Original Investigation

Recurrent Melanocytic Nevi and Melanomas in Dermoscopy
Results of a Multicenter Study of the International Dermoscopy Society

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IMPORTANCE Differentiating recurrent nevi from recurrent melanoma is challenging.

OBJECTIVE To determine dermoscopic features to differentiate recurrent nevi from melanomas.

DESIGN, SETTING, AND PARTICIPANTS Retrospective observational study of 15 pigmented lesion clinics from 12 countries; 98 recurrent nevi (61.3%) and 62 recurrent melanomas (38.8%) were collected from January to December 2011.

MAIN OUTCOMES AND MEASURES Scoring the dermoscopic features, patterns, and colors in correlation with the histopathologic findings.

RESULTS In univariate analysis, radial lines, symmetry, and centrifugal growth pattern were significantly more common dermoscopically in recurrent nevi; in contrast, circles, especially if on the head and neck area, eccentric hyperpigmentation at the periphery, a chaotic and noncontinuous growth pattern, and pigmentation beyond the scar’s edge were significantly more common in recurrent melanomas. Patients with recurrent melanomas were significantly older than patients with recurrent nevi (mean [SD] age, 63.1 [17.5] years vs 30.2 [12.4] years) (P < .001), and there was a significantly longer time interval between the first procedure and the second treatment (median time interval, 25 vs 8 months) (P < .001). In a multivariate analysis, pigmentation beyond the scar’s edge (P = .002), age (P < .001), and anatomic site (P = .002) were significantly and independently associated with the diagnosis of recurrent melanoma in dermoscopy.

CONCLUSIONS AND RELEVANCE Dermoscopically, pigmentation beyond the scar’s edge is the strongest clue for melanoma. Dermoscopy is helpful in evaluating recurrent lesions, but final interpretation requires taking into account the patient age, anatomic site, time to recurrence, growth pattern, and, if available, the histopathologic findings of the first excision.

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Dermoscopy is used in pigmented and nonpigmented lesions of the skin, nail apparatus, hair, and volar and mucosal areas.\textsuperscript{1-7} Scars revealing recurrence of pigment following a biopsy or other procedures performed on melanocytic neoplasms can be difficult to interpret both clinically and dermoscopically. Numerous case reports have been published.\textsuperscript{8-13} Botella-Estrada et al\textsuperscript{14} performed the largest study and analyzed the clinical, dermoscopic, and histopathologic characteristics of 57 recurrent melanocytic lesions. To obtain a larger number of cases, the International Dermoscopy Society (IDS) launched a multicenter retrospective, observational study to determine dermoscopic characteristics to differentiate recurrent nevi from recurrent melanomas.\textsuperscript{15}

**Methods**

**Patient Selection and Design**

In this retrospective observational study, patients’ data and dermoscopic images of histopathologically diagnosed recurrent nevi and recurrent melanomas were included from 15 pigmented lesion clinics in 12 countries (Argentina, Austria, Belgium, Brazil, France, Germany, Italy, Japan, Mexico, Romania, Spain, and the United States).

Lesions were collected from January through December 2011 via an e-mail request sent to all IDS members.\textsuperscript{15} For each lesion, a patient data intake form and clinical and digital dermoscopic polarized and/or nonpolarized, high-resolution, and in-focus images in JPEG format were required. It was also required that dermoscopic images of all lesions visualize the scar from the first procedure. The following patient data were collected for each lesion: sex; age; skin type; anatomic site; type of procedure performed at time of first intervention; initial histopathologic report and diagnosis at first procedure, if available, including tumor thickness for melanomas; time between the first and second procedures; and histopathologic diagnosis of the second procedure, including tumor thickness for recurrent melanomas. The anatomic sites were classified as head and neck, upper extremities, trunk, lower extremities, and nails. Mucosal lesions were excluded.

