

Accuracy of the first step of the dermatoscopic 2-step algorithm for pigmented skin lesions

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ABSTRACT **Objectives:** To evaluate the frequency of misclassifications of equivocal pigmented lesions according to the first step of the dermatoscopic 2-step algorithm.

Patients and Methods: 707 consecutive cases from 553 patients of central Europe and Australia were included in the study. Dermatoscopic images were evaluated in a blinded fashion for the presence of features described in the 2-step algorithm to determine their melanocytic or non-melanocytic origin. Mucosal, genital and non-pigmented lesions were excluded.

Results: The sensitivity of the first step was 97.1% for patients from Australia and 96.8% for patients from central Europe. The specificity was 33.6% for Australian patients and 67.9% for European patients. The most common reasons for misclassification were the presence of a pigmented network in a non-melanocytic lesion (n=68, 25.2%) and the absence of dermatoscopic features of melanocytic and non-melanocytic lesions in 69 (25.6%) non-melanocytic lesions.

Conclusion: The first step of the dermatoscopic 2-step algorithm, if applied consistently, has high sensitivity but low specificity. Many non-melanocytic lesions, especially solar lentigines and seborrheic keratoses, are wrongly classified as melanocytic. The worse performance of the first step algorithm in Australian patients is probably due to a higher rate of solar lentigines in patients with severely sun-damaged skin.

Introduction

Dermatoscopy improves diagnostic accuracy for melanocytic [1, 2] and non-melanocytic [3] skin lesions. Several diagnostic algorithms have been created [4-8] and tested [4-10]. Nearly all of them have been designed to distinguish between

benign and malignant melanocytic lesions and are based on the 2-step method [9,10]. The 2-step method requires differentiation between melanocytic and non-melanocytic lesions in a first step. The 2-step algorithm was reviewed and confirmed by leading experts in the field [9] and is widely accepted in teaching dermatoscopy. Nevertheless, the first

TABLE 1. Frequencies of diagnosis according to study center

Histologic Diagnosis	Europe	Australia
Melanocytic	187 (77.9%)	245 (53.0%)
Melanoma	62 (25.8%)	29 (6.3%)
Nevus	125 (52.1%)	216 (46.8%)
Non-Melanocytic	53 (22.1%)	217 (47.0%)
Actinic keratosis	2 (0.8%)	14 (3.0%)
Angiokeratoma	1 (0.4%)	0 (0.0%)
Basal cell carcinoma	17 (7.1%)	72 (15.6%)
Dermatofibroma	2 (0.8%)	4 (0.9%)
Hemangioma	3 (1.3%)	0 (0.0%)
Intracorneal hemorrhage	1 (0.4%)	0 (0.0%)
Inflammatory diseases	0 (0.0%)	2 (0.4%)
Ink spot lentigo	0 (0.0%)	1 (0.2%)
Lichen planus-like keratosis	3 (1.3%)	21 (4.5%)
Nevus sebaceous	1 (0.4%)	0 (0.0%)
Bowen's disease	0 (0.0%)	18 (3.9%)
Squamous cell carcinoma	0 (0.0%)	5 (1.1%)
Seborrheic keratosis	18 (7.5%)	43 (9.3%)
Solar lentigo	3 (1.3%)	37 (8.0%)
Tungiasis	1 (0.4%)	0 (0.0%)
Viral acanthoma	1 (0.4%)	0 (0.0%)

step especially runs the major risk of misclassification and can therefore lead to wrong diagnoses eventually, regardless of how good the algorithm of the second step is.

A few publications have reported single dermatoscopic features of the first step to be prone to misclassification [11,12], but the overall rate and reasons for wrong classifications have not been reported yet and this is the aim of this study.

Patients and methods

The cases originated from a tertiary referral center at a university hospital in Europe (Department of Dermatology, Medical University of Vienna) and from the Primary Skin Cancer Clinic in Brisbane, Australia. All documented cases between December 28, 2006, and May 20, 2009, were col-

lected. Mucosal and genital non-pigmented lesions and cases without histopathologic diagnosis were excluded.

Dermatoscopic images were evaluated in a blinded fashion by two of the authors (P.T., H.K.) for the presence of every melanocytic and non-melanocytic feature described in the 2-step algorithm [9]. A lesion was regarded of melanocytic origin if either at least one melanocytic feature was present or no dermatoscopic feature was present at all ("melanocytic by default"). If no melanocytic but at least one non-melanocytic feature was present a lesion was classified non-melanocytic. Lesions histologically proven to be a collision lesion of both origins were histologically classified as melanocytic.

