Digital Dermoscopic Monitoring of Atypical Nevi in Patients at Risk for Melanoma

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BACKGROUND Atypical nevi are a common risk factor for melanoma.

OBJECTIVES The objective was to determine the utility of monitoring dermoscopic photographs of atypical nevi in a high-risk population.

METHODS Over a 4.5-year period, digital dermoscopic photographs were taken of clinically atypical nevi at initial and follow-up visits, such that side-by-side comparisons could be made.

RESULTS A total of 5,945 lesions were monitored in 297 patients over 3 to 52 months (median, 22 months), and 324 lesions were biopsied. Photographic (dermoscopic) changes were noted in 96 of 5,945 (1.6%) lesions, which included 64 dysplastic nevi (67%), 25 common nevi (26%), and 1 melanoma (1.0%). Of 6 melanomas biopsied during the follow-up period, only 1 was detected by dermoscopic photographic change at follow-up.

CONCLUSIONS Most clinically atypical melanocytic nevi are stable over time, and lesions exhibiting dermoscopic changes are most likely to be dysplastic nevi. Although dermoscopy is a useful tool for clinical examination, the sensitivity of dermoscopic monitoring is limited by melanomas that may arise in normal skin or in clinically benign nevi that were not initially photographed.

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preexisting nevi, but may not provide sufficient detail to detect clinically significant changes in a specific nevus. Alternatively, multiple studies have described monitoring nevi by comparison of serially taken digital dermoscopic photographs. Although this approach is highly sensitive for detection of morphologic changes over time, it is not useful for detection of new lesions.

Here we report our experience using this latter approach in which baseline dermoscopic images of atypical nevi were archived and then serial dermoscopic photographs were repeated at each follow-up visit.

Methods

Patients

This study was approved by the Institutional Review Board at the University of Utah (IRB No. 16799). During the period from November 1999 to July 2004, patients with atypical nevi were seen and followed in the Mole Mapping Clinic at the Huntsman Cancer Institute. All patients undergoing dermoscopic monitoring had clinically atypical nevi and, in addition, approximately 25% had a personal history of melanoma and 10% had a positive family history of melanoma. All patients were counseled regarding the importance of sun protection, regular self–skin examinations, and the ABCD criteria for detecting melanoma and were asked to return every 6 to 12 months. Patients were also provided hard copies of regional and macro photographs taken on the first visit to facilitate detection both of new nevi and of gross changes in existing nevi during self–skin examinations at home.

Photography

All patients at the initial visit had baseline digital dermoscopic photographs taken of their clinically atypical nevi (>2 mm in diameter) using an imaging and archiving system (MoleMaxII, Derma Instruments, San Diego, CA). Inclusion criteria for photography were lesions with one or more of the following characteristics: asymmetry, irregular or fuzzy borders, nonuniform pigmentation (color variation), and size greater than 1 cm. Digital dermoscopic images were taken at 30-fold magnification and stored as jpeg files with a resolution of approximately 600 × 400 pixels. At each follow-up visit, dermoscopic images were taken of all previously photographed nevi, and new and prior dermoscopic images were compared side by side on a split screen by the dermatologist (GMB or DG). We did not employ rigid objective criteria for determining whether a lesion had changed, but rather dermoscopic photographs exhibiting interval asymmetric changes in size or pigmentation or the appearance of recognized dermoscopic structural changes were noted as having changed. Lesions demonstrating small symmetric changes in size or uniform changes in pigmentation were generally due to one or more of the following: expected lesion growth in proportion to skin area in young patients, seasonal sun exposure, variable intensity of the light source, or variable pressure applied to the lesion during photography and were not considered to have changed. In some cases, dermoscopic photographs were not helpful due to either poor photo quality or the presence of uniform dark pigmentation, which precluded assessment of potential changes. Determination of the dermatologist’s assessment of particular photographs was made by review of the chart notes.

Biopsies and Excisions

Biopsies were performed using either standard shave or punch technique, such that the entire clinical lesion was removed. With few exceptions, partial biopsies were not done. In some cases, excisional biopsy or reexcision for definitive lesion removal was performed. Standard histologic evaluation of hematoxylin and eosin–stained sections was performed by a trained dermatopathologist. All melanomas were rereviewed (by SRF) to confirm diagnosis and assess nevus origin. Diagnosis of dysplastic and common nevi and melanoma was based on well-established architectural and cytologic criteria. Specimens revealing nonmelanocytic
pathology such as carcinoma, and reexcisions of recently biopsied or recurrent melanocytic lesions including melanoma and cutaneous melanoma metastases, were not considered relevant for the study and were excluded. In addition, 31 biopsies (in 16 patients) were excluded because the photographic equipment was not available on the date of biopsy or the physician’s assessment of the photographs could not be ascertained by chart review.

