Comparative Analysis of Total Body and Dermatoscopic Photographic Monitoring of Nevi in Similar Patient Populations at Risk for Cutaneous Melanoma

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BACKGROUND Our previous experience monitoring nevi in high-risk patients using serial digital epiluminescence microscopy (DELM) photography achieved low biopsy rates but was limited by melanomas presenting as new lesions or arising from nevi that had not been photographed.

OBJECTIVE To determine whether biopsy rates, efficiency of melanoma detection, and melanoma origin (de novo vs nevus derived) differed in a similar patient population monitored using total body (TB) photography.

METHODS One thousand seventy-six patients (including 187 from a prior cohort) underwent TB photography and were monitored using photographs obtained at the initial visit. Risk factors and median monitoring periods for these patients were comparable with those of patients previously monitored using DELM photography.

RESULTS Two hundred seventy-five biopsies were performed in 467 patients on follow-up visits. Of 12 melanomas detected on follow-up, five were invasive, five presented as changing lesions and two as new lesions, nine arose de novo, and the remainder were nevus derived.

CONCLUSIONS In our experience with both approaches, monitoring patients at risk for melanoma using TB photography was associated with lower biopsy rates and lower nevus-to-melanoma ratios than using DELM and facilitated detection of new and changing lesions. In both cohorts, the majority of melanomas detected on follow-up arose de novo.

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Effective early detection of melanoma can greatly decrease patient mortality, and screening efforts are most effective when directed at patients with established risk factors, such as personal or family history of melanoma[1] and presence of numerous nevi or clinically atypical nevi,[2,3] but there is no consensus regarding the most effective melanoma screening modality or strategic approach to patients with nevi.[4]

Although multiple noninvasive modalities are currently available and on the horizon that may augment visual detection,[4] histologic examination after biopsy remains the criterion standard for melanoma diagnosis. Unfortunately, this often leads to numerous unnecessary biopsies in some patients. Morphologic change in a lesion may be the most sensitive indicator of melanoma development, with several monitoring studies having revealed that most early melanomas exhibit observable changes over a period of months,[5,6] hence the addition of the letter "E," for Evolving, to the ABCD acronym to increase its sensitivity and specificity.[7] Although patients are often able to detect new and changing lesions by self-skin examination,[8] confirmation of change can only be reliably accomplished with side-by-side comparisons in which individual lesions can be viewed simultaneously at two points in time. There are two established photographic approaches in which previously taken photographs are referred to during the clinical examination for the purpose of documenting changes in nevi over time. The

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first approach, described in several studies,[9–11] involves monitoring suspicious nevi using digital epiluminescence (dermatoscopic) microscopy (DELM) photographs taken at initial and follow-up visits and is geared toward detecting subtle changes in preexisting nevi. An alternate approach, also documented in several studies,[3,5,12,13] entails photographing existing nevi and uninvolved areas of skin using total body (TB) photography and then using these regional photographs as a baseline for comparison during follow-up examinations. This method is well suited to detecting new lesions, although the resolution of the photographs may limit its capacity to detect changing lesions.

We have had the opportunity over the past decade to use both of these methods of photographic comparison in our early melanoma detection program. During the period 1999 to 2004, we monitored 5,945 lesions on 297 patients at risk for melanoma using serial DELM photography.[14] Although we achieved a low biopsy rate (1.1 biopsies per patient over a 4.5-year period), only one in six melanomas detected on follow-up was biopsied because of photographic change, whereas the remaining melanomas arose de novo or from clinically nonsuspicious nevi not initially photographed. Over the past 5 years (2004–2009), we monitored a similar group of patients using TB photography. Our objective was to determine prospectively whether biopsy rate, rate of melanoma detection, and melanoma derivation (nevus derived vs de novo) differed in a similar patient population monitored using TB and DELM photography. We report here that monitoring patients using TB photography was associated with lower biopsy rates and lower nevus-to-melanoma ratios than DELM photography and facilitated detection of new and changing lesions. In addition, TB photography was found to be a more time-efficient approach.