All data and digital images were assigned a unique identifier, anonymized, and sent via e-mail to the study coordinator (A.B.). The institutional review board approval for this study was waived by the ethics committee (Medical Council Baden-Wuerttemberg, Stuttgart, Germany). Written informed consent was not necessary and was not requested.

The histopathologic diagnoses rendered by each participating institution’s dermatopathologist were accepted as the final diagnoses.

**Analysis of Dermoscopic Images**

All digital images were reviewed in consensus by 2 of us (A.B. and R.H.-W.), who were blinded to both histopathologic diagnoses. Each lesion was scored according to the principles of pattern analysis for the presence of the following basic elements\textsuperscript{16,17}: lines (classified as reticular, branched, parallel, radial, and/or curved), pseudopods, circles, globules or clods, and dots. Each element could form its own pattern; for example, a nevus consisting of reticular lines would result in a reticular pattern. If none of the basic elements was present, the pattern was termed structureless. Lesions revealing a combination of patterns were classified according to the number of presented patterns. The presence of a single dot or a single line does not constitute a pattern. In this study, the term pattern was defined as a collection of multiple basic elements of the same type, for example, multiple dots that cover a considerable part (≥20%) of the lesion. Colors were classified as black, brown, blue, gray, red, purple, and white, and the number of colors was counted. Each lesion was evaluated for degree of symmetry in 1 or 2 axes, the presence of eccentric hyperpigmentation at the periphery, growth pattern (centrifugal [like an outward force that draws a rotating body away from the center of rotation], chaotic, or neither), noncontinuous growth pattern, vessels within the scar and outside the scar, and presence of pigmentation beyond the scar’s edge (pigment traversing the scar edge, extending from the scar onto normal skin).\textsuperscript{10}

**Statistical Analysis**

Continuous data are given as means (SDs) or as the median (interquartile range). \(\chi^2\) Tests or Fisher exact tests were used for the comparison of proportions. Continuous data were compared with unpaired t tests or Mann-Whitney U test as appropriate. Logistic regression analysis was used for the multivariate model. We constructed 2 models for the diagnosis of recurrent melanocytic lesions. In the first model, we included those variables that were significantly associated with melanoma in the multivariate analysis (ie, age > 30 years, location on the head and neck area, and pigmentation traversing the scar’s edge). Positive criteria were added to a final score ranging from 0 to 3, and the area under the curve for this model was calculated. To calculate sensitivity, specificity, and negative and positive predictive values, we chose a cutoff of 2 (ie, if ≥2 criteria were present, the lesion was considered to be malignant). For this model, we disregarded the histopathologic diagnosis report associated with the first procedure. In the second model, we took the histopathologic report of the first procedure into account. For those lesions that were initially diagnosed as melanoma, we added 2 points, and for those lesions diagnosed as nevi, we subtracted 1 point. If no histopathologic report was available, then no value was added or subtracted from the final score. This resulted in scores ranging from −1 to 4. We chose the same cutoff as for the first model to calculate sensitivity, specificity, and negative and positive predictive values. All given \(P\) values are 2-tailed, and \(P < .05\) indicates statistical significance.

**Results**

**General Data**

The study consisted of 160 recurrent melanocytic nevi and recurrent melanomas from 98 females (61.3%) and 51 males (31.9%); for 11 cases (6.9%) the sex data were missing. The mean (SD) age of the patients was 43.1 (21.7) years. The final histopathologic diagnosis was recurrent nevus in 98 cases (61.3%)

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Table 1. Data of the Anatomic Sites of All Recurrent Lesions, Recurrent Nevi, and Recurrent Melanomas

<table>
<thead>
<tr>
<th>Site</th>
<th>Recurrent Lesions, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All</td>
</tr>
<tr>
<td>Head and neck</td>
<td>32 (20.0)</td>
</tr>
<tr>
<td>Upper extremities</td>
<td>11 (6.9)</td>
</tr>
<tr>
<td>Trunk</td>
<td>72 (45.0)</td>
</tr>
<tr>
<td>Lower extremities</td>
<td>41 (25.6)</td>
</tr>
<tr>
<td>Nails</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Missing</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Total</td>
<td>160 (100)</td>
</tr>
</tbody>
</table>

