

# Impact of clinical and personal data in the dermoscopic differentiation between early melanoma and atypical nevi

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**ABSTRACT Background:** Differential diagnosis of clinically atypical nevi (aN) and early melanomas (eMM) still represents a challenge even for experienced dermoscopists, as dermoscopy alone is not sufficient to adequately differentiate these equivocal melanocytic skin lesions (MSLs).

**Objectives:** The objectives of this study were to investigate what were the most relevant parameters for noninvasive differential diagnosis between eMM and aN among clinical, personal, and dermoscopic data and to evaluate their impact as risk factors for malignancy.

**Methods:** This was a retrospective study performed on 450 MSLs excised from 2014 to 2016 with a suspicion of malignancy. Dermoscopic standardized images of the 450 MSLs (300 aN and 150 eMM) were collected and evaluated. Patients' personal data (ie, age, gender, body site, maximum diameter) were also recorded. Dermoscopic evaluations were performed by 5 different experts in dermoscopy blinded to histopathological diagnosis. Fleiss'  $\kappa$  was calculated to measure concordance level between experts in the description of dermoscopic parameters for each MSL. The power of the studied variables in discriminating malignant from benign lesions was also investigated through F-statistics.

**ABSTRACT Results:** The variables age and maximum diameter supplied the highest discriminant power ( $F = 253$  and  $227$ , respectively). Atypical network, blue white veil and white shiny streaks were the most significant dermoscopic patterns suggestive of malignancy ( $F = 110, 104$  and  $99.5$ , respectively). Shiny white streaks was the only dermoscopic parameter to obtain satisfactory concordance value. Gender was not a discriminant factor. The specific statistical weight of clinical and personal data (ie, “patient’s age” and “lesion diameter”) surpassed those of atypical dermoscopic features.

**Conclusions:** The objective clinical and personal data collected here could supply a fundamental contribution in the correct diagnosis of equivocal MSLs and should be included in diagnostic algorithms along with significant dermoscopic features (ie, atypical network, blue-white veil, and shiny white streaks).

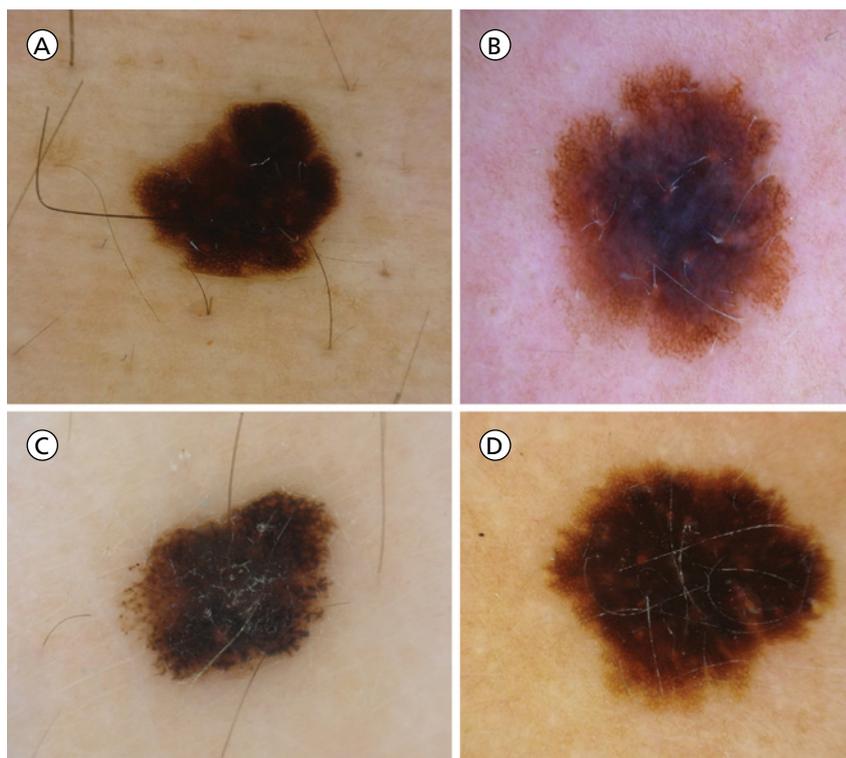
## Introduction

Dermoscopy is a useful noninvasive diagnostic method for differentiating benign from malignant melanocytic skin lesions (MSLs) [1]. In clinical practice, equivocal MSLs, including early melanomas (eMM), that do not yet exhibit clear-cut atypical features and atypical nevi (aN) showing clinical and dermoscopic features usually associated with malignancy are seen frequently. Early diagnosis of these equivocal MSLs can be challenging even for experienced dermoscopists [2-5]. In daily practice, dermatologists consider a patient’s risk factors that together form a basis for the decision “to leave or to excise” that include lesion dimension, localization, evolution in time, number of nevi, personal/familial history of melanoma, and skin phototype [6-8]. However, only 4 criteria—body site, maximum diameter, age, and sex—represent objective and standardized variables to assess for malignancy.