Methods

Patient Population

One thousand seventy-six patients were seen in the Mole Mapping Clinic at the Huntsman Cancer Institute during the study period: 889 new patients and 187 established patients (of 297 from our previously described cohort monitored using serial DELM photography using the MoleMax system from 1999 to 2004).[14] One hundred ten of the previously monitored patients were lost to follow-up and did not return during the study period. Patients were primarily from Salt Lake City and its environs but also included many patients referred throughout the intermountain West. Patients included those having one or more of the following melanoma risk factors:[1–3] three or more clinically atypical nevi (77%), more than 50 nevi (40%, 50–100; 28%, >100), personal history of melanoma (26%), and two or more family members with history of melanoma (10%). A small number of patients (1–2% of total) did not have one of these risk factors but were also monitored by photography if they had extensive lentiginosis (such that detecting new or changing nevi would be difficult) or were referred by other dermatologists who deemed them to be at high risk. The study population consisted of patients with roughly the same proportions of risk factors as those in the previous DELM-based study.[14]

Study Design

The Institutional Review Board of the University of Utah approved this study. From July 2004 to May 2009, biopsies of all melanocytic lesions and the physician notes dictated on the day biopsies were performed were reviewed during the course of the study. The identity of the lesion, the motivation for performing the biopsy, and the role of photographic comparison were ascertained. Biopsies of nonmelanocytic lesions and all re-excision specimens were excluded from the study.

Clinical Examination and Photography

At the initial visit, all patients underwent complete skin examination. In a separate dedicated room, approximately 27 regional photographs were taken based on standard poses[15] to capture nevus-bearing and nevus-free areas of skin. In some cases, additional photographs were taken to monitor more

closely clinically atypical lesions identified in other locations (such as the scalp, pubic area, between toes) or on curved surfaces (such as the shoulder or hip). A FinePix S2 Pro digital camera (Fujifilm U.S.A., Valhalla, NY) was used, with a SB-800 AF Speedlight flash (Nikon Inc., Melville, NY). All photographs were taken at a resolution of $3{,}024 \times 2{,}016$ pixels and stored using password-protected MIRROR DermaGraphiX software (Canfield Imaging Systems, Fairfield, NJ) on our institution's server. For most patients, the photography session was completed in approximately 15 minutes. Photographs were also stored as jpg files on a CD-ROM that was placed in the patient's chart to be used in the event of a problem with the wireless connection or the server. Patients were charged for the physician visit but not for photography. Patients were asked to return at 6- or 12-month intervals (based on perceived risk) for follow-up and were counseled on the importance of sun protection and monthly self-skin examinations.

At each follow-up visit, patients underwent complete clinical examination. All clinically suspicious lesions were then assessed using hand-held noncontact dermatoscopy (Dermlite II Pro HR, 3Gen, San Juan Capistrano, CA). Photographs from the initial visit were retrieved using a 50-Mb/s wireless connection and projected on a Compaq 8710w mobile workstation with a 17-inch screen (Hewlett-Packard, Palo Alto, CA). New lesions were appreciated using side-by-side comparisons with baseline photographs. To assess changes in preexisting lesions, comparisons were facilitated using the DermaGraphiX built-in zoom function to magnify particular lesions within baseline images.

Biopsies: Indications and Technique

Lesions suspicious for melanoma (including those representing "ugly ducklings"[16] or the most clinically atypical lesion on the patient) and those associated with patient concern (subjective change in appearance or symptoms) were biopsied before photography on new patients. In addition, lesions were removed if deemed poorly suited for photographic surveillance, such as dark lesions in which pigmentary changes would be difficult to assess. Indications for biopsy on follow-up visits included patient or physician concern for melanoma, new lesions that were clinically atypical or arising in patients aged 50 and older,[17] and preexisting lesions that demonstrated significant photographic (particularly asymmetric) changes.

Biopsies were performed using a standard shave or punch technique or in some cases elliptical excision such that the entire clinical lesion was removed. Shave biopsies were generally used for macular or larger lesions, whereas punch biopsies were performed on smaller and papular lesions. In some cases, re-excision was subsequently performed to ensure complete lesion removal.

Histologic Review

One of three dermatopathologists, one of whom (SRF) also re-reviewed all of the melanomas and any cases in which there was insufficient information in the pathology report, evaluated all biopsies. The histologic diagnosis of common nevus (CN, banal and congenital), dysplastic nevus (DN), and melanoma was based on architectural and cytologic criteria.[18] Pigmented spindle cell nevus, Spitz nevus, and blue nevus were grouped as "other nevi." For DN, architectural disorder was defined according to irregular placement of melanocytic nests along the tips and sides of elongated and fused retes. Concentric eosinophilic fibroplasia of the papillary dermis was present. Mildly atypical melanocytes were characterized by nuclear enlargement similar to the size of a keratinocyte nucleus with finely granular pigmented cytoplasms. Dermal melanocytes were arrayed in nests that showed nuclear and cytoplasmic maturation with progressive descent. Moderately atypical DN demonstrated prominent fibroplasia of the dermis with entrapment of dermal melanocytic nests and a host response of lymphocytes. Severely atypical DN demonstrated asymmetry, poor circumscription, and stretches where single

melanocytes predominated over nests with limited pagetoid scatter of single melanocytes above the dermoepidermal junction. Melanoma in situ (MIS) showed asymmetry, poor circumscription, and prominent pagetoid scatter of single and nested melanocytes. Invasive melanomas revealed atypical melanocytes forming irregular nests and sheets with lack of nuclear or cytoplasmic maturation with descent and mitotic activity in dermal melanocytes.[19]

