Correlation of Dermoscopic Structures of Melanocytic Lesions to Reflectance Confocal Microscopy

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**Objective:** To determine the utility of reflectance confocal microscopy (RCM) in the in vivo evaluation of dermoscopic structures of melanocytic lesions.

**Design:** For each described dermoscopic feature, we evaluated by RCM at least 2 melanocytic lesions. A digital camera connected to the confocal computer enabled direct analysis of the dermoscopic structures. To ascertain precision of correlation, the orientation of the dermoscopic and RCM images were compared using a superimposed grid.

**Setting:** Dermatology clinic specializing in pigmented lesions.

**Patients:** Eleven patients with melanocytic lesions, including 2 melanomas, 1 Spitz nevus, 7 dysplastic nevi, and 1 compound nevus.

**Main Outcome Measure:** Direct correlation of structures seen using dermoscopy with those seen using RCM.

**Results:** There was a good correlation between the global dermoscopic pattern and findings on the 4×4-mm mosaic of confocal images at the level of the dermoepidermal junction. The atypical network correlated with variability in the size and shape of dermal papillae. Globules corresponded with aggregates of bright cells, and darker shades of brown on dermoscopy appeared brighter on RCM. In peripheral streaks, RCM showed dense aggregates of pleomorphic cells of variable brightness and ill-defined cellular borders. These aggregates were continuous with the bright mesh that composed the central bulk of the lesion. A blue-white veil correlated with disruption of the rimmed papillae meshlike pattern and sometimes with the presence of bright cells corresponding to melanophages.

**Conclusion:** Correlating dermoscopic structures to RCM features is possible and a necessary step toward understanding the potential benefits of RCM in the clinical setting.

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**DERMOSCOPY IS A NONINVASIVE technique that allows for the visualization of subsurface structures by decreasing reflection at the stratum corneum–air interface. Recognition of these structures has generated a new set of clinical criteria in the assessment of pigmented lesions and, with appropriate interpretation, increases the clinician’s accuracy for melanoma diagnosis and can facilitate in differentiating melanoma from other benign and malignant pigmented lesions.**

Most dermoscopic structures have been shown to represent morphological alteration of the skin, ranging in location from the corneal layer to the superficial dermis. The accurate interpretation of these structures is thus important for differentiating benign from malignant lesions, for focusing a biopsy on the area most suggestive of malignancy in large lesions, and for guiding tissue sectioning of the specimen. To that end, histopathological analysis has been used to better understand the basis of dermoscopic structures. However, owing to the perpendicular plane in which a pathological specimen is sectioned, as opposed to the horizontal plane of view of dermoscopy, this correlation is hindered by technical limitations. Yadav et al presented the correlation of dermoscopic structures by showing the best available dermoscopic and histopathological photomicrographs, not necessarily from the same case. Subsequently, Soyer et al correlated a small series of case-by-case dermoscopic findings to histopathological features by providing the pathologist with a suture-marked tissue sample, a digital dermoscopic image highlighting the dermoscopic structures of interest, and a corresponding Polaroid image of the gross pathological features of the excised le-
sion with marking to guide sectioning. The authors stated that this method “is of sufficient quality to define fairly well the histopathological correlates”; however, “there still is certain bias.”6(p25) Later, Braun et al7 refined this dermoscopy-pathology correlation protocol by using a 1-mm micropunch to create a round, superficial notch around the area that contains the dermoscopic structure of interest within the excised specimen; this area is then easily identified during the histopathological examination. This technique is excellent for histopathological evaluation of a small, specific area that may be suggestive of malignancy on dermoscopy and further increases the confidence that structures seen in histopathological analysis truly correlate with the dermoscopic findings. However, it has been stated that the precise correlation of dermoscopy and histopathological features could only be achieved with serial horizontal sections of the specimen.8 To date, this sectioning method is technically complicated and not regarded as a standard pathological procedure.

