Characterization of 1152 lesions excised over 10 years using total-body photography and digital dermatoscopy in the surveillance of patients at high risk for melanoma

Gabriel Salerni, MD,[a] Cristina Carrera, MD,[a,b] Louise Lovatto, MD,[a] Rosa M. Martí-Laborda, MD,[a,c] Guillermina Isern,[e] Josep Palou, MD,[a,d] Llúcia Alós, MD,[d] Susana Puig, MD, PhD,[a,b] and Josep Malvehy, MD, PhD[a,b]

Barcelona and Lleida, Spain; and Rosario, Argentina

Background: The combined use of total-body photography and digital dermatoscopy, named "two-step method of digital follow-up," allowed the detection of incipient melanoma as a result of dermatoscopic or macroscopic changes during follow-up.

Objective: We sought to assess dermatoscopic features and dynamic changes leading to excision of melanocytic lesions during our 10-year experience of monitoring patients at high risk for melanoma.

Methods: We analyzed 1152 lesions excised during the surveillance of 618 patients at high risk for melanoma from 1999 to 2008.

Results: A total of 779 excised lesions had been previously recorded: 728 were removed because of dermatoscopic changes during follow-up and 51 were removed even though no significant change was noted. The remaining 373 excised lesions were new or undetected on previous total-body photography. A total of 98 melanomas were detected, 60 in the monitored lesions, and 38 among the "new" lesions. The most frequent dermatoscopic changes detected were asymmetric enlargement in almost 60% (n = 418), focal changes in structure in 197 (27%) and in pigmentation in 122 (17%), the latter two being more frequently seen in melanomas than in nevi (both $P < .001$). No significant differences were detected between dermatoscopic or histopathological characteristics of the melanomas in each group, with a considerable proportion of melanomas misclassified as benign in both groups (26.3% and 38.3%, respectively).

Limitations: The dermatoscopy pattern of stable lesions and the histopathology of lesions not removed were not included in the study.

Conclusion: The most frequent dermatoscopic features associated with melanoma were focal change in pigmentation or structure. Melanomas detected by dermatoscopic changes were remarkably similar to those detected in total-body photography. Almost 40% of melanomas diagnosed in individuals at high risk corresponded to lesions that were not under dermatoscopic surveillance. (J Am Acad Dermatol 2012;67:836-45.)

Key words: atypical mole syndrome; dermatoscopy; dysplastic nevus; follow-up; imaging techniques; malignant melanoma; outcome.

From the Melanoma Unit, Dermatology Department,[a] and Pathology Department,[d] Hospital Clìnic of Barcelona, IDIBAPS; CIBER de Enfermedades Raras, Instituto de Salud Carlos III, Barcelona[b]; Dermatology, Medicine Department, Hospital Arnau de Vilanova, Universitat de Lleida[c]; and Facultad de Ciencias Económicas y Estadísticas, Universidad Nacional de Rosario, Argentina.[e]

The research at the Melanoma Unit, Hospital Clìnic of Barcelona, is partially funded by grants 03/0019, 05/0302, 06/0265, and 09/1393 from Fondo de Investigaciones Sanitarias, Spain; by the CIBER de Enfermedades Raras of the Instituto de Salud Carlos III, Spain; by the AGAUR 2009 SGR 1337 of the Catalan Government, Spain; by the European Commission under the Sixth Framework Programme, Contract No. LSHC-CT-2006-018702 (GenoMEL); and by the National Cancer Institute of the US National Institutes of Health (CA83115).

Conflicts of interest: None declared.

Accepted for publication January 20, 2012.

Reprint requests: Susana Puig, MD, PhD, Melanoma Unit, Dermatology Department, Hospital Clinic Barcelona, Villarroel 170, 08036 Barcelona, Spain. E-mail: susipuig@gmail.com.

Published online April 23, 2012.

0190-9622/$36.00

doi:10.1016/j.jaad.2012.01.028

Early recognition and surgical excision is the most effective intervention for improving the prognosis of patients with primary malignant melanoma (MM).[1]

To distinguish between MM and benign lesions is often a challenge for the clinician. Furthermore, overlap of clinical features may lead to overlooking MM and excising an excessive number of benign lesions.[2]

Dermatoscopy has been shown to improve the diagnostic accuracy for early melanoma detection.[3-5] Nevertheless, MM may be not only clinically but also dermatoscopically indistinguishable from melanocytic nevi, especially in incipient lesions in which specific criteria for malignancy may not be present.[6,7]

On the basis that benign lesions usually do not change whereas MMs change significantly over time, digital follow-up (DFU) of atypical melanocytic lesions that are not suspicious for MM has been proposed as a strategy to recognize MMs that may lack distinct dermatoscopic features at baseline.[8] This approach has proved to be efficient in detecting early MMs without increasing the number of unnecessary excisions.[9-11]

The use of total-body photography (TBP) has been shown to be helpful in the detection of changes in shape, color, or surface eventually occurring in any lesion, and for the identification of new lesions aided by baseline and subsequent registries.[12-16]

The combined use of TBP and digital dermatoscopy, the so-called "two-step method of digital follow-up," was designed in our unit for the surveillance of patients at high risk for MM.[17] It has been proposed as a more sensitive strategy in MM screening, by allowing not only the detection of dermatoscopic changes over time, but also detection of macroscopic changes and the occurrence of new lesions not previously registered for follow-up.[18]

In this study, we analyzed the dermatoscopic features and dynamic changes leading to excision of melanocytic lesions during our 10-year experience in the surveillance of more than 600 individuals at high risk for melanoma using two-step method of DFU. The dual strategy of the two-step method of DFU allowed us to compare excised lesions that were under previous dermatoscopic monitoring (DM) with those excised lesions that were not under DM (notDM).