Statistics

Statistical analysis was performed using R 2.8.0 statistical software (The R Foundation for Statistical Computing, Vienna, Austria). $P \leq .05$ was considered statistically significant. For comparison of biopsy rates, a Poisson distribution was assumed, and a likelihood ratio test based on a Poisson regression model was used. A two-sided Fisher exact test was used for comparison of ratios (melanoma rates, melanoma detection rates, melanoma derivations).

Results

Patient Monitoring

During the study period, 1,076 patients underwent TB photography; 467 of these (43%) returned for at least one follow-up visit, 253 had at least two follow-up visits, and 141 had three or more follow-up visits. The fraction of patients not returning for at least one follow-up (57%) was lower than in our previous cohort[14] and consisted primarily of patients who changed their heath insurance carrier, moved out of state, or were not due for follow-up examination before the study end date (newly seen patients). The total monitoring period for individual patients with at least one follow-up visit ranged from 2 to 54 months (median 24 months) and was comparable to the previous cohort.[14] Of the 467 patients with at least one follow-up visit, 71 had less than 1 year of follow-up, 396 had at least 1 year of follow-up, 238 had at least 2 years of follow-up, and 30 had longer than 4 years of follow-up.

Biopsies Performed

A total of 548 biopsies were performed in 1,076 patients during the study period, corresponding to overall biopsy rates of 0.51 per patient and 0.27 per visit. Approximately half of the biopsies were performed at the initial visit, and the remainder were at follow-up visits. Biopsies on initial and follow-up visits yielded a similar distribution of melanocytic lesions; most were nevi (DN more predominant than CN), and the remainder were small numbers of Spitz nevi, DN with severe dysplasia, MIS, and invasive melanomas (Figure 1A).

Of 273 biopsies performed on the initial visit, 91% were nevi (53% DN, 38% CN). One hundred ninety-nine (73%) of these represented the most

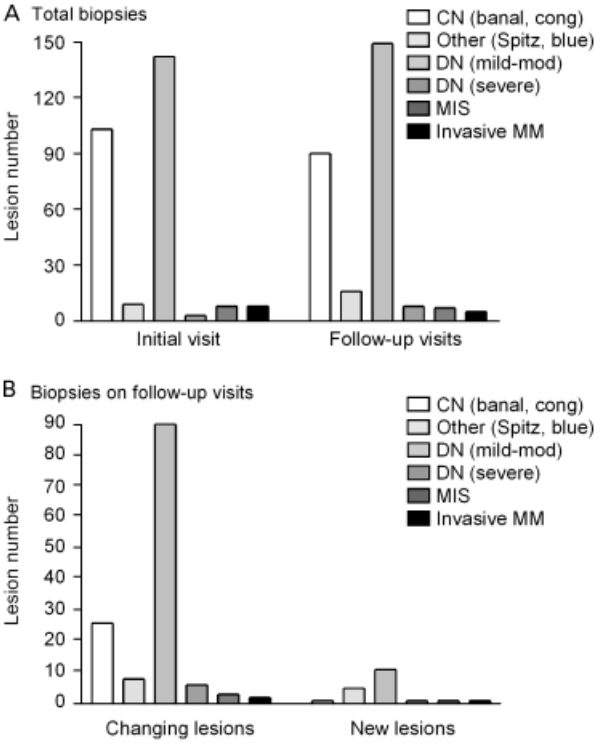

Figure 1. Histologic distribution of melanocytic lesions biopsied in this study. (A) Breakdown of total (548) biopsies according to initial and follow-up visits. (B) Breakdown of 275 biopsies performed on follow-up visits according to whether lesions were judged to be changing or new (based on comparison to baseline photographs).

atypical or "ugly duckling" nevi; 130 (65%) of these were DN (including three with severe dysplasia), 45 (23%) were CN, and 16 (8%) were melanomas (8/16 invasive, see below). Of 275 biopsies performed on follow-up visits, 243 (88%) were nevi, with DN (55%) predominating over CN (33%). Eight of the DN were severely dysplastic, and 12 melanomas (5 invasive, see below) were biopsied on follow-up visits.

