Dermatologists’ Accuracy in Early Diagnosis of Melanoma of the Nail Matrix

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Objective: To measure and compare the accuracy of 4 different clinical methods in the diagnosis of melanoma in situ of the nail matrix among dermatologists with different levels of clinical experience.

Design: Twelve cases of melanonychias (5 melanomas and 7 nonmelanomas) were presented following 4 successive steps: (1) clinical evaluation, (2) evaluation according to the ABCDEF rule, (3) dermoscopy of the nail plate, and (4) intraoperative dermoscopy. At each step, the dermatologists were asked to decide if the lesion was a melanoma.

Setting: The test was administered at 2 dermatological meetings in 2008.

Participants: A total of 152 dermatologists, including 11 nail experts, 53 senior dermatologists, and 88 junior dermatologists.

Main Outcome Measures: The answers were evaluated as percentage of right answers for each diagnostic step according to the different grade of expertise. Differences among the percentage of right answers in the different steps were evaluated with the z test at a 5% level of significance. The agreement was investigated using Cohen κ statistic.

Results: The only method that statistically influenced the correct diagnosis for each category (experts, seniors, and juniors) was intraoperative dermoscopy (z test; P < .05). Cohen κ statistic showed a moderate interobserver agreement.

Conclusions: Overall accuracy of dermatologists in the diagnosis of nail matrix melanoma in situ is low because the percentages of physicians who indicated the correct diagnosis during each of the first 3 clinical steps of the test ranged from 46% to 55%. The level of expertise did not statistically influence the correct diagnosis.

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EARLY DIAGNOSIS OF MELANOMA of the nail unit is still a challenge for dermatologists because the tumor usually presents with a longitudinal nail pigmentation (longitudinal melanonychia), which is not a specific sign for melanoma.

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Longitudinal melanonychia can also be caused by numerous nonmalignant conditions that include nevi of the nail matrix, benign melanocytic hyperplasia (nail matrix lentigo), and a number of inflammatory, traumatic, or iatrogenic nail disorders that induce the activation of the nail matrix melanocytes.1,4 Clinical examination can reveal features that are suggestive but not pathognomonic of melanoma. These include inhomogeneous pigmentation with bands or lines of different colors, presence of nail plate fissuring or splitting, rapid enlargement of the band, a proximal part of the band that is broader than the distal (triangular shape), blurred lateral borders, and pigmentation of the periungual skin.4

These features have been summarized in the ABCDEF rule for diagnosis of nail melanoma and this may help clinicians in distinguishing “nonalarming” from “alarming” bands and therefore in selecting the lesions that require excision and pathologic examination.5 Each letter indicates clinical and/or anamnestic features that are associated with an increased risk of melanoma: A (age as peak incidence of nail melanoma is between 50 and 70 years; A also reminds us of most commonly affected races: African American, Asian, and Mediterranean), B (bands), C (changes in size, shape, or color), D (dysfunction of the nail matrix), E (edema, induration, or erosion), F (fluctuation), and F (any features of inflammation).6

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Dermoscopy of the nail plate has recently been proposed as a noninvasive method to distinguish benign lesions from malignant lesions, and different dermoscopic patterns have been described in melanocyte activation, nail matrix nevi, and melanoma. The dermoscopic pattern associated with nail matrix melanoma is characterized by a brown band that contains irregular longitudinal lines of different color and thickness with loss of parallelism. Dermoscopic patterns, however, have not been validated by evidence-based studies, and the usefulness of this technique in the early diagnosis of nail matrix melanoma is still not proven.

