Dermoscopy: A Review of the Structures That Facilitate Melanoma Detection

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Melanoma is currently the fifth most common cancer in the United States, resulting in more than 9000 deaths each year. Despite numerous improvements in the management of advanced melanoma, the cornerstone to ensuring a cure remains early detection. Both patient and physician awareness regarding the signs and symptoms of early melanoma remain paramount. As a result, much effort has been and continues to be expended in developing and refining effective diagnostic algorithms to help identify melanomas and differentiate them from nevi, such as the ABCDE rule (A for asymmetry, B for border irregularity, C for color variegation, D for diameter >6 mm, and E for evolution in lesion size, shape, or color). To assist in the detection of more subtle melanomas requires technology to augment a visual examination.

Toward this end, a simple instrument called a dermatoscope has transformed not only the appreciation of the morphology of melanoma but also its growth dynamics. The discipline of dermoscopy has improved the detection of melanoma and other skin cancers, has resulted in the detection of thinner melanomas, and has helped improve the ability to differentiate nevi (benign lesions) from melanomas, which, in turn, has resulted in fewer biopsies of benign lesions. Since patients often first present to their primary care physicians for their health-related concerns, it is imperative that primary care physicians be able to recognize the lesions that are suspicious for melanoma. This review is intended to introduce osteopathic physicians to the dermoscopic features associated primarily with melanomas located on non-glabrous skin.

“Melanoma writes its message on the skin with its own ink and it is there for all of us to see. Unfortunately, some see but do not comprehend.” — Neville C. Davis, MD, 1978

With 178,560 cases of melanoma diagnosed in 2018 in the United States, resulting in 9320 deaths, this disease demands attention. Much research has gone into helping physicians recognize the morphologic features of early melanoma while it is confined to the skin and can be cured via surgical removal. Although finding sensitive means for detecting melanoma have remained paramount, it has also been important for physicians to differentiate nevi from melanomas, thereby improving specificity.
A significant breakthrough in our understanding of the clinical morphology of melanoma was the recognition that many melanomas are asymmetric and have irregular borders, multiple colors, and a diameter greater than 6 mm, which formed the ABCD rule (A for asymmetry, B for border irregularity, C for color variegation, and D for diameter >6 mm), first described in 1985.3 In addition, it became evident that the history of change and symptoms such as pruritus and bleeding are also important, leading to the addition of the E, standing for evolution in lesion size, shape, or color, to the ABCD rule in 2004.4,5 Although this knowledge helped detect countless melanomas, many remained elusive by being asymptomatic and lacking any ABCDE features. To address this gap, some proposed adding the “EFG rule” with E standing for elevation, F for firm, and G for growing.6,7 Others recognized that melanomas often appear as outlier lesions or as different compared with a patient’s other, benign, lesions (nevi), a concept known as the ugly duckling sign, described in 1988.8-10 Attempts were also made to amalgamate the aforementioned observations into the “Do UC” melanoma concept, with the D standing for different, U for uneven, and C for changing.11 Although all of these rules for examining the skin with the naked eye aided in detecting superficial spreading and nodular melanomas, many still escaped detection. It became clear that examination of the skin required harnessing technology to improve on the ability to detect melanomas and to differentiate them from nevi.

The technological advancement that transformed the world of skin cancer detection proved to be a relatively simple handheld device called a dermatoscope. This instrument provides ×10 magnification and illuminates the skin in a manner that minimizes light reflection off the skin surface, thereby facilitating the visualization of colors and structures located below the stratum corneum, which are not visible to the naked eye.12 This device is used by placing it on or near the skin with the light source turned on as the user looks through the magnifier at the lesion of interest. In a meta-analysis by Vestergaard et al,13 the diagnostic accuracy for melanoma, expressed as the diagnostic odds ratio (OR), was approximately 4 times higher for dermoscopy compared with the unaided eye. The sensitivity for the diagnosis of melanoma using dermoscopy (OR, 0.90; 95% CI, 0.80-0.95) was found to be higher when compared with that of the unaided eye (OR, 0.71; 95% CI, 0.59-82; P=.002).13 The physician’s diagnostic specificity also increased with the use of dermoscopy. In a study evaluating the impact of dermoscopy on the benign to malignant biopsy ratio, Carli et al14 showed that the biopsy ratio decreased from 1:18 before use of dermoscopy to 1:4 after the use of dermoscopy. Owing to improvements in diagnostic accuracy, this instrument is used by most dermatologists engaged in skin cancer detection and is now also used by nondermatologist physicians and other healthcare professionals, such as nurse practitioners.15,16