CAPSULE SUMMARY

- Two-step method of digital follow-up allows not only the detection of macroscopic changes and the occurrence of new lesions not previously registered, but also the detection of dermatoscopic changes over time.
- Melanomas detected by dermatoscopic changes are remarkably similar to those detected in total-body photography in terms of histologic and dermatoscopic characteristics.
- All atypical nevi showing substantial changes over time should be excised not to miss a melanoma.

METHODS

Study population

A total of 618 patients included in the surveillance program with TBP and digital dermatoscopy at the melanoma unit of a referral academic hospital (Hospital Clinic of Barcelona) were followed up between January 1999 and December 2008.[18]

The characteristics of the population included have been detailed in Salerni et al[18] and briefly, the cohort consisted of 618 patients with a mean age of 37 years (mean SD ± 13.3 years) at time of inclusion in the program; 45.5% were men. According to inclusion criteria, the vast majority of the patients (n = 556) had atypical mole syndrome (defined as having >100 nevi and/or >10 atypical nevi under dermatoscopic or histopathological analyses); 277 had a personal history of previous melanoma, including 73 with a history of multiple primary melanomas, before the start of the study; 8 patients with giant congenital melanocytic nevus and 3 patients affected with xeroderma pigmentosum were also included. Almost one third of the patients (n = 178) had a familial history of melanoma as well. Patients were followed up for a median of 96 months (range 13-120 months).

Baseline and follow-up registries

Images were obtained using a standardized digital system (MoleMax, Derma Instruments, Vienna, Austria), which is a digital DM device with a digital video camera and software adapted for the register and comparison of macroscopic TBP and dermatoscopy images. Examination procedure was performed according to the two-step method of DFU as previously described.[17,18] Patients were scheduled for follow-up in 3, 6, or 12 months according to the judgment of the dermatoscopy specialist who performed the evaluation and depending on the degree of risk of the patient.

Abbreviations used:

DFU:	digital follow-up
DM:	dermatoscopic monitoring
MM:	malignant melanoma
notDM:	not dermatoscopic monitoring
TBP:	total-body photography

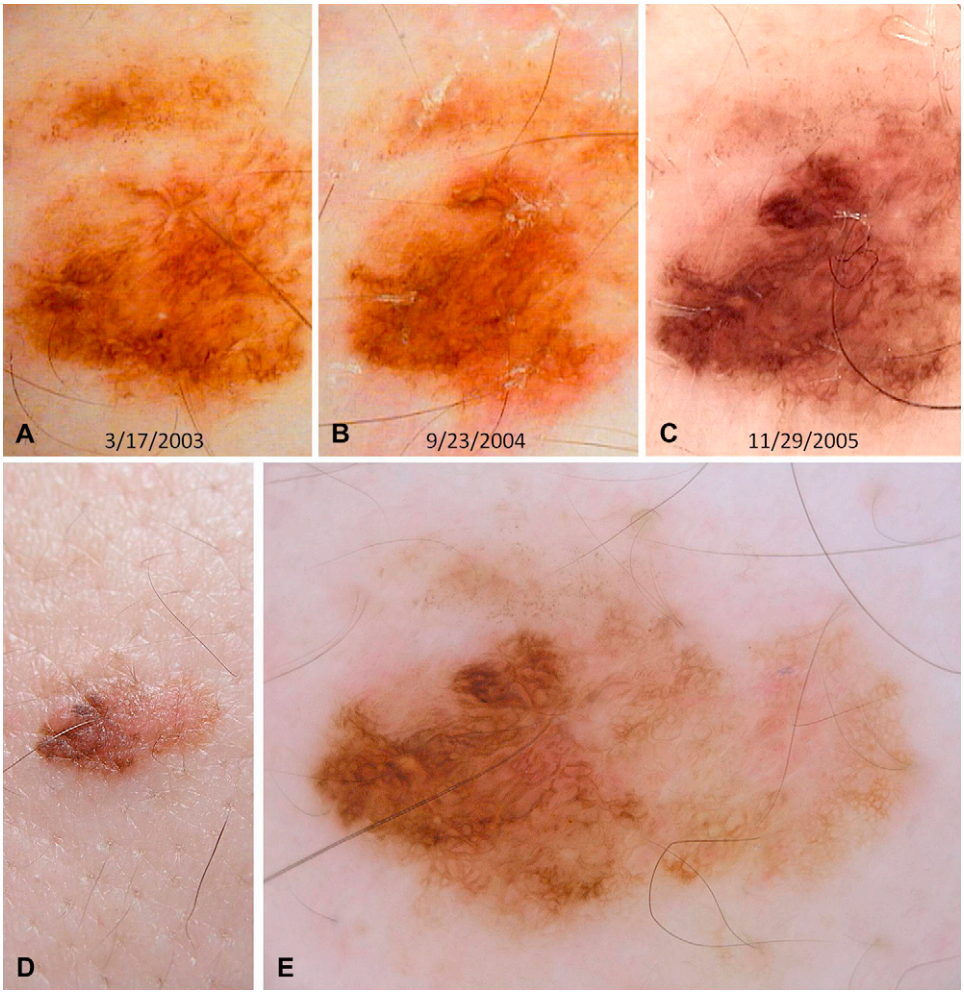

Fig 1. In situ malignant melanoma arising on congenital nevus excised on back of 51-year-old man with atypical mole syndrome and melanoma before inclusion in surveillance program. Lesion was followed for 42 months and 3 visits **(A** to **C)** until excision because of focal changes in structure and pigmentation. Clinical **(D)** and high-resolution dermatoscopic **(E)** images at time of excision. Total dermatoscopy score: 5.2.

