Dermatology Practical & Conceptual

Pigment Network Analysis in Melanoma and Nevi: Retrospective Study from Snippets to Full Dermoscopic Images

Noa Kremer[1,2*], Isabella N. Dana[1,3*], Emmanouil Chousakos[4], Larissa M. Pastore[5], Allan C. Halpern[1], Stephen W. Dusza[1], Jochen Weber[1]; Ofer Reiter[1,2], Aimilios Lallas[6], Cristian Navarrete-Dechent[1, 7], Ralph Braun[8], Harold S. Rabinovitz[9], Gustavo Carvalho[10], Rashek Kazi[1], Rozina B. Zeidan[1], Shirin Bajaj[1], Nicholas R. Kurtansky[1], Ashfaq A. Marghoob[1]

1 Dermatology Service, Memorial Sloan Kettering Cancer Center, New York, USA
2 Tel Aviv University Faculty of Medical and Health Sciences, Tel-Aviv, Israel
3 SUNY Downstate Health Sciences University College of Medicine, Brooklyn, New York, USA
4 1st Department of Pathology, Medical School, National & Kapodistrian University of Athens, Greece
5 Department of Internal Medicine, Cooper University Hospital, Camden, New Jersey, USA
6 First Department of Dermatology, Aristotle University School of Medicine, Thessaloniki, Greece
7 Department of Dermatology, Facultad de Medicina, Pontificia Universidad Catolica de Chile, Santiago, Chile
8 Department of Dermatology, University Hospital Zurich, Gloriastrasse, Zurich, Switzerland
9 Department of Dermatology, University of Miami Miller School of Medicine, Miami, Florida, USA
10 Cutaneous Oncology Department, A.C. Camargo Cancer Center, São Paulo, Brazil
***These authors equally contributed.**

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Corresponding Author: Noa Kremer, MD, 425 Main Street, New-York, NY 10044. ORCID ID: 0000-0002-9533-6222.
E-mail: kremern1@mskcc.org

ABSTRACT

Introduction: Atypical network is a dermoscopic criterion that helps in the diagnosis of melanoma. Despite its importance, the interpretation of atypical networks varies widely among experts.

Objective: This study examined the impact of viewing the whole lesion versus viewing foci of pigment network (i.e., snippets) in isolation from within the lesion on expert classification of pigment network in dermoscopic images.

Method: Six dermoscopy experts, blinded to the diagnosis, each evaluated a total of 92 images (80 nevi and 12 melanomas) for the presence of typical versus atypical pigment network. While 57% of images had consistent classification of the network between whole lesion and snippets, 43% shifted the network classification between the snippet to the whole lesion view. Melanomas were more prone than nevi to intra-rater discrepancy between whole lesion and snippets (54.2% vs. 41.7%; odds ratio (OR): 1.65; 95% confidence interval (CI): 1.11–2.47). The inter-observer agreement was higher for the snippet view (65.22%) than for the whole lesion view (55%).

Results: These findings suggest that both the objective morphology of the pigment network and the subjective interpretation of the network in context with other features within the lesion influence expert classification of pigment network.

Conclusion: Factors such as the variability in the distribution, thickness, and color of network lines, overall pattern, and other dermoscopic structures likely contributed to the classification changes.

Introduction

Atypical network is a dermoscopic criterion that helps in the diagnosis of melanoma[1]. The definition of an atypical network, according to the 2003 Internet Consensus Meeting [2] and the 2007 International Dermoscopy Society (IDS) consensus meeting [3], is "a black, brown, or gray pigment network with irregular holes and thick lines." Over time, this definition evolved from focusing primarily on the variability in color and line thickness to include the degree of symmetry in its distribution, leading to the 2016 IDS consensus meeting [4] definition of an atypical pigment network as "one with increased variability in the color, thickness, and spacing of the lines; asymmetrically distributed; gray color". However, since 2016, there remains a low-to-moderate agreement regarding the classification of atypical networks. Lallas et al. [5] reported that the inter-observer agreement for atypical network was low, with a kappa value of 0.39. In a more recent study conducted by Liopyris et al. [6], including dermoscopy experts, almost perfect agreement was achieved for the presence/absence of network in lesions, but there was variable agreement on the type and localization of the network within the lesion.