In vivo reflectance confocal microscopy (RCM) is a noninvasive imaging technique that allows for the en face visualization of microscopic structures and cellular detail in the epidermis and superficial dermis at histopathological resolution,9 offering the prospect of precise dermoscopy-confocal correlation. Reflectance confocal microscopy, similar to dermoscopy, images lesions in an en face plane, thus enabling direct correlations with dermoscopic images. Just as the pigment distribution in the tissue is the source of most dermoscopic structures seen in melanocytic lesions, melanin also provides a strong contrast to confocal images owing to increased backscattering of light, causing pigmented structures to appear bright.10 Thus, RCM may be a useful tool for evaluating melanocytic as well as nonmelanocytic pigmented lesions.11-17 The histopathological correlates of numerous confocal structures have been previously elucidated, providing the basis for studying the tissue morphology of melanocytic neoplasms using RCM.11,18-21

Recent advances in instrumentation have enabled the performance of real-time, in vivo correlation of dermoscopy to RCM findings. Herein, we present a case-by-case study of specific structures of melanocytic lesions using RCM. The RCM correlation of global dermoscopic patterns of melanocytic neoplasms is also described.

PATIENTS

The participants were patients presenting for clinical evaluation of melanocytic lesions at the Dermatology Service of Memorial Sloan-Kettering Cancer Center, New York, NY. Written consent was obtained before enrollment. The research protocol was approved by the institutional review board at Memorial Sloan-Kettering Cancer Center. The study was conducted on 11 selected melanocytic lesions at the Dermatology Service of Memorial Sloan-Kettering Cancer Center. The study was conducted on 11 selected melanocytic lesions of the skin of the trunk and limbs, not including facial and acral lesions, because the latter represent a distinct set of dermoscopic patterns. All but 1 lesion (case 6, a dysplastic nevus) prompted clinical concern, owing to a clinical history of changing lesion or atypical dermoscopic findings. Ten lesions considered suggestive of malignancy were excised and histopathologically analyzed.

INSTRUMENTS

Dermoscopic Evaluation

The clinical and dermoscopic features of the study lesions were documented using the Fuji S1 single-lens reflex digital camera and 60-mm Macro Nikkor lens (Nikon, Melville, NY) with a dermoscopy attachment (Epilume; Canfield Imaging Systems Inc, Fairfield, NJ). After the clinical image was obtained at a 1:1 ratio, a 70% alcohol spray was applied to the lesion and direct contact was made between the skin surface and the dermoscopy glass plate. The dermoscopic images were obtained with a ×1 magnification. The images were archived in an image database housed on a secured server at a resolution of 3 million pixels (DermaGraphix; Canfield Imaging Systems Inc).

Confocal Evaluation

We used a commercially available, near-infrared reflectance confocal microscope (Vivascop 1500; Lucid Inc, Rochester, NY) that has been described previously.11,12 Briefly, the microscope uses illumination with a near-infrared diode laser at 830 nm operating at a power of less than 20 mW. The skin contact device consists of a metal tissue ring with a coverslip window, which is attached to the skin surrounding the lesion of interest with a disposable medical adhesive after the application of a drop of immersion oil (Crodamol STS oil; Croda Inc, Edison, NJ). An ×30 objective lens of numerical aperture 0.9 was attached to the tissue ring after the application of an immersion medium (water [refractive index, 1.33] or ultrasound gel [reflective index, 1.36]) between the objective lens and the coverglass window. The RCM acquires horizontal tissue images at a 500 × 500-µm field of view (individual image), equivalent to ×30 magnification, with a resolution of 1024 × 1024 pixels. An automated stepper was used to scan a 4 × 4-mm field of view in the tissue, producing a square mosaic of 64 contiguous individual images (mosaic image). The 4 × 4-mm field of view displayed by the RCM is equivalent to ×5 magnification. In addition, the RCM has an automated stepper obtaining sequentially deeper individual images 3 µm apart, from the corneal layer to the superficial dermis (Z-axis stack), at the same point on the horizontal plane (XY-axis). A digital camera (Vivacam; Lucid Inc) connected to the RCM computer by USB cable enables direct viewing of the dermoscopic structures on the RCM monitor. The camera is based on a 1.3-cm (0.5-inch) sensor (6.6 × 5.3-mm array), with a rolling and half-global shutter providing 15 frames per second at 1280 × 1024 pixels (2.5-µm square pixels). The digital camera lens consists of 2 achromatic doublets oriented with their crown components toward each other to provide minimum spherical aberration and approximately 1.9 × magnification so that the resolution at the surface of the skin is 10 µm. The system computer samples a 1000 × 1000-pixel region from the 1.3-megapixel camera sensor, providing a 10 × 10-mm image of the skin. This full-color image is precisely registered with the RCM images by means of the skin contact device (ie, the tissue ring). The examiner can capture a dermoscopic image with the digital camera to be used as a reference when operating in the RCM mode. On this digital image, a square frame highlights for the user the 4 × 4-mm area that will be scanned by the RCM, which corresponds to the 4 × 4-mm area seen on the RCM mosaic image. Consequently, the RCM can be guided to provide subsampling of the region of interest on the dermoscopic image: pointing the cursor to a dermoscopic structure on the digital image will cause the RCM to scan at the corresponding location.
### Table 1. Global Dermoscopic Pattern and RCM Mosaic Image Findings