*Percentages may not total 100% owing to rounding.

and recurrent melanoma in 62 cases (38.8%). Patients with recurrent melanomas were significantly older than patients with recurrent nevi (mean [SD] age, 63.1 [17.5] years vs 30.2 [12.4] years; P < .001). No difference was found with regard to the sex distribution of patients with recurrent nevi (58.2% were females) and recurrent melanoma (66.1% were females). Regarding anatomic site, 32 recurrent lesions were located on the head and neck (20.0%), 11 on the upper extremities (6.9%), 72 at the trunk (45.0%), 41 on the lower extremities (25.6%), and 2 in the nail unit (1.3%); for 2 lesions, this data variable was not available (1.3%) (Table 1). Recurrent melanomas were more frequently located on the head and neck area than recurrent nevi (46.8% vs 3.1%; P < .001).

For most lesions (131 [81.9%]), the first treatment performed was a surgical procedure, such as shave, saucerization, punch, or excisional biopsy. One lesion was treated with surgery followed by imiquimod application (0.6%). In addition, 8 lesions were initially treated by cautery (5.0%) and 4 by cryotherapy (2.5%), 4 lesions recurred after trauma (2.5%), 3 were treated with cautery (1.9%), and for 9 lesions the procedure of the first encounter was not reported (5.7%). For 110 cases, the histopathologic diagnosis of the first procedure was available and included 66 nevi (41.3%) and 44 melanomas (27.5%); in 50 lesions (32 nevi and 18 melanomas) the histopathologic diagnosis of the first treatment was unavailable (31.1%). In all 160 recurrent lesions, the histopathologic diagnosis was available.

The median time interval between the first and second treatment was 18 months (25th-75th percentile, 6-41 months). Patients with recurrent melanomas had a longer time interval between the 2 treatment than patients with recurrent nevi (median, 25 months [25th-75th percentile, 12-48 months] vs 8 months [25th-75th percentile: 5-24 months]; P < .001).

Dermoscopic Patterns and Colors

Frequencies of dermoscopic features and colors according to the final diagnosis are given in Table 2. Radial lines were more common in recurrent nevi than in recurrent melanoma (29.6% vs 8.1%; P < .001). Because recurrent melanoma was recurrent melanoma was found more frequently on the face, circles were more commonly observed in recurrent melanomas than in recurrent nevi (33.9% vs 7.1%; P < .001). Dermoscopic pattern of recurrent nevi was more often symmetric and that of recurrent melanomas was asymmetric (18.4% vs 6.5%; P = .04). Eccentric hyperpigmentation at the periphery was more often visible in recurrent melanoma than in recurrent nevi (37.1% vs 21.4%; P = .045). A centrifugal pattern was more common in recurrent nevi than in recurrent melanoma (46.9% vs 12.9%), whereas a chaotic growth pattern was more often in recurrent melanomas than in recurrent nevi (59.7% vs 22.4%). A noncontinuous growth pattern was less often visible in recurrent nevi compared with recurrent melanomas (29.6% vs 53.2%; P = .004).

Pigmentation traversing the scar’s edge was less often found in recurrent nevi than in melanomas (42.9% vs 87.1%; P < .001). No significant difference could be demonstrated with regard to the pseudopods, globules or clods, dots, structureless areas, colors, number of features or colors, and vessels within or outside the lesion or scar (Table 2).

