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Dermoscopy—The Ultimate Tool for Melanoma Diagnosis

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"We are beginning to move away from clinicopathologic diagnosis into an era of clinico-imaging diagnosis." This vision became a fact, as the dermatoscope represents nowadays the dermatologist stethoscope. This is not only because dermoscopy reveals a new and fascinating morphologic dimension of pigmented and nonpigmented skin tumors, but also because it improves the recognition of a growing number of skin symptoms in general dermatology. Melanoma detection remains the most important indication of dermoscopy and in melanoma screening the aim of dermoscopy is to maximize early detection while minimizing the unnecessary excision of benign skin tumors. In the last few years, 3 meta-analyses and 2 randomized studies have definitely proven that dermoscopy allows improving sensitivity for melanoma as compared to the naked eye examination alone. This is the consequence of at least 3 issues: first, the presence of early dermoscopy signs that are visible in melanoma much before the appearance of the classical clinical features; second, an increased attitude of clinicians to check more closely clinically banal-looking lesions; third, an improved attitude of clinicians to monitor their patients.
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The Dermatologist Stethoscope

"We are beginning to move away from clinicopathologic diagnosis into an era of *clinicoimaging* diagnosis."[1] This is what Robinson and Callen wrote in 2005, a vision that, to our estimation, is slowly becoming true. The dermatoscope is, in fact, increasingly used as the dermatologist stethoscope, not only because it reveals a new and fascinating morphologic dimension of pigmented and nonpigmented skin tumors but also because it improves the recognition of a growing number of skin symptoms in general dermatology.

Dermoscopy can facilitate the diagnosis of scabies due to the presence of the pathognomonic "jet with contrail" sign.[2,3] Other skin infections and infestations may be differentiated with increased confidence, including pediculosis, phtiriasis, tungiasis, *Tinea nigra*, and molluscum contagiosum.[4-14] Among the most common inflammatory skin disorders—psoriasis and lichen planus—the use of dermoscopy allows the visualization of specific submacroscopic features, such as the "red dots" pattern in psoriasis and the "whitish striae" pattern in lichen planus.[15-20] In a recent review of the indications in dermoscopy, more than 35 different inflammatory and infectious skin diseases have been listed.[21] As reported in several case series, one of the newest applications is represented by trichoscopy, namely the dermoscopic observation of the scalp, which might be helpful for the diagnosis of different hair and scalp diseases.[22-32]

Because of the growing number of dermoscopy indications, it is not a surprise that the use of this noninvasive diagnostic tool is spreading worldwide. Currently, about 3500 clinicians joined the International Dermoscopy Society as regular members, from more than 110 different countries (see also http://www.dermoscopy-ids.org). As the number of dermoscopy users grows, also the number of scientific publications in dermoscopy increased significantly. As shown in Figure 1, almost 1000 articles have been published between 2003 and 2007, a magnitude 3 times higher than in the previous 5 years. About 300 dermoscopy articles have been referenced in PubMed just in 2008. The top 20 countries with the highest number of dermoscopy publications include nations from 4 continents, namely, Europe, North and South America, Australia, and Asia (Fig. 2).

To our estimation, the reason for the spreading interest in dermoscopy is 2-fold. On 1 hand, clinicians dealing with skin problems are usually passionate morphologists and dermos-

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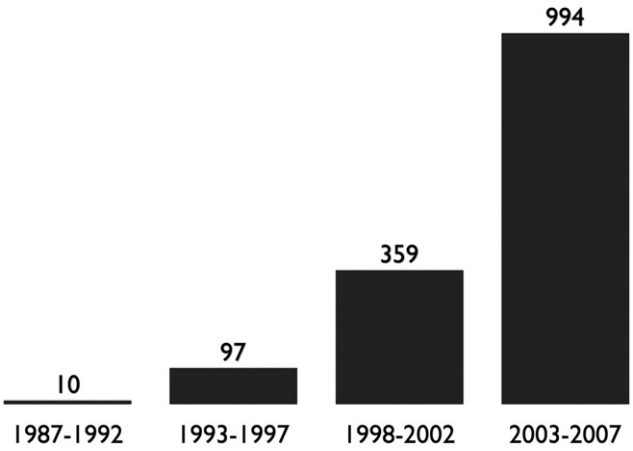

Figure 1 Number of published articles in dermoscopy as referenced at: http://www.scopus.com (search performed in April 2009).