<table>
<thead>
<tr>
<th>Case No./Sex/Age, y</th>
<th>Location</th>
<th>Description of Lesion</th>
<th>Global Dermoscopic Pattern</th>
<th>Arrangement of Specific Dermoscopic Structures</th>
<th>RCM Mosaic Image Findings at the Level of the DEJ</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F/75</td>
<td>Shoulder</td>
<td>7-mm brown papule</td>
<td>Reticular pattern, patchy type</td>
<td>Network areas separated by structureless areas</td>
<td>Irregularly arranged cells in the basal layer forming oval rings, cordlike structures, and a branching pattern; heterogeneous brightness in refractive basal cells; irregularly distributed DP</td>
<td>Dysplastic nevus</td>
</tr>
<tr>
<td>2/M/54</td>
<td>Chest</td>
<td>4.5-mm brown papule</td>
<td>Reticular pattern, diffuse type</td>
<td>Diffuse network</td>
<td>Round-to-elongated edged DP; irregularly distributed; focally, small bright round structures in the center of DP</td>
<td>Dysplastic nevus</td>
</tr>
<tr>
<td>3/M/48</td>
<td>Middle back</td>
<td>7-mm light brown with blue-gray hue papule</td>
<td>Multicomponent</td>
<td>Focal peripheral atypical network, structureless areas, and irregularly distributed peripheral globules</td>
<td>Disorganized architecture with refractive basal cells showing irregular, patchy distribution forming an irregular grid; clusters of refractive cells with variable brightness</td>
<td>Dysplastic nevus</td>
</tr>
<tr>
<td>4/F/85</td>
<td>Upper back</td>
<td>5-mm light brown macule</td>
<td>Reticular homogeneous</td>
<td>Patchy distribution of the refractive cells in the basal layer in the lesion, focally forming an irregular grid and curved and branching cordlike structures; remaining areas within the lesion are devoid of any specific pattern of the basal layer</td>
<td>Dysplastic nevus</td>
<td></td>
</tr>
<tr>
<td>5/F/32</td>
<td>Lower back</td>
<td>4-mm dark brown papule</td>
<td>Reticular globular</td>
<td>Diffuse network with central globules</td>
<td>Regular DP; round-to-oval in shape, uniformly distributed, along with dense clusters of bright cells</td>
<td>Dysplastic nevus</td>
</tr>
<tr>
<td>6/M/61</td>
<td>Chest</td>
<td>5-mm light and dark brown papule</td>
<td>Globular, cobblestone type</td>
<td>Numerous diffuse globules</td>
<td>Round-to-polygonal clusters of bright cells dispersed throughout the lesion</td>
<td>Compound nevus (with congenital pattern)†</td>
</tr>
<tr>
<td>7/M/29</td>
<td>Flank</td>
<td>7-mm dark brown papule</td>
<td>Globular homogeneous</td>
<td>Diffuse globules and mililike cysts</td>
<td>Round-to-polygonal clusters of cells, with heterogeneous brightness, dispersed throughout the lesion</td>
<td>Dysplastic nevus</td>
</tr>
<tr>
<td>8/M/14</td>
<td>Dorsal foot</td>
<td>4-mm bluish pink papule</td>
<td>Starburst</td>
<td>Central bluish veil and peripheral pseudopods</td>
<td>Central irregular mesh of cordlike structures with heterogeneous brightness; scattered small, bright structures in the center of the lesion; peripherally, sharply demarcated, fingerlike extensions budding in continuity from the meshed area</td>
<td>Spitz nevus</td>
</tr>
<tr>
<td>9/M/49</td>
<td>Thigh</td>
<td>7-mm dark brown–black and pink papule</td>
<td>Multicomponent</td>
<td>Upper part of lesion with atypical network and peripheral streaks; lower part with atypical network and bluish veil</td>
<td>Upper part of lesion with a mesh pattern, with well-demarcated bright peripheral extensions; lower part with a mesh pattern with focal loss of the grid along with scattered bright structures</td>
<td>Melanoma‡</td>
</tr>
<tr>
<td>10/M/79</td>
<td>Lower leg</td>
<td>15-mm light and dark brown patch</td>
<td>Reticular homogeneous</td>
<td>Mostly structureless with areas of thickened network and branched streaks as well as focal regression</td>
<td>Irregular branching and curved cordlike structures and dense aggregates of bright cells; structureless dark areas</td>
<td>Melanoma§</td>
</tr>
<tr>
<td>11/M/34</td>
<td>Upper abdomen</td>
<td>4-mm light brown with bluish gray hue papule</td>
<td>Multicomponent pattern</td>
<td>Central globules, broken-up network and bluish veil, peripheral branched streaks</td>
<td>Diffuse meshed pattern with focal increase in a brightness and thickening of mesh; foci with small bright structures</td>
<td>Dysplastic nevus</td>
</tr>
</tbody>
</table>