Intraoperative dermoscopy of the nail bed and matrix is an invasive technique that can be used by the surgeon to visualize the tumor margins and then possibly best select the margins of surgical excision. Intraoperative dermoscopy is performed with polarized devices that do not require the application of immersion fluids and allow examination with no direct contact in order to maintain aseptic conditions. Intraoperative dermoscopy examines the site of melanin production and may then offer new clues for distinguishing benign lesions from malignant lesions. In melanocyte activation, intraoperative dermoscopy shows gray lines. In melanocyte hyperplasia, it shows brown lines that are regular and associated with globules in nevi but that are irregular in melanoma (S.H.H., 2009, unpublished data). We measured and compared the accuracy of 4 different clinical methods (clinical evaluation, clinical evaluation using the ABCDEF rule, dermoscopy of the nail plate, and intraoperative dermoscopy) in the early diagnosis of nail matrix melanoma among dermatologists with different levels of clinical experience, including a group of dermatologists with specific expertise in nail disorders.
METHODS

The institutional review board of the Hospital do Servidor Público Municipal of São Paulo, Brazil, approved this study. We selected the images of 12 cases (5 in situ melanomas and 7 non-melanomas) of longitudinal melanonychias. The cases were selected by one of us (N.D.C.) and included all the cases of in situ melanoma diagnosed at the Hospital do Servidor Público Municipal of São Paulo from January 2006 to December 2007 and 7 consecutive cases of melanonychia not due to melanoma, which were excised during the same time period. All these cases were documented with clinical pictures, dermoscopy of the nail plate, intraoperative dermoscopy, and histopathologic examination of the excised lesion.

The test session was organized at 2 dermatological meetings in 2008: (1) Curso de Educação Medica Continuada em Dermatologia da Sociedade Brasileira de Dermatologia Regional de São Paulo, Brazil (attended by 119 dermatologists), and (2) the Annual Meeting of the Council for Nail Disorders San Antonio, Texas (attended by 46 dermatologists) (Figure 1). At the beginning of the session, each physician received a 4-page handout to fill out and return after the session. In the first page of the handout (Figure 2), physicians were asked to classify themselves according to 3 possible grades of experience: expert (physicians with specific interest in nail disorders including nail pigmentation), senior (general dermatologists with more than 10 years of experience), or junior (general dermatologists with less than 10 years of experience).

The images of the 12 cases were presented following 4 successive steps. At each step, the dermatologists were asked to indicate in the corresponding section of the handout if the lesion was a melanoma. Figures 3, 4, 5, and 6 illustrate the fourth step for 4 of the 12 cases.

1. Clinical features: Physicians were consecutively shown the clinical pictures of the 12 lesions.

2. Clinical features to be scored with the ABCDEF rule: The specific rules with guidelines were explained to the audience. In this case, we already scored A (age, race), C (duration of changes), D (digit), and F (family history), and each physician had to assign the B (band characteristics), and E (extension of the pigmentation) score.

3. Dermoscopy of nail plate: The dermoscopic pattern associated with nail matrix melanoma (brown band with irregular longitudinal lines of different color and thickness with loss of parallelism) was first illustrated, and then the dermoscopic features of the 12 cases were shown to the audience.

4. Intraoperative dermoscopy of nail bed and matrix: The dermoscopic patterns observed in melanocyte activation and hy-
perplasia (including melanoma) were first explained to the audience, and then the intraoperative dermoscopic features of the 12 cases were shown to the audience.

At the end of the test we collected the handouts and then presented the final diagnosis based on pathologic examination of the lesions. A total of 152 dermatologists returned their handouts; these included 115 dermatologists (5 experts, 40 seniors, and 70 juniors) in São Paulo and 37 dermatologists (6 experts, 13 seniors, and 18 juniors) in San Antonio. We obtained 48 answers from each physician (4 answers for each lesion).

To establish the validity of the selected images, we recently performed an intraobserver agreement to assess the reproducibility of the test. For this purpose we selected a panel of 5 Brazilian nail experts who had not participated in the original test. The test was administered twice, at an interval of 4 weeks, but with the 12 cases presented in a different order.

The answers were evaluated as a percentage of the right answers for each diagnostic step according to the different grade of expertise. To establish if there was any difference among the percentage of right answers due to dermoscopy examination, we performed a z test at a 5% level of significance using SPSS statistical software (version 10; SPSS Inc, Chicago, Illinois). The agreement was investigated using the Cohen $\kappa$ statistic, which incorporates a correction for the extent of agreement expected by chance alone. $\kappa$ Values of less than 0.40 indicate a fair agreement; $\kappa$ values of 0.41 to 0.60 indicate moderate agreement (with values of 0.60-0.80 indicating substantial agreement); and $\kappa$ values greater than 0.80 indicate an almost perfect agreement.

