Assessment of the Optimal Interval for and Sensitivity of Short-term Sequential Digital Dermoscopy Monitoring for the Diagnosis of Melanoma

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Objective: To determine whether 6 weeks could replace 3 months for short-term sequential digital dermoscopy imaging (ST-SDDI) of suspicious melanocytic lesions and determine the proportion of melanomas missed.

Design: Consecutive lesions (n = 2602) undergoing ST-SDDI monitored from 1859 patients were included. Half of the patients underwent 6-week monitoring followed by 3-month monitoring (range, 2.5-4.5 months) if changes were not seen. The remainder underwent 3-month monitoring only. Any change during this time led to excision. Lesions unchanged were then followed up over time.

Setting: A tertiary referral institution.

Main Outcome Measures: The proportion of changed melanomas (sensitivity) and odds ratios (ORs) for melanoma of changed lesions.

Results: Eighty-one melanomas were detected using ST-SDDI (Breslow thickness: median, in situ; maximum, 0.8 mm). Of 39 melanomas detected using ST-SDDI in the 6-week monitored lesions, 27 (69%) were detected at 6 weeks and 12 (31%) at 3 months. The OR for melanoma for a lesion changing at 6 weeks was 19 (95% confidence interval [CI], 10-35), and the overall OR for melanoma for a lesion changing during the short-term monitoring period (6 weeks to 4.5 months) was 47 (95% CI, 23-94). For lesions remaining unchanged at 3 months, 99.2% (1118 of 1127 lesions) were shown to be benign as defined by an unremarkable further follow-up. Seventy-five percent (15 of 20) of the lentigo maligna melanomas, 93% (40 of 43) of other in situ melanomas, and 96% (26 of 27) of the invasive melanomas were detected using ST-SDDI.

Conclusion: Three months remains the standard interval for ST-SDDI, where the sensitivity for the diagnosis of melanoma for changed (non–lentigo maligna) lesions is high but not 100%.

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Sequential digital dermoscopy imaging (SDDI) involves the capture and assessment of successive dermoscopic images, separated by an interval, of 1 or many melanocytic lesions, allowing detection of change.1-11 This imaging technique has been shown to allow the detection of melanoma lacking dermoscopic features of melanoma1,2 and is performed in 2 settings. Long-term monitoring examines nonsuspicious melanocytic lesions during standard surveillance periods (usually 6-12 months) often in the context of patients with multiple atypical nevi. Here, certain significant predictive changes in malignancy have been defined.1,6 In contrast, short-term digital monitoring (usually for 3 months and always <4.5 months) examines suspicious melanocytic lesions based on morphologic features or patient history but usually without any dermoscopic evidence of melanoma. Unlike long-term monitoring, any morphologic change seen with short-term SDDI (ST-SDDI) requires excision of the lesion.1,3

Currently, most of the data on ST-SDDI follows monitoring at a 3-month interval (range, 2.5-4.5 months).1,3,5,10 Here, the specificity for the diagnosis of melanoma is 83%, with only 17% of atypical benign lesions showing change at that interval.3 In the present study, we assess the diagnostic accuracy of SDDI at 6 weeks compared with the standard 3-month interval to test whether 6 weeks could replace 3 months as the standard interval for ST-SDDI.
Because 1 in 6 atypical benign lesions change during short-term monitoring and because some melanomas show changes after 6 days, it has been suggested that the sensitivity for the diagnosis of melanoma at 3-month monitoring would approach 100% (ie, all melanomas will show change at that interval). In the present study, by analysis of follow-up of lesions unchanged at the short-term monitoring period, we present the estimated sensitivity of the technique.

All the patients were examined in the tertiary referral center of the Sydney Melanoma Unit (Sydney Melanoma Diagnostic Centre) between April 1, 1998, and May 31, 2007. In this clinic, SDDI was performed on selected patients using the SolarScan system (Polartechnics Ltd, Sydney), which allows precise color calibration between imaging as previously described. In general, suspicious melanocytic lesions, usually flat or slightly raised, without overt dermoscopic evidence of melanoma, underwent ST-SDDI in 2 clinical scenarios: (1) lesions with mild atypia defined as symmetrical or, more frequently, near symmetrical in pigmentation pattern and that had a patient history of change and (2) lesions with moderate atypia defined as more asymmetrical with greater architectural disorder sometimes with a single dermoscopic feature of melanoma (as seen in some dysplastic nevi) but without a history of change.

All consecutive lesions undergoing ST-SDDI (<4.5 months) monitored from 1859 patients (median age, 39 years; age range, 1-90 years; 58% female) were included in the study. All the patients gave written consent for their clinical data to be used, and this study was approved by the ethics committee of the Central Sydney Area Health Service. A flowchart of recruited lesions is seen in Figure 1. Approximately half of the lesions underwent 6-week monitoring followed by 3-month (range, 2.5-4.5 months) monitoring if morphologic changes were not seen. The remainder of the lesions underwent 3-month monitoring without 6-week SDDI. Any visual change during this time was considered significant enough to warrant excision, except for an increase or decrease in milialike cysts or a uniform increase or decrease in pigmentation consistent with surrounding skin tanning changes.