Abbreviations: DEJ, dermoepidermal junction; DP, dermal papillae; RCM, reflectance confocal microscopy.

*Includes diameter in the longer axis, color, and elevation.
†Based on clinical evaluation in lesions that were not excised.
‡Breslow thickness, 0.55 mm; Clark level II with regression.
§Breslow thickness, 0.15 mm; Clark level II.

**DEFINITION OF DERMOSCOPIC GLOBAL PATTERNS AND SPECIFIC STRUCTURES**

The global dermoscopic pattern was based on the previously described pattern analysis method. The following 2 types of dermoscopic findings have been previously referred to as *streaks*: (1) *peripheral streaks*, a term that encompasses radial streaming and pseudopods and (2) *branched streaks*, which are foci of remnants of broken-up network. In addition, we used the descriptive term *blue-white structures* (BWSs) realized by prominent dermoscopy experts. The BWSs include blue pepperlike areas (peppering), structureless areas, and irregularly distributed peripheral globules.
whitish veil because these structures are often confounded by overlapping features.23

DERMOSCOPY-RCM CORRELATION PROTOCOL

For each dermoscopic structure, at least 2 melanocytic lesions were evaluated. The global dermoscopic pattern was correlated with the 4 x 4-mm mosaic image at the dermoepidermal junction (DEJ). In lesions with a diameter greater than 4 mm, RCM was performed in parts so as to cover the total surface area of the lesion. In the lesions included in this study, we found the level of the DEJ to be most useful for the correlation of the dermoscopic global pattern with RCM. A loss of resolution at depths greater than 250 µm limited the correlation with findings in the deeper portion of the dermis. We correlated specific dermoscopic structures—ataypical pigment network, globules, peripheral streaks, and BWSs—with the corresponding RCM findings at the individual image view. At areas of interest, individual RCM images were sequentially captured from the corneal layer to the superficial dermis using an automated stepper (Z-axis stack).

All dermoscopic images in the series were reviewed by 2 participating dermatologists (A.S. and A.A.M.) for the global pattern and the presence of specific structures. All RCM images were reviewed by 3 participating dermatologists (A.S., C.B.-A., and S.G.). To ascertain the precision of correlation that was performed in real time with the digital camera of the RCM, the orientation of the dermoscopic images obtained by the single-lens reflex camera with the dermoscopy attachment and the RCM-mosaic images were compared side by side using a 4 x 4-mm frame with a superimposed grid. Furthermore, we compared the location of the specific structure of interest on the dermoscopic image with the location of the corresponding individual RCM image on the RCM mosaic image. Precision of the dermoscopy-RCM correlation for each of the included lesions was ascertained by 3 of the participating dermatologists (A.S., S.G., and A.A.M.).

RESULTS

CORRELATING DERMOSCOPIC GLOBAL PATTERN WITH RCM

We enrolled 11 patients (8 male and 3 female; age range, 14-85 years) in the study and examined a single lesion in each. The lesions included 2 invasive melanomas, 1 Spitz nevus, 7 dysplastic nevi, and 1 compound nevus. Table 1 describes the case-by-case correlation of the dermoscopic global pattern with an RCM mosaic image at the DEJ level.