Inclusion criteria for melanocytic lesions

Melanocytic lesions with atypical clinical or dermatoscopic features were stored in the digital system. Lesions with clear-cut dermatoscopic features of melanoma (as described in pattern analysis,[19] the ABCD rule of dermatoscopic,[20] or the 7-point checklist[21]) were removed without DM. Lesions with definite dermatoscopic features conclusive of benign nevi were not considered for follow-up.[18] Lesions excised just after our first examination were excluded from this study because they were not followed up.

Lesions considered for excision and histopathological study

As described by Salerni et al,[18] changes leading to excision during DFU were any of the following: (1) asymmetric enlargement; (2) changes in dermatoscopic structures (expansion or decrease of pigment network; variation in the distribution or number of dots/globules; variation in shape; modification of depigmented areas or regression structures; appearance of scarlike areas, blue-whitish veil, streaks; and/or atypical vessels); (3) increase in the number of colors but not slight darkening or lightening of overall pigmentation of the lesion; (4) occurrence of regression structures; and (5) focal pigment modifications. All new lesions observed during follow-up and exhibiting atypical dermatoscopic features but no criteria for melanoma were registered and included in follow-up or excised according to the personal risk of the patient, and the criteria of the investigator. All lesions displaying sufficient criteria for melanoma suspicion were removed.

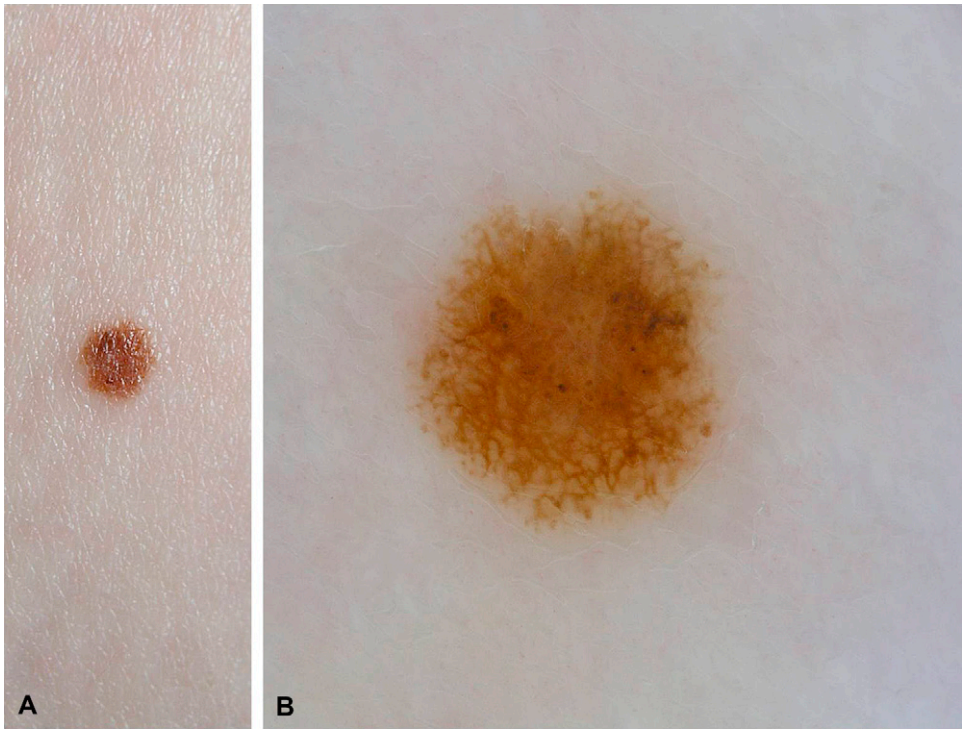

Fig 2. In situ melanoma located on left thigh of 32-year-old woman with atypical mole syndrome, history of personal and familial melanoma, and carrier of mutation in CDKN2A. Lesion was newly detected after 91 months since inclusion in follow-up program. Clinical **(A)** and dermatoscopic **(B)** images at time of excision. Total dermatoscopy score: 2.6.

Histopathology procedure

All lesions removed were step-sectioned and processed following the protocol in the pathology department of the melanoma unit that establishes that all melanocytic lesions excised to rule out melanoma should follow the current specified protocol: (1) the entire lesion shall be embedded; (2) the specimen should be trimmed at a right angle across the long axis in 3- to 4-mm−thick blocks; (3) from each block at least 2 to 3 sections representing different levels should be cut and hematoxylin-eosin stained; and (4) Melan A, HMB45, and Ki67 are performed in melanomas and in all atypical melanocytic lesions of concern for two dermatopathologists (L. A. and J. P.). Histology criteria for atypia were reported according to the National Institutes of Health Consensus Conference (1992).

Lesions excised during the study

Among the 11,396 lesions under surveillance, 1152 were excised in 407 patients with a mean of 2.83 lesions per patient (SD ± 2.39) during the 10-year period (global excision rate 1.86 per patient in 618 patients). In all, 598 (51.9%) lesions were excised in women and 554 (48.1%) in men, and at a median age of 37 years (mean, 39.4; SD ± 13.4 years) (detailed in Salerni et al[18]).

Lesions excised were located as follows: 496 (43.1%) on the back of trunk, 328 (28.5%) on the front of trunk, 195 (16.9%) on lower extremities, 78 (6.7%) on upper extremities, 38 (3.3%) on head and neck, 16 (1.4%) on acral skin of the feet, and one lesion (0.1%) was located on genital mucosa.

Histopathological diagnoses of lesions excised during follow-up were: 1016 nevi (88.19%), 98 melanomas (8.5%), 16 seborrheic keratosis (1.38%), 9 actinic keratosis (0.78%), 7 actinic lentigo (0.6%), 5 dermatofibromas (0.43%), and one basal cell carcinoma (0.1%).