As highlighted by Morris et al,17 only 15% of osteopathic physicians have ever used a dermatoscope; thus, it is critical to educate primary care osteopathic physicians about dermoscopy. This review is intended to familiarize the reader with the dermoscopic structures encountered in melanomas on nonglabrous skin, excluding the face. Melanomas located on the unique anatomical areas of the face, nail matrix, and mucosal and volar surfaces have additional features above and beyond those described in this review.

Literature Search
We undertook a comprehensive search of PubMed using the terms “dermoscopy” and “melanoma” from inception up to December 2018. This search resulted in 1835 articles. The title and abstract of these articles were reviewed to select 182 articles that dealt with melanoma detection and diagnosis. Studies of any design were considered. Exclusion criteria were studies that investigated melanomas on acral or volar skin, subungual melanomas, and melanomas located on mucosal and facial skin. The 182 selected articles were further reviewed to find articles that contained relevant statistical information, including sensitivity, specificity, and
ORs for dermoscopic structures associated with melanoma. Odds ratios were selected as the study measurement because they reveal how much more likely a lesion is to be a melanoma vs a nevus when a certain dermoscopic structure is present. Melanoma-specific structures are shown in the Table, Figure 1, and Figure 2 and are described below.

Melanoma Detection and Diagnosis

**Atypical/Irregular Pigment Network**

Recognizing an atypical network requires knowing the features of a typical network. A typical network consists of a gridlike pattern made up of lines and holes that are distributed in an organized manner (Figure 1A-C). The lines are usually brown to tan and display minimal variability in their thickness and hues. The holes of the network also display minimal variability in their sizes. In contrast, an atypical network consists of a web of lines of varying colors and thicknesses; the open spaces or holes in the web are also of varying diameters (Figure 2A).33 The appearance is a chaotic or disorganized network pattern. The color of the atypical network ranges from brown to black or gray, and it can appear smudged or out of focus. An irregular network is often associated with the in situ component of a superficial spreading melanoma. The lines of the network correspond histologically to the suprapapillary plates, and the lines correlate with the rete ridges.34 The irregular lines reflect the distorted rete ridges caused by the proliferation of malignant melanocytes. The black and gray colors are associated with increased melanization of surrounding keratinocytes and are due to proliferation and pagetoid spread of the malignant melanocytes. An atypical network confers an OR of 1.8 to 9.0 for melanoma.

**Negative Network**

The negative network can be described as hypopigmented serpiginous interconnecting lines that appear to wind through the lesion, creating a network and leaving islandlike regions of brown hyperpigmentation (Figure 2E).39 This dermoscopic finding may also be present in Spitz nevi. Because it is difficult to differentiate a Spitz nevus from a melanoma, the presence of a negative network should always raise concern for melanoma.40 A histologic correlate for a negative network has not been well established; however, it may represent bridging of adjacent rete ridges or elongation of the rete ridges in association with large melanocytic nests in the papillary dermis. The negative network is frequently observed in melanomas arising in association with nevi.41 The presence of a negative network has been found to have a 1.4 to 1.8 OR for melanoma.

