Short-term Digital Surface Microscopic Monitoring of Atypical or Changing Melanocytic Lesions

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Objective: To examine the outcome of short-term digital surface microscopic monitoring of suspicious or changing atypical melanocytic lesions.

Design: Digital surface microscopic (oil epiluminescence microscopy, and dermoscopy) images of clinically melanocytic lesions were taken with a color calibrated 3 CCD video instrument. In general, lesions were moderately atypical, flat or only slightly raised, without a history of change or surface microscopic evidence of melanoma, or were mildly atypical lesions with a history of change. Lesions were monitored during a 2.5- to 4.5-month period (median, 3.0 months). With the exception of overall change in pigmentation consistent with that seen in surrounding skin (solar exposure changes), any morphologic change after monitoring was considered an indication to excise.

Setting: Sydney Melanoma Unit, Sydney, Australia (a referral center).

Patients: A consecutive sample of 318 lesions from 245 patients (aged 4-81 years).

Main Outcome Measure: Specificity for the diagnosis of melanoma.

Results: Of the 318 lesions, 81% remained unchanged. Of the 61 lesions that showed morphologic changes, 7 (11% of changed and 2% of total lesions) were found to be early melanoma (5 in situ and 2 invasive with a Breslow thickness of 0.25 mm and 0.28 mm, respectively). None of these melanomas developed any classic surface microscopic features of melanoma and therefore could be identified only by morphologic change. The specificity for the diagnosis of melanoma by means of short-term digital monitoring was 83%.

Conclusion: On the assumption that all melanoma will change during the monitored period, surface microscopy digital monitoring is a useful adjunct for the management of melanocytic lesions.

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Because of the suboptimal diagnostic accuracy of melanoma at both the specialist and primary care physician level, instrumental methods have been developed to improve clinical accuracy. Surface microscopy (dermatoscopy, oil epiluminescence microscopy, and dermoscopy) greatly increases the morphologic features visualized in pigmented skin lesions and has been shown to increase the diagnostic accuracy of nearly all pigmented lesions, including melanoma.

Digital surface microscopy systems have undergone widespread investigation recently. These systems can be divided into 3 categories. First are those used to store images for viewing by clinicians in a conventional or telemedicine setting. Second are those used in combination with image analysis that aim for automated diagnosis. Third are those used for monitoring of lesions for morphologic change. While such instrumentations is being widely used in the field, little has been published regarding the technique.

Digital surface microscopic monitoring of melanoctic lesions can be found in 2 settings. Long-term surveillance of atypical nevi during periods such as 12 months is one useful application. Here, images are stored from lesions that are confidently diagnosed as nonmelanoma and can be used to detect early melanoma at standard follow-up surveillance periods. In contrast, we present data on short-term surveillance of lesions during a median interval of 3 months (range, 2.5-4.5 months).
MATERIALS AND METHODS

DIGITAL SURFACE MICROSCOPY INSTRUMENT

Single lesion monitoring was performed on a digital surface microscopy video instrument (MkII Skin Polarprobe, SolarScan prototype, Polartechnics Ltd, Sydney, Australia). The instrument uses a 3 CCD remote-head color video camera that produces 24-bit, 760×570-pixel images. The fixed focus system images an area of 24.2×18.1 mm, yielding a resolution of approximately 32 µm per pixel (×12.5 screen magnification). The light source is fiber optic coupled to an incandescent halogen lamp with a color temperature of 3000°K. Oil is placed on the lesion-camera interface to record digital surface microscopic images.

The calibration procedure comprises black balance, white balance, shading correction, setup of camera dynamic range, and capture of an image of a reference surface of known reflectivity. Black balance is performed once per month. The other 4 operations are performed once per session or when the system detects change in appearance of the reference surface. The image of the reference surface is used for lighting correction. In addition to the session-level calibration, the system comprises image-level calibration, which is facilitated by 4 gray-scale calibration targets present in each image. The calibration algorithm modifies the lighting-corrected images in such a way that each target average brightness experiences minimal variation against a preset value.