Of the 98 melanomas, 53 (54.08%) were in situ, and among the 45 invasive melanomas the median Breslow index depth of invasion was 0.50 mm (mean 0.54 mm), and none were ulcerated. According to histopathological subtype, almost 90% (n = 88) were superficial spreading, 8.16% (n = 8) lentigo maligna, and 2.04% (n = 2) acral lentiginous type. Sentinel node biopsy was not required in any of the melanomas diagnosed during follow-up.

Among nevi, 492 (48.4%) showed some degree of histologic atypia: 190 (18.7%) mild, 241 (23.7%) moderate, and 61 (6%) severe.[18]

Table I. Comparative analysis between lesions with and without previous dermatoscopic record

	Lesions			
	NotDM	DM	Total	*P*
Gender (%)				.67
Male	176 (47.18)	378 (48.52)		
Female	197 (52.82)	401 (51.48)		
Mean age at time of excision (SD), y	39.24 (±13.08)	39.99 (±14.27)		.387
Time from inclusion to excision (SD), mo	41.32 (±29.58)	36.14 (±25.9)		.004
Histologic diagnosis (%)				
Nevus	311 (83.3)	705 (90.5)	1016	.096
Melanoma	38 (10.19)	60 (7.7)	98	
Seborrheic keratosis	9 (2.41)	7 (0.9)	16	NA
Actinic keratosis	7 (1.88)	2 (0.26)	9	NA
Actinic lentigo	4 (1.07)	3 (0.39)	7	NA
Dermatofibroma	4 (1.07)	1 (0.13)	5	NA
Basal cell carcinoma	0	1 (0.13)	1	NA
Localization (%)				<.001
Back of trunk	143 (38.34)	353 (45.31)	496	
Front of trunk	95 (25.47)	233 (29.91)	328	
Upper extremities	31 (8.31)	47 (6.03)	78	
Inferior extremities	73 (19.57)	122 (15.66)	195	
Head and neck	27 (7.24)	11 (1.41)	38	
Acral foot	3 (0.80)	13 (1.67)	16	
Mucosa	1 (0.27)	0	1	
Regression (%)	80 (21.4)	239 (30.7)	319	<.001
Inflammatory reaction (%)	35 (9.38)	58 (7.45)	93	.259
Histologic fibrosis (%)	34 (9.12)	72 (9.24)	106	.944
Cytologic atypia in nevus (%)				
Any degree	121 (38.9)	371 (52.62)	492	<.001
Mild	44 (14.14)	146 (20.7)	190	.003
Moderate	60 (19.29)	181 (25.67)	241	.005
Severe	17 (5.46)	44 (6.24)	61	.485

DM, Dermatoscopic monitoring; *NA*, not available; *notDM*, not dermatoscopic monitoring.

Statistical analysis

Bivariate analysis was performed to assess differences between lesions under DM versus "new" lesions or previously not under DM; the χ^2 test was used for the comparison of qualitative variables, applying Fisher correction according to the sample sizes' need in tables of 2 × 2 and the Student *t* test was used to compare means of the quantitative variables. Differences were considered to be statistically significant when *P* was less than .05. Multivariable logistic regression analysis was used to obtain the odds ratio regarding type of change during monitoring in nevi and melanomas.

RESULTS

Lesions under DM versus new lesions or previously notDM

Of the 1152 lesions excised, 779 (67.6%) corresponded to lesions registered and under DM (Fig 1) whereas the remaining 373 (32.4%) corresponded to lesions detected during the prospective visits (Fig 2), which were new or not previously considered tributary for dermatoscopic record and DFU (notDM). In the DM group, the decision to excise relied mostly on the occurrence of microscopic changes during DFU and in the notDM group the detection of criteria of suspicion for melanoma was what justified the excision. Data showing comparative analysis between DM and notDM lesions are shown in (Table I).

DM lesions were excised in a mean of 41.32 months after the patient's inclusion in the follow-up program (Fig 3), whereas notDM lesions were excised after a mean of 36.14 months ($P = .004$).

According to the histology diagnosis, no statistically significant differences were found in the number of nevi and melanoma diagnosed as new lesions when compared with those with previous dermatoscopic record ($P = .096$). Histologic regression was present in 30.7% (n = 239) of DM lesions, but only in 21.4% (n = 80) of notDM lesions ($P < .001$). No differences were observed regarding presence of inflammatory reaction or fibrosis in the histologic evaluation.