Observations regarding dermoscopic criteria for melanoma diagnosis emphasize the importance of evaluating the number of colors, structures, and their distribution rather than focusing solely on specific structures such as network in isolation [1,7-9]. Consequently, interpreting pigmented network as typical or atypical is likely influenced not only by its objective morphology but also influenced by the subjective visual context based on the presence or absence of other structures and colors within the lesion [10].

Objectives

The primary objective of this study was to examine the impact of viewing the whole lesion versus viewing foci of pigment network (i.e., snippets) in isolation from within the lesion on expert classification of pigment network in dermoscopic images. The secondary objectives included examining inter-observer agreement regarding the classification of the pigment network and assessing whether expert reviewers' definitions of an atypical pigment network align with the current definition outlined in the literature [4].

Methods

This retrospective observational study was performed between November 2022 and August 2024. The study was approved by the Institutional Review Board (IRB) under approval number 16-458.

Image Selection, Network Annotation, and Generation of Circular Pigment Network Foci

Dermoscopic images of melanomas and nevi captured between 2002 and 2019 displaying a discernible pigment network were selected from a clinical database at Memorial Sloan Kettering Cancer Center (MSKCC) and from the ISIC Archive (https://www.isic-archive.com/). An expert dermoscopist (A.A.M) annotated the boundaries of network regions within each image, which were stored as binary mask images[11]. Pixels belonging to contiguous areas of the network were marked in white, while all other pixels were marked in black (Figure 1). Circular snippets were then extracted from these annotated regions using a Euclidean distance transform [12], ensuring that the snippets were centered within the network areas. The largest possible circular snippets were then automatically extracted from the network-patterned areas (Figure 2). To ensure that the snippets were informative enough for readers to determine the type of network, snippets with fewer than 10 holes were excluded from the dataset. The total number of snippets generated in this manner was 141, ranging from one to seven per lesion image. Most images

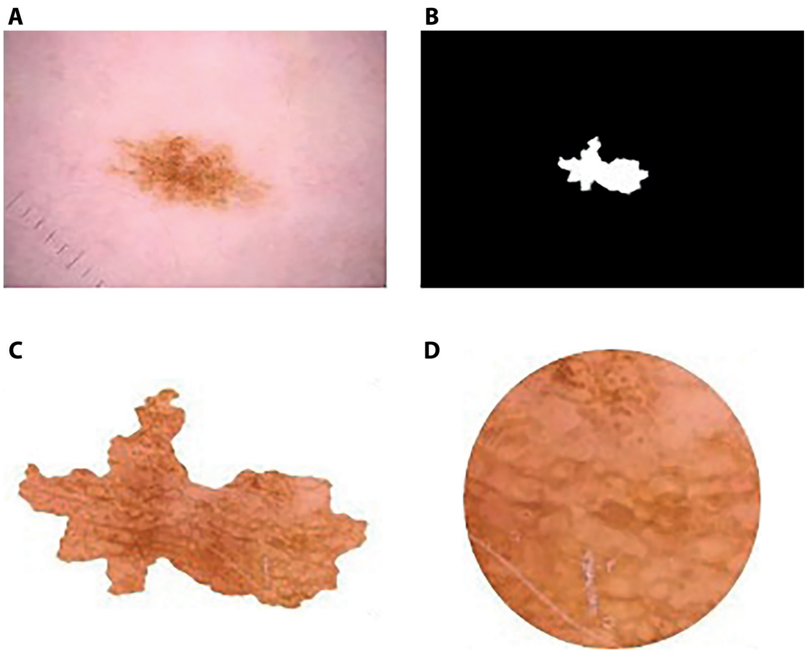

Figure 1. Creating Snippet. a. An expert dermoscopist (A.A.M) annotated the images to identify the regions of predominant pigment network. b. From these annotations, binary masks were created. c. The area of pigmented network extracted from the original whole dimension dermoscopy image. Euclidean-distance transform was applied to the binary masks. d. From the transformed images, circular areas were extracted.