**Atypical Streaks**

Streaks are linear pigmented projections emanating from the tumor and radiating toward normal skin. These structures may or may not have a bulbous ending. Those without a bulbous ending are known as radial streaming and those with a bulbous ending are known as pseudopods. Streaks correspond to the radial growth phase of either a pigmented Spitz nevus or a superficial spreading melanoma. Typical streaks, as seen in Spitz nevi, tend to be evenly distributed around the entire perimeter of the lesion in a symmetric or starburst manner (Figure 1F).42 In contrast, atypical streaks, as seen in melanomas, are irregularly and focally distributed at the periphery of the lesion.
Table.
Melanoma-Specific Structures and Associated Sensitivities and Specificities

<table>
<thead>
<tr>
<th>Melanoma-Specific Structures</th>
<th>Schematic</th>
<th>OR for Melanoma</th>
<th>Diagnostic Value</th>
</tr>
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</table>
| Atypical pigment network    | ![Schematic](image1.png) | 1.8-9.0<sup>18-21</sup> | Sensitivity: 21.0%-100.0%<sup>22-27</sup>  
Specificity: 46.0%-88.5%<sup>22-28</sup> |
| Angulated lines             | ![Schematic](image2.png) | 2.0-9.0<sup>21-23,29,30</sup> | Sensitivity: 16.7%<sup>29</sup>  
Specificity: 91.7%<sup>29</sup> |
| Negative network            | ![Schematic](image3.png) | 1.4-1.8<sup>30,31</sup> | Sensitivity: 22.0%-34.6%<sup>27,31</sup>  
Specificity: 77.2%-95.0%<sup>27,31</sup> |
| Atypical streaks            | ![Schematic](image4.png) | 1.5-5.8<sup>21-24,30</sup> | Sensitivity: 4.8%-23.0%<sup>22-27</sup>  
Specificity: 32%-58%<sup>23-28</sup> |
| Atypical dots/globules      | ![Schematic](image5.png) | 1.7-4.8<sup>21,22,24</sup> | Sensitivity: 13.0%-39.6%<sup>22-25</sup>  
Specificity: 74.3%-92.0%<sup>22-25</sup> |
| Blue-white veil             | ![Schematic](image6.png) | 1.74-13.0<sup>21,23,30</sup> | Sensitivity: 11.4%-92.0%<sup>22,23,25-27</sup>  
Specificity: 74%-99%<sup>22,23,25-28</sup> |
| Atypical blotch             | ![Schematic](image7.png) | 1.88-4.1<sup>21-23,30</sup> | Sensitivity: 18.0%-71.3%<sup>22-25</sup>  
Specificity: 30.5-92.6%<sup>22-25</sup> |
| Regression structures       | ![Schematic](image8.png) | 2.0-18.3<sup>21,23,24,30</sup> | Sensitivity: 11.4%-79.0%<sup>22,23,24-27</sup>  
Specificity: 63%-99%<sup>22,23,24-27</sup> |

(continued)
However, because spitzoid lesions can be difficult to differentiate from melanomas, a skin biopsy is recommended in patients older than 12 years presenting with symmetric spitzoid lesions. Histologically, streaks correlate with confluent melanocytic nests located at the DEJ at the periphery of a lesion. Atypical streaks have a 1.5 to 5.8 OR for melanoma.

Atypical Dots

Typical dots are associated with a typical network; they can be located in the center of the reticular nevi, on top of the network lines, or in the holes of the network. In contrast, atypical dots do not need to be associated with a network, but if a network is present, it is often atypical. Atypical dots are brown to black round structures measuring less than 0.1 mm in diameter. They tend to be distributed randomly and are often found toward the periphery of the melanoma (Figure 2A). Histologically, brown dots correlate with small clusters of melanocytes at the DEJ or in the epidermis; in contrast, black dots correspond to clumps of melanin in the stratum corneum. A lesion with atypical dots has a 1.7 to 4.8 OR for melanoma.

Atypical Globules

Typical globules display minimal variation in size, shape, and color; they can be symmetrically distributed around the periphery of a reticular nevus, in the center of a reticular nevus, or evenly dispersed throughout the nevus (Figure 1F-H). Histopathologically, globules correspond to nests of melanocytes in the DEJ or dermis. According to their location or cell type, globules can be brown (nests of melanocytes present at the DEJ or superficial dermis), blue (nests of melanocytes located deeper in the dermis), or white (balloon cell changes in melanocytes). Atypical globules are round to oval to angulated pigmented clods larger than 0.1 mm in diameter and present with varying size, shape, or color and may be distributed in a disorganized fashion within the lesion (Figure 2A). While most globules are round to oval, some are angulated, creating a cobblestone pattern. Atypical globules have an OR of 1.7 to 4.8 for melanoma.
Blue-White Veil