Devices used for taking dermatoscopic images were a DermLite Foto® (polarized imaging) and a DermLite Fluid®

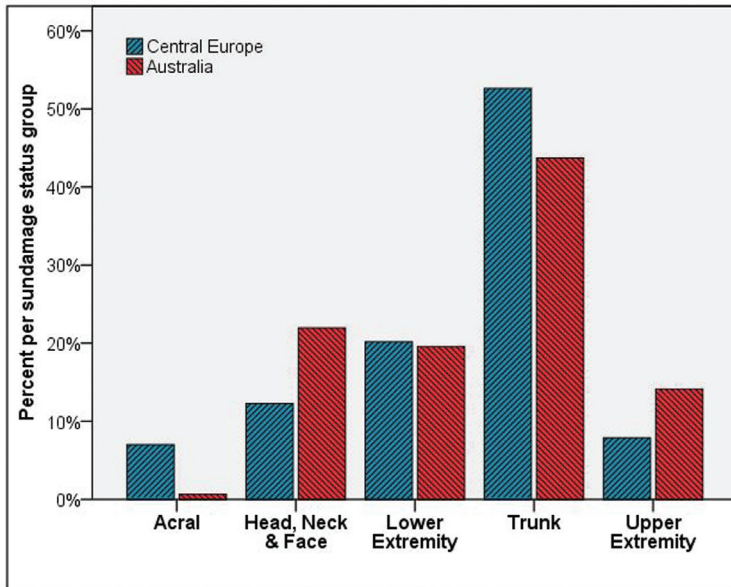


Figure 1. Distribution of lesions regarding body site and geographic origin. Given frequencies are calculated within each geographic group. [Copyright: ©2012 Tschandl et al.]

(non-polarized imaging). Pictures were taken at standard magnification (10x) and magnification encompassing the whole lesion. Images used for evaluation were in a JPEG format, had a resolution of at least 300 dots per inch, and a size not smaller than 800 x 600 pixels.

Statistical analysis

Sensitivity was calculated by dividing the number of correctly identified melanocytic lesions (according to the first step) with the total number of melanocytic lesions. Specificity was calculated by dividing the number of correctly identified non-melanocytic lesions (according to the first step) by the total number of non-melanocytic lesions. Continuous data are given as mean and standard deviation unless otherwise specified. Sensitivity, specificity, positive and negative predictive values were calculated according to standard formula.

Results

General data

We included 702 consecutive cases from 548 patients (mean age 54.6 ± 18.0 years, 59.9% males), of whom 331 (60%) were from Australia and 217 (40%) from Central Europe. Two hundred and seventy (39%) of the cases were non-melanocytic, 432 (61%) melanocytic, and the frequencies of histologic diagnoses are shown in Table 1. The lesions were located on head or neck in 18.4%, on the trunk in 45.7%, on the upper extremities in 11.8%, on the lower extremities in 19.4% and on acral sites in 2.7% (Figure 1).

Accuracy of the first step

The sensitivity of the first step was 97.1% for patients from Australia and 96.8% for patients from Central Europe. The

specificity was 33.6% for Australian patients and 67.9% for European patients. The positive and negative predictive values for melanocytic lesions were 0.62 and 0.91 for Australian and 0.91 and 0.85 for European patients, respectively.

Misclassifications

The most common reasons for misclassification were a pigmented network in 69 (25.6%) non-melanocytic lesions (Figure 2) and an absence of any given non-melanocytic features (“melanocytic by default”) in 74 (27.4%) non-melanocytic lesions (Figure 3). A list of dermatoscopic features leading to misclassifications can be found in Table 2. Seven percent ($n=13$) of misdiagnosed lesions were melanocytic but misclassified as non-melanocytic and 161 (92.5%) non-melanocytic were misclassified as melanocytic. Seborrheic keratoses and solar lentigines were most commonly misclassified. The frequencies of misclassification by feature are given in Table 3. Table 4 shows the positive predictive value by feature.