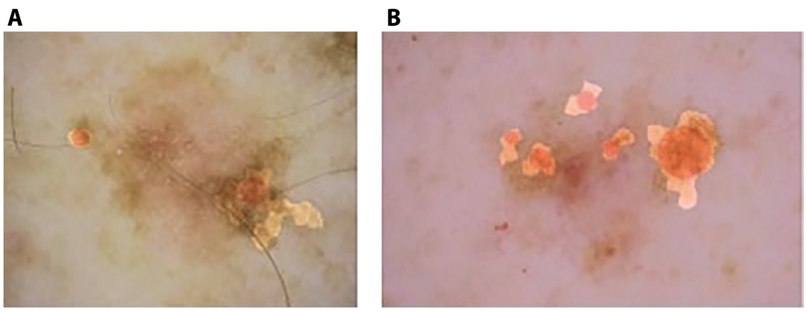

Figure 2. The largest possible circular cutouts were extracted from the network-patterned areas. (a) Melanoma with two circular areas. (b) Nevus with five circular areas. Two circles with fewer than 10 holes were excluded, and only 3 circles were shown to the six experts.

(60 out of 92) yielded a single circular snippet. The average number of snippets did not differ significantly between nevi and melanomas (approximately 1.5 per lesion).

Web-Based Data Collection Instrument

Six dermoscopy experts participated in the study, completing a web-based intake form with three modules. In the Preliminary Module, each participant provided his/her definition of an atypical network. In the Network Foci Module (Snippet), circular snippets from the same lesion were presented to each reader simultaneously, and readers classified the network as typical, atypical, or both (typical and atypical). In the Whole Image Module, whole dermoscopic images were shown, and readers classified the network in the image as either typical, atypical or both.

In each module, the cases were presented in a random order without diagnostic or demographic information. This random order was consistent for all readers to ensure uniformity in response (Figure S1). The same set of lesions was presented as cases in both the Network Foci Module and Whole Image Module.

Eligibility Criteria

Inclusion Criteria: melanocytic lesions with a discernible and in-focus pigment network visible on the dermoscopic images.

Exclusion Criteria: low-quality dermoscopic images and non-melanocytic lesions with a pigment network.

Statistical Analysis

The snippet and whole-image modules were independently assessed for network classification frequencies and inter-rater agreement, which was measured as percent agreement, Scott's/Fleiss' kappa, and Gwet's AC. Ninety-five percent confidence intervals (95% CI) were estimated.

Responses from snippet and whole-image modules were pooled to analyze intra-rater network classification consistency. Network classifications of a given lesion between the two modules by the same rater were viewed as a paired response and analyzed using confusion matrices and sankey diagrams. A binary variable indicated whether the rater's classification of a given lesion differed between the two modules. The relationship between network classification consistency and lesion type (nevus or melanoma) was analyzed using logistic regression and chi-square statistics.

Data management and analysis were performed using StataMP v16.1, StataCorp, and RStudio Build 524.

Results

Six dermoscopy experts, blinded to the diagnosis, each assessed 92 melanocytic neoplasms displaying network within the lesion, including 12 melanomas and 80 nevi. Across both snippet and whole-image modules, 1,104 observations were collected, resulting in 552 paired responses (72 of melanoma and 480 of nevi). All melanomas were confirmed as in situ by histopathology and 65% of the nevi were diagnosed as dysplastic nevi through histopathology, while the remaining 35% presented with benign and stable morphology during consecutive dermoscopic follow-up.