The resulting calibrated images of a single lesion taken from 2 to 4 different times were able to be viewed on the monitor simultaneously. The resolution of each of these images was 64 µm per pixel (×6.2 screen magnification).

The position of each monitored lesion was recorded on a body map, which can be either a pictorial representation of a human body or a photograph of part of the patient’s body. A patient history of change in color or pattern and size during the previous 2-year period was recorded when the first lesion image was taken. Responses were recorded as no change, change, or unknown.

CRITERIA FOR MONITORING PIGMENTED LESIONS

The clinical criteria for monitoring were as follows.

Only pigmented lesions considered melanocytic in origin were chosen. Criteria for such a decision included the presence of the surface microscopic features of brown globules, pigment network, branched streaks, or homogeneous blue pigmentation in the absence of classic patterns of non-melanocytic lesions13,14 with the use of ×10 magnification handheld surface microscopes (eg, Episcope; Welch Allyn Inc, Skaneateles Falls, NY, or Dermatoscope; Heine Ltd, Herrnsching, Germany).

All lesions had no surface microscopic features of melanoma on examination with a handheld surface microscope. A previously reported method achieving a 92% sensitivity for melanoma was primarily used.15 Here, for melanoma to be diagnosed, it must have neither of the 2 morphologic negative features of symmetry of pattern and a single color (scored from tan, dark brown, blue, black, gray, and red) and must have 1 or more of the 9 positive features, consisting of blue-white veil, multiple brown dots, pseudopods, radial streaming, scarlike depigmentation, peripheral black dots or globules, multiple (3-6) colors, multiple blue or gray dots, and broadened network.

In general, lesions monitored that satisfied the above criteria were chosen because of a recent history of change while exhibiting only minor clinical atypia or were mildly to moderately atypical lesions without a history of change. Minor atypical lesions show more symmetric patterns under surface microscopy, while more atypical lesions show increased asymmetry of pattern without demonstrating any positive features of melanoma. In the case of mild to moderate atypical lesions, these were mainly macules or only superficially raised. Lesions with the surface microscopic feature of multiple peripheral brown globules with symmetric pattern that often present with a history of change were not monitored, since these lesions are known to be benign.11,13

Lesions were scheduled to be monitored during a 2.5- to 4.5-month period (median, 3.0 months). All patients were instructed to observe their monitored lesion for change. If this occurred before their scheduled appointment, they returned earlier and an image was taken.

In general, any morphologic change resulted in an excision biopsy. The exception to this was overall increase or decrease in pigmentation without architectural change, which was consistent with change in pigmentation of the surrounding skin (solar exposure changes). In addition, the loss or appearance of milialike cysts was not considered significant. Changes were recorded as a function of shape, size (increase or decrease), interior architecture (pattern), and color (addition or loss of a preexisting color). Color change was defined spatially, ie, the loss or presence of a new color in a particular region of the lesion indicated change. Size changes were confirmed by means of an on-screen spatial measurement tool. No automated image analysis was used to determine change.

RESULTS

Three hundred eighteen lesions from 245 patients (median age, 38 years; range, 481 years; 54% female) were digitally monitored. The median planned follow-up was 3.0 months (range, 2.5-4.5 months). Eighty-one percent of lesions remained unchanged. The majority of these lesions were not excised (Table 1). Of the 61 lesions that showed morphologic changes, 7 (11%) were found to be early melanoma. Although all of these melanomas changed significantly within the monitoring period, none developed any classic surface microscopic features of melanoma. Five were in situ melanoma and 2 were early invasive melanoma (Breslow thickness, 0.25 mm and 0.28 mm) (Figures 1, 2, 3, 4, 5, and 6). With the criteria of morphologic change leading to the decision to exclude the diagnosis of melanoma, digital monitoring specificity for the diagnosis of melanoma was 83%.