Discussion

In this study we show that the accuracy of the first step of dermatoscopy is only moderate. It is very sensitive for melanocytic lesions but has low specificity. In other words, if the first step for dermatoscopy is used in the way it has been suggested many non-melanocytic lesions would be incorrectly classified as melanocytic lesions. The main reason for this is that criteria like the “pigment network” or “aggregated brown globules” are not specific to melanocytic lesions. Of 380 lesions with a pigment network, 69 (18.2%) were non-melanocytic. Of 96 lesions with “aggregated brown globules,” 19 (19.8%) were non-melanocytic. Many seborrheic keratoses and most solar lentigines have a pigment network when viewed by dermatoscopy. This comes as no surprise

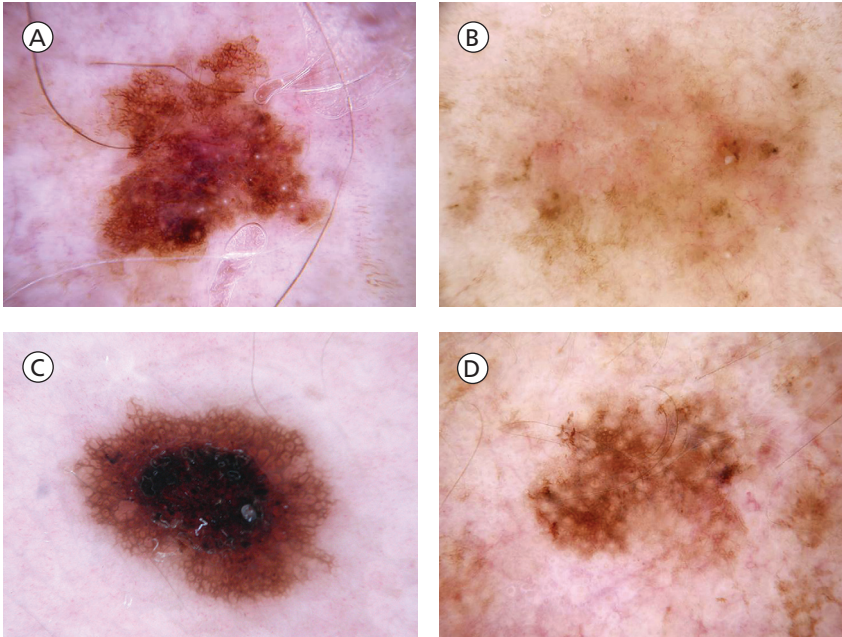


Figure 2. Pigmented network leading to a wrong classification. (A) Seborrheic keratosis. (B) Solar lentigo. (C) Seborrheic keratosis. (D) Solar lentigo. [Copyright: ©2012 Tschandl et al.]

because the reticular lines of the pigment network are due to hyperpigmentation of basal keratinocytes, which is common in seborrheic keratoses and a hallmark of solar lentigo. The high number of misclassified lesions with aggregated globules is more surprising. Most of them were seborrheic keratoses (n=8) and basal cell carcinomas (n=6) and one reason for their misclassifications might be the ambiguous distinction in the definition of terms of “aggregated globules” and “multiple blue-gray globules”.

Another common reason for misclassification was the absence of either melanocytic or non-melanocytic criteria. According to the rules of the first step, these lesions should be classified as melanocytic by default. However, 68.5% of pigmented lesions without any specific criteria were not melano-

cytic and would be classified incorrectly. The misclassification of non-melanocytic as melanocytic lesions was more common than the other way round. Only 13 melanocytic lesions (7.5%) were incorrectly classified as non-melanocytic because of the absence of a pigment network or brown globules and the presence of criteria for non-melanocytic lesions such as red-bluish to reddish-black homogenous areas (n=4) or milia-like cysts (n=2).

Originally, the differentiation of melanocytic and non-melanocytic lesions (the first step) was not part of pattern analysis. The first step was introduced to simplify dermatoscopy and to exclude non-melanocytic lesions from further analysis by short algorithms like the ABCD rule, the 7-point checklist, Menzies rule, or the CASH algorithm. The

Figure 3. An absence of any specific melanocytic or non-melanocytic (“melanocytic by default”) features, leading to a wrong classification. (A & B) Pigmented Bowen’s disease. (C & D) Seborrheic keratosis. [Copyright: ©2012 Tschandl et al.]