Classifications of Pigment Network by Image Type

The proportions of typical and atypical pigment network classifications were similar between snippets and whole lesion images (Table S1). Fifty-seven percent (N=315) of paired responses maintained consistent network classification across snippet and whole dermoscopic image evaluation (Figure 3). Of these, a slightly higher proportion of snippets were classified as typical networks (28%, N=153) compared to those classified as atypical networks (25%, N=139).

Forty-three percent (N=237) of paired responses shifted in network classification from the snippet to a whole image (Figure 3). A slightly higher proportion of snippets changed from typical network to atypical network in the whole lesion images, observed in 14% (N=77), compared to 10% (N=57) of snippets classified as atypical shifting to typical in the whole lesion images (Figures 3 and 4, sankey diagram).

Classifications of Pigment Network by Lesion Diagnosis

Of nevi, 58.3% (N=280) of paired responses maintained the same network classification from snippet to whole dermoscopic images (Table 1), with the majority (31.5%, N=151) classified as having a typical network, 22.9% (N=110) as atypical network, and 4% (N=19) as both types of networks (Figure 5A). Of the 41.7% (N=200) that underwent

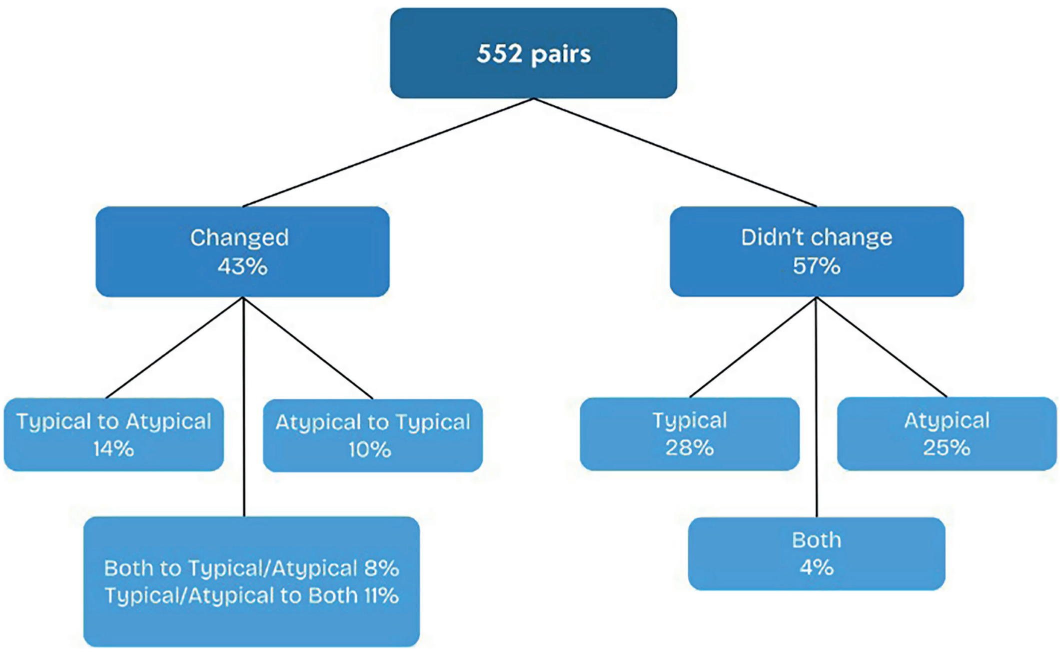

Figure 3. Chart of the relative frequency (%) of evaluations for the snippet and the whole dermoscopic image.