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The patterns of morphologic change between benign and malignant monitored changed lesions were analyzed (Table 2). Change in size or shape alone and change in all 3 features of size or shape, color, and architecture were all significantly increased in the monitored melanomas.

We analyzed the frequency of change in benign lesions as a function of age (Table 3). No significant

<table>
<thead>
<tr>
<th>Changed Lesions</th>
<th>No. (%)</th>
<th>Unchanged Lesions</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoma</td>
<td>7 (2)</td>
<td>Nonexcised</td>
<td>247</td>
</tr>
<tr>
<td>Invasive</td>
<td>2</td>
<td>Compound nevus</td>
<td>2</td>
</tr>
<tr>
<td>In situ</td>
<td>5</td>
<td>Dermal nevus</td>
<td>2</td>
</tr>
<tr>
<td>Nonexcised</td>
<td>2</td>
<td>Dysplastic junctional nevus</td>
<td>1</td>
</tr>
<tr>
<td>Nonexcised</td>
<td>5</td>
<td>Dysplastic compound nevus</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>61 (19)</td>
<td>Total</td>
<td>257 (81)</td>
</tr>
</tbody>
</table>

Table 1. Frequency of Morphologically Changed Lesions After Digital Monitoring

Figure 1. A, Original image. B, Image taken 3.6 months later. Note the change in shape, loss of foci of brown dots, and loss of central blue pigmentation. Diagnosis was melanoma with a 0.25-mm Breslow thickness.

Figure 2. A, Original image. B, Image taken 1.5 months later. The patient noted a change before his reappointment date, and hence the reimaging interval was shorter than usual. Note the broadening of the dark central extension (arrow). Diagnosis was melanoma arising from a compound dysplastic nevus with a 0.28-mm Breslow thickness.
difference was found between the frequency of change and any age group. However, the childhood group (0-15 years) had a possibly confounding small sample size.

In an attempt to show that the sensitivity for the diagnosis of melanoma should theoretically approach 100% when digitally monitored for the period of 2.5 to 4.5 months, 6 pigmented lesions identified as melanoma by standard surface microscopic criteria (median Breslow thickness, 0.5 mm) were reimaged after the short interval of 5 to 9 days (median, 6 days). Two of these melanomas (Breslow thickness, 1.5 and 0.42 mm) when re-
imaged on day 6 showed significant architectural change after a period that is one-fifteenth of our median planned monitoring interval of 3 months (Figure 7).

No difference was found in the outcome of monitoring for lesions for which patients gave a history of change. Specifically, there was no difference in a history of change in size, color or pattern, or any one of these changes (recorded when the lesion was first imaged) when changed and unchanged monitored lesions, or melanoma vs nonmelanoma were compared (Table 4).

**COMMENT**

Our study was designed to assess digital monitoring of single pigmented melanocytic lesions that may in a conventional clinical practice be excised or require clinical review by less objective methods. The main criteria chosen for monitoring were lesions that were mildly atypical with a recent history of change or moderately atypical lesions without a history of change. In the case of moderately atypical nevi, these lesions were usually flat or only superficially raised. This was to avoid monitoring an advanced melanoma. However, none of the monitored lesions had any classic surface microscopic features of melanoma (it should be assumed that the excised melanomas were malignant when first imaged). Indeed, even after the monitoring period, none of the melanomas developed classic surface microscopic features of melanoma. The decision to excise these lesions relied solely on evidence of morphologic change.

The time interval chosen for monitoring is clearly crucial for the effectiveness of the technique. Clearly, if the interval is too short, then monitored melanomas may not show any morphologic change. Conversely, if the interval is too long, the morbidity resulting from inadvertently monitoring invasive melanoma will increase and benign lesions may develop change. Stolz et al monitored 54 nevi by means of digital surface microscopy for a period of 10 to 21 months and found changes in 33% of lesions. Braun et al monitored 113 clinically benign nevi by means of digital surface microscopy for a median period of 6 months (range, 3-24 months) and found morphologic change in 69% of lesions. More recently, Kittler et al monitored 1612 clinically benign nevi by means of digital surface microscopy for a median interval of 11.4 months (range, 3.2-21.4 months). In their study, 31% of lesions showed morphologic change.