### RESULTS

Table 1 reports the percentages of right answers at each diagnostic step for each category of dermatologist. Our results showed that the only method that statistically influenced the correct diagnosis for each category (experts, seniors, and juniors) was dermoscopy of the nail bed and matrix ($z$ test; $P<.05$). No differences were found for the other methods considered.

Cohen $\kappa$ statistic showed a moderate interobserver agreement for clinical features, ABCDEF rule, and nail plate dermoscopy; interobserver agreement was higher for experts compared with seniors and juniors (Table 2). $\kappa$ Statistics showed a moderate agreement between clinical features and intraoperative dermoscopy in experts.
The main goal in the treatment of melanoma of the nail matrix is to diagnose and excise lesions that are still in situ because this provides the only real possibility of curative treatment. In situ melanoma, however, usually presents with a band of longitudinal melanonychia, which is hard to differentiate from melanonychia owing to benign conditions. A differential diagnosis between benign melanocytic hyperplasia and in situ melanoma can be a serious problem even for the pathologist, especially when the lesion is biopsied rather than excised. Several cases of delay in treatment of melanoma owing to false-negative findings from incisional biopsies are reported in the literature, and this is why we chose to excise bands of longitudinal melanonychia, using the nail matrix shave biopsy for large bands. Melanoma in situ is pathologically characterized by an increased number of enlarged and irregularly distributed melanocytes along the basal layer of the nail matrix. Amin et al recently evaluated the density and the characteristics of intraepidermal melanocytes in pathologic specimens of benign lentigo and in situ melanoma of adults and found that severe atypia is uncommon. Although they were not able to establish a cutoff value in the melanocytes’ density to separate in situ melanoma from benign lentigos, a melanocyte density of 40 or higher favors a diagnosis of melanoma. An additional problem is that the pathologic criteria that are considered consistent for a diagnosis of in situ melanoma in adults cannot be easily applied to melanocytic lesions in children because there are no data on melanocyte density in normal, benign, and malignant lesions in children, and because nevi in children often present with a mild degree of transepidermal melanocyte migration and some cellular atypia. The difficulties encountered in the early diagnosis of nail matrix melanoma are underscored by the recent literature showing that delay in the diagnosis is common with most lesions diagnosed in advanced stages and in situ lesions only accounting for 10% to 16.3% of melanomas.

A limitation of this study is that we did test accuracy in the diagnosis of difficult cases of melanonychia. All cases of melanonychia selected for our test were excised because the band had worrisome features that induced the dermatologist to excise the lesion and exclude the possibility of nail matrix melanoma; as a matter of fact, the decision to excise these bands was based on history and clinical examination and not on the results of intraoperative dermoscopy, which was used during surgery to examine the lesion and delimit surgical excision. We only included cases of in situ melanoma because the purpose of the study was to assess accuracy in the early diagnosis of melanoma and not in the diagnosis of advanced melanoma, which is associated with obvious alarming clinical signs. To assess the validity of the selected images, we decided to evaluate the reproducibility of the test with a panel of 5 nail experts who had not participated in the original study and obtained a high intraobserver agreement when the blinded images were reevaluated after 4 weeks.

Our results show that the accuracy of dermatologists in the clinical diagnosis of in situ nail matrix melanoma is low because the percentage of physicians who indicated the correct diagnosis during each of the first 3 clinical steps of the test ranged from 46% to 55%. The statistical analysis showed that the level of expertise did not statistically influence the correct diagnosis and that the interobserver agreement was moderate for all 3 different groups of dermatologists even if it was higher for experts than for seniors and juniors. The application of the ABCDEF rule did not influence the percentage of right answers compared with simple clinical examination. Nail plate dermoscopy did not improve diagnostic accuracy even among dermatologists who were trained in the techniques and classified themselves as experts in nail disorders. Although interpretation of dermoscopy criteria requires specific training, which cannot be acquired after a short teaching session, the statistical analysis did not show significant differences in the correct dermoscopic diagnosis of experts and nonexperts.