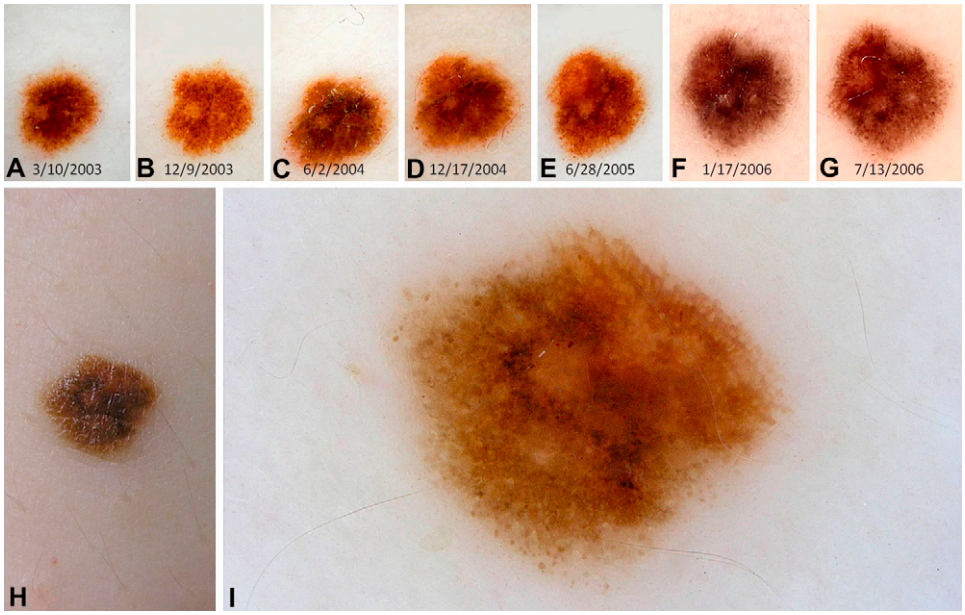

Fig 3. Superficial spreading malignant melanoma, Clark II, depth of invasion 0.5 mm, arising on melanocytic nevus, in 33-year-old man with atypical mole syndrome and personal and familial history of melanoma. Total dermatoscopic score at time of excision: 4.6. Lesion was followed for 40 months and 7 visits until excision after 67 months since beginning of patient's surveillance (**A** through **G**). High resolution clinical **(H)** and dermatoscopic **(I)** images at the time of excision.

Regarding the localization, DM lesions were more frequently located on front and back of trunk, and less frequently on extremities compared with notDM lesions ($P < .001$). Lesions removed from head and neck were more frequently excised as notDM lesions (7.26% vs 1.41%).

Regarding nevi excised during the study, 492 (48.42%) showed some degree of cytologic atypia, of them 371 (52.62%) corresponded to DM lesions and 121 (38.9%) were excised as notDM lesions ($P < .001$). Mild and moderate atypia were more frequent among DM lesions, 20.7% versus 14.14% ($P = .003$) and 25.67% versus 19.29% ($P = .005$), respectively; severe atypia was also more frequent among DM lesions (6.24% vs 5.46%), but differences were not significant.

The comparative analysis of dermatoscopic features of melanomas diagnosed as notDM lesions (n = 38) and those diagnosed as DM lesions (n = 60) (Table II) revealed no statistically significant differences in terms of asymmetry ($P = .919$), presence of abrupt borders ($P = .587$), number of colors ($P = .135$), and presence of dermatoscopic structures ($P = .332$). All lesions in both groups displayed at least the light-brown color, and the vast majority displayed also the dark-brown color. No differences were observed in the distribution of other colors (black, blue-gray, red-pink, white) between the two groups. The presence of structureless areas in more than 10% of the lesion, and more than two dots or globules were more frequent among melanomas diagnosed as notDM lesions, although differences were not significant. No significant differences between the two groups were detected according to total dermatoscopic score value ($P = .302$), neither for the presence of additional criteria (pseudopods, vascularization, and regression), nor different global dermatoscopic patterns.

Upon histopathological study, no statistically significant differences were observed regarding melanoma subtype, number of in situ melanomas, Clark level, mean Breslow depth, presence of ulceration, or proportion of melanomas arising in melanocytic nevus between DM and notDM lesions (Table III).

Dermatoscopic changes leading to excision

A total of 779 DM lesions were excised during the study. Of them 728, including 655 nevi, 60 melanomas, and 13 nonmelanocytic lesions, were excised as a result of dermatoscopic changes during DFU; whereas 51 lesions (50 nevi and one dermatofibroma) were excised despite no significant changes being observed. In the latter group, the decision to excise relied basically on dermatoscopic features and lack of confidence as to the nature of the lesion.

Significant changes during DFU were classified as: asymmetric enlargement, focal changes in pigmentation and/or structure, regression, and changes in

Table II. Comparative analysis of dermatoscopic features of melanomas diagnosed as new lesions versus those diagnosed as monitored lesions

	Lesions			
	NotDM, n = 38	DM, n = 60	Total	*P*
ABCD rule of dermatoscopy				
Asymmetry (%)				.919
Symmetric	3 (7.89)	6 (10)	9	
1 Axis	9 (23.68)	15 (25)	24	
2 Axes	26 (68.42)	39 (65)	65	
Abrupt borders				.587
0	10	26	36	
1 of 8	2	3	5	
2 of 8	6	7	13	
3 of 8	4	4	8	
4 of 8	11	9	20	
5 of 8	2	6	8	
6 of 8	2	4	6	
7 of 8	0	0	0	
8 of 8	1	1	2	
No. of colors (%)				
1	1 (2.63)	0	1	NA
2	5 (13.16)	12 (20)	17	.135
3	14 (36.84)	29 (48.35)	43	
4	16 (42.11)	14 (23.33)	30	
5	1 (2.63)	4 (6.67)	5	NA
6	1 (2.63)	1 (1.67)	2	NA
Colors (%)				
Light brown	38 (100)	60 (100)	98	NA
Dark brown	32 (84.21)	59 (98.33)	91	NA
Black	21 (55.26)	23 (38.33)	44	.101
Blue-gray	19 (50)	27 (45)	46	.629
White	6 (15.78)	8 (13.33)	14	.735
Red-pink	10 (26.32)	15 (25)	25	.884
No. of dermatoscopic structures (%)				.332
1	5 (13.15)	14 (23.33)	19	
2	18 (47.36)	30 (50)	48	
3	15 (39.47)	14 (23.33)	29	
4	0	1 (1.67)	1	
5	0	1 (1.67)	1	
Dermatoscopic structures (%)				
Pigment network	35 (92.11)	60 (100)	95	NA
Branched streaks	3 (7.89)	3 (5)	6	NA
Structureless area >10%	17 (44.74)	19 (31.67)	36	.191
>2 Points	17 (44.74)	17 (28.33)	34	.096
≥2 Globules	16 (42.11)	23 (38.33)	39	.71
Classification according to TDS (%)				.469
Benign	10 (26.32)	23 (38.33)	33	
Malignant	20 (52.63)	26 (43.33)	46	
Suspicious	8 (21.05)	11 (18.33)	19	
Additional criteria (%)				
Pseudopods	2 (5)	1 (1.67)	4	NA
Vascularization	4 (10.53)	6 (10)	10	NA
Regression	15 (39.47)	25 (41.67)	40	.83
Global dermatoscopy pattern (%)				.087
Reticulated	18 (47.37)	41 (68.33)	59	
Multicomponent	16 (42.11)	17 (28.33)	33	
Parallel	1 (2.63)	1 (1.67)	2	
Unspecific	3 (7.89)	1 (1.67)	4	