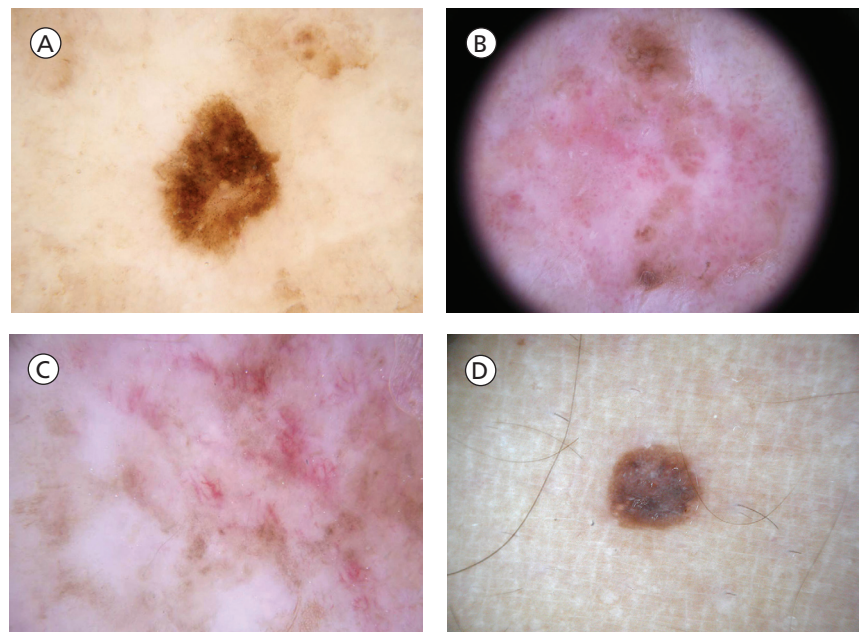


TABLE 2. Conflicting criteria in misclassified non-melanocytic lesions.

	Solar lentigo/ Seborrheic keratosis/ Lichen planus- like keratosis (n=125)	Actinic keratosis/ Bowen's disease/ Squamous cell carcinoma (n=39)	Basal cell carcinoma (n=89)	Ink spot lentigo/ Dermato- fibroma (n=7)	Inflamma- tory diseases/ Hematoma (n=3)
Pigment network	46	7	6	7	—
Aggregated globules	7	2	6	—	1
Streaks	1	—	—	—	—
Homogeneous blue pigmentation	—	—	1	—	—
Parallel pattern	—	—	—	—	—
None*	35	24	13	—	2
Pigment network & Aggregated globules	3	—	—	—	—

* “None” refers to the fact that, in the 2-step algorithm, all lesions without any non-melanocytic features are classified as melanocytic by default.

TABLE 3. Conflicting criteria in misclassified melanocytic lesions.

	Nevus	Melanoma
Multiple milia-like cysts	2	—
Comedo-like openings	—	—
Light brown fingerprint-like structures	1	—
Cerebriform pattern	1	—
Moth-eaten border	1	—
Arborizing vessels	—	—
Leaf-like structures	—	—
Large blue-gray ovoid nests	2	—
Multiple blue-gray globules	1	—
Spoke-wheel areas	—	—
Ulceration	—	—
Red-blue lacunas	1	—
Red-bluish to reddish-black homogeneous areas	—	4

TABLE 4. Positive predictive values for melanocytic lesion according to feature

Feature	Absolute No	No with wrong diagnosis	Positive predictive value
Pigment network	380	69 (18.2%)	0.82
Aggregated globules	96	19 (19.8%)	0.80
Streaks	12	1 (8.3%)	0.92
Homogenous blue	8	1 (12.5%)	0.88
Parallel pattern	0	0 (0.0%)	—
None *	108	74 (68.5%)	0.32

* “None” refers to the fact that, in the 2-step algorithm, all lesions without any non-melanocytic features are classified as melanocytic by default.

reason for introducing the first step probably was that many non-melanocytic lesions, especially seborrheic keratoses, would have been wrongly classified as melanomas. Although a structured approach to the analysis of pigmented skin lesions by dermatoscopy is reasonable, it is simply a matter of convention and convenience how the diagnostic procedure is structured. Simplicity, reproducibility and accuracy are among the most important criteria to evaluate the usefulness of a diagnostic algorithm. Given the fair performance of the first step and the fact that its application is rather complex and not simple, the question is whether its usage is still justified. There is no easy answer to this question because its usage strongly depends on convenience and habit. However, in a person with chronically sun-damaged skin and many solar lentigines the 2-step approach cannot be recommended. We have shown that the risk of misclassification is especially high in individuals from Australia with chronically sun-damaged skin. Solar lentigines are very common in this population [13,14]. Solar lentigines with a pigment network contributed largely to the low positive predictive value of the first step in the Australian group.