Multivariate Analysis and Diagnostic Model

A multivariate model, including all significant variables of the univariate analysis (age, anatomic site, time to recurrence, symmetry, presence of radial lines or circles, presence of eccentric hyperpigmentation, growth pattern, and presence of pigmentation beyond the scar’s edge), showed that location on the head and neck area (odds ratio [OR], 20.2 [95% CI, 3.0-137.2]; P = .002), age older than 30 years (OR, 48.5 [95% CI, 5.5-426.1]; P < .001), and pigmentation beyond the scar’s edge (OR, 4.0 [95% CI, 1.2-12.9]; P = .002) were independently associated with recurrent melanoma. Based on the multivariate analysis, we constructed 2 diagnostic models to aid the clinician with the decision regarding whether a recurrent lesion should be biopsied or not. The first model disregards the initial histopathologic report of the first procedure; the second model takes this report into account. In the first model, the number of recurrent melanoma-associated criteria (location on the head and neck area, age > 30 years, and pigmentation beyond the scar’s edge) were added to a score ranging from 0 to 3. If at least 2 of the criteria were present, the model reached a sensitivity of 88.7%, a specificity of 74.0%, a negative predictive value of 91.0%, and a positive predictive value of 63.8% for melanoma. This first model reached an area under the receiver operating characteristic (ROC) curve of 0.88 (95% CI, 0.83-0.94). In the second model, we added 2 points for those lesions that were diagnosed initially as melanoma and subtracted 1 point for those that were diagnosed as nevi. If no histopathologic report was available then nothing was added or subtracted from the total score. Thus, the scores for the second model ranged from −1 to 4. We chose the same cutoff of 2 points as was done in the first model to calculate sensitivity, specificity, and negative and positive predictive values. At a cutoff of at least 2 points the model reached a sensitivity of...
88.7%, a specificity of 85.7%, a negative predictive value of 92.3%, and a positive predictive value of 79.7% for melanoma. This second model reached an area under the ROC curve of 0.94 (95% CI, 0.90-0.98).

### Discussion

This multicenter, retrospective, observational study of 98 recurrent nevi (Figure 1) and 62 recurrent melanomas (Figure 2) by the IDS demonstrated that pigmentation traversing the scar’s edge is the strongest clue for recurrent melanoma in dermoscopy. Other significant factors associated with recurrent melanoma were circles, chaotic growth pattern, and noncontinuous growth in dermoscopy and the location on the head and neck area, age older than 30 years, and longer time to recurrence.

In daily clinical practice it is difficult to differentiate recurrent nevi from recurrent melanoma. Incomplete removals of melanocytic neoplasms by shave or punch biopsy, excision, laser treatment, or after trauma often present with recurrence of pigment. For many recurrent lesions it is difficult or impossible to obtain the original pathology report or slides. Furthermore, the presence of melanocytic hyperplasia or pseudomelanoma-like features can make it difficult for the pathologist to rule out a melanoma. Botella-Estrada et al.14 stated that 28% of the lesions in their study recurred after various surgical procedures and revealed pseudomelanoma-like features on pathologic examination. Also, inflammation can cause pigment or melanocytic hyperplasia in scars, which leads to confusion.14 A histological review of 722 reexcised scars after initial removal of nonmelanocytic tumors revealed that in 8% there was melanocytic hyperplasia, and in some cases a melanoma in situ was difficult to exclude.18 In 30% of melanoma scars and in 25% of nonmelanoma scars there was evidence of variable degrees of melanocytic hyperplasia.19 Thus, to ensure the most accurate diagnosis, it is recommended that whenever possible, the original pathology slides be reviewed, and, if the lesion is reexcised, that the pathologic findings be reviewed by a dermatopathologist. But should all recurrent lesions be reexcised? Naturally, any recurrent lesion that proved to be a melanoma on the original biopsy needs to be retreated appropriately. What about recurrent lesions that were originally diagnosed as nevi, or recurrent lesions for which the origi-
nal pathology slides are unavailable? It is precisely this question that the present IDS study was designed to answer.15