DM, Dermatoscopic monitoring; *NA*, not available; *notDM*, not dermatoscopic monitoring; *TDS*, total dermatoscopy score on ABCD.

Table III. Comparative analysis of histologic features between melanomas with and without previous dermatoscopy record

	Lesions			
	NotDM, n = 38	DM, n = 60	Total	*P*
Melanoma histologic subtype (%)				.255
Superficial spreading	32 (84.21)	56 (93.33)	87	
Lentigo maligna	5 (13.16)	3 (5.00)	8	
Acral lentiginous	1 (2.63)	1 (1.67)	2	
Nodular	0	0	0	
Clark level (%)				.799
I—MM in situ	19 (50)	34 (56.67)	53	
II	9 (23.68)	13 (21.67)	22	
III	10 (26.32)	13 (21.67)	23	
Ulceration (%)	0	0	0	
MM arising in nevus (%)	11 (28.95)	16 (26.67)	27	.806
Breslow depth (mean), mm	0.573 (0.25-0.9)	0.532 (0.3-1)		.377

DM, Dermatoscopic monitoring; *MM*, malignant melanoma; *notDM*, not dermatoscopic monitoring.

coloration. Lesions excised as a result of symmetric enlargement in the absence of other significant changes were also identified. The most frequent morphological change was asymmetric enlargement in almost 60% (n = 418) of the 728 monitored lesions. Focal changes in structure and pigmentation were seen in approximately 27% (n = 197) and 17% (n = 122), respectively. About 25% (n = 178) of excised lesions displayed changes in coloration, and 23% (n = 167) showed regression. A total of 52 lesions (49 nevi, one melanoma, one pigmented actinic keratosis, and one solar lentigo) were excised because of symmetric enlargement and absence of other significant changes.

Focal changes in pigmentation and in structure were more frequently seen in melanomas than in nevi during follow-up (odds ratio 2.988 and 5.47, respectively, both $P < .0001$). Asymmetric enlargement, regression, and changes in coloration were also more frequent in melanomas than nevi, but these differences were not statistically significant (Table IV).

DISCUSSION

The main goal of DFU is to improve early melanoma detection in populations at high risk for melanoma. Several strategies have been used for the surveillance of individuals at high risk to recognize early melanoma, such as the use of TBP,[12-16] dermatoscopy,[3,4,22] and DFU.[23-31]

It is well known that melanoma may arise on melanocytic nevi but also de novo.[32] It has been proposed that TBP might facilitate the detection of new lesions, and macroscopic visual changes in preexisting undetected lesions, by providing a comparative reference point for subsequent follow-up examinations.[16,17]

In 2007, Fuller et al[31] already raised a concern about the proportion of melanomas appearing de novo that strategies solely focused on DFU of registered lesions might overlook, because the total number of melanomas occurring in the population under study was not reported. In our study, 38 melanomas, almost 40% of melanomas diagnosed during a 10-year period, corresponded to lesions that were new or, being already present, had not been selected for dermatoscopic DFU (notDM). These findings underline the importance of comparing TBP in the surveillance of individuals at high risk, decreasing the threshold for considering a new lesion as suspicious, and therefore allowing the recognition of melanomas that otherwise might have been overlooked or, at least, would be detected at a later tumor progression phase once the lesion was included in follow-up and dermatoscopic changes could be noted.

Dermatoscopy has been proven to improve the diagnostic accuracy of nearly all pigmented lesions including melanoma,[3-5] and DFU of melanocytic lesions allows the recognition of early melanomas even in the absence of specific dermatoscopic criteria as a result of the identification of microscopic changes.[7]

DFU is based on the fact that benign melanocytic lesions remain stable whereas melanoma tends to change over time. In our study, 51 lesions were excised as a result of an increase in the physician's suspicion, despite no dermatoscopic change being noted, and none of these were melanomas. This observation confirms that DFU is not only a sensitive but also a specific strategy in melanoma detection.

This study reports, for the first time to our knowledge, the dermatoscopic features of melanomas detected as a result of TBP follow-up, because these lesions had not been previously recorded on digital dermatoscopy. Until now, whether melanomas detected by TBP might display different dermatoscopic characteristics compared with those detected as a result of dermatoscopic changes was a matter of speculation. According to our experience, melanomas diagnosed as new lesions and those as changing monitored lesions (notDM and DM lesions in our study) were very similar, displaying no significant differences regarding histologic and dermatoscopic features, with a considerable proportion of

Table IV. Type of dermatoscopic changes detected in melanomas and nevi during digital follow-up

	Melanomas, N = 60	Nevi, N = 655			
Type of change	**N (%)**	**N (%)**	**OR**	**95% CI**	***P***
Asymmetric enlargement	39 (65)	375 (57.27)	1.387	0.798-2.41	.245
Focal changes in pigmentation	21 (35)	100 (15.27)	2.988	1.687-5.293	<.0001
Focal changes in structure	38 (63.33)	157 (23.97)	5.47	3.146-9.543	<.0001
Regression	18 (30)	143 (21.83)	1.534	0.857-2.747	.147
Changes in coloration	20 (33.33)	152 (23.21)	1.655	0.939-2.916	.079

CI, Confidence interval; *OR*, odd ratio.

melanomas misclassified as benign in both groups (26.3% and 38.3%, respectively), pointing out that melanomas in both groups may be equally difficult to diagnose even with dermatoscopy.