The presence of blue in association with an overlying white ground glass haze defines the structure known as a blue-white veil (Figure 2D). Palpation reveals a raised lesion. Histologically, it correlates with melanocytes in the deeper dermis together with compact orthokeratosis. Differential diagnosis includes blue nevi; however, these benign tumors usually present with a uniform homogenous steel-blue color (Figure 1E). In contrast, blue-white veil in a melanoma does not encompass the entire surface of the lesion, and it often displays multiple hues of blue. The presence of a blue-white veil confers an OR for melanoma of 1.74 to 13.0.

Atypical Blotch

A blotch consists of a hyperpigmented structureless area that encompasses at least 10% of the surface area of a lesion. A typical blotch, as seen in nevi, is located in the center of a nevus with a reticular pattern (Figure 1D). In contrast, the presence of 1 or more off-center blotches is considered atypical and is highly suspicious for melanoma (Figure 2D). Histologically, it represents melanin located throughout all layers of the epidermis or heavy concentration of melanin in the stratum corneum. As a result, this area of high melanin concentration precludes the visualization of any other structures. Atypical blotches have an OR of 1.88 to 4.1 for melanoma.

Regression Structures

Scarlike areas and fine blue-gray dots (peppering) or granularity are known as regression structures. Dermoscopically, the scarlike area appears as a porcelain white structureless area that is lighter than the surrounding normal skin. Pepperering or granularity appears as tiny blue-gray dots (Figure 2C). Regression areas displaying peppering in association with scarlike depigmentation can manifest a bluish-white pattern usually seen in flat or macular lesions. In contrast, the blue-white veil is seen in raised or palpable lesions. In addition, areas of regression are devoid of blood.
Figure 2.
Melanoma presentation. Dermoscopic images displaying melanoma-specific structures. (A) Negative network, atypical dots and globules, atypical network and regression structures, peppering; (B) angulated lines; (C) regression structures: scarlike depigmentation and granularity; (D) atypical streaks, atypical globules, regression structures, and blue-white veil; (E) negative network and atypical dots; (F) shiny white lines; (G) atypical globules and atypical vessels (eg, polymorphous vessels consisting of dotted and linear irregular vessels); (H) peripheral tan structureless area, scarlike depigmentation, off-centered blotch, atypical network.
vessels and shiny white lines. Histologically, the peppering corresponds to melanophages or free melanin in the papillary dermis, and the scarlike depigmentation corresponds to dermal fibrosis. Regression structures have an OR of 2.0 to 18.3 for melanoma.

Peripheral Tan Structureless Areas
These homogeneous light brown areas located at the edge of the lesion are devoid of any other structures and encompass at least 10% of the surface area of the lesion (Figure 2H). A regular structureless area, as seen in nevi, is located in the center of a nevus with a reticular pattern (Figure 1E). In contrast, the presence of a peripheral tan structureless area is considered atypical and is highly suspicious for melanoma. Histologically, these structureless areas represent a flattened DEJ. Structureless areas have an OR of 2.9 to 27.9 for melanoma.

Shiny White Lines
These lines or streaks can only be seen with polarized light. They consist of short, bright, white lines that are usually oriented parallel or orthogonal to each other (Figure 2F). When seen in a melanocytic neoplasm, the differential diagnosis lies between a Spitz/Reed nevus and a melanoma. There are no specific features of shiny white lines that can help differentiate these 2 neoplasms, and, hence, all melanocytic lesions displaying shiny white structures should be viewed with suspicion. Histologically, shiny white lines correspond to stromal alteration and dermal fibrosis. Shiny white lines have a 2.5 to 9.7 OR for melanoma.

Atypical Vascular Structures
With the exception of intradermal nevi displaying comma-shaped vessels, blood vessels seen in melanocytic tumors should raise concern for melanoma. Vessels considered atypical include comma-shaped vessels in lesions without intradermal nevi and dotted, serpentine, and corkscrew vessels. Additionally, milky-red globules and milky-red areas are also considered atypical and probably reflect increased blood flow due to neoangiogenesis. The most common vessel pattern seen in melanoma is the polymorphous pattern (Figure 2G), which consists of 2 or more vessels within the same lesion. The presence of polymorphous vessels confers an OR of 2.0 to 3.04 for melanoma.