A global reticular pattern on dermoscopy corresponded to a meshed pattern on RCM, created by cords of bright cells of the epidermal basal layer (Figure 1A and B and Figure 2A and B). The holes in the dermoscopic network correlate with the darker papillary dermis on RCM that gives contrast to the pattern of the bright basal cells. A thinning dermoscopic pattern at the periphery corresponded to the ill-defined peripheral margins on RCM, in which the strands of basal cells appeared less bright and less prominent (Figure 1A and B). In cases of a reticular pattern...
dermoscopic pattern with structureless (homogeneous) areas on dermoscopy, such as reticular homogeneous patterns, the structureless areas correlated on RCM with a sparse or an absent pattern of the cells in the basal layer of the epidermis relative to the superficial dermis.

The dermoscopic globular pattern correlated with the appearance of nests of bright cells on RCM throughout the lesion. The density of globule distribution in the lesion on dermoscopy appeared to match that of the clusters on RCM. In the dermoscopic cobblestone globular pattern, RCM revealed large clusters of bright cells, dispersed throughout the lesion and separated by thin strands of relatively darker basal layer, giving the appearance of a multilobated lesion (Figure 3A and B). In the globular homogeneous pattern, these clusters were more widely separated by areas devoid of a specific pattern. In lesions showing the dermoscopic reticular globular pattern, clusters of bright cells were seen on RCM in con-

Figure 2. Dysplastic nevus in case 2. Squares a and b on dermoscopy (A) and the reflectance confocal microscopy (RCM) mosaic image (B) correspond to the RCM individual images (C) [irregular dermal papillae (DP) within a background of pigmented keratinocytes] and D [round structures connected to the DP rim (arrows)], respectively.

Figure 3. Nevus with cobblestone pattern in case 6. A pear-shaped nest seen on dermoscopy (A, arrow) can be precisely traced to the reflectance confocal microscopy (RCM) mosaic image (B, arrow) and individual RCM images (C, arrow).
junction with the meshed cords of bright cells. In 1 lesion (case 2 in Table 1), dermoscopy showed only a reticular pattern, whereas the RCM mosaic image clearly showed several foci of round structures, about 50 µm in diameter, appearing in the center of dermal papillae (DP), with brightness similar to the rim of basal cells. Going back to review the dermoscopy, we were scarcely able to correlate these findings with the minute, fuzzy brown globular structures in the holes of the network (Figure 2A [square b]).

A dermoscopic starburst pattern appeared on RCM as a variation of the reticular pattern, with a mesh of cords of bright cells in the center; at the periphery, however, this pattern was well delineated from the surrounding skin by bright knoblike extensions budding continuously from the mesh area (Figure 4B and Figure 5B). A multicomponent pattern on dermoscopy, with network, globules, and homogeneous areas, corresponded to a multistructural appearance on RCM, with foci of meshed cords, clusters of bright cells, and areas devoid of specific RCM structures.

**CORRELATING DERMOSCOPIC-SPECIFIC STRUCTURES WITH RCM**

**Table 2** describes correlation of specific dermoscopic structures with corresponding RCM individual images (500 × 500 µm).

**Atypical Pigment Network**

We studied 4 melanocytic lesions showing the foci of an atypical network (Table 2). The atypical network correlated with RCM findings in both the 500 × 500-µm individual images and the 4 × 4-mm mosaics of images (Figures 1 and 2). In all 4 lesions, the atypical network could be appreciated on the mosaic image: in 3 cases (1, 3, and 4), there was significant architectural disarray, with the cords of basal cells creating an irregular mesh with variable brightness and with holes of variable size and shape. In case 2, the architectural atypia was mild and consisted of variability in the size and shape of the DP, surrounded by basal cells with homogeneous brightness (Figure 2C and D). On individual RCM images, all cases showed variability in the size of adjacent DP and heterogeneity in the width of the layer of basal cells separating them. In case 1, disarray of the basal cells forming branching cordlike structures was also seen, corresponding on dermoscopy to faint branched streaks in the atypical network area. In 3 of the cases (2, 3, and 4), the basal cells surrounding the papillary dermis failed to form a confluent rim. In all cases, the bright cells at the basal layer appeared as small, round cells, and thus this dermoscopic feature consisted of architectural rather than cytological irregularity.
Globules