These findings are in contrast with those in the recent literature that report that dermoscopy is a useful tool for differential diagnosis of pigmented nail lesions. Until now, however, to our knowledge no studies have measured accuracy and interobserver agreement of this technique among dermatologists. The main shortcoming of nail plate dermoscopy in the evaluation of pigmented nail lesions is that the technique does not permit the evaluation of the anatomical site that produces the pigmentation but only of the deposits of pigment within the nail plate. To overcome this problem, intraoperative dermo-

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**Table 1. Percentages of Correct Diagnosis for Each Step of the Test in the 3 Groups of Dermatologists**

<table>
<thead>
<tr>
<th>Test Step</th>
<th>Experts</th>
<th>Seniors</th>
<th>Juniors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical features</td>
<td>55</td>
<td>51</td>
<td>52</td>
</tr>
<tr>
<td>ABCDEF rule</td>
<td>48</td>
<td>49</td>
<td>54</td>
</tr>
<tr>
<td>Nail plate dermoscopy</td>
<td>53</td>
<td>46</td>
<td>48</td>
</tr>
<tr>
<td>Intraoperative dermoscopy</td>
<td>76</td>
<td>71</td>
<td>72</td>
</tr>
</tbody>
</table>

**Table 2. Cohen κ Statistic: Interobserver Agreement for the 3 Different Groups on Clinical Features, ABCDEF Rule, and Nail Plate Dermoscopy**

<table>
<thead>
<tr>
<th>Group</th>
<th>Clinical Features</th>
<th>ABCDEF Rule</th>
<th>Nail Plate Dermoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experts</td>
<td>0.70</td>
<td>0.62</td>
<td>0.66</td>
</tr>
<tr>
<td>Seniors</td>
<td>0.62</td>
<td>0.58</td>
<td>0.46</td>
</tr>
<tr>
<td>Juniors</td>
<td>0.64</td>
<td>0.66</td>
<td>0.54</td>
</tr>
</tbody>
</table>

(κ = 0.53), seniors (κ = 0.50), and juniors (κ = 0.52) with no statistical difference among the different groups of observers. Reproducibility of the test was highly satisfactory. Intraobserver agreement showed a κ value equal to 0.89 for clinical diagnosis (95% confidence interval [CI], 0.85-0.92); κ = 0.85 for ABCDEF (95% CI, 0.81-0.89); κ = 0.87 for nail plate dermoscopy (95% CI, 0.80-0.91); and κ = 0.82 for intraoperative dermoscopy (95% CI, 0.78-0.86).
scopy of the nail matrix and bed has been recently introduced to provide a direct examination of the lesion as for skin dermoscopy. Our results show that intraoperative dermoscopy statistically improves diagnostic accuracy for each category of dermatologist. However, this is a new and invasive procedure that cannot be performed routinely to screen patients with nail pigmentation. In our experience, the technique is very useful to accurately assess the margins of the lesion during excision and can possibly reduce the chance of recurrence of melanonychia after excision.

Our results underscore the fact that in situ melanoma of the nail matrix is very difficult for dermatologists to diagnose, regardless of the level of their experience, and support the view that early excision and pathologic examination of all lesions with suspicious clinical features is presently the only way to avoid misdiagnosis.

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Author Contributions: Drs Di Chiacchio and Tosti had full access to all of the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis. Study concept and design: Di Chiacchio, Hirata, and Tosti. Acquisition of data: Di Chiacchio, Hirata, Enokihara, Fabbrocini, and Tosti. Analysis and interpretation of data: Di Chiacchio, Hirata, Michalany, Fabbrocini, and Tosti. Drafting of the manuscript: Hirata and Tosti. Critical revision of the manuscript for important intellectual content: Di Chiacchio, Hirata, Enokihara, Michalany, Fabbrocini, and Tosti. Administrative, technical, and material support: Hirata, Michalany, Fabbrocini, and Tosti.

Study supervision: Hirata, Enokihara, and Tosti.

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REFERENCES