We chose a short monitoring period of 2.5 to 4.5 months (median, 3 months). We believe that this represents a relatively safe monitoring period for early melanoma, which may be in contrast to 12-month monitoring. However, it must be acknowledged that there is no formal evidence for this statement. In addition, 3 months is believed to be an adequate period to detect change in melanoma. In a small sample of 6 melanomas, 2 changed in the very short time of 6 days. Our standard monitoring period of 3 months is therefore 15 times longer than the period shown to be able to detect change in some mela-
nomas. Furthermore, 17% of the nonmalignant lesions in our study showed some change after monitoring. For this reason, we are confident that all melanomas will show some morphologic change during the monitoring period. Nevertheless, this is difficult to prove.

Changes in the single feature of size or shape as well as change in all 3 features of size or shape, architecture, and color were significantly different in the monitored changed melanomas vs changed nonmelanomas. This is consistent with the work of others. Nevertheless, in 1 of the 7 monitored melanomas, change in architecture without color or size occurred. For this reason, with the use of our digital surface microscopy system for short-term monitoring, we do not recommend distinguishing any particular type of change that would exclude a benign or malignant diagnosis. It should be noted that, although no significant difference was found in the frequency of color change in monitored changed melanomas vs changed nonmelanomas, this may reflect a problem with statistical power due to the small melanoma sample size.

Our study contrasts with the recent report by Kittler et al., in which digital surface microscopy monitoring was performed on 202 patients with multiple atypical nevi during a longer period (median follow-up interval, 12.6 months). Consistent with the longer interval of monitoring, they classified changes as either significant, indicating the need for excision, or nonsubstantial, indicative of change in benign lesions. Significant changes found in 4% of lesions were defined as enlargement, changes in shape, regression, color, and appearance of surface microscopic structures known to be associated with melanoma. Of these significantly changed lesions, 8 (12%) were early melanoma. The nonsubstantial changes found in 28% of monitored lesions were a darker or lighter appearance, changes in the number or distribution of brown globules, decrease in the number of black dots, disappearance of an inflammatory reac-

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Table 4. Outcome of Digital Monitoring With a Patient History of Change*

<table>
<thead>
<tr>
<th>Patient History of Change†</th>
<th>Monitored Changed‡</th>
<th>Monitored Unchanged§</th>
<th>Melanoma</th>
<th>Nonmelanoma¶</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color or pattern</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>12/61 (20)</td>
<td>69/257 (27)</td>
<td>1/7 (14)</td>
<td>80/311 (26)</td>
</tr>
<tr>
<td>No change</td>
<td>21/61 (34)</td>
<td>86/257 (33)</td>
<td>3/7 (43)</td>
<td>104/311 (33)</td>
</tr>
<tr>
<td>Unknown</td>
<td>28/61 (46)</td>
<td>102/257 (40)</td>
<td>3/7 (43)</td>
<td>127/311 (41)</td>
</tr>
<tr>
<td>Size</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>8/61 (13)</td>
<td>34/257 (13)</td>
<td>0/7</td>
<td>42/311 (14)</td>
</tr>
<tr>
<td>No change</td>
<td>20/61 (33)</td>
<td>104/257 (40)</td>
<td>3/7 (43)</td>
<td>121/311 (39)</td>
</tr>
<tr>
<td>Unknown</td>
<td>33/61 (54)</td>
<td>119/257 (46)</td>
<td>4/7 (57)</td>
<td>146/311 (48)</td>
</tr>
<tr>
<td>Any change</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>14/61 (23)</td>
<td>79/257 (31)</td>
<td>1/7 (14)</td>
<td>92/311 (30)</td>
</tr>
<tr>
<td>No change</td>
<td>17/61 (28)</td>
<td>67/257 (26)</td>
<td>3/7 (43)</td>
<td>81/311 (26)</td>
</tr>
<tr>
<td>Unknown</td>
<td>30/61 (49)</td>
<td>111/257 (43)</td>
<td>3/7 (43)</td>
<td>138/311 (44)</td>
</tr>
</tbody>
</table>