Role of Photographic Comparison

Of the 275 biopsies performed at follow-up visits, 168 (61%) were motivated by photographic comparison, which identified a new or changing lesion. The remaining 107 (39%) biopsies corresponded to lesions in which there was no photographic change (primarily biopsied because of patient concern) or the photograph was not helpful (lesion out of focus or obscured). In a few cases, the photograph was not reviewed. Changing lesions were more commonly biopsied than new ones, but in both groups, there was a similar distribution of melanocytic lesion subtypes, with DN being most common for each (Figure 1B). There were 148 lesions that demonstrated significant photographic change, 91% of which proved to be nevi, with DN (74%) predominating over CN (17%). The remaining lesions were eight pigmented spindle or Spitz nevi, three MIS, and two invasive melanomas (Figure 1B). Thus, for lesions exhibiting significant photographic change, the majority proved to be DN, and only five were melanomas (see below). The most common types of observed changes prompting biopsy were altered (usually greater) pigmentation or color that was nonuniform throughout the lesion, asymmetric enlargement, change in shape or border, or a combination of these features. Lesions demonstrating symmetric enlargement (particularly in younger patients) or uniform pigmentary or color change (thought to be secondary to sun exposure or irritation) were generally not biopsied. Of 148 lesions biopsied because of photographic change, patient concern was noted in only 22 (15%), two of which proved to be melanoma.

Of 20 new lesions detected using photography that were biopsied, 13 (65%) were nevi that were almost exclusively DN (12 DN vs 1 CN); the remaining lesions consisted of four pigmented spindle cell or Spitz nevi, two melanomas (1 invasive, see below), and one blue nevus (Figure 1B). We identified many additional new lesions, but the majority of these were not biopsied because, in most cases, the patient was not concerned or the lesions presented in younger patients,[17] tended to be symmetric and uniformly pigmented, and did not represent ugly duckling–type lesions. Thus, although TB photography was useful in identifying new lesions, these other factors often played a role in the decision to biopsy. Nevertheless, only five of 20 (25%) new lesions biopsied were associated with patient concern, and two of these proved to be melanoma.

There were 56 lesions biopsied at follow-up that did not appear to have changed according to photographic comparison, and in all 56 cases, patient concern motivated the biopsy. In most cases, the lesion had been irritated, traumatized, or was associated with subjective symptoms such as itching. Forty-six (82%) of these lesions proved to be CN, and the remainder consisted of eight DN and two pigmented spindle cell nevi.

Finally, 51 lesions were biopsied for which the baseline photograph was not deemed useful. The most common reasons for this included the lesion of interest being covered by undergarments or hair or lacking sufficient focus in the photograph. In 13 cases, the physician did not review the photograph, usually because the lesion did not clinically appear to be melanocytic, or the patient was concerned about a lesion that clinically appeared benign. Three lesions for which the photograph was not viewed proved to be melanoma (see below).

Melanomas

Twenty-eight melanomas were detected during the study period, 16 of them on the initial visit and 12 on

follow-up visits (incidence 0.026 per patient) (Figure 1A). Of the 16 melanomas diagnosed on the initial visit, eight (50%) were invasive, ranging from 0.25 to more than 3 mm in depth (average depth 0.83 mm, median 0.39 mm). Figure 2A illustrates the role that TB photography played in the detection of melanomas and DN with severe dysplasia. Melanomas were categorized with respect to motivation for biopsy and the role of photographic comparison. As indicated, all 16 melanomas represented the most clinically atypical lesion on initial examination (Figure 2A).

Of the 12 melanomas detected on follow-up, five were invasive, ranging from 0.19 to 0.65 mm in depth (average depth 0.38 mm, median 0.36 mm). For three of five patients diagnosed with invasive melanoma on follow-up, an extended period of time had elapsed since the previous visit (1 patient, 1.5 years; 2 patients, 3 years). Five melanomas were detected because of morphologic changes (Figure 3A), and two presented as new lesions (Figure 3B). The two melanomas presenting as new lesions were 3 and 4 mm in diameter at the time of biopsy. As indicated in Figure 2A, for two melanomas it was unclear from prior photos whether the lesion had changed, and there were three melanomas in which prior photos were not assessed (2 of which were clinically amelanotic and biopsied to exclude basal cell carcinoma). No melanomas were detected when there was no photographic change (Figure 2A).

