S, Vinceti M, Rabinovitz H, Longo C, Menzies SW: The impact of in vivo reflectance confocal microscopy on the diagnostic accuracy of lentigo maligna and equivocal pigmented and nonpigmented macules of the face. J Invest Dermatol 2010, [Epub ahead of print].

30. Scope A, Benvenuto-Andrade C, Agero AL, Malvehy J, Puig S, Rajadhyaksha M, Busam KJ, Marra DE, Torres A, Propperova I, Langley RG, Marghoob AA, Pellacani G, Seidenari S, Halpern AC, Gonzalez S: In vivo reflectance confocal microscopy imaging of melanocytic skin lesions: consensus terminology glossary and illustrative images. J Am Acad Dermatol 2007, 57:644-58.

31. Marghoob AA, Swindle LD, Moricz CZ, Sanchez Negron FA, Slue B, Halpern AC, Kopf AW, Instruments and new technologies for the in vivo diagnosis of melanoma. J Am Acad Dermatol 2003, 49:777-97.

32. Mogensen M, Thrane L, Jorgensen TM, Andersen PE, Jemec GB: Optical coherence tomography for imaging of skin and skin diseases. Semin Cutan Med Surg 2009, 28:190-5.

33. Paoli J, Smedh M, Ericson MB: Optical coherence tomography for the diagnosis of melanoma using surface microscopy. Br J Dermatol 2009, 161:591-604.

34. Paoli J, Smedh M, Ericson MB: Optical coherence tomography for the diagnosis of melanoma using surface microscopy. Br J Dermatol 2009, 161:591-604.

35. Rosado B, Menzies S, Harbauer A, Pehamberger H, Wolff K, Binder M, Zalaudek I, Kittler H: Accuracy of computer diagnosis of melanoma: a quantitative meta-analysis. Arch Dermatol 2003, 139:361-7.

36. Rajpara SM, Botello AP, Townend J, Ormerod AD: Multiphoton laser scanning microscopy-a novel diagnostic method for superficial skin cancers. Semin Cutan Med Surg 2009, 28:190-5.

37. Kreher V, Cawthorn T, Dhillon S, Cooper J, Koo J, Lai SS, Abou-Daoud S: Optical coherence tomography of skin. Clin Exp Dermatol 2007, 32:568-71.

38. Drexseitl S, Binder M, Hable K, Kittler H: Computer versus human diagnosis of melanoma: evaluation of the feasibility of an automated diagnostic system in a prospective clinical trial. Melanoma Res 2009, 19:180-4.

39. Rosado B, Menzies S, Harbauer A, Pehamberger H, Wolff K, Binder M, Kittler H, Accuracy of computer diagnosis of melanoma: a quantitative meta-analysis. Arch Dermatol 2003, 139:361-7.

40. Rajpara SM, Botello AP, Townend J, Ormerod AD: Systematic review of dermoscopy and digital dermoscopy/artificial intelligence for the diagnosis of melanoma. Br J Dermatol 2009, 161:591-604.

41. Wong R, Tran V, Talwalker S, Benson NR: Analysis of RNA recovery and gene expression in the epidermis using non-invasive tape stripping. J Dermatol Sci 2006, 44:81-92.

42. Menzies SW: A method for the diagnosis of primary cutaneous melanoma using surface microscopy. Dermatol Clin 2001, 19:299-305.

43. Argenziano G, Fabbrocin G, Carli P, De Giorgi V, Sammarco E, Defino M: Epiluminescence microscopy for the diagnosis of doubtful melanocytic skin lesions. Comparison of the ABCD
rule of dermatoscopy and a new 7-point checklist based on pattern analysis. Arch Dermatol 1998, 134:1563-70.

40. Menzies SW, Kreusch J, Byth K, Pizzichetta MA, Marghoob A, Braun R, Malvehy J, Puig S, Argenziano G, Zalaudek I, Rabinovitz HS, Oliviero M, Cabo H, Ahlgren-M-Siess V, Avramidis M, Gutera P, Soyer HP, Ghiglotti G, Tanaka M, Perusquia AM, Pagnanelli G, Bono R, Thomas L, Pellacani G, Langford D, Piccolo D, Terstappen K, Stanganelli I, Llambrich A, Johr R: Dermoscopic evaluation of amelanotic and hypomelanotic melanoma. Arch Dermatol 2008, 144:1120-27.

41. Dermoscopy – Consensus Net Meeting on Dermoscopy. [http://www.dermoscopy.org/consensus/]

42. Pellacani G, Cesinaro AM, Seidenari S: Reflectance-mode confocal microscopy of pigmented skin lesions - improvement in melanoma diagnostic specificity. J Am Acad Dermatol 2005, 53:979-85.