Follow-up data for lesions remaining unchanged at 3 months were recorded using the clinic database records. Three categories of follow-up were recorded that were considered evidence of a benign lesion: (1) 6- to 8-month SDDI from baseline that showed no morphologic change; (2) greater than 8-month SDDI from baseline that showed none of the significant morphologic changes of size, shape, color, evidence of regression, or appearance of known dermoscopic features of melanoma, according to the criteria of Kittler et al; and (3) a routine skin examination more than 12 months after baseline imaging without detecting melanoma (Figure 1).

**RESULTS**

A total of 1331 suspicious melanocytic lesions underwent 6-week SDDI. If any morphologic change occurred at that time, excision was performed. If no change occurred, then conventional short-term monitoring at a median of 3 months (range, 2.5-4.5 months) after baseline imaging was performed. At this time, lesions undergoing any morphologic change underwent excision (Figure 1). Of the 39 melanomas detected using the 6-week to 3-month follow-up setting, 27 (69%) were detected at 6 weeks. At the 6-week interval, 96 benign lesions were excised because of change, resulting in a specificity for the diagnosis of melanoma of 93% (on the assumption of 1292 benign lesions in this set). The odds ratio (OR) for melanoma for a lesion changing at 6 weeks was 19 (95% confidence interval [CI], 10-35). Thirty-one percent of the melanomas (n = 12) required 3-month monitoring for detection (ie, changed at 3 months but not at 6 weeks). A further 118 benign lesions were ex-
cised because of morphologic change at this time. The OR for melanoma for a lesion changing at 3 months without change at 6 weeks was similar at 18 (95% CI, 7-49). The overall OR for melanoma for a lesion changing during the short-term monitoring period (6 weeks to 4.5 months) was 47 (95% CI, 23-94). Finally, 57% (46 of 81) of the melanomas detected using short-term monitoring had no dermoscopic features of melanoma on either the baseline or follow-up image using the method of Menzies et al. Examples of lesions that changed during ST-SDDI are shown in Figure 2 and Figure 3.

FOLLOW-UP OF LESIONS UNCHANGED AT 3-MONTH IMAGING

Of the 2602 lesions monitored during the short-term interval (<4.5 months; median, 3 months, incorporating lesions monitored with and without the 6-week interval), 81 melanoma and 406 benign lesions were excised because of change (Figure 1). To assess whether any melanomas were not identified during the short-term monitoring period (ie, false-negative melanomas remaining unchanged at 3 months), an assessment of the unchanged lesions in routine clinical follow-up was performed. Of the 2115 lesions that remained unchanged at 3 months, 1127 (53%) had significant follow-up records. These had medium-term imaging (6-8 months since baseline), where any change detected resulted in excision; long-term imaging beyond 8 months, where any “significant” morphologic changes as defined by Kittler et al resulted in excision; or routine clinical examination using dermatoscopy beyond 12 months after baseline imaging (Figure 1). Of those 1127 lesions, 9 false-negative melanomas were detected (8 of 9 were in situ and 1 was invasive [0.3-mm Breslow thickness]). Of these misclassified melanomas, 5 were lentigo maligna. Although there was a decrease in the proportion of correctly detected lentigo maligna at short-term monitoring (sensitivity, 75%) compared with 93% sensitivity for non-lentigo maligna in situ melanoma and 96% sensitivity for invasive melanoma, this was not statistically significant (Table) (with sensitivity values calculated assuming that no melanomas were present in the group lost to follow-up). There was no statistically significant difference between the median Breslow thickness of melanomas detected at ST-SDDI (in situ; range, 0-0.8 mm) compared with those misclassified (in situ; range, 0-0.3 mm) (P = .18, Wilcoxon rank sum test).

The specificity for the diagnosis of melanoma when excising a lesion for any change during short-term monitoring was 84%, with 406 benign lesions excised from 2512 imaged at baseline. For lesions remaining unchanged at 3 months, 99.2% (1118 of 1127 lesions) were shown to be benign on follow-up. The OR for melanoma for a lesion without change at 3 months was 0.02 (95% CI, 0.01-0.04).

COMMENT

The main aim of this study was to determine whether the interval for assessing suspicious melanocytic lesions using SDDI could be reduced from 3 months to 6 weeks. Because 31% of the melanomas detected during short-term monitoring did not change at 6 weeks and there was no significant difference in median Breslow thickness between melanomas detected at 6 weeks vs 3 months, there...
seems to be little advantage in reducing the recommended interval. However, when assessing suspicious pigmented macules of the face, the observation that only 75% of lentigo maligna lesions were detected at 3 months suggests the need for an additional long-term monitoring image to be taken before excluding malignancy. We suggest that this imaging occur 6 to 12 months after baseline imaging, but the evidence for this suggested interval lacks formal investigation.