Discussion
For the detection of any skin cancer, there exists a tension between maintaining a high sensitivity to identify cancer and a high specificity to avoid classifying benign lesions as malignant. Although removing every melanocytic neoplasm would confer a sensitivity of 100% for detecting melanoma, it would result in a specificity of 0% and lead to the unnecessary removal of thousands of benign lesions—clearly not a practical nor feasible approach in the management of melanocytic lesions. Fortunately, most nevi tend to display an organized pattern composed of networks, globules, and homogeneous areas (Figure 1). In addition, nevi tend to be devoid of any of the melanoma-specific structures listed in the Table. In contrast, melanomas tend to display 1 or more melanoma-specific structures and usually reveal a chaotic or disorganized distribution of colors and structures. Lesions that do not adhere to any of the nevus patterns shown in Figure 1 and do not display any of the melanoma-specific structures outlined in the Table must still be viewed with suspicion, and melanoma should also enter the differential diagnosis for these lesions. Additionally, nevi with multiple component patterns (Figure 1J) should also be interpreted with caution.

Melanoma-specific structures are dermoscopic structures that have been found to have a high specificity and OR for melanoma. There is no hierarchy in the significance of these structures and, thus, the presence of any one of these structures within a melanocytic lesion raises equal concern for melanoma. Naturally, the more structures that are present within a lesion, the higher the odds for the lesion to be a melanoma. While there is no hierarchy for the aforementioned 12 melanoma-specific structures, the presence or absence of specific structures may assist experienced physicians...
in predicting the melanoma subtype. For example, melanomas on sun-damaged skin most often reveal angulated lines and regression structures. In contrast, superficial spreading melanomas rarely display angulated lines, but they commonly have an atypical network or streaks. Nodular melanomas almost never display an atypical network or streaks but most often have a blue-white veil or atypical vessels. Not surprisingly, many of the melanoma-specific structures highlighted in this review also happen to serve as the foundation for numerous dermoscopy algorithms designed to assist physicians in differentiating nevi from melanomas.\textsuperscript{59,62,64,66,67}

Two Cochrane reviews of literature\textsuperscript{67,68} have shown that with proper training, dermoscopy is superior to naked eye examinations for the detection of melanoma. Thus, any physician engaged in skin cancer screening should learn to use dermoscopy and be able to recognize the aforementioned melanoma-specific structures. It is important to underscore that dermoscopy not only improves sensitivity for detecting melanoma but also helps reduce the number of biopsies of benign lesions, thus improving specificity, as well as facilitating in the detection of thinner tumors.\textsuperscript{70,71} Of course, competency in dermoscopy requires proper training. This review is intended to highlight only the most important dermoscopic features associated with melanoma and to bring awareness to physicians about the power of dermoscopy to diagnose melanoma. The ability of the physician to gain competency in recognizing the features outlined herein will require further study and experience. Knowledge acquisition can be obtained from attending dermoscopy courses, reading a dermoscopy atlas, using online resources (eg, https://www.dermoscopy.org, https://isic-archive.com, https://dermoscopy-ids.org), observing and learning directly from a dermoscopy expert, and, most importantly, practicing this technique daily. Terushkin et al\textsuperscript{72} showed that, along with time allotted to familiarize the physician with dermoscopic structures, 1 year of dermatoscope in the clinical setting was sufficient to achieve a benign to malignant ratio that was close to that of a specialist. The current review is intended to help physicians embark on this journey of learning to recognize the dermoscopic features associated with melanoma.

**Conclusion**

Dermoscopy is a valuable tool in the diagnosis of melanocytic tumors. It increases the sensitivity and specificity for melanoma detection, decreases the number of benign lesions biopsied, and allows the diagnosis of thinner melanomas compared with the naked eye examination. Any physician involved in skin cancer screening would benefit from being able to recognize the melanoma-specific structures through dermatoscope evaluation and, therefore, could refer patients with suspicious lesions for early treatment.

**References**