Besides case reports8-13 the largest study on this subject was performed by Botella-Estrada et al.14 They analyzed clinical and dermoscopic features of 57 recurrent melanocytic tumors with a classification into 4 categories: reactive pigmented scar with macular, banded, or diffuse pigmentation (72.6%); recurrent nevus (24.2%); recurrent melanoma (1.1%); and metastatic melanomas (2.1%). In the histopathologic examination, 56.1% were classified as reactive hyperpigmentation; 38.6% were recurrent nevi; 1.8%, recurrent; and 3.5%, metastatic melanoma. According to dermoscopic features they comprised 2 groups, 1 with reactive pigmentation and 1 with recurrent nevi and melanomas. Comparing the anatomic site, Botella-Estrada et al14 included 5.3% from the head and neck area (vs 20% in our study), 6.3% from the upper extremities (vs 6.9%), 75.8% from the trunk (vs 45%), 6.3% from the lower extremities (vs 25.6%), and 6.3% from the hands and feet (vs 1.3% from the nail area in our study). Based on differing methods of classification and numbers of melanomas, direct comparison of the study by Botella-Estrada et al with ours is difficult.

Our study revealed that patients with recurrent melanomas were significantly older than patients with recurrent nevi (63.1 vs 30.2 years). This age difference between the 2 groups could be a reflection of the higher pretest probability that a biopsied melanocytic lesion in an older individual will be melanoma, and, in contrast, that younger patients more often demand a treatment for cosmetic reasons.

The median time interval between the first and second treatment was 18 months (25 months for recurrent melanomas vs 8 months for recurrent nevi), but the interval lost its significance in multivariate analysis. A significant proportion of the recurrent melanomas may preferentially be of the slow-growing type.20,21 It is possible that lesions simply recur faster in youth and take longer to recur in older individuals. Unfortunately, the number of cases in our study was too small to evaluate “time to recurrence” as a function of (stratified by) age.

Botella-Estrada et al14 reported a mean time of 4 months (range, 1-14 months) to recurrent pigmentation in 43 scars, but no difference in time to recurrence between nevi and melanoma was specified. They14 named dermoscopic features as streaks, pigmented network, dots and globules, background homogeneous pigmentation, bluish white veil, heterogeneous pigmentation, and vascular structures. The presence of globules and heterogeneous pigmentation was the strongest dermoscopic finding ($P < .001$) for recurrent nevi, followed by prominent irregular network ($P = .045$) and absence of streaks ($P = .047$), and these features were helpful in differentiating

![Figure 1. Dermoscopic Images of Recurrent Nevi](image-url)
between reactive hyperpigmentation and recurrent melanocytic neoplasms. In contrast, our study was specifically designed to look for features to help differentiate recurrent nevi from melanoma. Radial lines, as well as a symmetric and centrifugal growth pattern, were more often seen in recurrent nevi (Box).

Circles, eccentric hyperpigmentation at the periphery, chaotic and noncontinuous growth pattern, as well as pigmentation traversing the scar’s edge were more often found in recurrent melanomas. Some of these observations have been described previously in a few case reports. The presence of circles is closely linked to the anatomic location of the lesion; they are more commonly found in recurrent melanoma of the face (65.5%) than in recurrent melanoma on other body areas (6.1%). Unfortunately, the number of cases in this study precluded us from stratifying the data based on location.

Helpful dermoscopic elements and patterns to differentiate recurrent nevi from recurrent melanoma are listed in the Box. Hocker et al showed that no melanomas developed during long-term follow-up after incompletely or narrowly removed dysplastic nevi. Tallon and Snow reported that in 1035 nevi and 196 dysplastic nevi the rate of recurrence requiring reexcision was only 0.3%. Goodson et al arrived at the same conclusion in their study with over 2 years of follow-up of incomplete removal of 271 nevi and 195 dysplastic nevi. All groups concluded that reexcision of incompletely removed nevi, including mildly to moderately dysplastic, may not be necessary. However, in cases of repigmentation in which the original diagnosis was melanoma, it remains imperative...
to rule out recurrent melanoma. Perhaps new noninvasive diagnostic tools, such as confocal microscopy, may also be helpful in the future.12