Seven percent of non–lentigo maligna in situ melanomas and 4% of invasive melanomas were not detected using ST-SDDI. Nevertheless, these melanomas remained thin when detected at longer follow-up, with 8 of the 9 remaining in situ and the 1 invasive melanoma having a Breslow thickness of 0.3 mm. The slow vertical growth of these misclassified melanomas was consistent with the slow growth seen by lack of morphologic changes noted during the short-term monitoring period.

Figure 3. A lentigo maligna lesion that changed during short-term sequential digital dermoscopy imaging. A, Baseline image of a 7.6-mm-diameter lesion on the cheek of a 61-year-old man. B, Six-week follow-up image showing changes, including extension of pigmentation (arrows), with an increase to 8.2 mm in diameter. Bar = 1 mm.

The estimates of missed melanomas were calculated on the assumption that there were no melanomas in the group lost to follow-up. For this reason, the sensitivities may be overestimated. However, because all the patients are instructed to return if any change occurs with their monitored lesion and many of the patients lost to follow-up underwent monitoring more than 12 months before the closing date of the study, this assumption seems more appropriate than extrapolating an incidence of missed melanoma in the follow-up group. Furthermore, the estimates of missed melanoma assume that all the lesions subsequently proved to be melanoma on long-term follow-up were melanoma at baseline imaging, which in the case of the non–lentigo maligna melanomas may not be true because in high-risk patients we assume a certain rate of melanoma newly developing within nevi.

This study was not a randomized trial but rather a retrospective analysis of consecutive patients undergoing

Table. Histologic Subtypes of Melanomas Detected or Undetected by Short-term Monitoring

<table>
<thead>
<tr>
<th>Melanoma Subtype</th>
<th>Detected at 6 wk (n=27)</th>
<th>Detected at 3 mo (n=42)</th>
<th>All Detected at 6 wk to 4.5 mo</th>
<th>All Detected at Longer Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lentigo maligna</td>
<td>6 (22)</td>
<td>6 (14)</td>
<td>15 (75)</td>
<td>5 (25)</td>
</tr>
<tr>
<td>In situ non–lentigo maligna</td>
<td>13 (48)</td>
<td>19 (45)</td>
<td>40 (93)</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Invasive</td>
<td>8 (30)</td>
<td>17 (40)</td>
<td>26 (96)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Breslow thickness, median (range), mm</td>
<td>In situ (0-0.8)</td>
<td>In situ (0-0.5)</td>
<td>In situ (0-0.8)</td>
<td>In situ (0-0.3)</td>
</tr>
</tbody>
</table>

a Data are given as number (percentage) of column total unless otherwise indicated.
b Data are given as number (percentage) of total of both rows unless otherwise indicated.
c There was no significant difference between the proportion of lentigo maligna melanomas correctly identified by change at short-term sequential digital dermoscopy imaging compared with in situ melanoma (P= .10) and invasive melanoma (P= .07) (Fisher exact test).
d There was no significant difference in median Breslow thickness between melanomas detected at 6 weeks vs 3 months (P= .47, Wilcoxon rank sum test) or those detected during the short-term digital monitoring period (<4.5 months) vs longer follow-up (P= .18, Wilcoxon rank sum test).
SDDI at a single institution. Although the same criteria were used in patients undergoing 6-week or 3-month monitoring, a possible limitation exists because of the lack of randomization into the 2 monitoring arms. Another confounder that may occur in sequential digital monitoring is pseudochange due to compression differences or stretching of the skin. Artifactual change due to stretching of the skin is usually easily identified by an increase in diameter of 1 lesion axis with a corresponding shortening of the perpendicular axis.

The safety of SDDI is again underlined in this study. As previously reported in a series of melanomas detected by short- and long-term monitoring, all the melanomas in this study were less than 0.8 mm in Breslow thickness, with a median Breslow thickness of in situ melanoma. Suspicious nodular lesions are never monitored using SDDI.

Five studies previously published on SDDI show that the technique allows the detection of melanomas that lack dermoscopic evidence of malignancy. In particular, in 1 prospective study of melanomas diagnosed by a variety of clinical means, 34% were detected exclusively using the findings of SDDI and were dermoscopically featureless. In the present study, 57% of melanomas detected at short-term monitoring had no dermoscopic features of melanoma. Furthermore, changes detected using SDDI are subtle and would not be detected using routine dermoscopic examination without the aid of an archiving facility that allows comparison of lesions tiled on the computer screen. Finally, the specificity for the diagnosis of melanoma when excising a lesion for any change during short-term monitoring was 84% (ie, 16% of suspicious benign melanocytic lesions changed during short-term monitoring). This reproduced the original findings.

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Author Contributions: Drs Altamura and Menzies had access to the data collected, and Dr Menzies is responsible for its analysis. Study concept and design: Menzies.

Acquisition of data: Altamura, Avramidis, and Menzies. Analysis and interpretation of data: Menzies. Drafting of the manuscript: Menzies. Critical revision of the manuscript for important intellectual content: Altamura and Avramidis. Statistical analysis: Menzies. Obtained funding: Menzies. Administrative, technical, and material support: Menzies. Study supervision: Menzies.

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REFERENCES