Results

Biopsies of Monitored Lesions

In 297 patients with atypical nevi, 5,945 lesions (range, 1–71; median, 19 per patient) were monitored over 3 to 52 months (median, 22 months). In 136 patients, 324 relevant biopsies (see Methods) were performed. Most of the monitored lesions were stable and did not exhibit change during the observation period (stable dysplastic nevus; Figure 1A). By contrast, only 96 lesions, or 1.6% of those monitored, were noted to have changed by comparison to a previous dermoscopic photograph. All lesions that demonstrated significant change—most commonly increased focal pigmentation and/or changes in lesion border—were biopsied. The remaining biopsies were categorized into three additional groups as depicted in Figure 2. The most common category was represented by 145 lesions (45% of biopsies) that had not been previously photographed, because they either represented a new lesion or were not selected for dermoscopic photography on the initial clinical exam (Figure 2). In 51 cases (16% of biopsies), lesions were biopsied despite lack of dermoscopic photographic change due to patient concern or request (i.e., new-onset itching or bleeding) or physician concern (i.e., to rule out melanoma; Figure 2). Finally, in 32 cases (9.9% of biopsies), prior dermoscopic photographs were not helpful; most commonly this was due to uniform dark pigmentation of the lesion, which precluded determination as to whether the lesion had changed, but occasionally prior dermoscopic photographs were not of sufficient resolution to appreciate interval changes.

A histologic breakdown of these categories of biopsies of monitored lesions is presented in Figure 3. Of the 145 lesions that were not photographed, the majority (92%) proved to be nevi, represented by a greater percentage of common than dysplastic nevi (52% vs. 41%; Figure 3A). Four melanomas (of 6 diagnosed in follow-up) were included in this category, as well as 5 lentigines and 2 Spitz nevi (Figure 3A). Of the 96 lesions that had changed prior to dermoscopic photograph, almost all (93%) were nevi, with dysplastic nevi predominating over common nevi (67% vs. 26%), and the remaining lesions were Spitz nevi, lentigines, and 1 melanoma (Figure 3B). Thus, although dermoscopic photographic change was more commonly associated with dysplastic nevi (Figures 1B and 3B), many lesions in this category proved to be common nevi without dysplasia (Figures 1C and 3B) and only 1 lesion was melanoma (Figures 1D and 3D). Changes in lesions that proved to be common nevi were usually the development of dark dots or eccentric pigmentation. Of 51 lesions that were biopsied despite lack of dermoscopic photographic change, almost all (98%) were nevi, with common nevi predominating over dysplastic nevi (67% vs. 31%), and none was melanoma (Figure 3C). Finally, of 32 biopsies where dermoscopic photographs were not helpful in assessing change, almost all were nevi (97%) with roughly equal representation of common and dysplastic nevi (Figure 3D).

Of the six melanomas diagnosed on follow-up visits, two were lentigo maligna or melanoma in situ, two were lentigo maligna melanoma, and two were superficial spreading melanoma. The depth for invasive lesions ranged from 0.23 to 0.35 mm. Of the two lesions of superficial spreading melanoma, one showed histologic evidence of a preexisting (dysplastic) nevus.

Role of Photography

Of the 324 biopsied lesions, a prior dermoscopic photograph was available in 179 (55%) cases (Figure 2). When available, a dermoscopic
photographic comparison made a difference in the clinician’s decision to biopsy in 96 of 179 (54%) cases, whereas in the remaining 83 (46%) cases the prior photograph either was not helpful or was irrelevant because either patient or physician concern motivated the biopsy (Figure 2). Of the 6 new melanomas biopsied at follow-up, in 4 of 6 (67%) there was not a previous dermoscopic photograph.
Among photographed lesions, no melanomas were detected in lesions that had not demonstrated dermoscopic photographic change. Although all patients were provided hard copy photographs of regional and macro photographs, their compliance in reviewing them and performing self-skin examinations was highly variable. No melanomas or dysplastic nevi requiring definitive excision were detected by patients using these (nondermoscopic) photographs. Dermoscopic monitoring was associated with an increase in the proportion of dysplastic to common nevi, as most lesions demonstrating dermoscopic photographic change were dysplastic nevi (Figure 3B) whereas most stable (Figure 3C) or unphotographed (Figure 3A) lesions were more likely to be common nevi. Finally, the biopsy rate was extremely low during follow-up visits as only 324 biopsies of melanocytic lesions were performed in 297 patients, corresponding to a rate of only 1.1 biopsy per patient over the 4.5-year study period.

Figure 2. Role of photography in lesions biopsied at follow-up visits. The 324 lesions biopsied at follow-up visits were categorized as indicated. Number of lesions indicated in parentheses adjacent to bars.