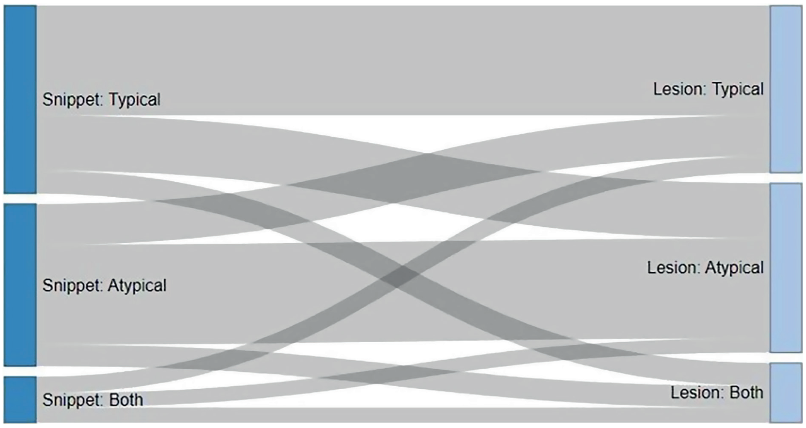

Figure 4. Sankey diagram depicting flow of pairs of lesion observations from snippet to whole dermoscopic image evaluation of the lesions.

Table 1. Distribution of Classification Flux Between Snippet and Whole Dermoscopic Image Observations Stratified by Lesion Diagnosis.

		Overall (n=552)		Lesion Diagnosis			
				Nevi (n=480)		Melanoma (n=72)	
		n	proportion	n	proportion	n	proportion
Classification from snippet to whole image	Same	313	56.7%	280	58.3%	33	45.8%
	Changed	239	43.3%	200	41.7%	39	54.2%

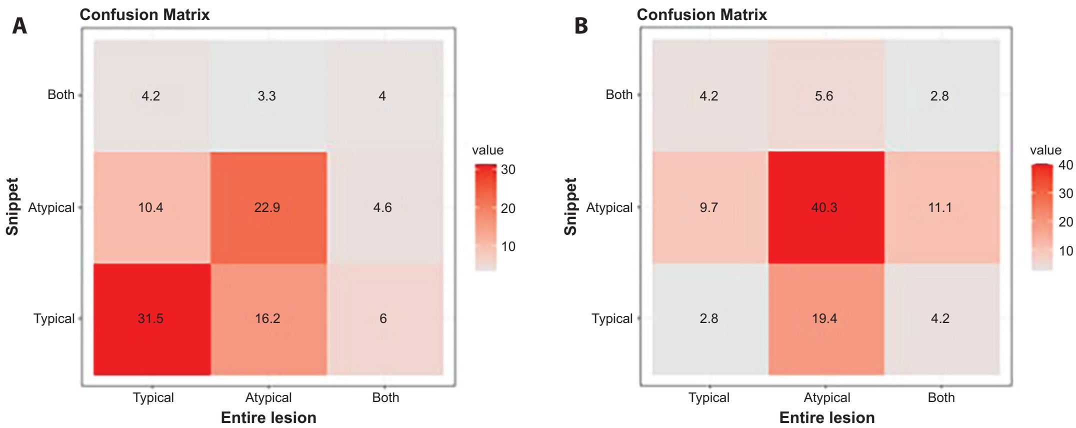

Figure 5. Confusion matrix of the relative frequency (%) of evaluations for the snippet and the whole dermoscopic image for nevi (a) and melanoma (b).

a change, there was a slightly higher shift from a typical network to an atypical network, observed in 16.2% (N=63) of paired responses, compared to a 10.4% (N=50) shift from atypical to typical.

In melanoma, 45.8% (N=33) of paired responses maintained the same network classification (Table 1). Among these, 40.3% (N=29) were identified as having an atypical network (Figure 5B), while only 5.6% (N=4) were classified as either typical network or both types of networks. Of the 54.2% (N=39) that had a change in network classification, the most notable shift was from a typical network to an atypical network, occurring in 19.4% (N=14) of cases, compared to 9.7% (N=7) that shifted from an atypical to a typical network. Paired responses involving melanomas were more likely than those of nevi to have inconsistent network classification, with an odds ratio (OR) of 1.65 (95% CI: 1.11–2.47). Additionally, the classification in melanomas shifted to having both network types slightly more frequently

Table 2. Breakdown of Atypical Network Features According to 6 Experts' Definitions.