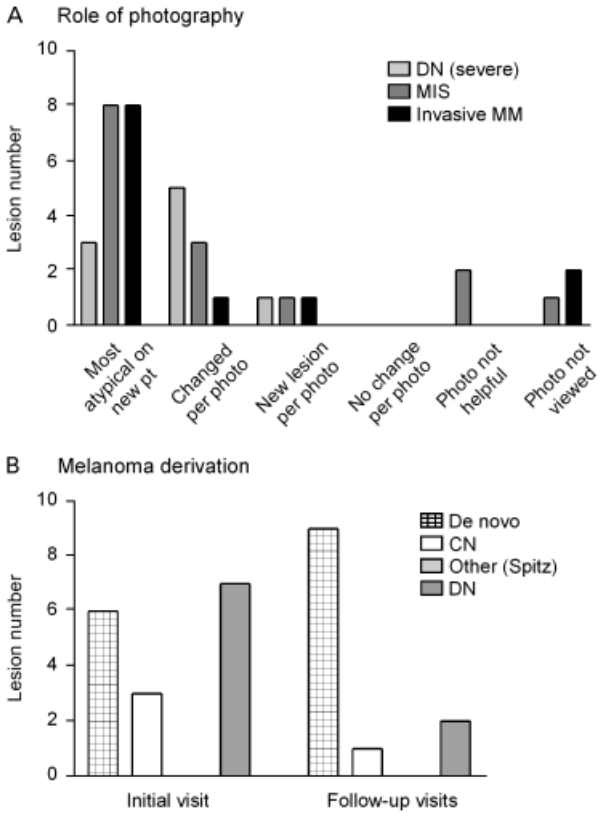

Figure 2. Analysis of melanomas detected in this study. (A) Dysplastic nevus with severe dysplasia, melanoma in situ, and invasive melanoma categorized according to presentation and role of photography in the decision to biopsy. (B) The 28 melanomas in the study are categorized according to detection on initial and follow-up visits and broken down as to whether they arose de novo or from a preexisting nevus.

Slides for all melanomas were re-reviewed to assess whether they arose within preexisting nevi. Melanomas detected at initial and follow-up visits are categorized in Figure 2B with respect to derivation. Although only six of 16 (38%) of melanomas diagnosed on the initial visit arose de novo, this was the case for nine of 12 (75%) lesions diagnosed on follow-up visits. For initial and follow-up visits, the nevus-derived melanomas were more likely to have arisen from preexisting DN than CN (Figure 2B). For the MIS, nine of 15 (60%) arose de novo; of the six remaining lesions, five were associated with DN and one with CN. For the invasive melanomas, six of 13 (46%) arose de novo, four were associated with DN, and three were associated with CN. There were no melanomas derived from preexisting Spitz nevi (Figure 2B).

In addition to the 28 melanomas detected during the course of this study, 11 DN with severe dysplasia were also re-reviewed. The majority of these lesions were identified according to photographic comparison. Six DN with severe dysplasia presented as changing lesions, one was identified as a new lesion (Figure 3C), and three were identified as the most atypical lesion on new patients.