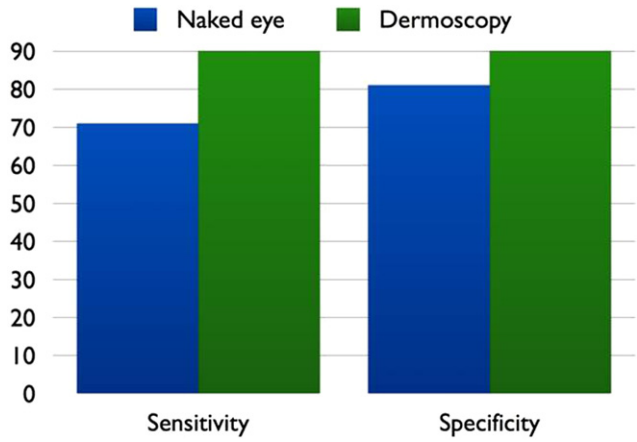

Figure 3 Average sensitivity for melanoma of naked eye and dermoscopy examinations. Adapted from Vestergaard et al.[37]

copy made a new submacroscopic morphologic world visible to them. In most cases, dermoscopy does not change the management of the individual lesions as judged using eye examination. However, by looking at a lesion under the dermatoscope, the clinician feels more confident and his clinical judgment is subsequently reinforced. By contrast, patients like dermoscopy, as well, because it makes them feel more in touch with their doctors, who are asked to come closer when they use a dermatoscope.

Country	Publications
Italy	203
USA	169
Germany	107
Austria	75
Spain	54
Japan	43
Switzerland	35
Australia	30
France	24
United Kingdom	23
Turkey	20
Belgium	18
Denmark	17
South Korea	12
Canada	10
Brazil	9
Taiwan	9
Poland	7
Sweden	6
Mexico	5

Figure 2 Top 20 countries with the highest number of dermoscopy publications as referenced at: http://www.gopubmed.org (search performed in April 2009).

Improved Performance in Melanoma Screening

Dermoscopy in 2009 should not to be considered as a young technique anymore but an established tool improving the clinical recognition of several different skin disorders. However, melanoma detection remains the most important indication of dermoscopy. The big problem in melanoma screening is that although this tumor is relatively uncommon, its benign counterpart, the mole, is extremely frequent in the general population. Many benign pigmented lesions are, thus, usually excised to detect melanoma early enough to prevent the dramatic consequences of the advanced disease. The aim of dermoscopy in melanoma screening is to maximize early detection while minimizing the unnecessary excision of benign skin tumors.

In the last few years, 3 meta-analyses and 2 randomized studies have definitely proven that dermoscopy allows improving sensitivity for melanoma as compared to the naked eye examination alone.[33-37] The last piece of evidence has been provided by Vestergaard et al in 2008.[37] These authors carried out a meta-analysis of dermoscopy studies performed in a clinical setting and found the relative diagnostic odds ratio for melanoma, for dermoscopy compared with naked eye examination, to be 15.6 ($P = 0.016$). As shown in Figure 3, the average sensitivities for melanoma of the naked eye and dermoscopy examinations were 74% and 90%, respectively. The latter result occurred without a decrease in specificity, suggesting that better melanoma detection (16% improvement) occurs without increasing the number of unnecessary excisions of benign lesions. In a randomized study, Carli et al demonstrated that combined eye and dermoscopy examination determined a significant reduction in the percentage of patients referred for biopsy (9.0% vs 15.6%; $P = 0.013$).[35] The use of dermoscopy is thus associated with both a significant increase of number of excised melanoma and a significant reduction of number of benign pigmented skin lesions excised for diagnostic verification.