Figure 3. Histologic diagnoses of lesions biopsied at follow-up visits. Lesions were categorized as (A) not previously photographed, (B) changed per prior photograph, (C) unchanged per prior photograph, and (D) unclear if changed. Number of lesions indicated in parentheses above bars. CN, common nevus; DN, dysplastic nevus; MIS, melanoma in situ; MM, invasive melanoma.
Discussion

The two primary goals of early melanoma detection are clear: first, biopsy melanomas while monitoring nevi, and second, avoid unnecessary biopsies/excisions. There is, however, currently no consensus as to the best screening approach—that is both sensitive and practical—to meet these goals in high-risk patients. Clinical evaluation with the naked eye, dermoscopy, and photographic comparison represent increasingly complex levels of examination that may be applied to individual melanocytic lesions. Of these, only photographic comparison allows assessment of change—now considered to be the most important clinical characteristic of developing or growing melanoma.5

Photographic comparison has been incorporated into two general screening approaches as described in the literature. First, Lucas and coworkers7 and Banky and coworkers10 used baseline regional photographs to detect new lesions and changes in preexisting lesions at follow-up visits. Dermoscopy was then applied to selected lesions to guide biopsy decisions. In these two studies, the fraction of melanomas that were in situ was 11 of 167 and 2 of 18,10 respectively. Although this approach appears effective in detecting melanomas, it is unclear if the invasive melanomas presenting as changing lesions could have been detected earlier with higher resolution photographs. A second approach, involving comparison of sequentially taken digital dermoscopic photographs, has been more frequently described.13–16 In these studies, the fraction of in situ melanomas was 5 of 8,13 5 of 7,14 4 of 4,15 and 9 of 18.16 Haenssle and colleagues16 reported that monitoring of dermoscopic photographs increased the sensitivity of melanoma detection over that associated with dermoscopy alone. Although this approach appears more sensitive for early melanoma detection, in that a relatively higher percentage of melanomas were missed because they either presented as new lesions or arose from nevi that were not monitored by dermoscopic photographs because total melanomas that developed in these patients was not reported.

It was reassuring to find that the vast majority of atypical nevi in our patients were quite stable over time, as only 1.6% of monitored lesions were noted to have changed by photographic comparison. This rate of change compares with rates of 4% to 6.4% reported in other studies13,15,17 in which dermoscopic photographs were monitored. Although some nevi did exhibit change, in the majority of our cases these changes were not histologically concerning, revealing only common or dysplastic nevi usually not requiring further excision. The availability of dermoscopic photographic comparison was associated with an extremely low biopsy rate of 1.1 nevi per patient during the 4-year monitoring period. By contrast, it is common for some dermatologists to remove several atypical nevi at each visit, and it is not unusual in our practice to see new patients who have had 20 to 30 nevi removed by other dermatologists over a period of years. One study of patients with atypical nevi by Cohen and coworkers18 documented a mean of 17.7 nevi removed per patient over a 4-year period. In that study, photographic comparison was not used, and removal of 3,361 atypical nevi yielded only 15 melanomas (0.4% of biopsies); in the subset of patients without prior history of melanoma, melanoma was detected in only 0.17% of biopsies.18 In their university-based pigmented lesion clinic, Carli and colleagues3 reported excision and melanoma rates of 15.6% (9% when dermoscopy was used) and 1%, respectively, without photographic monitoring. Thus, these prior studies are consistent with our experience that biopsies may be overused in the routine management of atypical nevi and that using photographic change as a criteria for biopsy was quite effective in minimizing unnecessary biopsies.

We diagnosed 6 melanomas on follow-up visits in 324 (1.9%) biopsies. If the 51 lesions that were biopsied without dermoscopic photographic change are excluded, the melanoma detection rate during follow-up increases to 2.2% (6/273). This rate is
comparable to rates of 1% to 4% reported in prior studies. Our melanoma-to-nevus ratio is likely to be lower than in some other studies because we biopsied all changing nevi. In some studies, particularly those from Europe and Australia, dermatologists may be operating in a different medicolegal environment that may not exert the same pressures to biopsy all changing nevi. Nevertheless, unless the number of changing lesions was very large, it would be predicted that biopsy of lesions demonstrating photographic changes would be associated with reduction in the melanoma rate by removal of nevi that are in transition to melanoma, and we did observe multiple lesions that proved to be dysplastic nevi demonstrated initial stability followed by subsequent photographic changes. It is notable, however, that of the 6 melanomas we biopsied, 5 did not arise from a preexisting nevus and in only 1 case did we detect a melanoma by photographic change at follow-up. Our findings are in accordance with those of Lucas and colleagues, in which none of the melanomas detected arose from clinically atypical nevi. Thus a general melanoma screening strategy focused solely on atypical nevi will likely miss melanomas presenting as new lesions or arising from nevi that are not clinically atypical.