On RCM, the globules corresponded to nests of melanocytes. A darker shade of brown on dermoscopy corresponded to increased brightness on RCM. Wherever the individual globules were well defined on dermoscopy, the clusters of the cells on RCM were brighter compared with basal cells in the same field and compactly aggregated. The best example of such cellular clusters is the globular cobblestone pattern (Figure 3), in which the shape and size of the individual globules are well matched to their appearance on RCM. On the other hand, clusters with lesser brightness, loose aggregation, or bright surrounding keratinocytes were more ill-defined on dermoscopy. In a nevus displaying a dermoscopic reticular-globular pattern (case 5) on RCM, cellular clusters were located in adjacent DP, with bright basal cells separating the DP; although several adjacent clusters appear as discrete structures on RCM, they were perceived as a single ill-defined globule on dermoscopy. Nests with a diameter greater than 50 µm tended to be more readily perceptible on dermoscopy (cases 5 and 6). In cases with regular globules on dermoscopy, the clusters seen on RCM were composed of bright, round, rather monomorphic cells. On the other hand, in 2 cases with irregular globules asymmetrically dispersed in the lesion and heterogeneous in size and shade, cellular clusters were found on RCM with ill-defined borders, variable brightness of cells, and some irregular, stellate-shaped cells.

Streaks

Peripheral streaks were studied in 2 cases. The first case was clinically diagnosed as a typical Spitz nevus (Figure 4). The second case was a 0.55-mm-thick melanoma (Figure 5) in which the upper portion had a starburst pattern with peripheral streaks; this portion was found to have Spitzoid features on histopathological evaluation as well.

On RCM, the peripheral streaks in both cases demonstrated dense aggregates of pleomorphic cells with ill-defined cellular borders. There was variable brightness of cells within the aggregates, with some cells standing out as brighter than others (Figure 5C). These aggregates were well delineated from the surrounding darker superficial dermis. In the Spitz nevus, streaks were seen on dermoscopy as pseudopods; these correlated with peripheral aggregates with a curved contour and a bulbous terminus (Figure 4D).

Blue-White Structures

On the RCM mosaic image, in areas of BWS, there was a noticeable architectural disarray of the basal cells at the DEJ level, and the meshed pattern was disrupted and re-
placed with areas of ill-defined brightness (Figure 4B [square a] and C). The individual RCM images showed a disarray of the cells in the basal layer in conjunction with bright cells in the superficial dermis, compatible with melanophages and, in some cases, melanocytes. Increased capillary blood flow in the superficial dermis was seen during the real-time RCM examination of the BWS areas. Although the whitish veil was previously correlated with compact orthokeratosis on the histopathological evaluation, we were not able to show a parallel finding in the RCM examination.

**COMMENT**

Precise dermoscopy-RCM correlation has several potential applications. First, it enables the study of the tissue correlates of specific dermoscopic structures, as in this report. Second, it may eventually prove to be useful in differentiating between benign lesions and those suggestive of malignancy: in areas of equivocal dermoscopic findings, RCM can be used to evaluate tissue morphology and to identify additional subtle clues, such as pagetoid spread, that may evade dermoscopic detection. In addition, it can help guide clinicians to perform a biopsy on a focused area that shows concerning confocal findings. Finally, it can guide histopathological sectioning of the specimen to areas found to be suggestive of disease on RCM, using the corresponding dermoscopy image as a gross pathology reference.

Similar to the histopathological approach to specimen analysis, which starts with an overview of the lesion at scanning magnification, we found it useful to view the initial RCM image of the lesion as a full 4-mm mosaic to ascertain the orientation of the mosaic image with respect to dermoscopy. In the studied cases, we found the level of the DEJ to be most useful for the correlation of the dermoscopic global pattern with the RCM mosaic image. To the best of our knowledge, this is the first publication that correlates the dermoscopic global pattern with RCM findings. From the level of the mosaic, the ob-

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**Table 2. Correlates of Specific Dermoscopic Structures and RCM Individual Images**