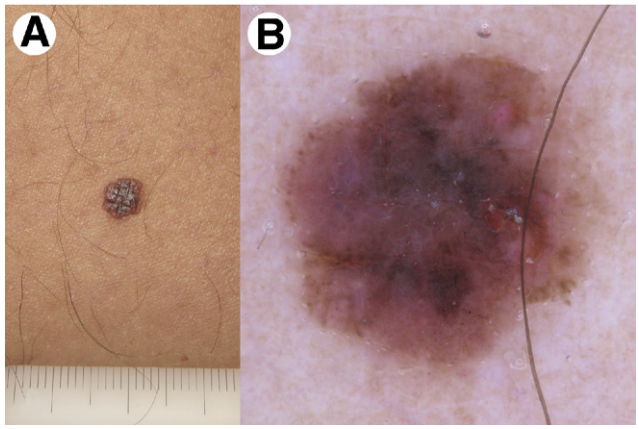

Figure 4 (A) Clinically benign-looking small melanoma located on the thigh of a 50-year-old woman. The lesion is symmetric, with regular border and homogeneous color. (B) Dermoscopically, there is asymmetry in color and structure, irregular dots/globules, and blue-white veil. The lesion is thus highly suspicious. Subsequent histopathologic examination revealed a 0.5-mm-thick melanoma.

Three Reasons for Improved Melanoma Detection

What are the reasons dermoscopy allows a better detection of melanoma? There are 3 possible explanations: first, the presence of early dermoscopy signs that become visible in melanoma much before the appearance of the classical clinical features; second, an increased attitude of clinicians to check more closely clinically banal-looking lesions; third, an improved attitude of clinicians to monitor their patients.

Early Dermoscopy Criteria

For years, the simple ABCD rule represented our clinical guideline to differentiate melanoma from benign moles. Undoubtedly, its introduction allowed a dramatic improvement in the early detection of melanoma. However, the ABC criteria (asymmetry in shape, border irregularity, and color variegation) are more evident when melanoma is already relatively large in size ($D > 6$ mm). Clearly, melanoma is already melanoma when it is smaller than 6 mm, and shape, border, and color might be relatively regular at this stage. The advantage of dermoscopy is that equivocal features are often present in very small melanomas already, thus increasing our index of suspicion even in the context of small and clinically banal-looking melanomas (Fig. 4).

Complete Skin Examination

As a consequence, clinicians are today more prone to examine dermoscopically even small and banal-looking lesions. This is in contrast to one of the guiding rules of a few years ago, namely, dermoscopy is best suited as a second-level diagnostic tool for clinically suspicious lesions. Indeed, dermoscopy has to be considered as a first-level screening tool to increase the number of early excised melanomas. In contrast to the cumbersome equipment used a few years ago, dermoscopy today is performed using inexpensive and hand-held instruments. Few of them are provided with a polarized light, avoiding the use of the fluid to render the epidermis translucent. This translates into a much faster screening in the clinical setting. In a recent randomized study, our group demonstrated that dermoscopy is indeed not time-consuming.[38] To determine the time required to perform a complete skin examination as a means of opportunistic screening for skin cancer both without and with dermoscopy, 1328 patients with at least 1 melanocytic or nonmelanocytic skin lesion were randomly selected to receive a complete skin examination with or without dermoscopy. The median time needed for complete skin examination without dermoscopy was 70 seconds and with dermoscopy was 142 seconds, a significant difference of 72 seconds ($P < 0.001$). However, a thorough skin examination, with or without dermoscopy, requires less than 3 minutes, which is a reasonable amount of added time to potentially prevent the morbidity and mortality associated with skin cancer.

Monitoring Patients With Multiple Moles

If dermoscopy is employed as a screening tool for complete skin examination, the number of early detected melanomas increases, but there is a variable percentage of melanomas that may still be missed at the first consultation.[34,39-43] This is because initial melanoma may be clinically but sometimes also dermoscopically indistinguishable from benign lesions, especially in the context of patients with multiple melanocytic nevi (Figs. 5-7).[44] In the management of these patients, 2 different strategies are employed. The first consists of removing all atypical lesions, resulting in a high number of unnecessary excisions of melanocytic nevi. The second strategy involves dermoscopic follow-up and excision of only those lesions that change over time. Digital dermoscopic monitoring of melanocytic lesions offers the dual advantages of increasing the likelihood that featureless melanomas are not overlooked while minimizing the excision of benign lesions.