The objective of this study was to define which clinical and personal data are the most relevant risk factors for malignancy and to investigate their impact in the dermoscopic differential diagnosis between eMM and aN.

## Methods

A total of 493 atypical MSLs were excised from 2014 to 2016 with suspected malignancy (Figure 1). MSLs localized on the face, palms, and soles were excluded *a priori* due to their pecu-



**Figure 1.** Examples of dermoscopically and clinically equivocal MSLs from the case study (polarized dermoscopy, 20 $\times$ ) diagnosed histologically. Atypical nevi exhibiting atypical network (A, B), blue-white veil and shiny white streaks (B). Early melanomas (C, D) showing only irregular dots and globules (C) and irregular pigmented blotches (D). Nevi were excised from the abdomen of a 43-year-old woman (A) and the arm of a 51-year-old man (B). Melanomas were excised from the upper back of an 83-year-old man (C) and a 79-year-old woman (D).

liar dermoscopic pattern. After selection for image quality, availability of patient data, and agreement of 3/3 experts on histopathological diagnosis, the final database consisted of 450 standardized dermoscopic micrographs—300 aN and 150 eMM—acquired at 17 $\times$  magnification. Dermoscopic evaluations were independently performed by 5 experts in dermoscopy. They were asked to assess the presence/absence of a series

of 18 dermoscopic structures designed to include only the features most commonly associated with atypical MSLs according to the current in literature. To ensure a thorough, blinded pattern recognition analysis, all experts were unaware of the histopathological diagnosis, clinical and personal data. Then, each one of the 18 selected dermoscopic structures was defined as absent/present within a lesion when 5/5 experts agreed.

**TABLE 1.** Discriminant analysis showing F-statistics (F) and P-value (P) of all dermoscopic, clinical, and personal variables (47) coded into 38 simple variables, 5 whole variables (bold), and 4 grouped variables (italics)

<b>Integrated Variables</b>	<b>F</b>	<b>p</b>	<b>Integrated Variables</b>	<b>F</b>	<b>p</b>
Age (years)	253	.000	Atypical vascular pattern (AVP)	21.2	.000
<b>Maximum Diameter</b> (mm)	227	.000	Shoulders	13.7	.000
Age cut-off ≥40 years	197	.000	<i>Group C: Seldom exposed sites</i>	13.5	.000
Age cut-off ≥60 years	167	.000	Hypopigmented areas	13.4	.000
Maximum diameter cut-off ≥8	152	.000	Blue-gray globules	13.3	.000
Age cut-off ≥50 years	146	.000	Arms + hands	12.6	.000
Maximum diameter cut-off ≥5	133	.000	<i>Group A: Chronically exposed sites</i>	12.1	.001
Maximum diameter cut-off ≥7 mm	129	.000	<i>Group D: Rarely exposed sites</i>	9.73	.002
Maximum diameter cut-off >10 mm	124	.000	Back	7.21	.007
Atypical network	110	.000	<b>Anatomical Site</b>	6.82	.009
Age cut-off ≥30 years	108	.000	Neck	6.78	.009
Blue-white veil	104	.000	Chest/breast	5.68	.017
Shiny white streaks	99.5	.000	Ankle + back of the feet	5.47	.019
Irregular pigmented blotches	67.6	.000	Side	4.35	.037
Irregular streaks	55.6	.000	Head	2.69	.102
Pink areas	52.3	.000	Multicolor pattern	2.68	.06
Blue-white veil >30%	47.6	.000	Broad network	2.57	.08
White scar-like areas	41.1	.000	Bottom	2.55	.110
Blue-gray peppering	39.2	.000	Abdomen	2.30	.130
<b>UV-exposed Body Areas</b>	39.2	.000	Radial streaming	2.6	.10
<i>Group B: Frequently exposed sites</i>	27.9	.000	Multiple brown dots	2.3	.12
Legs	23.5	.000	Light brown areas	2.1	.13
Irregular dots and globules (IDG)	22.6	.000	<b>Gender</b>	2.1	.28