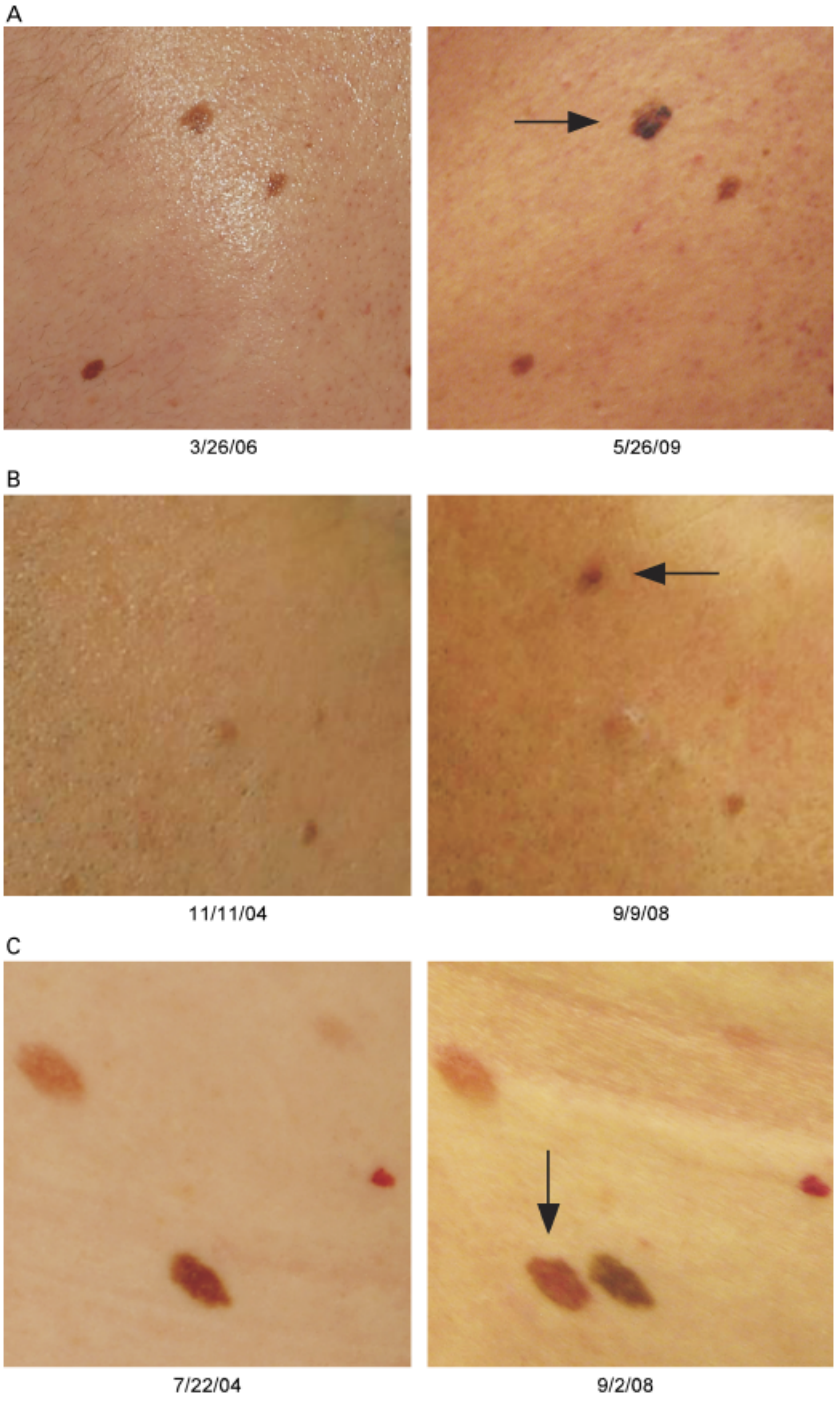

Figure 3. Examples of lesions identified using photographic comparison in this study. Baseline photographs in left panel and photographs taken of same region on follow-up visit (lesion of interest denoted by arrow) in right panel. Dates of each photograph are indicated. (A) Invasive melanoma (depth 0.20 mm) detected as changing lesion on the back of a 41-year-old man. It had been 3 years since his previous visit. (B) Lentigo maligna (melanoma in situ) detected as a new lesion on the cheek of a 47-year-old man. It had been 8 months since his previous visit. (C) Dysplastic nevus with severe dysplasia identified as a new lesion on the back of a 50-year-old woman. It had been 15 months since her previous visit.

TABLE 1. Comparison of Photographic Approaches

	*1999–2004**	*2004–2009*†
Photographic approach	Serial digital epiluminescence microscopy photography	Total body photography
Time for initial visit (clinical examination and photography), minutes	30–50	20–30
Time for follow-up visit (examination and photograph comparison), minutes	30–50	10–20
Patients with ≥ 1 follow-up visits, *n*	297	467
Monitoring period	3–52 (median 22) months	2–54 (median 24) months
Biopsies on follow-up visits, *n*	324 (1.1 per patient)	275 (0.59 per patient) $p<.001$
Melanomas on follow-up visits, *n*	6 (2 MIS, 4 invasive) 0.020 per patient	12 (7 MIS, 5 invasive) 0.026 per patient, $p=.81$, OR = 0.81 (95% CI = 0.24–2.28)‡
Melanoma detection rate on follow-up visits	1.9% (nevus:melanoma ratio 53)	4.4%, $p=.09$, OR = 2.41, 95% CI = 0.82–7.95‡ (nevus:melanoma ratio 22)
Excluding lesions biopsied without photographic change	2.2% (nevus:melanoma ratio 45)	5.5%, $p=.09$ OR = 2.57, 95% CI = 0.88–8.51 (nevus:melanoma ratio 17)
Depth of invasive melanomas on follow-up visits, mm	0.23–0.35	0.19–0.65
Derivation of melanomas on follow-up visits	1/6 nevus derived (1 dysplastic nevus)	3/12 nevus-derived, $p=1.0$ OR = 1.61, 95% CI = 0.096–100‡ (1 common nevus, 2 dysplastic nevi)

*As described in Fuller and colleagues.[14]
†Present study.
‡Odds ratios (ORs) and 95% confidence intervals (CIs) computed with second odds (present study) in numerator.
MIS, melanoma in situ.