The introduction of the 2-step algorithm was partly motivated by the relative importance of melanoma in comparison to non-melanoma skin cancer. However, we hold to the opinion that the differentiation between benign and malignant lesions is a better first step than deciding whether a lesion is melanocytic or non-melanocytic [3]. We prefer a system that differentiates between chaotic and symmetric lesions first. This system is not more accurate but conceptually simpler (Figure 4). Our study has a significant limitation. The authors are very critical with regard to the use of the first step and advocate another method instead [3]. We have tried to minimize any form of bias by blind assessment of the lesions and by selecting consecutive lesions from different parts of the world. We have used the criteria and the algorithm precisely in the way they are advocated. We acknowl-

edge that many seborrheic keratosis or solar lentigines with a pigment network can be diagnosed correctly based on other criteria. We are convinced that experienced dermatoscopists are tacitly aware of the limitations of the first step, i.e., its low specificity in solar lentigines and seborrheic keratosis and that they use other criteria to diagnose these lesions with specificity. However, this is not what the first step tells us to do. According to the first-step algorithm, the presence of a “pigment network” trumps all other criteria and thus would lead to a wrong diagnosis if used in a pedantic fashion.

Conclusion

The first step of the dermatoscopic 2-step algorithm, if applied consistently, has high sensitivity but low specificity especially in patients with severely sun-damaged skin.

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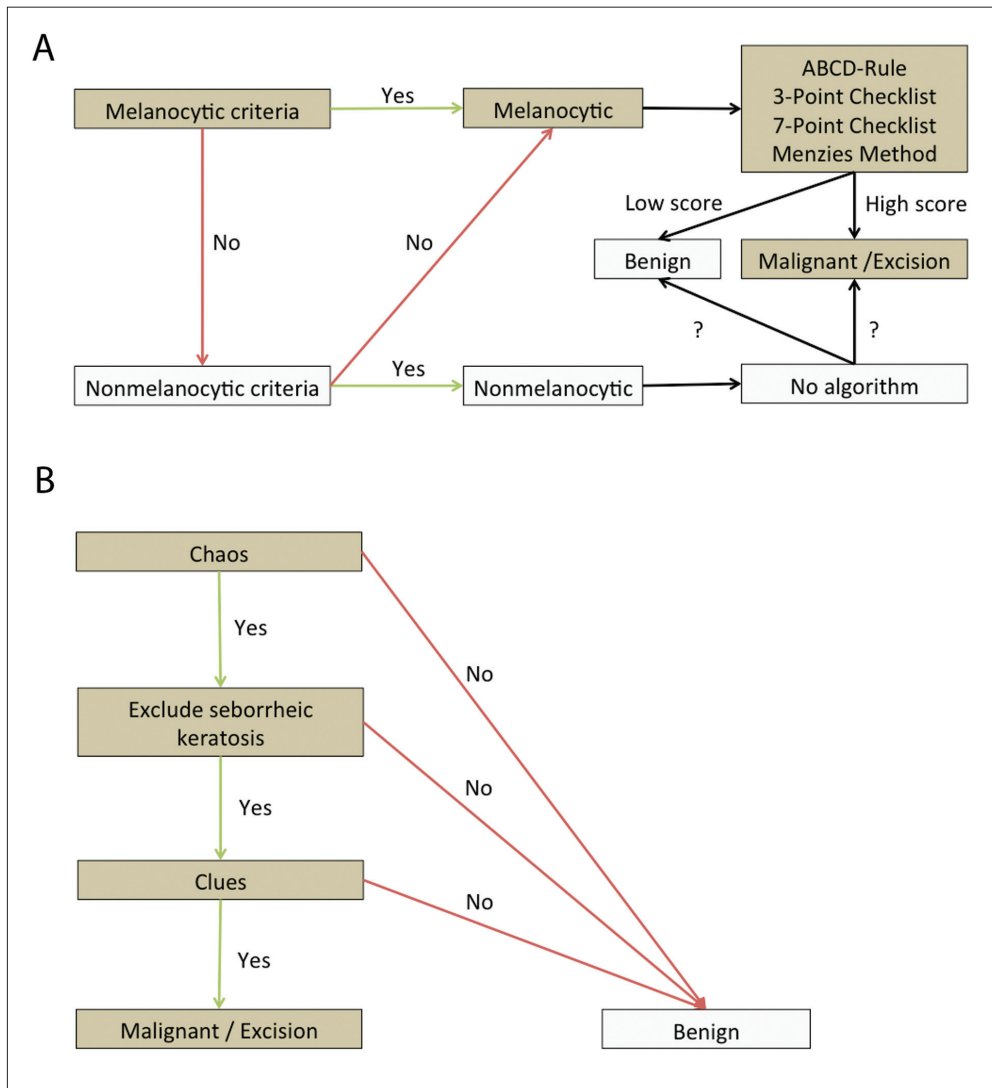


Figure 4. Difference between 2-step algorithm (A) versus “chaos and clues” algorithm (B). [Copyright: ©2012 Tschandl et al.]

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