At least, theoretically, we would expect to diagnose, upon histopathological study, melanomas appearing de novo as notDM lesions (being detected as new lesions or as a result of macroscopic changes during body-mapping comparison), and melanomas arising on melanocytic nevi as DM lesions that display changes over time. Interestingly we found no differences between both groups in the number of melanoma developing de novo or in association with melanocytic nevi. This unexpected observation could be explained as a result of slow-growing melanomas occurring in both groups, with no underlying nevi and a very slow evolution and banal appearance.

Dynamic changes in melanocytic lesions are not uncommon when performing DFU. The identification of changes that allow the recognition of early melanoma and those changes expected in benign melanocytic lesions might be challenging.[27] Over the last few years, evidence has accumulated in favor of DFU of melanocytic lesions with the aim of detecting microscopic changes that may predict the diagnosis of melanoma.[23,31] Currently, there is enough evidence to consider the use of sequential digital dermatoscopy imaging, in selected high-risk populations when available, to detect early melanomas even in the absence of specific dermatoscopic features.[6,7,17,18,33-35]

As expected, all types of changes considered significant during follow-up were more common in melanoma than in nevi. We found that focal changes in pigmentation and focal changes in structure were significantly more frequent in melanoma than in nevi (with an odds ratio of 2.988 and 5.47, respectively), but no considerable differences in terms of asymmetric enlargement, regression, or changes in pigmentation were demonstrated.

In our study, 53 lesions were excised only as a result of symmetric enlargement, a type of change not considered significant. Among these, we found one melanoma with a Breslow depth of 0.5 mm that was classified as benign according to the ABCD rule of dermatoscopy. Kittler et al[27] found that one melanoma initially diagnosed as an atypical nevus showed symmetric enlargement without structural dermatoscopic modifications. Our findings support their recommendation that all atypical nevi showing substantial modifications over time should be excised.

In conclusion, MMs detected as a result of dermatoscopic changes are remarkably similar in terms of histologic and dermatoscopic characteristics to those without previous dermatoscopy record detected during surveillance in high-risk populations with a considerable proportion of melanomas misclassified as benign in both groups. We support the current recommendation that all atypical nevi showing substantial modifications over time should be excised to not miss a melanoma.

This work is dedicated to all our patients and their families who have always collaborated with us and who are the objective of our work. We are indebted to our dermatologist colleagues, to our fellows, amongst them Isabel Kolm, Allison Bell Smythe, Renata Lorenzato, Florencia Cabrini, Myrna Hanke, Joane Portella, and nurses, who work together on a daily basis and whose effort is not always acknowledged in the research papers. We also thank Helena Kruyer for her help with the text edition.

REFERENCES

1. Kopf AW, Welkovich B, Frankel RE, Stoppelmann EJ, Bart RS, Rogers GS, et al. Thickness of malignant melanoma: global analysis of related factors. J Dermatol Surg Oncol 1987;13: 345-20.
2. Lindelöf B, Hedblad MA. Accuracy in the clinical diagnosis and pattern of malignant melanoma at a dermatological clinic. J Dermatol 1994;21:461-4.
3. Bafounta ML, Beauchet A, Aegerter P, Saiag P. Is dermoscopy (epiluminescence microscopy) useful for the diagnosis of melanoma? Results of a meta-analysis using techniques adapted to the evaluation of diagnostic tests. Arch Dermatol 2001;137:1343-50.
4. Kittler H, Pehamberger H, Wolff K, Binder M. Diagnostic accuracy of dermoscopy. Lancet Oncol 2002;3:159-65.
5. Vestergaard ME, Macaskill P, Holt PE, Menzies SW. Dermoscopy compared with naked eye examination for the