Thus although dermoscopic photographic comparison was effective at minimizing biopsies of benign lesions (particularly common nevi), its efficacy for the early detection of melanoma appears limited by melanomas presenting as new lesions or those not arising from preexisting atypical nevi. Most clinically atypical nevi were stable over time, and lesions exhibiting dermoscopic changes were most likely to be dysplastic nevi rather than melanoma. This suggests that most dysplastic nevi are not precursors of melanoma and that the value of digital monitoring lies not in the detection of change in nevi but rather, as recently described by Kittler and coworkers, in the detection of incipient melanoma. Others have reported that regional photography is highly effective in detecting new nevi. Photographic comparison simply needs to be able to answer the question: Is a given nevus new or changing? We suspect that regional photography, which is far less cumbersome than monitoring serially dermoscopic photographs, is a practical approach that may be sufficient (if the photographs are of sufficiently high resolution) for detecting clinically important changes in nevi. If, however, a small melanoma is photographed only by regional photography and not by dermoscopy, it will take a longer follow-up period to detect changes. In light of our experience described here, we are currently performing total body photography (to monitor the entire skin surface) and using high-resolution (6 MP) regional (rather than dermoscopic) photographs for monitoring atypical nevi in our patients at risk for melanoma.

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References

The well-conducted study by Fuller and coworkers is instructive for various reasons. First of all the study results indicate that the vast majority of so-called “dysplastic” or “atypical” nevi are not precursors of melanoma. It seems that even in patients with multiple “atypical nevi,” melanomas usually develop de novo—on normal skin—and not in a preexisting nevus. Only a small proportion of the 4,945 lesions diagnosed initially as dysplastic or atypical nevi changed during follow-up and the majority of changing lesions were melanocytic nevi and not melanomas. Only 1 of 6 melanomas that were detected during follow-up developed in a preexisting dysplastic nevus. What we can learn from this prospective study is that the misleading term “dysplastic nevus” has no legitimacy and should be abandoned once and forever because dysplastic nevi usually do not evolve into melanoma.

According to the results of the study by Fuller and coworkers, it is more likely to detect a melanoma developing on normal skin than to detect a melanoma arising in a preexisting nevus. Fuller and coworkers conclude that it is a better strategy to try to detect new lesions rather than to try to find changes in existing lesions. They advocate photographic overviews to monitor high-risk patients rather than monitoring single lesions by digital dermoscopy. With regard to the results of the study, their arguments are well taken. Four of six melanomas were not photographed initially, either because they were not present initially or because they were not chosen for photography. The criteria applied for choosing a lesion for dermoscopic photography (asymmetry, border irregularity, color variation, and size greater than 1 cm), however, are a major limitation of the study. As demonstrated recently, digital dermoscopic monitoring aims at detecting incipient melanoma when the only criterion is change over time and all other criteria are lacking. Incipient melanomas are not asymmetric, do not have border irregularity, are not multicolored, and are not larger than 1 cm. In other words small, incipient melanomas may look like “common nevi” (the term “common nevus” is usually used to indicate that the nevus looks completely inconspicuous whereas the term “atypical nevus” usually means that the nevus raises some concerns). If one wants to catch incipient melanomas, one must monitor small lesions that are completely inconspicuous but precisely these lesions were not chosen for photography in the study by Fuller and coworkers.
According to the study by Fuller and coworkers, the vast majority of monitored lesions did not change at all. This important observation was also made by others.\textsuperscript{2–6} It seems that the most prevalent application of digital dermoscopic monitoring is to reassure patients that a given lesion is a nevus and not a melanoma by demonstrating the absence of change during time. As correctly pointed out by Fuller and coworkers this should result in a reduction of unnecessary biopsies of melanocytic nevi for diagnostic reasons.

With regard to the optimal surveillance strategy of high-risk patients, I advocate a combined approach of digital dermoscopy monitoring to detect changes of single lesions and whole-body photographic overviews to detect new lesions. The addition of digital dermoscopy monitoring is important because a small inconspicuous lesion with a diameter of $< 5$ mm photographed at the patients’ first visit may already be an unrecognized melanoma. Because melanomas usually are slowly growing neoplasms, changes might be very subtle and easily missed by photographic overviews. Especially when follow-up time is short, melanomas sometimes show not signs of enlargement.\textsuperscript{1,7} It has been demonstrated that changes of dermoscopic structures like appearance dots and pseudopods might be the only clue to detect these melanomas.\textsuperscript{1,7} These changes will be missed when using only photographic overviews without dermoscopy.

In sum and in short, digital dermoscopy monitoring may be performed for only two reasons: first, to reassure patients (and physicians) that a given lesion is a nevus by demonstrating the absence of change during time, and second, to detect incipient, de novo melanomas as early as possible by demonstrating change over time when other criteria are still absent. There is no legitimacy to use digital dermoscopy monitoring to try to detect a melanoma developing in a preexisting nevus.

\textbf{References}