	Expert 1	Expert 2	Expert 3	Expert 4	Expert 5	Expert 6
Network / line thickness	+	+	+	+	+	
Network / line color		+	+	+	+	+
Network / line distribution		+		+		+
Network / lines shape	+	+				
Holes diameter / lines spacing			+	+		
Gray color						
Other			Deviation from the expected appearance.		More than 1 different networks in the same lesion.	Negative network, pseudopods, heavily pigmented dots and globules, veiling.

than that of nevi, with 15.3% (N=11) changing to having both network types compared to 10.6% (N=51) of paired responses involving nevi (Figure 5A-B).

Classifications of Pigmented Network by the Experts

The definitions of an atypical network provided by the six experts were different from the definition established at the 2016 IDS consensus meeting[4]. All six experts' definitions for atypical networks are detailed in Table S2. Five out of six experts include thickness, 5/6 color, 3/6 distribution, 2/6 shape, and 2/6 spacing of the lines (Table 2). None of the experts mentioned gray color, which was included in the 2016 IDS consensus meeting[4]. However, one expert included in his definition also negative network, dots, globules, and pseudopod, and another expert defined it as any network that deviates from the benign expected nevus pattern.

There were clear differences in the experts' classification of the pigment network, with some experts showing more discrepancies than others between the snippet and the whole dermoscopic image (Figure S2). The snippets showed better inter-observer agreement compared to whole lesion images across all three measures, with moderate agreement (65.2%) for the snippets and low-moderate agreement for the whole lesion images (55%); Gwet's AC was 0.51 for snippets versus 0.35 for whole lesion images; Scott/Fleiss' kappa was 0.41 for snippets versus 0.27 for whole lesion images (Table S3).

Discussion

This study investigated the classification of pigment network across snippets and whole lesion dermoscopic images of 80 nevi and 12 melanomas. Our findings reveal that a significant portion of paired responses (43.3%) had inconsistent classification between snippets and whole lesion images across the six experts, with variations observed associated with the lesion type, nevus, or melanoma.

Network classification inconsistencies were more common in melanomas, with an OR of 1.65. Conditioned on paired responses with network classified "typical" in snippet-view, 73% involving melanomas were classified "atypical" in whole-image view as compared to 30% involving nevi. This suggests that visual context plays an important role in interpreting the network as atypical in melanoma compared to nevi. Several factors in the visual context may influence the expert's classification of the network as atypical:

1. Network's distribution – Observing the distribution of the entire network can alter the classification especially if it is asymmetrically located at the periphery or the line thickness and color are unevenly distributed across the lesion[13], as demonstrated in Figure 6a.
2. Additional Dermoscopic Structures: Other dermoscopic structures[14], beyond atypical networks, which are correlated with atypia/melanoma can serve as diagnostic anchors that influence experts' interpretation of the network as atypical. Examples of such structures are illustrated in Figure 6b.
3. Overall Architectural Organization or Heuristic Method ('Blink' Approach): In melanoma, dermoscopic structures and colors are often distributed in a disorganized manner, resulting in a chaotic appearance within the lesion[7]. Experts frequently employ the heuristic method,