<table>
<thead>
<tr>
<th>Case No./Diagnosis</th>
<th>Description of Dermoscopic Specific Structure</th>
<th>RCM Findings at Corresponding Individual Images</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Atypical Network</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/Dysplastic nevus</td>
<td>Focal area of thickened network and branched</td>
<td>Round-to-oval edged DP of medium size with focal papillary disarray in which basal cells form branching cordlike structures</td>
</tr>
<tr>
<td></td>
<td>streaks</td>
<td></td>
</tr>
<tr>
<td>2/Dysplastic nevus</td>
<td>Focal area of thickened network with larger</td>
<td>Irregularly shaped edged DP of medium size with heterogeneous brightness within background of bright cells (pigmented keratinocytes); bright round structures, 50 µm in diameter, in center of several DP; some of them connected by bandlike structure to DP contour</td>
</tr>
<tr>
<td></td>
<td>holes</td>
<td></td>
</tr>
<tr>
<td>3/Dysplastic nevus</td>
<td>Focal thickened network</td>
<td>Irregular noneded DP; bundles of thick, scarlike collagen; isolated plump bright cells (melanophages) in superficial dermis</td>
</tr>
<tr>
<td>4/Dysplastic nevus</td>
<td>Focal thickened network</td>
<td>Irregularly shaped DP of variable size within background of bright cells (pigmented keratinocytes)</td>
</tr>
<tr>
<td><strong>Globules</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3/Dysplastic nevus</td>
<td>Atypical peripheral globules of different size and intensity of pigmentation</td>
<td>Dense oval-to-round nests composed of aggregate of cells with variable brightness; stellate cells in some aggregates</td>
</tr>
<tr>
<td>5/Dysplastic nevus</td>
<td>Homogeneous regular globules</td>
<td>Dense oval-to-round nests, 50-200 µm in diameter, composed of aggregates of bright cells</td>
</tr>
<tr>
<td>6/Compound nevus</td>
<td>Homogeneous cobblestone globules</td>
<td>Dense aggregates of bright cells forming nests that fill the DP</td>
</tr>
<tr>
<td>7/Dysplastic nevus</td>
<td>Mostly homogeneous regular globules with few darker central globules</td>
<td>Round to irregularly shaped nests composed of bright cells with ill-defined cellular outline; some nests appear to merge</td>
</tr>
<tr>
<td><strong>Streaks</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8/Spitz nevus</td>
<td>Peripheral streaks</td>
<td>Well-demarcated, round, knoblike, as well as polymorphic aggregates of poorly defined cells</td>
</tr>
<tr>
<td>9/Melanoma</td>
<td>Peripheral streaks</td>
<td>Well-demarcated dense aggregates of spindle-shaped cells of variable brightness and ill-defined cellular borders; numerous coarse dendritic structures in suprabasal epidermis</td>
</tr>
<tr>
<td>10/Melanoma</td>
<td>Structureless area with a few branched streaks</td>
<td>Aggregates of ill-defined elongated dendritic cells form cordlike structures</td>
</tr>
<tr>
<td>11/Dysplastic nevus</td>
<td>Branched streaks and broken-up network remnants</td>
<td>Poorly delineated aggregates of bright elongated cells overtide the lesion’s mesh</td>
</tr>
<tr>
<td><strong>Blue-White Structures</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8/Spitz nevus</td>
<td>Central blue-white veil</td>
<td>Aggregates of poorly defined cells with refractivity comparable to that of surrounding keratinocytes; in superficial dermis, numerous plump bright cells with ill-defined borders (melanophages) and dark round or canalicular structures (capillaries)</td>
</tr>
<tr>
<td>9/Melanoma</td>
<td>Blue-white veil partly overlying dark blotch</td>
<td>Bright dendritic pleomorphic cells with eccentric nuclei appear to ascend in epidermis on background of loss of keratinocytic demarcation suggesting pagetoid spread; dermal scattered, plump, bright cells (melanophages)</td>
</tr>
<tr>
<td>11/Dysplastic nevus</td>
<td>Bluish veil around central globules</td>
<td>Well-demarcated dense aggregates of bright elongated cells in patchy distribution; numerous dermal, plump, bright cells (melanophages)</td>
</tr>
</tbody>
</table>

Abbreviations: DP, dermal papillae; RCM, reflectance confocal microscopy.
server can then hone in on individual RCM images (500 × 500 μm) to analyze tissue morphology and cellular details. To facilitate the RCM procedure, the observer can specifically hone in on areas that correlate with dermoscopic structures that are suggestive of disease.

The dermoscopic appearance of a network has been correlated to histopathological findings; the thicker pigmented rete ridges correspond to the dark brown lines and the thinner pigmented suprapapillary plates correspond to the tan holes. The variation of shapes and sizes of the network holes was attributed to the disparity of DP and their suprapapillary plates. Atypical pigment network, with focal broadening of the net, was found in 35% of invasive melanomas with a specificity of 86% and was correlated on histopathological evaluation with shortened, widened rete ridges. We showed that the atypical network in nevi can result from an architectural disarray of the basal layer around the papillary dermis without cytological irregularity. Pellicani et al20 studied the RCM aspects of pigmented network and found irregular architecture of the DP in atypical nevi and melanoma. Cellular atypia was present in half of the melanomas but, as in our findings, in none of the nevi studied.20