Overall interobserver agreement was estimated by Fleiss'  $\kappa$  and its 95% confidence interval (CI). In a second phase, we retrospectively collected 2 clinical data (diameter and body site) and 2 personal data (age and sex) sets for each of the 450 MSLs, obtaining an integrated database of 450 images associated with 18 subjective (ie, dermoscopic data) and 4 objective variables (ie, clinical-personal data). In order to be tested for risk factors for malignancy, they were evaluated both in their original form as 5 whole variables and in their binary-coded form as 42 simple variables. Age and maximum diameter were dichotomized to account for some interesting cut-off values. The lesion site was described according to ana-

tomical criteria and further grouped into 4 body areas according to UV exposure, ie, Group A, chronically photoexposed body sites (head, neck, arms/hands); Group B, frequently photoexposed body sites (thighs, legs, ankle, back of the feet); Group C, seldom photoexposed body sites (shoulders, chest/breast, back); and Group D, rarely photoexposed body sites (abdomen, bottom, side).

## Results

Univariate discriminant analysis of all 47 integrated variables, shown in Table 1, was performed taking the histopathological diagnosis as outcome. Univariate power to discriminate between

eMM and aN was quantified by means of F-statistics. Statistical significance ( $P < 0.05$ ) was obtained by 37/47 variables. Taken together, the results of this analysis showed that: 1) age and diameter exhibited the highest discriminant power for eMM when considered as whole or simple variables; 2) the classification of anatomical sites into 4 body area groups according to UV exposure resulted in association with malignancy (eg, body site "head" obtained  $P > 0.05$  and  $F < 2.69$  as simple variable, but  $P < 0.05$  and  $F = 12.1$  when as part of Group A, chronically exposed body areas); 3) none of the dermoscopic features reached  $F > 110$ , demonstrating moderate impact; and 4) as reported in Table 2, agreement between experts

**TABLE 2. Concordance levels of experts (D<sub>1</sub>-D<sub>5</sub>) in recognition of dermoscopic structures (only variables that obtained P > 0.05 are shown)**

Dermoscopic Variable	Fleiss' κ [95% CI]	Strength of Agreement
Shiny white streaks	0.418 [0.403-0.432]	Intermediate
Irregular dots and globules	0.375 [0.360-0.389]	Poor
Blue-white veil	0.334 [0.320-0.349]	Poor
Blue-gray globules	0.302 [0.287-0.316]	Poor
Hypopigmented areas	0.297 [0.283-0.312]	Poor
Irregular streaks	0.254 [0.239-0.268]	Poor
Atypical network	0.238 [0.224-0.253]	Poor
White scar-like areas	0.214 [0.200-0.229]	Poor
Pigmented areas	0.163 [0.148-0.177]	Poor
Blue-white veil >30	0.151 [0.137-0.166]	Poor
Atypical vascular pattern	0.100 [0.085-0.114]	Poor
Blue-gray peppering	0.098 [0.084-0.113]	Poor
Irregular pigmented blotches	0.077 [0.063-0.091]	Poor

was generally poor, with the exception of white shiny streaks ( $\kappa = 0.418$ , 95% CI 0.403-0.432) albeit of intermediate level, which was probably due to the clear-cut appearance of this pattern.

## Conclusions

The method of combining clinical and personal data with dermoscopic variables proved to be highly useful diagnostically in differentiating regressing MM from regressing nevi [8]. Here in this dataset of eMM and aN, the relative impact of dermoscopic structures was moderate and their recognition was confirmed to be a rather subjective and equivocal method with unsatisfactory agreement [1,2]. Our findings are in line with recent epidemiological data in that eMM shows a trend to be increasing in prevalence in the elderly with no gender predominance [5,6], a strong correlation with lesion maximum diameter [7,8], and a moderate correlation with UV exposure ( $F=39.4$ ). This probably reflects only a fraction of eMM

that develop due to UV exposure [5-7]. In conclusion, despite the contemporary presence of an atypical network, blue-white veil, and shiny white streaks within an equivocal MSLs, which may indicate malignancy, the objective clinical and personal data collected could supply a fundamental contribution in the correct diagnosis of equivocal MSLs and should be included in diagnostic algorithms.

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