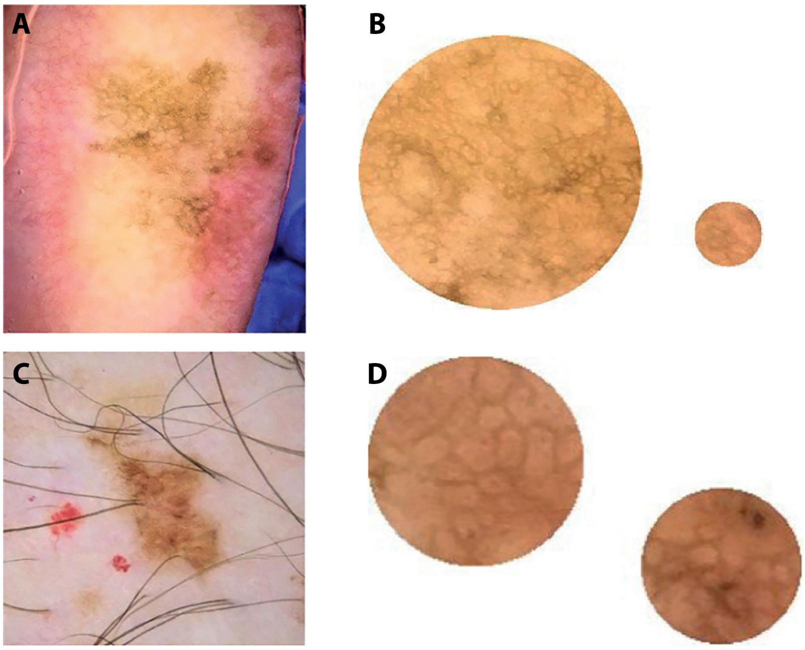

Figure 6. Melanoma in (A) and (C): lower snippet, upper whole image. (A) Classification changed from typical to atypical for 4 readers with asymmetric distribution of the network line thickness and color in the whole lesion image. (C) The streaks (peripheral radial lines) in the upper left quarter could explain why 3 out of 6 experts changed their classification from typical to atypical.

which involves recognizing the overall dermoscopic pattern of a lesion and relying on intuition or a "gut feeling"[15]. Evaluation of the whole dermoscopic image can change the expert's classification from typical to atypical network due to the disorganized context or "gestalt", rather than simply relying on the morphology of the network itself.

Because many melanomas exhibited a combination of asymmetric network distribution, other melanoma specific dermoscopic features, and overall architectural disorganization as illustrated in Figure 7a-b, it is not possible to pinpoint which specific factor in the visual context influenced the experts' change in network classification. Additionally, individual expert interpretations, which rely on different contextual elements based on their definitions of an atypical network, likely contributed to the change in network classification[16]. However, this shift in classification of networks emphasizes the importance of the entire dermoscopic lesion assessment, as the context provided by the whole image impacts the classification of network beyond just the morphology of the network as viewed in the snippets.

Unlike melanoma, which exhibits greater architectural complexity, nevi tend to be more symmetric and organized[13] (Figure S2). Since all nevi included in the study were required to have a reticular network, and because the primary morphological feature in our nevi likely had a

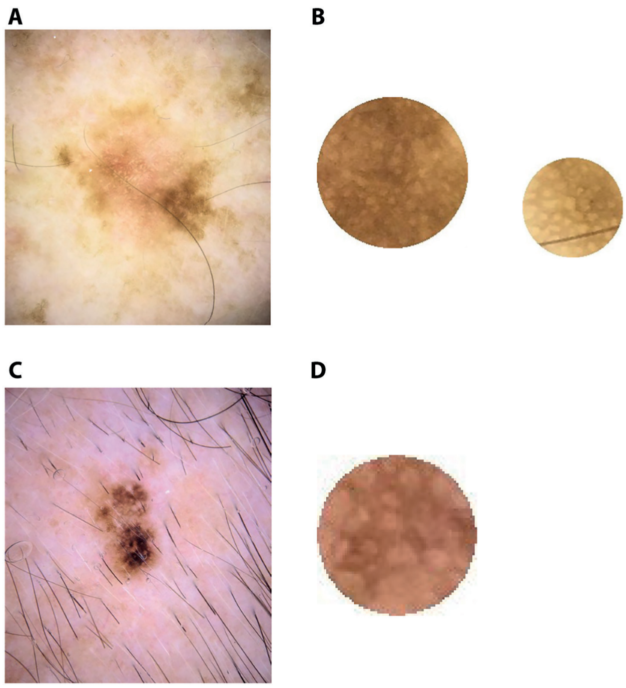

Figure 7. Melanoma in (A) and (C): lower snippet, upper whole image. (A) Melanoma with disorganization in colors and structures, shiny white lines (chrysalis), pink structureless areas and red dots in addition to atypical network unevenly distributed. Classification changed from typical to atypical for 3 readers (C) Melanoma with disorganization in colors and structures, linear angulated lines (polygons) and black blotch in addition to atypical network unevenly distributed. Classification changed from typical to atypical for 4 readers.