diagnosis of primary melanoma: a meta-analysis of studies performed in a clinical setting. Br J Dermatol 2008;159:669-76.
6. Kittler H, Guitera P, Riedl E, Avramidis M, Teban L, Fiebiger M, et al. Identification of clinically featureless incipient melanoma using sequential dermoscopy imaging. Arch Dermatol 2006; 142:1113-9.
7. Puig S, Argenziano G, Zalaudek I, Ferrara G, Palou J, Massi D, et al. Melanomas that failed dermoscopic detection: a combined clinicodermoscopic approach for not missing melanoma. Dermatol Surg 2007;33:1262-73.
8. Stolz W, Schiffner R, Pillet L, Vogt T, Harms H, Schindewolf T, et al. Improvement of monitoring of melanocytic skin lesions with the use of a computerized acquisition and surveillance unit with a skin surface microscopic television camera. J Am Acad Dermatol 1996;35:202-7.
9. Carli P, De Giorgi V, Crocetti E, Mannone F, Massi D, Chiarugi A, et al. Improvement of malignant/benign ratio in excised melanocytic lesions in the 'dermoscopy era': a retrospective study 1997-2001. Br J Dermatol 2004;150:687-92.
10. Carli P, de Giorgi V, Chiarugi A, Nardini P, Weinstock MA, Crocetti E, et al. Addition of dermoscopy to conventional naked-eye examination in melanoma screening: a randomized study. J Am Acad Dermatol 2004;50:683-9.
11. Kittler H, Binder M. Follow-up of melanocytic skin lesions with digital dermoscopy: risks and benefits. Arch Dermatol 2002; 138:1379.
12. Halpern AC. Total body skin imaging as an aid to melanoma detection. Semin Cutan Med Surg 2003;22:2-8.
13. Banky JP, Kelly JW, English DR, Yeatman JM, Dowling JP. Incidence of new and changed nevi and melanomas detected using baseline images and dermoscopy in patients at high risk for melanoma. Arch Dermatol 2005;141:998-1006.
14. Wang SQ, Kopf AW, Koenig K, Polsky D, Nudel K, Bart RS. Detection of melanomas in patients followed up with total cutaneous examinations, total cutaneous photography, and dermoscopy. J Am Acad Dermatol 2004;50:15-20.
15. Goodson AG, Florell SR, Hyde M, Bowen GM, Grossman D. Comparative analysis of total body and dermatoscopic photographic monitoring of nevi in similar patient populations at risk for cutaneous melanoma. Dermatol Surg 2010;36:1087-98.
16. Risser J, Pressley Z, Veledar E, Washington C, Chen SC. The impact of total body photography on biopsy rate in patients from a pigmented lesion clinic. J Am Acad Dermatol 2007;57: 428-34.
17. Malvehy J, Puig S. Follow-up of melanocytic skin lesions with digital total-body photography and digital dermoscopy: a two-step method. Clin Dermatol 2002;20:297-304.
18. Salerni G, Carrera C, Lovatto L, Puig-Butille JA, Badenas C, Planas E, et al. Benefits of total body photography and digital dermoscopy ("two-step method of digital follow-up") in the early diagnosis of melanoma in high-risk patients J Am Acad Dermatol doi: 10.1016/j.jaad.2011.04.008. Published online June 17, 2011
19. Pehamberger H, Steiner A, Wolff K. In vivo epiluminescence microscopy of pigmented skin lesions, I: pattern analysis of pigmented skin lesions. J Am Acad Dermatol 1987;17:571-83.
20. Stoltz W, Braun-Falco O, Bilek P, Landthaler M, Cognetta A. A color atlas of dermoscopy. Germany: Blackwell Science; 1994.
21. Argenziano G, Fabbrocini G, Carli P. Epiluminescence microscopy for the diagnosis of doubtful melanocytic skin lesions: comparison of the ABCD rule of dermatoscopy and a new 7-point checklist based on pattern analysis. Arch Dermatol 1998;134:1563-70.
22. Argenziano G, Soyer HP, Chimenti S, Talamini R, Corona R, Sera F, et al. Dermoscopy of pigmented skin lesions: results of a consensus meeting via the Internet. J Am Acad Dermatol 2003;48:679-93.
23. Schiffner R, Schiffner-Rohe J, Landthaler M, Stolz W. Long-term dermoscopic follow-up of melanocytic nevi: clinical outcome and patient compliance. Br J Dermatol 2003;149:79-86.
24. Haenssle HA, Krueger U, Vente C, Thoms KM, Bertsch HP, Zutt M, et al. Results from an observational trial: digital epiluminescence microscopy follow-up of atypical nevi increases the sensitivity and the chance of success of conventional dermoscopy in detecting melanoma. J Invest Dermatol 2006;126: 980-5.
25. Bauer J, Blum A, Strohhacker U, Garbe C. Surveillance of patients at high risk for cutaneous malignant melanoma using digital dermoscopy. Br J Dermatol 2005;152:87-92.
26. Robinson JK, Nickoloff BJ. Digital epiluminescence microscopy monitoring of high-risk patients. Arch Dermatol 2004;140: 49-56.
27. Kittler H, Pehamberger H, Wolff K, Binder M. Follow-up of melanocytic skin lesions with digital epiluminescence microscopy: patterns of modifications observed in early melanoma, atypical nevi, and common nevi. J Am Acad Dermatol 2000;43: 467-76.
28. Haenssle HA, Korpas B, Hansen-Hagge C, Buhl T, Kaune KM, Johnsen S, et al. Selection of patients for long-term surveillance with digital dermoscopy by assessment of melanoma risk factors. Arch Dermatol 2010;146:257-64.
29. Argenziano G, Mordente I, Ferrara G, Sgambato A, Annese P, Zalaudek I. Dermoscopic monitoring of melanocytic skin lesions: clinical outcome and patient compliance vary according to follow-up protocols. Br J Dermatol 2008;159: 331-6.
30. Menzies SW, Gutenev A, Avramidis M, Batrac A, McCarthy WH. Short-term digital surface microscopic monitoring of atypical or changing melanocytic lesions. Arch Dermatol 2001;137: 1583-9.
31. Fuller SR, Bowen GM, Tanner B, Florell SR, Grossman D. Digital dermoscopic monitoring of atypical nevi in patients at risk for melanoma. Dermatol Surg 2007;33:1198-206.
32. Weatherhead SC, Haniffa M, Lawrence CM. Melanomas arising from nevi and de novo melanomas—does origin matter? Br J Dermatol 2007;156:72-6.
33. Australian Cancer Network (ACN). Clinical practice guidelines for the management of melanoma in Australia and New Zealand (2008). Available from: URL:http://www.nhmrc.gov.au/_files_nhmrc/publications/attachments/cp111.pdf. Accessed March 30, 2012.
34. Carrera C, Palou J, Malvehy J, Segura S, Segura S, Aguilera P, et al. Early stages of melanoma on the limbs of high-risk patients: clinical, dermoscopic, reflectance confocal microscopy and histopathological characterization for improved recognition. Acta Derm Venereol 2011;91:137-46.
35. Salerni G, Lovatto L, Carrera C, Puig S, Malvehy J. Melanomas detected in a follow-up program compared with melanomas referred to a melanoma unit. Arch Dermatol 2011;147: 549-55.