Comparative Analysis of Photographic Approaches

We determined the overall biopsy rate, melanoma detection rate, and origin (nevus derived vs de novo) for all the melanomas. A comparison of these important parameters with those obtained in the previous cohort monitored using DELM photography[14] is detailed in Table 1. Two hundred seventy-five biopsies were performed in 467 patients on follow-up visits, giving a rate of 0.59 biopsies per patient (vs 1.1 per patient in the prior cohort, $p<.001$). Twelve melanomas were represented in these 275 biopsies, corresponding to a melanoma detection rate of 4.4% (vs 1.9% in the prior cohort, $p=.09$). If lesions biopsied without photographic change are excluded, the detection rate increases to 5.5% (vs 2.2% in the prior cohort, $p=.09$), and in both cases the difference approaches statistical significance. Of the 12 melanomas detected on follow-up, only three (25%) were nevus derived (vs 1/6 or 17% in the prior cohort, $p>.99$). Thus, we found that monitoring patients using TB photography was associated with a lower biopsy rate and higher melanoma detection rate (lower nevus:melanoma ratio) than in our prior study using DELM photography. Similar to our finding in the prior cohort, more melanomas detected on follow-up arose de novo than from preexisting nevi.

Discussion

Several groups have recently reported their experiences monitoring patients at risk for melanoma with serial DELM photography[10,11,20] or TB

photography.[5,12,17,21] Compared to prior studies using TB photography reported in the literature,[3,5,12,17,21–25] our study describes the largest number of patients and melanomas detected (to our knowledge). More importantly, we have been able to evaluate this approach in the context of our prior experience with serial DELM photography[14] involving the same physicians and a similar patient population. Five years ago, we began using TB photography to address critical limitations we found in our preceding experience with serial DELM photography[14]—namely melanomas presenting as new lesions or arising in benign-appearing nevi that had not been previously photographed.

There was potential for bias arising from inclusion of the prior patient group in the current study in that this population could have been preloaded with higher-risk patients. The dropout of 110 patients from the first group represented patients who were not adherent to follow-up and thus did not participate in the current study, but we do not feel that this biased the current study group because, with the exception of better adherence of the patients who were retained for the current study, the patient populations in the previous and current study were of comparable risk based on several factors. First, there was a similar composition of melanoma risk factors in the patients from each cohort. Moreover, we found comparable rates of melanoma incidence in the two groups (0.026 vs. 0.020 per patient, $p = .81$) monitored using TB and serial DELM photography, consistent with the two populations representing individuals with similar melanoma risk. We monitored a greater number of patients with TB photography (467 vs 297), but the range (2–54 vs 3–52 months) and median (24 vs 22 months) for the monitoring periods were comparable (Table 1). Thus, comparing the results here with those from our previous photographic study[14] appears justified.

For both cohorts, far fewer lesions were biopsied than what one might expect from the common practice of many dermatologists to remove one or two atypical nevi at each visit.[4] One study of melanoma patients (approximately one-third with numerous nevi) in which photography was not used, reported an average of 17 nevi (from those with numerous nevi) and three nevi (from entire cohort) removed per patient over a 4-year period.[26] By contrast, we achieved low biopsy rates on follow-up visits with both approaches (0.59 biopsies per patient with TB photography vs 1.1 per patient with DELM photography,[14] $p < .001$, Table 1). The significantly higher biopsy rate with DELM photography may be a consequence of the greater sensitivity for detecting morphologic changes in nevi because of higher resolution of these photographs and the fact that we were more likely to biopsy lesions exhibiting photographic change, although in the previous study,[14] we had only one case in which a changing nevus proved to be a melanoma. Thus, serial DELM photography appears more likely to identify morphologic changes that are histologically (or clinically) insignificant.

We found a higher rate of melanoma detection in patients monitored using TB photography (5.5% vs 2.2%, Table 1). Our previous finding that lesions exhibiting subtle dermatoscopic changes rarely proved to be melanoma[14] may account for the lower detection rate with DELM monitoring. On the other hand, the higher detection rate found with TB photography suggests that this method may be more specific for melanoma detection. Although the invasive lesions detected in both cohorts on follow-up were all stage IA, a greater fraction of melanomas were in situ (7/12 vs 2/6, Table 1) in patients monitored using TB photography. We might have expected to detect more melanomas with TB photography given its predicted capacity to detect melanomas arising de novo and from clinically nonatypical nevi, although prescient removal of DN with severe dysplasia (8 lesions) on follow-up visits could have decreased the detection rate because some of these lesions may have progressed to melanoma and been detected later.