Dermoscopic globules were correlated with nests of melanocytes at the DEJ or the papillary dermis on the histopathological findings. In some cases, such nests were not found in the histopathological analysis, and thus it was assumed that they correlated with clusters of melanophages and melanocytes, was indeed lacking the epidermal component but showing similar compact hyperkeratosis overlying the superficial dermis and the pigmented structures in the deeper dermis correlated with melanophages and melanocytes, was indeed highly specific for melanoma; blue areas without a veil, lacking the epidermal component but showing similar pigmented cells in the dermis, were seen in nevi. Other clinicians dispute the ability to consistently differentiate between the 2 dermoscopic findings in daily practice. Because BWSs often consist of an area rather than a discrete structure, it could be argued that the precision of the correlation with RCM has no clear advantage compared with the histopathological examination. Moreover, RCM is limited in identifying compact orthokeratosis and the pigmented structures in the deeper dermis reported in the histopathological correlation of the blue whitish veil.3 However, RCM added a complementary horizontal overview of the architectural arrangement at the DEJ level and clearly showed in the studied cases that BWSs were associated with focal disruption of the arrangement of the basal cells. The presence of bright, plump cells compatible with melanophages and of some melanocytes in the superficial dermis confirms previous findings associated with BWSs.

Our study has several limitations. Interpretation of RCM findings depends on the observer and, as such, relies on cumulative experience. In that sense, this observer dependency is not dissimilar to histopathological interpretation. The findings of the dermoscopy-RCM correlation apply to the lesions studied herein and may not be generalized to all melanocytic lesions displaying these patterns and structures. We anticipate that these dermoscopic structures will demonstrate diverse morphological tissue perturbations as we extend the study to a larger series of melanocytic neoplasms. Finally, we studied RCM image overviews at the level of the DEJ because this yielded the best correlation with dermoscopy. We intend to further this analysis to the suprabasal level of the epidermis and the deeper level of the dermis.

Peripheral streaks can be seen circumferentially in Spitz nevi and focally with asymmetric distribution in melanoma. Studies are dermoscopic structures that represent radial extension of the lesion, ie, at the en face plane. Thus, streaks are difficult to correlate with the histopathological findings. Soyer et al20 correlated streaks in Spitz nevi with junctional nests of pigmented, spindle-shaped melanocytes. Dermoscopy-RCM correlation showed that peripheral streaks were aggregates of elongated cells, well delineated from the bordering dermis and contiguous with the central mesh of the lesion. Some aggregates appeared to be round, curving around existing DP and producing a pseudopodlike appearance. Other aggregates produced an arrowlike arrangement, representing more linear streaks. These findings are in line with a previous RCM analysis of Spitz nevi21 and confirm the previous assumption, based on the correlation of dermoscopic and histopathological findings, that in Spitz nevi the junctional nests of melanocytes form a tubular arrangement in the horizontal plane.6

For consistency, we used the term blue-white structure,20 which encompasses overlapping terms described in the literature, ie, blue hue,9 gray-blue veils, whitish veil,10,26 gray-blue areas,9,27 and blue whitish veil.2 A bluish hue is generally considered a clue to malignancy in clinically equivocal cases.8 The BWSs can also be seen, albeit more rarely, in Spitz and atypical nevi.23 Massi et al8 conducted a dermoscopy-to-histopathology correlation of the blue hue in melanocytic lesions. They found that a blue whitish veil, correlating with an acanthotic epidermis with compact hyperkeratosis overlying the superficial dermis with melanophages and melanocytes, was indeed highly specific for melanoma; blue areas without a veil, lacking the epidermal component but showing similar pigmented cells in the dermis, were seen in nevi.8 Other clinicians dispute the ability to consistently differentiate between the 2 dermoscopic findings in daily practice.23 Because BWSs often consist of an area rather than a discrete structure, it could be argued that the precision of the correlation with RCM has no clear advantage compared with the histopathological examination. Moreover, RCM is limited in identifying compact orthokeratosis and the pigmented structures in the deeper dermis reported in the histopathological correlation of the blue whitish veil.3 However, RCM added a complementary horizontal overview of the architectural arrangement at the DEJ level and clearly showed in the studied cases that BWSs were associated with focal disruption of the arrangement of the basal cells. The presence of bright, plump cells compatible with melanophages and of some melanocytes in the superficial dermis confirms previous findings associated with BWSs.

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