In a retrospective analysis of 600 lesions from 405 patients, we assessed patient compliance and clinical outcome in patients with multiple atypical melanocytic lesions undergoing sequential dermoscopy imaging during short-term, medium-

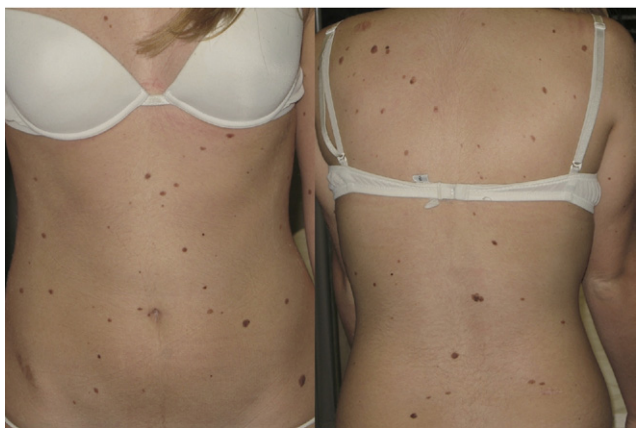

Figure 5 Multiple melanocytic nevi in a 23-year-old woman.

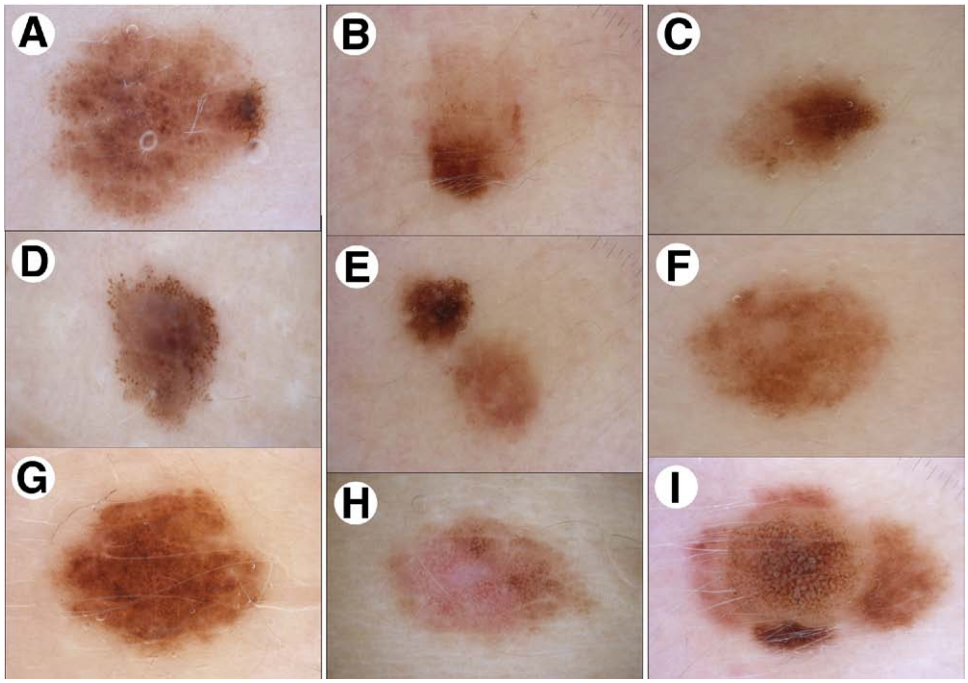

Figure 6 A sample of the nevi of the patient shown in Figure 5. Dermoscopically, all lesions show various degrees of atypical features. Lesions D, H, and I have been excised and histopathologically diagnosed as compound melanocytic nevi. Lesions A-C and E-G have been monitored and showed no changes over time.

term, or long-term follow-up.[45] In a median follow-up period of 23 months, 54 (9%) lesions were excised, revealing 12 early melanomas. The melanoma/benign ratio of excised lesions was 1:3.4. An earlier study showed that the use of dermoscopy led to a decrease in the number of unnecessary excisions of benign lesions compared to clinical examination alone, with an improvement in the malignant/benign ratio from 1:18 to 1:4.3.[35] In our study sequential dermoscopic imaging allowed a melanoma/benign ratio of 1:3.4, reflecting a very low number of unnecessary excisions.[45]