Although not a primary motivator for changing our monitoring approach, we had found serial DELM

photography to be cumbersome given the time required (up to 45 minutes) to photograph numerous atypical nevi on the initial and (every) follow-up visit. Although most patients required 30 to 50 minutes at each visit for clinical examination and photography or photographic comparison, we found that, with TB photography, the photographs could be obtained in 15 minutes, such that the initial visit required 20 to 30 minutes and follow-up visits only 10 to 20 minutes (Table 1). Thus, TB photography was more time efficient and may have accounted for greater follow-up adherence than we observed in our prior study.[14]

In evaluating the role of photography on the physician's decision to biopsy, we acknowledge the influence of several potential confounding factors. These include patient concern, which motivated biopsies in cases in which there was no photographic change, and patient age and lesion morphology, which played a significant role in the decision to biopsy new lesions. In comparing our two cohorts, it is worth noting that patient concern also probably played a role in the prior study in which the same physicians operating in the same medicolegal environment monitored a similar patient population. However, of 168 lesions biopsied as a result of photographic comparison, patient concern was only noted in 27 (16%). Thus, TB photography identified many new and changing lesions that patients were unaware of. Photographic change may be more reliable than patient history, because the melanoma detection rate was three out of 141 (2.1%) for lesions biopsied in which there was photographic change but no patient concern and none out of 56 (0%) for lesions biopsied solely because of patient concern. Although a new lesion is more likely to be melanoma in patients aged 50 and older,[17] we biopsied few (only 20) new lesions, and none of these were in patients aged 50 and older. The majority of new lesions identified were not biopsied because, in most cases, the patient was not concerned, and the lesions tended not to exhibit suspicious dermoscopic features.

We recognize that these two photographic approaches have inherent limitations that may bias which lesions are selected for biopsy. Although serial DELM photography is highly sensitive for detecting changes in nevi over time, this approach is necessarily limited to detecting changes in a subset of preexisting nevi and cannot detect new lesions. On the other hand, TB photography is geared toward detecting new lesions, and the resolution of the photographs necessarily limits its capacity to detect changing lesions. Given these considerations, we might have expected a greater proportion of melanomas detected using DELM monitoring to be nevus derived and a greater fraction of those detected using TB photography to present as new lesions, although in both cohorts, we found that a similarly small fraction of the melanomas (17% and 25%) detected on follow-up were nevus derived, with the majority arising as de novo lesions (Table 1). Our findings are consistent with other monitoring studies[3,5] and histologic studies,[27–29] suggesting that most melanomas arise de novo rather than from preexisting nevi. Given this trend of melanoma origin, one would predict that TB photography would be better suited than serial DELM as a solitary strategy for early melanoma detection. Such would be particularly true for older patients with fewer nevi in whom melanoma would be more likely to present as a new lesion than as a changing nevus. Serial DELM, however, may be better suited for young individuals with a few clinically atypical nevi who will probably develop many new lesions, making it difficult to establish a baseline using TB photography. Thus a combined approach, in which selected regional photographs are used along with DELM monitoring or in which DELM photographs of a subset of the most clinically atypical nevi are taken in patients monitored by TB photography, is probably optimal. However, incorporating two photographic systems will not be feasible for most practitioners. When we switched from serial DELM monitoring to TB photography 5 years ago, our hope was that the photographs would be of sufficient resolution to detect clinically significant changes. Although it is possible that DELM monitoring could have detected some of the melanomas earlier, most (4/5) invasive melanomas

we detected on follow-up were not nevus derived. Thus DELM monitoring may have resulted in earlier detection of these lesions only if photography was performed after the melanomas developed. In these cases of invasive melanoma detected on follow-up, the most important factor associated with delayed diagnosis was longer amount of time since the previous visit (1.5 years for 1 patient, 3 years for 2 patients). Therefore, as with any planned medical intervention, patient adherence is always a significant limitation of efficacy.

In summary, we have had the unique opportunity to compare two conventional photographic approaches in a similar patient population at risk for melanoma. In our experience, monitoring using TB photography appears to have advantages over serial DELM photography; it is more time efficient and is associated with lower biopsy rates and higher melanoma detection rates. Its greatest limitation appears to be patient adherence to timely follow-up examinations.

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