Our study has several limitations: the design was retrospective, and there was no assurance that all consecutive recurrent lesions seen in each participant’s clinic were entered into the study. This may have inadvertently led to the inclusion of only the atypical cases because they were more likely to be photographically documented than recurrent lesions with minimal pigment or lesions with uninteresting dermoscopic morphologic characteristics. The histopathology slides of the first and second procedures were not reviewed by a central study pathologist with an acknowledgement and acceptance of interobserver agreement among pathologists. In addition, the lesions’ elements and colors were classified by consensus, and thus no interobserver concordance was reported. Finally, there were numerous significant discriminating features found on univariate analysis (Table 2 and the Box); however, on multivariate analysis, only older age, location on the head and neck area, and presence of pigmentation traversing the scar’s edge retained significance. The number of cases included in this study precluded us from evaluating the significance of features (Table 2) stratified by age and location.

In summary, recurrent melanomas were strongly associated with age older than 30 years, longer time of recurrence, circles on the head and neck area, eccentric hyperpigmentation at the periphery, chaotic and noncontinuous growth pattern, and pigment traversing the scar’s edge (Box). Recurrent nevi were associated with age younger than 30 years, shorter time to recurrence, radial lines, symmetry, and a centrifugal growth pattern; in these lesions dermoscopic monitoring in 2 to 3 months is a reasonable option.15,20 However, an excision biopsy of any doubtful recurrent lesion in dermoscopy is the gold standard treatment at present.

REFERENCES
A Short History of Tattoo

Filippo Pesapane, MD; Gianluca Nazzaro, MD; Raffaele Gianotti, MD; Antonella Coggi, MD

Tattoo is a permanent pigmentation of the skin resulting from the introduction of exogenous substances. If this happens unintentionally—for example, after road injuries—it is called traumatic tattoo. However, the most common tattoos are decorative, related to current fashion or to a symbolic meaning.

The etymological origin of the word tattoo is believed to have 2 major derivations: the first is from the Polynesian word “to” which means “striking something,” and the second is the Tahitian word “tatau” which means “to mark something.” This word was introduced in Europe by the English explorer James Cook, who described the Polynesian technique of “tattaw” in his narrative of the voyage.

The oldest example of tattoo dates back to 3000 BC and is represented by a mummy called “Otzi the Iceman” discovered from the area of the Italian-Austrian border in 1991.1 Radiological examination of his bones showed osteochondrosis in areas where tattoos had been present. It has been speculated that these tattoos may have been related to pain relief treatments similar to acupuncture. If so, this practice may have existed at least 2000 years before its previously known earliest use in China.2

In ancient times the tattoo spread throughout Egypt and Rome until it was banned by the Emperor Constantine after his conversion to Christianity. Constantine believed that the human image was a representation of God and should not be disfigured or defiled. The practice of tattooing the body was never fully accepted by any of the 3 great monotheistic religions (Christianity, Judaism, and Islam). Although tattoos were forbidden among Christians by Pope Hadrian I in 787, the habit of tattooing the body survived secretly, especially in some places of Christian worship, like the Sanctuary of Loreto, where the “Friars-Tattooist” (“Frati-marcatori”) tattoo, a small devotional sign to the pilgrims, was used.

The reintroduction of the tattoo in the Western world occurred after the ocean expeditions of the 18th century. At the end of the 19th century the use of tattooing spread among highest European social classes: famous “celebrity” tattoos included those of Tsar Nicholas II and Sir Winston Churchill. In recent decades the practice of tattoo has widely spread in the Western world to all social classes, with an increase of complications related to it, such as allergic, lichenoid, granulomatous, and pseudolymphomatous reactions or induction of skin diseases.3

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