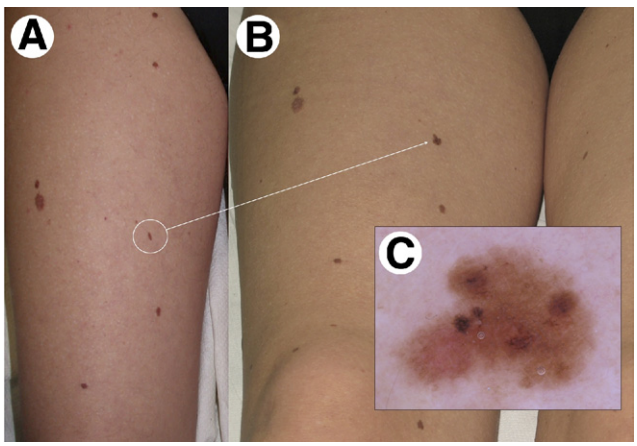

Figure 7 Same patient as shown in Figure 5. (A) At the baseline consultation the small lesion within the circle was regularly shaped and pigmented and, thus, not considered suspicious as compared to the lesions shown in Figure 6. (B) After 14 months the lesion is remarkably enlarged and highly suspicious for melanoma both clinically and dermoscopically (C). Subsequent histopathologic examination revealed a melanoma in situ.

In our study sequential imaging not only increased specificity but also improved sensitivity in the diagnosis of melanoma. Although 1 study failed to detect melanoma after a median 24-month follow-up,[46] there are many reports of sequential imaging resulting in the identification of melanomas that were not suspected as such at baseline examination.[41,42,45,47-51] Based on these studies, the average prevalence of patients with multiple nevi who can be discovered with melanoma during follow-up seems to be about 3%.

Although most studies were performed using long-term monitoring, a short-term monitoring protocol proposed by Menzies et al[42] recently achieved the greatest consensus because of the logical assumption that melanoma grows faster than melanocytic nevi and changes can be seen after only 2-4 months. However, in our study 7 of 12 melanomas detected during follow-up showed changes after 2-4 visits, corresponding to 8-54 months of follow-up.[45] We believe that a form of indolent, slow-growing melanoma exists, and only a prolonged surveillance can detect the subtle changes over time that characterize this type of melanoma.[52,53]

Nevertheless, short-term monitoring is the best strategy to optimize patient compliance. In our study, the rate of compliance was 84.2% with short-term monitoring protocol, 63.4% with medium-term monitoring, and 29.9% with long-term monitoring.[45] Since compliance is a sine qua non condition for the success of sequential imaging protocols,[34,54] recommending patient reevaluation after only few months will minimize the risk of leaving a melanoma untreated.

The bottom line is, in patients with multiple nevi sequential dermoscopy imaging is a useful strategy to avoid missing melanoma while minimizing unnecessary excision of benign lesions. For better compliance, the first re-examination should be scheduled at 3 months after the baseline visit. Regular annual follow-up monitoring is also needed to detect slow-growing melanomas, in which subtle changes may become apparent only over time.

Dermoscopy Facts and Fictions

From what is previously mentioned, it becomes evident that a few of the classical obstacles to the application of dermoscopy in the clinical setting—lack of time and insufficient evidence in term of diagnostic validity—should be considered today as a fiction. Instead, it is a proven fact that the use of dermoscopy is not time-consuming in the clinical setting and its application in the context of a complete skin examination will result in a higher number of early excised melanomas. Another obstacle is represented by the notion that dermoscopy requires long training and vast experience to be of benefit in diagnostic accuracy.[55] Clearly, some training is necessary to handle the new features that become apparent with dermoscopy. However, already a 1-day course can be sufficient to improve the recognition of lesions suggestive of skin cancer, as demonstrated in a randomized study.[36]