*No statistically significant difference was found in patient history of change in color or pattern, size, or any one of these changes when changed and unchanged monitored lesions, or melanoma vs nonmelanoma lesions, were compared (χ² analysis).
†On first presentation for monitoring of a lesion, the patient history was recorded for change in size or in color or pattern during the last 2 years.
‡Lesions showing morphologic change after digital monitoring.
§Lesions showing no change after digital monitoring.
¶Lesions either excised with benign pathological findings or monitored without change.
tion, disappearance of parts of the pigment network, and replacement by a diffuse light-brown pigmentation. Similarly, Braun et al. in a study of digital surface microscopy monitoring of 113 nevi during 3 to 24 months (median, 6 months), classified 2 types of changes. Type 1 changes corresponded to an increase in the pigment content of the lesion (black dots, brown globules, or pigmentation of the network) without modification of the size or other architectural features of the lesion. Type 2 changes included an increase in size and variations in the architecture of the lesion. They found the trend that atypical nevi had a greater incidence of type 2 changes and suggested that type 1 changes may be due to solar exposure in common nevi. As stated above, with our short-term monitoring system, most of the nonsubstantial and type 1 changes would be considered as an indication for excision. This is because such minor changes become significant when they occur during a short time. The exception to this was overall increase or decrease in pigmentation without architectural change consistent with change in pigmentation of the surrounding skin (solar exposure changes). In addition, the loss or appearance of millilike cysts was not considered significant.

Exposure to UV-B for a mean duration of 8 weeks (range, 2-17 weeks) has been documented to alter the surface microscopic features of nevi. In particular, exposed lesions showed increased irregularity and darker pigmentation. In a further study, solar changes may have been responsible for seasonal variations found in surface microscopy patterns of nevi; however, true cohorts were not analyzed. For these reasons it is important to stress to patients the need for protecting monitored nevi from solar irradiation.

As reported elsewhere, lack of enlargement of melanoma after monitoring is not uncommon. Indeed, as shown in Figures 1 and 6, melanoma can appear morphologically more benign over time, at least during our short monitoring period. We therefore underline the need for caution when monitored lesions show less atypia after short-term monitoring.

No difference was found in the monitoring outcome of lesions (change vs no change) when the patient noted a history of change at the time of first presentation. Clearly, in our study, a patient history of change in size or in color or pattern of a lesion does not reflect what will be seen after short-term monitoring. For this reason, short-term digital monitoring is a useful tool in assessing the stability of historically changing lesions.

One of the possible risks of monitoring involves noncompliance. Twelve percent of patients offered monitoring did not return for follow-up imaging. A significant proportion of these patients would have decided on surgical excision for management. However, formal investigations of the reasons for noncompliance have not been performed.

In conclusion, we have described a technique using a strictly calibrated imaging device that is designed to allow monitoring of suspicious lesions that do not meet standard criteria for the diagnosis of melanoma. On the basis of the theoretical assumption that all melanomas will be detected after short-term monitoring (sensitivity, 100%), the technique of excising all changed lesions after 3 months of monitoring showed a specificity for melanoma diagnosis of 83%, since only 17% of clinically suspicious nonmelanomas required excision. For this reason, we believe that this is a useful adjunct in the assessment of melanocytic lesions, since it enables early detection of featureless melanomas while decreasing the need for excision of suspicious benign lesions.

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