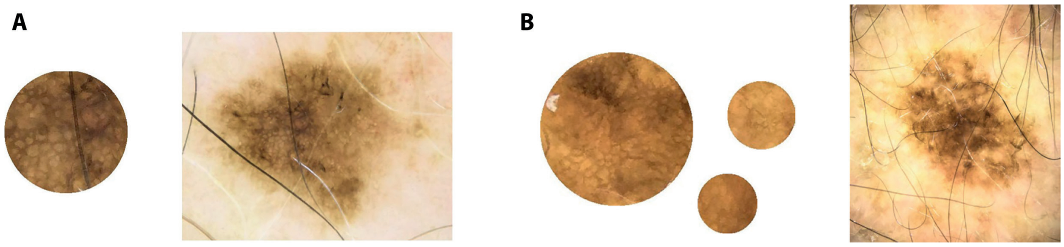

Figure 8. Melanoma in (A) and (B): left snippet, right whole image. Both with dominant morphologic structure of atypical pigment networks with thickened lines. (A) Classification remained the same (atypical) for 6 readers. (B) Classification remained the same (atypical) for 4 readers.

typical network appearance, the context of the lesion was less critical in classifying the network. These findings are consistent with the literature, which indicates that melanoma is usually diagnosed based on a combination of morphologic structures rather than a single feature[1]. Additionally, melanomas that did not change in network classification for most experts had atypical pigment networks as their main feature (Figure 8a-b). For these melanomas it is most likely that the thickened lines were noticed as atypical in the snippet and in the whole image (Figure 8a-b). However, in the nevus cases where there was a shift in the network classification, there was likely an influence on the network distribution and overall pattern in the whole image (Figure S4a). In contrast to melanoma, where additional dermoscopic structures could contribute to the change in classification this was true for only one nevus case (Figure S4b).

The definitions of an atypical network provided by the six dermoscopy experts were not consistent with the definition established during the IDS 2016 consensus meeting[4]. There were notable variations in how they interpreted the typicality of the network with low inter-observer agreement for the whole image view and low-moderate inter-observer agreement for the snippet view. Some experts showed more significant discrepancies between the snippet and the whole lesion image. This variability in the interpretation aligns with existing literature; for example, a study by Lallas et al.,[5] (2018) reported interobserver agreement of approximately 0.393 (kappa) for atypical network and a study by Carrera et al.,[16] indicated that interobserver agreement ranged from poor to fair. These findings highlight the lack of a unified agreed-upon definition of what constitutes a typical versus an atypical network[16]. The higher inter-observer agreement for the snippet supports our assumption that context provided by the whole dermoscopic image influences the classification of the network. When focusing only on the snippet, the interobserver agreement was higher, likely due to the removal of confounding visual context information and forcing the readers to focus only on the objective morphology of the network in its classification. However, when examining the whole image, the additional context led experts to interpret the network both objectively and subjectively, resulting in more disagreements among experts regarding the classification of the network as typical, atypical or both.

Limitations

Limitations of the study include the reliance on a single dermatologist's annotations for the pigment network, rather than employing more objective methods such as automated pigment network detection techniques[17]. Additionally, we were unable to precisely determine which factor in the context affected the change in classification of the network.

Conclusions

Factors such as variability in the network distribution, thickness or color of the network lines, overall pattern, and other dermoscopic structures likely contributed to changes in classification. This study highlights that the classification of a pigment network depends not only on its objective morphology, as seen in the snippets, but also on its subjective interpretation within the visual context of the whole lesion. Future studies should focus on identifying and defining the objective features that distinguish typical from atypical network. Additionally, further research is needed to determine the exact contextual factors that influence the classification of a network as typical or atypical. Identifying both the objective and subjective features involved in pigment network classification will be valuable for clinicians and could help improve AI algorithms.

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