The aim of that study was to determine whether the adjunct of dermoscopy to the standard clinical examination improves the accuracy of primary care physicians to triage lesions suggestive of skin cancer.[36] Seventy-three doctors were given a 1-day training course in skin cancer detection and dermoscopic evaluation, and were randomly assigned to the dermoscopy evaluation arm or naked-eye evaluation arm. During a 16-month period, these physicians, previously inexperienced in skin cancer screening, evaluated 2522 patients with skin lesions, which were scored as benign or suggestive of skin cancer. All patients were then reevaluated by expert dermatologists. The most significant result was that the use of dermoscopy allowed general physicians to perform 25.1% better triage of suspicious skin tumors compared to naked-eye examination alone ($P = 0.002$). The latter result occurred without a decrease in specificity (71.8%), suggesting that better triage of possible malignant skin tumors could occur without increasing the number of unnecessary expert consultations. Doctors using dermoscopy performed significantly better also in negative-predictive value ($P = 0.004$), resulting in a very low risk (1.9%) for patients with suspicious lesions not to be referred by general physicians for a second expert opinion.[36]

Another fiction is related to the correct approach to the dermoscopic differentiation of the various types of pigmented skin lesions. The so-called "analytic" approach requires the knowledge of the various global and local patterns and features that become apparent with dermoscopy. Once the dermoscopic alphabet is acquired, then the individual features are scored by the clinician and the diagnostic conclusion is reached by the calculation proposed in one of the algorithms that have been published in the last few years.[56-59]

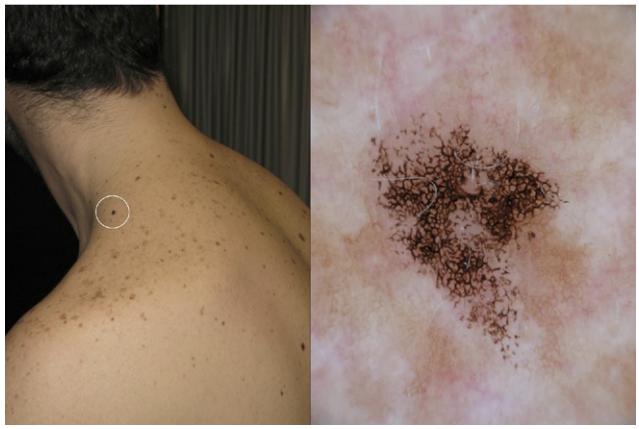

Figure 8 Flat, heavily pigmented lesion on the shoulder of a 38-year-old man. Dermoscopically, a special reticular pattern can be seen, characterized by a black broken-up network in the absence of any additional features. This pattern is virtually diagnostic of ink-spot lentigo.

The fact is that those algorithms have been shown to be of value only for beginners to facilitate their evaluations during their dermoscopy training. By that time, as soon as the experience increases in distinguishing the different faces of melanocytic and nonmelanocytic skin lesions, just the so-called "heuristic" approach will be used. The term derives from the Greek word "eureka," which means "I've got it," and refers to the ability of our brain to recognize instantly the overall pattern of the given lesion. This is especially true for clinicians used to practicing in morphologic fields of medicine, and dermoscopy is not an exception. In Fig. 8 an example of an ink-spot lentigo is given. The knowledge of such a specific type of reticular pattern allows the correct interpretation using the heuristic approach; instead, the analytical approach would have probably led the clinician to the wrong conclusion that the lesion could be a melanoma due to the irregularity of the network.

The last fiction is related to the patient expectations concerning the dermoscopic evaluation of his/her lesions. Many patients, especially in Europe, tend to overestimate the role of digital machine vision in general, and mole mapping in particular. They have the feeling that a "machine" is more accurate than a doctor in evaluating their lesions. Consequently, in many countries there is an increasing demand for mole mapping. As previously mentioned, the fact is that mole mapping is a valuable method to improve diagnostic accuracy when used for patients with multiple nevi. In the context of a patient with a single atypical lesion, especially if palpable, digital machine vision is virtually contraindicated, whereas a simple biopsy will solve the diagnostic issue. The bottom line is, in daily practice there is just a small and inexpensive dermatoscope that lies in our pocket. As the dermatologist stethoscope, dermoscopy is a remarkable screening tool to be used in the daily routine to decrease our diagnostic gray zone and to increase our confidence in managing patients with skin lesions.

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